Abstract Book

fNIRS 2016
October 13-16, 2016

Université Paris Descartes
12 rue de l’Ecole de Médecine
Paris
Welcome to Paris!

The fNIRS community can be proud of the continuing increase in the number of contributions to our biannual conference on functional near-infrared spectroscopy, now reaching over 255 abstracts submitted. From the many excellent contributions, we have aimed to arrange a program that will spur discussions and inspire everyone to produce new and exciting work in the field. To evaluate the submissions and organize the sessions, many colleagues have been helping us and we thank them all for their work. Following on Boston, London, and Montreal, we hope you enjoy the setting of Paris for this year’s conference and wish you a great time!

Joe Culver & Judit Gervain  
co-chairs
Acknowledgements

Many people have contributed to the organization of the conference. We are grateful to all of them for their help.

We have relied on the program committee for their valuable input on the program: Heather Bortfeld, Frédéric Dehais, Turgut Durduran, Adam Eggebrecht, Joy Hirsch, Fumitaka Homae, Jana Kainerstorfer, Sarah Lloyd-Fox, Chuck Nelson, Hellmuth Obrig, Nadege Roche, and Fabrice Wallois.

The abstracts were reviewed this year by Nawal Abboub, Cédric Albinet, Maria Arredondo, Richard Aslin, Hasan Ayaz, Wesley Baker, Sara Basso Moro, Adam Bauer, Katarina Begus, Silvia Benavides-Varela, Karla Bergonzi, Anna Blasi, Camillia Bouchon, Emilie Bourel-Ponchel, Sabrina Brigadoi, David Busch, Laurianne Cabrera, Mickael Causse, Tom Chau, Davide Contini, Robert Cooper, Kimberly Cuevas, Dean D'Souza, Ippeita Dan, Irene De La Cruz Pavia, Hamid Dehghani, Maryse Delaunay-El Allam, Swethsari Dravida, Gerard Dray, Thomas Dresler, Gautier Durantin, Lauren Emberson, Eve F. Fabre, Qianqian Fang, Silvina Ferradal, Marco Ferrari, Alissa Ferry, Andrew Fishell, Allison Fox, Maria Angela Franceschini, Amir Gandjakhche, Martina Giovannella, Theodore Gliga, Edgar Guevara, Ramon Guevara Erra, Angela Harrivel, Masahiro Hirai, Joseph Hollmann, Yoko Hoshi, Theodore Huppert, Daniel Hyde, Cécile Issard, Kurtulus Izzetoglu, Metlem Izzetoglu, Philip Jackson, Kaja Jasinska, Michal Kacprzak, Ioulia Kovelman, Chuen Wai Lee, Kevin Mandrick, Andrei Medvedev, Rickson Mesquita, Yasuyo Minagawa, Monika Molnar, Noman Naseer, Ryota Nishiyori, Adam Noah, Ahmet Omurtag, Ashwin B Parthasarathy, Katherine Perdue, Stephane Perrey, Luca Pollonini, Valentina Quaresima, Manon Ranger, Raphaëlle Roy, Dima Safi, Angelo Sassaroli, Hiroki Sato, Sébastien Scannella, Felix Scholkmann, Mohinish Shukla, Keith St Lawrence, Jens Steinbrink, Clara Suied, Ilias Tachtsidis, Gentaro Taka, Fenghua Tian, Yunjie Tong, Teresa Wilcox, Xian Zhang

We wish to thank the coordinators of the training course, Frédéric Dehais and Stéphane Perrey, as well as the other instructors Ardalan Aarabi, Hasan Ayaz, Kevin Mandrick, and Fabrice Wallois, for their work.

This conference could not have been organized without the enthusiasm, encouragement and hard work of the Society’s President, David Boas, its President Elect, Clare Elwell and its Secretary, Martin Wolf.

Gary Boas did a wonderful job at creating and updating the conference website. The help we received from Stacey Ladieu and Lucie Martin was instrumental in making the conference happen.

We are grateful to the volunteers who helped before and during the conference.

Last, but not least, we wish to thank our host and our sponsors, for their support.
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Training Course venue

Room Lavoisier A
Université Paris Descartes
Centre Universitaire des Saints-Pères
45 rue des Saints-Pères
75006 Paris

subway (métro): line 4 Saint-Germain-des-Près station, line 10 Mabillon station, line 12 rue du Bac station
public transport information and route planner: [www.ratp.fr](http://www.ratp.fr)
Conference venue

Main Building
Université Paris Descartes
12 rue de l’École de Médecine
75006 Paris

subway (métro): line 4 Odéon station, line 10 Cluny-La Sorbonne station
public transport information and route planner: www.ratp.fr
Social event venue & information

Saturday, Oct 15th, 8pm-midnight

Pavillon Daunou
18 rue Daunou
75002 Paris

Only cash will be accepted
- Soft 3€
- Wine/Beer 4€
- Hard 5€
- Champagne/Vodka Redbull 7€
- Bottle of wine 28€
- Bottle of champagne 65€

- 30 min walking

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**BUS** line 21 or line 27:

*Les Écoles* station (direction *Gare Saint-Lazare*) to *Opéra-4 Septembre* station

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![Map of Paris showing the route from Pavillon Daunou to Opéra-4 Septembre station](image-url)
# Program at a Glance

**Université Paris Descartes Main Building, 12 rue de l’Ecole de Médecine, Paris**

**Oral Presentations:** Grand Amphithéâtre, Posters: Grand Hall, Galerie Saint-Germain

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CSJP Building
Université Paris Descartes
45 rue des Saints-Pères
Detailed Program

Oral presentations: Grand Amphithéâtre
Poster presentations, lunch and coffee breaks: Grand Hall & Galerie Saint Germain

Locations other than the main venue are indicated separately in the program below.

Oct 13th THURSDAY

9:00-4:30: Training Course
CUSP Building, 45 rue des Saints-Pères, 75006, Paris
Note that this event is not part of the main conference program and requires separate registration and payment.

5:30-6:00: Opening remarks
Judit Gervain, co-chair
Claude Meunier, president, Institut Neurosciences & Cognition, Université Paris Descartes

6:00-7:00: Keynote: Maria Angela Franceschini [chair: Joseph Culver]
Clinical neuro-monitoring with NIRS-DCS

7:00-8:00: Reception

Oct 14th FRIDAY

8:30-10:00 Neurodevelopment 1 [chairs: Heather Bortfeld & Nadège Roche]

8:30-9:00 Invited talk
Yasuyo Minagawa: Neuroimaging the developing brain: From the neonatal period to adolescence

9:00-9:15 Silvia Benavides-Varela, Roma Siugzdaite, David. M. Gómez, Francesco Macagno, Luigi Cattarossi, Jacques Mehler: Functional interactions among cortical regions supporting word learning in newborns

9:15-9:30 Laurianne Cabrera, Judit Gervain: The processing of slow and fast temporal cues in phonetic perception at birth, an EEG-NIRS study

9:30-9:45 Lauren Emberson, Alex Boldin, Julie Riccio, Ronnie Guillet and Richard Aslin: Deficits in Top-Down, Sensory Prediction in Infants At-Risk Due to Premature Birth

9:45-10:00 Simone Cutini, Dénes Szűcs, Natasha Mead, Martina Huss, Usha Goswami: Atypical right hemisphere response to slow temporal modulations in children with developmental dyslexia

10:00-11:00 Poster Session 1 & Coffee
11:00-12:15 Brain and Systemic Physiology [chairs: Turgut Durduran & Gemma Bale]

11:00-11:30 Invited talk
Ursula Wolf: A novel methodology to better understand what is happening in the brain: Systemic physiology complemented functional near-infrared spectroscopy (SPC-fNIRS)

11:30-11:45 Davide Tamborini, Parisa Farzam, Bernhard Zimmerman, Kuan-Cheng Wu, Jason Sutin, David Boas and Maria Angela Franceschini: Multi-wavelength, multi-distance diffuse correlation spectroscopy for simultaneous measurement of blood flow and hemoglobin oxygenation

11:45-12:00 Matthew Caldwell, Felix Scholkmann, Ursula Wolf, Martin Wolf, Clare Elwell and Ilias Tachtsidis: Computational modelling of the effects of systemic physiology on brain haemodynamics suggests that physiological confounding is able to both mask and mimic functional activation

12:00-12:15 Yoko Hishi, Yukari Tanikawa, Eiji Okada, Hiroshi Kawaguchi, Manabu Machida, Masahito Nemoto, Toru Kodama and Masataka Watanabe: Estimation of optical properties of the cerebral tissue using time-resolved spectroscopy of femtosecond laser pulses

12:15-1:15 Early Investigator Award Presentations [chair: Clare Elwell]
Meryem Ayse Yucel, Juliette Selb, Christopher Aasted, Pei-Yi Lin, David Borsook, Lino Becerra and David Boas: Mayer waves reduce the accuracy of estimated hemodynamic response functions in functional Near-Infrared Spectroscopy

Sarah Lloyd-Fox, Anna Blasi, Greg Pasco, Theodore Gliga, Clare E Elwell, Tony Charman, Declan Murphy, Mark Johnson: Neural signature of autism evident before six months of life

Robert Cooper, Sabrina Brigadoi and David Boas: Array Designer: automated optimum array design for functional near-infrared spectroscopy

1:15-2:00 Lunch

2:00-3:30 Clinical Applications 1 [chairs: Joy Hirsch & Juliette Selb]

2:00-2:30 Invited talk
Ippeita Dan: fNIRS-based neuropharmacological assessment on children with attention deficit/hyperactivity disorder

2:30-2:45 Carly Anderson, Ian Wiggins, Padraig Kitterick, Douglas Hartley: Cortical activation measured using fNIRS: a predictor of cochlear implant outcome?

2:45-3:00 Willy Mattheus, Sonja Rossi, Dirk Mürbe, Anja Hahne: Speech and Music processing by postlingually deafened cochlear implant patients

3:00-3:15 Mana Manoochehri, Mahdi Mahmoudzadeh, Victoria Osharina, Fabrice Wallois: Fast Optical Signal Changes during Epileptic Spikes in the Human Model

3:15-3:30 Martina Giovannella, Guillem Mitjà, Clara Gregori-Pla, Michal Kacprzak, David Ibañez, Giulio Ruffini, Turgut Durduran: Concurrent diffuse optical measurement of cerebral hemodynamics and EEG during transcranial direct current stimulation (tDCS) in humans
3:30-5:00 Poster Session 2 & Coffee

5:00-6:45 Multimodal Monitoring [chairs: Adam Eggebrecth & Tanja Dragojevic]

5:00-5:30 Invited talk
Solomon Diamond: Multimodal fNIRS and EEG for studying neurovascular coupling

5:30-5:45 Takashi Numata, Masashi Kiguchi and Hiroki Sato: Multimodal measurement of brain responses to word memory task extracted from EEG, NIRS, and pupil diameter signals

5:45-6:00 Adrian Curtin, Jijun Wang, Junfeng Sun, Shanbao Tong, Banu Onaral and Hasan Ayaz: Concurrent fNIRS and TMS for comparison of Evoked Responses to Pulse-Matched High Frequency and Intermittent Theta Burst Stimulation


6:15-6:30 Dariusz Janusek, Piotr Lachert, Przemyslaw Pulawski, Daniel Milej, Piotr Sawosz, Michal Kacprzak and Katarzyna Blinowska: Simultaneous measurement of brain activity by functional near infrared spectroscopy and electroencephalography during motor task

6:30-6:45 Mahnoush Amiri, Alexandru Hanganu, Frédéric Lesage and Yves Joanette: A multimodal approach to evaluate the effect of cortical morphology of normal aging on the hemodynamic response measured by fNIRS: A language study

Oct 15th SATURDAY

8:30-10:00 Clinical Applications 2 [chairs: Ippeita Dan & Hasan Ayaz]

8:30-8:45 Claus Lindner, Ivette Chocrón Da Prat, Ángela Sánchez-Guerreiro, Joseph L Hollmann, Michal Kacprzak, Udo M Weigel, Olga Martinez Silva, Miriam de Nadal, Juan Sahuquillo, Turgut Durduran: Microvascular cerebral metabolism and blood flow and bispectral index

8:45-9:00 Bettina Sorger, Laurien Nagels-Coune, Amaia Benitez Andonegui, Michael Lührs, Lars Riecke, Rainer Goebel: Brain-based communication via online-decoded fNIRS signals

9:00-9:15 Androu Abdalmalak, Daniel Milej, Mamadou Diop, Mahsa Shokouhi, Lorina Naci, Adrian Owen, Keith St. Lawrence: Feasibility of fNIRS as a Brain Computer Interface for Studies of Disorders of Consciousness


9:30-9:45 Juliette Selb, Jason Sutin, Pei-Yi Lin, Parisa Farzam, Bernhard Zimmermann, Kuan Cheng Wu, Davide Tamborini, Zachary Starkweather, Sophia Bechek, Apeksha Shenoy, Siddharth Biswal, David Boas, Eric Rosenthal, Maria Angela Franceschini: Prolonged monitoring of cerebral blood flow and autoregulation in subarachnoid hemorrhage and stroke patients with diffuse correlation spectroscopy
9:45-10:00  Adam Eggebrecht, Karla Bergonzi, Andrew Fishell, Hamid Dehghani, Jin-Moo Lee, Joseph Culver: Bedside mapping of brain function during acute stroke recovery using High-Density Diffuse Optical Tomography

10:00-11:00 Poster Session 3 & Coffee

11:00-12:30 Hardware 1 [chairs: Alessandro Torricelli & Anna Gerega]

11:00-11:30 Invited talk
Frédéric Lesage: Towards wearable NIRS

11:30-11:45 Davide Contini, Mauro Buttafava, Edoardo Martinenghi, Alberto Dalla Mora, Marco Renna, Antonio Pifferi, Alberto Tosi, Alessandro Torricelli: A compact low-power Time-Domain fNIRS system

11:45-12:00 Tanja Dragojevic, Joseph L. Hollmann, Davide Tamborini, Mauro Buttafava, Joseph P. Culver, Franco Zappa, Turgut Durduran: Speckle contrast optical spectroscopy of the adult brain with a novel, compact system

12:00-12:15 Karla Bergonzi, Adam Eggebrecht, Joseph Culver: Lightweight high-density diffuse optical tomography using scCMOS detection

12:15-12:30 Phong Phan, David Highton, Jonathan Lai, Ilias Tachtsidis, Martin Smith and Clare Elwell: A New Multichannel Broadband Near-Infrared Spectroscopy System to Measure the Spatial Distribution of Cellular Oxygen Metabolism and Tissue Oxygenation

12:30-1:30 Lunch

1:30-2:45 Neurodevelopment 2 [chairs: Sarah Lloyd-Fox & Cécile Issard]

1:30-1:45 Nawal Abboub, Thierry Nazzi, Judit Gervain: Prosodic grouping at birth

1:45-2:00 Katherine Perdue, Julia Cataldo, Sarah A. McCormick, Alissa Westerlund, Charles A. Nelson: fNIRS reveals distinct infant emotional face processing

2:00-2:15 Vanessa Reindl, Christian Gerloff, Wolfgang Scharke, Kerstin Konrad: Brain-to-brain synchrony of parent and child during cooperation revealed by fNIRS hyperscanning

2:15-2:30 Alexa Ellis, Xiaosu Hu, Rebecca Marks, Pamela Davis-Kean, Craig Smith, Ioulia Kovelman: Shedding Light On Precursors to Division: An fNIRS Study

2:30-2:45 Lourdes Delgado Reyes, Sobanawartiny Wijekumar, Vincent Magnotta, John P. Spencer: Connecting the Dots: Brain-Behavior Relationships Between Looking Tasks and Explicit Decision Tasks

2:45-4:30 Poster Session 4 & Coffee

4:30-6:00 Special Session “Global fNIRS” [chair: Charles A. Nelson & Katherine Perdue]

4:30-4:40 Charles A. Nelson: Global fNIRS: An Introduction

4:40-5:00 John P. Spencer, Sobanawartiny Wijekumar, Lourdes Delgado Reyes, Aarti Kumar, Vishwajeet Kumar: Infant brain health in India: Assessing working memory capacity using image-based fNIRS

5:00-5:20 Pei-Yi Lin, Jason Sutin, Parisa Farzam, Juliette Selb, Fang-Yu Cheng, Peter Ssemunya, Edith Mbabazi, John Kimbugwe, Joyce Nalwoga, Esther Nalule, Brian Kaaya, Katherine Hagan, P. Ellen Grant, Benjamin Warf, Maria Angela Franceschini: Cure Forward: A novel diagnostic tool to improve infant hydrocephalus outcomes in the developing and the developed worlds

5:40-6:00  Charles A. Nelson, Katherine L. Perdue, Swapna Kumar, Alissa Westerlund, Sarah Lloyd-Fox, Clare Elwell, Sarah Jensen, Annie Berens: *The use of fNIRS in the study of early cognitive development in Dhaka, Bangladesh*

6:00-6:30  **fNIRS Society General Assembly**

8:00-  **Social Event**  
Pavillon Daunou, 18 rue Daunou, 65002, Paris

**Oct 16th SUNDAY**

8:30-10:00  **Neonatal & Pediatric Applications [chair: Fabrice Wallois & Ardalan Aarbi]**

8:30-9:00  Invited talk
Gorm Greisens: *Testing the benefit and harms of cerebral oxygenation monitoring in preterm infants*

9:00-9:15  Fumitaka Homae, Hama Watanabe, Gentaro Taga: *The Characteristics of the Cortical Functional Networks in Individual Infants*

9:15-9:30  Laura Dempsey, Robert Cooper, Maria Chalia, Samuel Powell, Chuen Wai Lee, Andrea Edwards, Nicholas Everdell, Dimitrios Airantzis, Andrew Michell, Adam Gibson, Simon Arridge, Topun Austin, Jeremy Hebden: *Time-resolved diffuse optical tomography of the infant brain during neuropathological events and passive arm movement*

9:30-9:45  Fang-Yu Cheng, Katherine Hagan, Yvonne Sheldon, Meryem A. Yücel, Kuan-Cheng Wu, P. Ellen Grant, Maria Angela Franceschini, Pei-Yi Lin: *Maturation of cerebral hemodynamic response in premature infants*

9:45-10:00  Yoko Hakuno, Yasuyo Minagawa: *Neural activations to mutual gaze and contingent responsiveness during live interactions in infancy*

10:00-11:00  **Poster Session 5 & Coffee**

11:00-12:30  **Data Analysis and Hardware 2 [chairs: Frédéric Dehais & Kevin Mandrick]**

11:00-11:15  Thomas Vincent, François Tadel, Alexis Machado, Zhengchen Cai, Giovanni Pellegrino, Louis Bherer, Jean-Marc Lina, Sylvain Baillot, Christophe Grova: *NIRSTORM: a brainstorm plugin dedicated to joint EEG/fNIRS analysis*

11:15-11:30  Michael Lührs, Rainer Goebel: *A novel Neurofeedback and BCI toolbox for real-time fNIRS: Turbo-Satori*

11:30-11:45  Andrew Fishell, Adam Eggebrecht, Steven Petersen and Joseph Culver: *High-Density Diffuse Optical Tomography during Movie Viewing: Response Reproducibility and Functional Mapping*

11:45-12:00  Frederic Lange, Luke Dunne, Ilias Tachtsidis: *Evaluation of Hemoglobin and Cytochrome using a Broadband Time Resolved NIRS system*

12:00-12:15  David Highton, Danial Chitnis, Phong Phan, Robert J Cooper, Simone Quaggio, Ilias Tachtsidis, Nicholas Everdell, Jeremy Hebden, Martin Smith, Clare Elwell:
Multiwavelength Diffuse Optical Tomography to Resolve Cytochrome C Oxidase
12:15-12:30 Dominik G. Wyser, Olivier Lambercy, Felix Scholkmann, Martin Wolf, Roger Gassert: A wearable fNIRS device for measuring human brain activity in everyday environments

12:30-1:30 Lunch (and Board Meeting)

1:30-3:00 Poster session 6

3:00-4:30 Neurocognition [chairs: Fumitaka Homae & Felix Scholkmann]

3:00-3:30 Invited talk
Frederic Dehais: Monitoring human performance under realistic operational settings

3:30-3:45 Hemel Modi, Harsimrat Singh, Thanos Athanasiou, Guang-Zhong Yang, Ara Darzi, Daniel Leff: Random Effect Modelling of Prefrontal Cortical Haemodynamics to Determine the Influence of Surgical Expertise on Executive Control during Temporal Stress in the Operating Room

3:45-4:00 Guillermo Borragán, Céline Guillaume, Hichem Slama, Carlos Guerrero-Mosquera, Philippe Peigneux: Performance decrease associated to cognitive fatigue is regulated by connectivity disruption more than reduced activity

4:00-4:15 Joy Hirsch, J. Adam Noah, Xian Zhang, Swethasri Dravida, Ilias Tachtsidis: Identification of Neural Systems Involved in Interpersonal Eye-to-Eye Contact: An fNIRS Hyperscanning Investigation

4:15-4:30 Anna Gerega, Stanislaw Wojtkiewicz, Piotr Sawosz, Lukasz Dziuda, Mariusz Krej, Paulina Baran, Krzysztof Kowalczyk, Roman Maniewski, Adam Liebert: fNIRS-based methodology for assessment of tolerance for reduced brain perfusion in air force pilots using lower body negative pressure test

4:30-5:00 Closing remarks
Joseph Culver, co-chair

POSTER PROGRAM

Oct 14th FRIDAY
Poster Sessions 1 & 2

2 Antonio Chiarelli, Edward Maclin, Kathy Low, Monica Fabiani and Gabriele Gratton: Mapping the effective attenuation coefficient of the human head: A multi-distance approach applied to high-density optical recordings

7 Hideyuki Taura and Amanda Taura: fNIRS case studies tracking L2 proficiency development

9 Blanca Marin Bosch, Aurelien Bringard, Guido Ferretti, Sophie Schwartz and Kinga Igloi: The effect of physical exercise on memory, a NIRS study
10 Quan Zhang, Vladimir Ivkovica, Gang Hu and Gary Strangman: *Ambulatory diffuse optical tomography and multi-modality physiological monitoring system and applications*

12 Stefania Lancia, Marika Carriero, Marco Ferrari and Valentina Quaresima: *Could “Corsi Block Tapping test” be considered a real working memory task?*

14 Rachida El Kaddouri, Annabel Nijhof, Jelle Demanet, Marcel Brass and Roeljan Wiersema: *The Role Of The Temporo-Parietal Junction In Implicit Mentalizing*

15 Amir Gandombakhche, Elizabeth Smith, Afrouz Anderson, Audrey Thurm and Fatima Chowdhry: *Lateralization and Cerebral Hemodynamics at Rest in Toddlers at Risk for Language Delay*

17 Masashi Kiguchi, Tsukasa Funane, Takashi Numata and Hiroki Sato: *Optical module with SoC for wearable fNIRS system*

18 Sigita Venclove, Osvaldas Ruksenas and Algis Daktariunas: *Gender Differences In Frontal Lobe Hemodynamic Response During Cognitive Task Performance*

21 Ross T Aitchison, Uma Shahani, Laura M Ward, Graeme J Kennedy, Xinhua Shu and David C Mansfield: *Haemodynamic Response in Diabetes: An fNIRS Study of the Visual Cortex*

29 Juanning Si, Xin Zhang, Yujin Zhang and Tianzi Jiang: *Hemispheric differences of hemodynamic responses during visual stimulation with graded contrasts*

30 Evelyne Mercure, Sarah Lloyd-Fox, Mark H. Johnson and Mairead MacSweeney: *Influence of early language experience on brain activation to language: A study of hearing infants with Deaf mothers*

35 Ahmet Omurtag, Haleh Aghajani and Hasan Onur Keles: *Classifying the Brain's Functional Status in Verbal Fluency Task: EEG+fNIRS*

40 Takeaki Shimokawa, Toshihiro Ishii, Yoichiro Takahashi, Satoru Sugawara, Masa-Aki Sato and Okito Yamashita: *Diffuse optical tomography by using multi-directional sources and detectors*

41 Muhammad Raheel Bhatta, Keum-Shik Hong and Seong-Woo Woo: *Development of portable fNIRS, EEG and tDCS system for real time brain monitoring during rehabilitation*

43 Tanja Dragojevic, Joseph L. Hollmann, Hari M. Varma, Claudia P. Valdes, Joseph P. Culver, Carles Justicia and Turgut Durdurian: *Three-dimensional blood flow imaging in small animals with speckle contrast optical tomography*

46 Evgenii Kim, Eloise Anguluan and Jae Gwan Kim: *Monitoring cerebral hemodynamic change during transcranial ultrasound stimulation using near infrared spectroscopy*

47 Alexander von Lüllmann, Heidrun Wabnitz, Tilmann Sander and Klaus-Robert Müller: *Miniaturized CW NIRS for integration and hybridization with mobile EEG / ECG / EMG and Accelerometer*

49 Kourosh Zare, Mohammad Ali Ansari and H. Sahraee: *The study of prefrontal cortex activation with fNIRS during video gaming*

56 Seung-Ho Paik, Zephaniah Phillips V and Beop-Min Kim: *A portable, multi-channel fNIRS system for prefrontal cortex: Preliminary study on neurofeedback and imagery tasks*

61 Paul Burgess, Clarisse Aichelburg, Paola Pinti, Frida Lind, Sarah Power, Elizabeth Swingler, Arcangelo Merla, Sam Gilbert, Ilias Tachtisidis and Antonia Hamilton: *Prefrontal activation differences associated with social vs. non-social prospective memory in a naturalistic setting.*

62 Thien Nguyen, Olajide Babawale, Hanli Liu and Jae Kim: *Exploring brain functional connectivity in resting state and during sleep using functional near infrared spectroscopy*
Sergio Novi, Alex Carvalho, Rodrigo Forti, Clarissa Yasuda and Rickson Mesquita: The complex brain: characterizing NIRS-based networks at rest with complex systems’ approaches

Fares Al-Shargie, Tong Boon Tang, Nasreen Badruddin and Sarat Dass: Prefrontal cortex connectivity under neutral-control and stress condition using fNIRS

Sabrina Brigadoi, Jessica Dunn, Robert J. Cooper and Adam P. Gibson: A 4D pediatric head model for diffuse optical imaging of 4.5 to 18.5 years old children

Lauren Emerson, Stephen Crosswhite, James Goodwin, Andrew Berger and Richard Aslin: Isolating the effects of surface vasculature in infant neuroimaging using short-distance optical channels: a combination of local and global effects

Daniel Chitnis, Robert Cooper, Simone Quaggia, Laura Dempsey, David Highton, Jeremy Hebden, Clare Elwell and Nicholas Everdell: MicroNIRS: A Fibreless, High-Density Diffuse Optical Tomography System


Heidrun Wabnitz, Mikhail Mazurenka, Laura Di Sieno, Gianluca Bosco, Davide Contini, Alberto Dalla Mora, Alberto Tosi, Wolfgang Becker, Yoko Hoshi, Simone Kühn, Evgeniya Kirilina, Rainer Macdonald and Antonio Pifferi: Localized cerebral responses and heterogeneity of superficial signals revealed by non-contact scanning time-domain fNIRS

Jason Sutin, Bernhard Zimmerman, Danil Tyulmankov, Davide Tamborini, Kuan Cheng Tony Wu, Juliette Selb, Alberto Tosi, David Boas, Angelo Gulinatti, Ivan Rech and Maria Angela Franceschini: Time-Domain Diffuse Correlation Spectroscopy

Paola Pinti, Clarisse Aichelburg, Frida Lind, Sarah Power, Elizabeth Swingler, Arcangelo Merla, Antonia Hamilton, Sam Gilbert, Paul Burgess and Ilias Tachtsidis: Real-world neuroimaging: the use of a fiberless and wearable fNIRS system to monitor brain activity in the real-life on freely moving participants

Susanna Tagliabue, Laura Di Sieno, Alberto Dalla Mora, Edoardo Martinenghi, Andrea Farina, Turgut Durduran, Alessandro Torricelli and Antonio Pifferi: Compact 8 channels time-domain diffuse optical tomography system based on SiPMs for functional brain imaging

Meltem Izzetoglu, Lori Severino and Mary Jean Tecce Decarlo: Brain Based Assessment of Reading Skills in Adolescent Students using fNIRS

J. Adam Noah, Swethasri Dravida, Xian Zhang and Joy Hirsch: Deoxyhemoglobin changes in right lateralized DLPFC represent conflict processing in a color-word Stroop task

Daniel Hyde and Charline Simon: Functional brain organization for theory of mind in 7-month old infants

Manob Jyoti Saikia, Mohammadreza Abtahi and Kunal Mankodiya: Development of a Wireless Wearable fNIRS System


Shelby Putt, Sobanawartiny Wijeakumar, Robert Franciscus and John Spencer: The Neural Correlates of Prehistoric Stone Tool Manufacture

Rebecca Re, Edoardo Martinenghi, Alberto Dalla Mora, Davide Contini, Antonio Pifferi and Alessandro Torricelli: Fiber-free SiPM detectors for TD fNIRS: in-vivo demonstration
Chuen Wai Lee, Maria Chalia, Laura Dempsey, Topun Austin and Rob Cooper: *Investigating superficial layer effects on fNIRS signals the in term-age infant*

Lorenzo Spinelli, Andrea Farina, Tiziano Binzoni, Alessandro Torricelli, Antonio Pifferi and Fabrizio Martelli: *Statistics of photon penetration depth in diffusive media*

Cécile Issard and Judit Gervain: *Parametric vs permutation tests to analyze newborns fNIRS data: analyzing the same dataset in three different ways*

Florian Haeussinger, Alexander Mann, Andreas Fallgatter, Ann-Christine Ehlis and Martin Schecklmann: *Temporal muscle hemodynamics overlaying cortical fNIRS*

Matteo Chincarini, Lina Qiu, Alessandro Torricelli, Michela Minero, Nicola Ferri, Isa Fusaro, Massimo Mariscoli and Giorgio Vignola: *fNIRS technology applied on animals: a study on sheep*

Ambika Maria, Kalle Kotilahti, Ilkka Nissilä, Jetro Tuulari and Hasse Karlsson: *Studying the processing of affective and non-affective touch in the developing brain of 2 year old children*

Anna Blasi, Barbara Manini, Sabrina Brigadoi, Rob Cooper, Gareth Barker, Stephen Wastling, Sarah Lloyd-Fox, Mark Johnson and Clare Elwell: *Simultaneous fMRI and fNIRS analysis in young infants*

Stanislaw Wojtikiewicz, Piotr Sawosz, Michał Kacprzak, Anna Gerega, Karolina Bejm, Roman Maniewski and Adam Liebert: *High-resolution diffuse optical tomography setup for measurements at quasi-transmission geometry on an adult human head*

Marisa Biondi and Teresa Wilcox: *Increased Cortical Activation to Human Versus Mechanical Hands in Infants*

Stefano Di Domenico, Marc Fournier, Achala Rodrigo, Mengxi Dong, Richard Ryan, Hasan Ayaz and Anthony Ruocco: *Relationship Need Fulfillment Predicts Self-Other Overlap in the Medial Prefrontal Cortex During Self- and Other-Referential Cognition*

Pardis Kaynezhad and Ilias Tachtsidis: *Miniature Broadband NIRS System for Brain Tissue Oxygenation and Metabolism*

Jessica Gemignani, Randall Barbour and Christoph Schmitz: *Improved optode design for efficient hair displacement and fast setup time*

Dennis Hueber and Beniamino Barbieri: *A new instrument for simultaneous frequency-domain NIRS and DCS measurements*

Zhengchen Cai, Rasheda Arman Chowdhury, Alexis Machado, Thomas Vincent, Giovanni Pellegrino, Amanda Spilkin, Jean-Marc Lina and Christophe Grova: *NIRS 3D Reconstruction Based on Maximum Entropy on the Mean (MEM)*

Terje Gjøvaag, Peyman Mirtaheri, Hilde Sylliaas, Jette Schack, Ane Eggebø, Katrine Svartsrød Grue, Martine Skonnord, Evin Güler and Inger Marie Starholm: *Frontal brain activation during heavy resistance exercise with and without the Valsalva maneuver*

Heloïse Auger, Louis Bherer, Étienne Boucher, Richard Hoge, Frédéric Lesage and Mathieu Dehaes: *Time-domain Near Infrared Spectroscopy of Extra-cerebral and Cerebral Hemoglobin Concentrations During Incremental Intensity Exercise*

Victoria Dumont, Daniel Zuba, Sylvain Lebargy, Martina Giovannella, Marc Zabalia, Bernard Guillois and Nadège Roche-Labarbe: *Perception of temporal regularity in tactile stimulation: a diffuse correlation spectroscopy study in preterm neonates*

Randall Barbour and Harry Graber: Characterization of Hemoglobin Dynamics as a Co-Varying System in the Resting State: Evidence of Functional Bias of Preferred States and Sensitivity to Disease

Eve F. Fabre, Kevin Mandrick, Maryel Othon and Frédéric Dehais: Disobeying an immoral rule is associated with a greater emotional reaction than obeying it: An exploratory fNIRS study

Yingwei Li, Blaise Frederick, Sinem Erdogan, Kimberly Lindsey, Kenroy Cayetano, Lia Hocke and Yunjie Tong: Studying the propagation of systemic hemodynamic oscillations in human body using peripheral near infrared spectroscopy measurements

Nassim Nasseri, Stefan Kleiser, Daniel Ostoic, Tanja Karen and Martin Wolf: The influence of superficial layers on near infrared spectroscopy data

Chandran V. Seshagiri, Tanmay Oruganti, Jason W. Trobaugh, Joseph P. Culver and Bertan Hallacoglu: Demonstration of the spatial sensitivity of a compact HD-DOT system using a retinotopy paradigm

Drew Halliday, Bryce Mulligan, Stefan Schmidt, Douglas Garrett, Sandra Hundza, Mauricio Garcia-Barrera, Robert Stawski and Stuart MacDonald: Neural Variability as an Indicator of Age-Related Cognitive Function

Stefan Carp, David Boas and Juliette Selb: Improved accuracy of brain oxygen metabolism measurements using multi-distance diffuse correlation spectroscopy and near infrared spectroscopy together with a Monte Carlo light transport model

Oct 15th SATURDAY

Poster Sessions 3 & 4

Antonio Chiarelli, Mark Flecher, Edward Maclin, Kathy Low, Fabiani Monica and Gabriele Gratton: Regional Optical Measures of Cerebrovascular Status Associated with Cortical Volume in Healthy Aging

Toshinori Kato: Vector-based analysis of local cerebral activation for quantitative fNIRS study

Marika Carrieri, Stefania Lancia, Alessia Bocchi, Marco Ferrari, Laura Piccardi and Valentina Quaresima: The “Key Search Task” activates prefrontal cortex

Rosalyn Hithersay, Carla Startin, Robert J Cooper, Clare Elwell and Andre Strydom: Executive functioning and pre-frontal activity in adults with and without Down syndrome: an fNIRS pilot study

Fares Al-Shargie, Tong Boon Tang and Masashi Kiguchi: Mental Stress Localization on PFC Subregion Based on fNIRS

Emilie Bourel-Ponchel, Mahdi Mahmoudzadeh, Aline Delignières, Patrick Berquin and Fabrice Wallois: Non-invasive, multimodal analysis of cortical activity, blood volume and neurovascular coupling in infantile spasms using EEG-fNIRS monitoring

Catharina Zich, Stefan Debener, Ann-Kathrin Thoene, Ling-Chia Chen and Cornelia Kranzioch: Simultaneous EEG-fNIRS reveals age-related changes in cortical signatures of motor imagery neurofeedback

Ling-Chia Chen, Pascale Sandmann, Maren Stropahl, Marc Schoenwiesner and Stefan Debener: Tracking functional reorganization in cochlear implant users with simultaneous EEG-fNIRS

Isabel de Roever, Gemma Bale, Robert J Cooper and Ilias Tachtsidis: Investigation of cytochrome-c-oxidase as a more robust marker of frontal lobe activation

Andreas J. Fallgatter, Beatrix Barth and Ann-Christine Ehlis: NIRS Neurofeedback in ADHD
Mina Nourhashemi, Guy Kongolo, Mahdi Mahmoudzadeh, Sabrina Goudjil and Fabrice Wallois: \textit{rCBF - rCMRO2 Interrelation of Neonatal Premature Brain}

Elise Vantroys, Sofie Boterberg, Herbert Roeyers and Rudy Van Coster: \textit{Screening for mitochondrial dysfunction using functional near-infrared spectroscopy}

Clara Gregori-Pla, Gianluca Cotta, Peyman Zirak, Igor Blanco, Pau Bramon, Ana Fortuna, Anna Mola, Isabel Serra, Mercedes Mayos and Turgut Durduran: \textit{What happens to cerebral hemodynamics during an obstructive sleep apnea?}

Jessica Defenderfer, Anastasia Kerr-German, Mark Hedrick and Aaron Buss: \textit{Auditory cortex activation as measured by fNIRS associated with speech perception in normal hearing adults}

Lauren Emberson, Benjamin Zinszer, Rajeev Raizada and Richard Aslin: \textit{Decoding the Infant Mind: Multichannel Pattern Analysis (MCFA) using fNIRS}

Dominic Oliver, Ilias Tachtidis and Antonia Hamilton: \textit{The role of parietal cortex in imitation: a study with fNIRS}

Sabrina Brigadoi, Sara Basso Moro, Federica Meconi, Silvia Benavides-Varela, Iulian E. Tampu, Mattia Doro, Paola Sessa, Francesca Simion, Simone Cutini and Roberto Dell’Acqua: \textit{A multi-modal fNIRS/EEG investigation of the fronto-parietal network during audio-visual matching}

Daniel Milej, Androu Abdalamalak, Mamadou Diop and Keith St. Lawrence: \textit{A Subtraction-Based Approach for Enhancing the Sensitivity of Time-Resolved fNIRS}

Kristin Shumaker, Matthew Brook O’Donnell, Ralf Schmaelzle and Emily Falk: \textit{Accuracy, Authenticity and Intersubject Correlation in Storytelling}

Benjamin D. Zinszer, Laurie Bayet, Lauren L. Emberson and Richard N. Aslin: \textit{Decoding semantic representations from fNIRS signals}

Thibaud Gruber, Sasha Frühholz, Coralie Debracque, Kinga Igloi, Blanca Marin Bosch and Didier Grandjean: \textit{Human recognition of emotions in voices: a fNIRS study}

David Davies, Michael Clancy, Z Su, Sam Lucas, John Bishop, Peter Hansen, Antonio Belli and Hamid Dehghani: \textit{A Point of care FD NIRS device equivalent to fMRI in detecting clinically relevant physiological changes}

Vrinda Kalia, Bryan Vonder Vellen, Kira Osowski, Aaron Luebbe and Karthik Vishwanath: \textit{Using fNIRS to Measure Hemodynamic Changes in the Prefrontal Cortex Due to Acute Stress}

Luca Pollonini, Heather Bortfeld and John Oghalai: \textit{PHOEBE: a software tool for optimized guided placement of fNIRS optodes}

Bridget Walsh, Fenghua Tian and Meryem Yucel: \textit{Hemodynamic profiles of speech production in children who stutter}

Shonosuke Kurita, Kazuki Kurihara, Hiroshi Kawaguchi, Shinpei Okawa, Takayuki Obata and Eji Okada: \textit{Influence of extracerebral blood vessels in subject-specific head models on image reconstruction of diffuse optical tomography}

Cécile Issard and Judit Gervain: \textit{On the use of alternating/non-alternating designs in infant research with fNIRS}

David Perpetuini, Roberta Bucco, Michele Zito and Arcangelo Merla: \textit{Study of memory deficit in Alzheimer’s Disease by means of complexity analysis of fNIRS signal}

Cristine Sortica Da Costa, Michal Placek, Marek Czosnyka, Brenno Cabella, Magdalena Kasprowicz, Peter Smielewski and Topun Austin: \textit{Complexity of Brain Signals is Associated with Outcome in Preterm Infants}

Michael Clancy, Antonio Belli, David Davies, Zhangjie Su, Samuel Lucas, Stanislaw Wojtkiewicz, Piotr Sawosz and Hamid Dehghani: \textit{Monitoring the Injured Brain -}
Using high density near infrared probes and registered subject specific atlas models to improve cerebral saturation reconstruction accuracy

117 Sobanawartiny Wijekumar, John Spencer and Vincent Magnotta: Age-related changes in visual working memory for multiple object features

122 Meltem Izzetoglu, Shadi Malaeb, Niraj Arora, Erol Veznedaroglu and Baruch Ben Dor: Near Infrared Spectroscopy Based Non-Invasive Cerebral Edema Monitoring System

127 Chris C Duszynski, Lia M Hocke, Brian W Benson and Jeffrey F Dunn: fNIRS measures cortical communication during KINARM robotic assessment

132 Reyhaneh Nosrati, Joshua Lee, Ermias Woldemichael, Steve Lin, Tom Schweizer and Vladislav Toronov: Development of Hyperspectral Functional Near Infrared Spectroscopy

137 Irfan Dar, Nasser H Kashou and Sudarshan R Jadcherla: Assessing Neonatal Cortical and Motor Activation during Swallowing in the NICU

138 Lia M Hocke, Chris C Duszynski, Chantel T Debert and Jeffrey F Dunn: Could fNIRS be the next concussion assessment tool? Studies of network integrity

160 Ardalan Aarabi, Viktoriaya Osharina and Fabrice Wallois: Assessing the effect of confounding factors on estimates of the NIRS hemodynamic response function using single-type event-related designs – A comparative study between averaging and deconvolution analysis

162 Chiara Bulgarelli, Carina de Klerk, Victoria Southgate and Antonia Hamilton: Gaze modulates functional connectivity between STS and IFG during a mimicry task in 4-month-old infants: a PPI study on fNIRS data

164 Ernesto Elias Vidal Rosas, Daniel Coca and Stephen Billings: Reduced-order modelling of light transport in tissue for real-time monitoring of human brain absorption changes using High-Density Diffuse Optical Tomography

170 Zahra Einalou, Keivan Maghooli, Seyed Kamaledin Setarehdan and Ata Akin: Decision tree using Graph Theory Approach to Functional Connectivity in Schizophrenia

171 Gemma Bale, Aleh Sudakou, Subhabrata Mitra, Judith Meek, Nicola Robertson and Ilia Tachtsidis: Using near-infrared spectroscopy to measure cerebral blood flow in neonatal brain injury

173 Lorenzo Spinelli, Lucia Zucchelli, Davide Contini, Matteo Caffini, Jacques Mehler, Ana Fló, Alyssa L. Ferry, Luca Filippini, Francesco Macagno and Alessandro Torricelli: In vivo measure of neonate brain optical properties and hemodynamic parameters by time domain Near Infrared Spectroscopy

174 Lina Qiu, Alessandro Torricelli, Fabrizio Martelli, Andrea Farina, Lorenzo Spinelli, Alwin Kienle and Adam Liebert: The reliability test of Mesh-based Monte Carlo method for photon migration studies

175 Peyman Mirtaheri, Jette Schack, Hilde Syllaas, Inge Marie Starholm, Ane Eggebø, Katrine Svartsrød Grue, Martine Skonnord, Terje Gjøvaag and Evin Güler: The effect of Valsalva maneuver on mean arterial blood pressure and brain activity measured by near infrared spectroscopy

179 Andreas J. Metz and Ursula Wolf: Comparison of low-frequency oscillations in multi-distance and single-distance functional near-infrared spectroscopy

180 Clémence Roger, Julie Depraetere and Jeremie Jozefowicz: Identification of the metabolic correlates of the activation/inhibition pattern: a study combining fNIRS and EEG methods

186 Michael Lührs and Rainer Goebel: A novel Neurofeedback and BCI toolbox for real-time fNIRS: Turbo-Satori
Laura Kischkel, Laura Pirazzoli, Anna Blasi, Katarina Begus, Drew Halliday, Momodue Darboe, Andrew Prentice, Sophie Moore, Clare Elwell and Sarah Lloyd-Fox: Developing an fNIRS working memory paradigm for infants in rural Africa and the UK

Udo Michael Weigel, Bjørn Andresen, Victor Chamizo, Davide Contini, Agnese de Carli, Roger Donat, Turgut Durduran, Rainer Erdmann, Monica Fumagalli, Martina Giovannella, Gorm Greisen, Simon Hyttel-Sørensen, Niels König, Kristian Lauritsen, Marco Pagliazzi, Antonio Pifferi, Matthias Rehberger, Ignacio Rocchetti, Tino Röhliche, Lorenzo Spinelli, Michael Wahl and Alessandro Torricelli: The BabyLux project - an optical neuro-monitor of cerebral oxygen metabolism and blood flow for neonatology

Hendrik Santosa, Theodore J. Huppert and Keum-Shik Hong: Decoding multiple sound-categories in the auditory cortex using independent component analysis

Theodore Huppert: Introduction to the nirs-toolbox

Theodore Huppert, Pat Sparto and Joe Furman: Concurrent EEG-NIRS of vestibular function

Cristen Olds, Luca Pollonini, Heather Borfeld, Michael Beauchamp and John Oghalai: Cortical activation patterns correlate with speech understanding after cochlear implantation

Yingwei Li, Yunjie Tong, Sinem Erdogan, Kimberly Lindsey, Kenroy Cayetano and Blaise Frederick: A low cost multichannel NIRS spectrometer for monitoring global physiological hemodynamic fluctuations

Randall Barbour and Harry Graber: Hemodynamic Imprinting: A Novel Approach to Disease Detection

Nicholas Barone, Ji Hoon Ryoo and Erin Kamarunas: How we determine baseline measures and its impact on results: A reflective discussion

Sinem Erdogan, Yunjie Tong, Lia Hocke, Kimberly Lindsey, Blaise Frederick: Denoising task related fMRI data with time delay processing of concurrently recorded peripheral NIRS


Arefeh Sherafati, Adam T. Eggebrecht, Joseph P. Culver and Tracy M. Burns-Yocum: A novel global metric to detect motion artifacts in optical neuroimaging data

Masahito Mihara, Hiroaki Fujimoto, Hironori Oтомune, Yuichi Hiramatsu, Kuni Konaka, Noriaki Hattori, Yoshiyuki Watanabe, Teiji Kawano, Megumi Hatakenaka, Hajime Yagura, Ichiro Miyai and Hideki Mochizuki: FNIRS-mediated Neurofeedback enhances gait recovery after stroke: double-blind randomized clinical trial

Lindsey Powell and Rebecca Saxe: Identifying a neural predictor of infants’ social preferences

Hasan Ayaz, Sarah Levin, Amanda Sargent, Noah Sideman, Christine Hammond, Lei Wang, Jaime Slonim, Prithvi Narayan, Denah Appelt and Brian Balin: fNIRS based cognitive function assessment following concussion in adolescents

Laurien Nagels-Coune, Niels Reuter, Björn Zierul, Denizhan Kurban, Lars Riecke, Rainer Goebel and Bettina Sorger: Shedding Light on Awareness: Towards Functional Near-Infrared Spectroscopy-based Detection of Consciousness

Danielle Forster, J Holberton, V Saxton, G Fedai and E Koumoundouros: Modelling The Cerebrovascular Haemodynamics Of Neonates Using Frequency Resolved Nirs And Doppler Sonography

Oct 16th SUNDAY
**Poster Sessions 5 & 6**

5 Ata Akin: Why prefer partial correlation to compute functional connectivity for fNIRS data?

6 Ingo Helmich, Alisa Berger and Hedda Lausberg: Neuro-motor control of posture in individuals with persistent post-concussion symptoms

16 Zhenhu Liang, Lei Cheng, Yue Gu, Yunjie Tong and Xiaoli Li: Depth of anesthesia monitoring based on the multi-channel fNIRS system

27 Maria Arredondo, Xiao-Su Hu, Lara Stojanov, Akemi Tsutsumi, Rachel Wlock and Ioulia Kovelman: Bilingual Children Show Left-Hemisphere Activation During Non-Verbal Attentional Networks

32 Mohamad Issa, Xiao-Su Hu, Silvia Bisconti, Juan San Juan, Ioulia Kovelman, Paul Kilieny and Greg Basura: Tinnitus leads to increased brain connectivity in primary auditory and non-auditory brain regions as measured by functional near infrared spectroscopy (fNIRS)

34 Sarah Steele, Christopher Aasted, David Borsook, Lino Becerra, David Boas, Meryem Yucel, Barry Kussman and Peter Kelsey: Frontal Lobe Activations Across Different Levels Of Consciousness

37 Glen Tellis, Cari Tellis, D'Manda Price, Cara Imbalzano, Danielle Spagnuolo, Erin Roberts and Tia Spagnuolo: Using fNIRS to compare hemoglobin concentration changes in typically-fluent-speakers and persons-who-stutter

38 Cari Tellis, Erin Roberts, Tia Spagnuolo, Danielle Spagnuolo, Glen Tellis, Cara Imbalzano and D'Manda Price: Using fNIRS to Assess Brain Changes as a Result of Voice Therapy

42 Borja Blanco, Cesar Caballero Gaudes and Monika Molnar: The influence of bilingual exposure on early brain network development

45 Jinung An, Sang Hyeon Jin, Seung Hyun Lee, Gwang Hee Jang, Soyong Lee and Eunju Kim: Clinical Observation using fNIRS Imaging of Body Weight-Supported Treadmill Training for Sub-acute Stroke Patients

51 Hoang-Dung Nguyen and Keum-Shik Hong: Real-time adaptive filtering for noise reduction in fNIRS data

52 Cari Tellis, Erin Roberts, Tia Spagnuolo, Danielle Spagnuolo, Glen Tellis, Cara Imbalzano and D'Manda Price: Use of fNIRS in Assessing Motor Learning and Voice


66 Glen Tellis, Cari Tellis, D'Manda Price, Cara Imbalzano, Danielle Spagnuolo, Erin Roberts and Tia Spagnuolo: Using fNIRS to measure cerebral hemoglobin concentration changes of typically fluent speakers using delayed auditory feedback

70 Mojtaba Soltanlou, Christina Artemenko, Thomas Dresler, Ann-Christine Ehlis, Andreas J. Fallgatter and Hans-Christoph Nuerk: The neural correlates of arithmetic complexity in children differ from those in adults: An fNIRS study

74 Sara Basso Moro, Sabrina Brigadoi, Silvia Benavides-Varela, Simone Cutini, Paola Sessa, Francesca Simion and Roberto Dell’Acqua: Cross-modal matching of numerosity is subserved by the left parietal cortex in the developing brain


88 Maria Chalia, Robert J Cooper, Chuen Wai Lee, Laura A Dempsey, Jeremy C Hebden and Topun Austin: Can diffuse optical tomography provide early detection of perinatal arterial ischaemic stroke (PAIS) at the cot side?
Nicholas Barone, Erin Kamarunas and Christy Ludlow: Changes in Cortical Control for Singing Onset with Increases in Task Difficulty

Aaron Buss and Anastasia Kerr-German: Dimensional label learning drives the development of attention to visual dimensions

Anastasia Kerr-German and Aaron Buss: Neural Dynamics of Selective and Flexible Attention Development

David Davies, Michael Clancy, Z Su, John Bishop, Emma Toman, Sam Lucas, Antonio Belli and Hamid Dehghani: Can a clinically viable Frequency Domain NIRS device reliably detect changes in brain tissue oxygen tension of patients with severe traumatic brain injury?

Felicia Zhang, Richard N. Aslin and Lauren L. Emberson: Investigating auditory prediction in young infants using fNIRS

David Rosenbaum, Katja Hagen, Florian B. Häußinger, Andreas J. Fallgatter, Florian G. Metzger and Ann-Christine Ehlis: State-dependent connectivity in late-life depression

Paola Pinti, Arcangelo Merla, Clarisse Aichelburg, Frida Lind, Sarah Power, Elizabeth Swingler, Antonia Hamilton, Sam Gilbert, Paul Burgess and Ilias Tachtsidis: An extended GLM-based algorithm for recovering functional events in real-world fNIRS neuroimaging outside the lab with freely moving subjects

Bahareh Behboodi, Kyungsoo Kim and Ji-Woong Choi: Eye Blinks Motion Artifact Removal using Kurtosis-based Wavelet Algorithm in Prefrontal Area

Hannah Felicitas Behrendt, Katherine Perdue, Kerstin Konrad and Christine Firk: Investigating neural correlates of face-to-face mother-infant interaction and infant affect regulation in response to maternal cues with the use of real-life display: A pilot fNIRS study

Alex Boldin and Lauren Emberson: Role of Frontal Cortex in Infant Top-Down Sensory Prediction

Shender-Maria Avila-Sansores, Gustavo Rodríguez-Gómez, Carlos Gerardo Treviño-Palacios, Adam Noah, Xian Zhang, Joy Hirsch, Felipe Orihuela-Espina and Ilias Tachtsidis: Manifold based modelling of brain connectivity in fNIRS


Swethasri Dravida, J. Adam Noah, Xian Zhang and Joy Hirsch: Consistency in fNIRS Recordings during Digit-Manipulation Tasks

Luuk van de Rijt, Roos Cartignij, Emmanuel Mylanus, Ad Snik, John van Opstal and Marc van Wanrooij: Speech perception outcome of cochlear implantation predicts cortical activation measured with functional near-infrared spectroscopy

Xian Zhang, J. Adam Noah, Swethasri Dravida and Joy Hirsch: A comparison of fMRI and fNIRS deoxygenated signals: A global component removal approach

Meryem Yucel, David Harper, Jim Ellison, Tony Fantana and David Boas: Memory encoding assessed by functional Near-Infrared Spectroscopy

Rodrigo Forti, Marilise Katsurayama, Lenise Valler, Victor Hugo Souza, Oswaldo Baffa, Wagner Avelar and Rickson Mesquita: Monitoring critical patients at the neuro-intensive care unit in real-time: how can diffuse optics help?

Guilherme Zimeo Morais, Joana Balardin, Rogério Akira Furucho and João Ricardo Sato: Exploring the correlation between oxygenated and deoxygenated hemoglobin signals

Hama Watanabe, Naoto Takahashi and Gentaro Taga: Hemoglobin phase of oxygenation and deoxygenation (hPod) in preterm- and term-born infants
Diane Dreikan, Runze Yang and Jeff F. Dunn: Quantification of Cerebral Hemodynamics with Age in Brain of Healthy Adolescents and Adults Using Frequency Domain Near-Infrared Spectroscopy

Nawal Abboud, Judit Gervain and Maria Dolores de Hèvia: Representing number and time in the newborn brain

Novri Suhermi, Judit Gervain and Themis Palpanas: Time Series Analysis for Near-Infrared Spectroscopy Data

Silvia Benavides-Varela and Judit Gervain: Learning word order at birth

Laura Pirazzoli, Sarah Lloyd-Fox, Ricarda Braukmann, Teodora Gliga and Mark H. Johnson: Hand, Spoon or Toothbrush? Cortical responses to social and non-social touches in 5 month old infants

Lina Bunketorp Käll, Robert Cooper and Malin Björnsdotter: The role of adaptive plasticity in tetraplegia patients following grip reconstruction

Samuel Montero, Ilias Tachtisidis, Paola Pinti, Clarisie Aichelburg, Antonia Hamilton, Sam Gilbert, Paul Burgess, Carlos Treviño, Luis Enrique Sacar and Felipe Orhuela-Espina: Analysis of Connectivity Symmetry Between Ox- and Deoxy-Haemoglobin in Freely Moving Subjects Performing Real-World Cognitive Tasks

F. Konrad Schumacher, Florian Amtage, Lena Köstering, Andreas Horn, Tobias Piroth, Cornelius Weiller, Björn O. Schelter, Volker A. Coenen and Christoph P. Kaller: Deep brain stimulation of the subthalamic nucleus alters the hierarchical organization of the prefrontal cortex in Parkinson’s disease: Modulating effects of disease duration at surgery

Gemma Bale, Savvas Savvidis, Subhabrata Mitra, Judith Meek, Nicola J. Robertson and Ilias Tachtisidis: NIRS-Measured Frontal Cortex Asymmetry in Neonatal Brain Injury

Mehrdad Dadgostar, Seyed Kamaledin Setareh dan and Ata Akin: Motion Artifact removal for Functional Near-Infrared Spectroscopy

Maheen Siddiqui, Sarah Lloyd-Fox, Pardis Kaynezhad, Clare Elwell, Ilias Tachtisidis and Mark Johnson: The role of cytochrome in neural responses in infants

Ippeita Dan, Minako Uga and Daisuke Tsuzuki: Update for spatial registration and statistics tools for fnNIRS with emphasis on anchor-based registration, effective multiplicity approach and adaptive GLM

Carina de Klerk, Antonia Hamilton and Victoria Southgate: Using fnNIRS to investigate the neural correlates of facial mimicry in infancy

Céline Issard and Judit Gervain: Adult-like perception of time-compressed speech at birth

Simon Skau, Lina Bunketorp Käll, Georg Kuhn and Birgitta Johansson: Change in cortical activation over time in individuals with mental fatigue

Marisa Biondi and Teresa Wilcox: Cortical Basis of Social and Mechanical Object Processing in Infancy

Marta Zanoletti, Giacomo Giacalone, Davide Contini, Rebecca Re, Lorenzo Spinelli, Luisa Roveri and Alessandro Torricelli: Reproducibility, hemispheric variability and range of normal values of cerebral oxygenation parameters measured by TD fnNIRS in healthy volunteers in view of an application to acute ischemic stroke patients

Bryan Brown, Sobanawaritny Wijekumar, Patricia Zebrowski and John Spencer: Cortical Activity Related to Speech Motor Planning and Execution in Adults Who Stutter

Thomas Vincent, Alexis Machado, Jean-Marc Lina and Christophe Grova: Bayesian fnNIRS smooth adaptive deconvolution

Iliza Butera, Erin Nelson and René Gifford: Neural correlates of music perception in cochlear implant users
Randall Barbour and Harry Graber: *Enhanced resting-state dynamics of the hemoglobin signal as a novel biomarker for detection of breast cancer*

Randall Barbour and Harry Graber: *Factors Influencing the Diagnostic Performance of Breast Cancer Detection by Hemodynamic Imprinting*

Silvia Bisconti, Renee Lajiness-O'Neill, Neelima Wagley, Keti Lengu, Tristin Nyman, Ana-Mercedes Flores, Tiffany Andersen, Casey Swick, Annette Richard, Elise Hodges, Xiaosu Hu, Anne-Michelle Tessier and Ioulia Kovelman: *Do you know these sounds? Left hemisphere shows greater activation to high frequency language phonotactics in infants but not in adults*

Katherine Perdue, Swapna Kumar, Alissa Westerlund, Julia Cataldo and Charles Nelson: *Resting State fNIRS with awake infants and children*

Kimberly A. Brink, Lindsay C. Bowman, Xiaosu Hu and Henry M. Wellman: *Differential activation during mental state reasoning in the temporoparietal junction*

Alexis Machado, Thomas Vincent, Zhengchen Cai, Jean Marc Lina, Eliane Kobayashi and Christophe Grova: *Robustness of the general linear model to noise misspecification in fNIRS*

Gentaro Taga: *A model of hemoglobin phase of oxygenation and deoxygenation (hPod) in spontaneous neurovascular and metabolic activity*
Abstracts
Invited Program
Clinical neuro-monitoring with NIRS-DCS

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Functional near-infrared spectroscopy (fNIRS) typically measures oxy- and deoxy-hemoglobin concentration changes in the brain following stimulation. Temporal and amplitude differences in the hemoglobin responses across individuals provide insights into brain development and brain health. In our lab we are developing advanced NIRS technology to provide quantitative hemodynamic measures to assess brain development and health through baseline measures instead of changes. We use frequency-domain near-infrared spectroscopy (FDNIRS) to quantify hemoglobin concentration and oxygenation. We complement this information with diffuse correlation spectroscopy (DCS) to quantify an index of blood flow (BF), and estimate an index of cerebral metabolic rate of oxygen (CMRO₂). With this method and simple point measurements we have reported developmental increases in hemodynamic and oxygen consumption in healthy infants and demonstrated alterations with disease. With the foundation of our seminal FDNIRS-DCS efforts with neonates established, we are now developing novel devices and approaches to better quantify cerebral blood flow and oxygen metabolism in children and adults both in the clinical settings and in developing countries. I will present the first fully integrated FDNIRS-DCS commercial system. I will show results from our technology, including measurements in infants and children in remote villages in Africa as well as measurements in pediatric and adult patients in intensive care settings in Boston. In parallel with the clinical translation of the established FDNIRS-DCS technology, we have also advanced the field and developed entirely new approaches that have the potential to be rapidly translated into a clinically viable, noninvasive, comprehensive cerebral hemodynamic monitoring method with significant advantages over existing methods. In particular, time-domain diffuse correlation spectroscopy (TD-DCS) is a novel technology that enables us, for the first time, to employ time-gating strategies used in TD-NIRS in DCS cerebral blood flow measurements and to realize improvements that are not possible with either of the two techniques alone. The use of novel long coherence light sources allows us to quantify both hemoglobin concentration and blood flow with standalone DCS. The development of DCS devices with fast acquisition rates allows us to acquire cerebral blood flow variations due to the cardiac cycle. We are the first to explore the possibility of using the pulsatile blood flow to assess intracranial pressure continuously and noninvasively. Our long-term goal is to develop a noninvasive bedside monitor that provides real-time brain physiological information with enough accuracy to guide the clinical care of neuro-ICU patients, protecting neurocognitive function and reducing the overall morbidity and mortality.
**Invited Talks**

**Neurodevelopment 1 (Friday, Oct 14th, 8:30-9:00)**

**Neuroimaging the developing brain: From the neonatal period to adolescence**

Yasuyo Minagawa (Keio University, Department of Psychology)

The human brain continues to develop until adolescence, and there are remarkable changes in cognitive systems throughout this period of development. Functional near-infrared spectroscopy (fNIRS) is ideal for use in young populations; therefore, we used fNIRS to assess dynamic cognitive systems at several stages of development. This talk will discuss such fNIRS data, as well as additional behavioral and physiological data. The talk will focus on the cerebral bases of speech perception and phonetic learning in neonates and infants, followed by the results of our longitudinal study that examines the cerebral substrates of critical periods for perceptual and cognitive learning. Neuronal plasticity of three age groups including children, adolescents, and young adults will be compared based on functional connectivity, as well as comparison of cerebral activation before and after training for two different tasks.

**Brain & Systemic Physiology (Friday, Oct 14th, 11:00-11:30)**

**A novel methodology to better understand what is happening in the brain: Systemic physiology complemented functional near-infrared spectroscopy (SPC-fNIRS)**

Felix Scholkmann\(^1,2\), Timo Hafner\(^3\), Martin Wolf\(^2\), and Ursula Wolf\(^6\)

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Previous studies showed that stimulus or task evoked changes in fNIRS signals are also influenced by changes in systemic physiology (e.g. pCO\(_2\), blood pressure). These changes are interesting in their own right and they are confounding effects with significant importance for fNIRS studies. The aim was to analyze how SPC-fNIRS can be applied to investigate physiological and cerebral changes elicited by short-time color light exposure (STCLE) and how they differ from subject to subject.

14 healthy subjects (35.4 ± 10.5 years) were measured in 3 different experimental conditions, i.e. single-color wide-field visual STCLE: red, green, or blue in a randomized and crossover design. Each measurement lasted 33 min (8 min pre-baseline, 10 min STCLE, 15 min recovery). STCLE followed an event-related design: light on/off sequence with 15 events (event duration: 20s). Subjects sat opposite a color screen. Cerebral hemodynamics/oxygenation (HD/OX) was measured bilaterally over the prefrontal (PFC) and visual cortex (VC) by a multi-channel frequency-domain NIRS
Systemic physiology parameters recorded and analyzed were: heart and respiration rate (HR, RR), pulse-respiration quotient (PRQ), end-tidal pCO$_2$ (P$_{ET}$CO$_2$), continuous mean arterial blood pressure (MAP), and the high-to-low frequency ratio (LF/HF) of heart rate variability.

Significant changes in systemic physiology were detected. A large intersubject variability was found in changes in HD/OX in the PFC and VC as well as in systemic physiology parameters (an example is displayed in Fig. 1). The results of a correlation analysis comparing the magnitudes and signs of physiological changes with personal psychological traits will be presented.

In conclusion, in our SPC-fNIRS study we found that STCLE caused different changes in cerebral HD/OX and indeed also systemic physiology depending on the specific subject. Possible causes and the significance of these findings for other fNIRS studies will be discussed. Since STLC is not a strenuous task, we expect that changes in systemic physiology may occur in many neuroscientific tasks and were neglected so far.

**Fig. 1:** Examples of individual changes in cerebral HD/OX and systemic physiology. The red lines mark the start and the end of the STCLE (duration: 20 s). Data are presented as median values ± standard error of the median.
Clinical Applications (Friday, Oct 14th, 2:00-2:30)

fNIRS-based neuropharmacological assessment on children with attention deficit/hyperactivity disorder

Ippéita Dan1, Yukifumi Monden2, Masami K Yamaguchi3, So Kazanawa4 and Ryoichi Sakuta1 on behalf of RISTEX ADHD Diagnosis Consortium.

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fNIRS exhibited its potential as a tool for neuropharmacological assessment from the early period on its invention, but its actual implementation in clinical situations has yet to be realized. While fNIRS offers technical advantages such as affordability, motion-tolerance and accessibility to allow large-scale group analyses to study neuropharmacological effects of several kinds of drugs on either healthy subjects or patients, it has not been regarded a powerful enough tool to realize individual-level analysis.

In a series of fNIRS studies on neuropharmacological effects of atomoxetine (ATX) and methylphenidate (MPH) on children with Attention Deficit Hyperactivity Disorder (ADHD), we have shown that fNIRS can successfully discriminate differences in how these drugs affects neurocognitive functions of ADHD children. We monitored the oxy-hemoglobin signal changes of ADHD children performing go/no-go or oddball tasks before and 1.5 h after ATX, MPH or placebo administration, in a randomized, double-blind, placebo-controlled, crossover design. We also included age- and gender-matched typically-developing (TD) controls without medication. In TD children, the go/no-go task recruited the right inferior and middle prefrontal gyrri (IFG/MFG), and this activation was absent in pre-medicated ADHD children. The reduction of right IFG/MFG activation was acutely normalized after ATX and MPH administration but not placebo administration in ADHD children. In TD children, the oddball task recruited the right IFG/MFG and the inferior parietal cortex. The right prefrontal activation was normalized after ATX and MPH administration in ADHD children, but the right inferior parietal normalization was specific to ATX. These results led us to conclude that fNIRS successfully visualized differential neuropharmacological effects of ATX and MPH to up-regulate the noradrenaline and dopamine systems in the inhibitory and attentional networks in the brains of ADHD children.

Moreover, we aimed to explore a method of individual differentiation between ADHD and TD children using fNIRS, emphasizing how spatial distribution and amplitude of hemodynamic response are associated with inhibition-related right prefrontal dysfunction. Thirty ADHD and thirty typically developing control children underwent a go/no-go task, and their cortical hemodynamics were assessed using fNIRS. We explored specific regions of interest (ROIs) and cut-off amplitudes for cortical activation to distinguish ADHD children from control children. The ROI located on the border of inferior and middle frontal gyrri yielded the most accurate discrimination with approximately 80% of sensitivity and specificity. Thus, the right prefrontal hypoactivation assessed by fNIRS would serve as a potentially effective biomarker for classifying ADHD children at the individual level.

In extension of these studies, projects for exploring neuropharmacological analysis of MPH and ATX on ADHD children at individual level are now under way. In this talk, we will describe the current status of this project, obstacles regarding neuropharmacological analyses, and future perspectives.
Multimodal monitoring (Friday, Oct 14\textsuperscript{th}, 5:00-5:30)

Multimodal fNIRS and EEG for studying neurovascular coupling

Solomon Diamond
Dartmouth College

In this on-going study, we are examining neurovascular coupling in multiple sclerosis (MS) using the simultaneous acquisition of electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS). These neurovascular coupling results are then used to optimize functional magnetic resonance imaging (fMRI) analyses of brain activity in patients with MS performing a working memory task. Challenges in multimodal data acquisition, modeling of neurovascular coupling, and functional neuroimaging analysis in the context of neurological diseases that alter the physiology of brain activation are addressed.

Hardware Development 1 (Saturday, Oct 15\textsuperscript{th}, 11:00-11:30)

Towards wearable NIRS
Frédéric Lesage
Polytechnique Montréal

In this talk we'll present efforts made in recent years to render NIRS portable: we'll present a design with low power consumption, high sensitivity and small footprint to enable acquisitions in a natural setting. Performance, when compared to off-the-shelf systems, and acquisition in movement will be presented. Efforts to further decrease size and build a system based on monolithic integrated chips will be discussed providing a perspective for the future of wearable NIRS.

Neonatal & Pediatric Applications (Sunday, Oct 16\textsuperscript{th}, 8:30-9:00)

Testing the benefit and harms of cerebral oxygenation monitoring in preterm infants
Gorm Greisen
Neonatology, Rig hospitalet, University of Copenhagen, Denmark, on behalf of the SafeBoosC consortium

The SafeBoosC project aims to examine the clinical benefit and harms of monitoring of cerebral oxygenation by NIRS in extremely preterm infants during the first 3 days of life. This period of cardio-respiratory transition to extra-uterine life is difficult for the immature child and a large proportion of the mortality and brain injury leading to survival with neurodevelopmental impairment occurs in these days. Cerebral hypoxia is likely to play an important role and therefore it is appealing to try to monitor cerebral oxygenation directly to allow timely and individualized
adjustments of the intensive life support these infants usually require. A randomized trial involving 166 such infants, carried out in eight neonatal intensive care units in eight European countries, demonstrated that it was possible to reduce the burden of cerebral hypoxia by more than half. There was a tendency towards improved clinical outcomes, but the trial was not statistically powered to demonstrate that. Therefore, a larger clinical randomized trial is required. Such a trial needs to be pragmatic since funding will be limited. This means that a number of different oximeters are likely to be involved. Therefore a robust way of calibrating oximeters is needed so as to ensure that the hypoxic alarm limit, i.e. the threshold of intervention, is comparable. This was achieved using a blood-lipid-yeast phantom.

Neurocognition (Sunday, Oct 16th, 3:00-3:30)

Monitoring human performance under realistic operational settings

Frédéric Dehais
ISAE, Toulouse, France

Safety analysis reveals that the complexity of modern transportation systems and operational pressure can overwhelm even the most experienced human operators when something goes wrong. Generally, humans are confused and face perseveration, a behaviour that leads them to neglect critical information (e.g. auditory alarms) and to persist in irrational decision-making. An innovative way to address these challenging safety issues is to merge knowledge and methods from cognitive psychology, system engineering and neurosciences. This approach known as Neuroergonomics aims at designing systems for safer and more efficient operation, and understanding human brain functioning in workplace (Parasuraman & Rizzo, 2007). This talk presents recent ISAE studies using brain-imaging techniques such as fNIRS to understand the underlying mechanisms of perseveration, inattentional deafness and mental overload. The results of this research pave the way to implement brain computer interface under realistic settings (flight simulator, light aircraft) and to design cognitive countermeasures to mitigate human error.
Special Session “Global fNIRS”  
Saturday, Oct 15th, 4:30-6:00

Infant brain health in India: Assessing working memory capacity using image-based fNIRS

John P. Spencer¹, Sobanawartny Wijeakumar¹, Lourdes Delgado Reyes¹, Aarti Kumar², Vishwajeet Kumar²

¹School of Psychology, University of East Anglia, Norwich, UK  
²Community Empowerment Lab, Lucknow, IN

Striking progress has been made in reducing infant mortality in some of the most impoverished regions on Earth; however, moving children from surviving to thriving in such settings remains an immense global challenge. At the core of this challenge is early brain health: during the first year alone, the brain doubles in size with profound changes in functional brain networks extending across the first 5 years. Not surprisingly, significant adversity can have a major impact on these emerging brain networks, yielding deficits that extend into adulthood.

Here, we present data on the first cross-sectional study using image-based fNIRS to examine the emergence of visual working memory from 4 months to 4 years. Our data establish a normative developmental trajectory for the task-based functional brain network that sub serves this critical cognitive system. We then use this normative trajectory as a basis for comparison to preliminary data collected at a field site in Uttar Pradesh, India. Our question was whether we could a neurodevelopmental toolkit to assess early infant brain health in this setting.

Our project took place at a field site in Shivgarh, IN operated by the Community Empowerment Lab. We collected data from 37 children: 10 6 mo (M=9.8, SD=1.2), 11 1yo (M=19.9, SD=2.1), 7 2yo (M=30.8, SD=2.3), 6 3yo (M=36.7, SD=2.6), and 3 4yo (M=46.3, SD=0.3). Children tolerated the NIRS cap well (see Fig 1), and robustly engaged in the VWM task. The top left panel in Fig 2 shows mean look durations: as with our sample from the USA (blue), there was an increase in look durations across set sizes as there were more items on the display; children in India had longer look durations overall suggesting they were more engaged. As a group, the India cohort robustly preferred the changing side, with a mean change preference of 0.55 which was significantly different from chance (p<.05) and robustly higher than the USA cohort (F(1130)=11.03, p<.001). On the other key metric—shift rate—children in India showed a decline over ages 1-4 (see above); this contrasts with the increase in shift rate in the USA sample that was predictive of higher capacity at 3-4 years.

We collected fNIRS data using an 8-channel portable device with optodes positioned over bilateral frontal cortex. We analyzed the fNIRS data using an AgeExSS ANOVA and then clusterized the results (α=.05). The significant clusters for the India (green) and USA (red) cohorts are shown in Fig 2 (confined to the regions we recorded from in India); brown clusters show the overlap across cohorts. There was overlapping activation in L-MFG and L-IFG. There was also a cluster unique to the India cohort in R-SFG. Interestingly, data from our US sample show that L-SFG activation was negatively correlated with WM capacity at 3-4 years. It is possible that early SFG activation is a biomarker for later VWM impacts.
Figure 1. Picture of fNIRS setup in field site in Shivgarh, India.

Figure 2. Top left shows mean look durations from preferential looking task comparing USA and India cohorts. Bottom left shows shift rates (rate of looking left and right) from preferential looking task in USA and India cohorts. Right image shows clusters of significant HbO activation in USA sample (red), India sample (green), and overlap (brown). We found significant overlapping activation in L-MFG and L-IFG across cohorts.
Cure Forward: A novel diagnostic tool to improve infant hydrocephalus outcomes in the developing and developed worlds.

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Eighty percent of infant hydrocephalus cases occur in the developing world, afflicting an estimated 250,000 infants in Sub-Saharan Africa alone. Unfortunately, most infants in lower-income countries go without treatment and, consequently, suffer severe brain damage and even childhood death. With proper treatment, the direct outcomes are preventable, and the children can grow up to have a better life.

CURE Hydrocephalus, an international non-profit organization dedicated to reducing the burden of hydrocephalus, has launched a surgical training network to equip developing world neurosurgeons with advanced surgical treatments for hydrocephalus. We are working with CURE to help eliminate untreated hydrocephalus by developing an inexpensive, and easy-to-use diagnostic tool rapidly evaluate disease progression and predict treatment outcomes.

Cerebral blood flow (CBF) is a promising biomarker for determining the extent of hydrocephalus and its effect on the brain. In hydrocephalus, compression of vessels and cerebral parenchyma from elevated intracranial pressure reduces CBF. Using new technology (Metaox, ISS Inc., USA) combining frequency-domain near-infrared spectroscopy (FDNIRS) with diffuse correlation spectroscopy (DCS), we can for the first time unambiguously measure cerebral indexes of microvascular blood flow (CBF) and oxygen metabolism (CMRO2) in the infant’s brain, right at their bedside.

In a clinical trial with a cohort of hydrocephalus infants at Boston Children’s Hospital (BCH), we have demonstrated the feasibility of conducting FDNIRS-DCS measurements in the clinic. We found successful hydrocephalus treatment increases cerebral blood flow and restores normal cerebral metabolism.

We performed a pilot trial at the CURE Children Hospital Uganda (CCHU) to investigate using the FDNIRS-DCS technique in measuring post-infectious hydrocephalus (PIH). In this pilot study, we enrolled 40 patients suffering PIH and adapted the FDNIRS-DCS measurements into their routine clinical care at CCHU. FDNIRS-DCS measurements were performed daily during their hospital stay to investigate the impact of PIH and surgical treatments on cerebral physiology. We found primary injuries from infection and the advance stage of the disease in the CCHU cohort resulted in significant brain structural pathology that was not observed in the BCH cohort.

These changes were readily detected by FDNIRS-DCS as distortions in the diffusion of light through the tissue. We used clinical CT scans taken before treatment to measure the extent of structural injuries. We found 25 percent of measured brain regions were destroyed by infection without any visible sign of cortex while 30 percent of the measured regions had more than 10 mm thickness of cortex remaining. NIRS measurements coincided with CT findings, reaching a sensitivity and specificity of 89 and 79 percent. We also found significantly lower oxygen saturation and CBF in brain regions with severe parenchymal edema and/or active inflammation. CBF also increased after hydrocephalus treatment regardless of pre-surgical conditions. The study is still ongoing to follow up outcomes after six months post-surgery. We will test whether the amount of CBF before treatment or the amount of change in CBF in response to treatment is a better predictor of outcome.

Based on the results from this pilot study, we plan to develop a larger and more comprehensive clinical trial to test the clinical use of this novel method in predicting neurodevelopmental outcomes. Success in the larger trial would lead to immediate improvements infant hydrocephalus care in both the developing and developed worlds.

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The Brain Imaging for Global Health Project (BRIGHT) in The Gambia and UK

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Brain development in human infants during the first 1000 days – the period from conception to two years of age - is critical, and risk of compromised development during this time can have a deep impact on physical growth and cognitive function into adulthood. Recent research has shown that exposures early in life, such as under nutrition, are linked to lifelong effects on adult health, however we still have a comparatively poor understanding of how such exposures effect brain development during this period. Non-invasive brain imaging techniques, such as functional near infrared spectroscopy (fNIRS), may provide information that to date has been unavailable with existing behavioural paradigms.

Recent fNIRS research in typically developing infants has shown robust and consistent activation to social versus non-social visual and auditory stimuli in the inferior frontal, anterior temporal and temporo-parietal regions of the cortex. Having established this signature response in infants from 4 to 6 months of age, here we applied this paradigm to the investigation of social responses in infants from the first days of life to the first year in two different settings: urban European and rural Gambian. This was a cross sectional study of infants in the Gambia and UK at 0-2, 4-8 and 12-16 months of age. Results revealed robust and consistent socially selective responses from 4 – 16 mths of life to both the visual and auditory stimuli. In contrast at 0-2 mths of age, in both the Gambian and UK infants, a stronger response was evidenced to the non-social auditory stimuli. These findings provide a key biomarker of cortical specialization over the first year of life.

We are now undertaking a two-centre longitudinal study of infants in the Gambia and UK from birth to two years of age using a range of measures. We believe fNIRS is ideally suited to the study of compromised development in global health research, particularly remote settings, where infants are exposed to a broad range of adversity early in life including poverty, under-nutrition and recurrent infections.

Figure 1: fNIRS studies being performed in a newborn, a 6 month old infant, 13 month old infant and a 2 yr old toddler in The Gambia.
The use of fNIRS in the study of early cognitive development in Dhaka, Bangladesh

Charles A. Nelson$^{1,2,3}$, Katherine L. Perdue$^{1,2}$, Swapna Kumar$^3$, Alissa Westerlund$^1$, Sarah Lloyd-Fox$^4$, Clare Elwell$^5$, Sarah Jensen$^{1,2}$, Annie Berens$^{2}$

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Advances in neuroimaging technology have opened a new avenue for research of the developing human brain. Functional near-infrared spectroscopy (fNIRS) is an example of a tool that is noninvasive, performs well early in life and is sufficiently portable that it can be used in low resource settings. Our team constructed a sophisticated neuroimaging lab in the Mirpur District of Dhaka, Bangladesh, including a 38-channel fNIRS system in order to study the effects of biological and psychosocial adversity on cognitive development. Study participants lived in a poor urban neighborhood (Figure 1a) and were exposed to a broad range of adversities early in life including poverty, malnourishment, recurrent infections, and lack of maternal education. We used a social cognition paradigm and resting state measures in a cohort of urban Bangladeshi infants (6-month-olds, $n=100$), and extended the work to study a cohort of 36 month-old ($n=130$) Bangladeshi children. Brain activity was recorded over the frontal and temporal cortices (Figure 1b). In the task-based experiment, social videos were alternated with control blocks of pictures of local modes of transportation. The oxyhemoglobin responses to each condition were calculated using HOMER2 by finding the mean response from 8-16 seconds after the start of the stimulus presentation. Statistical testing compared the silent visual social condition with the silent non-social condition, and the vocal (auditory social) with the non-vocal (auditory nonsocial) conditions to find channels that were selective for a particular condition. Disregarding background measures (of adversity), at the overall group level we find similar stimulus-selective channels in both ages, indicating that these brain responses are online from an early age (channels showing significant differences between visual conditions are shown in Figure 1c). These results are also similar to prior findings using the same stimuli with infants aged from 4-7 months in the U.K. and The Gambia. We are currently stratifying our data based on key background variables, juxtaposing measures of biological adversity (e.g., inflammation, stunting) with those of psychosocial adversity (e.g., maternal depression, education). These findings will be reported as well.

![Figure 1. A: Mirpur neighborhood, Dhaka, Bangladesh, B: Child with fNIRS probe. C: Channels that are selective for social vs. nonsocial visual stimuli (p<0.05)](image_url)
Contributed Talks
Infant perception and cognition have been traditionally investigated using habituation paradigms with the assumption that infants’ representations are best constructed after numerous repetitions of the very same stimulus, and in the absence of interference. However, it is a crucial yet open question how the brain regions react to stimuli presented in a fashion similar to everyday learning situations, namely in dispersed, rather than massive episodes. To address this question in the language domain, we tested forty healthy newborns with the functional near-infrared spectroscopy to establish the neonate brain’s ability to memorize the sound of a word in distributed episodes and the functional connections among brain regions during the phases of encoding and recognition of word-sounds. Forty healthy full-term newborns (14 males; mean age: 2.7 days, range: 2-5 days) participated in the study. The structure of the experiment consisted of an encoding phase and a test phase, separated by a silent retention interval. During the encoding phase, neonates heard 10 blocks containing two different randomly presented words. During the test phase, brain hemodynamic responses to one of the familiarized words (Same-word group) and a completely novel word sound (Novel-word group) were assessed. Hemodynamic responses were measured with fNIRS (ETG-4000, Hitachi) over 24 channels on the frontal, temporal, and parietal areas of both hemispheres. Areas involved in encoding were identified by means of robust linear regressions on the hemodynamic changes over-time. Differences between the two conditions in the test (using approximate permutation) were indicative of the recognition response to previously heard sounds (following Benavides-Varela et al., 2012). The results of the previous analysis (indicating the areas involved in the encoding and recognition responses) guided the network analyses. Effective connectivity analysis among the areas of interest was performed with structural equation modeling with AMOS software. Differences between the models were assessed using the “stacked model” approach (McIntosh & Gonzalez-Lima, 1994). The results evidenced an adaptation-like hemodynamic response during encoding in the left-frontal region, which was associated with a progressive decrement of the functional connections between this region and the left-temporal, right-temporal and right-parietal regions (Fig A). In the test, a characteristic neural signature of recognition recruited firstly the right-frontal area and subsequently the left-temporal and right-parietal regions. Connections originating from the right-temporal regions to these areas emerged when newborns heard the familiar word in the test phase (Fig B). These findings suggest a neural specialization at birth mainly characterized by the interplay between temporal and left-frontal regions during encoding; and between temporal and right-frontal regions during recognition of speech sounds. Most critically, the results show that these distinct configurations enable infants to retain speech sounds in distributed episodes despite the presence of interfering sounds.

A. ENCODING PHASE

B. RECOGNITION PHASE
Speech perception requires efficient auditory mechanisms to track differences in the spectro-temporal cues differentiating phonetic contrasts. For adults, slow temporal envelope cues (or amplitude modulation, AM) play the most important role in quiet for phonetic perception. The fast AM cues and the temporal fine structure (or frequency modulation, FM) play a more important role in noise and for speech prosody. Although infants have an immature auditory system, they show exquisite speech perception abilities early on. However, whether they rely on the same temporal information than adults when perceiving speech sounds is still not clear. The present study investigates how temporal information, slow versus fast AM cues, are used in phonetic perception at birth, when infants have yet limited experience with the auditory world.

Vocoders, which are speech analysis and synthesis systems, are used to manipulate the temporal modulations of speech in a specific number of frequency bands. Three vocoder conditions have been designed in order to preserve: (i) the original AM and FM cues (Intact), (ii) the fast AM cues (< 256 Hz) only (Fast), and (iii) the slow AM cues (< 8 Hz) only (Slow). French syllables varying in place of articulation on either the consonant /pa/-/ta/ or the vowel /pu/-/py/ were recorded from a female native speaker and processed in these three conditions. The Near-InfraRed Spectroscopy technique was used while infants were asleep in order to record hemodynamic brain responses in the temporal, parietal and frontal regions for the syllables processed in the three conditions. Time-locked electrophysiological brain responses to the syllables were also recorded using EEG. One group of 23 infants has been exposed to the consonant contrast and another group of 16 to the vowel contrast. Each infant was exposed to 6 blocks of 25 syllables in each of the three conditions.

Results show that the hemodynamic responses (Figure 1) differ between vowel and consonant groups according to the vocoder condition and the hemisphere. More precisely, different concentrations of oxygenated hemoglobin (oxyHb) are observed between Slow and Fast Conditions at birth, suggesting that these temporal cues are not processed similarly. Moreover, activations for Fast AM cues are more similar to Intact speech when newborns are exposed to a consonant change. This suggests that newborns are more sensitive to prosodic and formant transition cues preserved in both Fast and Intact conditions. Different activations are observed between vowel and consonant conditions: unlike adults, infants may require the fastest fluctuations (i.e., FM cues that convey primarily F0 fluctuations) to process vowels but can use only fast AM cues to process consonants.

Thus, processing of fast and slow speech temporal cues may not involve the same neural mechanisms at birth and the fast temporal information may play a significant role in early speech perception.

Figure 1. Oxygenated-hemoglobin concentration change in mmol x mm over the Left and Right Hemisphere for the Vowel (left panel) and Consonant (right panel) conditions, in each vocoder condition (Intact, Fast, Slow; black, red and orange bars respectively). The error bars represent the standard errors.
Deficits in Top-Down, Sensory Prediction in Infants At-Risk Due to Premature Birth

Lauren L. Emberson, Alex Boldin, Julie E. Riccio, Ronnie Guillet, & Richard N. Aslin

A prominent theoretical view is that the brain is inherently predictive and that prediction drives the engine of development. While neural signatures of top-down, sensory prediction are present in young infants, if prediction is important for development, developmental trajectories must be altered when prediction abilities are reduced or absent early in life. Here, we employed functional near infrared spectroscopy (fNIRS) to investigate top-down, sensory prediction in infants born prematurely, a leading cause of neuro-cognitive impairment worldwide. This at-risk group was targeted because prematurity leads to a broad range of behavioral deficits or delays and altered brain-behavior relationships suggesting that a fundamental aspect of development has been disrupted. Is that fundamental aspect of development the capacity to predict up-coming sensory input? We recorded neural activity of preterm and full-term infants at 6 months corrected age (i.e., controlling for maturational differences). While we found typical neural responses to presented auditory and visual stimuli, infants born prematurely exhibited altered neural responses to predicted stimuli. Importantly, while prediction and learning are linked (e.g., learning is required to predict upcoming stimuli), the current study was designed to isolate top-down prediction from simple associative learning to demonstrate selective impairments in premature infants. This assumption was confirmed in a separate behavioral control where both full- and preterm infants exhibited simple associative learning. These findings suggest that top-down sensory prediction plays a crucial role in development by showing that infants who will experience altered developmental trajectories and are at-risk for poor developmental outcomes exhibit differences in top-down prediction very early in life.

Figure 1

![Figure 1](image1.jpg)

Figure 2

![Figure 2](image2.jpg)
Atypical right hemisphere response to slow temporal modulations

in children with developmental dyslexia

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Phase entrainment of neuronal oscillations is thought to play a central role in encoding speech. Children with developmental dyslexia show impaired phonological processing of speech, proposed theoretically to be related to atypical phase entrainment to slower temporal modulations in speech (< 10Hz). While studies of children with dyslexia have found atypical phase entrainment in the delta band (~2 Hz), some studies of adults with developmental dyslexia have shown impaired entrainment in the low gamma band (~35 - 40 Hz). Meanwhile, neuroimaging studies of neurotypical adults suggest asymmetric temporal sensitivity in auditory cortex, with preferential processing of slower modulations by right auditory cortex, and faster modulations processed bilaterally. Here we compared neural entrainment to slow (2 Hz) versus faster (40 Hz) amplitude-modulated noise using fNIRS to study possible hemispheric asymmetry effects in children with developmental dyslexia. The recording optical unit was a multi-channel continuous wave fNIRS instrument (ETG-4000 Hitachi Medical Corporation, Tokyo, Japan). The present investigation made use of 32 laser diodes light sources (16 emitting light at 695 nm, and 16 at 830 nm) and 14 detectors. Probe arrangement enabled us to record hemodynamic activity bilaterally from parietal and temporal brain regions. The cortical regions underlying each optode and channel were estimated using the LONI Probabilistic Brain Atlas. The experimental procedure included two blocks of 5 minutes stimulation at each amplitude modulation rate used (2 Hz and 40 Hz), presented sequentially in a semi-random order. During each 5 minute block, 15 s periods of stimulation were interspersed with 15 s periods of silence. The children were watching a silent video during data acquisition. We also collected three measures of phonological processing which were administered as part of ongoing testing in the year that fNIRS was recorded, as were three psychoacoustic measures of sensitivity to non-speech amplitude envelope rise time.

We predicted atypical right hemisphere responding to 2 Hz modulations for the children with dyslexia in comparison to control children, but equivalent responding to 40 Hz modulations in both hemispheres. We performed an analysis for the HbO concentration on a single channel basis, aimed at identifying the core region that differed between the children with dyslexia and the control group. For each channel, we performed a mixed ANOVA with modulation rate as the within-participant factor (2 levels: 2 Hz and 40 Hz) and group as the between-participant factor (2 levels: control and dyslexic). We then collated those channels exhibiting a frequency x group interaction, which signified a differential effect of modulation rate between the two groups. Following these procedures, only the HbO response of channels 43 and 44, two adjacent channels in the right supramarginal gyrus, revealed a significant interaction after multiple comparison correction (ch. 43: F(1,28)= 16.64, p< .005; ch. 44: F(1,28)=11.11, p< .005). This region was significantly more active in children with dyslexia than in control children for 2 Hz stimulation (but not for 40 Hz stimulation). Furthermore, the hemodynamic response at 2 Hz was significantly associated with basic sensory processing of amplitude rise time and with vocabulary and reading development. We interpret the results with respect to a neural ‘temporal sampling’ framework for conceptualizing the phonological deficits that characterise children with developmental dyslexia across languages.
Multi-wavelength, multi-distance diffuse correlation spectroscopy for simultaneous measurement of blood flow and hemoglobin oxygenation

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Diffuse correlation spectroscopy (DCS) measures a microvascular blood flow index (BFi) by illuminating the tissue with a long coherence length laser, detecting fluctuations in the speckle pattern and fitting a physical model to the measured intensity autocorrelation curves\(^1\). Traditional DCS analysis is based on accurate knowledge of the optical properties of the medium, that is the absorption (\(\mu_a\)) and reduced scattering (\(\mu'_s\)) coefficients. To obtain this information, it is customary to use near-infrared spectroscopy (NIRS) in conjunction with DCS\(^2\).

Towards the development of a stand-alone DCS system, it was recently demonstrated that it is possible to uniquely determine \(\mu_a\), \(\mu'_s\), and BFi from multi-distance DCS measurements when using short-separations (i.e. \(r < 5 \text{ mm}\))\(^3\). The method fails to accurately separate BFi and \(\mu'_s\) at separations larger than 1 cm, distances that are needed to increase sensitivity to cerebral blood flow through the intact skull. We propose a novel approach that employs multiple wavelengths and multiple distances to uniquely separate the optical properties and BFi. The multi-distance DCS intensity measurements provide the intensity decay over distance, resulting in a slope proportional to the product \(\mu_a\mu'_s\). Measurements of the decay of the autocorrelation function at three or more wavelengths provide the remaining independent measurements to uniquely determine all the parameters of interest.

We have validated the method’s robustness by numerical simulations (Fig. 1 left). Following those promising results we have built a new state-of-the-art multi-distance and multi-wavelength DCS system (Fig. 1 right). This system exploits novel long coherence length lasers controlled by a custom laser driver board allowing fast multiplexing of three colors on the probe. The probe collects the light from different separation, measured by eight high efficiency single-photon APD detectors. The system employs a custom FPGA-based correlator board that we designed to record the arrival time of each detected photon. A USB 3.0 interface sends all the information to our software allowing us to select the desired measurement repetition rate in post-processing, based on the desired signal to noise ratio. The fast acquisition rate allows us to measure pulsatile blood flow for better physiological noise filtering and quantification of additional parameters such as cerebrovascular reactivity (CVR) and intracranial pressure (ICP). We are currently testing the performance of the device in layered tissue-like liquid phantoms to demonstrate accuracy and precision of the multi-distance multi-wavelength global fitting method on recovering \(\mu_a\), \(\mu'_s\), and BFi.

![Numerical simulations](image1.png)

![Simplified block diagram](image2.png)

Fig. 1: Numerical simulations (left) and simplified block diagram of the new DCS system (right).

In conclusion, we demonstrate the new generation of DCS with an extensive improvement in both instrumentation and data analysis that sets the stage for a new range of clinical applications.

Computational modelling of the effects of systemic physiology on brain haemodynamics suggests that physiological confounding is able to both mask and mimic functional activation


Functional brain activation can be identified in fNIRS data by its classic haemodynamic response: neurovascular coupling leads to increased regional blood flow, causing a rise in oxyhaemoglobin and a reduction in deoxyhaemoglobin. However, blood flow changes can also be driven by variations in systemic factors such as arterial pressure and blood concentration of CO₂. Moreover, it is known that such changes can occur spontaneously and even quasi-systematically in some kinds of functional experimental protocols [1, 2]. This has raised concerns about the risk of mistakenly interpreting fNIRS experimental data due to the confounding influence of such systemic changes [1, 2].

To test the plausibility of these concerns, we used a computational model of cerebral physiology [3, 4] to simulate the haemodynamic responses for changes in blood pressure and CO₂ in the presence and absence of functional activation. The simulated fNIRS signals were then classified according to their relative L₁ distances from four idealised target signals. We found substantial ranges of plausible variation for the systemic parameters that gave rise to both false positive (Figure 1A) and false negative (Figure 1B) classifications, suggesting that such false classifications may indeed occur in real data. These results underline the importance of measuring systemic physiological signals such as arterial pressure and blood concentration of CO₂ during functional experiments so that their potential confounding influence can be taken into account when interpreting the data.

**Figure 1.** Modelled oxyhaemoglobin (ΔHbO₂, red) and deoxyhaemoglobin (ΔHHb, blue) responses for parallel changes in arterial partial pressure of carbon dioxide (ΔPₐCO₂ from baseline 40 mmHg) and mean arterial pressure (ΔPₐ from baseline 100 mmHg) in the absence (A) or presence (B) of neuronal activation. Colours in the lower panels represent the distance metric used for classification. Positive values (magenta) are those classified as exhibiting functional activation. In the left panel, the magenta region identifies false positives, and in the right, the cyan region corresponds to false negatives.

Estimation of optical properties of the cerebral tissue using time-resolved spectroscopy of femtosecond laser pulses

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Introduction: Diffuse optical tomography (DOT) based on a model-based iterative reconstruction (MBIR) scheme has great potential for quantitative measurements of cerebral hemoglobin concentrations. The MBIR algorithm essentially consists of two parts: one is a forward model to calculate the light propagation and the resultant outward re-emissions at the boundary of the tissue, typically based on the diffusion equation (DE) or radiative transfer equation (RTE). The other is an inverse model searching for the distribution of optical properties. Because of the ill-posed nature of the inverse problem, accurate knowledge of background optical properties is crucial for quality of reconstructed images. In this study, we attempted to estimate absorption (μₐ) and reduced scattering coefficients (μₛ') in the rat and monkey brains.

Methods: 12 male rats (SD, 10-15 weeks, 395-550g) and one male monkey (Macaca, 11 years old) were anesthetized and an open-skulled cranial window was created. Incident and detecting light fibers (ϕ=50 μm, N.A=0.2) with a separation of 1.25 mm were inserted into the brain tissue and measured at different depths using femtosecond laser pulses (wavelength, 800 nm; pulse duration, 70 fs >) and a streak camera (temporal resolution, 312.5 fs). To estimate μₐ and μₛ' of the gray and white matters, a lookup table was created by the Monte Carlo simulation. The analytical solution of the RTE was also employed to estimate the optical properties.

Results: Figure 1 shows an example of the IRF (FWHM = 2.9 ps) and temporal profiles of intensity of detected light at different depths of the rat brain. Estimated optical properties of the rat and monkey brains are shown in Table 1.

Table 1 Optical properties

<table>
<thead>
<tr>
<th></th>
<th>μₐ (mm⁻¹)</th>
<th>μₛ'(mm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gray matter</td>
<td>0.037</td>
<td>0.8</td>
</tr>
<tr>
<td>White matter</td>
<td>0.009</td>
<td>3.7</td>
</tr>
<tr>
<td>monkey</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gray matter</td>
<td>0.036</td>
<td>1.2</td>
</tr>
<tr>
<td>White matter</td>
<td>0.004</td>
<td>2.6</td>
</tr>
</tbody>
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Fig. 1

Conclusions: There are remarkable differences in the μₐ and μₛ' between the gray and white matters. In contrast, there is hardly any difference in the optical properties of the brain between rodents and non-human primates.
Mayer waves reduce the accuracy of estimated hemodynamic response functions in functional Near-Infrared Spectroscopy

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Background: Analysis of cerebral hemodynamics reveals a wide spectrum of oscillations ranging from 0.0095 to 2 Hz. While most of these oscillations can be filtered out during analysis of functional near-infrared spectroscopy (fNIRS) signals when estimating stimulus evoked hemodynamic responses, oscillations around 0.1 Hz are an exception. These waves are defined as waves in arterial blood pressure with a frequency around 0.1 Hz (Julien, 2006). They are spontaneous hemodynamic oscillations in arterial pressure and can be distinguished from heart beat and respiratory cycles because of their frequency (Obirgi et al., 2000). Since they share a common spectral range with typical stimulus evoked hemodynamic responses from the brain, it is difficult to filter them out without affecting the hemodynamic response estimated. Here we investigate the effect of hemodynamic oscillations around 0.1 Hz on the estimation of hemodynamic response functions from fNIRS data.

Methods: The study was approved by the Institutional Review Board of the Massachusetts General Hospital. Seventeen healthy subjects were recruited and a total of 23 sessions were performed. Recordings were obtained using a multichannel functional near-infrared spectrometer operating at 690 and 830 nm wavelengths (TechEn Inc. MA, USA, CW7 System). The head cap contained 10 sources, 10 standard separation detectors, and 10 short separation detectors. A synthetic hemodynamic response function (HRF) was generated by introducing a signal change of 1 % from baseline for the 690 nm signal and 2 % for the 830 nm signal in the raw NIRS data. This synthetic HRF was then added to the raw signal at long distance channels with an inter-stimulus interval of 20 to 25 sec, which resulted in up to 18 stimuli over the 6 minute data set. We generated 25 such time courses with different randomly generated stimulus vectors for each of the 23 sessions. The raw fNIRS data (resting-state data with added synthetic HRFs) were then analyzed to estimate the evoked hemodynamic response following standard fNIRS analysis procedures.

Results and Conclusions: We have performed ROC analysis to estimate the true positive and false positive rate for estimation of the HRF with and without short separation regression at low and high Mayer wave powers. ROC curves have been produced using the t-statistic of the HRF estimation as the threshold for detection. Our results show that for an expected response of ~ 1 μM in oxygenated hemoglobin concentration (HbO), Mayer wave oscillations with an amplitude > ~ 1 μM at 0.1 Hz reduce the accuracy of the estimated response as quantified by a 3 fold increase in the mean squared error and decrease in correlation (R² below 0.78) when compared to the true HRF. These results indicate that the amplitude of oscillations at 0.1 Hz can serve as an objective metric of the expected HRF estimation accuracy. In addition, we investigated the effect of short separation regression on the recovered HRF, and found that this oscillations are present in fNIRS data.

Acknowledgements
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References
Neural signature of autism evident before six months of life


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Autism Spectrum Disorders (ASD) are common, highly heritable, developmental disorders, and later-born siblings of diagnosed children are at substantially higher risk for developing ASD than the general population. Although the emergence of behavioral symptoms of ASD in toddlerhood is well characterized, far less is known about brain and behavior in the first months of life of infants at familial risk.

Recent functional near infrared Spectroscopy (fNIRS) research in typically developing infants has shown robust and consistent activation to social vs non-social visual and auditory stimuli in regions of the social brain network. Having established this signature response in infants, here we apply this paradigm to the investigation of individual differences in infants at risk for autism. In a prospective longitudinal study we used measures of brain responses to social stimuli in 4 to 6 month old infants (N = 36) to assess the relationship between early brain function and ASD outcome at 3 years of age. Infants who went on to develop ASD at 3 years evidenced diminished activation to visual social stimuli across regions of the social brain network, and increased activation to non-social sounds in auditory areas, in contrast to typically developing infants who exhibited greater activation to social stimuli. Further, across the high-risk infants, the visual responses at 4 – 6 months of age were correlated with ASD symptomology in toddlerhood.

![Figure 1: Grand average HbO₂ hemodynamic response to visual social stimuli across social brain region ROIs (left panel), and average hemodynamic responses to social (positive y axis) and non-social (negative y axis) auditory stimuli (right panel). Low risk (green), high risk – no ASD (orange), high risk – ASD (purple).](image)

These findings are consistent with reported diminished social brain network responses in adults with ASD and are the first evidence of atypical functional brain responses in infants under the age of six months who later go on to develop ASD.

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Array Designer: automated optimum array design for functional near-infrared spectroscopy

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The necessity of carefully selecting appropriate source and detector positions for each experimental paradigm remains a major challenge in functional near-infrared spectroscopy (fNIRS). All fNIRS systems are limited in their channel number, and thus a balance must always be struck between sampling density and field-of-view. For the vast majority of fNIRS systems, full scalp coverage is not achievable, and even in cases where full scalp coverage is possible, the resulting sampling density can be inappropriately low. As a result, most fNIRS users must manually design a source and detector array for each experimental paradigm, given knowledge of the cortical regions of interest and given the limitations of the number of available source and detector fibres, their physical size and the dynamic range of the fNIRS system. This process is always likely to be flawed; the complex geometry of the cerebrum and the tendency for manual arrays to be uniform in design, coupled with the difficult question of what constitutes an ‘optimum’ array will ensure that arrays designed by hand are almost always sub-optimal, resulting in a lower sensitivity to the cortical regions of interest and thus poorer fNIRS data quality.

The advent of accurate anatomical and efficient photon-transport modelling approaches¹⁻³ has opened the possibility of automated fNIRS array design. The fundamental principle is that given a cerebral region of interest in an anatomical model, and given the number of sources and detectors, it is possible to select the source and detector locations from a set of possible positions on the scalp (e.g. the 10-20 system) that maximize some function that is used to quantify the quality of an array. While an example of this approach has been demonstrated for a clinical application⁴, no tools yet exist that enable fNIRS users to take advantage of this concept. This is likely due to the fact that automated array design can be computationally expensive, as it requires a dense solution space and the associated photon fluence distributions for each possible optode position.

We have developed a new tool, Array Designer, that uses the adult MNI 152 head model and a bespoke, high-density ‘10-2.5’ scalp coordinate system. Array Designer allows users to select a cortical region of interest (ROI) and automatically generate an optimum fNIRS array. This tool will soon become part of AtlasViewer⁵, within the Homer2 fNIRS processing package. Figure 1 shows three examples of selected ROIs and the associated optimized array designs and sensitivity distributions. These solutions were identified in < 45 seconds using a simple genetic algorithm that maximizes both the total array sensitivity to the ROI and a metric related to spatial overlap between the ROI and the array sensitivity distribution.

Fig. 1. Three examples of cortical ROIs, automatically generated optimum fNIRS arrays and associated sensitivity distributions. The red (resp. blue) circles indicate source (detector) positions in the possible 10-2.5 scalp locations.

²Schweiger and Arridge, JBO, 2014.
³Machado et al., JBO, 2014.
⁴Aastad et al., Neurophotonics, 2015.
⁵Brigadoi et al., Neuroimage, 2014.
Cortical activation measured using fNIRS: a predictor of cochlear implant outcome
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Introduction
A cochlear implant (CI) is an auditory prosthesis that can partially restore hearing to profoundly deaf individuals. While most individuals understand speech well with their CI, others receive far less benefit from their device. Currently, the factors underlying this individual variability in CI outcome are not fully understood[1]. Clinicians subsequently lack the tools to accurately predict individual outcomes. Emerging evidence suggests that activation to visual stimulation in temporal cortex may determine how well an individual can process and understand speech with their CI[2]. Unfortunately, research efforts in this field have been hindered by the incompatibility of most conventional neuroimaging techniques with a CI, due to electro-magnetic artefacts associated with the implanted device. Optical imaging by functional near-infrared spectroscopy (fNIRS) is a promising solution to these limitations since it is fully compatible with a CI, non-invasive and relatively inexpensive[3].

Methods
In a longitudinal design, fNIRS was used to examine how temporal brain regions responded to visual speech (lip-reading) before and after cochlear implantation. The aim of this research was to establish whether fNIRS measurements of cortical activation could help to more accurately predict future CI outcome. Adults with severe-to-profound deafness (n=17), who met NICE criteria for implantation, were tested at three time-points: (1) before implantation; (2) 1 month after CI activation; and (3) 6 months after CI activation. At each time point, fNIRS was used to measure cortical responses to lip-reading from bilateral superior temporal cortex. Behavioural measures of auditory speech perception and lip-reading ability were also obtained.

Results
Cochlear implantation enabled the significant recovery of auditory speech perception over the first six months of CI use, yet individual performance varied widely across CI users. Cortical fNIRS recordings in response to speech were free from CI-generated artefacts. Greater cortical activation to lip-reading measured before implantation was significantly predictive of poorer auditory speech perception after six months of CI use (r=-.75, p<.01). This pre-implant cortical measure was able to provide unique predictive value above that of known clinical factors, such as the age-at-onset and duration of deafness.

Conclusions
These results demonstrate the potential of fNIRS as a brain-imaging tool to examine cortical plasticity following cochlear implantation. Moreover, fNIRS might help to explain individual variability in CI success and to deliver more accurate clinical prognoses for CI candidates. Such a tool may help clinicians to better counsel patients’ expectations of their outcomes prior to implantation, and enable them to direct limited healthcare resources more effectively.

Acknowledgments
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References
Speech and Music processing by postlingually deafened cochlear implant patients

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Music perception is often not appreciated by cochlear implant users. Even more the differentiation of complex acoustic stimuli is constrained by the quality of the signal that is provided to the auditory nerve. The capability of the human brain of processing this quality reduced signal determines the differentiation and pleasure while listening to complex acoustic input such as music.

This study investigates the activation of the corresponding sound processing cortical areas by means of functional near infrared spectroscopy (fNIRS). Especially in case of cochlear implant usage fNIRS is a very suitable approach because fMRI studies are not possible and even harmful because of implanted magnetic components.

We presented acoustic stimuli of speech and music to 15 postlingually deafened cochlear implant users and to 15 control subjects matched in age and gender. During stimulus presentation we recorded the concentration levels of oxygenated and deoxygenated haemoglobin on 20 measurement volumes (channels) across the left and right hemisphere. Timecourses of the concentration changes were evaluated separately for each channel, using conditional averaging.

The following results were obtained:

1. Both groups exhibited significant hemodynamic responses across the auditory cortex, both for the left and right hemisphere when listening to speech and music stimuli.

2. For music processing the activation was higher over the right STG/STS than for sentence processing in the normal hearing group whereas there was no differential effect for language versus music in the CI group. Furthermore, activation in this region was higher for the control than for the CI group.

Recent studies about compensatory effects between auditory and visual cortex revealed significant differences in cortical processing of acoustic stimuli between normal hearing adults and cochlear implant users. This study confirms that processing of more complex sound stimuli, e.g. music, is also different for the group of CI users. This also validates the method of fNIRS as suitable to detect and analyze acoustic processing cortical areas in cochlear implant users. Furthermore, this study shall help to shed some light on the fact of adapted auditory processing by using a cochlear implant. Follow-up studies will clarify if these findings can be approved by using other, more fine-grained stimuli.
Fast Optical Signal Changes during Epileptic Spikes in the Human Model

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Introduction: Non-invasive Fast Optical Signal (FOS) uses near-infrared light to study changes in the neuronal optical properties in response to stimuli and endogenous events, and has high temporal (msec) and spatial (mm) resolution. These changes are assumed to be caused by changes in the light scattering properties of the neuronal tissue. The big challenge of measuring FOS non-invasively lies in the low signal-to-noise ratio. Thus, detectability of the FOS has been controversially discussed. We present detection of FOS in subjects with frontal lobe epilepsy, and investigate changes of these signals during epileptic spikes.

Methods: These signal were recorded from 4 male and female subjects with frontal lobe epilepsy. EEG was recorded using 64 surface electrodes (Easy cap®) with 1024Hz sampling rate, and the electrode positions included the 10—20 System location. Optical signals used two wavelengths (690 and 830nm) with a frequency-domain spectrophotometer (Imagent®,ISSInc). The configuration of the sources and detectors was rectangular with 3 lines. 16 detectors were placed on the higher and lower horizontal lines and the location of four sources was in the midline. Sources and detectors were placed on the forehead of the subjects. The intensity of the optical signals were first filtered between 1.6 and 11Hz. In this way, the slow fluctuations due to respiration and Mayer waves were removed from the optical signals. Then an independent component analysis (ICA) was used to reduce heart beat artifact. Also, time-frequency analysis was used to track the variations of (de)synchronization during Spikes.

Results: The refined signals showed a significant decrease from baseline from -95 to 140ms around “Zero Time” and a slight increase in two interval, from -180ms to -95ms, and from 140ms to 300ms. Time-frequency domain analysis revealed alternating desynchronization-synchronization-desynchronization almost concomitantly with the changes in FOS during spike. Figure 1 shows the averaging of fast optical signals on channels that contain response.

Conclusion: Our study demonstrated reliability of fast optical signals recorded non-invasively as well as their close relationship with EEG. We were able to detect small fast neuronal signals in the human with frontal lobe epilepsy during spikes. Generally, fast optical signals can provide a sensitive measure of brain activation which has a potential to contribute to the spatial and temporal characterization of various types of brain responses in a variety of basic research and clinical applications.

![Figure 1](image_url)

**Figure 1.** (A) Typical spike-related optical signal. (B) Typical spike in EEG channel F4. The horizontal axis shows time in seconds, “Zero Time” indicates the time of minimum-peak in EEG spike and the vertical axis shows intensity changes (AU) in (A) and amplitude of the signal (µV) in (B). (C) Typical time-frequency representation of channel F4. The horizontal axis shows time in seconds, the vertical axis shows frequency. (D) Place of main sources of spikes on a head model.
Concurrent diffuse optical measurement of cerebral hemodynamics and EEG during transcranial direct current stimulation (tDCS) in humans

Martina Giovannella¹, Guillem Mitjà², Clara Gregori-Pla³, Michal Kasprzak¹, David Ibañez², Giulio Ruffini²⁴, and Turgut Durduran¹²

We present measurements of cerebral blood flow (CBF) and cerebral tissue oxygenation, by a hybrid diffuse optical monitor, during transcranial direct current stimulation (tDCS). tDCS is a non-invasive form of brain stimulation that consists of applying weak direct currents to the brain through electrodes placed on the scalp. Such currents result in small cortical electric fields that modulate brain activity, depending on the polarity[1]. It is receiving increasing interest because effects have been demonstrated in a range of clinical conditions with a therapeutic potential in, e.g., stroke, depression, and epilepsy. There is a need to quantify the effects and, ultimately, the dosage of tDCS and EEG has its limitations for this purpose. Changes in cortical excitability and consequent ones in cerebral activity are associated to changes in the cerebral metabolism. CBF and cerebral tissue oxygenation can thus be used as a measure of the effects stimulation.

Measurement were performed with a hybrid diffuse optical cerebral monitor that integrates a diffuse correlation spectroscopy(DCS) [2] device, HemoFloMo (HemoPhotonics, SL, Spain) and a time resolved near infrared spectroscopy device (TR-NIRS) [3] device, TRS-20 (Hamamatsu Photonics K.K., Japan). Stimulation was driven by StarStim, by NeuroElectrics, which also allows for measurement of EEG. Twenty subjects were measured in two sessions, before, during and after 10 minutes of anodal and cathodal stimulation of the left frontal cortex. Twelve subjects were also measured during sham stimulation. EEG and optical signals were recorded during the entire protocol. Two optical probes were placed bilaterally in the frontal lobes with optical fibers around an electrode. Eight EEG electrodes were used.

As shown in the figure below, CBF in the frontal lobe, ipsilateral side, increases during both anodal and cathodal stimulation and does not recover in the 30 minutes after it, while in the sham stimulation we do not see a significant increase. In the contralateral hemisphere we also see a (smaller) increase during anodal and cathodal and not in the sham. Tissue oxygenation as measured by TR-NIRS shows a far smaller contrast than blood flow during and after the stimulation, detailed analysis will be shown, together with EEG results. This study shows that DCS, TR-NIRS and EEG are suitable techniques for concurrent monitoring of cerebral activity during tDCS.

![Graph showing CBF changes during tDCS](image)

**Figure 1** Evolution of CBF during the whole protocol. Grey shaded area represents the stimulation period.

References:
2. Durduran and Yodh, Neuroimage 85, 5163 (2014)
3. Torricelli et. al., Neuroimage 85 Pt 1, 28–50 (2014)
Multimodal measurement of brain responses to word memory task extracted from EEG, NIRS, and pupil diameter signals

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Attention plays a fundamental role in acquiring information and understanding its contents. Therefore, it is useful to evaluate the attentional state in various fields, such as education and mental care. To objectively evaluate attentional states, biosignals are effective. Previous studies have reported that responses to attention tasks were extracted from EEG (electroencephalogram) [1], NIRS (near-infrared spectroscopy) [2], or pupil diameter signals [3]. However, the differences in characteristics of their responses are not well understood. To clarify the characteristics of multimodal measurement and analysis of brain responses, we performed a word memory task, which is one of the attention tasks, while simultaneously measuring of EEG, NIRS, and pupil diameter signals.

In this study, participants memorized serially presented words as a word memory task. We hypothesized that the attentional state would be closely related to (1) the differences between success to recall a word (“recall words”) and failure to recall a word (“fail words”), (2) serial position of words, and (3) the number of recall words, i.e., the differences between trials with many words recalled (“well recalled trials”) and trials with few words recalled (“poorly recalled trials”). Then we evaluated the relationship between the attentional state and multimodal brain responses with those three types of time scales and extracted the differences in their responses.

We obtained the following results. (1) The ERP (event related potential; P300) induced by recall words was significantly higher than that induced by fail words in EEG data. (2) The increase in pupil diameter, which was averaged across three consecutive words, significantly differed depending on the serial position. (3) The functional connectivity between left prefrontal and parietal cortex was significantly higher in well recalled trials measured by NIRS than in poorly recalled trials.

Thus, different characteristics of brain responses related with the task were extracted. In particular, time scales of the responses were different. Therefore, we concluded that it should be effective to evaluate various time scales of attentional states by multimodal measurement and analysis of brain responses.

Reference:
Concurrent fNIRS and TMS for Comparison of Evoked Responses to Pulse-Matched High Frequency and Intermittent Theta Burst Stimulation

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Transcranial Magnetic Stimulation (TMS) is a non-invasive method used to excite or inhibit cortical activity for experimental, diagnostic, or therapeutic purposes. However, non-motor regions of the brain used in TMS therapies offer no measurable response to stimulation, potentially preventing the evaluation of effective therapeutic treatments. Functional Near Infrared Spectroscopy (fNIRS) is a technique which can be used to non-invasively monitor cortical changes associated with TMS stimulation and is not subject to magnetic interference. In this study, we non-invasively measured the cortical hemoglobin changes in the orbitofrontal cortex during simultaneous application of TMS at F3 in the left-dorsolateral prefrontal cortex. Seventeen healthy participants received short TMS trains using 4 different stimulation paradigms, Single Pulse, High Frequency, intermittent Theta Burst (iTBS), and Sham to determine the ability of fNIRS to measure and discriminate between the responses evoked by TMS stimulation protocols. Ten trials of each stimulation type were delivered with an inter-train interval of 40 seconds with 110% resting motor threshold used for Single Pulse and High Frequency, and 90% used for Theta Burst Stimulation. Comparison of 2 seconds of stimulations (30 pulses each) indicated that High Frequency stimulation produces a larger and more detectable response than comparable iTBS trains. These findings show that an LED-based fNIRS system can be used to measure TMS-evoked responses and future TMS applications can benefit from concurrent assessment of the localized cortical activation changes.

Figure 1: (A) Averaged response following stimulation for Optode 6, the gray curves denote the case of Sham stimulation; (B) Mean change (in window from 10s to 15s) from baseline (from -2s to 0s prior to stimulation).
Tri-Modal Simultaneous Investigation of Human Brain Function: Evidence for a Proof of Concept
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The link between spatial (where) and temporal (when) aspects of the neural correlates of most psychological phenomena is not clear. Elucidation of this relation requires integration across multiple brain imaging modalities and tasks that reliably modulate the engagement of brain systems of interest. Additionally, multi-modal recordings provide advantages for controlling effects such as habituation and/or memory, which is difficult to obtain across multiple uni-modal sessions. The goal of this project is to illustrate the feasibility of such an integration across three complementary imaging modalities (i.e., functional magnetic resonance imaging - fMRI, event-related optical signals - EROS, and electroencephalography/event-related potentials - EEG/ERP; see Figure 1), by overcoming the methodological challenges posed by simultaneous recordings using these methodologies. This project provides initial evidence for a proof of concept, based on integrating data from pilot investigations using several tasks (total n = 22), which confirm and extend the present results. The present focus is on the most relevant results from multi-modal investigation using an executive task with emotional distraction (i.e., the emotional odd-ball task), because this dual-task can dissociate between responses in large-scale dorsal and ventral brain systems involved in cognitive and affective processing. First, initial data from subjects performing this task (n = 5) provided validation of simultaneous bi-modal fMRI-EEG and EROS-EEG recordings, and identified prefrontal and parietal cortical responses consistent with spatial and temporal evidence from uni-modal recordings. Specifically, results showed 1) expected blood-oxygen-level dependent signal changes in the lateral parietal cortex (LPC) to targets and dorso-ventral dissociations to targets vs. distracters in the lateral prefrontal cortex (PFC), in the fMRI data (Figure 2.A), 2) similar dissociation in the dorsolateral PFC (dIPFC) vs. ventrolateral PFC (vIPFC) in the responses to targets vs. distracters, in the EROS data (Figure 2.B), and 3) ERP sensitivity such as P300 to targets, in the EEG data (Figure 2.C). Importantly, these data show that frontal dorso-ventral dissociations are effectively captured using fMRI, and similar dissociations are captured using EROS but in time windows similar to ERP responses, while the latter are captured at posterior locations. Therefore, tri-modal acquisition using tasks such as this can capture effects by simultaneously recording, in the fMRI scanner, EROS data using an optical array covering lateral PFC areas and a MR-compatible EEG cap, covering posterior locations. Noteworthy, this was recently confirmed by results from a pilot simultaneous fMRI-EROS-EEG recording (n = 1) (Figure 2.D). These results illuminate the overlaps and complementarity across measures of brain function, and point to ways in which distinct methodologies can be used simultaneously to study spatial and temporal correlates of psychophysiological phenomena.

Figure 1. Equipment configuration for tri-modal recording. In the fMRI scanner (A), EROS and EEG data were recorded using two patches to apply optical fibers (B) and a MR-compatible EEG cap (C).

Figure 2. Evidence for expected effects in fMRI, EROS, and EEG. A) Results showed expected fMRI BOLD response in LPC to targets and dorso-ventral dissociation to targets and distracters in the lateral PFC, B) similar EROS-related spatial dorso-ventral dissociations to targets vs. distracters in the PFC, C) ERP temporal sensitivity to targets over centro-parietal, and D) evidence for converging spatial and temporal EROS dissociations to targets and distracters using an optical array in the lateral PFC, during tri-modal simultaneous fMRI-EROS-EEG recordings.
Simultaneous measurement of brain activity by functional near-infrared spectroscopy and electroencephalography during motor task

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The aim of the study was to investigate the neurovascular coupling by the simultaneous measurements of brain activity by functional near-infrared spectroscopy (fNIRS) and electroencephalography (EEG) techniques. The correlation between changes in concentrations of oxyhemoglobin ($\Delta C_{HbO2}$) and brain rhythms during motor task was examined.

The time-resolved fNIRS system described in details elsewhere (Kacprzak, 2007)(Milej, 2014) was used in the study. $\Delta C_{HbO2}$ were derived from changes in the total number of photons of each distribution of times of flight of photons (DTOF) using molar extinction coefficients of the hemoglobin (Scott Prahl) and for assumed differential pathlength factor value (based on speed of light and mean time of flight derived from DTOF). The brain activity was measured simultaneously by means of fNIRS and EEG during right hand movement for four subjects. Thirty trials consisted of 20 s of movement followed by 30 s of rest. During the experiment signals from 32 active Ag/AgCl electrodes (10/20 system) and from eight NIRS optodes placed on the subject’s head were recorded. EEG was sampled at 512 Hz, referenced to “linked ears”.

EEG signals were subjected to Hjorth transform and time-frequency distributions were calculated. After a cue indicating the start of movement at the electrodes overlying primary motor cortex of the right hand (PMC), the desynchronization (amplitude decrease) in alpha (8-13 Hz) and beta (13-35 Hz) bands was observed and about 1.5 s later the synchronisation (amplitude increase) in the both bands occurred. During the desynchronisation period a rise in the concentration of oxyhemoglobin in PMC was observed. The values of Person correlation between $\Delta C_{HbO2}$ and the power of EEG signal in the alpha and beta bands are shown in the Table 1.

Table 1. Correlation between the changes in concentration of oxyHb and the power of EEG signal in the alpha and beta bands ($p < 0.001$

<table>
<thead>
<tr>
<th>Subject</th>
<th>$\Delta C_{HbO2}$ vs EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alpha</td>
</tr>
<tr>
<td>Pac 1</td>
<td>R = -0.71</td>
</tr>
<tr>
<td>Pac 2</td>
<td>R = -0.85</td>
</tr>
<tr>
<td>Pac 3</td>
<td>R = -0.79</td>
</tr>
<tr>
<td>Pac 4</td>
<td>R = -0.62</td>
</tr>
</tbody>
</table>

The values of correlation between $\Delta C_{HbO2}$ and EEG power in alpha and beta bands were high and negative with p-levels always lower than 0.001. In 3 cases the maximal (absolute) values of correlations occurred at position of electrode C3, for one person at position of electrode CP1, both overlying PMC of a right hand. The obtained values of correlation were higher than the correlation of oxyHb with the readiness potential ($R^2 = 0.235$) reported by (Zama and Shimada, 2015).

Acknowledgements

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References

Zama T., Shimada S. Scientific Reports (2015) 5:16438
Scott Phral. [http://omlc.org/spectra/hemoglobin/summary.html]
A multimodal approach to evaluate the effects of cortical thickness and neurophysiology of normal aging on the hemodynamic response measured by fNIRS; A language study

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As a hemodynamic based imaging technique, fNIRS signal is the result of a complex interaction between cerebral blood flow (CBF), blood volume and oxygenation (Ances 2004; Buxton et al. 2004). Moreover, the baseline values of these quantities change with aging in a heterogeneous fashion (Ances et al. 2009; Cabeza et al., 2005; D’Esposito et al., 2003). The importance of meeting this challenge has led us to calibrate fNIRS data by integrating modalities measuring complementary morphological and neurophysiological characteristics of individuals in the context of a language task. Despite some cognitive decline with normal aging, older adults show a good preservation of semantic knowledge. Thus, exploring the neural substrates underpinning word processing seems essential to understand how the brain confronts neurobiological declines.

To investigate the effects of morphological and neurophysiological parameters on the functional measurements, we acquired data from two modalities; magnetic resonance and diffuse optical imaging. We used a 32-channel continuous wave fNIRS system (TechEn CW6) to measure relative changes in oxy- and deoxyhemoglobin concentrations ([HbO₂] and [HbR] respectively) while participants undergoing the language task. Two groups of 23 French-speaking individuals (old= 69.6 ± 4.1, young=23.4 ± 2.7 years) were screened for their overall health and cognitive performance. A total of 240 words and pseudo-words were presented in a pseudo-random ISI fashion with SOA from 4s to 11s, in 3 sessions of 12 minutes. A home-made time-resolved spectroscopy (TRS) system was used to measure absolute hemoglobin concentrations of each participant at rest. We acquired anatomical MRI for coregistration of the optical channels using a stereotactic system (Brainsight; Rogue Research Inc.). An Arterial-Spin Labeling (ASL) sequence was acquired to quantify the individual’s baseline CBF at rest.

Group mean comparisons on absolute [HbO₂] and [HbR] revealed decreased prefrontal [HbO₂] in old adults (p<.0007). Analysis of tagged ASL images showed different group average of CBF measures over anatomical segmented gray matter images (p = .02). Cross-sectional analysis showed an age-related cortical thinning across almost the entire cortex. We applied a factorial 2-level analysis of variance on fNIRS data over all channels set contrasts from a general linear model (GLM) fit to the hemodynamic response function with time and dispersion derivatives. We observed an age-related difference at bilateral dorsolateral prefrontal cortex (DLPFC), inferior frontal (IF) and right posterior middle temporal (MT) gyr in Δ[HbR], and right posterior MT and DLPFC in Δ[HbO₂]. Including individual measures of cortical thickness and baseline [HbO₂] and [HbR] as regressors to the GLM, we observed a modified frontal age-different pattern of activity by diminished right DLPFC and accentuated IF engagement.

The present study supports the reliability of fNIRS application in neuropsychological aging studies whilst exerting caution in the interpretation of data. We showed that when controlling for baseline physiology, the degree and extension of neural activity could vary in some language-related brain regions in old adults. In studies aiming at exploring the age-related functional reorganization, it is thus essential to take into account individual morphological and physiological characteristics before drawing conclusions from relative hemodynamic changes.
Microvascular cerebral metabolism and blood flow and bispectral index

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Abstract: Cerebral blood flow and metabolic rate of oxygen during propofol-induced anesthesia were measured by time-resolved spectroscopy and diffuse correlation spectroscopy simultaneously with the bispectral index.

Introduction:
The bispectral index (BIS) is an electroencephalographic measure of brain activity that is widely used to evaluate the depth of propofol-induced anesthesia, often assumed to be a surrogate indicator for cerebral metabolism (CMRO₂) [1-3]. Hybrid diffuse optics can non-invasively measure microvascular hemodynamics via the oxygen saturation (StO₂) and a cerebral blood flow index (CBFI) and CMRO₂ [4]. Propofol reduces CMRO₂ and leads to a coupled decrease in rCBF, when neurovascular coupling is preserved [5]. We sought to compare two methods during controlled anesthesia in brain healthy.

Methods:
A combination of time-resolved spectroscopy (TRS) and diffuse correlation spectroscopy (DCS) were measured bilaterally on the frontal lobes during extracranial surgical procedures under general anesthesia with target-controlled infusion of propofol. The BIS was on the left brain hemisphere. A Pearson correlation test was performed in three steps. Step 1: the entire dataset; Step 2: all BIS data only significant changes (greater than the standard deviation) in optical data; Step 3: only significant changes in all variables.

Results:
Seventeen patients were included in the study. Figure 1 shows a representative time from the left hemisphere during the initiation of general anesthesia.

![Figure 1: Recorded variable changes (induction phase)](image)

rBIS decreases from 100% to ~ -40% and rCBF from ~ 70% to ~ -50. The two variables correlate significantly (R = 0.95; p < 0.001). The entire dataset correlates significantly (p < 0.001) between rBIS and rCBF with R = 0.33 (step I), R = 0.47 (step II) and R = 0.67 (step III). rBIS and rCMRO₂ correlate significantly (p < 0.001) with R = 0.32 (step I), R = 0.46 (step II) and R = 0.67 (step III).

Conclusion:
The first comparison of non-invasively, optically derived CMRO₂ and CBF by hybrid diffuse optics with the established BIS readings demonstrates the potential of diffuse optical techniques for monitoring the depth of anesthesia.

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Brain-based communication via online-decoded fNIRS signals

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Background. Human communication depends on the functional integrity of the neuromuscular system. In the so-called ‘locked-in’ syndrome (LIS), fully conscious and awake patients are incapable to communicate or interact naturally with their surroundings due to a severe motor paralysis including speech anarthria. Providing affected patients with convenient and robust motor-independent communication means, such as brain-computer interfaces (BCIs), is of high importance. Recently, we1,2 and others1 have successfully tested communication BCIs based on differently timed mental-imagery tasks and hemodynamic brain responses as measured with functional magnetic resonance imaging (fMRI). However, fMRI is costly and tied to research and clinical institutions. Thus, we currently aim at transferring the fMRI-based communication approach to functional near-infrared spectroscopy (fNIRS) which is generally more accessible and practically applicable than fMRI. In the presented study, we introduce and test a novel four-choice fNIRS-BCI based on motor imagery and auditory input.

Material and Methods. Nine healthy volunteers (six female, seven right-handed, average age of 28.1 years) were asked multiple(four)-choice questions and instructed to encode their respective answers by repeatedly (five times) performing a motor-imagery task (right-hand mental drawing) for 10s during one of four distinct time periods (where each time period corresponded to a particular answer option). Answer encoding was guided by auditory cues. Evoked hemodynamic brain signals were obtained with a NIRScout-816 system (NIRx Medizintechnik GmbH, Berlin, Germany) equipped with eight sources and eight detectors covering large parts of the scalp above the left-hemispheric sensorimotor cortex. Based on a short (ca. 12min) localization procedure in which participants alternated between mental-drawing (10s) and resting periods (20s), the most promising recording channel – showing clear hemodynamic brain responses (i.e., expected oxy- and deoxy-hemoglobin changes) during mental-task performance – was selected for each participant individually by performing online general-linear-model (GLM) analysis and adding together the observed oxy- and deoxy-t-values. Then, each participant performed eight answer-encoding runs of 6:05min. Immediately after, participants’ answers were decoded by performing online GLM analysis employing four hemodynamic reference functions representing the four distinct answer periods. Answer options (1st-4th) were sorted according to the sum of their associated oxy- and deoxy-t-values (highest value determining 1st answer option etc.). Post-hoc offline analysis was performed to obtain single-trial (vs. five-trial) decoding accuracies. Online and offline analysis (including conversion to oxy- and deoxy-hemoglobin values and standard preprocessing) was done using Satori (v0.8, Brain Innovation B.V., Maastricht, the Netherlands).

Results and Conclusion. Online, participants’ answers were correctly decoded in 76.4% of the cases (chance level being 25%). Individual accuracies varied from 37.5%-100% (see Figure). In four participants, a 100%-accuracy was achieved. The mean of the offline obtained single-trial decoding accuracies was 62.8% (ranging from 25%-97.5% across participants). In eight of the nine participants, single-trial decoding accuracies were significantly above chance level as assessed by permutation testing (p<0.05). We consider the suggested novel fNIRS-based four-choice communication BCI a promising approach and encourage testing it in clinical trials involving affected LIS patients.

References
Feasibility of fNIRS as a Brain Computer Interface for Studies of Disorders of Consciousness

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There has been an increasing interest in developing brain computer interfaces (BCI) for patients who are aware but lack the physical ability to follow commands. Owen and colleagues have previously shown using functional magnetic resonance imaging (fMRI) that some patients diagnosed as being in a vegetative state can communicate by performing a motor imagery task in response to commands. Although promising, this study highlights the need to explore alternative techniques considering the cost and limited accessibility of MRI. An attractive alternate is functional near infrared spectroscopy (fNIRS) given the technology is inexpensive and portable, which enables studies to be conducted at the bedside. Furthermore, brain regions associated with motor imagery (the supplementary motor area (SMA) and the premotor cortex (PMC)) can be interrogated by fNIRS. However, the reliability of fNIRS – which is critical to this application – is challenged by a number of factors, most notably signal contamination from the scalp that can potentially mask true activation. Time-resolved (TR) NIRS has been proposed as one approach for enhancing the sensitivity of fNIRS to brain activity since late-arriving photons have a higher likelihood of interrogating the brain. The objective of this study was to assess the reliability of TR-fNIRS in detecting brain activity associated with motor imagery. For validation, all participants performed the same task in a 3T MRI scanner.

Data were acquired with an in-housed developed TR-NIRS system consisting of one emission fiber ($\lambda = 830$ nm) and four detection channels. The detection fiber bundles were placed at a distance of $3$ cm around the emission fiber, each in a separate quadrant, to interrogate the SMA and PMC. Twelve healthy subjects were recruited (4 females, mean age 25.5, right handed). The experimental paradigm consisted of five 30-s cycles of rest and motor imagery. The order of fMRI and fNIRS were randomized to avoid possible training effects. Depth sensitivity was achieved by analyzing the TR-NIRS data in terms of statistical moments of the distribution of times of flight (DTOF) since higher moments are more sensitive to late-arriving photons.

In 8 of 12 subjects, significant activation ($p<0.05$) in the SMA and/or PMC was observed by both fMRI and fNIRS. Of the remaining 4 subjects, 3 showed activation with fNIRS only and 1 had no detectable activation with either modalities. The use of higher moments in the analysis of the TR data appeared to improve sensitivity as 8 subjects showed activation with the zero moment, 9 with the first moment and 10 with the variance. Unexpectedly, activation was detected by fNIRS in more subjects than by fMRI, tentatively suggesting that this new technique may prove to be even more sensitive for detecting changes in SMA and/or PMC activity than the more established method.

This study demonstrates the robustness of fNIRS for detecting brain activity during motor imagery. The next aim is to apply the same fNIRS protocol to disorders-of-consciousness patients who are confirmed by fMRI to be responsive.

Assessing the quantitative accuracy of near infrared spectroscopy using simulated hypoxia as a model for traumatic brain injury

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Introduction

Traumatic brain injury (TBI) is the most common cause of mortality or disability amongst otherwise healthy young people [1]. TBI is associated with tissue hypoxia, the level of which will have significant consequences for clinical outcome. Consequently, identifying and managing cerebral oxygenation in TBI care has significant clinical relevance. While near infrared spectroscopy (NIRS) is capable of accurately measuring temporal changes in cerebral oxygenation, questions remain over the validity and reproducibility of absolute cerebral oxygenation measurements for cerebral NIRS. Frequency domain (FD NIRS) devices represent a refinement in available clinically viable devices and potentially offer more consistent parameters to guide therapy. Using simulated hypoxia in healthy participants, we examined the quantitative accuracy and the variability within and between participants in classifying normal and hypoxic brains for absolute oxygenation measurements using a FD NIRS device.

Materials and methods

Eight healthy adult volunteers took part in this study. An ISS OxiplexTS FD NIRS system measuring at wavelengths of 690 and 830nm was used. One probe was placed across the forehead, 2 cm above the superior orbital ridge, while the other probe was placed across the zygomatic arch to compare neurological to somatic tissue changes. Isocapnic hypoxia was induced using a dynamic end-tidal forcing system (DEF), which precisely adjusts the composition of inspired air in order to produce desired end-tidal gas values. The DEF allows accurate manipulation of arterial gases and thus arterial oxygenation. Cerebral hypoxia was induced over two steps, with the aim of emulating hypoxic conditions similar to that seen in TBI patients during the second step. The most severe hypoxic stage (P_{ET}O_2 = 40 mm Hg) was compared to baseline (P_{ET}O_2 = 100 mm Hg) using a paired non-parametric T-test.

Results

The simulated hypoxia induced a significant decrease in oxygen saturation from normoxic baseline at both placement sites (Mean change: Forehead 61.8 to 54.8%; Zygoma 72.7 to 64.1%). However, the coefficients of variation seen during baseline for each anatomical location varied between 6.8% and 9.7%. To illustrate the scale of these variations, a 5-10% drop in NIRS-derived saturation has been associated with a magnitude of change for fainting, and at the upper end of this range predictive of poor clinical outcome during cardiac surgery.

Conclusions

These results illustrate that while the FD NIRS device can detect changes induced by simulated hypoxia, it cannot currently diagnose a healthy or injured brain using absolute oxygenation values alone (i.e., without knowledge of a patient’s individual healthy resting baseline), and therefore indicating that these absolute measures are not accurate enough to be used in the neurotrauma clinic. This underlines the need for improvement in quantitative accuracy of cerebral NIRS through a deeper understanding of inter-patient variation in oxygen saturation measures (e.g., via refinement of reconstruction algorithms to account for contamination from superficial layers (i.e., skin and skull)). Finally, simulated hypoxia can be used to effectively induce clinically relevant levels of brain ischaemia, and be used as a model to investigate NIRS technology development.
Prolonged Monitoring of Cerebral Blood Flow and Autoregulation in Subarachnoid Hemorrhage and Stroke Patients with Diffuse Correlation Spectroscopy

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Cerebral autoregulation is a protective mechanism of the brain vasculature that maintains adequate cerebral perfusion in response to varying cerebral perfusion pressure (CPP)1. Autoregulation is frequently impaired in patients suffering from brain injuries such as stroke, subarachnoid hemorrhage (SAH) and traumatic brain injury2,3. In turn, impaired autoregulation can lead to secondary ischemic or hemorrhagic insults. Monitoring of cerebral blood flow (CBF) and autoregulation are therefore essential components of neurocritical care, but continuous non-invasive methods for CBF monitoring are lacking. Transcranial Doppler (TCD)4 measures CBF velocity in the large cerebral arteries, but it is impractical over long monitoring epochs. Parenchymal probes can provide a focal measure of CBF or tissue oxygen tension5, but they are invasive and uni-regional. Diffuse correlation spectroscopy (DCS) is a non-invasive optics modality that measures a CBF index (CBFI) in the cortex microvasculature by monitoring the rapid fluctuations of near-infrared light diffusing through moving scatterers (red blood cells)6-7. Here, we present DCS data collected in at-risk patients in the Neurosciences Intensive Care Unit (NeuroICU) demonstrating the potential of the modality for non-invasive, long-term monitoring of cerebral perfusion and autoregulation.

Seven patients with stroke or aneurysmal SAH were recruited from the Massachusetts General Hospital NeuroICU. After the patient’s legally authorized representative provided informed consent, a DCS probe was positioned on the patient’s scalp where permitted by clinical equipment, and attached with gauge and a clinical adhesive (collodion). DCS data were acquired continuously for up to 20 hours as permitted by clinical care. Systemic and cerebral physiological parameters monitored as part of the patient’s clinical care were recorded synchronously: mean arterial pressure (MAP), intracranial pressure (ICP), CPP, EEG. In two patients, white matter (WM) perfusion was recorded by an invasive probe (Hemedex Inc.) based on the thermal diffusion technique, through a cranial bolt. DCS autocorrelation curves at each time point were converted to CBFI using the analytical solution of the correlation diffusion equation for a semi-infinite medium, and assuming typical baseline optical absorption (\(\mu_s = 0.15 \text{ cm}^{-1}\)) and scattering (\(\mu_s' = 10 \text{cm}^{-1}\)) for the head. A relative CBFI (rCBFI) was obtained by normalizing each subject’s CBFI by its mean value at MAP = 90±5 mmHg. A static autoregulation curve was obtained by plotting the DCS-derived rCBFI vs. CPP or MAP over the whole duration of the recording.

Figure 1a presents an example of MAP and CBFI recordings over 2 hours in a SAH patient (SAH6), showing that the CBFI fluctuations follow closely the MAP variations, indicative of impaired autoregulation. The corresponding static autoregulation curve is presented in Fig.1b (median and interquartile range), and accordingly presents a linear dependence between MAP and CBFI with a slope of about 2% CBFI/mmHg. Figure 1c shows the autoregulation curves for all 7 patients, displaying different levels of autoregulation disruption (SAH=subarachnoid hemorrhage, Str = Stroke).

![](map_cbf.png)

Our results demonstrate the feasibility of long-term monitoring of CBF with DCS in challenging conditions (NeuroICU), and the potential for monitoring autoregulation.

References
Bedside mapping of brain function during acute stroke recovery using High-Density Diffuse Optical Tomography

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Ischemic stroke typically begins with the occlusion of an artery in the brain [1]. In the first hours after onset, a patient’s neurological status can be highly unstable. Though current standards of care, MRI and CT provide clinicians with mere snapshots of brain structural health [2]. An imaging modality that continuously measures brain function at the bedside could provide near-real-time monitoring to better assess changes in neurological status and potentially inform clinical decisions. We have developed a portable high-density DOT system (Fig. 1a,b) that contains 48 sources and 34 avalanche photodiode detectors coupled to the head via optical fibers that are held in a rectangular grid by a comfortable neoprene cap (Fig. 1b,c). The field of view includes regions involved in sensory, motor and cognitive brain functions (Fig. 1d). To establish that the portable HD-DOT system is sensitive to disruption in brain function during the acute stages of stroke recovery, we have imaged 44 patients within the first 72-hours since their last known normal behavior. Up to an hour of resting state data was acquired in each subject. The National Institute of Health Stroke Scale NIH-SS provided a behavioral metric of stroke-induced functional deficit at the time of the scan. Functional data sets ranging from 15 - 50 minutes of quiet rest with eyes closed were used for further analyses. Standard DOT functional connectivity analyses (fcDOT) were performed on the [HbO] data [3]. Due to the added challenges of obtaining high-quality low-noise data in the clinic, new data quality metrics such as real-time cap coupling and automated motion artifact detection augmented the standard HD-DOT pipeline. Seed-based functional connectivity (fc) maps were generated using regions of interest (ROI) located at every voxel within the field of view for both the stroke patients and for an independently acquired set of healthy adult subjects (Fig. 1e). For each ROI-based fc map, the spatial correlation (called ‘similarity’) was calculated between the fc maps of the stroke patient and the healthy population (Fig. 1f). The distribution of similarity values across the entire field of view reveals a skewness (Fig. 1g) that is significantly sensitive to NIH-SS, p<7e-4 (Fig. 1h). Herein, we have demonstrated that HD-DOT is sensitive to altered brain function brought about by ischemic stroke as measured within the first 72 hours of stroke onset.

Figure 1 | a The portable HD-DOT system is deployed at the bedside and does not impair standard clinical care. b The imaging cap is composed of wearable Neoprene, (c) couples 48 sources and 34 detectors to the head in a regular grid that (d) covers multiple functional domains. e Anatomical CT and functional connectivity map of a healthy subject and a stroke patient reveals clear disruption in brain function. f A map of similarity is generated by calculating the spatial correlation between the fc map from an ROI and the fc map of the stroke patient vs. that in an average fc map of a healthy population. More disruption is seen across the field of view in subjects with a higher NIH-SS, as seen in the skewness of the distribution of similarity values (g). h The correlation between NIH-SS and the skewness of the similarity values across the field of view is significant at a level of p<4e-7.

References

A compact low-power Time-Domain fNIRS system

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Abstract

We proposed a novel compact time domain fNIRS system based on solid state technology. We developed a one-channel system with two wavelengths in order to estimate the hemoglobin content in tissue, in particular the brain cortex. The system is composed by three different parts: laser sources, detector, and acquisition electronics (Fig. 1(a)). As pulsed light source, we opted for two laser diodes operating in gain switching and thermalized by means of a thermoelectric cooler. The laser driving and cooling electronics are home made. The two laser sources emit pulse trains at 685 nm and 830 nm with a repetition frequency of 40 MHz, an average power of 0.3 mW and 2.5 mW respectively and a FWHM of the single pulse around 200 ps. The two wavelengths are sequentially shined into the sample by switching on and off the two lasers, implementing in this way a space multiplexing scheme [1]. The laser light is coupled by means of a proper optical system in two glass step index fibers (200 µm core diameter) in order to drive the light on the sample. The diffused light is collected by means of a graded index plastic optical fiber with a core diameter of 1 mm. The collected light is focused by a proper optics on a silicon photomultiplier (SiPM) of 1 mm<sup>2</sup> (C30742-11-050-T1, Excelitas) with a detection efficiency of around 15%. All the driving, cooling and read out electronics are home made. The detection module shows a time response of about 100 ps and a photon noise level of around 90 kcps [2]. The last part of the instrument is the acquisition electronics based on a Time to Digital Converter chip developed by Politecnico di Milano that shows the following characteristics: 10 ps of channel width, 40 ps FWHM single shot precision and 3.5 Mconv/s of maximum conversion rate. Photons arrival times are directly sent to a PC using a standard USB connection, a custom software controls the instrument and data management, while data analysis is performed off-line using a proper software. We are working towards a unique software for instrument control and on line data analysis. Fig. 1(b) shows the final instrument response function at the two wavelengths. We can observe a FWHM around 260 ps, the long tail is due to the typical time response of the SiPM detector. The system is suitable for oxygen saturation determination in tissue in particular for brain monitoring. The compactness of this device and the possibility to be battery operated (power consumption is < 10 W) pave the way to numerous applications, even for developing countries. Fully phantom characterization and first in vivo applications will be also presented.

Fig. 1 (a) Picture of the compact TD fNIRS system; (b) normalized IRF at the two wavelengths.

References

Speckle contrast optical spectroscopy of the adult brain with a novel, compact system

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Objectives: Speckle contrast optical spectroscopy (SCOS) is a new method for deep tissue blood flow measurements [1]. It utilizes correlation diffusion models with point sources and a multi-exposure speckle contrast (MESI) approach to measure deep tissue flow in a similar way to diffuse correlation spectroscopy (DCS), but with reduced constraints on the instrumentation. Previously, it was demonstrated on the human arm and on phantoms [1, 2]. Here, we present a novel instrument using a single-photon avalanche photo diodes (SPAD) array with embedded field programmable gate array (FPGA) as a compact, self-contained MESI system. We demonstrate the system on the adult human brain.

Methods: SPAD array is a high frame rate imager with single-photon sensitivity. The benefit of this imager is that it has high frame rate and is not affected by readout noise, allowing for effective multi-exposure SCOS measurements. This unique SPAD technology can be scaled in a low-cost manner and by using arrays, we are able to improve the signal-to-noise ratio drastically. Fig 1(a) shows the SPAD array composed by 64 detectors and FPGA system for real time processing. As shown in panel (b), source was placed at a 2.5cm distance and mounted on a bicycle-helmet. The whole system is embedded in standard 1” optical tubing. In parallel with the SCOS measurement, DCS was measured on the other hemisphere. Subjects were asked after acquiring the baseline to hold their breath for 30s, and afterwards to continue breathing normally. The challenge was repeated three times.

Results: Fig. 1(c) shows a typical cerebral blood flow (CBF) trace during breath-hold challenge from SCOS and DCS. Both methods are in agreement within noise and a typical bi-phasic response is obtained in response to breath-hold. We will present statistical results and the findings on other challenges. As well as the further miniaturized device.

Conclusion We demonstrate multi-exposure speckle contrast for deep tissue blood flow measurement on the adult human brain by implementing a compact SPAD array system.

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References
Lightweight high-density diffuse optical tomography using sCMOS detection

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Objective: The widespread adoption of optical neuroimaging has been restricted by the tradeoff between cap wearability and brain coverage [1]. Increased coverage requires more fibers and larger imaging consoles, however these changes drastically reduce the wearableity of the imaging cap and the portability of the entire system. The size of the detection fibers, which is driven by signal-to-noise considerations, is the primary obstacle to fabricating more wearable and portable optical neuroimaging arrays. Here we report on a design that leverages the low-noise of scientific CMOS cameras, along with binning and noise reduction algorithms to use fibers with approximately 30x smaller cross-sectional area than current high-density diffuse optical tomography (HD-DOT) systems [2].

Methods: We have developed a Super-Pixel sCMOS Diffuse Optical Tomography (SP-DOT) system (Fig. 1a) that uses 200um diameter source and detector fibers, with a lightweight low-profile, wearable design. A super-pixel algorithm leverages pixel binning to provide dynamic range (DNR), Noise Equivalent Power (NEP), and cross-talk (CT) specifications comparable to previous HD-DOT [2].

Results: We have demonstrated retinotopic mapping with a SP-DOT system (Fig. 1). The system has a high DNR (>10^3), high frame rate (>6Hz) and low NEP (< 9fW/Hz).

Discussion: The sCMOS-based SP-DOT system design provides an interesting approach to improving the weight/coverage tradeoff and has promising signal-to-noise that may open up HD-DOT a greater variety of applications. While the prototype presented here is limited to the visual cortex, the weight reduction to the cap should enable full-head and effectively wearable imaging caps.


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Figure 1. A) Wearable retinotopy cap. B) Source- and detector-pair light levels versus distance. C) Top: Subject position and visual stimuli (clockwise rotating flickering checkerboard). Bottom: Logmean 830nm light levels showing the response of the upper left visual cortex to the stimulus in the lower right visual field. Vertical lines show when the stimulus occurred. D) Reconstructed activations of the stimulus in the four corners of the visual field showing retinotopic mapping of the cortex. Colorbar denotes percentage of the maximum value.
A New Multichannel Broadband Near-Infrared Spectroscopy System to Measure the Spatial Distribution of Cellular Oxygen Metabolism and Tissue Oxygenation

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There is an unmet clinical need for a continuous, non-invasive cerebral monitor of oxygenation, haemodynamics and cellular oxygen metabolism across multiple regions simultaneously. We present a novel multichannel near-infrared spectroscopy (NIRS) system to measure changes in haemoglobin concentrations ($\Delta[\text{HbO}_2]$, $\Delta[\text{HHb}]$), the oxidation state of cytochrome-c-oxidase ($\Delta[\text{oxCOC}]$) and absolute tissue oxygenation saturation (TOI) at multiple locations simultaneously. The system employs halogen light sources emitting broadband light from 504 to 1068 nm, 2 CCD cameras and customized optical fibres. 24 channel NIRS measurements with source-detector distances from 20mm to 35mm were acquired from nine healthy adult volunteers during a Stroop task. Changes in systemic physiology were monitored to investigate its influence on the measured NIRS signals. $\Delta[\text{HbO}_2]$, $\Delta[\text{HHb}]$ and $\Delta[\text{oxCOC}]$ were calculated using the UCLn algorithm in 19 channels with high intensity count (figure 1a) and TOI values were calculated using Spatially Resolved Spectroscopy (SRS) across 4 regions indicated by black arrows in figure 1a. Figure 1b presents block-average concentration changes calculated across all repeats and subjects. The haemodynamic changes agree with previous study employing similar Stroop protocol². Mean TOI was calculated for each of the 4 regions in each subject and then averaged across subjects. Group average TOIs ± standard deviations in 4 regions from left to right are 75.4±2.1, 75.3±2.9, 78.6±2.5 and 79.1±3.4%. Using the new system, we have demonstrated the spatial distribution of oxicCO response to functional activation as well as tissue oxygenation saturation across the frontal lobe in healthy volunteers. This new system will enable the investigation of the relationship between regional changes in haemodynamics and cellular oxygen metabolism during functional activation as well as the balance between oxygen supply and demand across multiple regions in the brain.

Fig 1. a) Positions of 19 NIRS channels and 4 TOI channels on the forehead. The size of circle indicates the source-detector separations of each of the channels ranging from 20 - 35 mm. b) Block average of $\Delta[\text{HbO}_2]$, $\Delta[\text{HHb}]$ and $\Delta[\text{oxCOC}]$ with standard error of means in 19 channels from 10 repeats of the Stroop Task. The shaded area indicates the 60 s stimulation period. Plots with solid, dashed and dotted black borders are from channels with 35 mm, 30 mm and 20 mm separations respectively.

Prosodic grouping at birth
Nawal Abboub, Thierry Nazzi & Judit Gervain

The goal of the present study was to explore the developmental origins of prosodic grouping, also known as the iambic-trochaic law (ITL). The ITL states that sounds contrasting in duration are perceived as forming rhythmic groups with final prominence, i.e., iambic (short-long), while those contrasting in intensity/pitch form rhythmic groups with initial prominence, i.e., trochaic (strong-weak or high-law). Some authors (Bolton, 1894; Hayes, 1995; Hay & Diehl, 2007) believe that the ITL is a universal property of the auditory system, while recently, others have proposed that the ITL can be modulated by language experience in adults and infants (Yoshida et al., 2010; Bion et al., 2011; Iversen et al., 2008; Bhatara et al., 2012). By investigating whether newborns show the ITL bias, and if yes, whether it is influenced by the language heard prenatally, the current study seeks to clarify this issue.

We addressed these questions by conducting four experiments, using near-infrared spectroscopy (NIRS). First, we explored the earliest foundations of the crucial ability to detect and process prosodic patterns. In particular, no study has yet tested newborns’ prosodic grouping biases; a gap that the present study intends to fill. We tested prosodic patterns that varied along one of three acoustic dimensions that characterize speech prosody (duration: Exp. 1.; intensity: Exp. 2.; pitch: Exp. 3.). French, the language that our monolingual participants were exposed to prenatally, mainly uses durational contrasts in its prosody, in particular final lengthening. Second, we investigated how these abilities are modulated by language exposure, comparing prosodic grouping biases in monolingual French-exposed newborns and newborns exposed to French and another language using a pitch contrast, a dimension for which even non-linguistic animals show a grouping preference (Exp. 4). The second languages of our bilingual newborns in Experiment 4 make use of pitch in their prosody to a much greater extent than French does. In each experiment, the stimuli either followed the ITL-predicted grouping patterns (consistent condition: short-long or high-low or strong-weak) or the non-predicted grouping pattern (inconsistent condition: long-short or low-high or weak-strong) or did not provide any grouping cues (no grouping condition: equal duration, pitch, intensity).

We observed differential brain activations in favor of the inconsistent condition, suggesting that neonates already show prosodic grouping preferences at birth (Figure 1). Specifically, a stable bias was found for the duration cue in French-exposed monolinguals, whereas these babies showed a much weaker bias for the intensity and the pitch cues (Experiments 1, 2, 3). French-others language-exposed bilinguals showed a strong differential response in the pitch contrast condition (Exp. 4), which was not the case in our monolingual French newborns. These effects were observed most strongly in the left hemisphere. Because duration is the acoustic cue most typically used to mark prosodic prominence in French phrases and pitch is used in our bilingual babies’ other languages, prenatal language experience seems to have an effect on prosodic grouping at birth. Taken together, these results provide the first evidence that automatic perceptual biases for prosodic grouping may be present at birth, but are heavily influenced by prenatal exposure.

![Figure 1: Statistical maps indicating p-values from cluster-based permutation tests comparing the responses to consistent vs. inconsistent sequences in each experiment.](image)

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*Note: The figure shows statistical maps indicating p-values from cluster-based permutation tests comparing the responses to consistent vs. inconsistent sequences in each experiment.*
**fNIRS reveals distinct infant emotional face processing**

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Functional near-infrared spectroscopy (fNIRS) allows us to ask questions about how infants perceive the world despite their limited behavioral repertoire. In this study, fNIRS was used to measure infants’ brain activity during the presentation of happy, angry and fearful faces. We additionally investigated brain-behavior associations based on looking behavior.

Separate groups of 5-month old (n = 43) and 7-month old (n = 37) infants were tested with a 46-channel NIRS system that recorded brain activity over the frontal, temporal, and parietal cortex. The experimental stimuli presented were photographs of female faces with happy, angry or fearful expressions in a block design. Oxyhemoglobin (HbO) responses to each emotional condition were calculated using HOMER2. Simultaneous eye-tracking recorded infants’ looking behavior to the eyes or mouth of the images.

Activation patterns differed between emotional categories at each age (Fig 1). Happy faces elicited the broadest temporal and parietal activation at both ages. However, at 5 months the response was bilateral, while at 7 months the response was lateralized to the right hemisphere. At both ages, only fearful faces elicited negative frontal responses, which were decreases in HbO. Frontal activation to happy, fearful and angry faces was correlated with looking time to the eyes and mouth, but not overall looking time. Overall looking time did not differ between emotional categories or ages.

While there was no difference in overall looking time between emotional conditions, there was a difference in brain activation patterns, indicating that infants discriminated emotional categories at both ages despite a lack of overt behavioral differences. Infant’s larger responses to happy faces may indicate either more experience with this emotional category, or perhaps its particular salience to infants. Responses to happy faces lateralized between 5 and 7 months. Frontal activation patterns were negative overall, and correlated with looking to eyes or the mouth of the image, indicating a link between brain and behavior.

![Figure 1: Active channels for each emotional category and age (p<0.05)](image-url)
Title: Brain-to-brain synchrony of parent and child during cooperation revealed by fNIRS hyperscanning

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Introduction: Primate and human brains contain networks that resonate in real time to the states, actions, and emotions of conspecifics. Such systems show brain-to-brain coupling during human interaction which has been successfully demonstrated for adults in a variety of tasks. The present study aimed to examine neural synchrony between parent and child within a naturalistic setting. It has been proposed that biological synchrony may fine-tune the child’s brain to the caregiver-child dyad with long-lasting effects on the emotional, social and cognitive development of the child. Hence, the relationship between brain-to-brain synchrony within parent-child dyads and emotion regulation in the child was examined.

Methods: Brain-to-brain synchrony within parent-child dyads was studied during a cooperative and a competitive computer game using a single NIRS instrument for simultaneous measurements of brain activity. Additionally, the child performed both task conditions with an adult stranger. Wavelet coherence was calculated for corresponding channels within each dyad as well as between random participant pairs not playing together.

Results: In the frontopolar cortex (FPC), higher coherence was observed during parent-child cooperation in contrast to parent-child competition and stranger-child cooperation. In comparison to random pairs, coherence in the FPC was elevated only during parent-child cooperation. This coherence was negatively associated with the child’s emotional lability.

Conclusions: These results suggest that during cooperation the neural activities of parent and child synchronize in brain regions related to social cognition. fNIRS hyperscanning is a promising tool to further explore the biological foundations as well as the developmental outcomes of parent-child synchrony, in particular for future longitudinal studies in at-risk dyads or children in care.
Research suggests that school-aged children’s understanding of fractions and division is key to their successful acquisition of complex arithmetic in later grades (Siegler et al., 2012). Yet, little is known about the developmental antecedents of children’s understanding of division and how these relate to their emerging mathematical abilities. Interestingly, from a young age, children pay attention to whether or not they received a fair share of toys or food from frequent experiences with resource allocation. Division is required for these equality- and merit-based sharing activities. In our study we tested the hypothesis that early resource allocation experiences relate to children’s emergent arithmetic abilities and that sharing taps into similar brain regions as arithmetic.

**Method.** To test this hypothesis we asked children (ages 2-14, n=131) and adults (ages 18-23, n=28) to complete a Social Division task (see Figure 1) both behaviorally (children and adults) and during neuroimaging (adults only) using fNIRS. **Results.** Consistent with our hypotheses, children’s performance on the Social Division Task correlated with and explained a significant amount of variance in children’s mathematical abilities, especially in preschool children ($r(17)=.531, \beta=-.60, p < .05$). Similarly, the neuroimaging results revealed that both the Social Division and the Numerical Division tasks engaged similar bilateral parietal regions in adults (task > control task contrasts, $p <0.01$, see Figure 2). **Conclusion.** Emerging theories of mathematical development suggest that division might be foundational to the mastery of complex arithmetic. Here we offer new evidence to suggest that social sharing activities might foster the brain and cognitive mechanisms of division starting at a preschool age. These findings shed new light on the antecedents of mathematical development and suggest that social sharing activities might foster children’s later success in math acquisition.

*Figure 1.* Participants are asked to determine which character is being nicer in three different conditions. (A) Baseline: the character with more candy gave a larger proportion, (B) Absolute: both characters gave the same proportion, (C) Conflict: the character with less candy gave a higher proportion.

*Figure 2.* Adults showed similar activation in bilateral parietal regions during both Social Division, and Numerical Division tasks (task > control task contrasts, $p <0.01$)
Visual working memory (VWM) is a core cognitive system with a highly limited capacity. These limitations have a profound impact on the development of a broad range of cognitive abilities (Conway et al., 2003). Studies examining the development of VWM in infancy have relied on looking behavior, while longer-term cognitive outcomes are assessed using tasks that require explicit ‘same’ and ‘different’ decisions. We report findings from a study relating these behaviors at the levels of brain and behavior with 3- and 4-year-olds.

We recorded optical neuroimaging data from bilateral frontal, temporal, and parietal cortex while 3- and 4-year-olds (N=24 & 22, respectively) completed a Preferential Looking task (PL; Ross-Sheehy et al., 2003) and a Change Detection task (CD; Simmering et al., 2012). Behaviorally, results from the PL task showed an increase in mean look durations as the set size increased, as well as a decrease in the rate of shifting between displays. Consistent with data from Simmering (2016), there were 3 significant positive correlations with higher shift rates (SR) related to higher change preference scores (CP). Results from CD, showed that max capacity (K), the index for performance in this task, was higher for 4yo (M=2.09, SD=0.61) than 3yo (M=1.84, SD=0.62). To examine how children’s performance in CD related to their performance in the PL task, we correlated performance in PL (SR, CP) with Max K. Children with higher SRs at SS2 had higher WM capacities (r=.28, p<.05). Children with higher SRs at SS1 also had higher CPs at SS2 (r=.34, p<.05).

We analyzed the fNIRS data using an image-based fNIRS approach (Wijeakumar et al., 2016) and conducted task-specific ANOVAs (Age x SS for PL and Age x SS x Type for CD) across voxels common to both ages. Results from both ANOVAs showed significant effects within the VWM network that included frontal, temporal, and parietal regions (fig. 1). Interestingly, 1-IPL clusters that showed significant effects across both tasks, showed a developmental reorganization in the CD task with higher activation on ‘different’ trials at 3 years and higher activation on ‘same’ trials at 4 years. This pattern was negatively related to children’s WM capacity in the CD task.

To further explore how the tasks are related, we conducted an Age x SS x Task ANOVA. One important question we wanted to examine with these data is whether any brain areas engaged in PL were also engaged in CD and correlated with the standard measure of capacity—Max K. Two areas emerged from our correlational analysis: R-MFG and L-MFG. L-MFG activation, which was significantly higher for 4yo than for 3yo, showed a positive correlation with CP at SS3 and a positive correlation with Max K. Thus, MFG activation was significantly related to key indices of performance across both tasks.

In all, we found robust correlations between the two tasks, replicating behavioral and modeling findings from Simmering. Moreover, fNIRS findings localized areas in the brain—most notably, L-MFG—that subserve VWM functions in both tasks. These data are important in that they link measures of early neurobehavioral function with good predictors of childhood and adult outcomes (Max K).
The Characteristics of the Cortical Functional Networks in Individual Infants

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The functional networks revealed by various neuroimaging methods reflect both anatomical connections and functional relationships between distant regions. Several recent fMRI studies in adult participants showed that functional connectivity profiles in a resting state can be a clue in identifying a single participant within a large group (e.g., Finn et al., 2015). We have previously reported that the cortical network for language processing in early infancy consists of the frontal, temporal, and parietal regions of the brain. In the present study, we examined the possibility that the spatiotemporal organization of the functional network is determined individually in each infant. Twenty full-term healthy infants (104–123 days old) participated in this study. All infants were asleep while Japanese speech sounds (duration: ~4 s) were presented to infants every 10 or 20 s (63 sentences over 920 s). Cortical activation was measured using 94-channel NIRS. The continuous oxygenated hemoglobin (oxy-Hb) signal data were separately filtered using multiple band-pass filters (0.009–0.02 Hz, 0.02–0.04 Hz, 0.04–0.2 Hz, and 0.009–0.2 Hz), and divided into former and latter segments of 450 s of data prior to analysis. We then calculated correlation coefficients between the continuous time course of oxy-Hb signals, obtained from a single channel, and that of all other channels (Homae et al., 2010; 2011) in each segment. Based on these correlation-coefficient matrices, we calculated intra-infant correlation between the former and latter segments, and inter-infant correlations, which were the highest values of correlations between an infant and the other 19 infants. We compared the intra-infant and inter-infant correlations. These analyses revealed a highly significant consistency in intra-infant correlation when continuous data contained broad-band frequencies including, low frequencies. Specifically, when the filter was set at 0.009–0.2 Hz, 19 out of 20 infants showed higher intra-infant correlation in comparison with inter-infant correlation (p < 0.001). The difference between intra-infant and inter-infant correlations was not spatially uniform, but distinct cortical regions such as the left and right temporoparietal regions, as well as the left frontal region, showed marked differences between the correlations. Our findings demonstrate that functional networks in the speech-stimulated state reflect individual differences between infants. The temporal characteristics of an individual infant’s network may be embedded in broad frequency bands, and spatial characteristics of the network would appear in language-related regions. These results suggest that each individual brain has unique characteristics from early infancy.

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Time-resolved diffuse optical tomography of the infant brain during neurodevelopmental events and passive arm movement

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We present the first three-dimensional images of infant brain activity using fast time-resolved diffuse optical tomography (TR-DOT). There is a clinical unmet need for non-invasive monitoring of cerebral function at the cot-side in the neonatal intensive care unit (NICU). Electroencephalography (EEG) measures cerebral electrical activity but yields limited spatial information and does not always detect brain pathology in infants [1]. However, diffuse optical imaging (DOI) measures changes in blood volume and oxygenation in the infant brain. Continuous wave (CW) DOI systems illuminate the head with near-infrared light, and the change in intensity of light scattered back to the surface can be used to calculate oxygen saturation as well as the relative changes in oxy- and deoxy-haemoglobin concentration ([HbO] and [HbR], respectively). Metrics of brain function derived from [HbO] and [HbR] measurements can potentially be used to predict neurodevelopmental outcome as well as to develop biomarkers for guiding neuroprotective therapies. CW systems are limited to a depth sensitivity of 1-2 cm, but the ability to image the entire infant brain would provide more information about pathologies arising from deep-brain structures. TR-DOT is the only optical imaging technique which is capable of full transmission measurements across the infant brain. However, it typically requires expensive photon counting technology, has low temporal resolution, and requires complex mechanical components (such as variable optical attenuators) to achieve adequate dynamic range.

At University College London, we have developed a bespoke portable TR-DOT device known as MONSTIR II which is capable of acquiring whole-head tomographic data whilst mitigating some of the inherent disadvantages of TR methods [2]. MONSTIR II incorporates a supercontinuum laser and acousto-optic tuneable filters that allow data to be acquired simultaneously at any four near infrared wavelengths. Light is delivered sequentially to 32 source optical fibres coupled to the head, and temporal point spread functions (TPSFs) are collected by 32 independent photo-multiplier tubes routed to four time-correlated single-photon counting units. Ultimately up to 1024 channels of data can be acquired in a single illumination sequence. Datatypes extracted from the TPSFs, such as intensity and mean time of flight, allow us to determine changes in absorption and reduced scattering coefficients within the interrogated tissue (which can later be converted to changes in [HbO] and [HbR]). To enable fast TR-DOT imaging, the effective temporal resolution of our system is improved by reconstructing images using a variational Kalman filter [3]. This allows us to image transient haemodynamic changes in real time.

Using MONSTIR II and these novel reconstruction techniques we have successfully imaged changes in absorption and reduced scattering coefficients in dynamic 2D and 3D phantoms [3]. We have also scanned several infants, including some with hypoxic ischaemic encephalopathy (HIE), at the cot-side (Figure 1). We present our preliminary findings in infants from 1) functional activation caused by passive arm movement and 2) those with neuropathology.

Figure 1. Top: Flexible headgear was 3D printed to hold the optical fibres. Bottom: Scanning an infant with HIE. A) EEG system, B) optical fibres connect to MONSTIR II, C) headgear attached to the infant’s head.

References
Maturation of cerebral hemodynamic response in premature infants

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Objectives: Premature infants are at high risk of neurological complications that may affect brain development. In addition to the vulnerability to neurological insult associated with premature birth and physiology, premature infants' exposure to extraterine sensory experience can alter somatosensory cortical development. Functional near-infrared spectroscopy (fNIRS) measures regional cortical activation in response to stimuli and is a suitable tool for studying neural maturation in neonatal populations. The aim of this study is to use advanced fNIRS methods to investigate the influence of (early- or late-preterm) prematurity and sensory experience on brain development in premature infants. Materials and methods: We enrolled 11 infants (Gestational age: 25-32 weeks), aged 32 to 42 weeks postmenstrual age (PMA), and performed a total of 28 measurements in the Neonatal Intensive Care Unit (NICU) at Brigham and Women’s Hospital. We integrated continuous wave near-infrared spectroscopy techniques (CWNIRS) with diffuse correlation spectroscopy (DCS) to derive changes of hemoglobin concentrations (HbO) and cerebral blood flow (CBF) in response to somatosensory stimuli. For each measurement, we used differential pathlength factors and baseline hemoglobin obtained with frequency-domain NIRS to quantify relative vascular and metabolic changes (rHbO, rCBF and rCMRO2) (Roche-Labarbe et al., 2012). Results and discussion: We observed typical hemodynamic responses in infants measured at term equivalent age (PMA≥38 wks). In infants measured before term age (PMA≤36 wks), the characteristic “preterm” hemoglobin response with longer time to reach peak amplitude was more prominent (Figure 1a). This observation is consistent with results modeled from previous fMRI findings (Arichi et al., 2012). In addition, infants measured at older PMA tend to have responses with a larger undershoot. The larger undershoot may result from insufficient hemoglobin supply to overcome oxygen demand induced by functional activation during a low hematocrit period (Figure 1b) (Zimmermann et al., 2011). The functional responses among infants of the same PMA did not differ regardless of GA (Figure 1c), suggesting the influence of ex-utero, experience-dependent processes during the premature infant’s development prior to term age (Allievi et al., 2016). Conclusion: Preterm infants revealed a faster response time with increasing PMA characteristic of a more mature response. However, the developing of hemodynamic responses are also confounded by changes in systemic physiology during the period of maturation.


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Figure 1(a) Average of relative changes in oxy-hemoglobin (HbO) for two groups divided by PMA (b) Average of relative changes in HbO for two groups divided by Hemoglobin (HGB). (c) Average of relative changes in HbO for two groups divided by GA (PMA<38 wks). Red stars indicate significant difference between the two groups.
Neural activations to mutual gaze and contingent responsiveness during live interactions in infancy

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Social and linguistic input from other people during infancy and childhood plays an essential role for typical development. Yet, early development of the social brain network associated with social perception remains poorly understood. Especially, very little is known about neural activity in infants while they are socially interacting with others (see Lloyd-Fox et al., 2015; Urakawa et al., 2014). In this study, we observed 6- to 19-month-old infants’ brain activity in response to mutual gaze and contingent responsiveness during natural interactions across the temporal (temporoparietal junction: TPJ and superior temporal sulcus: STS) regions using fNIRS.

Twenty-two 6- to 19-month-old infants participated in the study. During the experiment, a female experimenter spoke to the infant using a picture book and puppets. There were two experimental conditions: the eye contact (E) and contingent (C) condition. Within the E condition, the experimenter always looked at the infant to make eye contact during interactions. Within the C condition, the experimenter not only made eye contact but also responded contingently to the infant’s behavior (e.g. smiled immediately after eye contact). During the baseline, the experimenter behaved in the same manner except that she always looked down and made no eye contact. The two types of experimental condition trials (20 s), E and C, were presented in between baseline trials (20/25 s). To investigate infants’ cortical activation, we used a multichannel NIRS system (ETG-7000, Hitachi Medical Co.). Two 3 × 5 rectangular probes (8 sources and 7 detectors) with a total of 2 × 22 channels were placed in each temporal lobe.

The fNIRS recordings indicated increased activation from baseline in the right TPJ and posterior STS region only for the C condition (Figure 1), suggesting that these regions are already responsive to a highly communicative behavior of others as part of the social brain network. Moreover, the activation in the right TPJ region was related to the occurrence of eye contact during mother-infant free-play interactions. Our study, thus, indicated an early involvement of the TPJ in natural social interactions, which presumably play an important role in the development of theory of mind.

![Figure 1. The grand averaged time courses of the hemodynamic responses in Channel 44 (right TPJ) and 40 (right angular gyrus or posterior STS).]
NIRSTORM: a brainstorm plugin dedicated to joint EEG/fNIRS analysis

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Wearable neuro-imaging devices allow designing experiments in ecological environments, with the possibility to handle long duration recordings [1]. The main modality involved is EEG, for which Brainstorm is a recognized and widely used analysis software platform, mainly offering preprocessings, detection and advanced EEG/MEG source reconstruction [2].

FNIRS is a promising imaging modality providing complementary information to EEG, i.e. hemodynamics-related variations linked to the neuro-vascular coupling occurring at the time of bioelectrical events detected using EEG. EEG and fNIRS signals similarly involve long duration scalp measurements, with excellent temporal resolution, and for which spatial localization might be improved by solving a so-called inverse problem using anatomical constraints. Aiming at the fusion of these two modalities, the proposed Brainstorm plugin, entitled Nirstorm, benefits from powerful and ergonomic features already available, such as database and pipeline management, event labeling, signal processing and visualization tools. In order to handle the specificity of fNIRS data, Brainstorm visualization has been enriched to allow navigation through pairs of sensors and also to visualize multiple time-courses per sensors (Fig. A).

The plugin offers the classical fNIRS preprocessing steps: filtering, detrending, movement correction based on [3] and [Hb] quantification via Modified Beer-Lambert Law. In addition to the typical window-averaging processing (Fig. B), Nirstorm also integrates a novel Bayesian regularized deconvolution approach inspired by [4] which provides temporally smooth estimates of the hemodynamic impulse response. Last, with the aim to jointly explore EEG source localization with fNIRS results, Nirstorm proposes a nonlinear reconstruction method: the Maximum Entropy on the Mean, developed in the context of EEG/MEG source localization [6,7] (Fig. C) and applied on a fNIRS forward model imported from [5]. All these tools will be further developed to reach joint EEG/fNIRS analysis by proposing advanced 3D tomographic and cortical reconstruction of fNIRS data as well as statistical analysis (group or individual level) along the cortical surface.

![Fig. A: Finger tapping experiment. Window averages of Δ[HbO] (red), Δ[HbR] (blue) and Δ[HbT] (green) with their standard deviation for a given pair of the montage in Fig. B. The red marker at 14 sec. corresponds to Fig. B. Fig. B: motor montage with mapped averaged Δ[HbO] values at time point t=14sec. Fig. C: MEM 3D reconstruction of Δ[HbO].

3 Scholkmann S., Spichtig S., Muehlmann T., Wolf M. (2010). Physiol. Meas., vol. 31-5,
7 Zerouali Y., Lacourse K., Chowdhury R., Hedrich T., Lina JM, Grova C., Best: Brain Entropy in space and time http://neuroimage.usc.edu/brainstorm/Tutorials/TutBEST
A novel Neurofeedback and BCI toolbox for real-time fNIRS: Turbo-Satori

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Introduction: Turbo-Satori is a novel real-time processing and analysis tool for functional near-infrared spectroscopy (fNIRS) data which was acquired using a NIRx recording device [1]. The software is optimized for real-time applications such as neurofeedback and brain computer interfaces (BCI’s).

Methods: The software calculates and shows relative oxy and deoxygenated haemoglobin concentration changes in real-time and provides this information in time course and neurofeedback / BCI displays. Relative Oxy/deoxy concentration changes are calculated in real-time. A selection of different IIR filters can be used to remove physiological confounds like heart-beat fluctuations or high frequency noise. A RLS GLM is calculated incrementally and the resulting statistics are indicated in the row headers in the channel selection area as well as in the specific rows and columns. The underlying events can be defined using received triggers or a predefined protocol containing the different conditions and timings. The contrasts used in the t-test can be changed online to support the channel selection procedure. Turbo-Satori is based on incremental procedures which can be performed in a run-time of O(1) for each data-point. We measured the processing time using two different datasets, the first datasets using 20 channels and the second using 64 channels. For the first experiment a mean processing time of 2.22 milliseconds (sd=1.47ms) per data point, sampling rate 10.42Hz (~98ms, 20 Channels), was measured. The second dataset performed similar: mean processing time 2.76ms (sd=2.57ms) for each data point, sampling rate 7.81Hz (~128ms, 64 Channels). To fulfill the real-time condition a processing time below the sampling rate is required. The software also includes network interface solutions to export data to 3rd party applications using the TCP/IP network protocol.

Discussion: Data driven analysis methods may be implemented in the future to provide more possibilities in the direction of explorative experiments. Additional improvements can be made in making use of multiple threads to process the data simultaneously for each channel.

Conclusion: A novel fNIRS toolbox was introduced including different preprocessing and analysis procedures in real-time with a processing time for each data point of O(1).

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References: [1] NIRx Medical Technologies, LLC
High-density diffuse optical tomography (HD-DOT) offers a broad cortical field-of-view and, like other near infrared spectroscopy techniques, affords high participant comfort and tolerance of small head movements, making HD-DOT well suited for developmental imaging studies. However, typical neuroimaging tasks require participants to attend to many repetitions of the same task to achieve adequate signal-to-noise, limiting their usability for populations requiring simple but highly engaging tasks (e.g. toddlers). We have developed analysis methods to extract localized, task-evoked cortical responses during passive viewing of feature films to meet the demand for rich and simple imaging tasks. We used HD-DOT [1] to continuously image cortical changes in oxy-hemoglobin concentration in healthy adults during passive viewing of The Good, The Bad, and The Ugly. First, we assessed response reproducibility between repeated viewings of the same 10-minute clip, hypothesizing that responses in sensory regions would show the most reproducible responses. As shown in Figure 1, we observed the highest reproducibility in cortical regions related to auditory and visual processing, replicating a signature effect of movie viewing shown with fMRI [2]. We next coded the movie clip for features of interest to generate a timecourse representing the intensity of a particular feature over the course of the movie [3]. We correlated time traces of these features to voxelwise time courses to map movie features to cortical areas. Figure 2 illustrates example results from this procedure for an auditory feature (spoken language) and a visual feature (hands). The strongest correlations between the spoken language feature and HbO are found in regions known to be active during speech processing, while the hands feature is most strongly correlated with visual and somatomotor regions, indicating that this feature-based correlation strategy is able to map functionally defined cortical regions [1,3]. Future work will be aimed at using movie viewing as a tool for imaging task-evoked responses in populations (e.g. toddlers) unable to comply with more complex task instructions.

**Figure 1:**
(A) Reproducibility for a single region (red region on cortex) is assessed by taking the Pearson’s correlation of HbO measurements from two repetitions of the same movie (red and blue time traces)
(B) Voxelwise response reproducibility across the entire field-of-view.

**Figure 2:**
Models of feature intensity (blue = auditory speech; orange = visual hands) during the movie (top) was correlated with voxelwise HbO to identify cortical regions related to processing each feature during movie viewing (bottom).

**References:**
Evaluation of Hemoglobin and Cytochrome using a Broadband Time Resolved NIRS system

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Abstract: We demonstrate the ability of a multiwavelength Time Domain NIRS system to monitor the changes in oxy-, deoxy- haemoglobin ([HbO₂] [HHb]) and the oxidation of cytochrome-c-oxidase ([oxCCO]). We first test the ability of the system to quantify the changes in [oxCCO] concentration in the presence of large haemoglobin changes during forearm ischemia. Then we test the ability of our system to resolve the changes in those 3 chromophores during a brain activation. The instrument uses a supercontinuum laser, photomultiplier detectors and a Time-Correlated Single Photon Counting Module for the detection and counting of photons [1]. The system is wavelength multiplexed and can measure the temporal point spread function (TPSF) of up to 16 wavelengths between 650-890 nm. In Figure 1, we present data from one study, were we used 16 wavelengths, from 780 to 870, to quantify the chromophore’s concentration changes during forearm ischaemia. The optical fibres were placed on the forearm with a source / detector distance of 3 cm. After 4 minutes of baseline measurements, we inflated the cuff at 200 mmHg for 5 minutes and then, monitored the muscle recovery for 5 minutes.

We quantified the changes in the [HbO2], [HHb] and [oxCCO] concentration in two different ways. For method 1 we used the change in attenuation and the modified Beer Lambert law utilizing the measured pathlength for each wavelength. For the second method used the change of the absorption coefficient, obtained by fitting the solution to the diffusion equation for a semi-infinite homogenous medium to the TPSF. The concentration results are plotted on figure 1.a and 1.b.

Both methods show a significant decrease in [HbO2], increase in [HHb] and no change in [oxCCO]. Same observations were seen before by Matcher and colleagues using continuous wave broadband NIRS [2]. During the forearm ischaemia there were significant scattering changes which could explain the quantitative differences between the two methods; as method 1 assumes no scattering changes. Here we demonstrate the capacity to resolve [oxCCO] in the presence of large haemoglobin changes during forearm ischemia using multiwavelength time domain NIRS.

We will finally present results from our current study that investigate the change in the [HbO2], [HHb] and [oxCCO] concentration in response to functional challenges in various area of the brain.

Figure 1: a) Concentration changes for [HHb], [HbO2], [HbT] ([HbT] = [HbO₂]+[HHb]), and [oxCCO] from method 1. b) Concentration changes for [HHb], [HbO₂], [HbT], and [oxCCO] from method 2. The wavelengths used were: 780, 786, 792, 798, 804, 810, 816, 822, 828, 834, 840, 846, 852, 858, 864, and 870 nm.

Multiwavelength Diffuse Optical Tomography to Resolve Cytochrome C Oxidase

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Functional near infrared spectroscopy (NIRS) indirectly identifies neuronal activity by measuring task evoked functional hyperaemia rather than directly measuring neuronal metabolic activity. The oxidation state of cytochrome c oxidase (CCO) the terminal electron acceptor in the mitochondrial respiratory chain can be measured non-invasively using broadband near infrared spectroscopy, and directly reflects neuronal metabolism. CCO measurement enables the investigation of cerebral energetics and neurovascular coupling across a wide range of experimental and clinical scenarios\textsuperscript{1}. However present systems are typically limited to a small number of channels due to the constraints of broadband spectroscopy. We present the first dense fibreless multiwavelength NIRS array based on light emitting diodes (LED) which for the first time promises to enable high spatial resolution CCO tomography, with the potential to develop into a wearable system.

Figure 1a illustrates the array consisting of 8 multi wavelength LED sources and 16 photodiode detectors. Each LED source contains eight LED die (780, 811, 818, 842, 850, 882, 891 and 901 nm) assembled in an area of 1.5x1.5mm. The optoelectronics are described in detail in Chitnis et al\textsuperscript{2}. Figure 1b demonstrates typical recordings during a visual functional activation in a single subject. The array was centered over the primary visual cortex (O1 position). A repeated inverting checkerboard stimulus of 20 sec duration was repeated 15 times and averaged. Chromophore concentration was derived using the UCLn algorithm\textsuperscript{3}. Figure 1c illustrates the residual from fitting the NIRS attenuation data at the peak of activation for two chromophores (oxyhaemoglobin (HbO\textsubscript{2}) and deoxyhaemoglobin (Hb)) and three (HbO\textsubscript{2}, HHb and the difference between the oxidized and reduced CCO spectrum (oxCCO)). The residual of the two chromophore fit resembles the oxCCO extinction spectrum whereas that residual of the three chromophore fit is minimal- suggesting oxCCO has been resolved.

Although further work is required to optimise the measurement technique across a range of physiological and pathophysiological scenarios, this approach has potential to deliver high spatial and temporal measurements of cerebral energetics. Work is presently ongoing employing image reconstruction techniques to produce the first CCO tomographic images, and this has considerable potential for the development of an inexpensive, wearable, continuous monitor to investigate cerebral energetics in multiple clinical and investigational scenarios which cannot be delivered by other modalities.

Figure 1. (a) schematic of source detector geometry across array, (b) changes in HbO\textsubscript{2}, HHb and oxCCO during visual activation of channels indicated in (a) showing a typical activation pattern, (c) two and three component fits from measured data

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A wearable fNIRS device for measuring human brain activity in everyday environments

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Functional near-infrared spectroscopy (fNIRS) allows non-invasive measurement of brain activity and has been successfully applied in brain-computer interfaces. fNIRS-based brain-computer interfaces for home rehabilitation could enlarge the scope of therapeutic paradigms, since task-specific training (e.g. arm training supported by a brain-triggered exoskeleton) can be provided in addition to clinical therapy. However, fNIRS devices for measuring brain signals are typically bulky and expensive, and there exist very few small and wearable devices with potential for home use – which still have several shortcomings (e.g. few optical channels, low light sensitivity, or difficult to don). In this project, a modular, wearable and low-cost fNIRS device is being developed, which targets the shortcomings of the other devices. The newly developed device consists of a freely selectable number of small modules; each has a size of 20x20x15 mm, and contains four individually selectable LEDs and one silicon-photomultiplier (SiPM). By deploying four wavelengths, the calculation of the concentration of four chromophores – instead of typically two – can be realized, and, thus, increasing the accuracy of brain activity classification. The modules are placed in a dense arrangement over the brain region of interest, and are controlled by a myRIO device (National Instruments, TX, USA) – a powerful tool that also enables online data processing. Compensation for confounding physiological effects is considered by including a short source-detector separation of 7.5 mm for short-channel regression. This hardware is expected to become a cutting-edge tool for reliably and robustly measuring brain activity using NIRS. Our device will help to advance the fNIRS technology to a state where it can be applied in clinics and at home, with the potential to open novel avenues in non-invasive brain-machine interfaces and neurorehabilitation therapy.

Figure 1: Small, wearable and low-cost fNIRS device with two modules – each containing four LEDs and one silicon-photomultiplier –, and the myRIO device – used for measurement triggering and data processing.
Random Effect Modelling of Prefrontal Cortical Haemodynamics to Determine the Influence of Surgical Expertise on Executive Control during Temporal Stress in the Operating Room

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INTRODUCTION
Temporal demands in the operating theatre (e.g. unexpected bleeding) increase cognitive workload and may impair surgical performance. Our prior work suggests that during temporal stress, senior surgeons maintain technical performance and demonstrate sustained prefrontal cortical (PFC) activation, whereas performance degradation and relative PFC disengagement typify junior surgeons. The aim of random effect modelling (REM) was to account for clustering in repeated measures data to further clarify the impact of surgical expertise and time pressure on the prefrontal haemodynamic response.

METHODS
28 surgical trainees (15 junior trainees, 8 intermediate trainees, and 5 senior trainees) performed a laparoscopic (key-hole) knot tying task under two conditions: (1) “self-paced” (SP), in which trainees were permitted to take as long as required to tie each knot, and (2) “time pressure” (TP), in which a maximum of 2 minutes were allowed. Each subject performed the task 5 times under each condition with inter-trial rest periods of 30 seconds. Subjective workload was quantified using the Surgical Task Load Index (SURG-TLX). A 24-channel optical topography system (ETG-4000, Hitachi Medical Corp., Japan) was used to measure prefrontal changes in oxyhaemoglobin (HbO₂) and deoxyhaemoglobin (HHb) concentration. Technical skill was assessed using task progression scores (au), error scores (mm), leak volumes (ml), and knot tensile strengths (N). REM analysis was carried out to appreciate the influence of expertise (junior vs intermediate vs senior) or condition (self-paced vs time-pressure) on task-induced changes in cortical haemodynamics (ΔHbO₂ or ΔHHb).

RESULTS
In junior and intermediate trainees, TP led to an increase in subjective workload (mean SURG-TLX score: junior trainees: SP=160.27 vs TP=202.07, p<0.001; intermediate trainees: SP=123.00 vs TP=172.50, p<0.01), and a significant deterioration in performance (mean normalised performance score: junior trainees: SP=0.53 vs TP=0.38, p<0.01; intermediate trainees: SP=0.52 vs TP=0.43, p<0.05). In contrast, no change in subjective workload (p=0.055) was observed amongst senior trainees who demonstrated no overall performance deterioration (p=0.116) under time pressure. In both self-paced and time pressure conditions, expertise was observed to be a predictor for ΔHHb (self-paced: z = -2.65, p = 0.008; time pressure: z = -1.99, p = 0.047). Among junior and intermediate trainees, condition was found to be a predictor for ΔHbO₂ (z = -2.84, p=0.004) and ΔHHb (z = 4.52, p <0.001) respectively. Whereas in senior trainees, condition was not a predictor for either ΔHbO₂ (z = 0.09, p = 0.925) or ΔHHb (z = 0.07, p = 0.944).

DISCUSSION
Senior trainees are better able to cope with intra-operative cognitive demands and stabilise their performance under pressure, perhaps due to enhanced PFC recruitment and task engagement. Future work will seek to develop cognitive training strategies that will maintain task engagement among more junior trainees, allowing them to improve performance under pressure.

REFERENCES
Performance decrease associated to cognitive fatigue is regulated by connectivity disruption more than reduced activity

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A situation of resource unavailability following sustained demands and a drop of performance are generally associated with the triggering of cognitive fatigue (CF) (Lim, Wu, Wang, Detre, & Dinges, 2010). There is not yet a clear agreement about the origin of this lack of resources (Hockey, 2013). To provide further insight in this issue, the present study investigated the neural dynamics of CF in a sleep deprivation situation where resources are naturally compromised. Using functional near infrared spectroscopy (fNIRS), we recorded cortical brain activity in 16 participants during the triggering of CF at three different times during the night (beginning-20h, middle-2h and end-7h). Results showed that although hemodynamic levels remain comparable at all sessions, lower performance levels were associated with a loss of connectivity at the end of the night in the left prefrontal cortex. These results support the dynamics models of stress and performance (Hancock & Warm, 1989; Hockey, 1997) which posits a disruption in the access to the pool of resources as a cause of performance drop during sustained attention.

References

Identification of Neural Systems Involved in Interpersonal Eye-to-Eye Contact: An fNIRS Hyperscanning Investigation

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Eye-to-eye contact between two humans is a universal form of natural social interaction, and although it is often speculated that eye-to-eye contact generates highly specific neural effects, a theoretical framework is lacking. Conventionally, neuroimaging techniques focus on single subjects and task-related paradigms, and investigations of neural correlates that underlie interpersonal interactions such as eye-to-eye contact are not well-studied. This knowledge gap is addressed by hyperscanning using functional near-infrared spectroscopy (fNIRS) to investigate neural systems engaged during natural interactive conditions (Scholkmann et al., 2013). We test the hypothesis that eye-to-eye contact between dyads engages language- and face-related processes to a greater extent than mutual gaze of a static face picture. In this study, 38 subjects (19 dyads) alternated their gaze between either the eyes of their partner or the eyes of a picture-face vs. a rest (+) target (Fig. 1). Blood oxygen level-dependent signals were acquired via a Shimadzu LABNIRS system with 84 channels distributed bilaterally on both heads covering anterior and posterior regions. Temporal resolution was 27 ms and the deoxyhemoglobin signal was used for analysis. Eye-to-eye contact was confirmed by eye-tracking (SMI ETG2) synchronized to the NIRS acquisitions. General linear model contrasts using global mean removal techniques (Zhang et al., 2016) revealed an eye-to-eye effect ([eye-to-eye]-[eye-to-picture]) consisting of a cluster centered at (-54, 8, 26) extending over left pars opercularis (40%), part of Broca’s Area specialized for speech production; left premotor and supplementary motor cortex (45%), part of the sensorimotor face network; and the left subcentral area (12%), consistent with the language and face-related hypothesis (p<0.01, Fig. 2).

Functional connectivity analyses (psychophysiological interaction (PPI), Friston et al., 1997) using the eye-to-eye effect cluster centroid as a seed (filled black circle) revealed increased connectivity to a cluster containing: left superior temporal gyrus (STG, 40%), a canonical node for receptive language processing and a component of Wernicke’s Area; left primary somatosensory cortex, a component of the sensorimotor face network (18%); and left subcentral area (35%), p<0.02. Right side homologues to Broca’s Area also increased connectivity to the eye-to-eye effect seed (Fig. 3). These findings are also consistent with co-engagement of eye-related and language systems during eye-to-eye contact.

Cross-brain coherence using wavelet analyses (MATLAB 2016a) between pairs of brains confirmed that STG and the supramarginal gyrus increased coherence (Fig. 4) during eye-to-eye contact (red) relative to eye-to-picture gaze (blue), known to be sensitive to social cues (p<0.03, Bonferroni corrected). Together, these findings are consistent with the discovery of a neural complex that integrates visual and language systems and is sensitive to the continuous exchange of socially meaningful face and eye signals across subjects during eye-to-eye contact.

References


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fNIRS-based methodology for assessment of tolerance for reduced brain perfusion in air force pilots using lower body negative pressure test

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The authors present a methodology for assessment of the reaction to reduced cerebral perfusion and orthostatic stress leading to ischemic hypoxia and reduced muscular tension which are frequently experienced by pilots of highly maneuverable aircrafts.

Studies were carried out using the system consisting of a chamber which generates a vacuum around the lower part of the body - LBNP (Lower body negative pressure) placed on the tilt table. The system contains in addition modules for ECG, EEG, EMG and blood pressure measurements for monitoring of physiological parameters. Above all, the system is equipped with the custom-made near infrared spectroscopy (NIRS) module allowing for continuous registration of cerebral oxygenation changes.

The authors developed the 6-channel NIRS system to assess the oxygenation of the cerebral cortex, based on measurements of diffusely reflected light from the near infrared region in reflectance geometry. The light is emitted into the subject’s head by the 12 LEDs which generate light at 735 nm and 850 nm wavelengths alternately modulated at frequencies of 10 Hz. The detector module allows to measure the attenuation of the light after it passed through a investigated tissue and consist of photodiodes with the developed and constructed active amplifying circuits. The emitting and detecting fiber bundles were fixed, on a subjects’ head, with the use of optodes’ holder combined with standard EEG cap. The optode holder, consisting of set of ports and fiber’s holders, was designed and 3-D printed. The source and detector pairs were separated by a distance of 3 cm. The measurements were carried out on a group of 38 active pilots and cadets of the Polish Air Force Academy in order to evaluate the dynamic changes in cerebral oxygenation. Measurement protocol consisted of two main parts:

1. Stepwise reduction of the pressure around the lower part of the body down to -100 mmHg.
2. At the pressure of -60 mmHg, stepwise tilting of the bed at a speed of 40°/sec; 30 seconds in each of 9 positions in the range from -20º to +40º (24 subjects) or from -20º to +70º (14 subjects).

The repetitive pattern of changes in the concentration of total hemoglobin (ΔCHbTot) in response to the rapid decrease of the pressure around the lower part of the body was observed. In some subjects, after the sudden drop of total hemoglobin concentration, it increased during the maintenance of a stable position of the body and pressure around the lower part of the body. For other subjects, ΔCHbTot signal remains at constant level during this period, or after a sudden drop of ΔCHbTot, its further decrease was noticed.

The differences of patterns of changes in signals of total hemoglobin concentration observed in different subjects may be related to differences in efficiency of compensation of ischemia’s effects by different subjects. The observed patterns of changes in hemoglobin concentration may be useful for proposing parameters allowing for evaluation of CNS response to sudden ischemia. The results of the measurements, based on the differences in behavior of the observed changes in concentrations of hemoglobin, allow to propose a potentially useful parameter for assessing predisposition of a subject to be a military of a pilot.
Posters
Friday, Oct 14th
NIR light has been widely used to study optical changes of the human brain tissue related to hemoglobin concentration. Baseline characterization of human head and brain optical properties is a more challenging but rather interesting application of NIR technology and it affects optical changes estimation. Separate determination of absorption and reduced scattering coefficients across the whole head is challenging. However, sufficiently far from the scalp surface, as in the brain structures, the effective attenuation coefficient (EAC), which is proportional to the geometric mean of absorption and reduced scattering coefficients, governs light propagation. We developed a procedure to map the EAC in each subject based on the light decay as a function of source-detector distance in an extended, high-density recording array. This procedure, which can be applied to standard continuous-wave optical recordings, yields maps with a resolution of a few cm. We present simulation and phantom data demonstrating that the procedure can accurately retrieve the EAC of a scattering medium and map its inhomogeneities. Moreover, application of the procedure to human fNIRS data indicates the importance of venous sinuses in determining regional variations in the EAC, a factor typically overlooked in the current literature.
Title: fNIRS case studies tracking L2 proficiency development

Presenters: TAURA, Hideyuki (Ritsumeikan University, JAPAN) and Amanda TAURA (Setsunan University, JAPAN)

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[abstract]

Six Japanese junior high school students learning English as a Foreign Language, were tracked in the first three years of their language development. Both linguistic and fNIRS data were collected three times after classroom learning had commenced – (1) in the seventh month (year one) (2) in the nineteenth month (year two) and (3) in the thirty-first month (year three). The English production data, which were elicited in both spontaneous spoken and written formats were analyzed in terms of accuracy, fluency, vocabulary, and writing skills. For the fNIRS data, a verbal fluency task was used to examine the brain activation in the Broca’s area.

In the linguistic analysis of the four sub-skills, one of the students examined showed a sudden boost in proficiency in (3) the thirty-first month as seen in Table 1.

<table>
<thead>
<tr>
<th>Time</th>
<th>Writing scores</th>
<th></th>
<th>Accuracy</th>
<th></th>
<th>Fluency</th>
</tr>
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<tr>
<td></td>
<td>Time</td>
<td>CC</td>
<td>CL</td>
<td>StC</td>
<td>*Quotient</td>
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<tr>
<td>7th month</td>
<td>4</td>
<td>6</td>
<td>3</td>
<td>64</td>
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</tr>
<tr>
<td>19th month</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>79</td>
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<tr>
<td>31st month</td>
<td>9</td>
<td>13</td>
<td>12</td>
<td>109</td>
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</table>

*90 < NS norm < 110 in Quotient

The timing of the improvement was echoed in the fNIRS data where a mixed-design analysis of variance was carried out using English letter fluency tasks, collected at the same three times as above, observing both brain hemispheres (F(5,68)=72.09, p<.001, Partial Eta Squared=.841). Post-hoc Bonferroni analyses revealed that the brain activation in Broca’s area stayed the same for the first two years of the experiment but increased significantly in the third year. In comparison, the homologous area in the right hemisphere showed an increasingly greater amount of brain activation each time. A hemispheric comparison carried out each of the three times disclosed that the left hemisphere was activated significantly more than its right equivalent in the first two years but no differences were apparent in the third year.

Thus, both linguistic and brain-imaging data showed a similar trend of a boost in proficiency and activation at the thirty-first month. Additional data collected from the remaining five students will be analyzed to examine whether the same results will occur.
The effect of physical exercise on memory, a NIRS study

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Regular physical exercise has been shown to benefit neurocognitive functions, especially enhancing neurogenesis in the hippocampus (Hillman, et al., 2008). However, little is known on the effects of a single exercise session on cognitive functions. To address this issue, we investigated the effect of acute exercise on memory.

Healthy young participants performed an associative memory task twice. Each visit consisted of an encoding, an exercise or rest and a test session. We used Near InfraRed Spectroscopy (NIRS) to track changes in oxygenated hemoglobin concentration over the prefrontal cortex, during the sport or rest and the test session. Our NIRS setup was composed of eight optodes forming seven channels. For six of the channels the emitters and receivers were 35mm apart, thus measuring effects in the brain. The remaining channel was a short separation channel with emitter and receiver 15mm apart to measure superficial layers only. We used Homer2 (Center of Biomedical Imaging, University of Harvard) to analyze changes in oxyHb: our processing stream allowed us to identify and exclude any motion artifacts as well as to subtract the effect of superficial layers, recorded by the short separation channel, from the rest of the channels.

We report a significant increase in performance in the memory task after exercise, compared to after rest. Memory improvement correlated with deactivation over prefrontal regions using NIRS during physical exercise, especially for the most difficult trials. This result may suggest that prefrontal deactivation during exercise might be involved in memory consolidation, an effect that has already been shown in sleep studies (Dang-Vu, et al., 2010).


Ambulatory diffuse optical tomography and multi-modality physiological monitoring system and applications

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1. Introduction: Ambulatory near infrared spectroscopy (aNIRS) and diffuse optical tomography (aDOT) enable a user to wear a NIRS device for noninvasive, continuous monitoring or imaging of tissue oxygenation and hemodynamics with minimal restrictions on their activities. Wearable devices are rapidly expanding from the traditional electrocardiography (ECG) and electroencephalography (EEG) monitoring to pulse oximetry, blood pressure, and various metrics of activity and exercise. NIRS is distinct from these other modalities in that it can monitor tissue blood oxygenation and oxygen utilization. These are particularly useful capabilities for functional brain and muscle assessment during and following tasks or exercise, and to evaluate certain disease states or recovery processes1,2.

2. Method: We developed a novel prototype aDOT system, called NINscan-M, capable of ambulatory tomographic imaging as well as simultaneous auxiliary multimodal physiological monitoring. Powered by 4 AA size batteries and weighing 577 grams, the NINscan-M prototype can synchronously record 64-channel NIRS imaging data, 8 channels of ECG/EMG/EEG or other analog signals, plus force, acceleration, rotation, and temperature for 24+ hours at up to 250Hz. We describe the system’s design, characterization, and performance characteristics.

3. Results and Discussion: The NINscan-M device is pictured in Fig 1A. With an auto-gain design, it can be operated with a single on/off switch. Tomographic muscle imaging data were acquired at 25 Hz during examples of isometric, cycle ergometer, and free running ambulatory exercise (Fig 1B,C), as well as during brain activation tasks. Device sensitivity up to 56 mm source-detector separations supported tomographic imaging up to 20 mm in depth. The results demonstrate a new, multi-modal (Fig 1D,E) tool for muscle and brain physiology studies and clinical assessment.

Could “Corsi Block Tapping test” be considered a real working memory task?

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Introduction. The Corsi Block Tapping (CBT) is a well-known neuropsychological non-verbal task that assesses the visuo-spatial working memory (WM). The CBT requires the storage and reproduction of the spatial locations of visual stimuli sequences. This ability is defined as “memory span forward”.

Beblo (2004), raising the issue that “memory span forward” is a lacking indicator of WM, developed a new paradigm based on the original CBT: the Block-Suppression-Test (BST). The BST requires a higher level of executive control to actively inhibit distractors which appear together with target stimuli. Toepper (2010) proposed a CBT/BST computerized version highlighting, by fMRI, an involvement of ventrolateral/dorsolateral prefrontal cortex (VLPFC/DLPFC) and the parietal cortex. The aim of the present study was to assess, by fNIRS, if the CBT and the BST are real working memory tasks which involve VLPFC/DLPFC.

Methods. Thirty-eight right-handed healthy volunteers (age: 23.9±3 y; level of education: 14.8±1.7 y) were asked to perform a CBT/BST computerized version and a control task (CT). A 20-channel fNIRS system (including 4 short-separation channels, SS) was employed to measure the PFC hemodynamic response. The CBT and BST can be subdivided into an encoding phase (target stimuli presentation) and a response phase (target stimuli reproduction). During the encoding phase, twenty sequences of visual stimuli were randomly presented to subjects. The sequence length was varied from three to six blocks. The location of the target blocks was changed either in the CBT or in the BST, while the distractor blocks were simultaneously presented only in the BST. During the response phase, subjects were asked to reproduce the sequence by making three to six (depending on sequence length) sequential decisions between two alternative response options. The CT was a simple motor task that required pressing a button, without any memory involvement.

Pre-processing fNIRS data. Motion artefacts were corrected by applying Wavelet motion correction method implemented in Homer2. In order to correct fNIRS signals for physiological and surface noise contamination, a “general linear model” approach was adopted (regression of SS channel signals with greatest correlation).

Results and Discussion. To the best of our knowledge fNIRS has never been used to monitor PFC hemodynamic response during CBT and BST. In this study, no significant activation was found in VLPFC/DLPFC in response to CBT, BST and CT execution. This could be reasonable for CBT which requires the maintainance of positional information involving parietal brain regions rather than the VLPFC. It’s still unclear why DLPFC was not activated during BST considering that for its execution the inhibition control of irrelevant information is required. Therefore, these results, obtained from a consistent sample size, suggest that CBT and BST couldn’t be considered as elective working memory tasks.

References: 
THE ROLE OF THE TEMPORO-PARIETAL JUNCTION IN IMPLICIT MENTALIZING

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Autism spectrum disorder (ASD) is a pervasive neurodevelopmental disorder, assumed to be caused by brain abnormalities appearing very early in life, which is characterized by qualitative impairments in social interactions and communication. A deficit in ‘Theory of Mind’ (ToM) or ‘mentalizing’, which is the ability to attribute mental states to oneself and others, has been argued to play a causal role in ASD.\textsuperscript{1} Previous studies on ToM have not been unequivocal because children and adults with high-functioning autism (HFA) often do well on standard explicit mentalizing tasks, so preserved ToM might be due to compensatory strategies. Different results might be expected when ToM is tested implicitly, which is less susceptible to these strategies and better parallels daily life. Recent findings from fMRI studies suggest a crucial role for the TPJ (temporo-parietal junction) in implicit ToM\textsuperscript{2} and earlier research reported that impaired TPJ function may play a crucial role in the pathophysiology of ASD.\textsuperscript{3}

In the first part of this project, we want to investigate if we can localize the TPJ with functional Near-Infrared Spectroscopy (fNIRS) using a well-validated ToM Localizer\textsuperscript{4} and an implicit ToM task (Buzz Lightyear task) in a group of 25 typically developed adults. The Buzz Lightyear task is recently developed in our lab and measures mentalizing by means of an implicit measure (ball detection time). Preliminary findings will be presented, as data collection is still ongoing.

In the second part, the aim is to evaluate implicit ToM and activation in the TPJ in children with HFA compared to typically developing children, using fNIRS. We hypothesize that children with HFA have an implicit mentalizing deficit, resulting in a deviant reaction time pattern, accompanied by less TPJ activation, relative to controls.

Lateralization and Cerebral Hemodynamics at Rest in Toddlers at Risk for Language Delay

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Symptoms of language delay and autism typically emerge in the toddler years, when brain imaging is especially challenging due to 1) intolerance of imaging apparatuses and 2) effects of motion on data quality. It is therefore difficult to study early brain differences in children with emerging language delays and autism, particularly in awake toddlers. The aim of our study is to show whether changes in Oxy and DeOxy Hemoglobin measured by fNIRS in toddlers with and without language delays, while passively watching engaging videos, can predict developmental outcomes, including both autism diagnosis and continued language delay.

We used a continuous wave fNIRS system (fNIRS Devices LLC, MD), with 16 source-detector pairs covering the frontal lobe. We focus on two aspects of resting cerebral hemodynamics—lateralization index and oxygenation variability—which were measured in the prefrontal cortex in toddlers ages 18-36 months. Toddlers also completed comprehensive diagnostic and developmental evaluations, including administration of the Autism Diagnostic Observation Schedule (ADOS-2) and the Mullen Scales of Early Learning (MSEL). We investigated hemodynamic variation by hemisphere by calculating a lateralization index (i.e., Left HB-Right HB). We also completed the Oxygenation Variability Index (OVI), a measure of cerebral autoregulation (Anderson et al., 2014). In this sample of 42 toddlers, 84% tolerated the NIRS equipment. This rate did not differ by age group or by diagnosis at study entry. This supports general feasibility of the fNIRS method in toddlers, including those with emerging delays. After accounting for data lost to technological error and changes in the study protocol, the final sample within which we analyzed lateralization index and oxygenation variability included 8 toddlers at risk for language delay along with 20 toddlers with typical development. Regarding cerebral hemodynamics, toddlers with language delay (including those with autism diagnoses at study outcome) showed more unilateral activation when compared to typically developing toddlers, as indicated by the absolute value of each toddler’s lateralization index. In other words, the degree to which oxygenation levels varied between left and right hemispheres was associated with early language delay (F=6.76, p=.01). This is consistent with findings regarding lateralization in sleeping toddlers with autism via fMRI (Eyler, Pierce, and Courchesne 2012) and lateralization of EEG phase coherence to face stimuli in infants at risk for autism (Keehn et al., 2015). Also, differences in lateralization were associated with cognitive ability across the total sample (r=-.4, p=.03) and within the typically developing group (r=-.52, p=.02). In addition, toddlers with language delays had a lower OVI across both hemispheres, which continued to be significant after accounting for group differences in overall cognitive ability (t=-2.97, p<.01). This could signal differences in physiological processes related to motility of oxygenated blood in the cerebrum in toddlers with language delay. These findings indicate that measuring hemodynamic properties of the resting brain with fNIRS may prove feasible and useful in predicting and understanding language delays and autism in toddlers.
Optical module with SoC for wearable fNIRS system

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System-on-chip (SoC) incorporated light-emitting diode (LED) and avalanche photodiode (APD) modules were developed to reduce the size and improve the usability of a wearable fNIRS system [Fig. 1]. SoC has a microcontroller unit and programmable circuits. The time division method and the lock-in method were used for separately detecting signals from different positions and signals of different wavelengths, respectively. Each module autonomously worked for this time-divided-lock-in measurement with a high sensitivity for haired regions. By supplying +3.3 V of power and the base and data clocks, the LED module outputted both 730 nm and 850 nm of lights, whose amplitudes were modulated in each lock-in frequency generated from the base clock, and the APD module provided the lock-in detected signals in the data rate.

SoC provided many functions, e.g., auto-power-control of LED, auto-judgement of detected power level, auto-gain-control of the programmable gain amplifier (PGA), and temperature compensation of APD sensitivity. The controller had only two tasks: (1) writing parameters in the I2C buffer of each module for controlling it, (2) reading data from the I2C buffer of each module. The full digital interface was helpful to easily design the new high-sensitivity system.

The number of modules and the arrangement of modules can be adaptively changed by connecting the modules in the daisy chain and setting the parameters dependent on the probing position. Therefore, we can easily realize a variety of arrangements of them including a freely exchangeable one.

![Fig. 1 Schematic of optical modules. All analogue circuits are built-in. MCU and HV represent Micro Controller Unit and High Voltage Supplier, respectively.](image-url)
GENDER DIFFERENCES IN FRONTAL LOBE HEMODYNAMIC RESPONSE DURING COGNITIVE TASK PERFORMANCE

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Executive functioning is one of the main traits of higher-level cognition in humans. However the mechanism of neurovascular coupling is far from being fully understood. The aim of this work is to compare gender differences in hemodynamic response obtained during computerised and clinically used Wisconsin Card Sorting Test (WCST), in order to assess normal subject variability.

The WCST was performed with equal number of healthy male and female in total n=30, 21.6±2.6 years old, without diagnosed mental or cardiovascular disorders. All participants had an average 12 years of education. No significant differences in WCST performance were obtained. Results collected during experiment show quantitative and qualitative differences in PFC activation related to the gender. This may explain the disagreement on this test activated brain areas comparing different studies (Nyhus and Barceló 2009).

Possibility of hemispheric activation differences during cognitive task performance has been mentioned by authors who represent their results collected from healthy subjects’ with EEG, fMRI, PET and recently fNIRS studies. Our results support these findings.

Haemodynamic Response in Diabetes: An fNIRS Study of the Visual Cortex

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Purpose: Functional near-infrared spectroscopy (fNIRS) is a non-invasive neuroimaging technique capable of measuring cortical haemodynamic changes. The aim of this study was to use fNIRS to investigate the haemodynamic response of the primary visual cortex to visual stimulation in diabetes.

Methodology: We used a two-channel frequency-domain fNIRS oximeter (OxiplexTS, ISS, Champaign, IL) to record the oxyhaemoglobin [HbO] and deoxyhaemoglobin [Hb] chromophore concentrations in response to visual stimulation at occipital locations O₁ and O₂ over the primary visual cortex. Utilising a slow event-related design, participants viewed binocularly at a distance of 1 m a full field pattern reversal checkerboard (check size= 30 min of arc; temporal frequency= 7.5 Hz; contrast= 100 %). Visual stimulation comprised 60 s baseline (luminance-matched grey screen) followed by 7 duty cycles (30 s checkerboard; 30 s grey screen). Participants were optically corrected during visual stimulation. The diabetic group (n= 11, mean age= 69 ± 20 years, M:F= 6:5) and control group (n= 12, mean age= 71 ± 23 years, M:F= 7:5) were matched for age (p= 0.83) and gender (p= 0.86). Prior to the study, participants’ Hb1Ac level, a measure of plasma glucose concentration, was measured (A1cNow® System, PTS Diagnostics, Indianapolis, IN).

Results: Intraclass correlation coefficient (p) analysis revealed a moderate interhemispheric relationship between O₁ and O₂ during checkerboard stimulation (p[HbO]= 0.67; p[Hb]= 0.66) and grey screen (p[HbO]= 0.63; p[Hb]= 0.65). Moreover, we found a strong interhemispheric relationship for the change in chromophore concentration between checkerboard stimulation and grey screen (ρ₃[HbO]= 0.78; ρ₃[Hb]= 0.72). As such, further analysis considered an average ‘occipital’ response. We found a characteristic increase in [HbO] (p< 0.001) and decrease in [Hb] (p< 0.001) in response to checkerboard stimulation compared to baseline (Figure 1). There were differences in the change in chromophore concentration between diabetic and control groups (p< 0.05), with the diabetic group having a greater increase in [HbO] (p< 0.05) and greater decrease in [Hb] (p< 0.05) to checkerboard stimulation than controls. We found that the change in [HbO] was strongly positively correlated with participants’ Hb1AC level (r= 0.601; p< 0.01), and that the change in [Hb] was moderately negatively correlated with Hb1Ac level (r= -0.522; p< 0.05) (Figure 2).

Conclusions: Our data suggest that fNIRS can be used as a quantitative technique to measure the haemodynamic response to checkerboard stimulation in diabetes. We have found that diabetic individuals have a larger haemodynamic response (reflected as increased [HbO]) to checkerboard stimulation than do age-matched controls. Moreover, this increase in [HbO] is correlated with Hb1Ac level.

**Fig 1. Chromophore concentrations (normalised around baseline)**

Diabetics’ [HbO] values are in dark red (n=11); controls’ [HbO] values are in light red (n=12); diabetics’ [HbO] values are in dark blue (n=11); controls’ [Hb] values are in light blue (n=12). Error bars= ±1 SEM.

**Fig 2. Relationship between Hb1Ac and change in chromophore concentration**

[HbO] values are in dark red (n=23); [Hb] values are in dark blue (n=23).
Hemispheric differences of hemodynamic responses during visual stimulation with graded contrasts

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Retinotopy is the fundamental mapping principle of visual input from retina to visual cortex [1]. It has been confirmed that visual stimuli had stronger responses over the contralateral visual cortex. Moreover, owing to the functional asymmetry of hemispheres of the brain, the spatial resolution and contrast sensitivity have been found asymmetric under stimuli in distinct visual fields [2]. Because visual stimuli with various contrasts presented significant advantages of investigating ways in which the visual information is organized and encoded, they have been employed in several studies to probe the relationship between the stimulus contrasts and corresponding hemodynamic responses. However, most of those studies concentrated on either distinct stimulus contrasts in full visual field or distinct visual fields with constant contrast. As far as we are concerned, the hemispheric differences in hemodynamic responses under distinct stimuli with graded contrasts remain unknown.

In this paper, the retinotopic mapping and the hemispheric differences are investigated using functional near-infrared spectroscopy (fNIRS). Hemifield checkerboard reversal stimuli with graded contrasts levels (1%, 10%, and 100%) are randomly presented to five healthy participants to compare the lateralization and magnitude of the hemodynamic response corresponding to each stimulus. As shown in Fig. 1, the functional activations are significantly stronger in the contralateral hemisphere. The amplitudes of the oxygenated hemoglobin (HbO) concentration at the three contrast levels are also significantly different from each other. Moreover, the HbO concentration increases with the increase of the contrast level. It should be noted that the changes of HbO concentration are higher for the left field stimulus than the right field stimulus. A possible explanation of this horizontal asymmetry lies in the superiority of the left visual field in visual spatial attention.

Fig. 1 a) Experimental paradigm. b) The amplitudes of the HbO concentration over the contralateral hemisphere as a function of the stimulus contrast levels; error bars show the SE. c) The group-averaged spatial distribution maps of the HbO concentration changes at different contrast levels: 1%, 10%, and 100%, in left and right visual field, respectively. The color bar indicates the changes of HbO concentration in μmol/l. Insets indicate stimulus types.

Reference:
Influence of early language experience on brain activation to language: A study of hearing infants with Deaf mothers

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Hearing infants with Deaf parents (HoD) have a very different early experience of speech and language to that of hearing infants with hearing parents (HoH). When the parents’ dominant language is a signed language, such as British Sign Language (BSL), their speech and language input differs from that of HoH infants. First, HoD infants have reduced exposure to spoken language in the prenatal and early postnatal period. Many deaf signing individuals use speech to communicate with hearing people, but the extent to which they actually ‘voice’ this speech and produce sound, as opposed to silently mouth, is extremely variable. Second, the postnatal experience of HoD infants includes both a language in the visual modality, e.g. BSL, and one in the auditory modality, e.g. English, which can be used by the parents, as well as by hearing relatives and the rest of the hearing community. This study investigates the impact of early language experience on brain representation for language. Since HoD individuals grow up learning two languages, they are compared to HoH individuals growing up learning two spoken languages. Three groups of hearing infants (4-7 months) were recruited: 30 infants from a monolingual English speaking family, 30 infants from a bilingual family in which two spoken languages are frequently used by the parents, 30 infants with a Deaf mother for whom BSL is the dominant language.

Functional near infrared spectroscopy (fNIRS) was used to study brain activation during spoken and sign language perception. Sentences were presented in infant-directed English and French (familiar and unfamiliar spoken languages), as well as in BSL and French Sign Language (familiar and unfamiliar sign languages). Results suggest strong activation to spoken language in the temporal cortex in all groups, which appears more left lateralised in HoH infants than HoD infants. Activation to sign language was found in a more restricted area of the temporal cortex. These results suggest an influence of early language experience on brain representation for language and will be discussed in relation to the particular experience of each group.

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Classifying the Brain’s Functional Status in Verbal Fluency Task: EEG+fNIRS

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**Introduction.** We performed verbal fluency task (VFT) studies with eight human subjects in order to determine the ability of multimodal data to discriminate between distinct functional brain states. VFT has been used to investigate the frontal and temporal lobe activation and relative impairments in diseases such as mild Traumatic Brain Injury \(^1\). Our methods based on multimodal data were able to classify functional brain states more accurately than those based on unimodal data.

**Methods.** We created a basic sensor unit consisting of a module made of three components: a thin plastic holder, NIRS optodes and an EEG electrode as in our previous work \(^2\)–\(^4\). Nineteen triplet holder modules were attached to subjects’ scalp at the standard International 10-20 sites. Data were recorded with commercially available EEG and fNIRS equipment (NIRScout 24x32, NIRx Medizintechnik GmbH, Germany and the FDA 510k approved microEEG, BioSignal Group, US). We used a block design with a 30 s resting period, followed by a 30 s task activation, another 30 s resting period, and a 30 s control period. Each subject executed three consecutive blocks. During the resting state, the subject was instructed to keep her eyes closed and relax without focusing on anything particular while not falling asleep. During the Task period the subject was instructed to name words from a randomly chosen category (e.g. animals, fruits, flowers). Neural (EEG), hemodynamic (fNIRS), and neurovascular (EEG+fNIRS) features were extracted from non-overlapping time windows of data. Feature space was constructed by converting each type of channel based time-series into a set of distributed activity maps by principal components analysis (Fig. 1C). Time windows were classified using linear Support Vector Machine and cross validated (Fig. 1B).

**Results.** The accuracy of EEG+fNIRS was drastically greater than that of the individual systems alone (Fig. 1A). Furthermore, principal components allowed better segregation of relevant vs. noisy signals into distinct components and aided the physiological interpretation of those features that are most descriptive.

**Conclusion.** Our results were consistent with previous reports of synergistic cooperation among different types of signals \(^5\). This increase in accuracy is thought to be a consequence of the relatively greater scope of underlying physiological processes accessed by multimodal data, exemplified by their respective activation maps, Fig. 1C) and the fact that the quantification of neurovascular coupling, as an additional source of information, is accessible only with the concurrent use of EEG and fNIRS.

**References**


![Figure 1](image-url)

**Figure 1** Analysis outline and results of automated classification of Task v Rest. Verbal Fluency Task with eight subjects. (A) Accuracy of the classification (\(\Delta T=15\) s). The maximum number of features for each system is different. Shaded regions indicate the variability of 10-fold cross validation. (B) Flowchart of the analysis steps. (C) Examples of Principal Components from each subsystem.
Diffuse optical tomography by using multi-directional sources and detectors

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Diffuse optical tomography (DOT) is an advanced imaging method used to visualize the internal state of biological tissues as 3D images [1]. However, current continuous-wave DOT requires high-density probe arrays for measurement (less than 15-mm interval) to gather enough information for 3D image reconstruction, which makes the experiment time-consuming. In this study, we propose a novel DOT measurement system using multi-directional light sources and multi-directional photodetectors instead of high-density probe arrays (Fig. 1) [2]. We evaluated this system’s multi-directional DOT through computer simulation and a phantom experiment. In these experiments, we generated a localized absorption change inside turbid media, performed DOT, and calculated the localization error of the estimates (Fig. 2). In solving inverse problems, we used our previously proposed hierarchical Bayesian estimation algorithm [3,4]. From the results, we achieved DOT with less than 5-mm localization error up to a 15-mm depth with low-density probe arrays (30-mm interval), indicating that the multi-directional measurement approach allows DOT without requiring high-density measurement.

Fig. 1. Conceptual diagram of multi-directional measurement.

Fig. 2. Example of 3D reconstruction image of phantom experiment. (a) True absorber position. (b) Reconstructed image.

Development of a combined fNIRS, EEG and tDCS system for real time brain stimulation and monitoring during rehabilitation

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Functional near-infrared spectroscopy (fNIRS) systems are widely used for the functional brain imaging because they are portable, noninvasive, low cost, and easy to use [1-3]. Transcranial direct current stimulation (tDCS) is one of the noninvasive electrical brain stimulation techniques that are used to modulate the cortical neural activity. During such modulation, the electric potentials are generated from the modulated brain tissues which can be recorded from the scalp using electroencephalogram (EEG). Respective neural activity is closely related to the cerebral blood flow that supplies glucose to the activated brain tissues. fNIRS is widely used to capture the hemodynamic response of the neural activity. Our aim is to develop a combined fNIRS-EEG system to monitor the brain activation in real time during the tDCS brain stimulation.

As a first step to achieve our goal, we have developed a new wireless fNIRS system compatible with EEG, and also developed a pad-type tDCS with variable current limits. Our wireless fNIRS system is composed of a microcontroller (dsPIC33FJ256MC710A, Microchip technologies, U.S.A.), a flexible probe, tri-wavelength light emitting diodes (L735/805/850-40B32, Epitex Inc., Japan), photodiodes (S1223-01 Si Photodiode, Hamamatsu Photonics, Japan), WiFi communication module (RN131 EK, Roving Network, U.S.A.) and battery. The developed tDCS system can generate the current in the range of 0.8 ~ 2.2 mA. To test the functionality of the systems, fNIRS data was recorded before and after the tDCS stimulation. The results of this study show that the anodal tDCS excites the neurons in the region of interest and this excitability is monitored using the fNIRS system.

Figure 1. Complete developed system: (a) fNIRS control and operation circuitry, (b) flexible probe with LEDs and Photodiodes, (c) tDCS system

Three-dimensional blood flow imaging in small animals with speckle contrast optical tomography

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Objectives: We demonstrate a new method for high-density, three dimensional, in vivo, imaging of cerebral blood flow (CBF) in small animals. This method is based on speckle contrast optical tomography (SCOT) [1, 2].

Methods: Speckle contrast is defined as the ratio of standard deviation to the mean intensity, which allows blood flow measurement, [2]. Continuous laser diode (L785P090, Thorlabs) was focused to spot size of 200µm with power of 3mW on the surface of the skull. The source was scanned over skull surface, with the total of 5x5 source positions. Images were collected with CCD camera (scA640-120fm, Basler) with the exposure time set at 5ms.

Male mice, four months old (C57/BL6, 30g), were placed in stereotaxic frame, anesthetized with isoflurane, and scalp was removed. Baseline measurement were acquired followed by localized photothrombosis in nine animals. For photothrombosis a photosensitizing dye (Rose Bengal) was injected through the intraperitoneal cavity. The activation of the dye was done with white light lamp in the right hemisphere. After waiting for the dye to clear from the body, perturbation measurement was acquired. Tomographic image was compared with image obtained from 7T MRI(Bruker, BioSpin, Germany) T2 multi-slice multi-echo (MSME) map.

Results: In the Fig. 1(a) one source position with the surrounding detectors is shown. The source was scanned over skull surface, with the total of 5x5 source positions. Images were collected with CCD camera (scA640-120fm, Basler) with the exposure time set at 5ms. Male mice, four months old (C57/BL6, 30g), were placed in stereotaxic frame, anesthetized with isoflurane, and scalp was removed. Baseline measurement were acquired followed by localized photothrombosis in nine animals. For photothrombosis a photosensitizing dye (Rose Bengal) was injected through the intraperitoneal cavity. The activation of the dye was done with white light lamp in the right hemisphere. After waiting for the dye to clear from the body, perturbation measurement was acquired. Tomographic image was compared with image obtained from 7T MRI(Bruker, BioSpin, Germany) T2 multi-slice multi-echo (MSME) map.

Conclusion: We presented SCOT as a new method for non-invasive, high-density tomographic reconstruction of deep tissue CBF in small animals. We will show statistical results and quantitative comparison to MRI findings from a group of mice.

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References
Monitoring cerebral hemodynamic change during transcranial ultrasound stimulation using near infrared spectroscopy

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Brain stimulation plays an important role in general neuroscience. It is also shown as an effective technique for treating some neurological disorders. The stimulation is realized by various techniques, but most of them are either invasive or have poor spatial resolution. Recently, ultrasound stimulation has been used for noninvasive brain stimulation with spatial resolutions of up to several mm [1]. The mechanism of ultrasound stimulation is still unclear, and further investigation is needed. Ultrasound stimulation has been combined with fMRI and PET, to observe brain functionality during sonication [2]. However, the use of fMRI and PET is too costly and bulky for animal studies. Thus, we propose to apply near infrared spectroscopy as a noninvasive, low cost, portable technique to observe cerebral hemodynamics during transcranial ultrasound stimulation.

Two adult male mice (C57BL/6, 37g) were used in this study. The mice were anesthetized with an intraperitoneal injection of ketamine/xylazine cocktail and fixed to a stereotaxic frame to minimize motion artifact. The NIRS system consisted of two laser sources with (773 nm and 838 nm) and a spectrometer as light detector. Hemodynamic changes were monitored by placing 400 µm core diameter optical fibers onto the mouse head with a source-detector separation of 1 cm. The signal was acquired at a sampling rate of 20 Hz. Oxy- and deoxyhemoglobin concentration changes were calculated using the modified Beer-Lambert law. Transcranial ultrasound stimulation was achieved using a low frequency focused acoustic wave from a commercial ultrasound transducer. We used 350 kHz with spatial peak pulse average (Isppa) and spatial peak time average intensity (Ispta) of 0.23 W/cm² and 64.5 mW/cm² respectively.

The NIRS signal was recorded during ultrasound stimulation which was able to elicit a motor response in the mouse. We believe the multi-location measurement of cerebral hemodynamics may provide critical information to reveal the underlying mechanism of ultrasound-based brain stimulation.

Keywords— NIRS, hemodynamic, ultrasound, brain stimulation.

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REFERENCE

Miniaturized CW NIRS for integration and hybridization with mobile EEG / ECG / EMG and Accelerometer

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Introduction: The increasing computational capacity and miniaturization of modern microprocessors in wearable computers and smartphones pushes the trend towards mobile body sensors and telemedicine. In contrast, brain activity assessments and Brain Computer Interfaces (BCI) are only slowly leaving static, lab based domains. At the same time, an increase in hybrid approaches to improve overall performance and robustness by combining several modalities (e.g. hybrid BCI [1]) can be observed. To contribute to advance hybrid neurotechnology further out of the lab, we present solutions to significantly miniaturize and mobilize CW functional Near Infrared Spectroscopy (fNIRS) and hybridize it with EEG, ECG, EMG and accelerometer technology.

Device and Performance: We designed a highly miniaturized next-generation device for Mobile (Bluetooth) Modular Multimodal Biosignal Acquisition (M3BA = “MEBA”) [2], integrating improved miniaturized stand-alone emitter/detector units from our published openNIRS design [3] into a high performance electrophysiological acquisition framework. The openNIRS emitter and detector units are based on Epix L750/850-04A multi wavelength LEDs and BurrBrown OPT101 Si photo diodes with integrated trans-impedance amplifiers, and provide current regulation (stabilization), square wave modulation for phase sensitive detection and programmable emission intensities and detection gains. Also, they enable a low supply voltage, safe and highly miniaturized design. In a novel hybrid shared acquisition approach, the Texas Instruments ADS1299 integrated EEG Analog Front End (AFE) with its outstanding electrical characteristics (e.g. 1μVpp input noise), and a high performance microcontroller were used for the simultaneous acquisition of EEG- and NIRS, enabling electrical crosstalk optimization (current path, common ground and shielding optimization) and phase sensitive demodulation in the digital domain. The ultra-low noise and exceptional linearity performance were amongst others demonstrated by optical and electrical phantoms and in-vivo tests at PTB [2].

![Figure 1: M3BA Module](image)

The resulting M3BAs are fully stand-alone battery powered modules, each providing 6 EEG/EMG/ECG channels (@500Hz/24Bit), 4-6 fNIRS channels (@16,66Hz/24Bit, 750/850nm LED) and a 3-axis accelerometer and can be combined to increase the channel count.

Discussion and Outlook: M3BA is a new customizable research tool designed for the use in multimodal mobile fNIRS-EEG applications in and outside the lab and is aimed to facilitate a better identification and use of common and complementary information in multiple (bio-)signals. By this, we hope to improve the robustness against non-stationarities and artifacts in our signal analysis and machine learning based approaches. The use of multiple modalities measured by miniaturized mobile hardware could contribute to bringing (hybrid) neurotechnology further out of the lab and into real-world scenarios – clinical or non-clinical, where potential users can benefit from it the most.

References
The study of prefrontal cortex activation with fNIRS during video gaming

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In this study, we investigated the variation of hemodynamic signals in prefrontal cortex during video game using functional near-infrared spectroscopy (fNIRS) [1]. To assess the effects of video gaming play on concentration of oxy-hemoglobin [HbO2] and deoxy-hemoglobin [Hb], we measured these concentrations using fNIRS in 60 normal volunteers (male), age range 16-22 years. We used a low cost homebuilt LED-based fNIRS (wavelengths of 730-850 nm, and a SD of 3 cm) calibrated with dynamic four-layer silicone-resin phantom. For all participants, the video game Mortal Combat as a famous violence game was played. After a 10 seconds rest, the subjects were asked to play for two rounds. In first round, each subjects took a seat in front of 42 inch monitor with an approximated distance of 1.5 m. A mirror in front of this monitor was located to reflect images of Mortal Combat. After 60 seconds, this participant was asked to rotate and look in mirror and continue to play video game (as second round). Due to high level of violence of this video game and need to rapid responses of participant, the motion artifact strongly affected on fNIRS signals. In addition, the rotation of subject to look in mirror was an excessive motion artifact after 70 seconds that it can be easily seen in unprocessed plots (Fig. 2 (a)). To remove motion artifact, first derivation of measured signal with analysis of variance can be used to indicate the location of motion artifacts. Then an averaging over some nearest neighborhoods can be used to remove this artifacts. To evaluate the ability of this method, we could remove the motion artifacts from a simulated signal (Fig. 1). As shown in Fig. 2, the motion artifacts are omitted from hemodynamic signals. As we expected the variation of [HbO2] and [Hb] in second round are more than first round [2].

Fig.1. Removal motion artifact from simulated signal. Raw signal is colored green and processed signal is indicated by red color.

Fig.2. Changes in oxy-hemoglobin and deoxy-hemoglobin during video game task performed by a subject with motion artifact (left) and processed plot (right).

References:

A portable, multi-channel fNIRS system for prefrontal cortex: Preliminary study on neurofeedback and imagery tasks

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Cerebral hemodynamic measurements can be thought as an indirect measurement of the brain’s response to various stimuli. In this study, we developed a portable, multidistance prefrontal fNIRS system to measure cerebral hemodynamics. The system consisted of 12 light sources and 15 detectors for a total of 108 channels, with a sampling rate of 5 Hz (Figure 1(A)). The wavelengths of the light source are 780nm and 850nm, alternating sequentially. ATxmega128A1, an 8bit of Micro controller unit (MCU) with 200-4095 resolution, along with a Matlab interface was utilized for data acquisition.

In addition to developing a multidistance fNIRS system, we also show significant activation from the prefrontal area of the brain during motor imagery tasks for five subjects. We performed left and right finger tapping motor imagery tasks that produced statistically significant changes of oxyhemoglobin concentrations in the contralateral prefrontal area (Figure 1(B)). Our results show that it is possible to observe hemodynamic activity during motor imagery tasks in the prefrontal area, rather than solely in the motor cortex. We were able to localize the hemodynamic response in the contralateral hemisphere by implementing neurofeedback training, during which their real-time hemodynamic response was given to the participating subject. We tested neurofeedback with sham feedback, and did not see the same localization of the hemodynamic response as with real hemodynamic feedback (Figure 1(C)).

Our portable fNIRS system may be useful in non-constraint environments for various clinical diagnoses. In addition, our motor imagery results show the possibility of obtaining relevant hemodynamic signal from the prefrontal area, which is significantly easier to access on a subject than the motor cortex. Neurofeedback of our NIRS signal proved to be an effective tool in localizing the response in the contralateral hemisphere for the subject and may be a useful tool for clinicians in rehabilitation.

Figure 1 – (A) The 108 channel NIRS probe used for this study. (B) Task averaged left and right hand motor imagery task for one subject, with prominent activation in contralateral hemisphere. (C) Task averaged left hand motor imagery task for one subject with neurofeedback and sham feedback. Sham feedback produces a less localized response in the contralateral hemisphere.
Prefrontal activation differences during social vs. non-social prospective memory in a naturalistic setting.

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Prospective memories (PM) that have a pro-social aspect seem to have a special status for humans. We rate them as particularly important, and are more likely to remember to carry them out. However, it is difficult to investigate the neural substrates of social intentions in a typical neuroimaging environment since the participant is separated from other people, and there are constraints on voluntary movement which alter the ways people behave. Accordingly, we used wireless fNIRS to contrast prefrontal cortex activations during the maintenance and execution of intentions relating to pro-social (Figure, panel C) vs. non-social cues (Figure, panel B) in a naturalistic environment. The experiment was conducted outside, on a typical London street, with participants free to move and act as they would normally (Figure, panels A-C). We considered as notable only those contrasts where independent significant changes (p<0.05) were obtained for both oxy- and de-oxymyoglobin concentration, and that these were mirror relations to each other. Relative to walking and observing the environment, prospective memory demands significantly increased HbO₂ with corresponding HHb change in a wide number of medial and lateral PFC regions. Most critically however, the social PM condition saw a significant increase in HbO₂ (with significant decrease in HHb) in lateral prefrontal cortex regions (Figure, panel F, top is HbO₂, bottom is HHb). These results suggest that the advantage for pro-social prospective memory is reflected in differences in activation within prefrontal cortex, and that this can be detected using fNIRS even in naturalistic settings.
Exploring brain functional connectivity in resting state and during sleep using functional near infrared spectroscopy

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Abstract—Brain functional networks were investigated using whole head fNIRS in resting and sleeping states. Three networks including frontal-parietal, auditory, and visual networks were found in both states.

I. Introduction
What happens in the brain when people are sleeping? Why during sleeping, people do not respond to the external stimulations, such as sound or smell? Up to date, there are plenty of studies, which investigate the brain during sleeping using many different techniques. However, the underline mechanism of the brain during this state is still unclear. In order to answer these questions, we measured fNIRS signal in resting and sleeping states to calculate and compare the functional connectivity in two states.

II. Materials and methods
Eighteen healthy subjects (mean age: 24) were recruited from University of Texas at Arlington (UTA) with the approval of the Institutional Review Board at UTA. Before participating in the experiment, all subjects signed in a consent letter. NIRS optodes from LABNIRS system (Shimadzu, Japan), with 40 sources and 40 detectors, making 133 channels, were placed on subject’s whole head. The experimental protocol consists of resting and sleeping states. During resting state, subject was asked to relax, stay still, and stare at a blank computer screen for five minutes. To confirm the sleeping state of the subject, additional EEG signal was used. fNIRS data were recorded for ten minutes when EEG signal showed the sign of sleep. Hemodynamic changes were preprocessed to remove motion artifacts and physiological noises. Noise free signal was used to calculate temporal correlation between 133 channels. Correlation coefficient matrix were then used to find brain functional network.

III. Result and Discussion
Among 18 subject, during sleeping state, there were 2 subjects could not fall asleep, 5 subjects woke up during experiment, and 11 subjects slept well. The data in both resting and sleeping states of 7 subjects, who could not sleep throughout the experiment were excluded. The correlation matrix of other 11 subjects were calculated and compared between two states. From the correlation coefficient matrix of 11 subjects, we found three groups of channels, which have high correlation coefficient (fig. 1) in both states. These groups cover fNIRS channels in frontal and parietal areas (frontal-parietal network), auditory areas (auditory network) and visual area (visual network).

[Fig.1] Correlation coefficient matrix from 133 channels in resting and sleeping states

VI. Conclusion
We were able to find three common networks, frontal-parietal, auditory, and visual networks in both states. Further analysis should be done to find the difference between two states’ network.

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The complex brain: characterizing NIRS-based networks at rest with complex systems’ approaches

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Measuring cerebral dynamics during the resting state has been a useful approach to explore the brain’s functional organization. Recent studies from near-infrared spectroscopy (NIRS), functional magnetic resonance imaging (fMRI), electroencephalography (EEG) and magnetoencephalography (MEG) have showed that the human brain activity across different regions is connected through some network structure, and it presents several complex features such as highly connected hubs, hierarchy and small-worldness. In this work, we present and validate a novel approach combining NIRS and graph theory to deeply analyze complex features of functional connectivity, as measured by NIRS, during the resting state.

We worked with continuous-wave (CW) NIRS data of the whole head from two different datasets. The first experimental dataset was previously published 1-3. Briefly, measurements of 11 healthy subjects were performed using a CW-NIRS system (CW6, TechEn, Inc.). For the second cohort, we simultaneously acquired data with NIRS and fMRI from 21 healthy subjects. In both situations, all subjects were instructed to not focus on any specific task (resting state), and both optical geometries were designed to cover the whole head, including frontal, parietal, temporal and occipital lobes. For each subject, 300-sec baselines runs were performed from 2 to 6 times.

Our results suggest that NIRS-based networks present a high density of local connections with a few long-range links. Brain regions (or regions that share the same functionality) symmetrically located are highly connected. For each subject, networks extracted from all NIRS contrasts (oxy-hemoglobin, deoxy-hemoglobin and total hemoglobin) can be quite variable over time. However, the global network metrics (as measured by the average degree, the clustering coefficient, the average pathlength and the diameter of the network) are stable, independently of the run. In addition, there are robust connections between different regions that repeat over time and across subjects. With our graph theoretical algorithms, we could also verify whether there were highly connected nodes (hubs) that could drive the networks. We identified that most of the hubs were located in the frontal and parietal lobes, with slightly predominance in the left hemisphere. Regarding differences in the NIRS contrasts, networks derived from total-hemoglobin contrast provided the most reproducible networks. However, global network parameters from the deoxy-hemoglobin signal correlated well with the BOLD-based networks. Oxy-hemoglobin and total-hemoglobin contrasts exhibit a different behavior from BOLD and deoxy-hemoglobin networks. Overall, our results introduce new insights in NIRS-based functional connectivity at rest and enhance the importance of combining NIRS and fMRI to better understand how the brain works and is organized at rest.

2. R. C. Mesquita et al., [doi: 10.1364/BOE.1.000324].
Prefrontal cortex connectivity under neutral-control and stress condition using fNIRS

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Introduction: Stress is one of the risk-factors for major disorders in the prefrontal cortex (PFC), including bipolar, schizophrenia, depression and anxiety. Excessive stress leads to alter the structure and functional network on the PFC. In this study we investigate the effects of stress on the connectivity of intra and inter-hemispheric PFC based on functional near infrared spectroscopy (fNIRS).

Methods: Twenty-two male, right-handed adults were recruited to perform mental arithmetic task experiment under neutral-control and stress conditions. The task involves three single digits with plus and/or minus operation. Under stress condition, time pressure and negative feedback about current performance were used as stressors. The entire experiment took approximately 20 minutes. Brain activities were acquired at the full PFC using OT-R40 fNIRS system (Hitachi Medical Corp, Japan) with 16 optodes (equivalent of 23 fNIRS channels, Fig.1 (a)). We investigated the effects of mental stress on functional connectivity of intra and inter-hemispheric PFC by calculating the average squared coherence of oxygenated hemoglobin concentration change between all channel pairs of participants in the frequency bands (0.009-0.02 Hz, 0.02-0.04 Hz, 0.04-0.06 Hz, 0.06-0.08 Hz, and 0.08-0.10 Hz). Similarly as [1], we applied Welch’s averaged modified periodogram technique to estimate the cross-spectral and power spectral density to obtain the squared coherence. The functional connectivity was then mapped based on squared coherence threshold of 0.90.

Results: The results in Fig.1 (b-d) showed functional connectivity of the intra and inter-hemispheric PFC under control condition whilst Fig.1 (e-g) shows the functional connectivity under stress condition, both at the frequency band of 0.08-0.1 Hz. A significant reduction in intra- and inter-hemispheric PFC connectivity from control to stress condition was found, with p-values < 0.001. Similar results were obtained for frequency bands (0.009-0.02 Hz, 0.02-0.04 Hz, 0.04-0.06 Hz), with p-values < 0.001. The reduction in functional connectivity in our experiment result is in line with recent fMRI study [2].

Fig.1. FNIRS channel arrangement on PFC (a); Under neutral-control condition: intra-hemispheric connectivity at right PFC (b) and left PFC (c), and the inter-hemispheric connectivity (d); Under stress condition: intra-hemispheric connectivity at right PFC (e) and left PFC (f), and the inter-hemispheric connectivity (g).

Reference:
A 4D pediatric head model for diffuse optical imaging of 4.5 to 18.5 years old children

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Diffuse optical tomography (DOT) is particularly suitable for studying the pediatric population in natural settings, without major restrictions to the child’s movements, and provides useful and important markers of cognitive development. Image reconstruction is more accurate when individual MRI data are available that can be used both as spatial priors in the forward model solution and to aid visualization of reconstructed changes in oxy- and deoxy-hemoglobin concentration. However, acquiring MRI data for each individual undermines many of the advantages of DOT (e.g., portability and applicability to challenging populations) and it is mostly unfeasible for cognitive studies in the pediatric population. The use of a registered atlas as a model for the individual anatomy is therefore becoming common-place in DOT. Whilst standard adult head models [1,2] and a 4D neonatal head model from the preterm to term age range have been recently presented [3], little has been produced for the pediatric age range. The use of a child’s MRI data as a template, e.g. [4], is far from being standard. Furthermore, the development of the brain during childhood makes the use of a single template over a large age range inappropriate.

We present a 4D pediatric head model that provides all the structural data required to perform DOT image reconstruction. We provide templates for the pre-puberty (4.5-8.5 years old), pre- to early puberty (7-11 years old), pre- to mid puberty (7.5-13.5 years old), early to advanced puberty (10-14 years old) and post-puberty (13-18.5 years old) age ranges. These head models were created by using standard pediatric MRI templates computed using data from 324 children enrolled in an NIH-funded MRI study of normal brain development [5,6]. For each age range, we segmented the structural MRI data into five tissues: scalp, skull, cerebrospinal fluid (CSF), grey (GM) and white (WM) matter. The extra-cerebral tissues were segmented using FSL [7], while brain tissues were segmented using tissue probability maps provided in [5]. Volumetric tetrahedral meshes and surface meshes for the scalp, GM and WM were created for each age range with iso2mesh toolbox [8]. Cranial landmarks coordinates (nasion, inion, pre-auricular points, and Cz) were identified and 10-5 positions computed accordingly to assist with registering the head model to the subject’s head and optimising probe location. By providing voxelized, surface and volume mesh data, our model allows the user to employ their preferred method of solving the forward and inverse problems. It will soon be freely available online. Fig. 1 shows an example of the data provided for one age range.

Fig. 1: Examples of tetrahedral head mesh, 10-5 positions and cranial landmarks, GM and WM surface meshes for the 4.5-8.5 years old age range.

Isolating the effects of surface vasculature in infant neuroimaging using short-distance optical channels: a combination of local and global effects

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Functional near-infrared spectroscopy (fNIRS) records hemodynamic changes in the cortex arising from neurovascular coupling. However, (noninvasive) fNIRS recordings also record surface vascular signals arising from noncortical sources (e.g., in the skull, skin, dura, and other tissues located between the sensors and the brain). A current and important focus in the fNIRS community is determining how to remove these non-cortical vascular signals to reduce noise and to prevent researchers from erroneously attributing responses to cortical sources. The current study is the first to test a popular method for removing signals from the surface vasculature (removing short, 1 cm, channel recordings from long, 3 cm, channel recordings) in human infants, a population frequently studied using fNIRS. We find evidence that this method does remove surface vasculature signals and indicates the presence of both local and global surface vasculature signals (Fig.1). However, we do not find that the removal of this information changes the statistical inferences drawn from the data (Fig.2 black and grey lines indicates changes in signal after removal of short channel info). This latter result not only questions the importance of removing surface vasculature responses for empiricists employing this method, but also calls for future research using other tasks (e.g., ones with a weaker initial result) with this population and possibly additional methods for removing signals arising from the surface vasculature in infants.

Fig.1

Fig.2
**MicroNTS: A Fibreless, High-Density Diffuse Optical Tomography System**

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**Abstract:**

We present the first functional images obtained using a fibreless, high-density diffuse optical tomography system. This technology has the potential to provide high-quality functional images of the human cortex using a wearable, wireless methodology that will provide almost unlimited experimental freedom.

Diffuse Optical Tomography (DOT) is an extension of multi-channel NIRS that facilitates the production of three dimensional images of changes in tissue chromophore concentrations. However, DOT has struggled to become a standard functional neuroimaging methodology because of the technique’s sensitivity to superficial tissues, its limited resolution, precision and field of view, and the cumbersome nature of optical fibre bundles. Several research groups have achieved significant success in addressing the challenges of resolution, precision, field of view and superficial signal contamination by significantly increasing channel density and scalp coverage.\(^1\)\(^2\) It has been demonstrated that high-density DOT, initially proposed by Zeff *et al.*\(^1\) in 2007, can produce functional images of the adult human cortex with a precision and resolution comparable to that of a typical fMRI scan.\(^3\) However, increasing the technology’s sampling density means increasing the number of optical fibres, which makes high-density (HD) DOT more challenging to implement, and potentially undermines one of the key advantages of the technology: its portability.

To address the significant problem of fibre burden, while maintaining the advantages of high sampling density, we have developed the first high density, fibreless diffuse optical tomography system. The system currently incorporates 8 dual-wavelength LED sources and 16 photodiode detectors, providing up to 128 channels over an area of ~60 x 60 mm\(^2\) (see Fig. 1a). An exceptional detector dynamic range is achieved using a charge integration methodology as described by Chitnis *et al.*,\(^4\) which allows source-detector separations of up to 60 mm *in-vivo*.

![Figure 1](image_url)

**Figure 1.** a) The source-detector layout of the fibreless high-density probe. b) The average HRF obtained across channels in the range 50-60 mm in one subject. c) the peak HbO and HbR images reconstructed for the same subject.

As a preliminary validation of this technology, a series of motor stimulation experiments have been performed on adult volunteers. Figure 1b. shows the average (and standard deviation) functional responses to a finger-tapping task for channels with separations in the range 50-60 mm in one subject. Figure 1c shows the reconstructed HbO and HbR changes (created using a registered adult head atlas) at 12 seconds post-stimulus onset, again in a single subject.

Through an extended series of in-vivo functional imaging experiments, we intend to demonstrate the efficacy and utility of this novel fibreless, high-density functional DOT system.

**References:**

\(^1\)Zeff *et al.*, PNAS 2007

\(^2\)Habermehl *et al.*, Neuroimage 2012

\(^3\)Eggebreet *et al.*, Nat. Photonics 2014

\(^4\)Chitnis *et al.*, RSI 2016, in press.
How to Co-Position EEG Electrodes and fNIRS Optodes in Multi-Modal Functional Brain Imaging Experiments?

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Multi-modal imaging of the human brain function offers a unique opportunity to simultaneously study the brain function across multiple spatial and temporal scales. One such approach is to combine Electroencephalography (EEG) and functional Near-Infrared Spectroscopy (fNIRS). EEG measures the electrical activity related to active neurons, on the scalp, offering high temporal resolution (ms) with relatively modest spatial resolution (cm). fNIRS on the other hand, uses light in the near infrared range, to measure the local changes in the oxyhemoglobin and deoxyhemoglobin concentrations associated with brain activity. Combining high-density array EEG with fNIRS in a multi-modal imaging setting, would enable observing the brain function simultaneously from two perspectives, and thus provides an appropriate tool for studying spatio-temporal relationship between neuronal activity and vascular response.

In this work, through simulation and experiments, we investigate how to best co-position EEG electrodes and fNIRS optodes, such that recorded signals from each modality are representative of brain activities initiated from the same region, with good accuracy. Three possible electrode/optode configurations are considered (Fig. 1). Simulations are conducted to investigate how the position of the EEG electrode on the scalp with respect to the location of underlying cortical active neuron impacts the accuracy of the estimated signal in the source space. For the experimental part of the study, using a customized cap allowing for different EEG-fNIRS electrode/optode configurations, brain activities are recorded in response to a modified Go/No-Go task. General linear model (GLM) is used to detect significantly activated regions, associated with the response inhibition effect, from fNIRS data. A new metric, based on the time-frequency power of spatially filtered signals, is then employed to examine the same effect from signals recorded via EEG electrodes for different electrode/optode configurations (Fig. 2).

Results from both simulation and experimental studies reveal that overlapping the position of EEG electrodes with the position of fNIRS channels is the best configuration choice, in terms of accuracy in acquiring signals of common origins across two modalities. The outcome of this study can be used as a guideline for designing and planning EEG-fNIRS multi-modal experiments.

Fig. 1. Possible EEG electrode/fNIRS optode configurations.

Fig. 2. Results of EEG-fNIRS experiment in response to Go/No-Go task: group-level activation indices for different frequency bands, and EEG electrodes, and GLM result for recorded fNIRS signals.
Localized cerebral responses and heterogeneity of superficial signals revealed by non-contact scanning time-domain fNIRS

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Introduction: Two major methodological challenges of fNIRS which currently prevent broader application are limited lateral spatial resolution and hemodynamic artefacts from superficial layers. Non-contact scanning imaging combined with time-gated detection promises to overcome these limitations by providing superior lateral spatial resolution for deep as well as for superficial responses to brain activation. Our recently presented non-contact system scans a tissue area with dimensions of several cm, with a fixed, small (few mm) separation between the illumination and detection spots, a 32×32 pixel resolution and a frame time of 1 s. After proof-of-concept tests on phantoms [1] and first successful in-vivo tests [2] in this contribution we report results of in-vivo applications of an upgraded system with two detection channels [3], [4].

Methods: A supercontinuum laser with acousto-optical tuneable filter provided picosecond pulses. A second generation compact fast-gated SPAD module with embedded gating and signal conditioning circuitry [5] was employed for selective detection of late photons that carry information on deep absorption changes. A second parallel detection channel was equipped with a non-gated detector, to separately record purely superficial absorption changes. We obtained arrays of photon time-of-flight distributions by means of a 2-axis galvanometer scanner operated in conjunction with imaging time-correlated single photon counting [6]. The wavelength was switched line by line between 760 nm and 860 nm. For details of the upgraded system and its performance characterization by phantom measurements refer to [4]. Data processing was based on a time-window analysis for both detection channels. The concentration changes of oxygenated and deoxygenated hemoglobin in each pixel were estimated by means of the time-resolved Beer-Lambert law.

In-vivo tests of the upgraded system included (1) a motor stimulation experiment on a bald subject with finger tapping and hand grip exercises, (2) a self-referential task [7] with an expected localized response in the frontopolar region (8 subjects, 10 trials, 8 sentences per task period of 33 s, separated by 33 s rest).

Results: The motor stimulation experiments revealed localized cerebral responses, with lateral extensions differing for finger tapping and hand grip experiments. For the cognitive stimulation we could not identify clear cerebral responses. However, the temporal-spatial pattern of task-evoked artefacts found in several subjects were studied with high spatial resolution. These signals were clearly confined to the location of superficial veins (see Fig. 1), confirming the findings of Kirilina et al. based on skin fMRI [8] and paving the way for new methods to separate superficial venous from cerebral signals.

Conclusions: Non-contact scanning with a dense, flexible grid of measurement positions has the potential to become a useful tool to separate brain activation and accompanying superficial responses and to study the details of their lateral spatial extension. Future technical efforts will focus on improving the detection efficiency, mainly by developing gated detectors with larger active area.

References:
Physiological monitoring of oxygen delivery to the brain has great significance for improving the management of patients at risk for brain injury. Diffuse correlation spectroscopy (DCS) is a rapidly growing optical technology able to non-invasively assess an index of blood flow (BFI) at the bedside. Current limitations of DCS are the contamination introduced by extracerebral tissue and the need to know tissue optical properties to correctly quantify BFI. To overcome these limitations we have developed a new technology for time-resolved diffuse correlation spectroscopy. By operating DCS in the time domain (TD-DCS) we are able to simultaneously acquire the temporal point spread function (TPSF) to quantify tissue optical properties and the autocorrelation function to quantify BFI. More importantly, by applying time-gated strategies to the DCS autocorrelation functions, we are able to differentiate between short and long photon paths through the tissue and determine BFI for different depths. Here, we present the novel device and we report the first experiments in tissue-like phantoms and in rodents. The TD-DCS method opens many possibilities for improved non-invasive monitoring of oxygen delivery in humans.

This figure reports results of TD-DCS measurements on a diluted milk phantom to demonstrate the dependence of BFI on time gate width. Panel a) shows the TPSF with superimposed gates of different widths all starting right before the peak at t= 250 ps. The gate labeled CW is 3000 ps wide. Panel b) shows the measured path-length dependent normalized intensity temporal autocorrelation functions for the corresponding gates. c) The correlation amplitude BFI as a function of gate width for the corresponding gates. BFI increases with narrower time gates as predicted by Bellini et al.¹

Using the same phantom data, this figure shows the linear dependence of the decay rate of g₁₀ on the light path-length. a) TPSF with superimposed twelve gates of fixed width (48 ps) starting at different time delays. b) Measured path-length dependent normalized field autocorrelation functions for the corresponding gates. c) Slope of the field autocorrelation functions at the 12 gates as a function of path-length (i.e. time delay · speed of light in water). The linear fit is done considering all of the slopes, the intercept is t₀ and the slope is proportional to Dᵣ·µ₄. The resulting Dᵣ is 1.0e⁸ mm²/s, in close agreement with the Dᵣ measured using a CW-DCS system (0.85e⁶ mm²/s).

Real-world neuroimaging: the use of a fiberless and wearable fNIRS system to monitor brain activity in the real-life on freely moving participants.

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Cognitive abilities supported by the prefrontal cortex can be difficult to study in conventional laboratory settings, especially in case frontal lobe dysfunctions, as the formal and physically constrained situations in the labs can change our behaviour and reduce the measurement validity. Prospective memory (PM) is one of the prefrontal cortex functions that present significant disagreement between measurements taken in everyday life and the lab.

In this abstract we discuss the experimental procedure of using a fiberless and wearable fNIRS system to conduct a neuroscience outside the lab on freely-moving participants. Prefrontal cortex functional activity was monitored using a 16-channels wireless and fiberless fNIRS system. The fNIRS probe was shielded from the environmental elements (rain, sunlight) with a shading cap. In addition, acceleration, heart and breathing rate were measured through a monitoring belt. Participants performed a PM task outside the lab. The experiment lasted approximately 1 hour and consisted of a baseline condition (i.e., the experimenter showing the experimental area to the participant), two Ongoing conditions (i.e., walking around the streets counting the number of certain items) and a social and non social PM task (i.e., performing the Ongoing task while responding to social and non social PM cues, e.g., fist bumping an experimenter and parking meters, respectively). Two rest phases were included at the beginning and the end of the experiment. Three video cameras were used to record the entire experimental session for behavioural examinations. fNIRS data were converted into haemoglobin concentration changes using the modified Beer-Lambert law and down-sampled to 1 Hz. Slow drifts were removed through a linear detrend. fNIRS signals were then corrected for motion artifacts and physiological noises were removed by means of a 3\textsuperscript{rd} order Butterworth band-pass filter (0.008-0.2 Hz).

Haemoglobin changes secondary to neuronal activation can be observed in proximity of functional events (Figure 1), showing the feasibility of wireless fNIRS for real-world neuroimaging.

![Figure 1. Example of oxygenated and deoxygenated haemoglobin changes in response to non-social PM cues.](image_url)
Compact 8 channels time-domain diffuse optical tomography system based on SiPMs for functional brain imaging


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Abstract

Diffuse Optical Tomography (DOT) is a non-invasive technique exploiting near-infrared light propagation in diffusive media to retrieve 3D maps of the distribution of optical properties down to 2-3 cm of depth [1]. In particular, in Time-Domain DOT approach, the information about depth is encoded in the photons time-of-flight. Unfortunately, this technique is affected by high cost and large dimensions of the main components. Aiming at overcoming these limits, we propose a compact system featuring low cost and small size. These features are feasible thanks to the use of: i) a pulsed laser diode at 689 nm as source (PicoQuant GmbH, Germany), ii) 8 Silicon Photomultipliers chips (Hamamatsu Photonics KK, Japan) with suitable front-end electronics developed at Politecnico di Milano [2] as time-resolved single-photon detectors, and a Time-to-Digital Converter (Surface Concept GmbH, Germany) as photon-timing electronics. With respect to the more traditional approach of fiber-based detectors, this system takes advantage of an improved harvesting of the diffused light since detectors are directly in contact with the head of the subject with their wide photosensitive area of 1.69 mm² each and their large numerical aperture (~1). The neoprene probe with the light-injection fiber in the center and the embedded 8 detectors all around (3 cm source-detector separation) is shown in Fig. 1.

![Fig. 1 Two photographs of the designed probe.](image)

We firstly investigated the performance of the system with both simulations and measurements of an inhomogeneous solid switchable phantom in which a cylinder embedding an absorbing inclusion ($\mu_s = 0.04 \text{ mm}^{-1}$) was moved through a homogeneous background ($\mu_s = 0.01 \text{ mm}^{-1}; \mu_s = 1 \text{ mm}^{-1}$) [3]. In both cases, we achieved good tomographic reconstructions of the embedded inhomogeneity using a linear reconstruction algorithm based on the Born-approximation [1]. However, its depth is slightly underestimated (about 5 mm). In addition, some superficial artifacts are visible in the tomographic images, probably related to the different sensitivity of the Jacobian matrix to the depth. It is worth noting that the reconstruction is efficient essentially only within the area covered on the surface by the source-detectors distribution. We also performed preliminary in-vivo measurements to prove the system suitability in detecting the hemodynamic variations during brain activation. We successfully recovered 3D maps of the activation during a finger tapping exercise. The tomographies show a good time and spatial localization: in fact, we can clearly identify that in time, in a specific position, the activation appears and then fades, thus restoring the initial condition. Despite the need for further investigation and optimizations, the obtained results are promising, confirming the suitability of this system to provide 3D maps of brain activations.

Bibliography

Brain Based Assessment of Reading Skills in Adolescent Students using fNIRS

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Learning to read is a crucial skill to be successful in today’s society. However, the 2005 report of the U.S. Department of Education indicated that 36% of fourth grade students cannot read at a basic level. Reading includes three components: decoding, comprehension and fluency. There are widely accepted and used tools for the assessment of fluency in elementary school, but there are only a few reading assessment tools for older students. These tools often focus on fluency alone and are not broadly implemented. Teachers of secondary school students find it difficult to assess reading comprehension. If the reading skills, specifically comprehension, are not appropriately assessed and remedied to reach benchmark levels during middle school, students will continue to struggle with reading through high school which can then affect their success in college and in the modern workforce.

With recent advances in neuroscience, reading processes are being studied by employing established brain-imaging technologies (e.g., functional magnetic resonance and electroencephalography). In recent years, functional near infrared spectroscopy (fNIRs) has been employed in the study of frontal lobe activation in reading related tasks. Since reading is a complex task a number of cognitive factors that range from low-level sensory to high-level cognitive processes, are activated involving different brain regions. Specifically, previous fNIRs studies support the notion that the frontal lobe is involved in the process of reading, providing higher executive functions such as memory and attention to the process of reading¹². With its portable, noninvasive, safe, affordable, and easily applicable nature fNIRs poses as an appropriate neuroimaging modality to be used in brain based assessment of reading skill development longitudinally which can be easily utilized in classroom settings.

At Drexel University, we are developing a computerized Adolescent Comprehension Evaluation (ACE) tool to assess students’ comprehension skills in 6th-8th grade. ACE provides a student with a reading passage and 10 multiple choice comprehension questions related to the passage. It can record passage reading time, number of times the passage is reviewed, correct and incorrect answers in a graded fashion, and the response times.

Assessment of reading comprehension evaluation in ACE will be based on behavioral measures obtained through the ACE outcome dashboard as well as brain based measures obtained through fNIRs recordings from the frontal lobes. In our pilot study on three 8th graders where one student was measured twice using two different passages, positive correlations were found between the oxygenated hemoglobin (Oxy-Hb) values and overall testing time (R=0.67), number of times the passage has been viewed (R=0.79), and the averaged response time (R=0.89).

These results may mean that as certain subjects take more time to complete the test and revisit the passage more frequently, they have to put more effort in it and hence their response times and the corresponding Oxy-Hb values increase. Furthermore, all cases had more correct answers than incorrect ones and on the average incorrect answers took more time to respond and more Oxy-Hb. Currently, we are collecting data from 8th graders in three middle schools within Philadelphia area which will be analyzed next.


Deoxyhemoglobin changes in right lateralized DLPFC represent conflict processing in a color-word Stroop task

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The classic Stroop task [1] introduced conflict between written and perceptual domains of colors and words, and subsequent Stroop tasks have varied stimulus dimensions and response choices to investigate neural correlates of conflict monitoring and resolution [2, 3]. Delays in reaction time to incongruent stimulus/response trials represent interference between conflicting stimulus and task dimensions, and associated activity in specialized neural circuits is taken as a marker of conflict processing [4]. Previous studies using functional near-infrared spectroscopy (fNIRS) have attempted to describe superficial cortical activity associated with conflict processing in the traditional Stroop color-word task [5, 6]. While these findings provide consensus that activity in the dorsolateral prefrontal cortex (DLPFC) represents conflict processing, there is disagreement as to the laterality and consistency of results in oxy- and deoxyhemoglobin concentration changes. Our goal was to repeat the traditional color-word Stroop task using multichannel fNIRS to clarify specific activity associated with conflict processing with the long-term goal of utilizing fNIRS in tasks designed to investigate domain-general and domain-specific activity in emotion, social, and language conflict tasks. We hypothesized deoxyhemoglobin would display significant increases in activity in the DLPFC for incongruent compared to congruent trials. Thirty-three subjects provided consent prior to participating in the six-minute event-related color-word Stroop task. Four trials were presented in 15 second blocks followed by 15 seconds of rest repeated six times for a total of 48 trials. Each block had a 3:1 ratio of congruence, resulting in a pseudo-block design trending toward either incongruence or congruence. Subjects were asked to indicate the word’s color by pressing assigned keys on a keyboard. Prior to task presentation, subjects were fitted with a Shimadzu LABNIRS cap with 98 channels defined by 30 emitters and 29 detectors designed to optimize coverage of frontal, temporal, and parietal lobes. Raw data was converted to oxy- and deoxyhemoglobin values using a modified Beer-Lambert equation and wavelet detrending was performed prior to hemodynamic modeling. A Gaussian spatial filter was applied to remove systemic artifacts [7] and subsequent group analysis determined differences between incongruent and congruent trials. Behavioral results were consistent with previous studies showing significantly longer mean reaction times for incongruent trials (p=0.0043). Functional imaging for incongruent > congruent trials showed activity specific to the right hemisphere DLPFC for deoxyhemoglobin only (Figure 1). A conjunction of incongruent and congruent trials indicated bilateral activity in the supplementary motor area for both oxy- and deoxyhemoglobin. According to prominent models of conflict and control mechanisms, the DLPFC is engaged primarily in reducing conflict [2]. These models suggest the cingulate-DLPFC-parietal network underlies conflict detection and resolution. Although precise locations of component functions may vary, the right dorsal cingulate is suggested to control processes consistent with resolution of conflict. The trended block paradigm used here may have contributed to lateralization. Our results further suggest deoxyhemoglobin changes best represent this processing and that oxyhemoglobin, even with spatially-consistent systemic artifact removed, may contain additional sources of variability that require caution in interpretation.

Functional brain organization for theory of mind in 7-month old infants

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Human adults and children reliably engage a network of brain regions, including superior temporal sulcus (STS), temporal-parietal junction (TPJ), and various regions of the prefrontal cortex (PFC), when thinking about what others are thinking or theory of mind. How and when functional organization for theory of mind arises, however, is unclear, despite behavioral evidence suggesting that humans may begin tracking the mental states of others’ within the first year of life. Here we use the emerging technology of functional near-infrared spectroscopy (fNIRS) to measure the brain response across the inferior parietal, superior temporal, and lateral prefrontal cortex in 7-month old infants as they viewed video scenarios of portraying actresses with different knowledge or beliefs about the location of a hidden object. We observed that regions of the TPJ of infants distinguished between scenarios where the actress held an accurate or true belief about the location of a hidden object from scenarios where the actress’s belief about the location of a hidden object was inaccurate or false, mirroring results recently obtained with the same methodology in adults. These results suggest that the TPJ region of the social-cognitive network is functionally active, engaged spontaneously, and continuous for theory of mind by 7-months.
Development of a Wireless Wearable fNIRS System

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Introduction: Near infrared (NIR) light as a probe to image functional activity of brain has got increasingly attention among the neuroimaging research community in recent decades. The increasing number of commercially available functional Near Infrared Spectroscopy (fNIRS) systems in recent years, proves the potential usage of the fNIRS for its unavoidable benefits over other well-established imaging modalities. Though there has been a significant advancement in portable fNIRS system design, most of the available systems are constrained to operate for the bedside monitoring of brain, which hinders imaging the brain when a subject is in motion or performing a physical activity.

Methods: Designing a multi-channel fNIRS system that is wearable, low-cost and wirelessly accessible for real-time BCI application is a very challenging process, involving designing a chain of complex electronics. We have explored the possibility of designing such a system that has the potential to address all of the above challenges. Our design includes a flexible 3D printed headband patch that holds four LED sources at two NIR wavelengths, 770 and 850 nm and four photodetectors. The controlling circuit is made of Intel Edison and high-resolution ADC, linking with optodes on the patch.

Results: Our fNIRS design is configured wirelessly via Intel Edison that streams data to a host computer for the data processing and visualization of the brain functional activities. We have tested our system on forehead of a subject, while performing physical activities to check the system functionality.

Conclusion: The 30 mm source-detector separation of our 10 channels system provides acceptable depth sensitivity and SNR. We are further investigating to increase the fNIRS channel density and incorporating different modulation techniques to image whole brain and to have a better time and spatial resolution.

References
Impact of posture on cerebral blood flow


The impact of posture on cerebral perfusion has been widely studied in healthy and diseased populations. Management of ischemic stroke, for example, is focused on maximizing cerebral blood flow (CBF) to minimize further damage to the ischemic penumbra. However, management strategies are generally empirical due to the absence of bedside CBF monitoring. Indeed, most stroke patients are kept flat after stroke onset to increase perfusion pressure. Furthermore, the optimal time-window for patient mobilization is still debated. Here we summarize the results of quantitative optical monitoring of CBF during postural manipulation, in both adults and children. The results highlight the need for bedside noninvasive monitoring during therapy and suggest subject posture ought be considered in functional protocols.

Several previous studies have shown that CBF is generally higher in the supine versus sitting position, consistent with guidelines that a stroke patient should be kept supine as much as possible. Our prior work demonstrated that CBF generally increases with decreased HOB angle. However, a paradoxical decrease in CBF was observed when the head-of-bed is lowered from an elevated position in ~20% of stroke patients; thus, a supine position may be detrimental for these subjects. We have extended these preliminary findings to CBF measurements during postural manipulation of 126 subjects, including stroke patients, patients with chronic obstructive sleep apnea, and controls aged 5 to 93 years.

Consistent with our prior measurements, we observe lower CBF in the supine position, compared to the seated position in ~25% of stroke patients and ~6% of healthy subjects across a wide range of ages and pathologies. Further, we identified a ‘hysteresis effect’ per supine blood flow; when subjects were brought back to a supine position after postural manipulation, ~80% of subjects showed an increase in CBF compared to initial pre-manipulation supine flow.

Taken together these results suggest that bedside monitoring of microvascular CBF is desirable for identification of patients for whom the standard of care supine position could be deleterious. Additionally, the suggestion that postural manipulation can itself raise cerebral blood flow - and the potential for hysteresis in baseline hemodynamics - requires further investigation per proper/effective study design. We will discuss this meta-analysis of data from different populations and compare our results to the available systemic physiological data.
The Neural Correlates of Prehistoric Stone Tool Manufacture

Shelby S. Putt, Sobanawartiny Wijeakumar, Robert G. Franciscus, John P. Spencer

This study aims to shed light on how and when mechanisms of the human brain evolved to support complex cognition and language. The field of evolutionary cognitive archaeology asserts that prehistoric technologies, as products of past cognition in action, are informative of the minimum cognitive and linguistic abilities that early humans needed to possess for their production. Previous researchers attempted to reconstruct the neural correlates of two Early Stone Age (ESA) tool industries, including the 2.6 million-year-old Oldowan industry and the 0.5 million-year-old late Acheulian industry. These studies used positron emission tomography (PET) to observe the functional activation occurring in the brains of human participants after they replicated the production (knapping) process of these different tool types. Because of evidence for overlap between the knapping and language circuits of the brain and increased anterior frontal activity during Acheulian tool production, they argued that their results 1) indicate increased cognitive demands for late Acheulian tool production relative to Oldowan tool production and 2) support a technological origin for language, meaning that certain language functions co-opted the neural substrate and functions that were already established for toolmaking and tool use. Because of the motion limiting aspects of PET, however, these studies were unable to record the hemodynamic response of naturalistic stone knapping in real-time. Furthermore, any conclusion regarding a technological origin for language is problematic if it relies on data obtained from participants who learned to knap with verbal instruction.

To test these two claims, this study utilized functional near-infrared spectroscopy to explore the neural correlates of real-time, naturalistic Oldowan and Acheulian stone knapping among 31 trained, right-handed, adult participants, who were separated into two training groups. Both groups trained by watching the same video tutorials showing hands making stone tools, but those in the verbal group heard spoken instructions, while those in the nonverbal group watched a version with the sound turned off. Functional brain images were reconstructed from digitized optode locations and 10-20 landmarks of each participant’s head and from the optical data (see Wijeakumar et al., 2016). A two-way analysis of variance revealed that only the Acheulian task recruited a frontotemporal cognitive control network, and the presence or absence of language during training dictated which higher-order cognitive areas of the brain become engaged. Selection for prehistoric individuals with increased working memory capacities, which would have allowed them to make increasingly complex tools to gain access to novel diets, may have spurred the evolution of larger brain size in the genus Homo during the ESA. Furthermore, this study demonstrates that the results of previous experiments reflect a very specific condition of stone knapping skill acquisition that involves linguistic instruction, which may not be analogous to how skills were transmitted during the ESA. Finally, evidence of overlap between left hemisphere language and stone knapping circuits among the participants in the nonverbal group lends additional support for the technological origin for language hypothesis.
Fiber-free SiPM detectors for TD fNIRS: in-vivo demonstration

R. Re, E. Martinenghi, A. Dalla Mora, D. Contini, A. Pifferi, and A. Torricelli

Abstract

We report on the development of a compact probe for Time Domain (TD) functional Near Infrared Spectroscopy (fNIRS) measurements based on fast Silicon Photomultiplier (SiPM). Recently, we demonstrated the possibility to employ SiPMs for TD diffuse optics\(^1\), obtaining timing resolutions down to 57 ps full-width at half maximum (FWHM). Since SiPMs were used in contact with the sample we obtained an high diffused photons harvesting efficiency thanks principally to the possibility to avoid the use of cumbersome fibers and lenses, thus exploiting the whole device numerical aperture (close to 1). The high quantum efficiency (>20% at 600 nm), the broad spectral coverage (350-1000 nm) and the good responsivity (10\(^2\) m\(^2\)sr at 690 nm), made SiPMs good candidates as TD fNIRS detectors. As additional advantages, SiPMs are inexpensive and require very compact and cheap front-end electronics, thus allowing the possibility to directly integrate the detector together with the electronics on the probe. In this way, the detection chain of the instrument can be very compact, rugged, easy to use and low cost.

In this work, the probe has been embedded in an instrument for TD fNIRS\(^2\). With respect to our previous probe, we directly integrated an avalanche signal amplification stage close to the SiPM, thus further reducing the size of the detection channel and improving the signal immunity to electromagnetic interferences. The whole electronics was placed in a plastic screw cap compatible with the EEG standard cap for measurement on brain. The presence of a resin avoids the direct contact of the scalp with the 100-V bias voltage and guarantees the electrical isolation. In this way, it is possible to integrate in a safe and easy way the new SiPM detector with the clinical standards methods for 10-20 electrode/optode positioning. Figure 1 (left) shows a photo of the integrated SiPM.

The system was firstly characterized on tissue phantoms in terms of temporal resolution, responsivity, linearity, and capability to detect deep absorption changes.

Furthermore, for the first time, we present in-vivo measurements on an adult volunteer. We monitored the hemodynamic changes on the adult arm during venous and arterial cuff occlusions and on adult motor cortex during a finger tapping exercise in order to demonstrate the capability of the whole system, employing fiber-free SiPM detectors, to non-invasively monitor human tissue’s hemodynamics changes. In Figure 1, an example of cortical activation it is shown. The volunteer performed a right hand finger tapping composed of 4 repeated blocks consisting in: rest (20 s), task (20 s), and recovery (20 s), for 240 s of total experiment length. The acquisition rate was set at 1 s and the source-detector separation was fixed at 3 cm. The two source-detector pairs were place around C3 and C4 positions. An increase of Oxy-hemoglobin [O\(\text{Hb}\)] combined with a decrease of deOxy- [H\(\text{Hb}\)] in the contra-lateral hemisphere is observed. The lines are the variations of the hemodynamic parameters with respect to the baseline averaged over the repetitions, the error bars are the correspondent standard deviations.

References

Investigating superficial layer effects on fNIRS signals in the term-age infant

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Over recent years, functional near-infrared spectroscopy (fNIRS) has been increasingly adopted as a non-invasive neuroimaging technique in infant studies of cerebral function and cognitive development. Advances in the technique, including improved headgear design and integrating image reconstruction to produce images of cerebral haemodynamic responses, have made this a potentially attractive tool for researchers and clinicians.

The measurement of cerebral haemodynamic changes using fNIRS provides an indirect measure of cortical function. The distance between an optical source emitting near infrared light and a detector that measures transmitted light will influence the depth of tissue sampled. The optimal source-detector (SD) distance to sample infant cortex is 25-30mm. However, due to the nature of the path of photons in biological tissue, a proportion of the optical signal measured will contain physiological information from non-cortical vasculature contained in the scalp and skull. A practical approach to minimising this surface artefact is to simultaneously measure the haemodynamic signal in the superficial layers using short SD separations (SS) and remove this from the overall fNIRS signal to isolate cortical activity.

The range of reported SS varies from 5 – 15mm in adults. A shorter distance closer to 6mm has been shown to provide a better signal as a larger SS may sample cortex. In infants, the optimal SS would ideally be scaled down and a distance of around 2.13mm was recommended in a simulation study using a Monte Carlo simulation for photon transport in anatomically informed multi-layered brain models. This short distance poses hardware challenges due to the physical size of the optical source and detector, and the potential detector saturation effect. For these reasons, infant studies adopting SS regression to date have typically used a distance of 10mm.

The objective of this study is to investigate the superficial layer effects on the measured haemodynamic signal using multiple SD distances. For this study, we have designed an optode containing a source and detector fibre bundle with a SS distance of 3mm. Using this optode in a multi-distance array (3mm, 6mm, 11mm, 16mm, 26mm, 36mm), we are recording resting-state data over the frontal and temporal regions in healthy newborn infants.

At present in two infant subjects, we have observed a layer effect for the resting-state (RS) frequency band (0.08 – 0.2Hz). Figure 1 shows two plots, one from each subject, demonstrating changes in the spectral power of light intensity in the RS band with SD distance measured at different locations. There is a gradual increase in spectral power peaking at 26mm followed by a decrease at 36mm which may be due to increased noise at this longer SD distance. We are currently recruiting more newborn infants and will also be investigating other physiological components of the signal including heart beat. This study will explore the contamination effect of superficial physiological artefact and determine the optimal SS distance for future infant studies.

References:
The study of photon migration through highly scattering media opens the way to the noninvasive investigation of biological tissues well below the skin surface [1]. Usually, the medium is addressed in reflectance geometry, where light injected and collected from the same side of the surface carries information on medium properties seen by photons along their paths. For this reason, a key issue is often to increase as much as possible the depth reached by migrating photons. Depth information is crucial, for instance, in brain functional imaging or in neuro-monitoring [2], where a key challenge is the extraction of specific brain-cortex signals out of the overwhelming systemic superficial contamination (e.g. scalp, skull and cerebrospinal fluid). The problem of determining the penetration depth of photons in a turbid medium has been addressed in the literature by several research groups [3, 4] but there is a lack of a general formulation of the problem.

For a laterally-infinite slab of thickness $s_0$ the probability density $f(z|\rho, t)$ that photons detected at a distance $\rho$ from the source at the time $t$ have reached a maximum depth $z_{\text{max}}$ between $z$ and $z + dz$ can be calculated as:

$$f(z|\rho, t) = \frac{1}{R(s_0, \rho, t)} \frac{R(s = z + dz, \rho, t) - R(s = z, \rho, t)}{dz} = \frac{1}{R(s_0, \rho, t)} \frac{\partial R(s, \rho, t)}{\partial z},$$

where $R(s, \rho, t)$ is the time-resolved (TR) reflectance for a slab with thickness $s$ and $0 \leq z \leq s_0$. From $f(z|\rho, t)$ it is possible to calculate the mean value of the maximum penetration depth $\langle z_{\text{max}} | \rho, t \rangle = \int_0^{s_0} z f(z|\rho, t) dz$, and, then, to have an estimation of the mean value $\langle z | \rho, t \rangle$ at which detected photons have undergone scattering events, resulting $\langle z | \rho, t \rangle \approx \langle z_{\text{max}} | \rho, t \rangle / 2$. Similarly, we can define in the continuous-wave (CW) domain a probability density function $f(z|\rho) = \frac{1}{R(s_0, \rho)} \frac{\partial R(s, \rho)}{\partial z}$, with $R(s, \rho) = \int_0^\infty R(s, \rho, t) dt$, and, then, the mean value of the maximum, $\langle z_{\text{max}} | \rho \rangle = \int_0^{s_0} z f(z|\rho) dz$, and of the mean, $\langle z | \rho \rangle \approx \langle z_{\text{max}} | \rho \rangle / 2$, penetration depth. We note that, in contrast to the TR approach, in the CW domain both $f(z|\rho)$ and $\langle z_{\text{max}} | \rho \rangle$ depend on the absorption coefficient of the diffusive medium.

In Fig. 1, the mean value of the maximum penetration depth is reported for a semi-infinite homogeneous diffusive medium and for a slab with $s_0 = 20, 40$ mm, for TR approach and CW domain. These values have been calculated exploiting both a Monte Carlo code and the diffusion approximation (DA) of the Radiative Transport Equation. Work is in progress to evaluate the same quantities in the frequency domain and in a diffusive heterogeneous medium.

![Fig. 1](image_url)
Parametric vs permutation tests to analyze newborns fNIRS data: analyzing the same data set in three different ways

Traditionally, fNIRS infants data have been analyzed using parametric statistical tests such as t-tests or ANOVA to compare the hemodynamic response evoked by the different conditions in each channel and in regions of interest manually defined. Due to the large number of channels tested, the results are affected by the multiple comparisons problem, an increase of type I error (i.e. an increase of the probability of false positive) and need to be corrected. Different method exist (e.g. Bonferroni, False Discovery Rate), but they all significantly decrease statistical power and may thus not be adapted to noisy data that already have low statistical power such as newborns data. Introduced into the functional neuroimaging literature by Holmes et al. (1996), permutation tests deals with the multiple comparisons problem (Maris & Oostenvald, 2007) and, as opposed to t-tests or ANOVAs, they don’t require any condition to be matched regarding the distribution of the data. This is particularly interesting since these conditions are rarely matched in developmental populations.

To assess for the relevance of permutation tests for newborns fNIRS data, we analyzed the same dataset in three different ways: First with a classical parametric approach, then with single threshold permutation test, and finally with cluster permutation test. The data consisted of the response to normal, moderately (60% of initial duration) and highly compressed (30% of initial duration) speech in 24 channels placed symmetrically (12 per hemisphere, see Figure 1) on the temporal, fronto-temporal and temporoparietal regions of 21 newborns (1-3 days). Single threshold permutation tests (Nichols & Holmes, 2000) consisted of characterizing each of the images generated by permutation of the three conditions by its maximum t-value among the 24 channels and replacing the real t-value of each channel in the distribution generated. This approached yielded similar results to uncorrected t-tests without the need of statistical correction (no t-test survived to the correction). Cluster permutation tests didn’t yield any significant clusters, although ANOVA on manually defined regions of interest revealed an effect in the frontal region. Because the fNIRS signal is highly auto-correlated in time, we define the clusters only in space dimension. The threshold of significance was 5 adjacent channels with a effect, which did not occur in the data. This was expected since 5 channels in the same hemisphere cover a too large region to constitute a cognitively meaningful brain region.

We conclude that single threshold permutation tests constitute a promising statistical tool to analyze noisy infants fNIRS data that does not survive to corrections applied to results of parametric tests. Single-threshold permutation tests offer a solution to the multiple comparisons problem without killing the statistical power of the data, making them very useful to analyze infants fNIRS data.

<table>
<thead>
<tr>
<th>Main effect of compression rate</th>
<th>Permutation test</th>
<th>Parametric tests (ANOVA and t-tests, uncorrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vs 60%</td>
<td>Ch. 10: p=0.002</td>
<td>Ch. 10: p=0.006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 15: p=0.0146</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 22: p=0.0142</td>
</tr>
<tr>
<td>Normal vs 30%</td>
<td>n.s.</td>
<td>Ch. 10: p=0.003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 12: p=0.020</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 15: p=0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 22: p=0.007</td>
</tr>
<tr>
<td>60% vs 30%</td>
<td>Ch. 10: p=0.011</td>
<td>Ch. 10: p=0.026</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 14: p=0.021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 15: p=0.046</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ch. 20: p=0.028</td>
</tr>
</tbody>
</table>

Table 1: comparison between parametric and single-threshold permutation tests

![Figure 1: Placement of the channels on the newborns' head](image)
Temporal muscle hemodynamics overlaying cortical fNIRS

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Introduction: The fNIRS is capable to measure oxygenation changes within the light penetrated tissues using the absorption abilities of the two hemoglobin types. Therefore, not only cerebral but also extra-cerebral hemodynamics are detected (Haeussinger et al., 2011). In humans the temporal muscle covers a large area of the (fronto-)temporal brain region, such as Broca’s area, which is especially important in speech-related tasks. Towse et al. (2011) showed that the constriction of skeletal muscles leads to a hemodynamic response, whose shape is very similar to the cerebral response. In this work we aimed to investigate the influence of muscular hemodynamics on the measurement of temporal brain activation.

Methods: In the 1st part we provoked activation of the temporal muscle by teeth-clenching. Muscle constriction strength was measured using Electromyography (EMG). Hemodynamics was measured using multi-distance NIRS (31 subjects) and simultaneous NIRS-fMRI (1 subject). In the 2nd part we measured cerebral activation evoked by speech noise stimuli (32 subjects). The sample was split into a “bite”- and a ”non-bite”-group by visual data inspection based on the knowledge from the pre-study. Effects of ”bite event” exclusion on the auditory activation were investigated.

Results: We found a reliable and strong bite induced response in temporal channels (see figure 1). The short-distance NIRS (10 mm) displayed partly poor correlation with default NIRS (30 mm optode distance). The maximal EMG-amplitude correlated significantly with the peak-amplitude of the bite-related NIRS-response. The BOLD-signal extracted from the temporal muscle reflected strongly the NIRS-signal during bite events (see figure 2). For the auditory task we found 16 subjects comprising bite-typical artifacts in temporal channels. Excluding artifact-related blocks from the model-based analysis led to an increase of derived t-values in auditory regions (see figure 3).

Discussion: NIRS is clearly affected by muscular hemodynamics caused by temporal muscle constriction. To avoid muscle artifacts we recommend a careful subject instruction regarding movements, which could lead to temporal muscle constriction, such as teeth-clenching or swallowing. The simultaneous assessment of EMG is capable to detect constriction events. In combination with a system identification approach this could an effective way to handle temporal muscle artifacts. The application of short-distance NIRS is - according to our results - limited probably due to constriction-induced scalp movement. We are further working on the development of filter methods based on the Independent Component Analysis (ICA) or the Wavelet-transformation.

References


Figure 1: T-map (left) of averaged oxygenated hemoglobin (oxy-Hb) amplitudes for three bite events and 31 subjects between 3 and 34 seconds after the bite onset. The temporal courses (right) of the event-related averages for the positive and negative significant channels. A clear hemodynamic response can be seen in the temple region. The amplitude and peak-time is distinctly increased as compared to normally observed cerebral responses.
Figure 2: (A) shows the results of the temporal muscle extraction and the position of the NIRS channels exhibiting the muscle artifact. (B) Comparison of the gray- and muscle-BOLD signal. A clear connection between the NIRS and the muscle-BOLD signal can be seen. (C) A voxel-wise correlation analysis between fMRI and oxy-Hb gives evidence that the anatomical origin of the bite artifact is the temporal muscle.
Figure 3: Oxy-Hb t-maps for the auditory task. The group with temporal muscle artifacts ("biter") shows lower activation in Broca’s area. An exclusion of artifact events leads to an increased measured auditory activation (higher t-values, increased number of significant channels).
Abstract

The lack of data concerning the organization of the central nervous system of the animals farmed for milk and meat production is a potential handicap for the study of cognition processes, important for the assessment of animal welfare, and a gap in comparative neuroscience. We conducted several trials in order to study the functional organization of the cerebral cortex of free-moving sheep through the non-invasive application of functional near-infrared spectroscopy (fNIRS), a developing technology that has started to be applied in animals (Muehlemann et al., 2011). We intended to record the oxygen consumption of selected areas of the brain involved in the performance of behavioural motor and associative tasks and to assess the brain activity when animals were anticipating either a positive or negative event. We used the continuous-wave fNIRS OxyPrem device and recorded the data with Tubis software (version 4.5).

Here we present the fNIRS results of the pilot phase that was conducted on three sheep undergoing to a series of stimuli for 20 s, each followed by a 20 s interval. The stimuli applied were: 1) auditory, consisting in a neutral sound repeated 8 times; 2) visual, involving the application of the Finnoff light intermittently on the pupil, repeated 4 times per eye and 3) physical, entailing the application of a pressure of 250 mmHg with a tourniquet on the forelimb, 4 times per limb. We repeated the protocol recording the brain activity with electroencephalography (EEG). In addition, we set up an experiment to assess the brain activity when animals were anticipating either a positive or negative event. We trained eight sheep to anticipate two events with a supposed different value via classical conditioning. Two pairs of audio-visual stimuli anticipated either the presence of feed (positive event) or the absence of it (aversive event) in a testing area hidden behind screens. On test day, each sheep performed two sessions of six trials. A session consisted in 3 positive and 3 negative trials randomly distributed (always starting with a positive). During the task sheep were wearing the fNIRS device on the head. We focused on the brain activity during the 20 s of latency between submission to stimuli and events. Furthermore, we analysed the behaviour of the sheep during the anticipation period using validated ethograms (Reefmann et al., 2009; Boissy et al., 2011).

fNIRS represents an innovative non-invasive method to conduct more objective assessments of animal behaviour and helps to improve the evaluation of animal welfare. The data will allow the identification of the cerebral areas involved in the physiological regulation of complex and integrated behaviours with different emotional valences. Combining the exploration of the neural substrates underlying cognitive functions with existing behavioural and physiological measures will strengthen knowledge of how animals perceive different environmental situations. Validation of the data will also promote the use of large herbivores’ brains as suitable models in neuroscience.

References

Studying the processing of affective and non-affective touch in the developing brain of 2 year old children

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Background: A special set of neurons called C-tactile (CT) afferents mediate affective touch that is typical in infant-parent interaction. CT fibers project to the insula, temporal regions and orbitofrontal cortex (Olausson et al., 2002) [Francis et al., 1999] and [Rolls et al., 2003]. However, the brain responses to affective touch are relatively unstudied in children.

Aim: To study how the developing brain processes affective and non-affective touch at 2 years of age using near-infra red spectroscopy (NIRS).

Methods: 20 children of 2 years of age were randomly recruited from the FinnBrain Birth Cohort. The child was held by his mother and we positioned the imaging probe on the fronto-temporal region of the left hemisphere of the child. Then, we slowly stroked the child’s contralateral forearm skin with a soft brush at a velocity of around 3 cm/s (CT fiber stimulation) followed by fast stroking at a velocity of around 25 cm/s (control stimulation). The stimuli was randomized and presented in an event-related fashion, where the stimulus is applied for 2 seconds, with an average inter-stimulus time of 20 seconds. An average of 58 stimuli (29 slow and 29 fast) were provided. The session was video recorded in order to identify epochs where the child was restless or the stimulus could not be applied. The brain activation to the stimuli was studied using a 16-channel intensity modulated diffuse optical imaging system (Nissilä et al. RSI 2005). Photogrammetry was used to record 3D coordinates of the optodes relative to landmarks as well as head shape so that a geometrically accurate model of the head can be used for image reconstruction and visualization.

Results
Preliminary results suggest that affective touch (slow brushing) increases HbT in frontotemporal areas and non-affective (fast brushing) causes an insignificant decrease or no change in that same region.

![HbT response time courses averaged across stimuli and subjects in the ROI.](image-url)
Simultaneous fMRI and fNIRS analysis in young infants

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Functional brain imaging for infant development has seen an exponential growth in the past decade. Functional magnetic resonance (fMRI) and functional near infrared spectroscopy (fNIRS) in particular provide complementary information in terms of temporal and spatial resolution of task related haemodynamic responses, however they both present different challenges when used with infant populations. For infant fMRI there is a trade off between the quality of the data and the need for the infants to be asleep to minimise data corruption due to movement. For fNIRS, depth sensitivity and issues with probe placement can be a problem. We undertook a study of simultaneous fMRI and fNIRS data acquisition to help understand the fNIRS-fMRI correlations in infants. In this work we present a methodology that optimises the computation of the averaged fMRI-BOLD time series for correlation with the fNIRS time series from each channel (based on [1]) by taking in account the position of the fNIRS optodes with respect to the fMRI activation. Each fMRI-active voxel contributes to the average through a weighting factor obtained from the photon measurement density function (PMDF), which gives the probability that a photon migrating from the source to the detector will travel through a given region of tissue. PMDFs for each source-detector pair are calculated using models of light transport in tissue and anatomical information provided by the infant’s own structural scans (using TOAST++ [2]). We present here this methodology as applied to data from a single participant.

We analysed the fNIRS data (acquired with the UCL Optical Imaging System [3]), and fMRI data (acquired from a 1.5T GE HDx scanner), from a single participant (183 days-old) during natural sleep using an experimental set up similar to our previous publications [4]. The infant listened to environmental sounds interleaved with silence in a protocol previously tested with fNIRS and fMRI separately [4]. The fMRI data were analysed in native space using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/), and the fNIRS oxy- and deoxy-haemoglobin (HbO2 and HbHb, respectively) were calculated channel wise using in house Matlab code. ΔHbO2 and ΔHbHb were normalized to maximum change and were correlated with Δ(1/BOLD) (BOLD~1/T2*, as it is a measurement of exponential signal decay).

Table 1. Pearson correlation coefficients between PMDF-weighted fMRI-BOLD from active clusters and fNIRS time series (HbO2 and HbHb), with their significance levels.

<table>
<thead>
<tr>
<th>channel</th>
<th>Δ[HbO2]:Δ(1/BOLD) r</th>
<th>p-val</th>
<th>Δ[HbHb]:Δ(1/BOLD) r</th>
<th>p-val</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.526</td>
<td>0.0364</td>
<td>0.5465</td>
<td>0.0285</td>
</tr>
<tr>
<td>8</td>
<td>0.88257</td>
<td>&lt;0.0001</td>
<td>0.8979</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Figure 1. PMDF for a single fNIRS channel (red-yellow colormap) and fMRI active clusters (blue). The arrows on either side of the fiducial marker showing the channel location represent source and detector positions for that channel.

We calculated the “sensitivity” of each channel to the underlying fMRI activation (see Figure 1) from the PMDFs (% normalised PMDF in active clusters). According to this metric, channel 8 showed the highest sensitivity and channel 1 the lowest sensitivity to the infant’s activation. Table 1 shows that correlation between the weighted fMRI-BOLD and fNIRS data is stronger in channel 8 than in channel 1.

The use of spatially-weighted fMRI-BOLD time series when quantitatively comparing simultaneously acquired fMRI and fNIRS data in infants enables the selection of regions of interest for both data sets and allows the analysis to be limited to brain regions most likely accessible to both techniques.

References:

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High-resolution diffuse optical tomography setup for measurements at quasi-transmission geometry on an adult human head
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Introduction
We have developed a continuous wave measurement setup operating at a dense mesh of sources and detectors with spatial and frequency coding of source-detector pairs [1, 2]. The main goal of our studies was to significantly increase the sensitivity of the NIRS measurement on oxygenation changes in a brain tissue. As it was reported the sensitivity to oxygenation changes increases with source-detector separation [3, 4]. In order to increase the separation designing a detector of high dynamic range was necessary. Moreover, the system was adapted for bed-side monitoring and for simultaneous functional magnetic resonance imaging. We show that our system allows to measure in-vivo optical signals simultaneously at source-detector distances from 1 cm up to 12 cm (source and a detector located on both sides of an adult human head).

Instrumentation
The high-resolution diffuse optical tomography (HD-DOT) system is presented in fig. 1.

Fig. 1. The HD-DOT system (a) and its emission and detection modules (b).

Results
We carried out Valsalva maneuver on healthy volunteers. The maneuver procedure is as follows: 40 s of rest state, 10 s of Valsalva and 1 minute of rest. The influence of the extracerebral tissues on the measured attenuation signals was removed using methodology presented in [1, 5]. Changes in attenuation observed during the Valsalva increases with the source-detector separation. However, an attenuation drop is visible for source-detector distances larger than 8 cm.

Conclusions
We have developed first high-density diffuse optical tomography device capable of collecting signals at extremely large source-detector separations. Results of the Valsalva maneuver test suggest that the signals measured at quasi-transmission geometry are strongly affected by a presence of cerebrospinal fluid. Monte Carlo studies which we carried out support this suggestion. Furthermore, for the large interoptode distances on a human head the photons pathlengths start behave similar to the diffusion transport in a transmission geometry. The Valsalva maneuver results for short (<8 cm) source-detector separations are in a good agreement with signals recorded during the Valsalva maneuver reported in [6, 7].

Acknowledgements
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References
Increased Cortical Activation to Human Versus Mechanical Hands in Infants
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Introduction: In the first year, infants can distinguish between human and mechanical agents and have different expectations for how they should move and interact (Woodward, 1998). Infants are also sensitive to the functional nature of objects (Wilcox & Chapa, 2004), and show increased cortical activity to events possessing a functional purpose (Wilcox, et al., 2014). These findings raise questions about whether there are distinct, early emerging systems for the processing of human and mechanical agents, and whether these systems are influenced by functional relevance of objects. To address this question, the current research uses fNIRS to assess patterns of cortical activation to events involving human and mechanical hands, in the context of events that are either functionally relevant or non-functionally relevant.

Design: Infants aged 7-9 months were tested in one of four conditions formed by crossing hand type (human or mechanical) and event type (functionally relevant or non-functionally relevant). In the functional event, infants saw pound and pour events (a hand used a tool to pound a nail, or scoop and pour rice) on alternating trials. The non-function events were identical to the functional events, except the tools did not come in contact with the nail or rice. About an equal number of infants were assigned to each condition: human hand, function (n = 19); human hand, non-function (n = 16); mechanical hand, function (n = 16); mechanical hand, non-function (n = 18). Events were presented in a puppet-stage apparatus. Infants saw 12 trials (15 s each); each trial was preceded by a 10 s baseline during which a curtain occluded the stage. Prior to test, infants were fitted with a custom-made headgear (Figure 1). Changes in HbO, compared to baseline, were averaged over 8-15 s of each trial; then averaged over trials and participants to obtain a grand average for each group.

Results and Discussion: In the left hemisphere, four spatially contiguous channels (Figure 1a: 1, 5, 6, and 9) showed a significant agent x event interaction, which were averaged to form a left middle temporal ROI. Paired comparisons on the mean left ROI responses revealed that the human hand, function event elicited significantly greater activation than the mechanical hand, function event, $t(33) = 3.577$, $p < .001$, Cohen’s $d = 1.245$. No other comparisons were significant. In the right hemisphere, four spatially contiguous channels (Figure 1b: 11, 14, 15, and 19) showed a significant main effect of agent, $F(1,65) = 14.502$, $p < .001$, $\eta^2 = 0.963$ were averaged to form a right middle temporal ROI. The main effect of event and the agent x event interaction were not significant, $p > .05$. Infants viewing action sequences performed by the human hand showed significantly greater activation than those viewing action sequences performed by the mechanical hand. In summary, the left middle temporal cortex responded selectively to human as compared to mechanical agents, but only in the context of functionally relevant actions on objects. In contrast, the right middle posterior temporal cortex responded selectively to events involving human as compared to mechanical hands, independent of event type. These results reveal discrete processing networks, contributing to understanding the cortical basis of infants' processing of agents, physical objects, and functionally relevant events.

Figure 1 (Left and center). International 10-20 system overlaid on the left and right hemispheres. Red dots are sources, blue dots are detectors, and channels are numbered between each source-detector pair. The gold circles indicate the spatially contiguous channels that evidenced significant activation in each hemisphere. Figure 2 (Right). Mean hemodynamic responses in the left hemisphere of infants in condition: (a) human hand, function; (b) human hand, non-function; (c) mechanical hand, function; and (d) mechanical hand, non-function.
Relationship Need Fulfillment Predicts Self-Other Overlap in the Medial Prefrontal Cortex During Self- and Other-Referential Cognition

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Overview: Social neuroscience studies have shown that regions within the medial prefrontal cortex (MPFC) are reliably recruited by cognitive tasks that entail self-referential thinking such as reflecting upon one’s own physical attributes, feelings, and personality traits. Studies comparing self-referential judgments with judgments about close others inconsistently report comparable levels of MPFC activity across self- and other-referential conditions, suggesting that relationship characteristics may moderate the degree to which the MPFC differentially represents knowledge about the self and others. The present study used continuous-wave functional near-infrared spectroscopy to examine if the degree to which relationship partners support people’s fulfillment of psychological needs for competence (feeling effectual), relatedness (feeling connected), and autonomy (feeling volitional) moderates MPFC activity during self- and other-reflection. Participants (N = 109) were asked to judge the relevance of trait adjectives for both themselves and a friend. While those who reported lower levels of need fulfillment with their friend showed elevated activity only in the self-referential condition, those who reported higher levels of need fulfillment with their friend showed similarly high levels of MPFC activity in both the self- and other-reflection conditions. These results are consistent with the idea that the MPFC differentially represents others on the basis of the need fulfillment experienced within the relationship and that people may incorporate fulfilling relationship partners in to their sense of self.

Method: One hundred nine students (78 females) from the University of Toronto participated in this study either for course credit in their introductory psychology course or for monetary compensation at a rate of $15 CAD ($10.44 USD). Participants nominated a friend and completed the Friendship Autonomy Support Questionnaire (FASQ; Deci et al., 2006) and the Need Satisfaction in Relationships Scale (NSRS: La Guardia et al., 2000). Sample items from these measures were as follows: “I feel that my friend provides me with choices and options” (FASQ) and “When I am with my friend, I feel free to be who I am” (NSRS). Scores on these scales were highly correlated (r = .75) and therefore aggregated to form a composite measure of the need fulfillment experienced within the relationship. While undergoing neuroimaging with continuous-wave functional near-infrared spectroscopy (fNIRS), participants were asked to judge the relevance of trait adjectives for both themselves and their nominated friend (e.g., How accurately does this word describe YOU, talkative?); How accurately does this word describe YOUR FRIEND, reliable?). With its low cost and compact design, fNIRS holds promise for social and personality neuroscience because it affords larger sample sizes and ecologically valid designs. The present study therefore represents an important methodological extension of previous research examining the involvement of the MPFC during self- and other-referential processing and demonstrates the utility of fNIRS for social and personality neuroscience.
Miniature Broadband NIRS System for Brain Tissue Oxygenation and Metabolism

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Abstract: Brain injuries such as neonatal hypoxic-ischaemic encephalopathy (HIE), a common result to birth asphyxia, as well as acute brain injuries in adults, have high rates of mortality and morbidity worldwide. It is therefore important for clinicians to be able to monitor the status of the injured brain at the bedside in real-time, in order to assess patient outcome and redirect clinical care. NIRS is a cheap cerebral monitoring technique compared to other methods such as MRI that provides this monitoring through measuring tissue oxygen levels (oxy and Deoxy-haemoglobin [HbO2 and HHb]). Our group is interested in developing broadband NIRS systems which also enable the measurement of Cytochrome-c-oxidase [oxCCO], an indicative of cellular oxidative metabolism in the mitochondria. We previously developed a high-performance broadband NIRS system, CYRIL (CYtochrome Research Instrument and appLication system), that monitors brain oxygenation and metabolism in the HIE babies within the neonatal intensive care unit (NICU). However, there is an urgent need for a compact and more accessible broadband NIRS system to monitor infants and adults at the bedside.

A single-channel compact broadband NIRS system called "Mini-CYRIL" was developed based on a miniature white light source (filtered>675nm) and a miniature broadband spectrometer (440-1100nm). Significantly reduced in size (figure 1b), Mini-CYRIL acquires the spectral data (integration time:22ms-4min) and uses the UCLn algorithm to convert changes in light attenuation through the tissue (780-900nm) to real-time changes in [HbO2] and [HHb] as well as [oxCCO]. Mini-CYRIL also accounts for the wavelength dependency of the differential path-length factor (DPF) and quantifies the changes in concentrations through real-time measurement of optical path-length at 840nm, using second differential spectroscopy of water. The miniature system was validated using standard cuff-occlusion measurements (figure 1c). Due to its portability, Mini-CYRIL has been deployed in various studies including preclinical HIE and baby fNIRS studies, as well as spinal cord and retinal measurement.

Figure 1: Comparison between the size of CYRIL (a) and Mini-CYRIL (b) broadband NIRS systems with respect to the size of a term baby doll. (c) Data from adult cuff occlusion measurement (source-detector: 28mm).
A principal challenge encountered with fNIRS studies is the difficulty to create an efficient, stable and comfortable optical interface with the scalp, especially in the presence of hair. Hair and hair follicles can act as strong attenuators leading to poor signal quality [1]. Often, significant time and effort can be invested to ensure that a minimum amount of hair remains under each optode especially for subjects with thick, darkly colored hair [2].

A variety of strategies have been implemented to deal with this issue. One approach involves use of small diameter optode tips. This is often combined with the application of a constant pressure onto the tip, either through some spring-loaded mechanism, or the use of elastomeric caps or bands. While effective, use of smaller diameter tips can cause significant discomfort and limits sensing area, thus reducing signal quality. Also, strategies to overcome the hair barrier may require careful scalp preparation involving local parting of the hair (possibly with the aid of gels or liquids) or ‘rubbing’ of the optodes through the hair. While the latter can improve setup times, it is prone to disturb other regions of the sensor array and can add to discomfort, thus limiting the population of subjects amenable to this method.

Here we describe an optode design that significantly reduces setup time without sacrificing comfort or signal quality. Key design features include dual-tip probes [3] housed within a spring-loaded assembly that supports rotary movement thus enabling a sweeping like motion for fast hair displacement. This design is suitable for fiber optic probes as well as fiber-less optodes (LED source, photodiode detector), see. Figure 1.

Figure 1: (a) Standard single-tipped fiber-optic probe. (b) Dual-tip LED-source (insert shows bottom view). (c) Dual-tip fiber-less (SiPD) detector. (d) Dual-tip fiber-optic probe. (e) Placement of optode in holder before securing with spring-loaded cap from top. (f) Optode seated in spring-loaded holder; arrows indicate the forces involved in hair separation: blue = twisting motion, orange = downward-directed spring tension.

Improved Setup Times. The twisting preparation requires only a few seconds of manipulation of each position and avoids the need for line-of-sight inspection otherwise required to ensure site proper preparation. This is equivalent to a ‘rubbing’ type preparation but is easier to perform and less disturbing to the headgear. The ‘traditional’ individual hair parting approach can require tens-of-seconds per position.

Optical Efficiency. Dual-tipped fiber-optic probes and LED sources have identical efficiencies compared to their single-tipped counterparts, while offering the advantage of fast setup. For fiber-less silicon photodiode (SiPD) sensors, such as employed with our ‘NIRSport’ instruments, sensing efficiency was improved by 2.7x by increasing the photosensitive area and efficiency of the optical elements. This value is within a factor of two (1.5x) that obtained using high-end fiber-based Avalanche-Photodiode (APD) solutions.

Conclusion. The dual-tip design affords efficient hair displacement with fast setup times comparable to the simple ‘rubbing-on’ approach while retaining the sensitive area and comfort of our previous designs. Sensitivity improvements of 2.7x have been achieved with a fiberless sensor.

References.
A New Instrument for Simultaneous Frequency-Domain NIRS and DCS Measurements.

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A new instrument combining multi-distance frequency-domain near-infrared spectroscopy (MDFD-NIRS) and diffuse correlation spectroscopy (DCS) capabilities is illustrated. The new instrument allows rapid and simultaneous acquisition of both signals in a single sensor. MDFD-NIRS measurements are made using laser-diodes at eight wavelengths between 670nm and 840nm. DCS measurements are made using a long coherence length 850nm solid state laser. DCS detection is accomplished with 8 photon-counting avalanche photo-diode channels, and the instrument uses 4 miniature photomultiplier for MDFD-NIRS detection. The sensor system is all fiber optic with collocated optics at the sensor working surface. An overall measurement rate 20 Hz has been achieved with real time FDNIRS and DCS calculations for real time signal evaluation. It is possible to record pulsatile signals in both modalities. Design choices are discussed and performance is evaluated.

Keywords: frequency-domain near-infrared spectroscopy diffuse correlation spectroscopy, instrumentation
NIRS 3D Reconstruction Based on Maximum Entropy on the Mean (MEM)

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Introduction: Not only does NIRS tomography project the measured data on the scalp to the cortical surface, it also significantly improves overall image quality and reliability. In the present study, we adapted a nonlinear EEG/MEG reconstruction method - Maximum Entropy on the Mean (MEM) to solve the inverse problem in NIRS reconstruction, considering its accurate and stable performance when recovering the locations of the generators together with their spatial extent along the cortical surface.

Method: MEM offers an efficient probabilistic framework to incorporate prior knowledge in the solution of the inverse problem. Our current implementation assumes brain activity is modeled by cortical parcels. These parcels are estimated using a data-driven parcellization of the full field of view considered for NIRS tomography. Each parcel is associated to a state variable controlling whether the parcel is active or not. While fitting the data through relative entropy maximization, MEM allows switching off inactive parcels of the model.

To evaluate the method, an optimal source-detector montage (Fig. 2a) was estimated for a focal region within the primary motor cortex, manually identified by a neurologist. This montage was used for 1) NIRS data acquisition on a healthy control using Brainsight (Rogue-Research Inc.) during a finger tapping task and resting state, and 2) realistic simulations obtained by simulating a hemodynamic response within this region, followed by applying a realistic NIRS forward model and addition of real resting state data.

Results: Fig. 1 shows the comparison of reconstructed activation map calculated by MEM and the standard Minimum Norm Estimate (MNE) inverse solution. Fig. 1c shows that MNE results extended outside the ground truth (SpatialDispersionHbO,HbR~4.5mm) and the reconstructed signals within this region were contaminated by noise. However, MEM results were more focal (SDHbO,HbR~1mm) while the reconstructed signal was less noisy. Fig. 2 shows the reconstruction results of real data, as expected, MEM provided more focal reconstruction along the primary motor cortex.

Frontal brain activation during heavy resistance exercise with and without the Valsalva maneuver

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Introduction
Repetitive resistance exercise (RE) causes rapid fluctuations in mean arterial blood pressure (MAP) and performing a Valsalva maneuver (VM) during RE will probably affect cerebral hemodynamics. The present study investigates how RE performed with and without a VM affect indices of blood flow and HbO2 and HHb concentration changes (Δ) in the prefrontal cortex of healthy adults.

Methods
Participants. Four female and six male, healthy volunteers (mean ± sd: 24.5 ± 2.3 yrs., 178 ± 7.2 cm and 75.9 ± 14.6 kg) participated in the study.

Procedures. RE was 3 Sets (S) of bilateral knee extensions performed in a training apparatus at 93 ± 1.5 % of the participants’ maximum strength. The RE sessions was conducted with and without VM (WVM) in a randomized order and separated by 48 hours. The weights were lifted to voluntary exhaustion (5.9 ± 1.1 reps) and with 3 min recovery between sets.

NIRS. Frontal brain activation was assessed using a 3-channel Portalite system (Artinis, The Netherlands). The Portalite was placed over the left (Fp1) frontal cortex region of the forehead. NIRS data was recorded at 10 Hz. Results are reported as concentration changes in oxy- and deoxyhemoglobin (Δ[HbO2], Δ[HHb]). Total Hb (Δ[TotHb] = Δ[HbO2] + Δ[HHb]) is indicative of changes in regional blood volume. MAP was measured by finger photoplethysmography (FMS, The Netherlands).

Results
Table 1. MAP and concentration changes of oxy- and deoxyhemoglobin during RE. Values are means ± SD. N = 11.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rest</th>
<th>Resistance exercise (RE)</th>
<th>With Valsalva Maneuver (WVM)</th>
<th>With Valsalva Maneuver (VM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Valsalva Maneuver</td>
<td>S1</td>
<td>S2</td>
<td>S3</td>
</tr>
<tr>
<td></td>
<td>With Valsalva Maneuver</td>
<td>S1</td>
<td>S2</td>
<td>S3</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>95±7.5</td>
<td>137±16</td>
<td>135±15</td>
<td>150±31</td>
</tr>
<tr>
<td></td>
<td>***</td>
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<td>***</td>
</tr>
<tr>
<td>Δ[HbO2], μm</td>
<td>0.57±0.92</td>
<td>3.99±2.4</td>
<td>5.69±2.6</td>
<td>6.83±3.9</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Δ[HHb], μm</td>
<td>-0.07±0.47</td>
<td>-0.39±0.98</td>
<td>-0.16±1.3</td>
<td>-0.04±1.3</td>
</tr>
<tr>
<td></td>
<td>-0.16±0.97</td>
<td>0.12±1.0</td>
<td>-0.03±1.0</td>
<td></td>
</tr>
<tr>
<td>Δ[TotHb], μm</td>
<td>0.50±0.96</td>
<td>3.60±2.1</td>
<td>5.54±2.6</td>
<td>6.79±3.9</td>
</tr>
<tr>
<td></td>
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</tr>
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</table>

*p < 0.001; Rest vs. S1, S2, S3. ¹p < 0.05; S1 WVM vs. S1 VM; ²p < 0.01; S2 WVM vs. S2 VM.
³p < 0.05, ⁴p < 0.01; S1 VM vs. S2 VM and S3 VM. ⁵p < 0.01; Set 1 VM vs. Set 3 VM and Set 2 VM vs. Set 3 VM. ⁶p < 0.05; S1 vs. S2 of S3 WOV. ⁷p < 0.05, S1 vs. S2 and S3 VM. ⁸p = 0.1; Set 3 WOWM vs. Set 3 VM

Conclusion
During RE with VM, MAP was higher compared to WOVM. From rest, cerebral blood volume (Δ[TotHb]) and Δ[HbO2], increased both during VM and WOVM, but there is a trend for lesser changes when RE is performed with VM (p = 0.1).
Time-domain Near Infrared Spectroscopy of Extra-cerebral and Cerebral Hemoglobin Concentrations During Incremental Intensity Exercise

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Introduction. Physical exercise is known to promote brain health. Changes in physical activity are related to functional and structural alterations in the brain. However, the understanding of immediate cerebral changes due to exercise is currently incomplete due to the lack of tools to measure brain function during exercise.

Methods. We used time-domain near infrared spectroscopy (TDNIRS) to quantify extra-cerebral and cerebral hemoglobin concentrations and oxygen saturation (SO2) in the prefrontal cortex of 15 young adults at rest and during incremental intensity exercise (40% and 80% of subject’s peak power output - PPO). Individual PPO was derived by the maximum oxygen volume consumption test (VO2max) performed on an ergonomic stationary bicycle allowing subjects to cycle at a constant power measured in watts. The TDNIRS system included a combined source of 4 pulse lasers (690, 760, 810 and 840 nm) positioned between 4 single photon counting avalanche photodiodes located at 10, 15, 25 and 30 mm from the source. Instrument response function (IRF) was measured for each condition. Data acquisition was 10 min. Hemoglobin concentrations were estimated with optical properties recovered using a 2-layer fitting model.1 Temporal point spread functions were first fitted with a homogeneous model to provide initial values to be injected in the 2-layer model. The thickness of the extra-cerebral layer was fixed and based on MRI data. The cerebral layer was considered semi-infinite. Hemoglobin was then quantified with cerebral optical absorption and known extinction coefficients. Absolute concentrations were compared between conditions with general linear mixed models.

Results & Discussion. In extra-cerebral tissue, an increase in deoxy-hemoglobin (HbR) and a decrease in SO2 were observed while only cerebral HbR increased at 80% (Fig. 1). Results in extra-cerebral tissue are consistent with thermoregulatory mechanisms2 to dissipate excess heat through skin blood flow, while cerebral changes are in agreement with cerebral blood flow redistribution mechanisms3 to meet oxygen demand in activated regions during exercise, such as the prefrontal cortex supporting executive function. No difference was observed in oxy-(HbO2) and total hemoglobin (HbT), which differ from some previous continuous-wave (CWNIRS) studies. This difference may be due to the extra-cerebral contamination observed in CWNIRS. Also, HbO2, HbR and HbT increased with subject’s PPO supporting previous results of increased total mass of red blood cells in athletes.

Conclusion. Our approach in quantifying both extra-cerebral and cerebral absolute hemoglobin during exercise may help to better interpret past and future CWNIRS studies that are prone to extra-cerebral contamination and allow a better understanding of acute cerebral changes due to physical exercise.

Perception of temporal regularity in tactile stimulation: a diffuse correlation spectroscopy study in preterm neonates

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An essential function of our brain is to identify temporal structures in the environment and use them to form predictions, allowing us to optimize our behavioral response and the use of attentional and energetic resources. Temporal predictions also form the basis of cognitive functions and social interactions. They have been recently described in 6 months old infants (Emberson et al., 2015). Our ability to process temporal regularity seems to appear very early, but the development of this process is not known. We only know that related skills are present at birth (Stefanics et al., 2007), suggesting that the ability to process temporal information emerges during the prenatal period, but this has not been studied.

In a previous study we found that preterm neonates are capable of behavioral response suppression (i.e. habituation) when presented with regular tactile stimuli (vibrations), and that they show response rebound when the inter-stimulus interval is extended, suggesting that the change in temporal properties of the stimulation sequence is perceived (publication in preparation). In the present study, our aim is to further investigate the ability of preterm neonates to use the inter-stimulus regularity to generate sensory predictions. We address this issue in the tactile modality as it is the earliest to develop, and is a fundamental sensory input in newborns for both object processing and social interactions.

Forty healthy neonates born between 31 and 32+6d weeks of gestational age are randomly assigned to two experimental groups. Measurements are performed at 33 and 35 weeks of corrected gestational age, during post-feeding sleep. The stimulation consists in 3 s long vibrations delivered to the palm of the right hand, interspersed with 5 s long regular intervals (group 1) or 3 to 7 s long irregular intervals (group 2). During the 13 minutes long stimulation sequence, 10 stimuli are randomly omitted. Diffuse correlation spectroscopy (αmax-FloMo, HemoPhotonics S.L.) is used to estimate changes in blood flow in the cortical tissues during stimulation (Durduvan & Yodh, 2013). A miniature probe is maintained over the subject's contralateral primary somatosensory cortex. We hypothesize that in group 1, regularity will induce an omission response when the stimulus is unexpectedly absent (as is observed in adults using BOLD fMRI, Chen et al., 2010) and/or a response rebound to the stimulus immediately following the omission. In group 2, we do not expect an effect of omissions. Data analysis is underway; preliminary findings and implications will be discussed.

During their stay in the neonatal care unit, premature neonates are subjected to constant, non-ecological tactile stimulation, at a most critical time of growth of their nervous system. They have an increased vulnerability to neurodevelopmental disorders involving atypical tactile and temporal information processing (Cascio, 2010). Recently, Sinha et al. (2014) proposed that clinical signs of autism could be explained by a prediction impairment. A better understanding of tactile and temporal processing in preterm infants would allow us to better understand the influence of early sensory experiences on the neurodevelopmental development of these vulnerable patients.


Development of a Portable functional Near-Infrared Spectroscopy Device

Brian Feild, Nishi Rochelle, Satoshi Yomota, Ryu Konoshita, Nobuyuki Akinaga, Hiroyuki Matsumoto, Rintaro Yamamoto, Eiji Ando and Shin Nakamura

With the development of brain science research, the demand of wearable device which features degrees of measurement freedom is increasing. In designing a portable system, the system must be lightweight, comfortable and not interfere with the task while maintaining a high quality signal. LIGHTNIRS (Shimadzu, Kyoto Japan), a wearable fNIRS system(Fig.1) was designed in order to meet these requirements for the following research field; (1) Neuro-marketing research which investigates the preferences and decision-making process of consumers, (2) Communication research which identifies the relationships between individuals in social groups, (3) Physical Therapy research which identifies neural mechanisms related to physical therapy benefits, (4) Brain-Machine Interface research which uses biofeedback to restore or supplement body functions.

LIGHTNIRS consist of 8 sets of transmitter and receiver fibers, providing 22 channel and images can be acquired at rate of 75 ms. Two type of holders (Fig.2A,2B) are specially designed to allow the arrangement of the fibers to measure any brain region of interest. Due to the small size and light weight, measurements, LIGHTNIRS is compact enough to be carried with a specialized carrying bag. Communication between PC enable to measure 4 subjects at the same time.

This presentation will focus on the development of a new portable fNIRS platform which includes system configuration, specification and features. This new wearable fNIRS system will open up brain function research for a variety of research fields.

Fig.1 LIGHTNIRS main unit       Fig.2A  Holder for cognitive function

Fig.2B  Holder for motor function
Characterization of Hemoglobin Dynamics as a Co-Varying System in the Resting State: Evidence of Functional Bias of Preferred States and Sensitivity to Disease

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Abstract:
The dynamics of an arbitrary system can vary, from those dominated by stochastic processes to those constrained in particular ways. Experience shows that the dynamics of the hemoglobin (Hb) signal is principally constrained by systemic and local autoregulatory factors that serve to establish a quasistatic equilibrium at rest, wherein the amplitude of the oxygenated and deoxygenated Hb components (oHb, dHb, respectively) vary about some temporal mean values. Further, a disturbance that restricts blood flow causing hypoxia (ischemia), followed by its release, will spontaneously elicit a transient compensatory response leading to hyperemia followed by spontaneous return to the resting state levels. While the preceding is widely appreciated, many commonly applied data analysis strategies do not attempt to exploit the coupling present in the (oHb, dHb) two-state system, which generates variations in the Hb signal that reflect behaviors in which elements of the Hb response necessarily co-vary. In a previous report we demonstrated that a simplified categorical scheme containing unique combinations of these co-variations and the accompanying changes in total Hb levels, appears to yield associations that are not observable from examination of the individual components [1]. This scheme, outlined in Table 1, is represented in the familiar case corresponding to the sequence of transitions accompanying a compensatory response to transient hypoxia.

For this report we have applied this methodology to evaluate measures of the hemoglobin signal acquired from the breasts of healthy subjects and those with confirmed breast cancer and benign disease. Observed categorical behaviors can be contrasted to a stochastic model as a basis for determining functional biases. Three distinct types of information are accessible from this examination. One involves measures of the likelihood of state transitions and their time dependence. Another considers regions of interest that share a common functional state. While time-varying on a local level, evidence that different regions of tissue exhibit preferred states is provided. Still another recognizes that determination of the time-varying amplitude of individual elements comprising these states provides a basis for defining a host of features that may serve to distinguish the expected influence of disease. Specifically considered was diagnostic performance provided by application of metrics comprising measures of the first and second moments of the pixel time series, over the space and time domains. Evidence provided demonstrates that the information retrievable from measures that consider the hemoglobin response as a co-varying system is significantly greater than is available from examination of its individual elements. Also identified are specific features of the system response that may serve as useful biomarkers for disease.

Table 1. Co-Varying Hb States

<table>
<thead>
<tr>
<th>Hb Component</th>
<th>State 1</th>
<th>State 2</th>
<th>State 3</th>
<th>State 4</th>
<th>State 5</th>
<th>State 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hboxy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hbdeoxy</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HbTotal</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Balanced</td>
<td></td>
<td>Uncompensated oxygen debt</td>
<td>Compensated oxygen debt</td>
<td>Balanced</td>
<td>Uncompensated oxygen excess</td>
<td>Compensated oxygen excess</td>
</tr>
</tbody>
</table>

Algebraic signs identify Hb component value relative to the temporal mean.

Reference:
Disobeying an immoral rule is associated with a greater emotional reaction than obeying it: An exploratory fNIRS study.

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In the last decades, various studies in neuroscience have highlighted the involvement of emotional processes in moral decisions (e.g., Moll et al., 2002; Greene et al., 2003). More precisely, the ventral-medial prefrontal cortex (VMPFC), which underpins the normal generation of social emotions, was found to play an important role in moral decision-making (e.g., Greene et al., 2003; Koenigs et al., 2007). Little is known on how individuals deal with their emotions when they are asked by a line manager to follow a rule that conflicts with their moral values (e.g., I should not kill people). The present experiment aimed at determining the neural correlates associated with 1) the choice to follow an immoral rule imposed by a line manager and 2) the choice to disobey a line manager and follow moral values in the context of military operations. Participants were acting as drone pilots and their brain activity was measured using a prefrontal 16-channel functional near-infrared spectroscopy (fNIRS). In each trial, the drone piloted by the participants suffered damage and the latter had to choose the best place to crash the drone between a “civilian site” where civilians were standing, and a “military site” with military facilities/equipment. Participants were informed that the drone crash would kill every person present at the crash site and that nobody would be killed if they chose to crash on the “military site”. In the first part of the experiment, participants were given no rule and had to choose the crash site according to their own preferences. However, in the second part of the experiment, they were explained that their mission was to protect military sites. The results revealed that participants chose to sacrifice civilians more frequently when they were given the order to protect military sites compared to when they were not given any rule. Moreover, participants were longer to make their decisions when they were confronted to a moral dilemma (i.e., following moral values versus obeying orders) than when they were not.

Lower central PFC activations were found when participants chose to follow the immoral rule (i.e., sacrificing civilians) compared to when they chose to disobey (i.e., not killing individuals). Central PFC regions were found to underpin the normal generation of social emotions (Koenigs et al., 2007). Taken together these results demonstrate that making the choice to disobey a rule given by a line manager is associated with a greater emotional reaction than choosing to obey it, although this rule is immoral and leads to kill innocent people. Choosing to disobey a rule may have a greater “emotional cost” than obeying it, which may explain why some individuals are likely to follow bad rules rather than oppose it.


Studying the propagation of systemic hemodynamic oscillations in human body using peripheral near infrared spectroscopy measurements

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Introduction: Low Frequency Oscillations (LFOs: 0.01-0.15 Hz) are slow, spontaneous variations, commonly observed in BOLD fMRI signals and in oxy- and deoxy-hemoglobin signals in functional near infrared spectroscopy [1]. It has been demonstrated with concurrent NIRS/fMRI that part of the LFO signal travels through the brain following the cerebral vasculature. Moreover, the same LFO signals have been observed in the periphery simultaneously with NIRS at various time delays [2]. To deepen our understanding of the propagation of sLFOs, especially in periphery, we used a custom built NIRS system to record the LFOs signals at different peripheral sites (i.e. earlobes, fingertips and toes) to assess the different arrival times of sLFOs.

Method and analyses: In this study, 13 healthy subjects were recruited. Six Nellcor type fingertip pulse oximeter probes were placed over the subject’s two earlobes, two index fingers and two 2nd toes, as shown in Fig.1(a). The NIRS data were acquired simultaneously with our MRO (Multichannel Research Oximeter), a 7-channel microcontroller-based NIRS device designed and assembled by our lab. The NIRS data were acquired continuously at 31.25 Hz for 30 minutes while the subject lay on a comfortable bed. The three 10-mins experimental blocks were: 1) resting state; 2) involuntary left leg lifting (the experimenter raises and lowers the subject’s leg in a predetermined pattern); 3) and a paced breathing task. For each subject, the oxy-, deoxy- and total hemoglobin concentration changes (∆[HbO], ∆[Hb] and ∆[tHb]) were calculated for each peripheral site and then filtered to the low frequency range. The power spectrum of these sLFOs and time delays between sLFOs of any two sites (e.g. left earlobes and right earlobes, left fingertip and left toe, etc.) were calculated in each experimental condition.

Result and conclusions: In Fig.1(b) to (d), we can see: 1) The sLFOs observed at symmetric peripheral sites (e.g. left and right earlobe) are highly correlated (correlation coefficient =0.8) with almost no relative time delay in all three conditions. 2) In the resting state, the LFO signal in the hands and feet are delayed by several seconds relative to the earlobes, and the LFOs are delayed in the feet relative to the hands. 3) A local perturbation, such as left leg lifting, is widely observed in other peripheral sites, which reflects some internal feedback mechanisms of human body. 4) In paced breathing, which is a global perturbation, we observed corresponding sLFOs at all the peripheral sites with shorter delays between them, indicating two interesting things. First, these sLFOs may be tightly linked to CO2 fluctuations in the lungs, then carried by the blood to different parts of the body [3]. Secondly, the shorter intrasite delay of the sLFOs at different sites may reflect the blood flow increase during the paced breathing. The goal of the pilot study is to deepen our understanding of sLFO, which is a confound signal to functional studies in both fMRI and fNIRS, moreover, it can be developed into a biomarker to assess central and peripheral blood circulation, symmetry and efficiency [4].

Reference:
Fig. 1 (a) Schematic drawing of the placements of the NIRS probes (i.e. over the two earlobes, two index fingers and two 2nd toes) in the experiments. (b) The paired LFOs (i.e. \( \Delta[HBO] \)) recorded from 3 symmetric peripheral sites of one subject and their calculated time delays in resting state. (c) Same experimental data recorded during involuntary left leg lifting; the lifting periods are indicated by the shaded areas with frequency of 0.05Hz. (d) Same experimental data recorded during paced breathing task indicated by the shaded areas with frequency of 0.1Hz.
The influence of superficial layers on near infrared spectroscopy data
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Abstract: Changes due to exercise in muscle tissue oxygen saturation (StO$_2$), measured by near infrared spectroscopy (NIRS) are known to be lower for subjects with higher adipose tissue thickness (ATT). This is most likely not physiological but caused by the superficial layer, which reduces sensitivity to the deep tissue. This is also true for the brain, which is covered by superficial layers of skull and skin. The aim of this project was to assess in vitro, how superficial layers influence deep tissue StO$_2$ measured by NIRS oximeters and how this influence can be removed.

Material and method: We prepared a liquid phantom with total hemoglobin concentration ($C_{htb}$)=70 µM and mounted 4 windows, resembling the optical properties of superficial layers such as adipose tissue. We conducted 4 cycles of oxygenation-deoxygenation of the liquid phantom and each time shifted the NIRS oximeters (Nonin adult, INVOS adult, OxyPrem v1.3, and OxiplexTS) to the next window. Hence after 4 repetitions, each oximeter had measured through 4 different $d_{\text{window}}$. We started deoxygenating by adding fresh baker’s yeast (3g) and re-oxygenated the hemoglobin by providing an oxygen flow (2L/min) into the phantom. In an in-vivo measurement, we acquired StO$_2$ data during an arterial occlusion measurement on the arm of the subject. With locally measured ATT, the results from the phantom and a measurement on the belly we calibrated StO$_2$ to reduce the effect of superficial layers.

Results and discussion: Figure 1 shows a comparison of the trend of sensitivity vs. $d_{\text{window}}$/APD, where APD is the average penetration depth, between the continuous wave (CW) oximeters and the frequency domain (FD) oximeter. It is visible that for $d_{\text{window}}$/APD <1 both trends look similar, but as $d_{\text{window}}$/APD increases, the FD oximeter retains higher sensitivity. Figure 1 also shows 50% relative sensitivity at $d_{\text{window}}$/APD = 1.5 for CW oximeters and at $d_{\text{window}}$/APD = 1.75 for the FD oximeter. This value is similar to the ones reported in the literature, investigating influence of ATT on absorption coefficient ($\mu_a$) and reduced scattering coefficient ($\mu'_s$) measured by an FD oximeter. By the in-vivo calibration we reduced the error in absolute StO$_2$ caused by adipose tissue by at least 43% and can reduce it to a minimum for measurements of StO$_2$ changes which are relevant for fNIRS and other types of activation studies.

Conclusion: We conclude that all the CW oximeters employed were sensitive to StO$_2$ of the liquid phantom even when $d_{\text{window}}$ was as thick as 16 mm. In comparison to the FD oximeter, the CW oximeters lost their sensitivity faster as $d_{\text{window}}$ increased. For the brain, since bone and skin have a higher scattering and absorption coefficient, the effects will even be aggravated. We also presented a method that reduces the error in absolute StO$_2$ caused by the layer of adipose tissue, which could be applied for measurements in the brain in a similar way.

![Figure 1. Trend of the sensitivity of oximeters vs. $d_{\text{window}}$/APD.](image-url)
Demonstration of the spatial sensitivity of a compact HD-DOT system using a retinotopy paradigm

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Traditional Diffuse Optical Tomography (DOT) systems rely on fiber optic cables to carry optical signals to and from the imaged tissue. As the number of channels increases, the weight and size of the fibers limits both the comfort and the practical utility of such systems in clinical use. We have developed a compact, non-fiber based high-density DOT (HD-DOT) sensor and used it for retinotopic imaging of the visual cortex in human volunteers. The sensor consists of 10 source optodes and 18 detector optodes printed on rigid-flex circuit boards for flexibility. Each source optode contains five lasers operating at five different wavelengths ranging from 690-850nm with source-detector separations ranging from 13-87mm. Data are digitized, processed, and transmitted to a laptop via Ethernet at 5Hz for post-processing.

Retinotopy recordings were performed on two subjects, where the sensor was placed above the inion over the visual cortex. During recordings, seated subjects were asked to stare at a rotating checkerboard wedge stimulus (RCWS) located ~30in away and rotating in 10°/sec steps. Ten full revolutions of the RCWS were presented. Raw optical intensity data were post-processed to generate images of oxy-hemoglobin changes (ΔHbO) using previously described methods. Estimated ΔHbO trends for three pixels from different regions of the imaging field reveal strong periodicity of the response to RCWS with a distinct phase for each region (Fig 1a). ΔHbO images for different RCWS positions (Fig 1b) demonstrate the spatial sensitivity of our HD-DOT system. Phase values of the temporal ΔHbO estimates were computed at the frequency of the RCWS rotation for each pixel and mapped to the polar angle of the RCWS position (Fig 1c). The phase map in Fig 1c shows the typical pinwheel pattern associated with retinotopic mapping of the primary visual cortex consistent with earlier works [1].

We have demonstrated the spatial sensitivity of our compact HD-DOT sensor to cortical neurovascular coupling using a retinotopic mapping experiment. Initial results from two subjects highlight the spatial sensitivity and the utility of this system for functional brain mapping applications.

Figure 1 – HD-DOT imaging results from the rotating checkerboard wedge stimulus (RCWS) for a subject. (a) Temporal ΔHbO trends for three arbitrarily chosen pixels are shown for five revolutions (Rev) of the RCWS revealing high signal-to-noise, periodicity, and phase distribution of the ΔHbO response. (b) ΔHbO images shown below five different RCWS positions, indicating the region of activation in the visual cortex of the brain. (c) Colormap of the wedge position (top); and the polar angle map of the ΔHbO response showing the typical pinwheel pattern associated with retinotopic mapping of the primary visual cortex (bottom).

Neural Variability as an Indicator of Age-Related Cognitive Function

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Variability in neural activity has historically been treated as noise, in favour of deriving estimates based on central tendency (e.g., mean). Recently, researchers have shown that variability and mean confer different sources of information and that increased variability in neural activity is associated with superior behavioural performance and that it decreases during late-life. Although mounting evidence suggests that increased neural variability is beneficial for cognitive function, it is less clear whether this positive association is driven by within- or between-person factors, or is further modulated by increasing age or recent falls (indicating executive impairment). Further, variability can be derived in several different ways, drawing into question its congruence across operationalizations. To date, the majority of age-related variability findings have been found using fMRI, with comparatively low temporal resolution. Given its superior temporal properties, fNIRS is well suited for deriving more densely sampled profiles of variability in cerebral oxygenation.

The present investigation decomposes within- and between-person sources of variance for three operationalizations of cerebral oxygenation; central tendency (mean), variability (standard deviation) and signal complexity (multivariate multiscale entropy). 25 older adults (71-81 years of age) completed a test of cognitive interference (the Multi-Source Interference Task (MSIT)) while undergoing fNIRS recording. The MSIT was derived from the Stroop, Eriksen Flanker and Simon tasks and was designed to activate the cingulo-frontal-parietal cognitive attention network. We used a multichannel, continuous-wave optical imaging system (CW6) developed by TechEn. The system contained an array of 8 sources (4 at 690nm, 4 at 830nm) and 8 detectors, for a total of 10 channels (source detector separations = 8 at 3cm and 2 at 1.5cm). The array was positioned over bilateral prefrontal cortex, and target brain regions were established a priori using Homer 2 software.

Time-varying covariation models were employed to estimate the effects of cerebral oxygenation on behavioural performance, as well as the moderating effects of age and fall status. Findings suggest that mean and variability estimates are differentially associated with behavioural performance (accuracy and RT) with both showing increases in older adults at greater fall risk. Whereas mean-based computations were positively associated with more accurate and faster responding, variability-based computations were primarily associated with faster responding only and occurred in non-overlapping channels across the prefrontal cortex. These patterns are in keeping with compensation-related hypotheses, suggesting that at-risk older adults recruit additional neural tissue relative to low-risk adults to achieve comparable levels of behaviour. Future studies of neural variability may consider examining within- and between-
person factors and operationalizing signal complexity in cerebral oxygenation over longer time periods to examine its effects over multiple time scales.
Diffuse Correlation Spectroscopy (DCS [1,2]) offers an alternative way to directly estimate cerebral blood flow (CBF), and the combination of DCS and near-infrared spectroscopy (NIRS) measurements can offer robust quantification of the cerebral metabolic rate of oxygen (CMRO$_2$). However, both techniques employ diffusely reflected light that has traveled mostly through extracerebral tissues. Recent studies indicate that depth sensitivity profiles are different for NIRS vs DCS measurements, with DCS appearing to be more sensitive to the brain than NIRS methods for a given source-detector separation [3,4]. This mismatch can lead to erroneous conclusions with respect to the amount and perhaps even the direction of change in CMRO$_2$. Previously, theoretical two or multi-layer theoretical models based on the correlation diffusion equation have been developed for improving the accuracy of DCS-based perfusion measurements in layered media [5,6]. However these models are limited by their assumption of a flat, infinite slab geometry. Recently, our group has demonstrated the use of Monte Carlo (MC) based multi-layer, multi-distance fitting [7], which offers increased accuracy for complex tissue structures such as the adult brain.

In this paper we employ a method based on a realistic head geometry that can be derived from MRI scans (if available) or approximated from head shape measurements. We combine DCS measurements taken at two or more distances with a MC based forward model (based on a version of the tMCimg Monte Carlo software package [8] modified to store momentum transfer at each scattering event). The MC head geometry is a variable thickness 2-layer model derived from the external head surface by sequentially eroding 22 $1$-mm thick tissue layers. Photon history from the superficial and deep layer groups, respectively, was concatenated to achieve an effective 2-layer representation.

Through simulations we explore the improvements offered vs. processing the measurements with a semi-infinite diffusion model and estimate the impact of errors in geometry and optical properties on rCBF and rCMRO$_2$ estimates. An example is shown in the figure below, based on simulated data from an actual segmented head MRI from an adult subject. A 100% increase in CBF was considered without changes in CMRO$_2$ (similar to a hypercapnia experiment). Using a homogeneous tissue model results in estimating an erroneous 12% increase in CMRO$_2$ even when accurate baseline optical properties were used in the inversion.

**References:**
Saturday, Oct 15th
Regional Optical Measures of Cerebrovascular Status Associated with Cortical Volume in Healthy Aging

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Aging is accompanied by anatomical and cerebrovascular deterioration. However, the relationship between regional cortical volume and cerebrovascular status is less clear, as only gross estimates of cerebrovascular health have been available. Recently, we developed a novel tomographic optical method allowing local estimates of cortical vascular status through the measure of arterial compliance. Here, we extracted MRI volumetric and arterial compliance estimates within multiple cortical regions. These regions were defined by the cortical boundaries of 47 healthy participants (18-75 years old), derived using FreeSurfer. Between participants analysis revealed a correlation between cortical volume and arterial compliance. Compliance also mediated age and cortical volume association. Regional correlations revealed an average stronger effect of aging on particular cortical areas. However, no consistent pattern of atrophy was identified in older adults. Within participants analysis highlighted volume and compliance spatial association. This association was stronger in older participants (age>48 years), and strengthened with age. By means of hierarchical clustering, this relationship was found to be significant for multiple levels of spatial resolution. These results suggest that some of the variance of sub-clinical atrophy found in ageing is associated with worsening of macro- and micro-vascular environments and it can help explaining the atrophy pattern of each individual.
Vector-based analysis of local cerebral activation for quantitative fNIRS study

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Vector-based fNIRS is a new analysis technique which can process simultaneously with oxyHb, deoxyHb, cerebral oxygen exchange (COE) and cerebral blood volume (CBV) on a two-dimensional plane such as Figure 1. The relationship between the change in ΔCOE and the change in ΔCBV can be detected by vector trajectories using Equation (1-4). The utility of this technique has been reported by detecting the initial dip (1, 2), a metabolic influence of the respiratory routes (3), and the driver’s brain activation during real operation (4-7). A unique advantage of fNIRS is the detectability of the plural hemodynamic indices, and fMRI does not provide this merit. Nevertheless, in fNIRS study, an important issue of the consistency among the indices which the functional images of each index show the different activation areas has not been resolved. It cannot be ensured that a statistical significance of qualitative single hemoglobin index demonstrates the physiological significance reflecting neural activity. This study shows that the simultaneous processing of the plural indices determines the degree of local brain activation based on a quantitative classification of oxygen metabolism. This vector-based analysis is enabled to emphasize the hidden brain activation by the single index processing.

\[ \Delta \text{COE}_1 = \frac{1}{2} (\Delta D_1 - \Delta O_1) \cdot \cdot \cdot \text{Equation (1)} \]

\[ \Delta \text{CBV}_1 = \frac{1}{2} (\Delta O_1 + \Delta D_1) \cdot \cdot \cdot \text{Equation (2)} \]

\[ L^2 = (\Delta \text{COE}_1)^2 + (\Delta \text{CBV}_1)^2 = (\Delta O_1)^2 + (\Delta D_1)^2 \cdot \cdot \cdot \text{Equation (3)} \]

The angle \( k = \text{Arc} \tan(\frac{\Delta D_1}{\Delta O_1}) = \text{Arc} \tan(\frac{\Delta \text{COE}_1}{\Delta \text{CBV}_1}) + 45^\circ \left( -135^\circ \leq k \leq 225^\circ \right) \cdot \cdot \cdot \text{Equation (4)} \]

![Figure 1 Definition of the vector coordinates.](image)

References


The “Key Search Task” activates prefrontal cortex

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Introduction. The executive functions are considered a set of cognitive processes (attentional/inhibitory control, planning, working memory, cognitive flexibility, etc.), which are crucial for the cognitive control of behavior. The “Key Search Task” (KST) is a subtest of the “Behavioural Assessment of Dysexecutive Syndrome” (BADS) which assesses planning and search strategy. Since this test requires to imagine and to plan several possible routes to be taken, it could be hypothesized that the KST assesses also the ability to plan spatial navigation in a given space. Therefore, this study was aimed at investigating the hemodynamic response of the ventrolateral/dorsolateral prefrontal cortex (VLPFC/DLPFC), by fNIRS, during the execution of the KST.

Methods. Thirty-eight right-handed healthy volunteers (age: 23.8±3.9 y; level of education: 14.3±1.9 y) were recruited for this study. A 20-channel fNIRS system (including 4 short-separation channels, SS) was employed for measuring the PFC hemodynamic response to the execution of both KST and Control Task (CT). Both during the KST and the CT, the subjects were given an A4-sized paper (placed on a bookstand) with a dark 100 mm square in the middle, and a small black dot 50 mm below it. In the KST, they are required: 1) to imagine to search for an imaginary key they have lost on a large field; 2) to draw a line, starting from the black dot, representing their search route. Participants are also asked to search everywhere as accurately as possible. In the CT, subjects are asked to automatically retrace an “X” letter placed at the centre of the dark 100 mm square.

Pre-processing fNIRS data. Motion artefacts were corrected by applying Wavelet motion correction method implemented in Homer2. In order to correct fNIRS signals for physiological noise and surface contamination, a “general linear model” approach was adopted (regression of SS channel signals with greatest correlation).

Results and Discussion. Neuroimaging studies provide evidence that the PFC is crucially involved in planning, the differential contributes of its subregions are still a matter of debate. In general, it plays a crucial role during the path-finding tasks. Here, we found an activation of the right VLPFC (rVLPFC) during KST execution, and a bilateral DLPFC activation during the CT execution. This finding contributes to define the differential role of the rVLPFC, that connecting with hippocampus, is involved in the recollection of several possible routes for the reaching of a behavioural goal. This finding suggests that the KST could be also adopted for evaluating spatial navigation planning. The DLPFC, activated during CT, has a role in regulating the eye-hand coordination necessary for tracing a figure as suggested from its connections with supplementary/pre-supplementary motor areas and cerebellum.

To the best of our knowledge, this is the first study in which fNIRS has been used during the KST execution. Our results also provide a suggestion for the potential relevance of the KST in assessing the spatial navigation planning in brain-damaged patients.
Executive functioning and pre-frontal activity in adults with and without Down syndrome: an fNIRS pilot study

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Executive functioning (EF) describes the cognitive processes used to guide and control thoughts and behaviour. These processes, which include planning, rule-learning, set-shifting and inhibition are associated in large part with activity in the frontal cortex. Individuals with Down syndrome (Trisomy 21; DS) show impairments in EF tasks and have been shown to have reduced volume in frontal areas compared to individuals without DS. DS is the most common genetic cause of intellectual disability and adults with DS are also at increased risk of developing Alzheimer’s disease (AD). In AD in this population, decline in EF may precede the memory decline more typically associated with AD. Measuring this decline however can be difficult, as many adults with DS would score at floor level in the standardised tests commonly used to assess decline in the general population.

Brain imaging may offer alternative ways of exploring changes in the brain relevant to the development of AD in people with DS, and may reveal changes prior to those seen on cognitive tests. However, there remains a paucity of functional imaging work in DS, due in part to difficulties administering imaging paradigms that often require participants to remain still while lying inside a scanner. Functional near infrared spectroscopy (fNIRS) may therefore offer a better-tolerated method for investigating cortical activity in adults with DS.

Our aim is to assess the feasibility of using fNIRS to measure cortical activity during EF tasks in the adult DS population. In this pilot study, healthy adults with (N=7) and without DS (N=7) completed four tasks covering different EF processes: go/no-go (inhibition), picture Stroop (interference/inhibition), dimensional change card sort (rule-learning and shifting) and verbal fluency (general executive function). fNIRS data was acquired with an NTS Optical Imaging System (Gowerlabs Ltd., London) with 16 light sources and detectors, arranged into 44 channels (42 x 30mm and 2 x 10mm channels) covering the pre-frontal and superior temporal cortex. Preliminary processing of data from 7 adults without DS shows a distinct pattern of activation for each active task versus rest, after motion artefact correction and short-separation regression (Fig 1). Detailed statistical analyses of the haemodynamic responses to each controlled task will be presented for adults with and without DS. These results will inform the design of a larger, 12-month longitudinal project using fNIRS to measure EF related cortical activity in adults with DS, to investigate age and decline related changes.

Figure 1: Group average haemodynamic response functions to experimental condition versus rest in each task

References
Mental Stress Localization on PFC Subregion Based on fNIRS

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Background: Prefrontal cortex (PFC) is the brain region related to regulating thought, action and emotion through connections with other brain regions. It has been identified as the region sensitive to the detrimental effects of stress exposure. However, it’s not clear which subregion of the PFC is most sensitive to stress. Identification of subregion enables portable neuroimaging technologies such as fNIRS to provide more targeted neurofeedback training as a means to improve stress coping.

Methods: Twenty male, right-handed adults were recruited to perform mental arithmetic task experiment at two levels of difficulty. Level one involves three single digits with plus and/or minus operation only; level two involves three single/double digits with the four basic operations. Two conditions were considered, i.e. neutral-control and stress conditions. Under stress condition, time pressure and negative feedback about current performance were used as stressors. The induction of stress was assessed by using salivary alpha amylase. Each session lasted for approximately 20 minutes.

Brain activities were acquired at the full PFC using OT-R40 fNIRS system (Hitachi Medical Corp, Japan) with 16 optodes (equivalent of 23 fNIRS channels) and sampling rate of 10 Hz. Channels were registered to three PFC subregions (frontopolar prefrontal cortex, FP-PFC: Ch-[9, 10, 11, 15, 16, 20, 21 and 22], ventrolateral prefrontal cortex, VL-PFC: Ch-[8, 13, 14, 19, 12, 17, 18 and 23] and dorsolateral prefrontal cortex, DL-PFC: Ch-[1-7]). Fig 1 (a) shows the fNIRS channel arrangement.

At each arithmetic difficulty level, we investigated the effects of mental stress on the PFC areas by measuring the significant difference in hemodynamic response between stress and rest conditions for each channel. From the t-maps (difference between control and stress), we localized the brain activities corresponding to the induced stress. We further calculated the value of lateral index, LI= (right-ch-left)/(right+left) for each pair of contralateral channels. One-tailed t-test was performed to determine if right or left PFC area was more affected by mental stress.

Results: The salivary alpha amylase assessment confirmed the induction of mental stress at two distinguishable levels. The fNIRS results showed significant reduction in oxygenated hemoglobin concentration from control condition to stress level one and level two, with p<0.001 and p<0.0001, respectively. Between stress level one to stress level two, the reduction in hemodynamic response was also significant, p<0.01. Fig 1 (b) and (c) show the t-maps at the two stress levels. The statistical analysis showed right VLPFC consistently appear at both stress levels as the PFC subregion most sensitive to stress, p<0.05. As expected, the LI result also supported the dominance of right PFC at both levels of mental stress. In short, the results of this study found that the right VLPFC was the most sensitive PFC subregion to mental stress among male subjects.

![Fig 1. (a) fNIRS channels registration on PFC, (b) t-map of stress level one, (c) t-map of stress level two.](image-url)
Non-invasive, multimodal analysis of cortical activity, blood volume and neurovascular coupling in infantile spasms using EEG-fNIRS monitoring

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KEYWORDS: infantile spasm, neurovascular coupling, cerebral blood volume, electroencephalography, optical imaging
SUMMARY

Although infantile spasms can be caused by a variety of etiologies, the clinical features are stereotypical. The neuronal and vascular mechanisms that contribute to the emergence of infantile spasms are not well understood. We performed a multimodal study by simultaneously recording electroencephalogram and functional Near-infrared spectroscopy in an intentionally heterogeneous population of six children with spasms in clusters. Regardless of the etiology, spasms were accompanied by two phases of hemodynamic changes; an initial change in the cerebral blood volume (simultaneously with each spasm) followed by a neurovascular coupling in all children except for the one with a large porencephalic cyst. Changes in cerebral blood volume, like the neurovascular coupling, occurred over frontal areas in all patients regardless of any brain damage suggesting a diffuse hemodynamic cortical response. The simultaneous motor activation and changes in cerebral blood volume might result from the involvement of the brainstem. The inconstant neurovascular coupling phase suggests a diffuse activation of the brain likely resulting too from the brainstem involvement that might trigger diffuse changes in cortical excitability.
Simultaneous EEG-fNIRS reveals how age and neurofeedback affect motor imagery signatures

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Stroke frequently results in motor impairment. Motor imagery (MI), the mental practice of movements, has been suggested as a promising complement to other therapeutic approaches facilitating motor rehabilitation. Of particular potential is the combination of MI with neurofeedback (NF). However, MI NF protocols have been largely optimized only in younger healthy adults, even though strokes occur more frequently in older adults. The present study examined the influence of age on the neural correlates of MI supported by electroencephalogram (EEG)-based NF, and on the neural correlates of motor execution. We adopted a multimodal neuroimaging framework focusing on EEG-derived event-related desynchronization (ERD%) and oxygenated (HbO) and deoxygenated haemoglobin (HbR) concentrations simultaneously acquired with functional near-infrared spectroscopy (fNIRS). ERD%, HbO concentration, and HbR concentration were compared between younger (mean age: 24.4 years) and older healthy adults (mean age: 62.6 years). During MI ERD% and HbR concentration were less lateralized in older adults when compared to younger adults. The lateralization-by-age interaction was not significant for movement execution. Moreover, EEG NF was related to an increase in task-specific activity compared to the absence of feedback for both older and younger adults. Finally, significant modulation correlations were found between ERD% and hemodynamic measures despite the absence of significant amplitude correlations. Overall, the findings suggest a complex relationship between age and movement-related activity in electrophysiological and hemodynamic measures. Our results emphasize that the age of the actual end-user of MI NF rehabilitation protocols should be taken into account when designing neurorehabilitation protocols.
Title:
Tracking functional reorganization in cochlear implant users with simultaneous EEG-fNIRS

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Abstract:
Using functional near-infrared spectroscopy (fNIRS) we recently confirmed both higher visual evoked activation in auditory cortex and higher auditory evoked activation in visual cortex in cochlear implant (CI) users compared to normal hearing (NH) controls. This pattern may reflect functional reorganizations induced by sensory deprivation during deafness and subsequent sensory restoration with a CI. However, functional changes in CI users are not restricted to cross-modal reorganization patterns and can also be observed in intra-modal sensory processing. Particularly, previous studies found lower cortical activation in both auditory and visual cortex. This effect may be due to an altered stimulus-specific adaptation pattern for visual and auditory stimuli in CI users, which may be associated to speech recognition abilities. Using concurrent EEG-fNIRS we investigated stimulus-specific adaptation in visual and auditory sensory systems. EEG was used to estimate the amount of activation in response to individual sounds presented within a train of stimuli. Each block-averaged response separately for each sequential stimulus was then convolved with a hemodynamic response function to simulate the block-accumulated hemodynamic response as measured by fNIRS. We found enhanced stimulus-specific adaptation for visual stimuli and decreased stimulus-specific adaptation for auditory stimuli in CI users compared to NH controls. Interestingly, stronger stimulus-specific adaptation yielded differences in the peak latency of the accumulated hemodynamic response. Stronger adaptation resulted in earlier peak latency and vice versa. The results point towards a higher efficiency in processing visual stimuli in CI users and may be related to advanced lip reading skills. Moreover, our study presents a new way of predicting hemodynamic (fNIRS) response patterns by concurrently recorded EEG signals.
Investigation of cytochrome-c-oxidase as a more robust marker of frontal lobe activation

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Functional near-infrared spectroscopy (fNIRS) is an increasingly used method for monitoring haemodynamic response to brain activation in terms of concentration changes of oxygenated-($\Delta$HbO$_2$) and deoxygenated- ($\Delta$HHb) haemoglobin. It is based on the tight coupling between neuronal activation and vascular response. However, fNIRS signals are susceptible to confounding factors from physiological-based systemic interference and extracerebral signals. These confounders may mask (false negative) or mimic (false positive) a neuronally-induced haemodynamic response, leading to misinterpretation of results\textsuperscript{1}.

Figure 1: Block average and standard error of mean during stimulus (17 subjects) without (left) and with (right) short-separation regression. Stimulus begins at 0s and continues until 30s

It has been shown that short source-detector separations of $\sim$0.8cm can effectively sample extracerebral layers in the head and facilitate the removal of superficial contamination from standard fNIRS channels and this significantly improves the reliability of fNIRS measurements\textsuperscript{2}.

Recently, our group used a multi-distance broadband NIRS system to additionally measure cytochrome-c-oxidase ($\Delta$oxCCO) during functional activation, a metabolic marker, and found a depth-dependence of cytochrome not seen in haemodynamic signals. This suggests CCO is a brain-specific signal\textsuperscript{3}.

The aim of this study was to investigate whether $\Delta$oxCCO can produce a more robust marker of functional activation due to its independence from scalp fluctuations. Continuous frontal lobe measurements from 17 healthy adults were collected during a working memory challenge using a broadband NIRS system. Short source-detector separations were used to remove extracerebral effects using short-separation regression.

Block averages for subjects showed an increase in $\Delta$HbO$_2$ in all detectors with the expected decrease in $\Delta$HHb only seen at the furthest channel. $\Delta$oxCCO showed little change at short separations with large increases at 3cm. Regression showed an improvement in haemodynamic signals, with a more apparent decrease in $\Delta$HHb. Regression made little change to $\Delta$oxCCO, corroborating findings it is brain-specific and therefore has the potential to be a more robust marker of functional activation.

\textsuperscript{1} I. Tachtsidis and F. Scholkmann, Neurophotonics 3 (3) 030401-1 - 030401-6 (2016).
\textsuperscript{2} S. Brigadoi and R. J. Cooper, Neurophotonics 2, (2) 025005-1-02005-9 (2015).
Title: NIRS Neurofeedback in ADHD

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Objectives: Psychiatric disorders like ADHD are currently mainly treated with pharmacotherapeutic and, to a lesser extent, with psychotherapeutic methods. The success measured as improvement of symptoms under is surprisingly good with high effect sizes (>0.8) in randomized controlled trials, in particular for pharmacological treatment with stimulants. However, there is still room and need for improvement.

Methods: Neurofeedback methods based on EEG and fMRI methods are increasingly applied as an alternative or add-on therapeutic approach. The rationale behind these therapies is to show the subjects an immediate feedback of their brain activity. So they can learn how to regulate their brain activity and transfer this ability to real life situations.

Results: We established a neurofeedback protocol for regions of the prefrontal cortex based on measurements of brain activity with Near-Infrared Spectroscopy (NIRS). This NIRS-neurofeedback was applied in children and adults with ADHD with promising results.

Conclusion: Due to its high ecological validity, NIRS-neurofeedback might develop to an alternative or add-on therapy also for ADHD patients in future.
Introduction

The coupling between cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO\textsubscript{2}) is a primary important function [1, 2] as the working brain requires a continuous supply of glucose and oxygen (O\textsubscript{2}), which must be provided by CBF [3]. Under resting physiologic conditions, identifying a causal relationship between CBF and CMRO\textsubscript{2} in neonatal brain helps to infer the principles of cortical hemodynamic during development. While the linear relationship between CBF and CMRO\textsubscript{2} changes was known for resting-state in adult [1], the nonlinear relationship has not been studied in preterms.

Methods

We simultaneously recorded CBF and CMRO\textsubscript{2} by two separate devices (CBF by Hemophotonics® and CMRO\textsubscript{2} by Hamamatsu®) relying on different approaches; the NIRS and the DCS, respectively. Continuous measurements during sleep were performed in healthy (n=9) and Intra-Ventricular Hemorrhage (IVH grade II) (n=1) preterm neonates (28-35 weeks GA). To determine the coupling between rCBF and rCMRO\textsubscript{2} and the dominance of this coupling, the transfer entropy (TE) and the Mutual Information (MI) were calculated. Based on the concept of causality as it was introduced by Wiener [4]. We improved the prediction of the future of a time series of rCBF (or rCMRO\textsubscript{2}) by the incorporation of information’s from the past of a second time series rCMRO\textsubscript{2} (or CBF). This technique can be presented as an indication of a causal interaction between CBF and CMRO\textsubscript{2} since the physiological process producing the variables (rCBF) and (rCMRO\textsubscript{2}) can be considered as autonomous dynamic sources. We applied the surrogate method to determine the statistical significance.

Results

To elucidate whether there is a dominant influence of CBF on CMRO\textsubscript{2} or inverse (CMRO\textsubscript{2} on CBF), the directionality index (D) between rCBF and rCMRO\textsubscript{2} was calculated. Statistical confidence for MI and TE were calculated using surrogate method determining the limits at 95\textsuperscript{th} percentile. The statistical evaluation of TE values robustly detected the correct direction of CMRO\textsubscript{2} on CBF for 10 subjects. In premature infant at rest during sleep, the consumption of oxygen (CMRO\textsubscript{2}) had a predominant driving influence on CBF, as indicated by the negative values of the index D with appropriate statistics.

Conclusions

This study focusing in the nonlinear CBF-CMRO\textsubscript{2} coupling in the resting state of neonatal brain conclude that even if their interactions are bilateral, the dynamics of metabolic rate as assessed by rCMRO\textsubscript{2} has a dominating influence over blood flow rate (rCBF). Here we confirm the Darwinian opinion that the need of oxygen in brain tissue (rCMRO\textsubscript{2}) creates the function rCBF. These results help to infer the principles of cortical hemodynamic during development in neonatal brain.

References

Mitochondria are the energy suppliers of the eukaryotic cell. Mitochondrial dysfunction (MD) is associated with a miscellaneous group of disorders, named the mitochondrial diseases. Especially tissues with great need for energy are hereby affected, such as brain, heart muscle, skeletal muscle, liver and retina.

Increasing evidence is found that MD is related to autism spectrum disorder (ASD). Over the past decade, several studies have shown that a subgroup of children with ASD suffers from concomitant MD. However, only 112 children with ASD+MD have been described in the scientific literature.

The diagnosis of a mitochondrial disease involves an invasive process which necessitates after a thorough clinical evaluation either skeletal muscle, cultured skin fibroblasts, liver, or heart biopsy. These samples are used for biochemical examination of the respiratory chain complexes using spectrophotometry and Blue Native Polyacrylamide Gel Electrophoresis. As these techniques are time-consuming and invasive, a simpler and non-invasive protocol is needed to screen for MD.

Functional near-infrared spectroscopy (fNIRS) might be an alternative screening method for MD. Mitochondria consume the oxygen from oxy-hemoglobin to produce energy. After release of the oxygen molecule, oxy-hemoglobin is converted to deoxy-hemoglobin. In tissues with MD the energy production is decreased and subsequently less oxygen is extracted from blood. This results in concentration changes of oxy- and deoxy-hemoglobin that are different from those in healthy controls. These differences can be detected with fNIRS.

Up till now, this screening approach has only been tested in forearm muscle from patients with mitochondrial myopathy. Therefore, the first goal of the present study is to test the oxy- and deoxy-hemoglobin concentrations in the brain of children with established MD and to compare these concentrations with those found in brain of healthy controls. In this study, both visual and auditory stimuli will be given to children with MD and healthy controls. By using an odd-ball paradigm, we hypothesize that the stimulation of the brain in the patients with MD will lead to a higher increase of oxy-hemoglobin concentration (see Figure 1) and a slower increase of deoxy-hemoglobin concentration (see Figure 2) as compared to healthy controls.

In case fNIRS can be used efficiently to screen for MD, this strategy can be used to screen larger groups of patients with diseases linked to MD such as ASD. The pilot data of this study will be presented at the conference.

Figure 1: Hypothetical changes in concentration of oxy-hemoglobin in the patients with mitochondrial dysfunction and in controls

Figure 2: Hypothetical changes in concentration of deoxy-hemoglobin between the patients with mitochondrial dysfunction and controls.
What happens to cerebral hemodynamics during an obstructive sleep apnea?

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Obstructive sleep apnea (OSA) syndrome leads to repeated, prolonged periods of interrupted breathing during sleep due to upper airway obstruction. Apnea events cause profound, periodic changes in cerebral and systemic hemodynamics including periods of hyper- and hypo-perfusion and intermittent hypoxia. A better understanding of the effects of the apnea would allow to understand their relation with cerebrovascular diseases.

In this work, we have used a hybrid ISS Imagent (ISS, Champaign, USA) frequency domain (FD) near-infrared diffuse optical spectroscopy (NIRS-DOS) and a custom build diffuse correlation spectroscopy (DCS) system [1] simultaneously with a standard polysomnography (PSG) system (Siesta, Compumedics, Melbourne, Australia). We have followed the apnea-induced changes of microvascular oxygenation, blood flow in the frontal lobes and the systemic parameters during four hours of night sleep in sixteen severe OSA patients, detecting 954 usable obstructive apneas.

We have identified the start and end of each OSA event and considered them independently. Both relative and absolute changes were calculated to enable inter- and intra-subject averaging. We were able to obtain robust data on cerebral blood flow, oxygenation and volume with sufficient signal-to-noise ratio to, for the first time, characterize each apnea.

We have also found that microvascular cerebral hemodynamics and systemic parameters respond to the apnea event at different times after the end of the cessation of airflow (figure 1). These delays have never been quantified before in the microvascular blood flow. In addition, linear models showed that the both microvascular and systemic responses of each apnea depend on the apnea duration. We will present parametric models characterizing different features related to the systemic parameters, patient demographics and clinical indicators. These features include: post-apnea peak amplitude and time, post-apnea drop amplitude and time, and the delays between them.

Fig. 1. Bootstrap and mean of peripheral arterial saturation (ΔSatO2), relative heart rate (rHR), relative cerebral blood flow (rCBF) and cerebral oxygen saturation (ΔStO2). All obstructive apnea events in this analysis are considered from -5 seconds to 40 seconds from the apnea end. Yellow area marks the apnea period. Grey and black dashed arrows indicate the systemic and cerebral apnea peaks, respectively.

References
The cochlear implant (CI) has become one of the greatest biomedical advancements of our time for individuals with severe to profound hearing loss (HL). The surgically placed electrode within the cochlea is designed to stimulate the auditory nerve directly, in hopes of giving the patient an improved ability to recognize speech. Despite improving technology, great variability in levels of functional success still remains among CI recipients. Unfortunately, the underlying neural mechanisms that may explain these differences are not well understood. Further, whether or not success with a CI can be accurately predicted prior to the surgical procedure has yet to be determined; however, if this were possible, it would radically improve candidate identification and the proper use of limited healthcare resources. The current study investigates the signal representation of non-degraded and degraded speech within the auditory cortex (AC) region of the temporal lobe. While magnetic resonance imaging (MRI) and electroencephalography (EEG) can be used to assess human cortical activity, their efficacy for recipients of CI remains limited due to the technical incompatibilities of the implanted device. Functional near infrared spectroscopy (fNIRS) is safe, non-invasive, relatively quiet, more tolerant of movement artifact and most importantly, not susceptible to the electrical signals of a CI, making it uniquely ideal for use with CI recipients. Prior research has demonstrated in normal hearing listeners larger areas of activation in the AC while passively listening to normal speech as opposed to largely delocalized activity observed in the AC when the same participants were presented distorted speech. For that reason, we implemented an event-related speech perception task to investigate cortical activation patterns of listeners with normal hearing in various listening conditions. Participants performed the Hearing in Noise Test (HINT) in the following conditions: quiet, speech-shaped background noise and simulated CI speech. Participants were instructed to repeat the sentences that were presented. A percent-correct score was calculated for each condition. During these tasks, hemodynamic changes were measured using fNIRS probes over bilateral auditory cortices. AC activation was observed across all conditions. Further, the magnitude of hemodynamic activation on a subset of channels varied across listening condition as a function of speech perception scores. The pattern of data revealed that higher activation in more difficult listening conditions was associated with higher speech perception scores. These data are the necessary first steps to formulating a convenient, clinical measurement that can predict patient prognosis. Results will be interpreted to predict outcomes in future studies with the CI population.
Decoding the Infant Mind: Multichannel Pattern Analysis (MCPA) using fNIRS

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The current abstract presents a method of multivariate pattern analysis for fNIRS that allows the authors to decode the infant mind (a key population in the fNIRS field). Specifically, multi-channel pattern analysis (MCPA) employs a correlation-based decoding method where a group model is constructed for all infants except one; both average patterns (i.e., infant-level) and single trial patterns (i.e., trial-level) of activation are decoded. Between subjects decoding is a particularly difficult task, because each infant has their own somewhat idiosyncratic patterns of neural activation. The fact that our method succeeds at across-subject decoding demonstrates the presence of group-level multi-channel regularities across infants. Moreover, we find significant decoding when univariate tests failed to find significant difference between conditions. Finally, we can employ this method to obtain spatial localization in the neural signals (restriction to the 3 most informative channels). The code for implementing these analyses has been made readily available online to facilitate the quick adoption of this method to advance the methodological tools available to the fNIRS researcher.

Figure 1.
The role of parietal cortex in imitation: a study with fNIRS
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Introduction
Imitation allows us to learn new skills and connect with other people. There has been increasing interest in understanding the mechanisms that determine when people imitate with high fidelity, especially when this compromises the efficiency of their own actions. A number of studies have examined neural mechanisms that detect if an action is rational or irrational (Jastorff et al., 2011; Marsh & Hamilton, 2011; Marsh et al., 2014), with straight actions judged as rational and curved actions as irrational. Other studies examine imitation fidelity (Frey & Gerry, 2006) but none have combined these two aspects. This is partly due to the physical restrictions of fMRI. In the experiment, we used functional near infrared spectroscopy (fNIRS) to monitor parietal cortex activation when participants observed rational and irrational actions, and performed actions themselves.

Methods
Participants completed a computerized “picture building” task with another person (Fig 1A). Puzzle pieces on the left could be moved to make a picture on the right, e.g. a butterfly. The top half of the screen belonged to the demonstrator and the bottom to the participant. First participants watched the demonstrator move a piece, in either a straight or curved movement (green arrow). After this, participants had to move the same piece on their half of the screen (yellow arrow).

An Artinis Medical Systems Oxymon Mk III fNIRS system and OxySoft software were used to record oxygenated and deoxygenated haemoglobin data (oxy- and deoxy-Hb) over parietal cortex. 2x2 optode arrays were placed on each side of the head over angular gyrus, temporoparietal junction, and anterior and posterior anterior IPL (Fig 1B). fNIRS data was analysed with SPM-NIRS to find regions showing differences between performance and observation or differences between curved and straight actions. Results are reported only when an increase in oxy-Hb was matched by a decrease in deoxy-Hb.

Results
Activation in left temporoparietal junction (Fig1C) and right angular gyrus (Fig1D) was greater during the observation condition compared to the perform condition (Figure 2). An interaction effect was seen in right anterior inferior parietal junction (aIPL) with observation of curved irrational actions producing the greatest activation (Fig 1E).

Conclusion
Using a novel computerized task, we were able to record fNIRS signals from typical adults during action observation and action performance. The results replicate prior fMRI results (Marsh et al., 2014), and demonstrate the feasibility of using fNIRS with motor tasks. Future studies can examine brain activation using fNIRS in clinical populations and a wider range of movement tasks.
A multi-modal fNIRS/EEG investigation of the fronto-parietal network during audio-visual matching

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The neural substrates of visual attention are known to be rooted in the fronto-parietal circuitry [1], and both frontal and parietal cortices have been hypothesized to play a crucial role in cross-modal matching of audio-visual information. Here we investigated the interplay between frontal and parietal regions both at the electrical and hemodynamic level using a cross-modal matching task.

A multi-modal fNIRS/EEG acquisition was performed by simultaneously acquiring fNIRS and EEG data on healthy adults. Participants were presented with auditory and visual stimuli as displayed in the figure. Auditory stimuli consisted of either 2 or 3 beep sounds. The number of beeps was either congruent or incongruent with the number of subsequently presented lateralized visual targets (i.e. either 2 or 3 filled circles). Participants were required to orient covertly their attention to the lateralized visual targets whilst maintaining their gaze at fixation, under the requirement to press the ‘yes’ key when the number of beeps matched the number of lateralized visual targets, and ‘no’ when it did not. During the experiment, bilateral fronto-parietal brain responses to the stimuli were monitored with an ISS Imagent™ system equipped with 8 detectors and 64 sources (36 channels at 3 cm and 2 short-separation (SS) channels, at 0.7 cm). Optodes were positioned to cover the bilateral ventrolateral and dorsolateral prefrontal cortices and the bilateral intra-parietal sulcus. Electroencephalographic data were recorded with a portable EEG system (Biopac®) with 8 channels. Two electrodes were located in PO7 and PO8 to monitor the N2pc component (an increment in negativity at posterior electrodes contralateral to an eccentric target relative to ipsilateral symmetrical electrodes); such event related potential (ERP) component is typically considered a neural marker of visual selection and is known to be modulated by target numerosity when targets have to be enumerated. The other electrodes were employed to monitor eye-movements. NIRS data were analyzed with the Homer2 package [2]. Channels with very low intensity were pruned, motion artifacts were identified and corrected applying spline interpolation, and a band-pass filter (0.01-0.5 Hz) was applied. The hemodynamic response was recovered with a GLM approach, simultaneously regressing the SS signals to reduce physiological noise [3]. Only trials associated with correct responses and not contaminated by eye movements were kept in the analyses. N2pc was computed (for each numerosity and audio-visual matching condition) as the difference between neural activity in the contralateral hemisphere to the lateralized targets (presented at either right or left hemifield) minus the ipsilateral activity. Preliminary results on 7 participants showed longer reaction times for incongruent vs. congruent trials, regardless of numerosity. An N2pc was observed at PO7 and PO8 sites modulated by congruency only when 3 targets where displayed. The fNIRS results suggested the involvement of the fronto-parietal network in the task, in so far as numerosity modulated the frontal cortex activation, whereas congruency modulated the activity in the left parietal cortex. Results on a larger sample will be presented and the localization and implications of the cross-modal matching processing will be discussed by combining ERP and fNIRS results.

A Subtraction-Based Approach for Enhancing the Sensitivity of Time-Resolved fNIRS

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Introduction: The most popular and widely used optical technique for mapping functional activation is multichannel continuous-wave (CW) NIRS. To improve sensitivity to brain activity and reduce the confounding effects of hemodynamic changes in the scalp, most CW systems take advantage of the fact that depth sensitivity is proportional to source-detector (rSD) separation. An alternative method with even greater depth sensitivity is time-resolved (TR) NIRS, which is based on analysis of the distribution of times-of-flight of diffusely reflected photons (DTOFs). One method of extracting depth information from DTOFs is by generating the statistical moments since late arriving photons have greater weighting on higher moments (i.e., $<r>$ - mean time of flight and $V$ – variance). In a previous study (Milej et al. Applied Optics, 2016) we proposed a subtraction method (referred to as sTR) to measure the optical properties of turbid media without the need of measuring the instrument response function. In this work, we will show that a further advantage of the sTR method is increased depth sensitivity, which could be useful in fNIRS applications.

Methodology: Monte Carlo (MC) simulations of heterogeneous media and 2-or-3 layer phantom experiments were used to assess the depth sensitivity of sTR compared to moment analysis of individual DTOFs (referred to as iMA). Depth sensitivity factors for a semi-infinite geometry were generated and the ability to retrieve the optical properties of the bottom layer of a two-layer phantom and a 1-cm thick middle layer in a 3-layer phantom was assessed. Finally, the sTR method was applied to fNIRS data consisting of 50 30-s alternating periods of finger tapping and rest to measure the oxygenation change during motor activation.

Results: MC simulations demonstrated that sTR for rSD = 1.5 cm could obtain the same sensitivity for an inclusion located at depth of 1 cm as iMA for rSD = 3 cm. Two-layer model simulations and the phantom experiments demonstrated that sTR was less sensitive to the superficial layer. Specifically, the error in the estimated optical properties of the deeper layer obtained by sTR was < 5%, while for iMA it was < 20%. The results of the three-layer phantom showed that the sTR method could estimate the optical properties of the 1-cm middle layer with an error < 15%. Finally, the in vivo results (Fig.1) showed that the magnitude of the hemodynamic response measured by sTR was considerably higher than that obtained by iMA analysis of DTOFs acquired at rSD = 3 and 4 cm.

Conclusion: The results from the MC simulations and phantom experiments illustrate that the sTR technique provides greater sensitivity to deeper layers. These results agree with the in vivo data showing the greater magnitude of the activation-induced increase in HbO2 obtained with this method. This promising technique could eliminate the need for complex algorithms used to minimize extracerebral contamination in fNIRS studies.

Fig. 1 Time courses of changes in concentration of oxyhemoglobin observed in the left hemisphere. Green box mark the beginning and end of the right hand finger-tapping task.
Accuracy, Authenticity and Intersubject Correlation in Storytelling

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Real-life autobiographical stories are a common way we share our experiences and opinions with others. During interpersonal communication, speakers and listeners reflect on both the perspective of their communication partner and the self-relevance of the story. Studies of persuasive communication show shared brain activity occurs across speakers and listeners in areas associated with perspective taking and self-related processing, including the bilateral TPJ, DMPFC and MPFC (Falk, Morelli, Welborn, Dambacher, & Lieberman, 2013). During the social sharing of autobiographical stories, the degree of neural synchrony between the speaker and listener in these regions predicts the listener’s factual recall of the speaker’s story (Stephens, Silbert, & Hasson, 2010). Sometimes, shared stories are so persuasive they are adopted by listeners and retold as though the events happened to them (Brown, Croft Caderao, Fields, & Marsh, 2015). We hypothesized that differential activity in perspective-taking and self-related processing regions during story listening would predict later accuracy and perceived authenticity of listeners’ story retellings.

Using fNIRS, we investigated intersubject correlation (ISC) in the bilateral TPJ, DMPFC and MPFC during a naturalistic storytelling task. Participants (N=36) were asked to watch a video of a gender-matched participant telling a real autobiographical story. After video viewing, they were then asked to retell the story in the first-person, as though the events had happened to them. The listeners’ retold versions of the story were scored on a 50-point scale for factual accuracy, and were separately scored by Amazon Mechanical Turk workers for the perceived authenticity of the story. ISC in the fNIRS data was measured channel-wise in 20 channels across the four ROIs. We found that a randomized split-half correlation of HbO shows positive ISC in the MPFC during story listening (Figure 1). This demonstrates how fNIRS can be used in a naturalistic task to track how individuals exhibit similar patterns of neural activity in a shared social context. Other analyses show the relationship between HbO concentration change during listening and the prediction of listener accuracy in retelling, and the prediction of perceived authenticity. As fNIRS is applied to studies of dyadic and live social interaction, ISC will be a valuable method for understanding neural synchrony in naturalistic verbal communication.

![Figure 1.](image)

Figure 1. A randomized split-half intersubject correlation (ISC) over 20 channels of fNIRS data. Oxygenated hemoglobin (HbO) data were collected from 36 female listeners while listening to a 270s personal story. Significant correlations are present in the MPFC, showing the possibility of gathering ISC data from fNIRS during interpersonal communication tasks.
Multivariate statistical analyses have provided a new window into the contents of neurocognitive representations, allowing neuroscientists to decode functional brain responses into signals of theoretical significance, such as semantic information. Integrating recently developed tools for representational similarity-based decoding (Anderson et al., 2016) and Multichannel Pattern Analysis (MCPA; Emberson et al., 2016), we test whether semantic information elicited by words and pictures can be decoded from fNIRS data. We thus reveal the semantic contents of this signal encoded in distributed patterns of functional brain responses measured by fNIRS.

Eight adults (3M, 5F) participated in a 15-minute passive viewing and listening task. Participants were presented with eight audio-visual stimuli, featuring a photograph of an object and simultaneous auditory presentation of the object’s name. Stimulus presentation lasted 3 seconds with a jittered 6 to 9 second interstimulus interval. This procedure was repeated over 12 blocks, with stimulus order randomized in each block. Meanwhile, participants’ blood oxygen levels were measured using the Hitachi ETG-4000 fNIRS system. The fNIRS probes were arranged in two arrays: 24 channels in a 4x4 array on the posterior occipital lobe, and 22 channels in a 3x5 array on the left temporal lobe. After standard preprocessing procedures, we performed a channel stability analysis adapted from fMRI decoding (Mitchell et al., 2008), selecting the 50% most stable channels for each participant. Responses to each stimulus were then epoched and averaged according to MCPA procedures. Each participant’s response patterns were abstracted to a representational similarity space and compared to (1) the group average (excluding that participant, i.e., leave-one-out cross-validation) and (2) the COMPOSES model of semantic representation (Baroni et al., 2014).

The group average analysis revealed an accuracy for between-subjects decoding of 0.65, significantly better than chance ($p<0.05$; Panel A). This finding indicates that a shared set of perceptual or semantic representations for the eight stimuli was encoded in the fNIRS data. The analysis based on the COMPOSES semantic model depended only on semantic information in the fNIRS signal, with a mean decoding accuracy of 0.63 ($p<0.05$). After applying Emberson et al.’s (2016) channel-subset analysis to identify the best 11 semantic decoding channels for each participant, accuracy increased to 0.74 ($p<0.001$; Panel B), indicating that we had isolated a component of the neural response that closely matched the COMPOSES model of semantic representation. To our knowledge, these preliminary results represent the first attempt to link the functional response pattern measured by fNIRS to a model-based representation and successfully decode semantic relationships in the fNIRS signal. The extension of these methods to fNIRS will expand the analytic tools available to the field and allow researchers to make direct inferences about the informational content of neural signals.

References:
Human recognition of emotions in voices: a fNIRS study

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Abstract

Human vocalizations can convey different kinds of information. For instance, variations of the vocal tone of the voice, known as prosody, can give information about the emotional state of the speaker. In recent years, the emergence of the study of affective neuroscience has allowed understanding how emotions are decoded by human brain, particularly through the use of functional imaging. While studies have suggested the role of the right inferior frontal cortex (IFC) in attentive decoding and cognitive evaluation of emotional cues in human vocalizations, recent studies also point out an important role of the left IFC. The bilateral IFC activation may depend on the nature of emotional vocalizations (emotional prosody versus nonverbal expressions) and on the level of attentive processing (explicit versus implicit processing), suggesting that several IFC subregions might integrate different acoustic information in order to attribute implicit or explicit meanings. In this study, our goal was to develop a protocol based on functional Near-Infrared Spectroscopy (fNIRS) to collect behavioral and functional data to investigate frontal lateralization of human emotion vocalizations during explicit and implicit categorization and discrimination. All participants were exposed to the same stimuli, consisting of speech-like but semantically meaningless words (e.g. “molen”, “belam”, “nikalibam”) extracted from the Geneva Multimodal Emotion Portrayal database. These pseudo-words were spoken in a neutral, an angry or a fearful tone by two male and two female speakers, resulting in 36 different stimuli. The stimuli were presented during a mini-block design in four different tasks defined by a 2 (decision target: emotion, word) by 2 (task: categorization, discrimination) design, with each task repeated two times and two additional passive listening blocks. 10 blocks, the order of which was pseudo-randomly assigned to each participant. In particular, the same stimuli were used in a discrimination or categorization task on the identity of the pseudo-words to test the hypothesis of lateralization of the processing of categorization and discrimination performed on different aspects of the auditory stimuli, namely the linguistic structure versus the emotional nature. We predicted that the emotion task would induce an increase of NIRS signal within the right IFC while the left IFC would show an effect during word discrimination compared to categorization. We expected that a subpart of the right IFC would be strongly involved in both categorizing and discriminating emotional voices compared to passive listening, while other subparts of the right IFC would be significantly modulated between categorization versus discrimination. We present here preliminary results on 18 adult subjects (10 females, age range: 22 - 40). Our preliminary analyses on the blood oxygenation signal suggest a task-by-laterality interaction, particularly the possibility that categorisation compared to discrimination processes in general may be more present in the right IFC. The analysis of the deoxygenation signal showed a target-by-task interaction, with word categorisation compared to word discrimination revealing increased deoxygenation signal. This experiment shows that NIRS is an adapted means to study different types of vocal emotion classifications in humans, fostering its application in extended paradigms to study emotional appraisal in humans.
A Point of care FD NIRS device equivalent to fMRI in detecting clinically relevant physiological changes

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Introduction
Despite relatively low cost, ease of use and non-invasive nature the use of NIRS within the context of traumatic brain injury (TBI) care (one of its most logical potential applications) is limited, and it been deemed not sufficiently consistent and accurate for these purposes. Frequency domain (FD NIRS) devices represent a refinement in available point of care (clinically viable) devices and potentially offer more consistent parameters to guide therapy.

Aims
To assess the correlation of the observations made by a commercially available, point of care cerebral FD NIRS device with those yielded by functional Magnetic Resonance Imaging (fMRI- Blood Oxygen Dependant Load signal BOLD) on brain activity during hyperventilation (provoking vaso-constriction a clinically relevant change in cerebral physiology).

Materials and Methods
Healthy individuals will perform a protocol of sequential (1 minute long) voluntary hyperventilations (punctuated by a 1 minute rest period, consistency/adequacy monitored by end tidal CO2) manoeuvres under observation by both a clinically viable FD NIRS device and fMRI. This induces cerebral vaso-constriction effect clinically relevant to changes in TBI. The ISS OptiplexTS™ is a clinically viable FD NIRS device. Tested in single detector / 4 source (at 30, 35, 40 and 45mm distances) form, with 2 (device standard) wavelengths of 680 and 830nm. For fMRI observations, a single shot EPI sequence (32 channel coil) was undertaken; region of interest was selected manually (frontal), corresponding to NIRS acquisition tissue (3x3x3mm voxel/no slice gap (ascending acquisition)/flip angle 80 degrees/echo time 30ms/repetition time 2ms).

Results
A total of 9 individuals (6m/3f, age 21-40) completed the protocol. Excellent agreement was observed between both modalities. All observed hyperventilations were consistent in terms of duration and end tidal CO2. Pooled ANOVA demonstrated a strong cross correlation affirming this (CCF of 0.954) with an indicated lag of 0 seconds between modalities.

Conclusion
Observations from this clinically viable FD NIRS device correlate well with those made by fMRI, within the same time frame. This confirms that an easily applied point of care FD NIRS device has similar abilities in detecting clinically relevant changes in cerebral physiology, along with its inherent potential advantages over this established gold standard.

References
Using fNIRS to Measure Hemodynamic Changes in the Prefrontal Cortex Due to Acute Stress

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Background
Research studies have well established that stress threatens homeostasis and stimulates a series of physiological responses in the human body and brain (McEwen, 2000). Recent neuroimaging research has shown that acute stress activates brain regions associated with emotions and vigilance (Wang et al., 2005). In particular, neural correlates associated with negative affect are generally elicited in the right prefrontal cortex (RPFC) whereas the left prefrontal cortex (LPFC) is associated with positive emotion (Wang et al., 2005). In addition, there is evidence indicating that the neural correlates of vigilance and sustained attention associated with acute stress are also localized in the right prefrontal cortex (RPFC), right parietal lobe, and right thalamus (Sarter, Bruno & Givens, 2001). Consequently, researchers have speculated that the right prefrontal cortex (RPFC) may play a significant role in the brain’s response to stress, since two aspects of acute stress, vigilance and negative emotion, have been localized to the RPFC.

However, the neural activation patterns associated with acute stress are less understood (Pruessner et al., 2008), even though they impact fundamental cognitive processes like memory. Additionally, most of the neuroimaging research on the hemodynamics associated with acute stress has been conducted with fMRI technology, which requires participants to be placed in a supine position with immobilized heads (Pruessner et al., 2008). These challenges can be overcome with fNIRS. The present study will examine the hemodynamic response associated with acute stress using fNIRS.

Methods
Twenty participants (10 = female) are targeted to be recruited for the study. Acute stress will be induced by asking participants to place their non-dominant hand in ice-cold water for 3 minutes (Lighthall et al., 2009). Hemodynamic responses in the pre-frontal cortex (PFC) will be assessed for 30 seconds prior to submersion of the participant’s hand, for the establishment of baseline, and then for 3 minutes during the activity. Participants will be given a questionnaire to assess their stress levels pre and post the acute stress induction as a manipulation check. Data for the hemodynamic response will be acquired using the NIRScout 8x8 (NIRx Medizintechnik GmbH). Data analysis will be conducted using nirsLAB and IBM SPSS Statistics 21.

Results and Conclusions
Data collection and data analyses for the study are currently ongoing. Consistent with previous research (e.g. Wang et al., 2005) we anticipate observing increased activation in the Right PFC, in comparison to the Left PFC, during the acute stress exposure. The findings of this study will provide evidence for the feasibility of fNIRS as a novel method for the examination of hemodynamic response, in the PFC, in response to acute stress. Potential applications for complex cognition (i.e. decision making) and future directions will be discussed.

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PHOEBE: a software tool for optimized guided placement of fNIRS optodes
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Functional near-infrared spectroscopy (fNIRS) is an optical imaging technique for mapping neural activity by measuring hemodynamic changes in the cerebral cortex associated with resting or evoked brain activity. With recent fNIRS instrumentation encompassing large numbers of optodes, it is possible to reconstruct a hemodynamic image of the entire cerebral cortex with a lateral resolution on the order of a few centimeters, which can be improved to a few millimeters when a regional cortical activity is investigated using a smaller but denser optode layout.

Despite these advantages, use of fNIRS with adult human subjects is currently limited by several unresolved issues. One of the main challenges encountered by fNIRS researchers is collecting optical signals from all channels with a signal-to-noise ratio (SNR) that is sufficient to carry out a reliable estimation of cortical hemodynamics. While the instrumental noise associated with photodetectors and front-end electronic amplifiers can be minimized with good engineering practices, collecting strong optical signals is mostly the result of an optimal experimental preparation whereby light-emitting and light-collecting optodes are placed in direct contact with the subject’s scalp to maximize the amount of light travelling though the cortex. Another issue that limits the use of fNIRS with humans is the considerable amount of time that placing individual optodes may take, particularly with individuals for whom achieving good optical coupling to the scalp is difficult due to thick or dark hair.

To address these issues, we developed a numerical method that: 1) computes an objective measure of the signal-to-noise ratio (SNR) for a given fNIRS channel in real time during optode placement, akin to electrode conductivity used in electroencephalography (EEG), and 2) determines and displays the coupling status of all individual optodes on a model of a human head to indicate which optodes require adjustment for optimum fNIRS data acquisition. The methodology described in this paper has been implemented in a software tool named PHOEBE (Placing Headgear Optodes Efficiently Before Experimentation) that is freely available for use by the fNIRS community.

The SNR measure of an optical channel relies on the notion that the photoplethysmographic signal associated with the cardiac cycle must be detected clearly in order for fNIRS measurements to be collected successfully. Since the cardiac pulsation in an fNIRS signal is attributed primarily to blood circulation in the scalp, its prominence is a strong indicator of the effectiveness of the optode-scalp coupling that is the basis for an fNIRS channel. To determine the coupling status of each individual optode on a generic fNIRS probe, the topology of the optical layout is represented as a connected graph in which nodes represent the individual optodes and edges represent the optode pairings weighed by their SNR (Figure 1). A system of Boolean equations is solved to determine which uncoupled nodes are contributing to low SNR values at the connected edges. Based on this information, optodes that are initially displayed as uncoupled or undetermined can be easily identified and adjusted to achieve optimum placement of the entire fNIRS probe (Figure 2).

![Figure 1](image1.png)

**Figure 1:** (a) Optical layout with 8 sources (red dots) and 12 detectors (black dots) and (b) connected graph of the optical layout.

![Figure 2](image2.png)

**Figure 2:** Screenshot of PHOEBE displaying scalp coupling of optodes in different colors: green (coupled), red (uncoupled) and yellow (undetermined).
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Title: Hemodynamic profiles of speech production in children who stutter.

Stuttering emerges in the preschool years as the brain develops the intricate and dynamically interactive networks underlying language formulation and speech production. Those who stutter know what they wish to communicate; however, involuntary disfluencies (e.g., blocks, syllable repetitions, and sound prolongations) disrupt the forward flow of their speech. Over two decades of neuroimaging research reveals clear anatomical and physiological differences in the speech neural networks of adults who stutter. However, there have been few complementary investigations in children who stutter. Thus, it is unclear whether the differences in stuttering adults are present at onset, or alternatively, reflect compensatory processes. Several neuroanatomical studies in children who stutter support decreases in gray matter volume in inferior frontal gyrus and subcortical regions bilaterally in children who stutter compared to controls, coupled with reduced integrity of white matter tracts interconnecting auditory and motor speech areas (Beal et al., 2013; 2015; Chang et al., 2008; Chang & Zhu, 2013; Chang et al., 2015). It may follow that these structural differences adversely affect speech neurophysiology in children who stutter, yet few studies have examined this empirically.

The primary goal of this foundational study is to examine the lateralization and timing of the hemodynamic response over neural regions integral to fluent speech production and implicated in the pathophysiology of stuttering with fNIRS. Based on earlier findings in adults who stutter, we hypothesize that connected speech, which maximally engages speech and language networks, will elicit atypical hemodynamic responses in terms of amplitude and lateralization in the group of stuttering children compared to controls. An alternative possibility is that atypical neural activation patterns in adults who stutter result from years of stuttering and compensating for their disfluencies, and thus, may not have yet emerged in children who stutter.

Twenty-five children between the ages of 7 and 11 participated in the study; 12 children who stutter and 13 matched controls. For the experimental task, participants described aloud 30 illustrated scenes. For the null (no speech) trials, the children fixated on a point on the monitor. Hemodynamic recordings were recorded with a continuous wave system (CW6; TechEn, Inc.). The optodes were held against the scalp with a custom-designed 3-D probe over regions of interest including inferior frontal gyrus, precentral gyrus (orofacial motor cortex), and superior temporal gyrus.

We found that children who stutter had distinctly different speech-evoked hemodynamic responses compared to their fluent peers. Whereas controls showed the expected, canonical hemodynamic response profile, children who stutter exhibited a diminished early peak in HbO₂ followed by significant deactivation in many channels. Between-group differences in neural activation patterns were significant over left hemisphere channels, including those over ventral inferior frontal gyrus and orofacial motor cortex. Potential neural mechanisms precipitating these differences are considered within the framework of the DIVA/GODIVA computational models of speech production and stuttering (Civier et al., 2013; Tourville et al., 2011).
References


Diffuse optical tomography (DOT) using high-density and multi-distance probe configurations has enabled us to improve the spatial resolution of the brain activation images. [1] The subject-specific head model of which the structure is based on an individual’s head images is used to accurately estimate the spatial sensitivity matrix for the image reconstruction in the DOT. The heterogeneity in absorption caused by the extracerebral blood vessels affects the reconstructed images and sensitivity of the DOT [2, 3]. In this study, the influence of the absence of the extracerebral blood vessels in the subject-specific head models on the image reconstruction of the DOT was investigated.

The MR head images were segmented into five regions, which were the scalp, skull, cerebrospinal fluid, gray matter and white matter, to generate a subject-specific head model. The structure of the extracerebral blood vessels was obtained by MR angiography. Light propagation in the models was calculated by Nirfast [4]. The changes in the optical density, $\Delta OD$, caused by the absorption change, $\Delta \mu_a$, in the gray matter due to brain activation detected by the probe pairs were estimated from the head model including the extracerebral blood vessels whereas both models including and excluding the extracerebral blood vessels were used to estimate the spatial sensitivity matrices $J$ for the image reconstruction. Source and detector probes were alternatively attached at 10-mm interval lattice points on the frontal or occipital regions. The images of the absorption change were reconstructed from the optical density detected by the first- to third-nearest neighbors of the source-detector probe pairs by using the spatial sensitivity matrices.

$$[\Delta \mu] = J^T(JJ^T + \alpha I)^{-1}[\Delta OD]$$  

(1)

where $\alpha$ is the regularization parameter and $I$ is the identity matrix. The regularization parameter was changed to evaluate its effect on the quality of the reconstructed image. The spatial extent of the absorption change in the images reconstructed using the model excluding the blood vessels was almost the same as that using the model including the blood vessels, however, the quantitative accuracy of the images reconstructed using the model excluding the blood vessels decreased with a decrease in the regularization parameter. The value of the absorption change spatially fluctuated and did not indicate the actual distribution. Although the unrealistic fluctuation in the absorption change is reduced with an increase in the regularization parameter, the spatial extent of the absorption change in the reconstructed images increased with an increase in the regularization parameter. This noisy fluctuation was also observed in the images reconstructed using both the models from the change in the optical density including the noise. The choice of a higher regularization parameter to reduce the noisy fluctuation in the absorption change in the reconstructed image caused by the inaccurate spatial sensitivity matrix and noise in the optical density detected by the probe pairs will result in broadening of the spatial extent of the brain activation measured by the DOT.

References  
On the use of alternating/non-alternating designs in infant research with fNIRS

Thanks to its easiness to set up on subjects, fNIRS offers a unique opportunity to investigate developmental neurocognitive questions at very young ages, especially at birth. Because of the slow time course of the hemodynamic response, stimuli are typically presented by blocks (Gervain et al., 2011; Rossi et al., 2012). Introduced by Best & Jones (1998), alternating and non-alternating designs, display an alternation of blocks with stimuli from the same condition in the non-alternating blocks, and blocks with stimuli from two different conditions in alternation in the alternating blocks. This type of design offers the opportunity to test fine-grained discrimination between two types of stimuli by pre-verbal infants, as evidenced by numerous successful implementations, both in behavioral (Maye, Werker, & Gerken, 2002) and fNIRS experiments (Gervain, Berent, & Werker, 2012; Gervain et al., 2016; Sato, Sogabe, & Mazuka, 2009).

In the current study, we compared the alternating/non-alternating design (Figure 1) to the more traditional block design (Figure 2) in two studies with newborn infants (1-3 days old) using the exact same stimuli. We presented 120 French utterances at their normal duration, compressed to 60% of their normal duration or compressed to 30% of their initial duration. Every utterance was presented once in each duration. In the first experiment, in one half of the experiment, the non-alternating blocks displayed only normal utterances or only 60% compressed utterances and the alternating blocks presented an alternation of normal and 60% compressed speech. In the other half of the experiment, non-alternating blocks displayed normal or 30% compressed speech only and alternating blocks displayed an alternation of normal and 30% compressed speech (Figure 1). Although the difference between responses evoked by alternating and non-alternating blocks was weak, we observed a differential response between normal and 30% compressed speech on the one hand, and between 60% and 30% speech on the other hand when we compared the responses evoked by the non-alternating blocks separately. With the simple block design, although the blocks were the same as the non-alternating ones in the first experiment, there was no significant difference between the responses evoked by the three compression rates.

Taken together, these results suggest that one advantage of the alternating/non-alternating design is that it highlights subtle differences in stimuli due to rapid alternations in the presentation. Newborns have a limited working memory capacity and alternations of two different stimulus types within the same blocks could facilitate the comparison. Alternating blocks serve as a prime for processing of the non-alternating blocks, making the differential encoding of stimuli from closely related conditions easier when memory capacity of the population studied does not resist the long inter-block interval required by NIRS.
Study of memory deficit in Alzheimer's Disease by means of complexity analysis of fNIRS signal
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The deficit of normal performances of working memory (WM) is a main signature of Alzheimer's Disease (AD). Free and Cued Selective Reminding Test (FCSRT) is an innovative clinical test used to evaluate memory deficits\textsuperscript{1}. In particular, the response to Immediate/Delayed Free Recall (IFR/DFR) is considered highly indicative of early AD\textsuperscript{1}. Neuroimaging studies of WM diagnosis are currently done with fNIRS, EEG and fMRI. However, it is very difficult and not ecological to use these techniques simultaneously with the clinical administration of the FCSRT, given the impossibility to create a proper matrix design and a proper modeling of the expected functional response. Therefore, alternative solutions must be searched for overpassing this limit.

In this study, we proposed to investigate whether the complexity of the fNIRS signal is correlated with memory deficit in early AD through a Multiscale Entropy analysis (MSE)\textsuperscript{2} of the fNIRS signal during the IFR/DFR. Sample Entropy (SE) of a signal is defined as the negative natural logarithm of the conditional probability that signal subseries of length \( m \) (pattern length) that match pointwise within a tolerance \( r \) (similarity factor), also match when their length is increased of one sample\textsuperscript{3}. The procedure to evaluate MSE consists of the construction of coarse-grained time series according to different scale factors and the calculation of SE of each coarse-grained time series. fNIRS signals in response to IFR/DFR were recorded over the Brodmann areas 8, 9, 10 and 46 using a multi-distance setup with 4 cm, 3 cm and 2 cm source-detector separations. In particular, we were interested on Brodmann areas 8 and 9 because they are involved in memory deficits and impaired abstract thinking\textsuperscript{3}. The measurements were performed in ecological conditions, during a clinical interview on six healthy subjects (mean age: 67.5 ± 5.0 years; 5M/1F) and on six early AD patients (mean age: 72.2 ± 4.5 years; 4M/2F). fNIRS measurements were performed by using a frequency-domain Imagent system instrument (ISS Inc., Champaign, IL). MSE for both oxyHB and deoxyHB changes time series during the baseline and the three repetitions of IFR and DFR for each channel were computed at different scales (\( m=1; m=2; m=3 \)) and with the similarity factor \( r=0.2 \). Group differences were tested through a Wilcoxon test (\( p<0.05 \)). We found that the majority of channels covering the Brodmann areas 8 and 9 presented significant differences at scale \( m=1 \) and \( m=2 \) in the two groups, while the other channels did not show any significant difference (Table 1). At scale \( m=3 \) the number of channels that presented significant differences decreased.

Our results, although extremely preliminary, demonstrate the feasibility of performing truly ecological studies of WM decline in early AD by fNIRS during clinical interview. Further measurements are currently performed to improve the capability of instrumental diagnosis. If confirmed over a larger cohort of subjects, our method could provide a potential support for diagnosis of early AD.

<table>
<thead>
<tr>
<th>Brodmann Area</th>
<th>oxyHB - p-value</th>
<th>deoxyHB - p-value</th>
</tr>
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<tbody>
<tr>
<td>8</td>
<td>0.0087</td>
<td>0.0260</td>
</tr>
<tr>
<td>9</td>
<td>0.0022</td>
<td>0.0152</td>
</tr>
</tbody>
</table>

Table 1 Statistical differences between the SE (\( m=1 \)) of the two groups evaluated during IFR.

References
**Complexity of Brain Signals is Associated with Outcome in Preterm Infants**

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**Introduction:** A healthy biological system has the ability to react and adapt to minute changes in its environment, a property that characterize complex control systems. Decreased complexity has been associated to aging and poor outcome. We applied Multiscale Entropy analysis to assess the complexity of systemic signals and the complexity of various cerebral near-infrared spectroscopy derived parameters. We further correlated the complexity index (CoI) of brain and systemic signals with outcome. **Methods:** Prospective observational study of 61 preterm infants with a median (range) gestation age (GA) of 26 (23 - 31) weeks with an indwelling arterial catheter. All infants were studied before 24 hours of age, following parental consent. A NIRS sensor (Hamamatsu Photonics, KK, Japan) was placed on the infant’s temporoparietal area of the head. NIRS signals as oxygenated haemoglobin (HbO₂), deoxygenated haemoglobin (Hb), tissue oxygenation index (TOI) and tissue haemoglobin index (THI) and systemic signals as continuous mean arterial blood pressure (MABP), heart rate (HR) and arterial saturation (SaO₂) were collected using ICM+ software. **Results:** Lower Col-HbO₂, Col-Hb and Col-TOI were observed in those infants who developed intraventricular haemorrhage (IVH) compared to those who did not (P=0.002, P=0.010 and P=0.003 respectively). Mean Col-HbO₂, Col-Hb and Col-THI were lower in those infants who died compared to those who survived (P=0.002, P=0.004 and P=0.003, respectively). Complexity of HbO₂ was an independent predictor of IVH (P=0.010) and mortality (P=0.047). Col-MABP was the only complexity index of systemic signals associated with outcome. **Conclusion:** This is the first study to apply Multiscale Entropy to assess the complexity of cerebral near-infrared signals in preterm infants. The results from our cohort revealed that decreased complexity of brain signals recorded within the first 24 hours of life was associated with mortality and brain injury in this population. Furthermore, the complexity index of brain signals had better correlation with outcome than the complexity index of systemic physiological signals.
Example of Multiscale Entropy

Results are mean ± 1.96*standard error of mean.
Monitoring the Injured Brain - Using high density near infrared probes and registered subject specific atlas models to improve cerebral saturation reconstruction accuracy

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Introduction
Monitoring is a key facet in the treatment of traumatic brain injury (TBI) patients and Near infrared spectroscopy (NIRS) is an emerging modality which has been shown to have significant potential advantages over current monitoring techniques, however its application to TBI is still a ‘work in progress’ [1, 2]. Currently the main limitation of NIRS is the lack of quantitatively accurate parameter recovery. Diffuse optical tomography (DOT) is a more complex form of NIRS that can use finite element model-based iterative reconstruction processes to produce spatial maps of recovered parameters from high-density (HD) datasets containing multiple overlapping NIRS measurements. It has been shown in simulation that by using a small hybrid NIRS/DOT pad, consisting of multiple sources and detectors, the high-density measurements obtained can allow for a semi-complex parameter recovery with improved quantitative accuracy over standard NIRS methodologies when combined with register atlas models [3].

Aims
This study aims to extend the previous work from simulations to the collection of high-density data from healthy volunteers in order to test the viability of the hybrid NIRS/DOT probe and the atlas-based reconstruction algorithm.

Materials and methods
Ten healthy volunteers (8 Male, 2 Female) performed a series of three maximal effort, 10-second, standing Valsalva Maneuvers (VM) under controlled laboratory conditions, using a HD NIRS probe over the prefrontal cortex (see Fig. 1). The probe consisted of 8 source positions illuminating at 750 and 850 nm with 6 detector locations. 96 overlapping measurements were collected at 10Hz with source-detector separations ranging from 1.5-5.5 cm over a 48 cm² region of interest. Reconstructions were performed in NIRFAST software using the ICBM152 atlas model as a structural prior. The Atlas was registered to the subject head using a non-iterative point-to-point algorithm, based on four data points taken on the head (Nasion-Inion and pterional-pterional).

Results
Reconstructions showed an average cerebral saturation change of 21±6% (Fig. 2) from baseline (standing rest) to VM peak, which is in keeping with the predicted 22% drop yet markedly different to the ~6% change seen in our previous NIRS studies with the VM. However, the quantitative accuracy of the baseline measurement was not consistent with the recovered values; being 99±3%, 70 ±8% and 72±24% for skin, bone and brain respectively. The large variation in the baseline measurements is due potentially to mismatch in the scatter properties and superficial layer thicknesses between the subjects and Atlas model, as was seen in the original simulation study.

Conclusions
Our HD NIRS probe greatly improves the accuracy of changes in cerebral saturation; however there is still room for further improvement with the quantitative accuracy of the Atlas models and initial scattering properties that derive baseline values.

Acknowledgements:
This work has been funded by the Engineering and Physical Sciences Research Council (EPSRC). The FEM code is distributed as part of the NIRFAST modeling software at http://www.nirfast.org.

References
Age-related changes in visual working memory for multiple object features

Previous functional neuroimaging (fMRI) studies have shown that the aging brain recruits more neural resources across more regions than the younger brain when engaging in executive functions. However, cost-efficiency, sensitivity to motion artifacts, supine-positioning, exclusion of participants with metal implants and ambiguity in the physiological basis of fMRI signals motivate the use of a more ideal tool such as functional near-infrared spectroscopy (fNIRS). Hence, the objective of the current study was to investigate age-related changes in behavior and neural activation using fNIRS in a canonical visual working memory task.

Twenty-six older and young participants were presented with trials that consisted of a sample array of objects that varied in set size (SS) with 1, 2 or 3 items. Following a brief delay, a test array was presented. Participants had to indicate whether the arrays were the same or different. The objects varied along the dimension of either Color or Shape. fNIRS data was recorded from frontal and parieto-occipital regions. fNIRS data were pre-processed and channel-specific betas were obtained using a general linear model. Optode positions were digitized and projected onto atlases created by segmenting age-specific structural MRI scans (Fig 1). Sensitivity profiles were generated for each channel by running Monte Carlo simulations with 100 million photons. Voxel-wise changes in hemoglobin concentrations were estimated for each condition and participant using an image reconstruction approach that combined sensitivity profiles and betas from each channel. ANOVAs were run using these voxel-wise changes in hemoglobin concentrations with Age, Dimension and SS as factors. Family wise corrections were applied to obtain clusters of activation.

Both ages performed better on the Color than on the Shape dimension. Young adults had higher capacities than older adults across the Color (Young=2.5; Old=1.7) and Shape (Young=1.4; Old=0.9) dimensions. Using our novel image-based analytical pipeline, we observed that our activation patterns overlapped with canonical feature processing and VWM regions reported in previous fMRI literature. Further, consistent with previous fMRI work, older adults recruited more brain regions than the younger adults. Specifically, a fronto-parietal VWM network composed of bilateral inferior frontal gyri, left angular gyrus, and inferior parietal lobule (IPL) showed increased activation in the older than the young adults (Fig 2). Feature-selective regions in the bilaera middle temporal gyri, left superior temporal gyrus and right inferior occipital gyru showed greater activation at SS1 and SS2 in older than young adults (Fig 3). However, at SS3, when more representation could not be maintained efficiently in the older adults, neural activation dropped. Further, older adults required greater neural activation in the Shape dimension than in the Color dimension in the right IPL, which has been implicated to play a role in feature binding. Finally, older adults showed decreased activation to incorrect trials across fronto-parietal regions such as the right middle frontal gyrus and bilateral IPL, suggesting failure to encode and/or consolidate items in working memory. Collectively, this study has demonstrated that fNIRS can be reliably used to investigate localized age-related effects of visual working memory processing.
Near Infrared Spectroscopy Based Non-Invasive Cerebral Edema Monitoring System

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Each year in the U.S. about 1.5 million people incur a head injury requiring medical care. Over 5.3 million people suffer severe disabilities due to past traumatic brain injury (TBI)1. One of the most common effects of TBI, in addition to intracranial hematomas (bleeding in the brain), is brain edema (accumulation of water in the intra- and/or extracellular spaces of the brain) that causes increased pressure inside the head and hence damage to brain cells. In the current practice, detection of the edema is usually performed through computed tomography (CT) scan which is standard of care but involves radiation and continuous bedside monitoring is not possible. Typically, monitoring is performed using intracranial pressure (ICP) monitoring device which is invasive and carries risk of complications like infection, hemorrhage, etc. Decompressive craniotomy (opening the skull through surgery) is the most widely used technique to control brain edema. Early detection of brain edema may help clinicians in timely identification of patients in need of surgery and may improve the outcomes of the surgery. However, currently there exists no portable, noninvasive and affordable device for the early detection and follow-up monitoring of brain edema.

The overall goal of this study was to design, develop and evaluate a Near Infra-Red Spectroscopy (NIRS) based mobile imaging device to monitor brain edema continuously and noninvasively. The specific aims of the study were: i) NIRS based clinical prototype design and development to monitor changes in the brain water content; ii) information processing algorithms development and their evaluation and optimization through laboratory phantom and animal testing; iii) human experimentation to test and validate the concept of detecting and monitoring brain edema in humans non-invasively.

In the literature, Thiagarajah et al.2 found in mice that NIR light scattering reversibly increased with brain edema (25% signal increase per 1% increase in brain water content), but was insensitive to changes in cerebral blood oxygenation or blood flow-related changes in ICP. This animal study demonstrated that NIRS technology offers a simple noninvasive solution to detect and monitor brain edema and hence provided a scientific basis for this study. We have designed and developed the first prototype of an NIRS based, non-invasive, affordable and portable edema monitoring device and its signal processing algorithms for blood and water content extraction. The performance of the device and the signal analysis algorithms were evaluated under various oxygen saturation conditions using a novel, multi-layer, dynamic head mimicking laboratory phantom where different types and sizes of edema and hematoma was modeled as shown in Figure 1. The prototype device was also tested on animal (piglet) models and on humans. The phantom, animal and preliminary human testing results suggested that the proposed device is capable of detecting changes in the water and blood content in the brain.

Figure 1: (a) Adult human head mimicking multilayer liquid phantom; (b) Focal edema test phantom results under various oxygen saturation conditions.

FNIRS measures cortical communication during KINARM robotic assessment
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Introduction: The KINARM End-Point Lab, developed by BKin Technologies (Kingston, Ontario, Canada), is a robotic device that objectively assesses functional performance across a range of neurological impairments including concussion1. Previously we used FNIRS coherence to measure interhemispheric cortical communication in healthy subjects2. Using this method we found reduced cortical communication in the motor cortex of children suffering persistent concussion symptoms3. In the current study, we apply FNIRS to investigate cortical communication in healthy controls, while they perform the KINARM neurological assessment. Measures of FNIRS coherence during KINARM exercise may lead to a better understanding of how brain activity relates to function during robotic assessment.

Methods: 8 healthy controls were recruited to participate in our pilot study combining FNIRS and KINARM. Hemodynamic signals were acquired at 50 Hz, using the TechEn NIRSOptix. FNIRS data were collected from bilateral motor (M1) and dorsolateral prefrontal (DLPFC) cortices while participants underwent the KINARM assessment. Participants performed 7 tasks designed to test a variety of functional brain markers including visual-spatial awareness, working memory, reaction time, coordination, cognition, decision making, and position sense. To investigate cortical communication in the brain during the KINARM tasks we used a coherence analysis, which observes the similarity of frequencies between two FNIRS signals.

Results: In this small pilot study we found evidence of increased interhemispheric coherence in the DLPFC during Trail-Making B assessment. This test is commonly used to assess cognitive function, and it has been shown to increase activation in the DLPFC. Our preliminary results show high variability in the visual-spatial and position sense tasks, as well as the Object Hit and Hit & Avoid tasks. This study indicates that interhemispheric coherence may change with cognitive function. It also shows that FNIRS can be a useful clinical adjunct to neurological assessment tools such as the KINARM robot.

References:

Figure 1: Interhemispheric communication in the DLPFC during KINARM assessment.
A) FNIRS brain signal is recorded bilaterally during KINARM tasks. B) We found increased DLPFC connectivity during high cognitive load.
Development of Hyperspectral Functional Near Infrared Spectroscopy

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Near infrared spectroscopy (NIRS) is a portable tool for real time measurement of tissue chromophores such as hemoglobin, water, Cytochrome-c-oxidase (Cyt-ox) and fat having specific absorption spectra in the waveband 650-1100 nm. Most of commercially available NIRS systems are multispectral (mNIRS) which are mainly capable of detecting changes in the tissue hemoglobin concentrations and blood oxygenation; mNIRS suffers low quantitative accuracy. In addition, the lack of spectral resolution makes mNIRS unable to measure changes in low concentration chromophores such as Cyt-ox. In order to improve the quantitative accuracy of NIRS and to include the intracellular oxygen metabolism marker (Cyt-ox) we developed the hyperspectral NIRS (hNIRS). Mitochondrial Cyt-ox redox changes provide critical information about oxygen metabolism level. The greatest mitochondrial concentration in cerebral tissue makes Cyt-ox much more brain-specific than hemoglobin because it is not contaminated by extra-cerebral tissue layers (scalp, skull, etc.) when measured non-invasively. hNIRS hardware includes the stabilized halogen lamps and the portable highly sensitive fibre-optic spectrometers, which can acquire spectra at typical rates of 10 Hz and spectral resolution of 3 nm (Fig. 1). In order to maximize the efficiency of the hNIRS we have developed a hyperspectral algorithm to measure absolute values of tissue chromophore concentrations and a robust hyperspectral signal processing algorithm to measure changes in hemoglobin concentrations and Cyt-ox (Fig. 2). The latter includes noise filtering by principal and independent component analysis and a step-wise chromophore detection algorithm relying on diffusion approximation and spectral features of chromophores. This algorithm allows for both relative and absolute measurements of chromophore concentrations including Cyt-ox redox changes, thus enabling monitoring of intracellular oxygen metabolism. We have assessed the reliability of the hNIRS (both hardware and software) in several test measurements including monitoring cerebral perfusion and metabolism in animal model during cardiac arrest, hypo/hyper-ventilation and FiO2 alternation. In addition, we have assessed the performance of invasive vs. non-invasive cerebral hNIRS measurements and the performance of hNIRS vs. a commercial mNIRS system.

Since hNIRS data includes hundreds of signal channels, it allows for the superefficient multichannel noise reduction techniques, which is very important in fNIRS. We successfully applied our hNIRS technique in combination with the wireless Emotiv EEG system (Fig. 3) to measure functional brain activity during driving and cognitive exercises. Our results have shown a superior performance of hNIRS over mNIRS. In future we plan to explore functional hNIRS in the assessment of mild traumatic brain injuries.
Assessing Neonatal Cortical and Motor Activation during Swallowing in the NICU
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Background: Feeding issues are a major concern for the successful development of neonates. Currently physiological markers of swallowing have been documented but the cortical influences are not well documented. Neonatal dysphagia is a known morbidity among infants with neurological injury.

Objective: To investigate the cortical activity during pharyngeal infusions of different volumes with Functional Near-Infrared Spectroscopy (FNIRS) and concurrent Electromyography (EMG) measurements in a NICU setting.

Methods: Neonates (N=10) were consulted for dysphagia and underwent a diagnostic manometry study to assess the swallowing capabilities of each infant. Saline infusions of .1, .5, and 1 mL were administered to each infant multiple times for each study. Concurrent FNIRS using a NIRx NIRScout CW system was collected as well as EMG from the buccinators and mylohyoid with a BioRadio from VivoSense Inc. Comparisons between response latency and magnitude of response of each hemisphere was compared for each infusion. Correlation between EMG data and NIRS was analyzed to determine the efficacy of concurrent acquisition.

Results: Table 1 displays the FNIRS characteristics of each infusion volume, and there was no significance (p>0.05) between the infusions. Figure 1 displays a NIRS hemodynamic response and concurrent EMG data showing an EMG magnitude increase in the buccinators during the hemodynamic response, as shown by the black arrows in the graph.

Table 1. Oxy-hemoglobin response latency and for the three infusion volumes. Values reported as Mean±SE.

<table>
<thead>
<tr>
<th>Latency Left Side (sec)</th>
<th>.1 mL (N=33)</th>
<th>.5 mL (N=33)</th>
<th>1 mL (N=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>.1 mL (N=33)</td>
<td>12.4±1.2</td>
<td>11.0±1.3</td>
<td>10.6±1.1</td>
</tr>
<tr>
<td>Latency Right Side (sec)</td>
<td>13.2±1.3</td>
<td>9.4±1.1</td>
<td>8.8±1.2</td>
</tr>
<tr>
<td>Magnitude Left (µmol/L)</td>
<td>2.3±0.5</td>
<td>2.0±0.5</td>
<td>1.8±0.4</td>
</tr>
<tr>
<td>Magnitude Right (µmol/L)</td>
<td>1.9±0.3</td>
<td>1.7±0.2</td>
<td>1.6±0.3</td>
</tr>
</tbody>
</table>

Conclusions: We demonstrated the use of FNIRS as a co-modality with EMG and manometry during diagnostic swallowing studies of neonates. There was no significance in latency and magnitude of hemodynamic response for each pharyngeal infusion, but activation was seen for each volume. Concurrent EMG and NIRS was shown as the timing of the hemodynamic response correlated to peaks in the EMG data. Further analysis of EMG data needs to be done along with manometry data in relation to the NIRS hemodynamic responses.

Figure 1. Representative illustration of simultaneous FNIRS and EMG data responses.
Could fNIRS be the next concussion assessment tool? Studies of network integrity
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Introduction: Concussion or mild traumatic brain injury (mTBI) is a major health concern. An estimated 30% of people will suffer an mTBI by age 251 and as many as 1 in 52 patients will experience persistent symptoms. Objective imaging measures are needed to more accurately assess injury and recovery. Many functional changes that occur following mTBI can be attributed to axonal damage, leading to disrupted network connectivity3. fNIRS may be an effective clinical tool to detect these changes. We used fNIRS to show that there was reduced coherence between motor cortices in pediatric cases with persistent symptoms4. The current study expands this research by studying adults and additional networks.

Methods: Continuous fNIRS signal was collected at 50 Hz from bilateral motor (M1, 16 channels) and dorsolateral prefrontal cortices (DLPFC, 8 channels) in 11 mTBI patients with persistent symptoms and 12 controls, using a TechEn NIRS0ptix. We used coherence analysis, which observes the similarity of frequencies between two fNIRS signals, to investigate potential network dysfunction in mTBI patients (Fig 1).

Results and Discussion: Our data show the relationships between coherence analyzed with different frequencies and between different regions. We found lower inter- and intra-hemispheric coherence values in mTBI patients compared to healthy controls during the 2-back test, but not in every task, indicating that the reduction in coherence may be amplified with high cognitive demand. As a step towards greater transportability and a user-friendly design we also show that these results are reproducible when analyzed using only a single channel in each region.

References:
Assessing the effect of confounding factors on estimates of the NIRS hemodynamic response function using single-type event-related designs - A comparative study between averaging and deconvolution analysis

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In fMRI and functional near infrared spectroscopy (fNIRS) experiments, slow and rapid event-related designs are usually used to characterize the brain hemodynamic response to discrete events using conventional averaging (CA) and the deconvolution method (DM).

In this study, we investigated the effect of main confounding factors including timing parameters of event sequences, different types of noise, signal-to-noise ratio (SNR), temporal autocorrelation and temporal filtering on the performance of these techniques in slow and rapid event-related designs. A series of numerical simulations was conducted with synthesized and real resting-state NIRS data. In our simulations, background (baseline) NIRS data consisting of physiological components were added to NIRS hemodynamic responses associated with neural activation, physiological nuisance and instrumental noise.

Our results demonstrated that DM was much less sensitive to the confounding factors. The event timing was the main factor largely affecting the accuracy of CA. In slow event-related design, both CA and DM provided similar results. In rapid event-related design, DM outperformed CA for all SNR especially above -10dB regardless of the event sequence timing and the dynamic of NIRS background activity. We also found that periodic low frequency hemodynamic fluctuations and phase-locked noise can highly affect the performance of both techniques for estimating the hemodynamic evoked response especially under low SNR. The temporal autocorrelation also distorted the time profile of the estimated hemodynamic response in low SNR NIRS signals. Finally, high-pass temporal filtering showed considerable effect on the performance of both techniques by removing low frequency components of the hemodynamic response profiles.

Our results demonstrated the importance of event timing, background noise and SNR in estimating the hemodynamic response profiles using CA and DM in single-type event-related designs.
Gaze modulates functional connectivity between STS and IFG during a mimicry task in 4-month-old infants: a PPI study on fNIRS data

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Mimicry, the tendency to spontaneously copy others’ behaviour, is thought to play an important role in social interaction 1, but very little is known about how it develops. Previous studies with adults have shown that parts of the mirror neuron system (MNS), such as the superior temporal sulcus (STS) and inferior frontal gyrus (IFG), are activated during mimicry. In adults, the strength of the connection between these areas is modulated by gaze direction 2. We have recently demonstrated that eye contact also modulates mimicry of facial actions in 4 month-old infants (de Klerk et al., in prep). The aim of the current project was to investigate whether perceived gaze direction modulates STS-IFG connectivity in the same 4-month-old infants.

We performed psychophysiological interaction (PPI) analyses on functional near-infrared spectroscopy (fNIRS) data. To our knowledge, this is the first time that PPI has been adapted for infant fNIRS data. We measured hemodynamic responses in 32 4-month-old infants using NIRS headgear (2 source-detector arrays, 26 channels - UCL topography system, NTS2), while they observed videos of models performing facial actions (e.g. mouth opening or eyebrow raising) accompanied by direct or averted gaze. Data preprocessing and artefact removal was performed using the HOMER2 toolbox. Data analysis was conducted using a combination of custom Matlab scripts and the SPM-NIRS toolbox 3. For each infant, a standard GLM design matrix was built. In order to explore PPI connectivity, a second GLM design was created with regressors for direct/averted gaze, the time series from the seed region, and the interaction term between these two regressors (Fig.1). Our seed region was STS, which is a key centre for processing of eye gaze 4 and a sensory input site to the MNS 5. As hypothesized, our PPI analysis revealed that the connection from STS to IFG was stronger under conditions of direct gaze than averted gaze, t=2.40, p=0.022. Moreover, the connection from STS to temporo-parietal junction (TPJ) was also modulated by direct gaze in the same way, t=2.22, p= 0.034 (Fig.2).

These results show that the modulation of connectivity from STS to IFG by gaze, previously shown in adults, is already present in infants by 4 months of age. Future analyses will test how these results relate to the infants’ mimicry behaviour. Another interesting result is the engagement of TPJ in relation to STS during mimicry. As TPJ is considered one of the core regions involved in ‘mentalising’, and in self-other differentiation 6, we might suppose an integration between the networks supporting these processes and the MNS during mimicry. Further investigations are required to disentangle this relationship, and to understand the development of functional integration in the social brain in infancy. This study can be considered an important step in understanding how brain connectivity can change as mimicry develops from early in life, and in utilising brain connectivity techniques applied to infant fNIRS data.

References
Reduced-order modelling of light transport in tissue for real-time monitoring of human brain absorption changes using High-Density Diffuse Optical Tomography

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Abstract. High-Density Diffuse Optical Tomography (HD-DOT) has demonstrated improved performance in both resolution and localization errors compared to traditional topographic near-infrared spectroscopy of the human brain\textsuperscript{1,2}. Due to the highly scattering nature of tissue, image reconstruction requires the solution of accurate models of light propagation based on the Finite Element Method (FEM), which significantly increases reconstruction time, and consequently it prevents HD-DOT to be used in real-time monitoring of brain function. To overcome this difficulty, a new reconstruction method based on Reduced-Order Models (ROM) of light propagation in tissue is proposed. The models are nonlinear functions that directly map absorption changes within the brain to flux measurements at detector locations. This approach reduces considerably the reconstruction time up to three orders of magnitude. The applicability of the approach is demonstrated through a numerical experiment. Results indicate that a full 3D reconstruction can be performed in <2 seconds per time point instead of several minutes or even hours with the conventional FEM approach\textsuperscript{3}, without compromising image quality.

Fig. 1a shows a 3D geometrical model of a human head derived from pixel images of an MRI scan, with a Region-of-Interest (ROI) indicated in green (L×W×D = 7×5×3 cm) from which a finite element mesh with high-resolution anatomical prior information was created (Fig. 1b). A perturbation was specified in the form of an absorber in the grey matter (Fig. 1c) with time-varying optical properties. Synthetic data was generated on a fine mesh (112275 elements) while the inverse problem was solved on a coarser mesh (66966 elements). Rendered volumes of images reconstructed from the first sample using both FEM and ROM approaches, are displayed in Figures 1d-e, respectively. Image quality during the reconstruction process (Fig. 1f) demonstrates that images of similar quality can be obtained in ~1sec with the proposed method. It also recovers accurately the relative changes of the time-varying signal (Fig. 1g) without compromising the quality (Fig. 1h).

![Fig. 1](image_url)

**Fig. 1** (a) 3D model derived from MRI scan. (b) High-density finite element mesh of the ROI. (c) Simulated perturbation (red object) embedded in grey matter. (d), (e) Volume rendering of synthetic absorber recovered using FEM and ROM approaches, respectively. (f) Evolution of reconstruction quality for the first sample measured using the Image Correlation Coefficient (ICC). (g) Reconstruction of time-varying optical parameters at the inclusion’s centroid. (h) ICC for each sample.

Decision tree using Graph Theory Approach to Functional Connectivity in Schizophrenia

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Objective: In this study, we aimed to investigate the change in the functional connectivity patterns in the prefrontal cortex (PFC) emerging during a modified version of the color-word matching Stroop task. This task consists of three different stimulus conditions: Neutral (N), Congruent (C) and Incongruent (IC). A continuous wave 16 channels functional near-infrared spectroscopy (fNIRS) device (ARGES Cerebro, Hemosoft Inc., Turkey) was used to measure the changes of HbO₂ concentrations from 12 healthy volunteers and 16 Schizophrenia subjects. The probe was placed on the forehead with approximate cortical sampling regions as depicted in Figure 1.

Methods: Wavelet based partial correlation (WPC) analysis allows us to observe the functional similarity between PFC regions based on activity in a defined frequency interval in each stimulus. WPC was computed for the frequency interval of [0.003 to 0.08] Hz. We considered the channels as a set of vertices V and computed the WPC between each pair of channels. WPC coefficients were assigned as weights on the set of edges E, leading to an undirected complete weighted graph G=(V, E). Degree can be evaluated for wide range of networks, including weighted graphs. The formal definition is as follows:

\[ D_i = \sum_{j \in N} a_{ij} \]

where N is the number of nodes in the network, aij is the number of connection between nodes i and j. The decision tree can be linearized into decision rules. Algorithm C5.0, purring 90% and 6-fold cross validation were used to classification (91.7±4.3).

Results: The rules have the form: If degree of channel 2 or 16 is less than 9, then subject will have schizophrenia. If degree of channel 2 or 16 is more than 9, then subject will be normal. These rules consist of three types of stimulus.

Conclusions: Degree exhibits a stable decrease in schizophrenia showing an attempt of the brain regions to promote a sparser connectivity with long-spanning connections. This is in line with the hypothesis that schizophrenia is a disorder of connectivity between components of large-scale brain networks.

![Figure 1: Placement of the fNIRS probe on the PFC](image-url)
Using near-infrared spectroscopy to measure cerebral blood flow in neonatal brain injury

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Abstract: Over 50 neonates with hypoxic-ischaemic brain injury were monitored using a broadband near-infrared spectroscopy (NIRS) system\textsuperscript{1} in the neonatal intensive care unit. During monitoring, spontaneous oxygen desaturation events were common. The aim of this work is to use the NIRS cerebral oxygenation data (HbD = oxyhaemoglobin - deoxyhaemoglobin) combined with arterial saturation (SpO\textsubscript{2}) recorded using a pulse oximeter to calculate cerebral blood flow (CBF) using a method based on spontaneous desaturation events.

The method is based on Fick’s principle which states that the rate of accumulation of a tracer in an organ is equal to the difference between its rate of arrival and departure. If a substance is introduced into the arterial blood and the time of measurement is less than the transit time through an organ, the tracer will not appear in the venous blood. Therefore the flow can be measured as the ratio of tracer accumulated to the quantity of tracer introduced. We have used a change in HbD as a tracer; when a sudden change in SpO\textsubscript{2} occurs, the change in HbD represents a change in tracer concentration and thus we can calculate CBF. CBF was successfully calculated with NIRS in 30 infants. For four neonates the CBF was measured with arterial spin labelling (ASL) MRI and a strong positive correlation was found between the NIRS- and ASL MRI-measured CBF values when measured on the same day ($R^2=0.96$, $p=0.04$, see Fig. 1). For infants with severe injury there was an increase in CBF with age.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{nirs_vs_asl.png}
\caption{CBF measured by NIRS against CBF measured by ASL MRI. $R^2=0.96$, $p=0.04$.}
\end{figure}

**In vivo** measure of neonate brain optical properties and hemodynamic parameters by time domain Near Infrared Spectroscopy

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By exploiting the relative transparency of biological tissues to near-infrared light, Near Infrared Spectroscopy (NIRS) is an optical technique suitable for non-invasively studying the physiological baseline characteristics of the brain in adults and infants [1]. In particular, the information about oxy and deoxyhemoglobin concentrations (O$_2$Hb and HHb, respectively) can be derived from the measured absorption properties of the brain. In this context, the time domain (TD) NIRS approach, based on the use of light pulses hundreds of picoseconds broad, allows the assessment of the absolute optical properties of the tissues, i.e. $\mu_a$ and $\mu'_s$ coefficients, by acquiring the time resolved tissue response and exploiting proper physical models for data analysis [2, 3]. Moreover, NIRS is particularly suitable and attractive for infants, because of its safeness, non-invasiveness and wearability characteristics. As a matter of fact, NIRS can integrate or substitute other imaging modalities that are usually limited in studying neonates, children or in general subjects without a full control of movements.

In this study, 33 healthy full-term neonates (13 male and 20 female, 3.2±0.9 days after birth) underwent to the measurement protocol at the Azienda Ospedaliera “Santa Maria della Misericordia” in Udine, Italy. All infants had an Apgar score higher than 7 at 1 and 5 minutes after birth. Written informed consent was signed by parents of every neonate prior to the enrollment, and the study was approved by the local ethics committee. Measures were performed using the class I multichannel medical device for TD functional NIRS (TD fNIRS) developed at the Physics Department of Politecnico di Milano [4]. In the experiment, we used as probes two soft silicon cushions, into which optical fibers for light delivery and detection are embedded, resulting in 12 source-detectors pairs on each probe. Infants were tested in a quiet and dimmed room, within their cribs. The silicon probes were placed one over each hemisphere, so as to cover from the frontal area until the central areas of the neonates’ head, centered on the perisylvian areas.

All subjects have a high percentage of channels registering an acceptable signal-to-noise ratio (94.1±5.6%), except 4 neonates (subjects 30, 31, 32 and 33) that were excluded from data analysis. The median values of O$_2$Hb, HHb, the total hemoglobin concentration (tHb = O$_2$Hb+HHb) and the oxygen saturation (SO$_2$ = O$_2$Hb/tHb), together with $\mu_a$ and $\mu'_s$, coefficients at 690 nm and 820 nm for the brain of all the babies are reported in Fig. 1.

![Fig. 1. Median values of O$_2$Hb, HHb, tHb and SO$_2$: (a), $\mu_a$ (b) and $\mu'_s$ (c) relative to the brain of the different neonates. Error bars represent the 25th and 75th percentile of the value distribution.](image)

**Reference**

The reliability test of Mesh-based Monte Carlo method for photon migration studies

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Abstract

The Monte Carlo (MC) method is widely used for simulating photon propagation inside general complex diffusive media for its excellent accuracy. The agreement of independent MC codes cannot be given for granted prior of standardization and cross validation tests among the codes. In principle, after a careful debug of the programs, independent MC codes should return consistent values within the statistics of the simulations. But when dealing with complex geometries there are many reasons that can generate differences among different codes. For instance, the use of a different modelling of the boundary conditions and of the geometry of the medium, the use of different normalization units, and the graininess of statistical procedures.

In 2010, Fang proposed a fast Mesh-based Monte Carlo (MMC) photon migration method for static and time-resolved imaging in 3D complex media that appears to be very powerful and flexible. In order to test the reliability and correctness of MMC, here we take two main categories of comparisons. Firstly, comparing the statistical moments of scattering point coordinates obtained from MMC simulation with the values calculated by the analytical expressions for different anisotropy factors. Secondly, comparing the time resolved reflectance obtained from MMC with that from other MC codes and with the solutions of the diffusion equation for homogeneous geometries (slab, cube) and inhomogeneous geometries (layered slab and slab with absorbing and scattering inclusions). Our current results show that MMC has very similar results compared with several independent MC methods in both homogeneous and multi-layered geometries. Fig. 1(a) shows the results of the time resolved reflectance calculated from four different MC codes for a two-layered geometry at d = 20.5 mm (source-detector distance). For the heterogeneous case (with small perturbations), our results show a good agreement between the MMC simulation and the perturbation model, as shown in Fig. 1(b). In both homogeneous and heterogeneous case, MMC simulation shows some numerical differences from other solutions, which may stem from the domain truncation due to a finite boundary in the MMC simulation, since the difference will be smaller when using a larger volume. Our study has demonstrated that MMC results are reliable for both homogeneous and heterogeneous medium, plus its flexibility and efficiency to image 3D complex media, like human brain, so we believe that it will have a lot of applications in bio-photonics.

References

The effect of Valsalva maneuver on mean arterial blood pressure and brain activity measured by near infrared spectroscopy

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Introduction: Near-infrared spectroscopy (NIRS) is widely used to reveal brain activation pattern as it is able to measure the hemoglobin concentration changes secondary to neuronal activity (1). However, a limitation of NIRS is that systemic changes influence the measured signals. With that regards, there is a need to map these effects in a combined settings. As an exercise may increase the blood pressure, repeated Valsalva Maneuver (VM) will alternate the blood pressure and respiration frequency further (2). Previous studies have reported a significant relation between MAP, ΔCO2 (End-tidal CO2) and ΔHbD (oxyhemoglobin-deoxyhemoglobin) in the brain (3). The purpose of this study was to clarify the relationship between the oxygenated and deoxygenated hemoglobin, the difference of the hemoglobin (ΔHbD), and the mean arterial pressure during moderate exercises with or without the VM.

Methods: Nine healthy volunteers (mean±SD; age, 25.2±2.5 years; height, 177.9±7.5 cm; weight, 71.2±13.0 kg, five females) participated in this study. The study was conducted according to the Helsinki declaration, and all participants provided a written informed consent. All subjects were free of any known cardiovascular or respiratory diseases and were not taking any medications. Each subject received verbal and written explanation of the study objectives. Subjects were seated on a chair in a quiet room and were instructed to perform the leg extension with or without VM. Each session was 3 sets of RE at 55 ± 3.9 % of the participants maximum strength (1RM), and the weight were lifted to voluntary exhaustion (14.8 ± 1.9 reps). Brain oxygenation was achieved by a 3-channel PortaLite system (Artinis, The Netherlands) that was placed over the left (Fp1) frontal cortex region of the forehead. A Finapres NOVA finger cuff was applied for the measurements of blood pressure.

Statistics: Comparing the average results of all three sets with or without VM there is an increase of averaged MAP (with VM, 151.8±24.3 mmHg; without VM, 141.9±24.4 mmHg). The averaged value for all three sets for oxygenated (HbO2), and the difference of the hemoglobin (ΔHbD) increased accordingly (with VM: HbO2=7.9±3.7, ΔHbD=6.4±1.0; without VM: HbO2=5.5±3.9, ΔHbD=3.9±1.1).

Conclusions: As VM introduces a blood pressure fluctuation, the percentage changes of both HbO2 and ΔHbD show an increase (%HbO2=43.6±5.4, %ΔHbD=64.1±10) compared to the changes observed by MAP with or without VM (%MAP=7.0±0.4). As CO2 is a vasodilator, the increase of HbO2 and ΔHbD may not only be due to an increase of blood pressure but also due to local blood flow regulation in the measured brain region.

References:
Comparison of low-frequency oscillations in multi-distance and single-distance functional near-infrared spectroscopy

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Background: Low-frequency oscillations (LFOs) in the cardiovascular system, e.g. Mayer waves or vasomotion, have increasingly drawn attention and can be measured by functional near-infrared spectroscopy (fNIRS). However, the influence of the methodology to calculate hemoglobin concentrations on these LFOs was not investigated in detail. Our aim was to study how LFO power depended on two calculation methods, the multi-distance (MD) diffusion approximation based approach and the single-distance modified Beer-Lambert law (MBLL) approach, respectively.

Methods: We analyzed data from 17 subjects (median 29, six females) from one of our studies. Subjects sat quiescent for 33 minutes and were exposed to colored light during 10 min. They repeated the experiment 3-4 times in a cross-over design with different colors. Data were recorded with a frequency-domain NIR-spectrophotometer (Imagent, ISS Inc.) at four distances (2, 2.5, 3, and 3.5 cm) over the left pre-frontal cortex. We calculated oxyhemoglobin concentration changes by the two different approaches: MD (1 signal) and MBLL (1 for each distance). Signals of deficient data quality were manually excluded. From these signals we obtained power spectral densities (PSD) by fast Fourier transformations. The PSD was split in four frequency bands: very-low frequency (VLF) 0–0.04 Hz, low frequency (LF) 0.04–0.15 Hz, high frequency (HF) 0.15–0.4 Hz, and very-high frequency (VHF) 0.4–1.5 Hz. For each band we calculated three measures: absolute and relative (to total power) band power, and the signal to noise ratio (SNR). SNR was only calculated for HF and VHF, which consistently showed a prevalent peak. Significance was tested by Friedman tests with either including the MD and MBLL data or the MBLL data from the different distance only (Benjamini-Hochberg corrected alpha = 0.04).

Results: For LF and VLF absolute and relative power were significantly higher when calculated from MBLL compared to MD. In the HF and VHF bands, absolute and relative powers were significantly lower but SNR was significantly higher when calculated from MBLL compared to MD. For the different MBLL distances the absolute power of all bands differed significantly. For relative power bands only LF power significantly increased with distance.

Discussion: LFO power depended on the calculation approach. One explanation may be the different tissue volumes sampled from the different light channels. Longer distances lead to sampling of larger and deeper volumes, whereas shorter distances are more sensitive to superficial layers (e.g. skin). The MD approach incorporates all four distances, which reduces influences from superficial layers. Hence, a larger portion of the LFO power is possibly due to superficial tissue, which can be reduced by using MD approaches. The difference between the MD and the MBLL may also be due to vasomotion, which is localized and hence different in the brain and the skin.

Conclusion: Power in all frequency bands depended on the employed calculation approach. The difference could possibly be utilized to study vasomotion.
Identification of the metabolic correlates of the activation/inhibition pattern: a study combining fNIRS and EEG methods

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The ability to choose an appropriate action under time pressure is an important feature of cognitive control. Neurophysiological evidence indicates that neural inhibition is an important component of motor processing in choice reaction time (RT) tasks. Thanks to Laplacian transformation on monopolar EEG data, Vidal et al [1] revealed two noticeable features of the motor command in between-hand choice RT tasks, called the activation/inhibition pattern. First, just before the response, a negativity develops over the contralateral primary motor cortex (M1) revealing an activation of the correct response. Second, a positivity over the ipsilateral M1 develops symmetrically, and reveals an active inhibition of the incorrect response. This activation/inhibition pattern has also been observed using transcranial magnetic stimulation and H reflex [2]. However, this specific pattern, in particular the presence of the ipsilateral inhibition, has not been observed using metabolic neuroimaging methods. The aim of the present study was to fill this particular gap using the functional Near-Infrared Spectroscopy (fNIRS) with an event related design in order to observe the metabolic correlate of the activation/inhibition pattern. For that purpose, participants performed a RT task in which they had to respond as a function of the direction of arrows presented on a visual display. For some participants, fNIRS recordings were combined with EEG in order to have a control of actual presence the activities of interest. Preliminary results confirmed the classical activation/inhibition pattern in EEG data. However, the hemodynamic response appearing in the fNIRS data is identical in the left and right hemisphere.

Acknowledgments
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References
A novel Neurofeedback and BCI toolbox for real-time fNIRS: Turbo-Satori

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Introduction: Turbo-Satori is a novel real-time processing and analysis tool for functional near-infrared spectroscopy (fNIRS) data which was acquired using a NIRx recording device [1]. The software is optimized for real-time applications such as neurofeedback and brain computer interfaces (BCI’s).

Methods: The software calculates and shows relative oxy and deoxygenated haemoglobin concentration changes in real-time and provides this information in time course and neurofeedback / BCI displays. Relative Oxy/deoxy concentration changes are calculated in real-time. A selection of different IIR filters can be used to remove physiological confounds like heart-beat fluctuations or high frequency noise. A RLS GLM is calculated incrementally and the resulting statistics are indicated in the row headers in the channel selection area as well as in the specific rows and columns. The underlying events can be defined using received triggers or a predefined protocol containing the different conditions and timings. The contrasts used in the t-test can be changed online to support the channel selection procedure. Turbo-Satori is based on incremental procedures which can be performed in a run-time of O(1) for each data-point. We measured the processing time using two different datasets, the first datasets using 20 channels and the second using 64 channels. For the first experiment a mean processing time of 2.22 milliseconds (sd=1.47ms) per data point, sampling rate 10.42Hz (~98ms, 20 Channels), was measured. The second dataset performed similar: mean processing time 2.76ms (sd=2.57ms) for each data point, sampling rate 7.81Hz (~128ms, 64 Channels). To fulfill the real-time condition a processing time below the sampling rate is required. The software also includes network interface solutions to export data to 3rd party applications using the TCP/IP network protocol.

Discussion: Data driven analysis methods may be implemented in the future to provide more possibilities in the direction of explorative experiments. Additional improvements can be made in making use of multiple threads to process the data simultaneously for each channel.

Conclusion: A novel fNIRS toolbox was introduced including different preprocessing and analysis procedures in real-time with a processing time for each data point of O(1).

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References: [1] NIRx Medical Technologies, LLC
Developing an fNIRS working memory paradigm for infants in rural Africa and the UK

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The ability to hold essential information in mind and manipulate it ‘online’ is one of the most crucial cognitive functions that children develop in infancy. Moreover, working memory has been shown to be highly predictive of academic attainment and later life outcomes [1].

Research on this important neurocognitive function has shown it is processed in structures within temporal regions relating to the hippocampal network. However, its developmental trajectory from early infancy remains relatively unknown and age-appropriate neuroimaging paradigms need to be developed. Furthermore, very little research has examined neurocognitive development of infants outside of high-income countries, and there is a significant need for new field-friendly techniques.

In this series of studies we developed a new paradigm to assess working memory that was first tested in a sample of infants in the Gambia, Africa, and is now being further refined and piloted in infants in the UK. We aim to study the cortical correlates of working memory in infants to better understand which cortical structures underpin working memory function during development and to describe what this development looks like in Gambian infants.

We used an object permanence paradigm, a task testing the ability to create and hold a mental schema of an object in mind, when it is no longer visually accessible, tapping into both executive functions and working memory.

In Study 1 we have collected data using fNIRS in 12-16 month old Gambian infants [2]. Two experimental conditions were tested, in which the object was either hidden for 3 or for 6 seconds. The results show significant HbO2 responses in channels over the temporal lobes when infants are presented with a hidden object, which extends from temporal into a more widespread response including frontal regions when the object is hidden for a longer period of time (Figure 1).

In Study 2 we added a control condition, in which the object remained visible to the child, thus allowing us to factor in infants’ attention. We presented a pilot sample of infants in the UK between 12 and 14 months with the adjusted paradigm and we are continuing to test more infants within this group.

Preliminary analyses suggest a trend for differential processing of the experimental and the control condition, as well as a differential time lapse in the haemodynamic response depending on how long the object remains hidden for. We are planning to further examine these differences and trends by increasing the number of participants to add to the robustness of our analyses. The findings will be discussed in relation to theories of object permanence and attention.

The BabyLux project - an optical neuro-monitor of cerebral oxygen metabolism and blood flow for neonatology

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Abstract

The BabyLux project (http://babylux-project.eu, grant agreement n. 620996, CIP-ICT- PSP-2013-7) started in 2014 with the aim to provide a precise, accurate and robust integrated system to continuously monitor cerebral oxygen metabolism and blood flow in preterm and critically ill newborn babies. BabyLux brings together a group of experts in the underlying optics technology (ICFO-The Institute of Photonic Sciences, Spain / Politecnico di Milano, Italy) with industrial partners (HemoPhotonics/Loop-Competitive Design Network, Spain/Fraunhofer Institut IPT, Germany) and clinical end users (Rigshospitalet Copenhagen, Denmark/ICCRS Ca’Granda Ospedale Maggiore Policlinico, Italy) to address this challenge with an overall concept taking up completed research and development work done by its partners and extending already tested prototypes to the level of demonstrators for the clinics. The project is driven by the end-users to address an important unmet need. Over the last two decades, the percentage of preterm births (i.e. born <37 weeks of gestational age) in the Western hemisphere rose by 20%, representing an estimated 15 million babies worldwide[1]. During early stages of brain development, injury from lack of blood flow and oxygen delivery may induce cognitive and physical handicaps. In fact, preterm births now account for a significant portion of children with cerebral palsy and cognitive, visual, and hearing impairments. A non-invasive, continuous, cot-side monitor of cerebral oxygen metabolism and blood flow is an unfilled niche in clinical care. The system is based on near-infrared diffuse correlation spectroscopy (DCS) and time resolved near-infrared spectroscopy (TRS) to non-invasively and safely measure cerebral oxygen metabolism and blood flow. This innovative approach combines the state-of-the-art in accuracy and robustness of TRS and DCS within a single instrument to provide medical practitioners in real time via an easy-to-use graphical user interface hemodynamic cerebral tissue parameters (e.g. oxygen saturation, blood flow index, cerebral metabolic rate of oxygen extraction). The instrument after a demonstration phase in laboratory settings entered an operational phase in real-life settings, conducted in parallel at two public partner hospitals. The particular interest of the BabyLux solution in proven user friendliness will be evaluated additionally by professional end-users during the validation tests carried out in conditions fitting in the clinical workflow, protocols and procedures. The device concept and initial laboratory and clinical evaluations will be presented.

Fig. 1 Left: Photo of the BabyLux demonstrator; Right: BabyLux hybrid sensor, soft cover dimensions approx. 25x40mm.

Decoding multiple sound-categories in the auditory cortex using independent component analysis

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The aim of this study is to decode the hemodynamic response (HRs) evoked by multiple sound-categories using functional near-infrared spectroscopy (fNIRS) in both offline and online processing. The HRs in both hemispheres using fNIRS were measured in 18 and 7 subjects while exposing them to four (English-speech, non-English-speech, annoying sounds, and nature sounds) and six (the same four previous categories plus classical music and gunshot sounds) different sound-categories, respectively.

The schematization of the proposed online processing is provided in Figure 1. An independent component analysis (ICA) algorithm for processing adaptively to the number of observations is employed to reduce the unwanted noise in fNIRS signals. Further, linear discriminant analysis (LDA) is utilized for training and testing using the data from both hemispheres. For classification, 14 different feature-sets each comprising different combinations of 8 features (i.e., the mean, slope, skewness, kurtosis values from the reconstructed independent components of HbO and HbR data) are tested. For comparative purposes, offline processing using averaged data from regions-of-interest in individual subject was performed using LDA and support vector machine (SVM) classifiers.

It is found that among all the feature-set combinations, the combination of all 8 features for four-class problems and the mean-HbO, slope-HbO, and skewness-HbO for six-class problems yielded the best online classification accuracies. Additionally, the computation times in every trial were about 0.40 sec and 0.44 sec for four- and six-class problems, respectively. In two-class problems, the highest accuracies were 66.67% (left) and 50.00% (right) in Subject 6. Meanwhile, in six-class problems, the highest accuracies were 33.33% using both left and right hemispheres’ data in Subject 24. Furthermore, the result from offline processing showed the classification accuracies above the chance levels. In details, the overall two-class classification accuracies of LDA were 70.53±8.79% (speech hearing) and 73.39±10.82% (sound hearing), whereas those of SVM 68.11±7.90% (speech hearing) and 72.24±9.61% (sound hearing), respectively. Therefore, it was concluded that LDA performs better than SVM in classifying the HR signals evoked by audio stimuli.

Introduction to the nirs-toolbox

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We will be introducing our new Matlab toolbox for fNIRS functional analysis. The toolbox is open source and can be downloaded at [www.bitbucket.org/huppertt/nirs-toolbox](http://www.bitbucket.org/huppertt/nirs-toolbox). This defines an array of new Matlab-derived data classes and namespaces for performing basic preprocessing methods as well as first and second-level statistical models. Additional tools for registration and forward model generation, which interface with the NIRfast, MCextreme, and tMCimg forward model solvers are included as well as several inverse model methods including our work on mixed effects inverse models. The toolbox also incorporates functional connectivity and hyperscanning processing including a number of graph-theory based metrics interfacing with the brain connectivity toolbox from the O. Sporn lab at University of Indiana (brain-connectivity-toolbox.net). The toolbox supports native data formats from the TechEn, Hitachi, NIRx, and Artinis systems as well as import through the popular *.nirs format used in the other HOMER and HOMER-2 programs.

Most distinguishing from other toolboxes, our new toolset provides a number of validation tools for evaluating the sensitivity/specificity (via receiver operator curves) and effective false-discovery rate estimates of the various processing modules and pipelines that can be implements. Particular focus has been placed on correcting type-I error rates in fNIRS analysis related to motion artifacts, systemic physiology, and serially-correlated noise which have significant negative impacts on both functional evoked activity and connectivity models in fNIRS.

Recently, the toolbox has also been extended to deal with multimodal EEG and MEG data and implements both unimodal and multimodal methods for principal component analysis (via parallel factor analysis; PARAFAC) and multimodal image reconstruction methods.
We have developed an integrated NIRS-EEG head cap for measuring brain activity associated with multi-sensory processing of vestibular and balance related activity during upright balance tasks. Previous work by our group has indicated the superior temporal gyrus and temporal parietal function in vestibular sensory processing (1-3). In this current study, we have recorded concurrent NIRS-EEG during dynamic posturography while measuring from these regions (figure 1).

**Figure 1. Concurrent NIRS-EEG was collected while standing for balance tasks.**

Subjects preformed transitions between sensory conditions (eye open/closed, fixed/sway-referenced floor, and optical flow scenes) while standing upright in a virtual reality immersive environment. FNIRS and EEG data (changes in frequency specific power) was analyzed as evoked changes between the sensory tasks. Figure 2 shows the reconstructed fNIRS and EEG signals for the transitions from SOT I (eyes open/fixed floor) to SOT IV (eyes open/swayed platform) and SOT II (eyes closed/fixed) to SOT V (eyes closed/swayed) showing corresponding activation patterns in the left temporal parietal junction during the tasks.

**Figure 2. Reconstructed NIRS and EEG evoked signals from balance transitions.**

**References.**


Cortical activation patterns correlate with speech understanding after cochlear implantation

Cochlear implants are a standard therapy for deafness, yet the ability of implanted patients to understand speech varies widely. This holds for both prelingually and postlingually deafened cochlear implant users. To better understand this variability in outcomes, we used functional near-infrared spectroscopy (fNIRS) to image cortical activity in postlingually deafened adults hearing through their cochlear implants. We then compared their fNIRS results to standard behavioral measures of their speech perception abilities. Thirty-two deaf adults hearing through cochlear implants were tested, along with 35 normal-hearing controls. Regions of interest measured using fNIRS were the left and right lateral temporal lobes. The speech stimuli included four conditions varying in intelligibility. These included normal speech, channelized speech (vocoded into 20 frequency bands), scrambled speech (the 20 frequency bands were shuffled in random order), and environmental sounds (a non-speech control stimulus). Behavioral measures of speech perception consisted of an individual’s speech reception threshold, as well as sensitivity to consonant-nucleus-consonant words and AzBio sentence tests measured in quiet. Both control and implanted participants with good speech perception (as measured behaviorally) exhibited greater amounts of cortical activation to natural speech than to unintelligible speech. In contrast, implanted participants with poor speech perception (also as measured behaviorally) had robust, indistinguishable cortical activation in response to all four classes of stimuli. The ratio of cortical activation to normal speech to that of scrambled speech directly correlated with patients’ scores on the consonant-nucleus-consonant words and the AzBio sentences. Critically, this pattern of cortical activation was not correlated with auditory threshold, age, side of implantation, or time after implantation. Moreover, turning off the implant reduced cortical activation across implanted participants, regardless of speech perception ability as determined behaviorally. Together, these data indicate that the responses we measured within the implant patients’ lateral temporal regions, including middle and superior temporal gyri, correlate with their behavioral measures of speech perception and in a counterintuitive direction, thus demonstrating a cognitive mechanism that we are able to substantiate with neural data for the variability in speech understanding outcome following cochlear implantation.
A low cost multichannel NIRS spectrometer for monitoring global physiological hemodynamic fluctuations

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**Introduction:** Systemic NIRS waveforms have shown utility for characterizing and removing physiological confounds from functional imaging data and for tracking blood circulation \[1\]. Comparison of the arrival time of these low frequency “noise” waveforms using correlation analyses offers a method for assessing the function and dysfunction of peripheral vasculature \[2\], but recording these signals generally requires dedicating at least one channel of a high end research NIRS device to each site being measured, which limits the potential clinical applications of the technique. In order to explore the potential uses of this type of analysis, we have developed a low cost, portable multisite NIRS system which combines low weight, compact size, ease of use, and clinical quality components. This device permits long duration, high accuracy, full bandwidth recording of peripheral physiological NIRS signals at multiple sites by using custom firmware to repurpose mass produced commodity components to perform this task.

**Methods:** We have developed an inexpensive multichannel oximeter which is a refined and expanded version of a single channel system shown previously \[3\]. The assembled device is shown in Figure 1(a); it has seven NIRS channels and one EKG channel. The core of each NIRS channel is an Olimex MOD-PULSE pulse oximeter development board (Olimex, LTD, Plovdiva Bulgaria), which implements Texas Instruments’ reference design for a Nellcor-compatible single chip pulse oximeter using a TI MSP430FG439 MCU. It uses a Nellcor type D-YS or DS-100A pulse oximeter probe, which measures transmission through fingers, toes, or earlobes at 660 and 920nm. The block diagram of the MOD-PULSE board is shown as Figure 1(b). The MOD-PULSE has a two stage input amplifier, with ADCs at the output of each stage and adjustable LED output power. As previously described \[3\], the onboard MCU was reprogrammed to perform a rapid, closed loop offset adjustment of the first amplifier stage to keep the 512 Hz digitized optical signals at a dithered target value. The offsets waveforms are filtered and downsampled by a factor of 16, achieving 14 effective bits of dynamic range at 31.25 Hz with a flat frequency response (DC to 15.625 Hz) with a 12-bit ADC. Sample pairs from each channel are sent at 31.25 Hz over a serial bus to a Teensy 3.2 (an Arduino-compatible development board with an ARM processor) for further signal processing and transmission over USB to a laptop (in this case a MacBook Pro). The Teensy 3.2 also generates the sample clock to synchronize the seven MOD-PULSE boards. The EKG channel uses an Olimex MOD-EKG board with firmware modified to permit external synchronization.

A Python application shown as Figure 1(c) on the laptop converts raw NIRS data to in (delta) oxy-(HbO), deoxy- (HbR) and total hemoglobin (tHb) concentration waveforms, separates them into frequency bands of interest, displays them, performs and displays correlations between the channels, and stores the data.

**Result:** The device we have built meets the target goal of a portable, low cost, high accuracy multichannel NIRS system which can be used to assess peripheral vascular physiology.

**References:**


Fig 1. Multichannel NIRS spectrometer. a) The assembled device, shown with Nellcor fingertip probes and EKG sensor. b) Block diagram of the microcontroller board (i.e. MOD-PULSE). c) The user-interface, shows real time changes in HbO, HbR, tHb, cardiac, LFO and EKG data for 8 channels.
Hemodynamic Imprinting: A Novel Approach to Disease Detection

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Abstract:
In this report we introduce a generalizable approach to early disease detection involving a novel composite methodology—referred to as hemodynamic imprinting—that explores the spatiotemporal response of the hemoglobin signal in soft tissues to a controlled viscoelastic deformation. Motivating this approach is the expectation that the principal constituents of tissue that determine its stiffness, vascular density and metabolic demand will be modulated by disease in a manner that allows for the emergence of specific features in the hemoglobin response. Different from other concurrent sensing methods, whose aim is to identify independent features, explored here are the dynamic interactions that arise as a consequence of the induced modulation.

As an exemplary demonstration applied to the problem of breast cancer detection, here we have employed the method of optomechanical imaging [1], adopted to acquire simultaneous bilateral measures of the breast. This methodology combines feedback-controlled viscoelastic deformation of tissue with concurrent high density diffuse optical tomography. This approach supports extension of measures of the hemoglobin signal into the time domain, allowing for the examination of spatiotemporal behaviors [2,3].

To appreciate factors affecting diagnostic performance with the aim of optimizing capabilities, parameter sweeps applied to elements of the hemoglobin signal have been conducted by varying conditions of measurement and approaches to data analysis. Findings obtained emphasize a close phenomenological coupling between the conditions of data collection, primitive behaviors of spatiotemporal phenomena, and the expected influence of elements of the tumor phenotype. Diagnostic performance obtained supports the feasibility of individual assessment of disease presence.

References:


Title: How we determine baseline measures and its impact on results: A reflective discussion.
Authors: Nicholas Barone, Erin Kamarunas, and Ji Hoon Ryoo

In the analysis of fNIRS data, the peak hemodynamic response (HDR) is compared to baseline values to determine cortical activation. For researchers new to fNIRS data analysis, determining the peak HDR and baseline values can present a challenge, because when examining the literature there does not appear to be a standard method for choosing how to define these values. Researchers are using a wide variety of baseline and HDR peak definitions (for example: Bortfeld et al., 2009; Harada et al., 2006; Hull et al., 2009; Jadcherla et al., 2014). Therefore, each research team must analyze their data as they determine best fits their individual protocol. The question arises as to whether there should be a standardized method for determining peak HDR and baseline. Upon the completion of a recent research project, we questioned whether the method we chose to determine these values had an impact on the statistical results. Therefore, we hypothesized that changing the definition of baseline and peak HDR would affect the results when using the same statistical analysis.

Using previously recorded fNIRS data comparing cortical HDR over 6 regions of interest during 2 singing conditions (n=9), we determined baseline and peak HDR using 5 methods derived from the literature (Methods in Table 1). A repeated measures ANOVA with between-subject variable (Baseline) comparing analysis methods 1-4 indicates statistically significant differences in Z-scores (p<.01). Furthermore, we ran a two-way ANOVA comparing 6 regions of interest across 2 conditions for each of the 5 methods. We observed large variability in the results of our original research question regarding cortical activation in the regions of interest between conditions depending on which analysis method was used (Results in Table 1). Comparisons between regions of interests by singing condition ranged from 0 to 6 of 6 regions showing significant differences.

The results indicate that how baseline and peak HDR are defined and measured does impact the results of the statistical analyses when comparing the same data. In this discussion-style presentation we will explore our different methods of data analysis and how they influenced the results. This allows for a thought-provoking conversation on optimal analysis methods that accurately represent the data, the ethical implications of determining the method of analysis, and the possibility of standardization for fNIRS researchers who do similar research protocols.

Table 1.

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References:


Denoising task related fMRI data with time delay processing of concurrently recorded peripheral NIRS

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Introduction

Near-Infrared Spectroscopy (NIRS) and functional Magnetic Resonance Imaging (fMRI) are independent methods for studying hemodynamic changes in vivo. Similar to its NIRS counterpart, a major component of fMRI signals come from systemic low frequency oscillations (sLFOs) of non-neuronal origin in the low frequency range (<0.15 Hz), and this phenomenon affects detection power for task related neuronal activation.

Previous work from our group demonstrated that sLFOs are intrinsic blood signals that propagate dynamically both in peripheral tissue with site dependent temporal delays [1] and throughout the brain with cerebral blood circulation [2-4]. sLFOs obtained from peripheral NIRS recordings were widely present in resting state fMRI data with varying time delays which suggested a global circulatory origin for this non-neuronal component.

Here, we evaluate a parsimonious and computationally efficient method for removing systemic low frequency noise from task fMRI signals by adapting our previously developed ‘Regressor Interpolation at Progressive Time Delays (RIPTiDe)’ resting state denoising method [5,6]. We will utilize fingertip NIRS signal as a dynamic systemic noise modeling regressor and examine a) functional contrast to noise ratio (CNR), b) sensitivity and c) specificity of the resulting activation maps at single subject and group level with and without using this method.

Methods

A concurrent NIRS/fMRI study was conducted on 11 healthy volunteers. 3 subjects were excluded due to poor signal quality and the results for 8 subjects will be shown for analysis (5 M, 3 F). Whole brain fMRI data were acquired on a Siemens TIM Trio 3T scanner (Siemens Medical Systems, Malvern, PA) using a multiband pulse sequence. A resting state fMRI scan was followed by a 4 minute serial subtraction experiment and five 3 minute visual stimulation runs, separated by 2 minutes of rest. NIRS data was simultaneously recorded with two optical probes, placed on the forehead over the right prefrontal area and on the right pointer fingertip (Imagent, ISS, Inc., Champaign, IL) at two illumination wavelengths (690 and 830 nm).

For each voxel BOLD time series, the noise modeling regressor was obtained by shifting the fingertip NIRS HbO signal with an ‘optimal’ time delay that maximizes its cross-correlation with that voxel’s BOLD time series. The optimal delay was determined using the RIPTiDe procedure with in-house built, custom software [7].

Results

Figure 1 demonstrates group level z-scores overlaid on the standard 2mm MNI brain from an event related checkerboard visual stimulation experiment. Denoising fMRI data with a voxel-specific optimally aligned low frequency fingertip HbO signal resulted in a better localized activation area (Fig 1A) with a higher contrast-to-noise ratio within the corresponding positive activation map when compared to analysis after standard preprocessing (Fig.1B).

Our preliminary findings suggest that a preprocessing pipeline utilizing dynamic fingertip HbO signal denoising after standard fMRI preprocessing steps (i.e., motion and slice timing correction, smoothing and temporal high-pass filtering) provides improved activity localization in the visual cortex with less false positives. This confirms and extends our previous findings from resting state fMRI [1-6].

References

Figure 1. Group level z-statistics results overlaid on the standard brain show improved activity localization after denoising fingertip NIRS-HBO signal (A) when compared to the same analysis obtained after standard preprocessing (B).

Figure 2. % Variance explained by the voxel-specific time delayed fingertip NIRS signal averaged over all subjects. Peripheral sLFOs explain up to 15 % of fMRI-BOLD signal variance especially in heavily perfused regions.
Abnormality of Low Frequency Cerebral Hemodynamics Oscillations in TBI Population

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Background
Traumatic brain injury (TBI) is a major cause of death and disability. In the United States alone, approximately 1.7 million individuals sustain a TBI each year, of which 52,000 die and another 275,000 survive, one-third of these with chronic disability. Traumatic Vascular Injury (TVI) is a well-established but relatively understudied pathologic component of TBI. Microscopic examination from TBI tissue identifies abundant microhemorrhages as well as diffuse intravascular microthrombi which may indicate a vascular cognitive impairment.

Objective
Measure, with fNIRS, low frequency oscillations in hemodynamic signal, attributed in the literature to cerebral autoregulation. They were assessed using Oxygenation Variability (OV Index), obtained from oxy/deoxy-hemoglobin variations in response to stimulus.

Compare our OVI metric between a group of healthy control (HC, n=14) and TBI (n=29).

Method
Participants responded to an action complexity judgment task (evaluating the complexity of daily life activities by classifying the number of steps as “few” or “many”) with a varying degree of cognitive load to produce brain activation. During the task, we measured Oxy- and Deoxy-hemoglobin variations ([HbO] and [HbR]) with fNIRS. For each channel (source/detector pair) instantaneous amplitudes \( A(t) \) and phase \( \varphi(t) \) of \([HbO]\) and \([HbR]\) variations were obtained from the filtered NIRS data. Combining the data for the two hemoglobin species ([HbO] and [HbR]) we were able to quantify instantaneous ratio of \([HbO]\) and \([HbR]\) signal amplitudes (as well as phase shift between the two components) in the given frequency band, as a function of time. For convenience, to characterize \([HbO]/[HbR]\) ratio we have used directly related parameter \( SO_2 \):

\[
SO_2 = \frac{[HbO]}{[HbO] + [Hb]}
\]

To better assess quite complicated behavior of \( SO_2(t) \) during task-rest cycle in each channel and, for simplicity, we have introduced a special metrics (one number) to characterize \( SO_2 \) level of variations during a given time interval, so-called Oxygenation Variability Index (OVI):

\[
OVI = \frac{\sigma(SO_2)}{\mu(SO_2)}
\]
Results

Mean OV indices, corresponding to high complexity tasks, are higher than that of low complexity tasks in the HC group, revealing strong parametric effect (0.039 +/- 0.017 for low, 0.057 +/- 0.036 for high, \( p \)-value=0.069). However, no significant difference has been recorded for the OV indexes for two different loads in the TBI group (0.055 +/- 0.033 for low, 0.054 +/- 0.035 for high, \( p \)=0.9).

Discussion

Our results indicate a novel metric to assess the level of cerebral hemodynamic variations using the low LFO band, which is related to cerebral autoregulation. This metric reveals a strong parametric effect, i.e., mean OV indexes, corresponding to high complexity tasks proved to be significantly higher than that of low complexity tasks, implying stronger CA response to more complicated tasks.

OV index metrics proves to be sensitive to chronic TBI and can potentially be used to separate subpopulations TBI vs. HC. Noticeable differences in OV index spatial distributions between subpopulations have been observed.
A novel global metric to detect motion artifacts in optical neuroimaging data

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As with other imaging modalities, motion can induce artifacts that corrupt optical neuroimaging data (both for fNIRS and high-density DOT). In clinical applications with limited data collection time, it is imperative to utilize optimal motion correction techniques to obtain quality maps of brain function. While multiple methods have been developed for detecting motion artefact in individual NIRS measurement channels, the large measurement numbers present in several multichannel fNIRS and HD-DOT systems provides an opportunity to use detection methods that integrate over the entire field of view. Here, we use a method that aims to quantify motion artifacts by calculating the global variance in the temporal derivative (GV-TD) across all voxels (e.g. from the temporal derivative of the time-course in each voxel, the method calculates root mean square across over all voxels) [1]. This calculation is a fast and automated and identifies motion by considering global aspects of data instead of looking at single channels (Fig. 1a). To test the performance we designed an experimental paradigm that intermixed controlled epochs of motion artifact with relatively motion-free epochs during a well-understood block design hearing-words (HW) language paradigm [2]. Data were collected from 9 subjects and comprised 348 blocks of HW in all, using a previously described HD-DOT system [2]. The subjects were instructed to perform specific movements (e.g. shaking the head to left and right) when cued (10% of the total number of blocks). We categorized the blocks into three groups by sorting the blocks based on the maximum of their GV-TD time-courses (Fig. 1b). Our results show that a higher signal-to-noise is achieved with data having the lowest set of maximum global-variance values (Fig. 1c-f). In summary, a censoring threshold based on the global variance of the temporal derivative time-traces provides a fast and direct way for identifying noise due to motion.

Figure 1: a) Timetrace of all voxels (N=13,107) for one session shows a clear global signature of motion-induced artifact that is reflected in the timecourse of a measure of the global variance of the temporal derivative (blocks 6 and 7, of 11 total, contain head movement). b) Categorizing 348 blocks across multiple sessions into three groups (G1, G2, G3; 116 blocks each), based on the maximum value of their GV-TD timetrace. c) Signal-to-noise maps (T-maps). Colorbar denotes 30%-80% of the maximum T-value of G1. d) Histogram of the thresholded maps in c. e) Block-averaged hemoglobin concentration in activation on right side (HW stimulus is on for 15s in each block). Errorbars (standard error) reveal that the within-time-point noise also increases from G1 to G3. Orange bars denote the 15 sec auditory word presentation followed by 15 seconds of rest per block. f) T-maps with group-specific thresholds based on 30%-80% of their own maximum.

References:
FNIRS-mediated Neurofeedback enhances gait recovery after stroke: double-blinded randomized clinical trial

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Background:
Balance impairment in the patients with brain injury severely affects their activities of daily living (ADL), and previous studies suggested that the important role of the dorsomedial portion of motor cortex including the supplementary motor area (SMA) in balance and gait control in human. Consistently, several studies suggested the SMA involvement in the gait and balance recovery after hemiplegic stroke. Based on these findings, we hypothesized that SMA facilitation using functional near infrared spectroscopy mediated neurofeedback system (fNIRS-NFB) could augment the gait and balance recovery after stroke.

Objective:
We conducted a randomized clinical trial to investigate whether fNIRS-NFB targeting the SMA activity combined with mental practice would augment the post-stroke balance recovery.

Methods:
Subacute stroke patients with subcortical lesions (N = 43, 32 males, Age : 59.8±11.3, 115.0±20.1 days from onset) with written informed consent have participated. In addition to the usual inpatient rehabilitation up to 180min/day, they participated 6 sessions of mental practice with motor imagery of gait and postural related task concurrent with neurofeedback of the SMA activation. Clinical measures including Berg Balance Scale (BBS), Gait speed, and 3m-Timed Up-and-go test (TUG) are assessed. Subjects are randomly assigned to 2 groups (REAL and SHAM). Neither patients nor physicians did not recognize which group they were assigned (double blinded).

Results:
Baseline clinical characteristics were comparable between two groups. There was significant interaction between gait and balance measures including BBS and TUG with significant improvement in the REAL group (F2,29=6.79, p<0.005 and F2,40=3.72, p<0.05, respectively). Comparing the before and after fNIRS-NFB, only REAL group showed significant increase of gait task related cortical activation in the SMA. There was no sideeffects associated with fNIRS-NFB in both groups.

Conclusion:
Our findings confirmed the feasibility and efficacy of fNIRS-NFB on post-stroke gait and balance recovery.
Identifying a neural predictor of infants’ social preferences

Lindsey Powell & Rebecca Saxe

Measurement of infants’ attention is one of the few windows we have into the early development of the mind. Despite revealing what infants can distinguish, however, differences in looking time often fail to reveal why infants devote more attention to one thing than another. It is clear that some attentional preferences are driven by the reward value of the stimulus (i.e. how much an infant ‘likes’ it) while others are driven by infants’ efforts to maximize learning about the world. The current experiments are part of a larger project to develop fNIRS measures that differentiate these underlying sources of infant attention. In particular, they test the hypothesis that neural activity in medial prefrontal cortex (MPFC) correlates with preferential attention toward socially rewarding individuals. In Experiment 1, infants observed one speaker producing positively valenced infant-directed speech (high social reward condition) and another speaker producing neutral, adult-directed speech (low social reward condition). We recorded from 32 channels over bilateral MPFC, and left and right dorsolateral prefrontal cortex (LDLPFC and RDLPFC). We employed an iterated leave one trial out procedure to identify candidate functional channels of interest (fCOI) likely to show higher HbO2 responses to high social reward vs. low social reward in individual participants in each of the three anatomical regions (MPFC, LDLPFC and RDLPFC); this approach increases statistical power and reduces noise due to variability in array alignment and functional region location across participants (Vul & Kanwisher, 2010; Powell, Deen & Saxe, under review). We observed higher activation in MPFC (mainly in left hemisphere) for the high social reward condition vs. the low social reward condition ($t(20) = 2.01, P = 0.05$; Figure 1). Channels recording from LDLPFC and RDLPFC did not differentiate the two conditions.

In a second (ongoing) experiment, 9- to 12-month-old infants again observe one infant-directed speaker and one adult-directed speaker. Following the fNIRS portion, participants also complete a 20 s preference test during which the speakers are presented side-by-side and looking time to each is recorded. With half the intended participants run, we again find higher HbO2 responses to the high vs. low social reward conditions in left MPFC ($t(12) = 1.62, P = 0.13$; attention-matched trials: $t(12) = 2.24, P < 0.05$; Figure 1). Moreover, there is a strong correlation between the differential response to high and low social reward trials and infants’ subsequent attention to the high social reward and low social reward speakers during the preferential looking test ($r(11) = 0.747, P < 0.01$; Figure 2). No similar relationship holds in LDLPFC or RDLPFC. These results thus break new ground by showing not only that responses in MPFC reflect the social reward value of a speaker, but also that they selectively predict individual infants’ subsequent preferential attention. The presentation will also discuss ongoing work aimed at identifying a distinct neural predictor in DLPFC of differential attention to speakers whose speech contains either high or low amounts of information (i.e. a statistically structure syllable pattern vs. random syllables).
fNIRS based cognitive function assessment following concussion in adolescents

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Concussion statistics estimate as many as 3.8 million occur annually in the United States and despite efforts, the number of children treated in emergency rooms for traumatic brain injuries (TBI) annually is increasing[1]. Patients with concussion report an average of 19 symptoms in the 3 months post-injury period, including difficulties in thinking and trouble remembering, as indications of cognitive impairment. There is an unmet clinical need for a safe, practical, reliable and low-cost tool to monitor changes in cognition and executive functioning especially in pediatric population. Functional near infrared spectroscopy (fNIRS) is an emerging technology and is a good candidate for this need as it can provide localized brain activity changes in the prefrontal cortex in natural out-patient settings. At Drexel University, we have developed wearable, wireless and battery operated fNIRS systems that can monitor prefrontal cortex hemodynamics in natural settings[2]. In this study seven adolescents (ages 14-17) participated so far and three subjects were within 4 weeks of concussion (diagnosed according to the International Consensus Conference) compared to healthy controls. Total participation time was approximately one hour and included neuropsychological, emotional, neuroimaging, molecular biological (miRNA), olfactory, and symptom reporting dimensions. The task battery included N-back working memory task (3 levels x 4 iterations), Wisconsin Card Sorting Task (WSCT), Math Fluency Test and University of Pennsylvania Smell Identification Test (UPSIT). The preliminary findings in behavioral profile of healthy controls and concussed subjects were comparable, however, there was increased brain activation, as measured by fNIRS suggested additional mental effort put forth by the patient group to keep up with the task. (See Figure 1). These initial findings confirm the potential of fNIRS and further results will be presented to assess the sensitivity of biomarkers related to clinical outcome measures.

References


Background. Patients with a disorder of consciousness (DOC) often survived severe brain injury and go through a comatose phase initially. When patients recover from this phase they progress either to the unresponsive wakefulness syndrome (UWS) in which awareness is absent or to a minimally conscious state (MCS) in which goal-directed/purposeful behavior is observed yet not consistent. Unfortunately, misdiagnosis is frequent with up to 41% of MCS patients being misdiagnosed as UWS. Misdiagnosis has tremendous consequences for prognosis and end-of-life decisions. Recently, attempts to improve differential diagnosis have been made employing mental-imagery tasks and functional magnetic resonance imaging (fMRI). Approximately 10% of DOC patients can modulate their brain activation following this approach. The current study explores an extension of this approach by transferring it to functional near-infrared spectroscopy (fNIRS). fNIRS has many advantages over fMRI such as portability, ease of use, inexpensiveness, and lower motion sensitivity.

Material and Methods. In this proof-of-concept study 18 healthy volunteers (average age of 24.5 years; nine females; three left-handed) were tested with a simple setup including three source and six detector optodes placed on the scalp above the left cerebral hemisphere. A NIRScout 816 system (NIRx Medizintechnik GmbH, Berlin, Germany) was employed with LEDs emitting wavelengths of 760 and 850 nm. Participants were asked to answer yes/no questions solely by mental imagery of either mental drawing (MD; for encoding a “yes” answer) or spatial navigation (SN; for encoding a “no” answer) in distinct time windows. Participants were auditorily guided with the NIRStim stimulation software (NIRx, Germany). This combination of mental tasks and time windows evokes spatio-temporal brain activity patterns that have proven informative in previous fMRI encoding paradigms. In one session, four localizers were performed – two for each employed mental task – and six yes/no questions, e.g., “Do you live in Maastricht?”, were answered. Participants encoded the chosen answer five times in a row, resulting in a total encoding time of 3.05 min per answer. The offline analyses were done with Satori (v0.8, Brain Innovation B.V., Maastricht, the Netherlands).

Results and Conclusion. After preprocessing each channel’s data a general linear model was fitted. Two channels of interest (COIs) – one for MD and one for SN – were chosen per participant using a high oxygenation increase and a high deoxygenation decrease (both assessed using t-values derived from two localizers) as selection criterion. We could identify a suitable channel for each of the tasks in seven subjects. The answer decoding was based on the inspection of the t-values for both COIs. In three subjects all questions could be decoded correctly. Mean decoding accuracy reached 86%. These preliminary results highlight fNIRS as a potentially promising method in the DOC context. After further advancement and extensive validation of the paradigm and analysis pipeline, the ultimate goal is to test the paradigm in affected patients.

References

MODELLING THE CEREBROVASCULAR HAEMODYNAMICS OF NEONATES USING FREQUENCY RESOLVED NIRS AND DOPPLER SONOGRAPHY

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The Resistance Index (RI), a measure of cerebrovascular resistance (CVR), is often used to aid the diagnosis of Hypoxic Ischemic Encephalopathy (HIE) (1). Results from a study of 38 normal term neonates conducted at the Mercy Hospital for Women in conjunction with The University of Melbourne observed that the RI is dependent not only on gestation and post-natal age, but also on the post-prandial time. Therefore, a perceived lack of reliability of the RI may be due to this multiple dependency.

In order to determine the RI, the cerebral blood flow velocities are measured using Doppler sonography and calculated from the Cerebral Pulse Pressure (CPP) divided by the Peak Systolic Velocity (PSV). An RI of lower than 0.55 suggests a lowered CVR indicative of the brain sparing effect associated with HIE (1). The brain sparing effect is a neuroprotective mechanism, the purpose of which is to preferentially direct blood flow to the brain in hypoxic-ischemic episodes. This mechanism is just one of many mechanisms that interact and contribute, in various degrees, to control the CVR and regulate the cerebral haemodynamics (2). A single snapshot variable such as the RI is unable to accurately and precisely describe variations to the CVR resulting from cerebral haemodynamic regulation (CHR) in response to pathophysiological events and multivariate approach is required (2).

Near-Infrared Spectrometry (NIRS) offers a non-invasive and continuous method for assessing cerebral haemodynamic regulation and cerebrovascular reactivity (3, 4). Frequency-resolved NIRS provides measurements of brain perfusion by measuring the haemoglobin content of the brain tissue and relative cerebral haemoglobin oxygen saturation (rSO₂) (5). The lowered CVR as seen in HIE strives to increase Cerebral Blood Volume (CBV). This physiological response should be reflected in a greater total haemoglobin content of the brain tissue which, without change to or reduced oxygen metabolism expected with therapeutic hypothermia, should have a higher oxy-haemoglobin ratio, and consequently a higher rSO₂. The Dehaes et al study confirmed that these alterations to cerebral blood flow, volume and rSO₂ could be detected with NIRS (5).

NIRS coupled with Doppler sonography has the potential to provide a more holistic description of, and better detect pathophysiological alterations to, cerebral haemodynamics. A current study at the Mercy Hospital for Women aims to formulate an adaptive control model (6) of cerebral haemodynamics to track the pathophysiological alterations in HIE neonates. The study involves measurements of rSO₂, oxy- (HbO₂) and deoxy- (Hb) haemoglobin concurrently with measurements of the cerebral blood flow velocities using Doppler sonography and determination of the RI in both normal and HIE neonates. A frequency-resolved NIRS which could measure haemoglobin content of the tissue as well as a measure of rSO₂ was required and the ISS OxipherTS which promises absolute measurements of both oxy- and deoxy-haemoglobin was selected. Preliminary results have yielded parameters upon which the adaptive control model may be trained (based on).

References


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Sunday, Oct 16th
Why prefer partial correlation to compute functional connectivity for fNIRS data?

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This paper aims to numerically prove that use of the partial correlation (PC) method provides a more accurate estimation of the underlying functional connectivity of the brain dynamics measured by the Functional near infrared spectroscopy (fNIRS) compared to conventional correlation based analysis. The proposed approach is based on the use of partial correlation to estimate the true connectivity between 16 regions measured by our system [2]. Let’s assume that any channel \( x_i(t) \) has a signal model as \( x_i(t) = h_i(t) + Ws_i(t) + n(t) \) where \( h_i(t) \) is the brain hemodynamic response function (BHRF) due to a neuronal activation taking place in the path of the \( i^{th} \) channel, \( s_i(t) \) is the systemic fluctuations of the brain and the skin that are not directly coupled to to cognitive activity weighted with \( W \) factor, and \( n(t) \) is the general additive noise [1, 4–6]. We define \( h_i(t) \) and \( s_i(t) \) as:

\[
\begin{align*}
\h_i(t - \theta^b_i) &= (t - \theta^b_i)^2 e^{-(\frac{(t - \theta^b_i)}{\tau_h})} \\
\s_i(t - \theta^s_i) &= \left[ \sin(2\pi f_1 f_s (t - \theta^s_i)) + \sin(2\pi f_2 f_s (t - \theta^s_i)) \right]
\end{align*}
\]

Functional connectivity is defined as the correlation of the hemodynamic activity between the distant cortical regions (i.e. \( r_{ij} = Corr(h_i(t), h_j(t)) \)). The challenge is to extract \( r_{ij} \) when all we have is access to \( r_{sx} \). The partial correlation coefficient between 1 and 2 after removing the influence of 3 is defined as follows [3]:

\[
r_{12,3} = \frac{r_{12} - r_{13}r_{23}}{\sqrt{(1 - r_{13}^2)(1 - r_{23}^2)}}.
\]

The 3rd signal is called the regressor. We computed the regressor by high pass filtering of \( s_i(t) \) to obtain HBO with a cutoff frequency at 0.09 Hz. Error between the FC’s computed from the original BHRFs and other processed signals are compared against the PC based FC maps.

Overall we see a drastic improvement in estimating the correlation coefficient by the PC method compared to conventional correlation based method. It should be remembered that this method works under the major assumption that the frequency range of the contamination is different than that of the hemodynamic response.

Acknowledgements

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References

Fig. 1. (a) A mixed signal simulation for channel 1 with $h_i(t)$ in red, the mixed signal $x_i(t)$ and and filtered signals $\hat{x}_i(t)$ in blue. The parameters of the simulation are: $\tau = 1$, $W = 0.3$, $f_1 = 0.1$ Hz, $f_2 = 0.25$ Hz, $f_s = 2$ Hz, $n(t) = \mathcal{N}(0,0.01)$. (b) Errors in estimating the true connectivity: $E_{CO}$: LPF of $x_i(t)$ @ 0.08 Hz with a $4^{th}$ order butterworth filter, $E_{BW}$: LPF of $x_i(t)$ @ 0.08 Hz with a $11^{th}$ order butterworth filter, $E_{CH}$: LPF of $x_i(t)$ @ 0.08 Hz with a $9^{th}$ order chebyshev filter, $E_{PC}$: PC based approach where the $HBO_R$ is the HPF of $x_i(t)$ @ 0.09 Hz with a $9^{th}$ order chebyshev filter.
Neuro-motor control of posture in individuals with persistent post-concussion symptoms

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Introduction: Postural instability has been shown to characterize individuals who suffered from long-term symptoms after mild traumatic brain injury (mTBI). However, recordings of neural processes during postural control are difficult to realize with standard neuroimaging techniques. Thus, we used functional NearInfraRed Spectroscopy (fNIRS) to investigate brain oxygenation of individuals with persistent post-concussion symptoms (pPCS) during postural control in altered environments.

Methods: We compared brain oxygenation and postural sway during balance control in three groups: individuals suffering from pPCS, individuals with a history of mTBI but without pPCS, and healthy controls. Individuals were investigated during postural control tasks with 6 different conditions: (i) eyes opened, (ii) eyes closed, and (iii) blurred visual input, each while standing (a) on a stable and (b) an unstable surface.

Results: In all groups, during the eyes closed / unstable surface condition as compared to the other conditions, the postural sway increased as well as the brain oxygenation in frontal brain cortices. In the most difficult balance condition, as compared to the other two groups, subjects with pPCS applied more force over time to keep balance with a significantly greater activation in frontopolar / orbitofrontal areas of the right hemisphere.

Conclusions: As subjects with pPCS applied more force over time to control balance, we propose that with regards to cognitive processes the increase of cerebral activation in these individuals indicates an increase of attention-demanding processes during postural control in altered environments.

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Depth of anesthesia monitoring based on the multi-channel fNIRS system

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Abstract: It is critically important to monitor the changes of cerebral oxygen metabolism and the state of consciousness during general anesthesia (GA). 11 patients under propofol and sevoflurane anesthesia were monitored based on a 12 channel continuous wave (CW) fNIRS system device in prefrontal area. The concentration changes of oxygenated hemoglobin (HbO2), deoxygenated hemoglobin (Hb) and cerebral tissue heart rate (CTHR) from the forehead were determined from the raw optical information based on the discrete stationary wavelet transform (DSWT). The results showed that the concentration changes of HbO2 and Hb could track the different states of consciousness under GA. The relative concentration of HbO2 and Hb in moderate anesthesia increased compared to awake state, and progressively decreased approaching baseline value during recovery state (Fig.1). Also, the CTHR (cerebral tissue heart rate) index had a clear changes in the induction and awakening process.

Key Words: Cerebral oxygen metabolism; General anesthesia; fNIRS; Discrete stationary wavelet transform

Loss of consciousness (LOC) is determined by the loss of response to a verbal command. The recovery of consciousness (ROC) is defined as the point when the patients could follow a verbal command.

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Title: Bilingual Children Show Left-Hemisphere Activation During Non-Verbal Attentional Networks

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Abstract: Non-verbal visuo-spatial attention tasks typically engage right frontal and parietal brain regions, could early bilingual exposure alter the functional organization of attention in the developing brain? Theories of bilingualism suggest that bilinguals’ languages are always active, and their parallel activation demands increased activity in left-hemisphere brain regions associated with language processing. Recent research (Arredondo et al., 2016) suggests the need to selectively attend and alternate between two languages impacts children’s left frontal lobe engagement during an attention task. Yet, little is still known about children’s brain activity during non-verbal visuo-spatial attention tasks; hence, the present study used functional Near-Infrared Spectroscopy (fNIRS) to investigate bilingual children’s brain activation across three non-verbal attentional networks. We hypothesize bilingual children will show left-hemisphere engagement across attentional networks.

Method: Forty Spanish-English bilingual children (M=8 years-old, range= 7 to 9) completed the Attentional Network Task child version (ANT; Fan et al., 2005), which is a non-verbal visuo-spatial attention task that builds upon a cue alerting and orienting scheme along with a flanker paradigm. The ANT requires participants to selectively attend and inhibit conflicting and non-conflicting information; it measures three attentional networks: alerting, orienting, and executive. A TechEN-CW6 system with 690 and 830 nm wavelengths was used. The setup included 14 emitters of near-infrared light and 12 detectors spaced 2.7 cm apart, yielding 44 data channels sampled at 50-Hz (22 channels per hemisphere). We examined brain activation in bilateral frontal, parietal, and temporal regions. The probe localization was established using the international 10-10 transcranial system positioning. Data preprocessing was completed using Homer2, preliminary analyses were completed using NIRS-toolbox.

Results: Consistent with our hypothesis, preliminary findings revealed that bilingual children activated left-hemisphere regions across non-verbal attentional networks. During the alerting network, children activated left inferior frontal gyrus and temporo-parietal regions. During the orienting network, children activated left middle and superior frontal regions. During the executive network, children activated left middle and superior frontal and right inferior frontal regions.

Conclusions: The greater recruitment of the left hemisphere (the hemisphere known to be critical for language abilities) in bilingual children is consistent with previous research suggesting that early dual-language experiences may indeed alter children’s neurodevelopmental mechanisms of attention. In particular, extensive bilingual experiences may strengthen the computational capabilities of children’s left hemisphere, which may thus become more efficient during non-verbal tasks of selective attention and possibly other cognitive functions. The present findings carry powerful implications for understanding the impact of early language experiences on neural plasticity and to inform theories of early cognitive development.
Tinnitus leads to increased brain connectivity in primary auditory and non-auditory brain regions as measured by functional near infrared spectroscopy (fNIRS)

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**Background.** Tinnitus, the phantom perception of sound in the absence of a sound stimulus, results in increased spontaneous neural activity and increases in neural synchrony in central auditory circuits in animal models. These putative physiologic correlates of tinnitus have not been effectively translated in brains of human subjects. We recently demonstrated that human primary auditory and adjacent, non-auditory cortices are hyper-metabolic in tinnitus subjects. **Objective.** The present study was designed to investigate changes in brain connectivity between auditory and non-auditory brain regions in tinnitus subjects and age-matched controls before and after auditory stimulation. **Methods.** Individuals with bilateral subjective tinnitus with near normal hearing and non-tinnitus controls were selected for the study. Hemodynamic activity was monitored over the region of interest (ROI, primary auditory cortex) and non-ROI (adjacent non-auditory cortices) and brain connectivity was measured during a 60 second baseline/period of silence before and after a passive auditory challenge consisting of alternating pure tones (750 and 8000Hz), broadband noise and silence. **Results.** Within tinnitus subjects prior to the auditory stimulus, non-ROI regions were more correlated/connected than ROI regions; an effect that was reversed after auditory stimulation. When compared to non-tinnitus controls, tinnitus subjects showed increased connectivity in both the ROI and non-ROI with that of other brain regions that was maintained after auditory stimulation. Interestingly, when assessing the power (measure of brain activation) of a specific brain region, greater levels were seen in controls relative to tinnitus in both ROI and non-ROI prior to stimulation. Post auditory stimulation, only non-ROI showed greater power in controls relative to tinnitus subjects suggesting that brain connectivity rather than magnitude of hemodynamic responses may be more important for the pathologic basis of tinnitus perception. **Conclusions.** When considered together these data demonstrate that tinnitus leads to plasticity and increased connections in both primary auditory and adjacent non-auditory regions, an effect that may contribute to the conscious perception of tinnitus in humans.
FRONTAL LOBE ACTIVATIONS ACROSS DIFFERENT LEVELS OF CONSCIOUSNESS

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Abstract:
The purpose of this research was to identify an objective hemodynamic biomarker within the frontal lobe, which correlates to perioperative nociception across various anesthetic regimens. This particular brain region was chosen due to numerous functional magnetic resonance imaging studies that report blood-oxygen-level dependent changes in the frontal lobe in response to nociception. In addition, the lack of hair in this region allows for easy access for fNIRS probe placement. This research is critical as insufficient analgesic control may induce a response in the brain referred to as central sensitization, which can ultimately result in increased pain and opioid use in the postoperative period, as well as initiate a chronic neuropathic pain process. In this fNIRS study, data were collected from three distinctive groups undergoing a painful procedure (awake, sedated and anesthetized). The data were analyzed using paired t-tests to identify significant difference between painful and non-painful conditions. The results are shown in the Figure. The left panel illustrates the group average (n=11) hemodynamic response to a noxious electrical stimulation applied to the left thumb of a group of awake, healthy subjects. The center panel depicts the group average (n=13) response to an insufflation of the colon in a cohort of sedated patients undergoing screening colonoscopy. The right panel shows the group average (n=5) response to a radio frequency cardiac ablation for a group of patients under full anesthesia in order to correct cardiac arrhythmias. The results show there is a consistent oxygenated hemoglobin response to noxious stimuli across different levels of consciousness (i.e., awake, sedated, and anesthetized subjects). This response is illustrated in the figure by the solid blue line. These findings demonstrate the ability for fNIRS to be used across various surgical environments to define pain and potentially provide a real-time measure of analgesic depth.

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Using fNIRS to compare hemoglobin concentration changes in typically-fluent-speakers and persons-who-stutter

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Functional near-infrared spectroscopy (fNIRS) has become a novel method to study hemoglobin concentration changes in the brain. The use of fNIRS in the field of fluency disorders is limited. In this study, we used fNIRS to measure hemoglobin concentration changes in typically fluent speakers (TFS) and persons who stutter (PWS).

The purpose of this study was to determine whether areas of increased oxygenated hemoglobin would differ between PWS and TFS during speech and non-speech tasks. NIRScout from NIRx Medical Technologies was used. The optical illumination information includes 760-nanometer wavelength as well as 850-nanometer wavelength, and LED emitter type. To take measurements, 12 sources, 16 detectors, and 26 total channels were used. Our participants ranged in age from 12 to 27. PWS were greater than 5% disfluent and TFS were greater than 98% fluent in speech samples. PWS were matched for age, gender, and handedness with TFS. Measurements were taken during four conditions for each participant: (1) reading aloud, (2) spontaneous speech, (3) silent reading, and (4) finger tapping.

Through trend analysis, we found differences in regional oxygenated hemoglobin concentration levels in PWS compared to TFS using fNIRS for reading aloud and free speech. During reading aloud, PWS showed increased oxygenated hemoglobin concentration levels compared to TFS in the following areas of the brain: bilateral pars opercularis, bilateral pars triangularis, bilateral dorsolateral prefrontal cortex, left premotor cortex, left primary motor cortex, bilateral angular gyrus, right middle temporal gyrus, right supramarginal gyrus, and right superior temporal gyrus. Furthermore, we found that when participants engaged in spontaneous speech, PWS showed increased oxygenated hemoglobin concentration levels compared to TFS in the following areas of the brain: bilateral pars opercularis, bilateral pars triangularis, bilateral dorsolateral prefrontal cortex, left premotor cortex, left primary motor cortex, bilateral supramarginal gyrus, bilateral angular gyrus, right middle temporal gyrus, and right superior temporal gyrus. During the other two conditions (i.e., silent reading and finger tapping), there was no difference between PWS and TFS. Using fNIRS in stuttering research is a promising avenue as it is non-invasive and allows us to conduct research with speech-related tasks in a clinical setting. Knowledge of differences in hemoglobin concentrations between PWS and TFS could promote better understanding of neurological differences underlying stuttering and other fluency disorders to guide future clinical practice and promote improved evidence-based treatment methods in the field of fluency.
Using fNIRS to Assess Brain Changes as a Result of Voice Therapy

Introduction: Though voice therapy has been shown to be empirically effective in the treatment of voice disorders, few well-controlled studies have been conducted. In addition, the measures most typically used to track improvement as a result of voice therapy are subjective and their results often vary due to a number of factors (e.g., clients, clinicians, environments). Functional near infrared spectroscopy (fNIRS) provides a more objective way to measure the effects of voice therapy in individuals with voice disorders through the measurement of changes in oxygenated and deoxygenated hemoglobin concentrations.

Purpose: The purpose of this pilot study was to investigate regional cerebral hemoglobin changes as a result of integrated implicit-explicit voice therapy in four individuals with voice disorders.

Methods: Each subject was run using the NIRScout by NIRx Technologies over the course of voice therapy with a 34-channel layout to measure regions of the brain including the inferior prefrontal cortex, premotor cortex, Broca’s area, postcentral gyrus, and superior temporal gyrus. Testing was conducted in four sessions: (1) at time of evaluation, (2) after four sessions of voice therapy, (3) after eight sessions of voice therapy, and (4) 12 weeks after the completion of voice therapy. In each testing session, the subjects completed three tasks as stimuli, each repeated 15 times: (1) sustained phonation in typical speaking voice, (2) sustained phonation in a target vocal quality, and (3) jaw movement. Tasks were preceded by a five-second preparation slide indicating which task was next, were randomly presented through E-Prime software for five-second stimulus periods, and were followed by 20-second rest periods.

Results: All subjects demonstrated increases in oxygenated hemoglobin in the inferior prefrontal cortex during the production of a novel voice quality over the course of voice therapy. In addition, several subjects showed increases in the premotor cortex, Broca’s area, postcentral gyrus, and superior temporal gyrus as compared to baseline at evaluation. In some subjects, changes in hemoglobin concentration during the target vocal quality task were similar to changes in the typical speaking voice task over time, though were generally larger in magnitude. The jaw movement task was used as a control, and in most subjects, showed limited similarities in hemoglobin concentration changes to both other tasks.

Discussion: Increases in oxygenated hemoglobin in the inferior prefrontal gyrus, premotor cortex, Broca’s area, postcentral gyrus, and superior temporal gyrus are all associated with explicit or implicit motor learning, an indicator that subjects acquired the target voice task through voice therapy. These findings are the first to suggest a change in pattern of oxygenated hemoglobin concentration due to learning in the field of voice. The continued use of fNIRS in subjects with voice disorders could help to improve understanding of motor learning in voice and ultimately improve therapy outcomes for patients.
The influence of bilingual exposure on early brain network development

Our previous study with 4-month-old infants indicated that exposure to one vs. two languages from birth affects the developmental trajectories of functional brain network configurations. We found a functional network showing higher synchronization in bilingually-raised infants, as opposed to their peers from monolingual homes. The topology of the network, involving connections that were mainly localized over typical areas of the auditory language network (i.e. left and right temporal regions and left frontal regions), indicates that bilingual infants might need to recruit different brain resources as a potential consequence of bilingual exposure [1]. The modulation of brain development by bilingual experience might be especially relevant in the auditory language network during the first postnatal months [2]. By testing older monolingual and bilingual infants, we will be able to disentangle whether the effect that we found in younger infants is a transient effect related to maturation rate differences across the two populations, or if it is a sustained effect reflecting long-term neural adaptations to a monolingual vs. a bilingual learning environment. Importantly, the assessment of the functional resting state networks of the monolingual and bilingual infants took place in a task-free setting while infants received no exposure to linguistic (or any other sort of) stimuli. Therefore the task demands in both populations were identical, unlike in most previous infant studies that required the two populations to perform specific linguistic tasks, which might have imposed different task demands on the monolingual and bilingual infants.

In the present study, we used functional Near-Infrared Spectroscopy (NIRS) to record spontaneous hemodynamic activity in the resting state in awake 8-month-old Spanish or Basque monolingual (n=20) and Spanish-Basque bilingual (n=20) infants. The degree of synchronization of the hemodynamic activity was evaluated by computing the correlation coefficient between pairs of time courses of oxyhemoglobin and deoxyhemoglobin independently on the region underlying each NIRS optode pair. Then, a network based statistical approach [3] was used to reveal potential differences in the connectivity patterns between groups. We present results showing how an early and continued bilingual exposure can lead to specific adaptations in the developing neural circuitry between 4 and 8 months of age.


Influence of bilingual exposure in early brain network development

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Results from our previous study indicate that infants exposed to one vs. two languages from birth follow different developmental trajectories in their functional brain network configuration that are detectable as early as 4 month of age. Concretely, we found a functional network showing higher synchronization ($\rho < 0.05$, corrected) in bilinguals than in monolingual infants. The topology of the network, involving connections that were mainly localized over typical areas of the auditory language network (i.e. left and right temporal regions and left frontal regions), indicates that bilingual infants might need to recruit more brain resources to deal with the additional cognitive demands that imply being exposed to two linguistic systems [1]. One possibility is that this differential brain functional activity in bilinguals might be able to modulate the organization of experience-dependent neural circuits [2]. Concretely, the bidirectional interaction between experience and brain development might be especially relevant for auditory language network configuration during the first postnatal months. Testing older monolingual and bilingual infants we will be able to disentangle whether the effect that we found in younger infants might be a transient effect related with maturation rate differences or if this is a sustained effect leading to specific adaptations that originate as a result of growing in a bilingual environment.

In the present study, we used whole-head Near-Infrared Spectroscopy (NIRS) to record spontaneous hemodynamic activity in awake 8-month-old Spanish or Basque monolingual (n=20) and Spanish-Basque bilingual (n=20) infants. Crucially, since the former study, data acquisition procedure improved substantially. As a result, we achieved longer recordings; we reduced the presence of artifact contaminated segments and we obtained a much better signal quality. We evaluated the degree of synchronization of the hemodynamic activity by computing the correlation coefficient between pairs of time courses of oxyhemoglobin and deoxyhemoglobin independently on the region underlying each NIRS optode pair. We used a network based statistical approach [3] to reveal potential differences in the connectivity patterns between groups. Here, we present results showing how an early and continued bilingual exposure can lead to specific adaptations in the developing neural circuitry. Currently, most of the evidence in the field comes from adult studies, and studies in which infants are tested on a task or presented with linguistic stimuli. Significantly, we address this question with a task and stimulus free experimental setup and in very young infants at different ages.


Real-time adaptive filtering for noise reduction in fNIRS data

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The functional near-infrared spectroscopy (fNIRS) can be utilized to measure the brain hemodynamic response (HR) [1,2]. However, physiological noises always exist in fNIRS data. The band-pass filter is not effective for canceling respiratory and blood pressure noises [3]. A real-time method for noise removal in fNIRS data is really necessary. In this work, a brain activity model is developed based on an autoregressive moving average model to reconstruct the HR and physiological noises as follows.

\[ y(t) = -\sum_{i=1}^{q} a_i y(t-i) + \sum_{j=1}^{p} b_j u(t-j) + \sum_{k=1}^{3} c_k \cos(2\pi f_k t) + b_0 + \varepsilon(t), \]  

where \( y(t) \) is the measured HR at the time step \( t \), \( u(t) \) refers the design HR generated based on the given stimuli using a state-space model [1], \( q \) and \( p \) indicate orders of input and output, respectively, \( f_k \) denotes the \( k \)-th frequency of the physiological noises (i.e., cardiac 1Hz, respiratory 0.25 Hz, and Mayer wave 0.1 Hz), \( b_0 \) refers baseline term, and \( \varepsilon(t) \) stands for the model error. \( a_i, b_j, c_k \), and \( b_0 \) are unknown parameters. They are estimated based on the recorded HR using the recursive-least square method. To validate our proposed method, the fNIRS dataset of arithmetic tasks from previous work (Subject 1) [4] was used. Fig. 1(a) plots unfiltered and filtered HbOs of two representative channels 4 and 8. As can be seen, noises do not effect as the same for all channels (see Fig. 1(b)); Ch.4 consists of data (i.e., 0.022 Hz) and low-frequency noise (i.e., 0.004 Hz) whereas for Ch. 8, noise frequencies appear at 0.004, 0.082, 0.2, 0.34, and 0.61 Hz. Those noise frequencies are effectively removed using our proposed method (see Fig. 1(c)). It is noteworthy the proposed method can use in real-time.

Fig. 1. (a) An example of unfiltered (blue curve) and filtered (red curve) HbOs and the spectrum of Chs. 4 and 8 before (b) and after (c) using the proposed method, respectively.

Use of fNIRS in Assessing Motor Learning and Voice

**Introduction:** While traditional voice therapy is known to be effective, it primarily utilizes implicit strategies such as auditory-perceptual models. These methods may contribute to clients’ decreased generalization and maintenance of tasks taught in therapy. Current motor learning theory suggests that an integrated implicit-explicit instructional approach results in a synergistic effect and enhances learning. There is, however, minimal research that supports this type of learning theory in voice therapy. Functional near infrared spectroscopy provides an objective, noninvasive method to assess the brain’s response to an integrated implicit-explicit voice therapy approach throughout the learning process.

**Purpose:** The study was conducted to compare hemoglobin concentration changes in the brain between a group of individuals who received integrated implicit-explicit voice instruction and age and gender matched individuals who received no voice training.

**Methods:** This study was a within-and-between groups pretest-posttest design. NIRScout by NIRx Technologies was used to assess hemoglobin concentration changes. A 34-channel layout that spanned the prefrontal, motor, somatosensory, and temporal regions of the brain was used to assess implicit-explicit learning. Participants were divided into two groups: one receiving integrated implicit-explicit training in a target vocal quality and a control group receiving no training. Each participant was run on fNIRS at four testing periods: (1) prior to training, (2) after training, (3) after a period of independent focused and deliberate practice, and (4) after a retention period. During each testing period, each participant completed two tasks, both randomly repeated 15 times: (1) sustained phonation in normal speaking voice and (2) sustained phonation in a target vocal quality. There was a 5 second preparation slide, followed by a 5 second stimulus duration, followed by a 20 second rest period.

**Results:** Significant increases in oxygenated hemoglobin (HbO) levels were observed in left and right inferior prefrontal gyri, left primary motor cortex, and left superior temporal gyrus in the experimental group at post-testing compared to pre-testing. The control group only exhibited a significant increase in HbO levels in the right pars opercularis at the same time frame. Results indicated that individuals demonstrated a significant increase in HbO in areas of the brain consistent with acquisition of a novel motor skill following implicit-explicit voice instruction compared to a control group of age and gender matched peers who received no training. The following figure illustrates a trend shown by each of the groups. The experimental group exhibits a focal change in HbO levels from pre-testing to post-testing compared to the control group, which illustrated little change in HbO over time.

**Discussion:** Increases in HbO levels in the aforementioned areas across the learning process (from pre-training to post-testing) are indicative of the acquisition of a non-speech motor skill in the experimental group. The individuals who received no training did not demonstrate a learning effect, supporting the use of an integrated implicit-explicit approach to voice training. Continued research using fNIRS can further validate the integrated implicit-explicit approach to voice therapy, enabling clinicians to create more beneficial and personalized treatment plans for clients that are based in motor learning theory.
We implemented a high density NIRS probe to monitor the hemodynamic response in the prefrontal area during the Valsalva maneuver for 15 elderly patients (mean age = 51 years old) who exhibit signs of orthostatic hypotension (OH). OH is caused by a poorly functioning autonomic nervous system and is marked by reduction in cerebral perfusion and a lack of oxygen supply to the brain [1].

The Valsalva maneuver (VM) can be used to monitor the autonomic nervous system. VM is marked by four phases in blood pressure (Figure 1(A)), as the nervous system adjusts to changes of intrathoracic pressure. VM also exhibits a clear cerebral hemodynamic response, varying by location. A previous MRI study of healthy subjects showed a delay of 21 seconds for the prefrontal area of the brain to reach peak oxygenation, compared to 5 seconds in the amygdala and hippocampus [2].

To measure the rate of change of oxyhemoglobin (HbO) changes, we fitted a line from the start of the VM to peak oxygenation. Our findings indicate that the patients group exhibit a slower rate of change compared to healthy subjects (n=3, trials=6). In addition, healthy subjects showed a larger amplitude of HbO changes. We then split the patient by diagnosis: Dysautonomia, Idiopathic Parkinson’s (IPD), or Stroke. As expected, Dysautonomia patients had the slowest rate of change and smallest amplitude of HbO changes. IPD patients had an HbO rate of change similar to healthy subjects (Figure 1 (B)), but Stroke patients showed an amplitude change much closer to healthy subjects than IPD (Figure 1 (C)).

In conclusion, we have shown there is a distinct delay for the VM to have a hemodynamic response for the prefrontal area, which can be observed by NIRS. In addition, we have shown that the hemodynamic response varies by diagnosis, and NIRS may serve as an enhanced tool in monitoring the autonomic nervous system.

References

Using fNIRS to measure cerebral hemoglobin concentration changes of typically fluent speakers using delayed auditory feedback

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In recent years, functional near infrared spectroscopy (fNIRS) has played a role in advancing research in the field of speech-language pathology. Specifically, fNIRS has helped uncover cerebral hemoglobin concentration differences in persons who stutter (PWS) during speech related tasks. As the exact etiology of stuttering is unknown, the use of fNIRS to compare the cortical activity of PWS and typically fluent speakers (TFS) has been instrumental in furthering our research. Currently, few studies have been conducted to evaluate the effects of delayed auditory feedback (DAF) on cortical brain activity in both TFS and PWS, and no studies have used fNIRS to investigate these effects. The purpose of this study was to measure differences in hemoglobin concentration in the brain in TFS while using DAF for speech and non-speech tasks.

DAF requires headphones to be placed over or in a person’s ears and projects environmental sound back to the ears in the form of an echo to the person wearing the device. In fluency therapy, DAF often has an effect on PWS that makes them speak more fluently. When the device is used on TFS, however, they become more disfluent during speech tasks, even causing them to be disfluent in some cases. This phenomenon enabled us to examine whether there were similar disfluencies exhibited by TFS and PWS. This study examined the differences in oxygenated hemoglobin in TFS while speaking both with and without DAF.

Participants in this study had no prior training with DAF and were at least 98% fluent in speech samples. All participants were over 10 years old. Probes were placed contralaterally across the prefrontal cortex, motor strip, parietal somatosensory areas, postcentral gyrus, auditory processing areas, and receptive and expressive language areas. Measurements were taken during three conditions for each participant: (1) spontaneous speech using DAF, (2) spontaneous speech without DAF, and (3) a rote nonverbal motor speech task. Each stimulus was presented for 5 seconds and was followed by a 20-second rest period. The NIRScout by NIRx Technologies was used to collect data. During collection, 16 sources, 16 detectors, and 32 channels were utilized to find measures.

Trend analyses completed on pilot data with TFS showed increased oxygenated hemoglobin concentrations in the right hemisphere of the brain when DAF was activated compared to when DAF was not activated. The results of this study have the capability to improve understanding of the neurological differences of PWS and TFS. In the future, this knowledge can be expanded upon to validate techniques used in the treatment of fluency disorders. Results of the entire participant pool will be presented at the conference.
The neural correlates of arithmetic complexity in children differ from those in adults: An fNIRS study

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The investigation of the neural underpinnings of arithmetic complexity in children is required for developing educational and therapeutic approaches. These approaches are mostly applied in training of complex calculations in children with poor arithmetic competence. A few studies in adults reveal engagement of bilateral brain regions, especially left frontal cortex and intraparietal sulcus (IPS) during complex calculation compared to simple calculation. However, little is known about underlying neurocognitive processing of this complexity in children.

To address this question, 24 typically developing fifth grade children (9 girls; age 11.1 ± 0.5 years old) underwent simple and complex multiplication tasks while functional near-infrared spectroscopy (fNIRS) data were collected from 44 channels over both hemisphere. The experiment was a block design, and the multiplication problems of simple and complex conditions were presented in 8 blocks of 45 s followed by 20 s of rest. The sequence of the blocks and of the problems was randomized. The task was self-paced with a limited response interval of 10 s for simple problems and 30 s for complex problems, respectively.

Behavioral data revealed that children were faster and more accurate in solving simple problems compared to complex problems. FNIRS data indicated that simple multiplication was associated with brain activity in the left superior parietal lobule (SPL) and IPS extending to the left motor area, but notably not the angular gyrus (AG). Complex multiplication was associated with activity in bilateral SPL, IPS, middle frontal gyrus (MFG) and left motor area. The contrast of complex against simple multiplication yielded greater activity in right MFG.

We suggest that activation in frontal areas indicates additional cognitive control and working memory demands for tasks of heightened arithmetic complexity in children. No difference in parietal activation suggests that in this developing age, children still rely on the magnitude processing not only for complex, but also for simple multiplication problem solving. This finding is in contradiction to studies in adults suggesting complex calculation relies on both cognitive processes and additional magnitude processes, which activate fronto-parietal network. We conclude that in children, arithmetic complexity is associated with additional domain-general processes but not with alteration of domain-specific magnitude processing.
Neural efficiency in children with higher and lower mental abilities using functional near-infrared spectroscopy: A preliminary analysis

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Background: Why people differ in intelligent behavior is an issue that has been occupying researches for more than a century. The neural efficiency hypothesis (NEH) is one discussed explanation. The hypothesis suggests that individuals with higher mental ability (MA) show less brain activity compared to individuals with lower MA. To the best of our knowledge, no study investigated the NEH with a working memory task and functional near-infrared spectroscopy (fNIRS). The aim of the present study was to examine neuronal efficiency in children solving a classical working memory task while measuring brain activity with fNIRS.

Methods: Six children with lower MA (intelligence quotient below the 40th percentile) and six children with higher MA (intelligence quotient over the 85th percentile) participated in the study (mean age of both groups: 12 years). The subjects were a subset of a larger study. Prior to the fNIRS measurement, intelligence was assessed with the Cattel’s Culture Fair Test (CFT 20-R). During the fNIRS measurement, children solved a letter-number sequencing task. This task comprised four blocks each lasting 40 seconds.

Brain activity was measured by a FOIRE-3000/8 fNIRS system (Shimadzu, Japan). Eight emitters and eight detectors were placed in an array with distances of 15, 30, and 42 mm above the left pre-frontal cortex (20 channels in total). The Saager/Berger approach was applied to minimize superficial influences by the 15 mm channels. Based on the modified Beer-Lambert law, oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) concentration changes were calculated. For each channel, movement artefacts were corrected with MARA. By subtracting the median of the last five seconds of activation from the median of the five seconds before the beginning of the task, final task responses were calculated. To obtain a block mean per subject, the four experimental blocks were averaged. Task responses were tested for significance by Wilcoxon Sign-Rank test (2-tailed, α < 0.05).

Results: Children with higher MA showed better working memory abilities than children with lower MA. fNIRS recordings indicated a positive O₂Hb concentration change for the lower MA group but no O₂Hb change for the higher MA group in three channels (all p < 0.05). However, another channel showed the opposite response, i.e. O₂Hb change in higher MA group. Five HHb task responses were obtained without corresponding O₂Hb responses.

Discussion and Conclusion: The two MA groups showed different O₂Hb responses in pre-frontal brain regions consistent with the NEH. Positive O₂Hb responses in the lower MA group may be interpreted as need for higher brain activation. However, responses in the high MA group and HHb responses were not necessarily in line with the NEH. Nevertheless, our results provide clear evidence for fNIRS as a feasible method to investigate the NEH in children.
Title: Can diffuse optical tomography provide early detection of perinatal arterial ischaemic stroke (PAIS) at the cot side?

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Introduction: PAIS occurs in 1:2500 infants. It is secondary to occlusion of a large cerebral artery and potentially results in hemiplegic cerebral palsy, cognitive impairment and epilepsy in childhood. Clinical management in the neonatal period is restricted to symptomatic treatment; a key contributing factor to this is the lack of investigating tools for rapid detection of PAIS. Brain MRI remains the gold standard in diagnosing PAIS, but logistically it cannot always occur in the time-critical acute phase. Diffuse Optical Tomography (DOT) is a safe, non-invasive neuro-monitoring tool, which allows changes in cerebral haemoglobin concentrations to be imaged at the cot-side. Low-frequency oscillations in cerebral haemoglobin concentrations are known to be associated with cerebral autoregulation processes and ‘resting-state’ functional brain networks. This study seeks to test the hypothesis that the power spectra of these LFOs differs between the healthy and PAIS-affected regions of the infant brain.

Methods: As part of a larger study, we have recruited healthy term infants as controls and infants who presented with seizures in the first 72 hours of life. These infants were scanned using the UCL Optical Imaging System for 1-2 hours. We retrospectively analysed data from 4 patients diagnosed with PAIS on MRI, 4 patients with no cortical changes or lateralised findings on MRI and 3 healthy term infants. Following manual motion artefact rejection and channel quality-checks the data were concatenated and mean-corrected. The data power spectra were then extracted using a fast Fourier transform. The LFOs were subdivided in 3 bands; very LFOs (VLFOs) 0.009-0.02 Hz, the resting state network (RSN) 0.02-0.1 Hz and the Mayer waves 0.1-0.5 Hz. We then applied a Bonferroni-corrected paired t-test and a two-tailed t-test to compare the mean spectral power content of the left hemisphere versus right hemisphere channels for the different LFO bands.

Results: All infants with PAIS had a significantly lower mean spectral power in one or more of the LFO frequency bands over the injured hemisphere. Subject 1 exhibited lower mean power over the left hemisphere compared to the right in the VLFO band (p=0.005); subject 2 had a lower mean power over the left hemisphere compared to the right in the Mayer wave band (p=0.0056); subject 3 had a lower mean power over the left hemisphere compared to the right in all the bands (p=0.0037, p=0.0164, p=0.00018 respectively); and subject 4 had a lower mean power over the right hemisphere compared to the right in the RSN and Mayer wave bands (p=0.00098, p=0.0075 respectively). No significant inter-hemispheric differences were observed in the two control groups.

Conclusions: Our results suggest a link between the site of PAIS and the loss of certain LFOs, potentially secondary to altered sympathetic tone, altered vascular smooth muscle architecture or other neurogenic or metabolic factors. These findings require further investigation, but there appears to be potential for DOT in the early detection of PAIS.

Title: Changes in Cortical Control for Singing Onset with Increases in Task Difficulty
Authors: Nicholas Barone, Erin Kamarunas, & Christy Ludlow

Professional singers learn to begin singing at target pitches at different lung volumes by learning to check forces of elastic recoil in the respiratory system (Sundberg et al., 1991). fMRI studies showed greater cortical activation for opera singing in trained singers than singing students and greater activity in singing students than in lay singers (Kleber, 2010). This was not expected as motor control learning usually results in diminished cortical activation with increased skill (Chen & Wise, 1995; Ojakangas & Ebner, 1992; Toni, et al., 1998). We expected that task difficulty might differentiate between singers and non-singers in cortical activation patterns in bilateral perisylvian regions. We hypothesized that singing onset at more difficult low volume would produce greater cortical activation in non-singers than singers.

We compared singers and non-singers on repeating the syllable “pea” at middle C for 3 seconds after a “start” signal at low (30% vital capacity), middle (50%), and high (80%) lung volumes. The singers were first year university vocal performance students; the non-singers had no singing practice or training. Participants performed 30 trials at each lung volume while viewing their lung volume in real-time on a computer screen. Measures of timing of airflow release for /p/ to vocal fold closure for voice onset measured task control at different lung volumes. BrainSight was used to fit a reference MRI into each subject’s head and locate 3 sites on each hemisphere using Talairach coordinates to locate the inferior premotor, inferior somatosensory and the posterior superior temporal gyrus auditory association cortex. A continuous wave fNIRS system (TechEn, CW6), at 50 sps, measured blood oxygenation and deoxygenation using event related averaging over 30 trials from “start” at each volume.

Based on physiological measures of singing, both groups took longer to begin expiration and voice after “start” at low lung volumes (p = .003) while singers took longer to close the vocal folds for singing after the /p/ than non-singers (p = .004), particularly at high lung volumes (p = .007).

Event related averaging showed similar cortical activation patterns in both groups: two peaks (P1, P2) occurred relative to “start” signal, P1 at ~4s and P2 at ~10s. Movement artifact may have affected P1 at high lung volumes at the auditory location due to airflow mask placement. No group differences were found in peak amplitudes when normalized as Z-scores relative to mean baseline readings. For P1, Z-scores at high compared to moderate and low lung volumes were reduced at all cortical locations. P1 responses at low lung volume showed significantly higher and more diffuse cortical activation in both groups (p = .003). No lung volumes effects or group differences were found for P2.

In conclusion, although physiological measures of voice control showed increased attention to timing control particularly at low lung volumes in the singers, early cortical activation was significantly increased during this more demanding task to the same degree in both groups at all cortical sites.

References
We use fNIRS with 3- and 4-year-olds to test the hypothesis that learning labels for visual features improves children’s ability to attend to those features. We measured functional activation related to the comprehension and production of dimensional labels (e.g., “red” or “color”), and the ability to match objects based on dimensional values. Additionally, children were given two tasks that measured dimensional attention abilities, specifically probing attentional selectivity and attentional flexibility. We recorded fNIRS data from frontal, parietal, and temporal regions that have been implicated in a frontal-posterior network of executive attention.

The data revealed various new insights into brain-behavior relationships during this period of early childhood. First, producing color labels elicited functional activation (defined as a significant difference between oxy-Hb and deoxy-Hb) across channels over bilateral frontal cortex, left temporal cortex, and right parietal cortex. Color comprehension, on the other hand, only elicited functional activation in left temporal cortex. Finally, color matching only produced functional activation in right parietal cortex.

We correlated performance in the selective and flexible attention tasks with these hemodynamic measures from the dimensional label tasks. Dimensional attention performance was positively associated with hemodynamic activity during color production in right parietal cortex and with hemodynamic activity during color matching in both left temporal and right parietal cortices. That is, stronger activity during these color tasks was associated with better performance in the dimensional attention tasks. Finally, dimensional attention performance was negatively associated with hemodynamic activity during color comprehension in left frontal cortex. That is, stronger activity in left frontal cortex during color comprehension was associated with poorer performance on the dimensional attention tasks. This makes sense, given that functional activity during color production was only observed in left temporal cortex. This suggests that children who did not selectively engage left temporal cortex during color production did worse on the dimensional attention tasks.

In summary, we provide data demonstrating that the neural dynamics involved with dimensional label knowledge predicts performance on dimensional attention tasks. This provides support for the central hypothesis that dimensional label learning provides a basis for attending to visual dimensions. This project provides a path for future research to probe how dimensional label learning tunes a frontal-temporal-parietal system that can be used to organize behavior in the real-world. As children learn labels for visual features, patterns of connectivity are established between frontal and posterior cortex. These connections are then used to direct cognitive processing toward features or dimensions that are relevant for the current context or goals.
Studies of attentional development are typically divided among different functions. For example, one specific function of attention is to selectively focus cognitive processing on a single dimension of stimulus features. In this context, data suggest that attention becomes more selective over development, as children are able to make decisions based on a single feature dimension rather than integrating information across multiple feature dimensions (Smith, 1989). A second function of attention is to flexibly shift cognitive processing across different visual dimensions as the context or internal goals change. In these studies, data suggest that attention becomes more flexible over development, as children are able to switch attention between dimensions rather than perseverating on a single dimension (Zelazo, 2006).

How is the attentional system able to balance these demands of being both increasingly selective as well as increasingly flexible? Buss and Spencer (2014) proposed a neurocomputational model to explain the emergence of flexible attention between the ages of three and five. This model implements a dimensional attention mechanism that can focus cognitive processing on feature dimensions (e.g., shape or color). The model grounds this mechanism in coupling between frontal regions representing labels for visual dimensions and temporal cortical regions representing the metric details of visual information. As associations between labels and visual features become stronger, dimensional attention strengthens and the model produces the pattern of behavior demonstrated by 3- to 5-year-olds.

In the current project, we generalize this model to explain the development of selective attention. The model demonstrates that this dimensional attention mechanism underlies the development of both flexible and selective attention. More importantly, the model also makes predictions about the neural signatures associated with these shifts in behavior. Specifically, the model predicts that development in these two aspects of attention is associated with increases in neural activation across a frontal-temporal cortical network.

In order to test this model, we collected event-related hemodynamic data utilizing functional near-infrared spectroscopy (fNIRS) with a group of 3- and 4-year-olds (n=48) while they performed a selective (Triad Classification, TC; Smith & Kelmer, 1977) and a flexible attention task (Dimensional Change Card Sort, DCCS; Brace, Morton, & Munakata, 2006). Behavioral performance between tasks was highly correlated ($r=.372$, $p=.013$). Further, analysis of the fNIRS data revealed Oxy-Hb levels in bilateral frontal channels, right parietal, and left temporal regions were significantly associated with performance in both the TC and DCCS tasks. This supports the model’s prediction that performance in these two tasks engage a common neural network and neural mechanisms.

As predicted by the model, these selective and flexible attentional functions recruited overlapping areas of cortex in a way that was sensitive to the level of performance on these tasks. Using a dynamic neural field model to interpret the pattern of behavioral and hemodynamic data,
we conclude that increasing the strength of attention to visual dimensions is driven through increased connectivity between frontal and posterior cortical regions. This theoretical approach, then, provides a unified framework that can explain the development of distinct attentional functions.


Can a clinically viable Frequency Domain NIRS device reliably detect changes in brain tissue oxygen tension of patients with severe traumatic brain injury?

**Introduction**

Monitoring modalities employed in the management of severe traumatic brain injury (TBI) involve the placement of invasive probes into the cerebrum. Of these the measurement of free brain tissue oxygen tension (PbtO2) is becoming a standard monitoring tool in advanced brain injury management centres. A previous investigation into whether a clinically viable Near Intra-Red spectroscopy (NIRS) device is able to detect changes in oxygen tension in TBI with sufficient sensitivity to negate the use of PbtO2 monitor have been unsuccessful\(^1\). The use of Frequency domain NIRS (FD NIRS) may improve on this.

**Aims**

To determine the capability of a commercially available FD NIRS device to predict severe brain hypoxia (oxygen partial pressure of <10mmHg, normal range 20-70mmHg) as measured invasively by a specific PbtO2 catheter placed in the brain of patients with severe TBI.

**Materials and Methods**

The ISS OptiplexTS™ is a clinically viable FD NIRS device. Tested in single detector / 4 source (at 30, 35, 40 and 45mm distances) form, with 2 wavelengths of 680 and 830nm. The Raumedic PbtO2 catheter is an invasive monitoring device utilised in enhanced neurosurgical monitoring utilising fluorescence quenching to measure free oxygen within the brain tissue. Consecutive patients admitted to the neurological critical care unit at the Queen Elizabeth Hospital Birmingham with severe TBI requiring PbtO2 within the first 72 hours after injury were enrolled. Simultaneous cerebral NIRS measurement was undertaken.

**Results**

16 patients were recruited, although 7 were excluded due to equipment error, or an absence of a hypoxic episode. Of the 9 remaining, a total of 576,347 paired data points were considered (over 143 hours), with 142,529 measurements representing severe hypoxia. In certain patients, corresponding data plots between NIRS and PbtO2 demonstrated good agreement on visual inspection, however in a number of cases this was not the case. Due to the variability in the change in NIRS parameters for a given change in brain tissue oxygen tension each patient data stream was considered separately. Area under receiver operated characteristic (AUROC – where a value of 0.5 represents predictive abilities similar to guessing at random) curve analysis of the 8 (patients) NIRS data streams was undertaken. 7 of these demonstrated that NIRS parameters had moderate discriminatory abilities in predicting the presence of severe hypoxia (AROC of 0.699, 0.75, 0.74, 0.84, 0.87, 0.71, and 0.81). The remaining data streams indicated a poor and relatively poor predictive ability (AUROC of 0.67 and 0.68 respectively).

**Conclusion**

This clinically viable FD NIRS device has moderate abilities in predicting the presence of severe tissue hypoxia in TBI. However promising, these findings support previous findings that indicate the NIRS modality is not yet sufficiently sensitive to be used in isolation or to replace the currently accepted invasive gold standard of brain tissue oxygen tension monitoring.

**References**

Investigating auditory prediction in young infants using fNIRS

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Learning does not only depend on bottom-up processes such as processing incoming sensory information, but it also relies on top-down processes such as the ability to make predictions about upcoming events. Prior experiences shape neural responses in sensory regions of the adult brain, but until recently evidence of expectation-based feedback had not been demonstrated in infants (Emberson, Richards & Aslin, 2015). To further investigate this phenomenon, we used fNIRS and MR co-registration to identify occipital and temporal channels. We took pictures of each infant to help locate the fNIRS optodes in relation to anatomical markers. Three average MR templates in the studied age range were used for co-registration to capture natural variability in infants’ head sizes. Co-registering the fNIRS channels for each infant with the appropriate MR template allowed us to record hemodynamic activity in the occipital and temporal cortices as infants participated in a cross-modal (audiovisual) omission paradigm. First, infants were familiarized to a sound and a picture such that they learned a picture always predicted a sound (statistically consistent trials, V+A+). Following the familiarization trials, infants viewed unexpected audio omission trials (V+A-), where the predictive visual stimulus was not followed by the expected auditory stimulus.

Recordings from 23 6-month-olds revealed increases in activity in the occipital and temporal cortex during statistically consistent (V+A+) trials. Recordings also revealed a strong response in the occipital cortex but no overall response in the temporal cortex for unexpected audio omission trials (V+A-), see figure. This result is surprising given previous studies showing expectation-based occipital responses on visual-omission trials in infants (Emberson, Richards & Aslin, 2015). Exploratory analyses of the oxygenated responses within the averaged time-window reveal a robust response for only from 7 to 9 seconds. Current work is being done to examine infant’s looking behavior during the study to determine whether infant looking patterns are driving this unexpected pattern.

State-dependent connectivity in late-life depression

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Background. There is a large body of studies concerning the effects of Major Depressive Disorder (MDD) on psychological and physiological functioning. Depression is, e.g. related to reduced cognitive functioning, aberrant brain functioning and cortical structure changes. Especially in late-life depression (LLD), cognitive impairments are associated with worse treatment progress and are considered a risk factor for neurodegenerative disorders. However, little is known about the differences in neural processing and coupling during rest and cognitive functions in patients with late-life depression compared to healthy elderly individuals. The study at hand aimed to investigate the cognitive control network (CNN) in LLD during a cognitive task and at rest by means of functional near-infrared spectroscopy (fNIRS).

Methods. Hemodynamic responses were measured at rest and during the Trail-Making-Test (TMT) using fNIRS in a matched sample of 49 depressed and 51 non-depressed elderly subjects (age range: 51–83 years; 64.1 ± 6.58 [mean ± SD]). Functional connectivity (FC) and network metrics were derived from the data and analyzed with respect to differences between the subject groups.

Results. Depressed and non-depressed subjects showed significant differences both at rest and during task performance in FC. Depressed subjects showed reduced FC in a left frontopolar cortical network during task performance and increased FC in a left fronto-parietal cortical network at rest.

Conclusions. Depressed elderly subjects showed altered FC and network organization during different mental states. Higher FC at rest may be an indicator of self-referential processes such as rumination that may reduce FC during task performance due to an overtaxed executive control system.
An extended GLM-based algorithm for recovering functional events in real-world fNIRS neuroimaging outside the lab with freely moving subjects

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Statistical analyses of fNIRS data require the knowledge of the event onsets timeline. Such a timeline is easy to recover for lab-based experiments, but it may be extremely challenging for real-world experiments conducted outside the lab on freely moving participants. In fact, functional events in the real-world arise from the integration of complex and highly variable behaviours, including the anticipation or thought of an action, the interaction with the environment, walking, avoiding obstacles and so on. Moreover, stimuli presentation in the real-world is not predetermined and event onsets are hard to predict or identify, especially from the examination of video recordings, which can be tedious and time-consuming. An automated method to disentangle all these events from neuroimaging data to support and improve the behavioural observations would be of great benefit.

More precisely, the algorithm is based on the GLM-based least square fit analysis and identifies functional events testing all the possible combinations of time location and duration of the events. The developed algorithm has been applied to real-world fNIRS data recorded during a prospective memory (PM) experiment outside the lab. Prefrontal cortex activity was continuously monitored using a 16-channels fiberless and wearable fNIRS system. The participant (healthy, 21 years old) performed a PM task outside the lab (i.e., walking around the streets and counting the number of certain items while responding to PM cues by fist bumping an experimenter). Three cameras recorded the experiment to recover the event onsets from a behavioural perspective and to validate the presented algorithm.

The algorithm has detected both event-based and activity-based PM targets from the background ongoing activity. More precisely, the recovered functional events have been found in correspondence or in close proximity to PM cues suggesting that event onsets are more likely to occur when the participant identifies the PM cue (Figure 1) rather than when it is reached.

Even though the present method is the first attempt to recover functional brain events from fNIRS data recorded during a naturalistic task and further improvements are needed, this study shows that “brain-first” rather than “behaviour-first” analysis is in principle possible, and this may solve some of the problems with real-world neuroimaging.

Figure 1. Example of an identified functional event position respect to a social PM (sPM) target within the experimental area and corresponding t-values map overlapped onto a brain template.
Eye Blinks Motion Artifact Removal using Kurtosis-based Wavelet Algorithm in Prefrontal Area
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Introduction: Functional near-infrared spectroscopy (fNIRS) which is a non-invasive neuroimaging technique benefits brain functional imaging modality which its applications have been rapidly spreading in brain imaging technologies. fNIRS measures the concentration changes in oxygenated and deoxygenated hemoglobin to provide functional information. However, motion artifacts have significantly been one of the major sources of noise in fNIRS data. Motion artifacts can be generated by not only the movement of the head, but also the decoupling between the source/detector optodes and the scalp [1], resulting in high-frequency spikes with higher amplitude level than that of signal caused by hemodynamic changes. Since blinking eyes is an unavoidable motion, the decoupling affected by eye blinks and skin movement in forehead causes motion artifact signal especially to prefrontal fNIRS imaging. Applying wavelet transform is one of the recent approaches in removing artifacts in case that there is no additional sensors to detect motion artifacts. Here, we used a kurtosis-based wavelet algorithm [2] to suppress the eye blinks motion artifacts from fNIRS data recorded in prefrontal area.

Methods: Two healthy subjects participated in this study. In the experiment, each participant was supposed to close the eyes during the rest period and to blink continuously during the task period while the data was collected in the prefrontal area with 13 channels. In order to obtain eye blinks motion artifacts multiple times, the rest period and task period lasted 10 seconds and were repeated 10 times. LABNIRS (Shimadzu) device was utilized for acquiring the fNIRS data which provided 3 different wavelengths (780, 805, 830 nm). After data acquisition, the kurtosis-based wavelet algorithm [2] was applied to the optical density (OD) signals in order to remove the eye blinks motion artifacts. In this project, 10 level of wavelet decomposition, was applied and the kurtosis threshold was fixed to 3.3 same as [2], as is shown in fig. 1.

Results: The signal before removal in blue in fig. 2 shows the OD signal for 40 seconds in channel 13 with 780 nm wavelength. The channel 13 was located 2 inches above the eyebrow. As shown in the signal before removal, during the signal in task period comparing the signal in rest period, several abrupt peaks are observed which are caused by eye blinks. By applying eye blinks artifact removal with 10 level wavelet decomposition, the abrupt peaks are suppressed as shown in the signal after removal in red. Consequently, the algorithm could selectively remove the eye blinks by cancelling abrupt significant OD changes.

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**Topic area:** Neurodevelopment

**Title:** Investigating neural correlates of face-to-face mother-infant interaction and infant affect regulation in response to maternal cues with the use of real-life display: A pilot fNIRS study

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**Abstract:** Children of depressed mothers present a high-risk group for development of psychopathology later in life. Previous studies have suggested that depressed mothers show low maternal sensitivity. As a consequence, children of depressed mothers have a higher risk of disturbed social-emotional development. To date, however, it is unclear how low maternal care impacts the developing brain. Innovative, non-invasive imaging techniques, such as fNIRS, allow us to investigate neurobiological mechanisms of infant’s emotion and stress regulation development within the mother-infant relationship. On a behavioral level, a variety of studies have investigated parent-infant interaction employing the still-face paradigm (infant and parent engage in a face-to-face interaction episode *(baseline)*; followed by a *still-face* episode, in which the parent ceases interaction and maintains a neutral facial expression; followed by a *reunion* episode, in which normal face-to-face interaction resumes) and found that the parent is an important modulator of infant’s physiological and behavioral stress regulation. Yet, neural correlates underlying parent-infant interaction and infant stress regulation capacity during the still-face paradigm have not been investigated. The main aim of the current study was to assess infants’ emotional reactivity to depressive and positive maternal cues (e.g. still versus happy facial expressions) employing an adaptation of the still-face paradigm, the adapted Still-Face Task, which consists of depressed versus non-depressed real-life, face-to-face mother-infant and stranger-infant interaction episodes, while infants undergo fNIRS imaging. Preliminary results (n=5 infants at age 6-8 months) indicate enhanced activation of the social brain including OFC during mother’s still-face (CH20, p<.05) and left posterior dPFC during mother’s happy-face (CH9, p<.01); brain regions also found to underlie maternal affect regulation in response to infant attachment cues, suggesting that the use of real-life display during fNIRS imaging could contribute to an essential understanding of early (social) brain development within its natural context. Still, results and task application need to be addressed with caution. Restrictions and implications will be discussed.
Previous work has established that infants can employ a recently learned audiovisual association to engage in top-down sensory prediction (Emberson, Richards, & Aslin, 2015). However, this previous work examined only the response in temporal and occipital cortices. Here, we extend these results to frontal ROI in an expanded dataset (N = 50). We also apply recently developed regression analyses to examine temporal changes in the fNIRS signal (Kersey & Emberson, under review).

Infants were familiarized with an audiovisual pairing where one sound always predicts a visual event. Then, infants were shown trials that either were consistent with familiarization (A+V+ trials, 80%) or that unexpectedly omitted the visual event (A+V-, 20% of trials). Previous analyses showed that infants exhibit an occipital response during both consistent trials and unexpected visual omissions that is similar in magnitude. By contrast, in the frontal ROI (identified through MR co-registration), we see a marginal increase ($p = 0.06$) in activity during unexpected visual omissions over learned audiovisual events suggesting the possibility of frontal lobe involvement in either responding to the violation of visual expectation or to the origination of the top-down prediction signal seen in the occipital lobe.

We sought to further understand the frontal involvement in these trials by analyzing the time-course of this response with mixed effects modeling. For omission trials (A+V-), we find no significant changes in signal over time indicating a robust response throughout with no adaptation. This contrasts with patterns in the A+V+ trials that broadly show a significant decrease in response over time during consistent (A+V+) trials (Kersey & Emberson, under review). We then examined patterns for a separate control group where visual omissions were expected and find the patterns of activation more similar to the statistically-consistent trials and not the unexpected visual omission trials indicating that violations of visual expectation may be driving these differences in the infant frontal lobe.

These findings provide convergent evidence of frontal lobe involvement in the detection of unexpected visual omissions after an auditory cue. Ongoing analyses are examining connectivity between occipital, temporal and frontal lobes during learning and detection of violations of expectation.
**Manifold based modelling of brain connectivity in fNIRS**

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It has been previously suggested that activity in the human brain can be visualized as a manifold using both fMRI [1] and fNIRS [2] methodologies. We present here a methodology to determine functional connectivity utilizing a manifold-based organization of synthesized topological fNIRS data. Our long-term goal is to implement this type of analysis for determining connectivity not only within the brain of an individual, but also in hyperscanning experiments that aim to investigate connectivity across brains of individuals in social environments. To determine functional connectivity with respect to fNIRS signals we specifically use the following convention; 1) observations $u(t)$ are projected to an ambient space $\Delta(u(t))$; 2) the manifold $M$ is defined by means of a distance function $d$ capturing the essence of brain connectivity, and 3) the solution is operationalized in terms of some representation $h(M)$. Channel recorded responses $u(t)$ are represented as points in the ambient space by assuming orthonormal samples. Geometry of the manifold $M$ is set to mimic signal similarities and differences in neurovascular responses e.g. $D(M)=\{d(u,u)\}$=Euclidean. The connectivity network arises from thresholding neighboring channels, e.g. $C=h(M;\varepsilon)=D(M)<\varepsilon$. Twenty-four channel synthetic data was generated by aggregating stimulus-evoked response, systemic noise (vasomotion, breathing and heart rate) and Gaussian noise (3%). Verification is achieved through simulation of two scenarios: (a) one in which all channels respond to a stimulus with different phase lag in their response, and (b) one with only a subset of responsive channels. Fig 1 depicts the generation of synthetic signals, the constructed manifold and the retrieved connectivity networks, illustrating the ability of the analysis to characterize varying phase differences between observation representations in different channels. These results suggest that manifold representation provides a flexible framework for the analysis of brain connectivity. We are currently implementing the method to investigate connectivity between brains in hyperscanning fNIRS investigations.

![Figure 1. Step 1-Projection: Each channel is projected to ambient space; Step 2-Manifold: Manifold geometrically proxying brain connectivity by distance function; Step 3-Solution: finally retrieved connectivity networks.](image)

**References**

[1] Friston, K. J.; et al. Cerebral Cortex, 1996, 6, 156-164,

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Hand Flipping Detection in fNIRS data using Support Vector Machine

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Introduction: Functional near infrared spectroscopy (fNIRS) is one of the most emerging portable brain scanners, and can be used in studying the motor cortex region for motion-related tasks. Some studies have been done to monitor the changes of cerebral oxygenation as a response to some motor tasks. One of the most useful methods in studying the motion tasks is to classify the fNIRS data based on different actions and some studies have been performed with this goal.

Method: In this study, we have recruited seven healthy participants to perform a motion task of flipping their hand (adopted from the Unified Parkinson’s Disease Rating Scale) and the goal is to classify the action and the rest periods in which the participants were asked to be stationary. Four of the participants were able to perform the task for 15 trails with the length of 30 seconds and 30 seconds rest time in between each trial. Figure 1 shows the montage of electrodes along with the timeline of the experiment. The other three participants were able to do it for just 2 trails, which because of the short length of the experiment, we had to exclude them for this processing. For the classification, we have used support vector machine (SVM), which is a supervised learning model and trains itself based on a portion of the data that is labeled into two different categories. As pre-processing, we have applied the least mean squared (LMS) filter on the data recorded from the NIRScout System (NIRx Inc., USA) using an 8x8 sensor array. The filter is an adaptive filter and takes out the noise and some motion artifacts from the signal.

Results: We have applied four different learning models in which the Kernel functions are different, along with two methods of evaluation, k-Fold Cross-Validation, and Hold-Out. We set k to be 10 for the cross-validation method and used the 2/3 portion for the Hold-Out method. The results show that the most complex SVM performs better than the other models and can reach above 95% accuracy in classifying the action and rest tasks for each participant separately. The table shows the accuracy of different models applied to the data from each participant.

<table>
<thead>
<tr>
<th>SVM Method</th>
<th>Evaluation</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear Kernel</td>
<td>10-Fold</td>
<td>80.87%</td>
<td>63.80%</td>
<td>66.56%</td>
<td>65.99%</td>
</tr>
<tr>
<td>C=100</td>
<td>Hold-Out</td>
<td>80.07%</td>
<td>64.28%</td>
<td>66.38%</td>
<td>66.25%</td>
</tr>
<tr>
<td>Polynomial Kernel</td>
<td>10-Fold</td>
<td>82.08%</td>
<td>79.94%</td>
<td>73.14%</td>
<td>76.38%</td>
</tr>
<tr>
<td>Degree=2, C=100</td>
<td>Hold-Out</td>
<td>83.25%</td>
<td>79.50%</td>
<td>74.44%</td>
<td>78.69%</td>
</tr>
<tr>
<td>Polynomial Kernel</td>
<td>10-Fold</td>
<td>93.83%</td>
<td>88.03%</td>
<td>89.55%</td>
<td>89.46%</td>
</tr>
<tr>
<td>Degree=3, C=100</td>
<td>Hold-Out</td>
<td>92.83%</td>
<td>87.17%</td>
<td>89.88%</td>
<td>87.99%</td>
</tr>
<tr>
<td>Radial Kernel</td>
<td>10-Fold</td>
<td>97.41%</td>
<td>95.14%</td>
<td>97.01%</td>
<td>96.64%</td>
</tr>
<tr>
<td>C=100</td>
<td>Hold-Out</td>
<td>97.58%</td>
<td>94.25%</td>
<td>96.65%</td>
<td>95.80%</td>
</tr>
</tbody>
</table>

Discussion: Using the LMS filter and SVM results in a high accuracy of classification between rest and task periods. The results are for each individual participant, and the system has trained based on that data. There is a problem in classifying the data from all the participants due to the fact that the NIRScout system uses different calibration gains for each individual recording, therefore it would not be feasible to apply the classification on the data from all the participants together, or train the system with the data from one participant and apply it to the data from another person to get the accuracy.
Functional near-infrared spectroscopy (fNIRS) could be uniquely suited for use in clinical populations to measure neural activity before and after treatment. However, in order to conduct “pre-post” studies on single subjects, consistency of fNIRS measurements must be ensured so that differences in neural activity detected after treatment can be attributed solely to the intervention and not to inter-scan variability. To test consistency of recordings, two subjects were scanned using a Shimadzu LABNIRS for ten consecutive days while performing right-handed digit-manipulation tasks. For the first run (“Ball-Squeeze”), subjects squeezed a ball in response to cues presented on a computer screen every second. During the second run (“Double Finger-Tap”), subjects tapped each finger consecutively against the thumb twice per second. For the third run (“Finger-Tap”), subjects tapped each finger consecutively against the thumb once per second. During the fourth run (“Follow-the-Number”), a number from 1 through 4 appeared randomly on the screen every second. Subjects were instructed to tap the first finger against the thumb in response to “1”, the middle finger in response to “2”, the ring finger in response to “3”, and the pinky finger in response to “4”. Each run consisted of six blocks. Each block consisted of 20 seconds of task followed by 10 seconds of rest, during which subjects were instructed to focus on a crosshair on the screen and stop moving. The fNIRS setup consisted of 30 emitters and 29 detectors in a 98-channel layout covering frontal, parietal, and temporal lobes. A modified Beer-Lambert equation was used to convert raw data to deoxyhemoglobin and oxyhemoglobin concentrations. Wavelet detrending was applied to these values prior to hemodynamic modeling. As expected, deoxyhemoglobin contrast results for each subject during digit-manipulation tasks (vs. rest) revealed activity in left pre-, primary, and supplementary motor cortices (p<0.01). To evaluate inter-scan variability, beta values from each channel were averaged over ten days per subject. The channel with the maximum average beta value was identified for each subject. Average beta values from the channel of interest are shown for each subject, task, and day (Figure 1). Mean beta values and standard deviations in the channel of interest for Subject 1 were as follows: 134.3±61.8 for “Ball-Squeeze”, 154.2±55.9 for “Double Finger-Tap”, 125.2±43.3 for “Finger-Tap”, and 133.2±51.9 for “Follow-the-Number”. For Subject 2, mean beta values and standard deviations in the channel of interest were: 198.5±84.4 for “Ball-Squeeze”, 223.2±106.6 for “Double Finger-Tap”, 170.6±78.2 for “Finger-Tap”, and 187.6±90.9 for “Follow-the-Number”. The average beta values over all tasks were 136.7±35.3 for Subject 1 and 195.0±56.9 for Subject 2 (see Figure 2). These results demonstrate that fNIRS data is highly consistent within subjects and tasks given adequate task repetition. Here we show that six 30-second blocks with alternating task/rest periods provide the minimum task-evoked signal to yield consistent deoxyhemoglobin measures, and multiple repetitions may compensate for variance in the data.
SPEECH PERCEPTION OUTCOME OF COCHLEAR IMPLANTATION PREDICTS CORTICAL ACTIVATION MEASURED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY

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Hearing loss disrupts normal functioning of the entire auditory system. The major question remains how restoration of peripheral hearing by implanting a cochlear implant (CI) would affect central auditory processing. Traditional neuroimaging methods such as fMRI, MEG, and EEG are impractical to study such processing because of artefacts induced by the CI. We will make use of functional near-infrared spectroscopy fNIRS to measure temporal cortical activity of CI users during an auditory-visual speech-in-noise perception task (based on the Dutch Matrix sentence test: Houben et al., 2014).

To avoid saturation and reduce idiosyncratic differences in fNIRS signals as observed in an earlier study for a supra-threshold auditory-visual stimulus presentation (Van de Rijt et al., 2016), we now present novel near- and sub-threshold stimuli, have subjects being actively engaged in the task, and apply a larger 48-channel NIRS setup. We determine how auditory, visual and auditory-visual speech perception performance of CI users is correlated with temporal cortical activation as measured by fNIRS. We have measured 14 normal-hearing subjects and 8 CI users. We aim to demonstrate some preliminary data on this topic.


A comparison of fMRI and fNIRS deoxyhemoglobin signals: A global component removal approach

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Background: Although speech is a primary human function, brain activity related to tasks with overt speaking cannot be measured using functional magnetic resonance imaging (fMRI) due to motion artifacts generated by head movement. Functional near-infrared spectroscopy (fNIRS) is less susceptible to motion artifact and enables the acquisition of blood oxygen level-dependent (BOLD) signals comparable to those obtained with fMRI. fNIRS has the potential for use in a wide range of tasks that cannot be performed within the confines of an MRI machine; however, it does have challenges that must be addressed. Systemic effects, including blood pressure and respiratory changes, can be prominent in fNIRS signals. Removal of systemic effects is challenging due to the fact that systemic waveforms are correlated with task-related BOLD signals [1]. The spatial pattern of systemic effects is global and has a very low spatial frequency; thus, the global component is distinct from that of localized neural activity.

Previously, we described a principal component spatial filter algorithm for removal of the global components (Clean) of fNIRS signals and reported the effectiveness of this approach for refining the oxyhemoglobin (OxyHb) signal obtained during a finger-thumb tapping task [2] (Fig. 1). Here we use fNIRS to measure neural activity during an overt (responses spoken aloud) Boston Naming task and compare our results with those of fMRI studies involving silent (imagined) speech tasks. In addition, we demonstrate the utility of removing systemic global effects from the deoxyhemoglobin (DeoxyHb) signal. Method: Twenty-two healthy subjects participated (mean age ± SD = 24.5 ± 9.0) and informed consent was obtained. fNIRS signals were acquired using a Shimadzu LABNIRS system. Thirty emitter and 29 detector optodes were used, providing a total of 98 channels per participant. Subjects were instructed to name and describe a picture aloud for 3 seconds per image. A standard 15-second task (5 pictures) and 15-second rest block design was used. Each run consisted of 6 blocks and 2 runs were performed for a total of 6 minutes.

Result: The raw fNIRS DeoxyHb (Fig. 2, right) signal shows widespread positive activity indicating the influence of global components that are not specific to neural resources required for this task. In contrast, the cleaned DeoxyHb signal (Fig. 2, center) shows both positive activity at the SMA and left Broca’s Area, consistent with previous fMRI results (Fig. 2, left) for a silent Boston Naming task [3]. Conclusion: The PCA global component removal method reduces systemic artifact and improves the utility of deoxyHb signals acquired with fNIRS. Although limited to detection of cortical activity near the brain’s surface, fNIRS provides a method for measuring neural activity related to tasks involving talking, and may extend neuroimaging capabilities to include active speech in natural human interactions.

Memory encoding assessed by functional Near-Infrared Spectroscopy

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Background: Alzheimer’s disease (AD) is a chronic neurodegenerative disorder which is the sixth leading cause of death in the United States [NI-A-NIH]. Early detection of AD is the key to preventing, slowing and stopping the disease. The earliest cognitive impairments in patients with Alzheimer’s disease are seen in learning and memory skills as in normal aging, however, with different underlying neurological changes [Sperling2003]. This preliminary study is performed to assess the NIRS’s utility to measure brain activation during memory encoding on young healthy adults. Paired-associate learning (PAL) is a suitable experimental task that involves the pairing of two items e.g. for face-name pairs, when the learner is prompted with the face, he responds with the appropriate name. The face-name encoding task activates the striate, fusiform, prefrontal cortices and the anterior hippocampus in young healthy adults [Sperling2001].

Methods: Paired-associate learning Task Protocol: The task requires a set of paired faces and names. For this, we have randomly combined neutral faces obtained from The Face Database [Minear2004] and the most popular given names for male and female during the last 100 years from varying age and ethnicity obtained from USA Social Security Administration. During the experiment, subjects were presented either a novel face or a repeated face. In each run, there were two novel-face blocks and two repeated-face blocks, each block with seven face-name pairs. Repeated faces were shown to the subject prior to the experiment. Each face-name pair was presented for 4.5 s and will be followed by the second pair after an inter-stimulus interval that varies between 0.3-2.2 s within a block. Inter-block interval will be set to 20 s.

INIRS Instrumentation: Our fNIRS imaging system supports up to 32 lasers (16 dual-wavelength sources) and 32 detectors (TechEn Inc.). We perform measurements using 690 and 830 nanometer wavelengths to obtain sensitivity to changes in HbO and HbR. The timing of stimulation events presented to the subject is recorded along with the optical data to maintain synchronization. Analysis protocol: The time series pairs from each detector will be converted from wavelength (absorption) to relative concentrations (of HbO/HbR). This will be done with the modified Beer-Lambert Law and the extinction coefficients of HbO and HbR [Cope&Delpy1988]. The heart rate (~1Hz), and fluctuations at lower frequencies (0.01 Hz) were filtered out using a bandpass filter. We performed short separation regression to regress out superficial contamination from scalp and skull [Gagnon2011]. Our significance level was set to p = 0.05.

Results and Conclusions: The results for the group average of 9 young healthy subjects are presented in Fig1. Our preliminary results show that fNIRS measurements on the frontal lobe are sensitive to regions activated by the PAL task. We have observed a statistically significant increase during the presentation of repeated faces compared to novel faces during the paired-associate learning task in the middle to superior frontal cortex (averaged response shown in Fig1) (paired t-test, p = 0.05). We believe this signal represents face-recognition of a familiar face, and will further be investigated.

References


Monitoring critical patients at the neuro-intensive care unit in real-time: how can diffuse optics help?

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Non-invasive assessment of micro-vascular physiology of deep tissue over long periods of time at the bedside has been a real clinical demand. In the neuro-intensive care unit (nICU) real-time physiological monitoring could lead to a more individualized and efficient treatment. Recent advances of diffuse optical techniques, such as frequency-domain diffuse optical spectroscopy (FD-DOS) and diffuse correlation spectroscopy (DCS), enabled the continuous monitoring of patient hemodynamics at the bedside. Concurrent measurements of tissue oxygenation (from FD-DOS) and relative cerebral blood flow (from DCS) also allow continuous assessment of relative changes in cerebral metabolic rate of oxygen (rCMRO2) in critical patients. This information could be used to better understand, and potentially guide, patient care during hospitalization. The goal of this work was to build a hybrid DCS/FD-DOS system for continuous real-time monitoring of rCMRO2, and to fully integrate the system into the nICU. We then evaluated the system’s performance as a bedside monitor of neurocritical patients during hospitalization.

The hybrid system consists of a homemade DCS module that employs 16 photon counters (SPCM-AQ4C, Perkin Elmer), a long coherence laser (785 nm, CrystaLaser) and a correlator board (Correlator.com). The FD-DOS module employs a commercial system (Imagent, ISS) with 4 detectors and 32 sources emitting in 4 different wavelengths. A graphical interface was built based on similar nICU instrument interfaces so that clinicians can assess all patient's hemodynamic and metabolic information in real time. In the software, we used a semi-infinite approach for estimating the absolute optical properties from the FD-DOS data, and the blood flow index from the DCS data. For the patient monitoring, the optical sensor was designed to allow measurements with 4 different source-detector distances (1.5-3.0 cm) for both FD-DOS and DCS. The injured region was accurately located in real-time using the patient’s computerized tomography image in the InVesalius Navigator software (df.ffclrp.usp.br/biomag) connected to a spatial tracker (FASTRAK, Polhemus). We monitored both the ipsi- and the contra-lesion hemispheres of all patients for periods ranging from 2 to 5 hours.

Our preliminary results suggest that the system can aid patient’s care with real-time bedside monitoring by evidencing differences between different patients’ diagnosis. For instance, the blood flow index (BFI) in the ipsi-lesion hemisphere of a patient with a frontal lobe ischemic stroke was an order of magnitude lower than the BFI found for patients with cerebellar ischemic stroke. In addition, the technique can be used to longitudinally monitor the injured region by comparison with the contra-lesion regions. For example, in a patient diagnosed with sub-arachnoid hemorrhage that could not be monitored with transcranial Doppler (TCD) during the pre-vasospasm phase, the BFI on the ipsi-lesion hemisphere was approximately 200% higher than the BFI in the contra-lesion hemisphere.

Overall, we presented the construction of a real-time hybrid optical system designed specifically to monitor patients in the critical state at the nICU. Although this is a pilot study, our preliminary results suggest that the real-time feature can help clinicians to identify worsening conditions of patients by continuously monitoring hemodynamic oscillations over time.
Exploring the correlation between oxygenated and deoxygenated hemoglobin signals
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¹NIRx Medizintechnik GmbH, Berlin, Germany, ²Federal University of ABC, São Bernardo do Campo, Brazil, ³Albert Einstein Hospital, São Paulo, Brazil

Introduction
Oxygenated and deoxygenated hemoglobin relative changes as measured with continuous wave fNIRS systems are expected to be negatively correlated [1]. Herein we identify areas of the brain, in which this theoretical assumption does not seem to be valid for topographical measures (i.e. no short-distance channels available).

Methods
Pearson correlation between oxygenated and deoxygenated hemoglobin was calculated based on a 5s sliding window. This was done with two different groups: (a) N = 8 adults, mental arithmetic block design collected with Hitachi ETG-4000 [2]; and (b) N = 14 adults, resting state data collected during 5 minutes with NIRx NIRScout16x16.

Results

Figure 1. Channels distribution on the MNI (left, figure adapted from [2]) and block average curves obtained from four different channels (right) for a representative subject (#08) and their resulting oxy-deoxygen correlation (rho).

Figure 2. Channels distribution on MNI (obtained with NIRS-SPM [3]) and boxplots of 10 regions of interest based on Brodmann areas [4] and the median correlation over all subjects. Highlighted are channels with positive correlation.

Conclusion
Datasets collected with systems from different manufacturers (Hitachi and NIRx) exhibited consistent positive correlation between oxygenated and deoxygenated hemoglobin signals on inferior frontal and middle temporal region. Moreover, the positive correlations in these regions are present on both evoked and non-evoked signals. Therefore, in addition to task-related paradigms (e.g. for language studies), resting state connectivity studies should also be mindful of these findings when interpreting and reporting results obtained from these regions. Further investigation (e.g. multi-modal with fMRI) is necessary to better understand the origins of the positive correlation.

References
Hemoglobin phase of oxygenation and deoxygenation (hPod) in preterm- and term-born infants

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A crucial issue in neonatal medicine is the impact of preterm birth on the developmental trajectory of the brain. In the present study using fNIRS, we propose a new method to detect subtle differences in neurovascular and metabolic functions in neonates and infants. We refer to the time-averaged phase differences between spontaneous oscillatory changes in oxy-Hb and those of deoxy-Hb as hemoglobin phase of oxygenation and deoxygenation (hPod) in the cerebral tissue of sleeping neonates and infants.

The 100 infants with no evidence of clinical issues were categorized into three groups according to their GAs at birth: (i) 24 term infants (GA ≥ 37 weeks, range: 37-41 weeks), (ii) 32 late-preterm infants (34 weeks ≤ GA ≤ 36 weeks), and (iii) 44 early-preterm infants (GA < 34 weeks, range: 23-33 weeks). In order to examine typical development around 2-4 months of age, data from 59 full-term healthy infants were also analyzed in the study.

Results shows that the values of hPod generally decrease from an in-phase to an anti-phase pattern as a function of age regardless of the group as classified by GA. This decrease consists of a rapid change occurring at birth and a gradual change lasting during the first 6 months of chronological age (CA). The rapid decrease of hPod with increasing CA until 8 weeks of age was observed in both term and late-preterm infants. The early-preterm infants had lower values of hPod in the neonatal periods until 44 weeks of postmenstrual age (PMA), suggesting that the early-preterm infants had an accelerated development. The early-preterm infants, however, also had a slower decrease in the hPod value after 8 weeks of CA. Thus, comparison of hPod among the groups revealed that developmental changes in hPod in early-preterm infants precede those in late-preterm and term infants at term equivalent age, but then progress at a slower pace.

This study suggests that hPod measured using fNIRS is sensitive to the developmental stage of the integration of neurovascular and metabolic functions in the brains of neonates and infants. Possible mechanism explained our data is an accelerated development of their circulatory processes after birth and structural and/or functional developments of the neurovascular system during the first half of the first year of life.
Quantification of Cerebral Hemodynamics with Age in Brain of Healthy Adolescents and Adults Using Frequency Domain Near-Infrared Spectroscopy

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Introduction: Frequency domain near infrared spectroscopy (fdNIRS) can be used to noninvasively measure microvascular oxygen saturation (StO2), oxy- (HbO), deoxy- (Hb) concentrations, and total-hemoglobin concentration (tHb) in the brain. Aging of the brain involves moderate shrinkage of the cortex and other gray matter structures, loss of white matter, and changes in cerebral hemodynamics. Due to the fact that there are known changes with age we need to have a good understanding of how age impacts fdNIRS data.

Methods: Ten adolescents (6 females, 4 males; age 17±0.8 years, mean ±SD) and twelve adults (8 females, 4 males; age 50.4±2.7, mean±SD) were recruited. Measurements were recorded from left and right frontal lobes using the OxiplexTS multidistance frequency domain spectrometer. The average between lobes was reported. The OxiplexTS uses the wavelengths of 824nm and 690nm, with source-detector distances ranging from 2.0-3.5cm. Data was sampled at 110MHz for approximately one minute, averaged to 2Hz, to provide a single value per person. Data was collected during resting state while sitting, under quiet and dim conditions.

Results/Discussion: There was a significant decrease of HbO, HHb, and tHb in adults (50.4±2.7 years) compared to adolescents (17±0.8 years) (Figure 1). This is consistent with previous results showing that younger subjects (28±4 years) had significantly higher HbO, HHb, and tHb compared to older subjects (85±6 years). Our results are also consistent with previously compared data looking at 35±11 years.

![Figure 1](image.png)

Figure 1. fdNIRS measured brain hemoglobin parameters with age (n=10 [adolescents]; n=12 [adults]). Values indicate overall averages of left and right frontal lobe measurements. (mean±SD)

Such absolute measures are important because they provide a better understanding of brain physiology with age, and of the control populations one would need when studying disease. These data show that when measuring absolute values and comparing between population it is important to have age matched data.

References
Representing number and time in the newborn brain
Nawal Abboub, Judit Gervain & Maria Dolores de Hevia

The ability to discriminate and represent information of magnitude (number, time and space) is foundational to human reasoning and central to mathematics, science and technology. The origin of these concepts is subject to a long-standing debate, although recent behavioral studies on newborns have brought new insight, showing that at birth humans are able to discriminate different numerosities (Izard et al., 2013) and to map number and time onto space (de Hevia et al., 2014). However, the origins of these abstract concepts in the developing brain are still debated and poorly understood. Therefore, the goal of the present study was to shed light on the neural origins of the ability to represent the dimensions of number and time in the newborn brain.

Contemporary cognitive neuroscience has only begun to investigate how these mathematical concepts are processed in the brain, primarily through studies of basic arithmetic. Two sets of brain areas have been associated with number processing. Bilateral intraparietal and prefrontal areas are systematically activated during number perception and calculation (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999), even in untrained monkeys (see Nieder & Dehaene, 2009). This circuit seems to be already present in infants by 6 months of age, although the response was found mostly in the parietal area in the right hemisphere (Edwards, Wagner, Simon, & Hyde, 2015; Hyde, Boas, Blair, & Carey, 2010). Critically, no study has yet investigated newborns’ brain responses in numerical tasks; a gap that the present study intends to fill.

We conducted two experiments with sleeping newborns, using near-infrared spectroscopy (NIRS). In a first experiment, we tested number discrimination using an alternating/non-alternating design (Gervain, Berent, & Werker, 2012). We presented newborns with two types of sequences of sounds: blocks alternating in numerosity where time and number were varied (Alt: 6/18; short/long), and blocks with no alternation containing the same number and duration (Non-Alt: 6 (short) or 18 (long)). In a second experiment, we tested another group of newborns with the same experimental design as in the previous experiment, but only the numerosity was varied (duration was controlled for by manipulating the length of the smaller sequences so that they matched the overall length of the longer sequence: Alt (6/18; constant duration), Non-Alt (6 or 18, constant duration).

Preliminary results from Experiment 1 (n=7) showed differential brain activations according to the type of block (Non-Alt/Alt), suggesting that neonates already show number discrimination at birth (Figure 1). We found a greater activation for Non-Alternating sequences than for Alternating sequences, in particular in the parietal area in both hemispheres.

These findings show that the newborn brain might recruit the same circuits as children and adults to process abstract mathematical concepts. However, results from Experiment 2 will provide crucial evidence on whether the dimensions of time and number are processed in the same way, which will contribute to a highly debated issue on common and shared and independent neural circuits for numerical and temporal processing.

Figure 1: Grand average results of Experiment 1. The x-axis represents time in seconds; the y-axis shows concentration in mmol*mm. The rectangle along the x-axis indicates time of stimulation. The continuous red and blue lines in the graphs represent oxyHb and deoxyHb concentrations, respectively, in response to the Non Alternating sequences. The dashed red and blue lines represent oxyHb and deoxyHb concentrations, respectively, in response to the Alternating sequence.
Near-infrared spectroscopy (NIRS) is an increasingly popular non-invasive brain imaging technique, often used in developmental cognitive neuroscience research [1]. As it is a relatively new method, standardized data analysis techniques are still lacking. Our understanding of the hemodynamic response in infants is also incomplete, rendering analysis methods that rely on strong assumptions about the underlying physiology impractical. Compromised data quality due to hair and strong movement artifacts, typical in babies, also plagues data analysis [1,2].

Here we put forward new analysis methods based on time series management and analysis techniques [3,4,5]. These techniques can efficiently operate on the original, fully detailed data set, taking into account the detailed trends that these data exhibit. Specifically, we have used similarity search to identify NIRS data that follow similar trends over time and subsequently group those together in clusters, and detect abnormal behaviors. We illustrate these novel methods (i) by comparing their results to previously published findings [2], as well as (ii) by applying them to previously unpublished data (both from experiments on newborn speech perception). In the first study, newborn infants listened to artificial speech sequences that either conformed to a repetition-based regularity (AAB: “babamu”, “nanape” etc.) or not (ABC: “bamuge”, “napefi” etc.), while their hemodynamic responses were measured in 12 channels per hemisphere over frontal, temporal and parietal sites. In the second study, the same sequences were used, but implemented by musical tones rather than speech.

As a first analysis, we used Euclidean distance in order to calculate the difference in the response of stimulus AAB and ABC. Based on the results in [2], we obtained significant differences between the conditions in left fronto-temporal and right frontal channels (Figure 1). Then, we performed a hierarchical cluster analysis to the AAB and ABC stimulation blocks in one significant channel. Preliminary results show that blocks of the same condition form a number of small clusters, although at the largest cluster levels such convergence is not always achieved (Figure 2). This implies that the responses to the AAB and ABC conditions indeed show different patterns. We are further refining this analysis to test for patterns characteristic not only of the two conditions, but of individual participants and different brain areas. If confirmed to be successful, this clustering algorithm has the potential to provide new analysis tools for NIRS data processing, possibly reliable at the individual level. Such an analysis would have immediate and important applications in basic as well as clinical NIRS research.

References
Learning word order at birth
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In language, the relative order of words in sentences carries important grammatical functions. However, the developmental origins of this ability and its neural correlates are to date poorly understood. The current study therefore investigates the origins of infants’ ability to learn about the sequential order of words, using near-infrared spectroscopy (NIRS) with newborn infants. Two groups of twenty newborn infants (age range 1-4 days) participated in one experiment each: in the first one a word order change was implemented in 4-word sequences recorded with a list intonation (as if each word was a separate item in a list; list prosody condition, Experiment 1) and in the second one the same 4-word sequences were recorded with a well-formed utterance-level prosodic contour (utterance prosody condition, Experiment 2). We used a NIRx NIRScout 8-16 system with a source-detector separation of 3cm, using pulsated LED lights at 760nm and 850nm for data acquisition. Both channel-wise t-tests and cluster-based permutation test were computed for comparing deviant (i.e. word-order changed, Dev) and standard blocks (i.e. word order did not change, Stad) within each experiment. In total, there were 24 [standard block – deviant block] pairs in each experiment. We found that newborns could detect the violation of the word order in the list prosody experiment (Fig. A), but not in the utterance prosody experiment (Fig B), as reflected by the significant differences between deviant and standard blocks in the former but not the latter. These results suggest that while newborns are already sensitive to word order in linguistic sequences, prosody appears to be a stronger cue than word order for the identification of linguistic units at birth.

Asterisks indicate channels with a statistically significant advantage for the deviant over the standard blocks. The ROIs obtained through the permutation test in the LH and the RH respectively are encircled using dotted lines.
It is known that pleasant touch is mediated by C-Tactile (CT) fibers and that CT targeted touch leads to broad cortical activations including posterior STS, a key region of the social brain [Gordon et al., 2011]. Our goal is to discover if a similar pattern of activation can be observed in young infants, or whether the development of this cortical specialization results from extensive postnatal experience. Over two studies, we use functional Near InfraRed Spectroscopy (fNIRS) to compare social to non-social touch. Across the studies the social touch stimulus is always a gentle caress (3-10cm/s) performed by the experimenter on the baby’s arm. In the first study (n=22) we contrasted the human caress to a caress performed with a spoon, both at the same speed, hypothesising that a difference in temperature and texture would be sufficient to elicit different activations. In our second study (n=17) we stroked the baby’s arm with an electric toothbrush, hypothesising that the features of this stimulation were so different from those of a human caress that it will not activate CT fibers, leading to a clearer distinction between the conditions. In the analysis we used a Region of Interest approach - with the use of a NIRS-MRI age appropriate co-registration map [Lloyd-Fox et al., 2014] - to define two ROIs, over the inferior frontal gyrus (IFG) and the posterior STS.

In the first study we found broad cortical activation to touch (social and non-social) versus baseline, but the contrast between social and non-social touch was not consistently different across infants (Figure 1a). In the second study we found broad responses to the toothbrush stimulus over both ROIs, but we failed to replicate the responses to the hand found in the previous study and found no activations to this stimulus (Figure 1b). In light of these results it is possible that at this age discrimination between social and non-social touch is still undergoing specialization. I will discuss how we are trying to elucidate the mechanisms behind these responses in future work with other age groups and different stimuli.

References:

The role of adaptive plasticity in tetraplegia patients following grip reconstruction

Spinal cord injury (SCI) is considered one of the most devastating injuries to afflict the human body and a significant global public health problem. Recovery from a complete SCI is exceedingly rare and the majority of the injured patients are disabled during the most productive periods of their lives. Surgical restoration of key functions, such as hand grip control has tremendous potential to offer functional gains for tetraplegic patients. Tendon transfers are the most common in which the distal end of a functionally intact muscle is detached, rerouted and reattached to a nonworking muscle to replace its original function. Brain plasticity is a core principle of brain function. It describes the ability of the central nervous system (CNS) to reshape and relocate structure and function, as an adaptive response to a functional demand. Cortical mapping and relearning are key factors in optimizing patient outcome following tendon transfers. However, the mechanisms of cortical plasticity and motor relearning following tendon transfer are exceptionally poorly understood. Reconstructive surgery amounts to a unique, focused stimulus for brain plasticity. The intervention therefore yields a rare opportunity to characterize the mechanisms involved.

The objective of the present study is to delineate patterns of cortical reorganization following advanced grip reconstructive surgery in tetraplegia patients using both functional near infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI). More specifically, we will map regained motor function of a thumb following surgical transfer of the brachioradialis (BR) muscle to the flexor pollicis longus (FPL) muscle (BR-FPL). We will compare cortical maps for elbow and thumb flexion using both imaging techniques. We plan to include a minimum of 6 patients who have undergone grip reconstruction at Center for Advanced Reconstruction of Extremities (C.A.R.E.) at Sahlgrenska Hospital/Mölndal, Gothenburg, Sweden at least a year earlier. Six healthy, gender and age-matched controls will be recruited. In the fNIRS assessment sources and detectors are placed over the sensory-motor regions of the left and right hemispheres, the covered area corresponding to the C3 and 4 positions in the international 10–20 system. Hemoglobin concentration is measured using the NTS Optical Imaging System (University College London). Results from the first control subject are presented below. Figure 1a and b show the hemodynamic response function (HRF) to the thumb flexion task in the sensory-motor channels of the left hemispheres.

![Figure 1a. The hemodynamic response function (HRF) to the thumb flexion task in the sensory-motor channels of the left hemispheres.](image1a)

![Figure 1b. A t-stat map showing the t-statistic value for fNIRS channels with a significantly larger HbO increase for the thumb than the elbow task.](image1b)

![Figure 2. The gross somatotopic organization of the primary motor cortex in the arrangement called motor homunculus.](image2)

![Figure 3. Spatial patterns of cortical brain activity during elbow and thumb flexion as measured with fMRI.](image3)
Analysis of Connectivity Symmetry Between Oxy- and Deoxy- Haemoglobin in Freely Moving Subjects Performing Real-World Cognitive Tasks

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Recent advances in mobile optical brain imaging have enabled monitoring brain function while cognitive tasks are performed in real-world scenarios for which neuroimaging modalities as fMRI and MEG were unsuited. Connectivity in brain fNIRS studies has revealed important insights about the brain human cognition; while most of the investigations have mainly focused on oxy-haemodynamic response, our aim here is to investigate the connectivity during these tasks considering both oxy- (HbO) and deoxy- (HbR) haemoglobin as well as systemic variables. Here we use data recently published by Pinti and colleagues [1] where changes in prefrontal cortex haemoglobin response were monitored during the performance of a real-world prospective memory task by using a 16-channels wireless fNIRS device on 19 freely moving volunteers. The within-subject protocol included a baseline condition (i.e., the experimenter showing the experimental area to the participant), two Ongoing conditions (i.e., walking around the streets counting the number of certain items) and a social and non-social PM task (i.e., performing the Ongoing task while responding to social and non-social PM cues, e.g., fist bumping an experimenter and parking meters, respectively). Changes in acceleration, heart rate, and breath rate were recorded using a monitoring belt in a subcohort of 7 subjects. fNIRS signal processing involved down-sampling to 1Hz, linear detrending, wavelet-based motion artefact removal, and band-pass filtering. A set of HbO and HbR connectivity matrices were produced by a Bayesian network considering subjects with systemic data. The similarity of the functional connectivity networks under HbO and HbR was quantified in terms of the symmetry of a combined matrix of both networks (Fig. 1 left). Symmetry was computed across conditions with and without systemic data. Fig. 1 right shows a summary of the symmetry per condition, also the percentages of channels related to systemic data are presented in the upper group. High symmetry between the networks recovered with HbO and with HbR is observable from Fig. 1 right. More precisely, when systemic data is considered the symmetry between HbO and HbR is near 90% across all conditions and 24-30% of the 16 channels are connected with systemic variables. However, only the Ongoing contaminated (OGc) condition shows a statistical difference in the symmetry with and without systemic data (Wilcoxon signed rank test, Fig. 1 right gray squares). This can be caused since OGc it was the most complex of the conditions and was at the end of the experiment. Even though the symmetry value between HbO and HbR connectivity maps is high, it is not 100%, perhaps due to differences in confounding factors within the signals (e.g. scalp influences). Through this study, we show that this probabilistic approach is capable of discovering the functional relationships between brain areas without the specification of a priori model. Furthermore, the approach is able to unravel the direction of the information flow, which we could be addressed in a future work.


Figure 1. (Left) Exemplary connectivity matrices. (Right) Symmetry between HbO and HbR-based connectivity, percentage of channels affected by systemic variables and p-values of Wilcoxon signed rank test.
Deep brain stimulation of the subthalamic nucleus alters the hierarchical organization of the prefrontal cortex in Parkinson’s disease: Moderating effects of disease duration at surgery

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Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is a common therapy for patients with Parkinson’s disease (PD). However, the alleviation of motor symptoms by DBS is partly offset by detrimental effects on the prefrontal cortex (PFC) and related executive functions [1]. Extant models of PFC functioning propose a rostro-caudal gradient of organization with rostral prefrontal regions modulating activity of caudal PFC [2, 3]. Capitalizing on the high temporal and adequate spatial resolution of multi-channel functional near-infrared spectroscopy (fNIRS), the purpose of the present study was to assess DBS-induced alterations in this functional hierarchy.

Methods

Intrinsic activity of the lateral PFC was recorded using an ETG-4000 fNIRS device (Hitachi Medical Systems, Japan) for 12 minutes during passive watching of nature movies in PD patients with STN-DBS (n = 26) and matched PD patients without DBS (n = 26). In PD patients with DBS, measurements were conducted ON stimulation (ON DBS) and – after a 2h interval – OFF stimulation (OFF DBS). Directed interactions between 38 fNIRS channels, evenly distributed over the lateral PFC, were calculated in the frequency band between 0.06 and 0.1 Hz using partial directed coherence (PDC), a measure of granger causality [4]. PDC values and clinical variables were analyzed in a linear mixed effects model using R statistics [www.r-project.org].

Results

In accordance with models of PFC functioning, PDC measures of Granger causality revealed an overall predominant direction of influence from rostral to caudal PFC. In PD patients with STN-DBS the stimulation effect on PDC values in rostro-caudal direction was moderated by the disease duration before DBS surgery (p = .02): The later patients underwent DBS surgery (i.e. the longer they were administered to conventional drug treatment) the more heavily the hierarchical gradient from rostro to caudal PFC was reduced ON DBS. Furthermore, an increased rostro-caudal gradient was positively correlated with the levodopa equivalent daily dose (p < .001) and with the volume of tissue activated by DBS (p < .001).

Conclusion

This study provides first evidence for STN-DBS-induced alteration of the PFC’s hierarchical organization, specifically suggesting that a late STN-DBS surgery has a detrimental impact on neural processing in the PFC. Thus, fNIRS-based measurements of PFC integrity can significantly enhance understanding of DBS-induced side effects and may help to optimize DBS applications in the future.

References

NIRS-Measured Frontal Cortex Asymmetry in Neonatal Brain Injury

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Abstract: Neonatal hypoxic-ischaemic encephalopathy (HIE) is related to neurodevelopmental problems and mortality. Broadband near-infrared spectroscopy (NIRS) can monitor cerebral changes in haemodynamics, via oxy- and deoxy-haemoglobin (HbO\textsubscript{2} and HHb), and metabolism via cytochrome-c-oxidase [1]. The aim of this study is to assess frontal cortex asymmetry of neonates suffering HIE using bilateral NIRS measurements in response to fluctuations in systemic physiology. 41 infants with HIE were monitored with broadband NIRS in the first days of life. Spontaneous arterial desaturation events were analysed using the laterality index (LI) method to assess the asymmetry of the cerebral response. LI has been previously used to assess laterality in functional NIRS studies [2]. Haemoglobin difference, analogous to oxygenation (HbD = HbO\textsubscript{2} – HHb), was used to calculate the LI (which varies from -1 to +1, representing dominance of the left and right sides):

\[ LI = \frac{QLH - QRH}{QLH + QRH} \]

where QLH and QRH correspond to HbD changes in the left and right side of the frontal cortex (see an example in Fig. 1). Desaturation events were identified from oxygen saturation (SpO\textsubscript{2}) decreases of >10% in 18 infants. Fig 2 shows LI values compared with a MRS marker of injury severity, lactate/n acetyl aspartate (Lac/NAA).

Fig. 1 Example of an oxygen desaturation event with corresponding changes in cerebral HbD. The LI for this event is +0.35 (left-side dominance).

Fig. 2 Average absolute LI against Lac/NAA per baby across days 2-4 of life. The red/black markers indicate right/left-side dominance.

2. Tanida et al., 2007, Brain Research, 1184:210-216
Motion Artifact removal for Functional Near-Infrared Spectroscopy

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Some methods were suggested to overcome movement or motion artifact in fNIRS signals. Motion artifact removal based on discrete wavelet transform (DWT) has been proposed by Molavi et al. [1]. In this study, a new algorithm for automatic selection of the threshold value in wavelet coefficients is proposed. Data were collected by a continuous wave dual wavelength fNIRS system with 16 channels (ARGES Cerebro, Hemosoft Inc., Turkey) and sampling rate of device is 1.7 Hz. To evaluate the proposed algorithm, synthetic fNIRS data were used which is a combination of rest data and motion artifact. Our algorithm is based on DWT but it is different to select threshold in each level. We applied DWT to decompose signal into 8 levels and Daubechies 5 (db5) is used for the mother wavelet. Then histogram of wavelet coefficients is calculated in each level that is an estimation of probability density function (PDF). The kernel smooth density estimator produces a function to represent a probability distribution using the sample data. Based on the probability of wavelet coefficients in each level, the function may be simple or a mixture of Gaussian functions. Hence, each function may have one or multiple mods. If there are more than one mods, it means that there is outlier data. The outlier data is produced because of motion artifact which is to be set zero. Accordingly, in each level in which there is more than one mod, a threshold can be defined to exclude wavelet coefficients. At first all the local minimum points are determined on PDF. Then the nearest local minimum on both sides of the mean of the estimated PDF are obtained. Right and left points obtained as largest and smallest threshold for the coefficients are selected, respectively. In other words, each of the coefficients in the range [low Threshold, High Threshold] remains unchanged. Considering the number of coefficients of each level is different, therefore each level has a different density function, so this method is adaptive thresholding. The normalized mean square error (NMSE) criterion to evaluate the effectiveness of the proposed method is calculated and the results were compared with Molavi [1] in Table 1.

Table 1. NMSE of before removal and after removal

<table>
<thead>
<tr>
<th>Clean Signal / Noisy Signal</th>
<th>NMSE (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal with Motion Artifact</td>
<td>-2.3454</td>
</tr>
<tr>
<td>Removal Motion Artifact [1]</td>
<td>-6.3882</td>
</tr>
<tr>
<td>Removal Motion Artifact (Proposed Method)</td>
<td>-10.2958</td>
</tr>
</tbody>
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The role of cytochrome in neural responses in infants

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Near-infrared spectroscopy (NIRS) has become an established research and clinical tool in neurodevelopmental research for measuring changes in cerebral oxygenation, in particular changes in oxyhaemoglobin (HbO2) and deoxyhaemoglobin (HHb). A novel multi-wavelength broadband NIRS system has been designed [1] that simultaneously measures these changes in addition to changes in cellular oxygen utilisation by measurement of the oxidation state of the mitochondrial respiratory chain enzyme cytochrome-c-oxidase (CCO). NIRS measurements of CCO provide a measure of oxygen metabolism within cells and may therefore provide a more direct and sensitive marker of neuronal activity than haemoglobin. Non-invasive measurement of CCO through NIRS, could therefore be utilised as a tool to further our understanding of cognitive development. The aim of this study was to pilot the use of the new broadband NIRS system to investigate the role of CCO in neural responses to functional activation in the developing human brain.

Studies were performed with 26 typically developing (TD) infants aged between 4 and 6 months. Infants wore custom-built NIRS headgear containing a single channel (1 source-detector pair: separation 2.8cm), which – with the use of a NIRS-MRI age appropriate coregistration map [2] - was placed over the right superior temporal sulcus – temporo-parietal region (STS-TPJ). The system “mini-CYtochrome Research Instrument and application” (mini-CYRIL) was developed at UCL and consisted of a white light source from an HL2000 light source and Ventana VIS-NIR miniature spectrometer from Ocean Optics and had a sampling frequency of 1Hz. Changes in HbO2, HHb and CCO were calculated using changes in attenuation of light at 120 wavelengths between 780-900nm. The experimental condition consisted of presentation of social visual and auditory stimuli for 10-12s, which included engaging videos of “peek-a-boo” and “incy-wincy spider” accompanied by human non-speech vocalisations such as laughter, followed by non-social baseline condition of still images of different types of transport, such as cars and helicopters, for 10-12s [3].

Figure 1 shows the measured changes in HbO2, HHb and oxCCO in a typical infant. Task related changes in all chromophores are clearly evident with the magnitude of changes in oxCCO within the physiological range expected from other oxCCO studies [4].

The results from this study show that measurement of CCO in response to functional activation is possible and may reveal information about oxygen metabolism during functional activation in the developing human brain.

1. Bale et al. (2014) Biomedical Optics Express, 5(10), 3450-3466.
Update for spatial registration and statistics tools for fNIRS with emphasis on anchor-based registration, effective multiplicity approach and adaptive GLM

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In recent years, we have made three lines of methodological contributions to help solving major problems involved in fNIRS data analyses. In this poster presentation, we will provide brief overviews for these methods and distribute the latest digital resources related to them, along with our stable classical tools (available at http://brain-lab.jp).

First, sometime ago, we introduced a probabilistic registration method that uses a reference MRI database instead of the subject’s own MRI, and probabilistically registers the fNIRS optode or channel positions onto a canonical brain template in the standard stereotactic brain coordinate systems. As an alternative method, we devised an anchor-based registration method utilizing roughly obtained anchor positions on the scalp instead of strictly defined landmarks such as 10/20 landmarks. This method uses a spherical coordinate system to seek a position in the reference MRI database that corresponds to the anchor position, and eventually presents fNIRS optode and channel positions in the standard stereotactic brain coordinate system. When any point located in the zenith region of the scalp was used as the anchor, this method yielded stable estimations for the probe and channel positions in the standard stereotactic coordinate system. Thus, anchor-based registration will be a practical alternative, especially to avoid burdening a subject and to reduce experimental time.

Second, recent advances in multichannel fNIRS allow wide coverage of cortical areas while entailing the necessity to control family-wise errors (FWE) due to increased multiplicity. Conventionally, the Bonferroni method has been used to control FWE. While Type I errors (false positives) can be strictly controlled, the application of a large number of channel settings may inflate the chance of Type II errors (false negatives). Bonferroni-based methods are especially stringent in controlling Type I errors of the most activated channel with the smallest p value. To maintain a balance between Type I and II errors, effective multiplicity (Mₑ) derived from the eigenvalues of correlation matrices is a method that has been introduced in genetic studies. The number of significantly activated channels remained almost constant regardless of the number of measured channels. We demonstrated that the Mₑ approach can be an effective alternative to Bonferroni-based methods for multichannel fNIRS studies.

Third, an increasing number of fNIRS studies utilize a general linear model (GLM) approach, which serves as a standard statistical method for fMRI data analysis. While fMRI solely measures blood oxygen level dependent (BOLD) signal, fNIRS measures the changes of oxy-hemoglobin (Hb), and deoxy-Hb signals at a temporal resolution several-fold higher. This suggests the necessity of adjusting the temporal parameters of a GLM for fNIRS signals. Thus, we devised a novel GLM-based method utilizing an adaptive hemodynamic response function (HRF). We sought the optimum temporal parameters to best explain the observed time-series data during verbal fluency and naming tasks. The adaptive HRF method could suitably explain the behaviors of both Hb parameters during tasks with different cognitive loads during a time course, and thus would serve as an objective method to fully utilize temporal structures of all fNIRS data.
Humans have a tendency to spontaneously and unconsciously copy or ‘mimic’ others’ behaviours. Although this mimicry plays an important role in communication and affiliation (1), little is known about its development. We are currently conducting a longitudinal study aiming to elucidate the cognitive and neural mechanisms supporting the development of mimicry from infancy to toddlerhood, from which the results of the first visit at 4-months will be presented.

Previous neuroimaging work with adult participants suggests that mimicry is supported by connections between the superior temporal sulcus (STS), which is thought to process the kinematics of observed actions, and the inferior frontal gyrus (IFG) that represents the motor commands needed to perform these actions (3). Although mimicry is often portrayed as an automatic consequence of this perceptual-motor link, it is clear that mimicry is modulated by social signals, such as group status (2), and eye contact (3) in adults. In the current study we manipulated the direction of the model’s gaze (direct vs. averted) to assess whether mimicry is modulated by eye contact early in infancy as well.

We presented infants with videos of models performing facial actions (e.g. mouth opening and eyebrow raising) accompanied by direct or averted gaze, while we measured activation of the infants’ mouth and eyebrow muscles using electromyography (EMG) to obtain an index of mimicry. After a nap infants observed the same stimuli while we used functional near-infrared spectroscopy to investigate the hemodynamic response over IFG and STS areas.

We found that 4-month-old infants showed more mimicry (see Figure 1), and greater activation over right STS areas (see Figure 2), when they observed facial actions accompanied by direct gaze compared to facial actions accompanied by averted gaze. These findings suggest that, like in adults, mimicry is modulated by social signals from early in infancy, and that this modulation is associated with activation in the right STS region.

**Figure 1.** Mimicry scores were calculated by subtracting EMG activity over the non-corresponding muscle from activity over the corresponding muscle (e.g. on an eyebrow trial EMG activity over the mouth muscle was subtracted from activity over the eyebrow muscle, so that a more positive scores indicates more mimicry).

**Figure 2.** Hemodynamic responses (oxyHb) measured over the right hemisphere during the observation of actions accompanied by direct, compared to averted gaze. Positivity indicates a greater activation for the Direct Gaze condition. The statistically significant channels (20, 21, 25) are indicated with a black circle.

**References**

Adult-like perception of time-compressed speech at birth

Human listeners are able to maintain a constant representation of speech despite a wide range of variations in the signal. Accent, emotional state, or gender can significantly modify the acoustic properties of speech but we still identify the same linguistic units it carries without efforts. In the time dimension, adults are able to adapt to time-compressed speech up to about 40% of the initial duration (Palier et al., 1998) in their native language or a rhythmically similar language, even if that is unfamiliar to them (Sebastian-Galles et al., 2000). Does this ability rely on listeners’ linguistic knowledge, or is it a more general auditory skill, possibly present before the existence of considerable linguistic knowledge, i.e. at birth?

In two functional near-infrared spectroscopy (fNIRS) experiments, we investigated how newborns perceive time-compressed speech. Specifically, we tested how newborns process speech compressed to 60% of its initial duration, a compression rate that adults can adapt to, and to 30% of its initial duration, a compression rate that adults cannot adapt. We used uncompressed speech as a basis of comparison. We measured newborns’ brain responses in the temporal, frontal, and temporo-parietal regions bilaterally, since these regions have been shown to be involved in speech processing at birth (Pena et al. 2003, Gervain et al., 2008, 2012).

In the first experiment, we exposed newborns to time-compressed speech in their native language, i.e. French, using an alternating/non-alternating design (Figure 1), a powerful design to test fine-grained discrimination (Best & Jones, 1998, Gervain et al., 2012). We found that newborns processed normal and 60% compressed speech similarly, as shown by a canonical hemodynamic response to these two speech rates in the non-alternating blocks, but could still discriminate them, as indicated by the significant difference between alternating and non-alternating blocks in the temporal region (p=0.014). By contrast, the non-alternating blocks with 30% compressed speech evoked a negative response in two left tempo-parietal and one right frontal channel (p=0.001, p=0.0204 and p=0.002), showing that like adults, newborns process this compression rate differently form normal and moderately compressed speech.

In the second experiment, we presented time-compressed speech in an unfamiliar but rhythmically similar language, Spanish. The experimental design and compression rates were the same as in the first experiment. Preliminary results suggest that the 30% speech rate is processed differently from the other two speech rates in Spanish, too. However, this difference is less pronounced than for French. Two channels, both in the temporal region, revealed a significant difference between normal and 30% compressed Spanish (ch. 3 p=0.026; ch 17 p=0.045). These results imply that newborns may be able to adapt to time-compressed speech in an unfamiliar language if it is rhythmically similar to the native language. However, this ability is relatively weaker than adaptation for the native language. This conclusion meshes well with the results of some existing NIRS studies with newborns, showing an advantage for the language heard in utero over other languages.

![Figure 1: Alternating and non-alternating design used in the two experiments. N: normal utterances. C: compressed utterances.](image-url)
Change in cortical activation over time in individuals with mental fatigue
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Background and aim
Mental fatigue can be a disabling consequence of traumatic brain injury (TBI), stroke, infection or inflammation in the Central Nervous System. The condition is characterized by pronounced mental fatigue after moderate mental activity. Pronounced fatigue can appear very rapidly and, when it does, it is not possible for the affected person to continue the activity. Individuals suffering from mental fatigue are able to perform as well as healthy individuals on regular neuropsychological tests for a limited time. In behavioral studies where larger test batteries are performed twice over a period of a couple of hours, it has been shown that healthy controls maintain their level of performance or improve, whereas individuals with mental fatigue do not. The aim with the present ongoing study is to investigate brain activation in the frontal lobe during focused activity and rest over time, in individuals with mental fatigue after TBI using functional near infrared spectroscopy (fNIRS).

Methods
We plan to include a total of 20 individuals with TBI and a matched control group. Up to now, 11 patients and 8 controls have been included. The test battery includes nine neuropsychological tests. All but one test is done twice, and brain activity is recorded with fNIRS during performance of all tests. Hemoglobin concentrations are measured using the NTS Optical Imaging System (University College London), with 16 sources and 16 detectors, resulting in 50 channels plus 2 short separation channels using the wavelengths 780 and 850nm. The 50 channels are divided into 10 ROI: left and right frontal polar area (FPA), anterior dorsolateral prefrontal cortex (DLPFC), posterior DLPFC, anterior ventral lateral prefrontal cortex (VLPFC) and posterior (VLPFC).

Preliminary Results
Patient data will be presented on the fNIRS meeting. Below we present data from 8 controls (five men and three females) from the 1st and 2nd conflict processing Stroop-Simon test (figure 1). The participant is asked to specify the color of the ink by pressing a button with either the left or right thumb on a gamepad and ignore the word meaning and location. It was approximately one hour of neuropsychological testing between the 1st and 2nd test. Control subjects are match with respect to patients’ age and education. Mean age 40 ±15 (range 26-58). Concentration data is calculated from the area under the curve between 4-8 seconds after stimuli for oxygenated hemoglobin (oxy-Hb) for every ROI. We hypothesized that the control participants would have less spread out brain activation in the 2nd test due to the order effect. A preliminary 3-way 2 (1st vs 2nd) x2 (Stroop Congruency) x2 (Simon Congruency) ANOVA with Bon Ferroni correction does indicate a 1st vs. 2nd effect in Left and Right FPA and aDLPFC, which is in support of our hypothesis. Figure 2 illustrates the activity in left aDLPFC for 1st and 2nd test.

![Figure 1. Stroop-Simon test. Stimuli on the left is a Congruent-Congruent. The stimuli on the right is an Incongruent-Incongruent.](image1)

![Figure 2. Average group response for an Incongruent-Incongruent stimulus in the 1st and 2nd test in Left aDLPFC.](image2)
Cortical Basis of Social and Mechanical Object Processing in Infancy
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Introduction: Infants distinguish between human and mechanical entities with different expectations for the way that they should move and interact, leading to speculation that the infant brain has specialized cortical networks for processing these entities. Researchers have used fNIRS to assess cortical responses in 5-month-olds to social events (e.g., human hands, faces) versus mechanical events (e.g., toys, machines), finding different patterns of activation in the temporal cortex to these events (Lloyd-Fox, et al., 2011). Other researchers (Grossmann et al., 2013; Biondi & Wilcox, 2014) have investigated cortical responses to human and robot entities, also finding different patterns of cortical activation for these types of events, providing insight about the neural basis for processing these entities. However, it is difficult to draw firm conclusions about the nature of specialized cortical networks from these findings, partly because the objects and events used, within and across studies, vary in many ways. Our current research investigates patterns of neural activation to carefully controlled events that were either social or mechanical in nature.

Design: Infants aged 6-10 months (n = 20) watched two types of events in a puppet stage. In the social event, a round object with animate properties (eyes, self-propelled, and an implied goal/intention of moving up the hill) was either helped or hindered by another shape also with animate properties (Hamlin, Wynn & Bloom, 2007) (Figure 1). The physical events were identical except, through mechanistic movements, the round object was pulled up or pushed down the hill by another non-social artifact. Behavioral research suggests infants interpret these events as social or mechanical, respectively. Each infant saw 12 trials (12 s each): 6 each of social and mechanical, in a blocked design. Each trial was preceded by a 10 s baseline, during which a sparkly pinwheel moved across the stage. Infants were fitted with a custom-made fNIRS headgear (Figure 2). Changes in HbO, compared to baseline, were averaged over 5-12 s of each trial; then averaged over trials and participants to obtain a grand average for each event condition.

Results and Discussion: Preliminary analyses of mean HbO responses at the channel level revealed two spatially contiguous channels in the left hemisphere (channels 5 and 9) and two in the right hemisphere (channels 15 and 18) that showed activation, which were averaged to form left and right temporal regions of interest (ROI) responses (Figure 2). Planned comparisons revealed during the mechanical event, the mean HbO response obtained in the right temporal ROI (M = 0.428, SD = .516) was significantly greater than the left temporal ROI (M = -0.025, SD = 0.420), t(19) = -2.632, p < .05 (one tailed). In contrast, the left (M = 0.236, SD = 0.489) and right (M = 0.378, SD = 0.356) temporal ROIs both showed activation in response to social event, the magnitude of which did not differ significantly, t(19) = .516, p > .05. Finally, within the left hemisphere, greater activation was obtained to social (M = 0.236, SD = 0.489) than mechanical (M = -0.025, SD = 0.420) trials, t(19) = -1.738, p < .05 (one tailed). In summary, we obtained bi-lateral activation in the posterior temporal ROI in response to the social events. In comparison, we found right lateralized activation in response to the mechanical events. These results suggest the presence of distinct functional networks for processing social and mechanical information in the infant temporal cortex.

Figure 1 (Left). (a) A social hinder event; (b) a social helper event; (c) a mechanical pull event; (d) a mechanical push event. Arrows indicate direction of movement. Figure 2. (Center and right). International 10-20 system overlaid on the left and right hemispheres. Red dots are sources, blue dots are detectors, and channels are numbered between each source-detector pair. Gold circles indicate the channels in the ROI.
Reproducibility, hemispheric variability and range of normal values of cerebral oxygenation parameters measured by TD fNIRS in healthy volunteers in view of an application to acute ischemic stroke patients

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Abstract

Background: Despite the widespread use of fNIRS for research and clinical applications, the range of normal values of deoxy-haemoglobin (Hb), oxy-haemoglobin (O2Hb), total haemoglobin (tHb) concentrations and tissue oxygen saturation (SO2) and their inter-hemispheric variability in elderly healthy volunteers are currently not known. This is mainly due to the limitations of classical single channel or topographic continuous wave (CW) NIRS instrument that can only provide relative hemodynamic changes. Conversely, Time Domain fNIRS (TD fNIRS), can discriminate absorption and scattering phenomena at different layers of the tissue, thus providing absolute hemodynamic data. In this work we have studied if TD fNIRS could be exploited to perform a bed-side monitoring in ischemic stroke patients.

Methods: a TD fNIRS medical device developed at Dept. Physics Politecnico di Milano was used. The system employs pulsed lasers at 635, 690, 785, and 830 nm as light sources, a graded index fiber and a grade index fiber bundle for injection and collection of photons, four hybrid photomultipliers with band pass filters for photo detection and a Time Correlated Single Photon Counting (TCSPC) board for the acquisition of the reflectance curves. The entire system was fully characterised following the BIP and MEDPHOT protocols [1-2]. Data were fitted with the diffusion model for infinite homogenous media. Seven healthy volunteers (43% female) with mean age 74.6 y (range 61.2-88.5 y) were enrolled. Three positions per hemisphere (F3-F5, C3-C1, P3-P5, F4-F6, C4-C2, P4-P6,) were identified by means of the 10/10 international topographic system in order to represent the putative vascular territories of middle and anterior cerebral artery. Each session was performed at 30° head-of-bed angle. In order to evaluate the reproducibility of the measurements, each position was investigated at 3 time-points separated from 5 minutes each.

Results: The average values of Hb, O2Hb, tHb and SO2 in healthy volunteers were respectively 13.41±2.51, 27.81±5.35, 41.23±6.85 µM and 67.27±4.63%. The mean intra-position coefficient of variation among 3 separated measurements were 1.05%(±0.56%). The mean percentage of inter-hemispheric differences between specular positions for Hb, O2Hb, tHb and SO2 were respectively 10.2%(±7.5), 12.0%(±9.3), 10.9%(±7.7) and 3.0%(±1.6).

Conclusions: from our preliminary results on elderly healthy volunteers we observed that the average reproducibility of measured concentration is <4% for HHb, O2Hb and tHb, while it is <1% for SO2. Among corresponding positions on different hemispheres, we detected a high variability in healthy volunteers. Next step will be fit the data with a multilayer model in order to further avoid the effect of extra-cerebral tissues. A clinical campaign on stroke affected patients (20 subjects), with onset of symptoms within 24 hours, has also started and the preliminary results will be presented at the conference.

Figure 1 Mean values and standard deviations of Hb and O2Hb among volunteers in different head locations.

References


Title: Cortical Activity Related to Speech Motor Planning and Execution in Adults Who Stutter

Authors: Bryan Brown, Sobanawaritny Wijeakumar, Patricia Zebrowski, John Spencer

Stuttering is a disorder of childhood characterized by disruptions in speech production that manifest as repetition or prolongations of parts of words, whole word and/or phrases. The incidence and prevalence of stuttering are stable across cultures and impact approximately 5% of children and 1% of adults (McKinnon 2007; Yairi, 1992). fMRI studies of speech production in adults who stutter (AWS) have revealed a pattern of neurocorrelates of stuttering briefly summarized as increased activity in right hemisphere regions and decreased activity in the left hemisphere. Frequently identified cortical sites of atypical activity include the inferior frontal gyrus, bilaterally, as well as the superior temporal gyrus, inferior parietal lobule and supplementary motor area in the right hemisphere (Chang, 2009, Lu, 2010).

While cortical activity of AWS has been studied for 20 years, the majority of studies have not examined speech-motor planning separately from speech-motor execution. Thus, in the vast majority of cases, it is not clear if the differences observed in the cortical activity of AWS reflect differences in the planning or execution of speech.

To address this, we completed two experiments, one isolating speech-motor planning and a second isolating speech-motor execution. In Experiment 1, we examined planning using a nonword repetition task. All nonwords had approximately the same level of motor execution demands (three syllables) but differed in the degree of planning necessary (one syllable repeated three times or three different syllables). Participants were seated in a comfortable chair and words were presented at a comfortable volume. Participants were instructed to repeat the nonword as quickly as possible.

Motor execution was examined by a go-no go picture identification task. A picture of a commonly known object (e.g., car, turtle) was displayed on a computer monitor. Participants were instructed to say the name of the object aloud during ‘go’ trials and to covertly name the object on ‘no-go’ trials.

15 AWS and 15 AWNS participated. Image reconstruction of brain activation was achieved by integrating results of channel-based general linear modeling of HBO and HbR with the sensitivity profiles of Monte Carlo simulations (see Wijeakumar et al., 2016). All analyses were completed in AFNI.

Results indicated that compared to AWNS, during speech-motor planning AWS demonstrated increased activity in the inferior frontal gyri bilaterally, the left middle frontal gyrus, and the right postcentral gyrus. Additionally, AWS demonstrated decreased activity in the right middle frontal gyrus. These results are consistent with previous literature, suggesting that AWS demonstrate atypical planning during speech production; however, advances the literature in demonstrating that the atypical planning is not related to lexical targets, but rather is a feature of non-speech movements.

During motor execution, AWS demonstrated decreased activity in the right inferior frontal gyrus, supramarginal gyrus, superior temporal gyrus, and the postcentral gyrus bilaterally, but increased activity in the left postcentral gyrus. However, rather than activity speech-motor execution, the results indicate we have also identified activity related to the inhibition of speech. AWS demonstrate increased activity related to the inhibition of speech relative to AWNS.
References:


Bayesian fNIRS smooth adaptive deconvolution

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Context: Classical fNIRS data analysis [1] mainly consists in window-averaging which might be biased by unproper baseline definition or GLM-based analysis which cannot properly provide evoked hemodynamics estimates. The current work addresses these issues with a new method to deconvolve the hemodynamic response function (HRF).

Method: Within a Bayesian framework inspired by [2], the novelty of this approach relies on the design of a spline-regularized prior to model the HRF. The covariance matrix of the HRF embeds local temporal dependencies in the form of piece-wise polynomials (Fig. 1). Another asset of the method is the joint modeling of a low-frequency trend to properly capture the resting baseline. The forward model reads: \( y_j = X f + T c + b \), for any channel \( j \), where \( y_j \) is the \( \Delta[Hb] \) time-course (HbO or HbR, which are treated independently), \( X \) the Toeplitz matrix encoding the experimental paradigm, \( f \) the HRF, \( T \) a low-frequency orthonormal basis, \( c \) the trend coefficients and \( b \), a white noise component. The prior on \( f \) is a multivariate normal with spline-based covariance matrix (Fig. 1) and unknown scale. The prior on \( c \) is normal with unknown variance. All hyper-parameters have non-informative Jeffreys priors. The model inference is performed by Markov Chain Monte Carlo and posterior mean and variance estimates are computed for all unknowns.

Results: This approach has been validated on realistic artificial data (1 source and 4 detectors) and is able to properly recover atypical response shapes in a low SNR situation (Fig. 3). Applied on a 30-second block tapping data set (motor patch of 4 sources x 8 detectors) with no detrending, the fitted time-course is adjusted to a sensible baseline and activation blocks are well captured, as shown in Fig. 4.

Conclusion: the proposed temporally regularized deconvolution approach is able to robustly recover atypical HRFs and provides sensible baseline fits allowing proper interpretation of the response variations.

Fig. 1: prior covariance matrix of the HRF (duration of 25 sec.), built from a uniform spline basis comprising 10 coefficients. Leading and trailing terms are zeros, enforcing starting and returning to baseline. Moving from diagonal terms in the anti-diagonal direction, the covariance coefficients decrease towards zero in around 2.5 sec., showing the temporal dependency of the response coefficients. Fig. 2: artificial data. In a given channel, HRF estimate (red) with its posterior standard deviation, superimposed on the ground-truth HRF (blue). Fig. 3: finger tapping experiment. Signal fits for \( \Delta[HbO] \) (red) and \( \Delta[HbR] \) (blue) superimposed on the observed signals (light red and light blue respectively) and the tapping stimulation blocks (pink).

Neural correlates of music perception in cochlear implant users

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Cochlear implants (CIs) allow those with severe-to-profound hearing loss to experience sound, some of them for the first time. Although this highly successful neuroprosthetic device can enable remarkable proficiency in understanding speech, poor spectral resolution due to the underlying etiology, discrete number of electrical contacts, and spread of intracochlear electrical activity leads to extensive difficulty with complex pitch perception. Despite these underlying physiologic and technical limitations, some users achieve the complex pitch discrimination necessary for music appreciation. This study aims to better quantify both behavioral and functional measures of variable music processing capabilities seen in CI users. To do so, we first categorized music perception as “low” or “high” by calculating a median split of CI users’ accuracy on a chord discrimination task (median 69%, range 52-92%). Our primary hypothesis was that in contrast to low performing CI users (<69% accuracy), high performing CI users and normal-hearing (NH) controls exhibit significantly greater auditory cortical activation in response to music stimuli.

As an optical neuroimaging technique, functional Near Infrared Spectroscopy (fNIRS) is ideal for testing this hypothesis due to its compatibility with both the electronic and ferromagnetic components of CIs. To date, we have conducted behavioral testing and fNIRS with 6 CI users and 6 NH controls passively listening to tones, noise, chords, and melodies. Collecting several clinical measures of speech and music perception including a consonant-nucleus-consonant (CNC) word test, AzBio sentence test, University of Washington Clinical Assessment of Music Perception (UW-CAMP), Melodic Contour Identification (MCI), and a major/minor chord discrimination task allowed us to characterize various spectral aspects of music perception. Scores on these behavioral measures are representative of the high diversity seen in CI users. Ongoing recruitment and analyses are aimed toward investigating the neural correlates of diversity in this clinical population. A future goal of this work is to refine clinical outcome measures of spectral resolution in CI users and how they impact music perception and quality of life.
Enhanced resting-state dynamics of the hemoglobin signal as a novel biomarker for detection of breast cancer

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Abstract:
Simultaneous bilateral breast measures of spatiotemporal features of the hemoglobin signal have been examined in healthy women, those with benign disease, and those with biopsy-confirmed breast cancer. Examination of the frequency response reveals notably enhanced amplitude in the vasomotor region in affected subjects, in agreement with prior reports obtained by dynamic thermography [1]. These studies also identified that the likely causative agent responsible for this feature is constitutively elevated nitric oxide production, a feature common to inflammatory responses.

In an effort to identify optimal measures of the diagnostic performance, we have systematically explored measures corresponding to different elements of the hemoglobin signal as a function of metrics sensitive to primitive forms of spatiotemporal behaviors. These measures were obtained by computing different permutations of the first and second moments, in the spatial and temporal domains, of the image time series, to generate a set of scalar cross-domain metrics. Examined were the spatial mean of the temporal standard deviation (SMTSD), spatial standard deviation of the temporal standard deviation (SSDTS), temporal mean of the spatial standard deviation (TMSDD), temporal standard deviation of the spatial mean (TSDSM) and temporal standard deviation of the spatial standard deviation (TSDSSD). Other considered quantities were the coefficient of variation of the spatial (CVSSD) and temporal standard deviation (CVTSD), and a metric sensitive to the phase of temporal features (SCI = SMTSD/TSDSM). Independently considered was a computational modeling effort intended to identify the forms of primitive spatiotemporal behaviors to which the preceding measures are sensitive. Results of the sensitivity computations are reported in Table 1. ROC analysis was used to identify the diagnostic performance of each metric, examined as either a univariate quantity computed from an individual breast, or as a bilateral difference or ratio. The considered analysis did not rely on specific prior knowledge of whether a tumor was present or which breast was affected.

Results obtained demonstrated that among the measures considered, those with primitive-behavior sensitivities that include Mean Amplitude yielded the highest AUC values (up to 87%), but that this selectivity was dependent on which element of the hemoglobin signal was examined. The most successful measures were those based on hemoglobin (Hb) oxygen saturation, while total Hb was the least successful (AUC ~81%). These findings are the first to identify that the known phenotype of a sustained inflammatory response, a feature considered necessary for tumor development and growth, is observable by dynamic near infrared optical tomography [2].

<table>
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<th>Table 1</th>
<th>Model-parameter dependence</th>
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<td>Metric</td>
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References:

Factors Influencing the Diagnostic Performance of Breast Cancer Detection by Hemodynamic Imprinting

Randall L. Barbour and Harry L. Graber
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Abstract:
Clinical experience shows that disease diagnosis invariably is based on a composite of information that spans the principal domains of tissue characteristics, namely its composition, spatial and temporal properties. Our working hypothesis is that surrogate measures that are sensitive to disease and that span these same domains can be captured from a noninvasive examination of the hemoglobin signal that is additionally subjected to the modulating influences of a controlled viscoelastic deformation. This hypothesis builds on the understanding that such maneuvers will affect blood flow, and hence the hemoglobin response, in ways that are sensitive to the principal macroscopic components of tissue; i.e., its stiffness, vascular density and metabolic demand. By extension, because each of these can differ by as much as an order of magnitude depending on tissue type and each is sensitive to disease, disease-sensitive behaviors of the hemoglobin signal may emerge in response to an applied force. We refer to this dependence as Hemodynamic Imprinting [1] in recognition that emergent features can be expected to depend on the details of the applied force and hence are imprinted as a consequence of the expected nonlinear interactions resulting from the controlled modulations.

The considered methodological framework comprises elements involving resources for applied sensing, experimental protocols and data analysis. To support systematic enhancement of these elements, in this report we have examined features of the information space associated with emergent hemoglobin responses. Experimentally controllable factors include details of applied force and strategies for data analysis (image reconstruction, feature extraction). Intrinsic factors include elements of the hemoglobin signal, as can be explored by examination of components (e.g., total Hb, deoxyHb, etc.) individually or as a co-varying system [2], as well as expected sensitivities to principal elements of the tumor phenotype (i.e., tumor angiogenesis, tissue stiffness and sustained inflammatory response [3]). Findings obtained indicate that the information value of derived features can be improved by examination of a composite of measures obtained from different experimental protocols (e.g., resting state, applied force), and from examination of Hb measures as a co-varying system.

References:


Do you know these sounds? Left hemisphere shows greater activation to high frequency language phonotactics in infants but not in adults.

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Topic Area: Neurodevelopment

Around the age of 12 months infants reach an important developmental mark - they produce their first words. How does the infant's brain prepare them for this key milestone? Behavioral research shows that before speaking their first words infants become increasingly sensitive to phonotactic frequencies of their native language. More specifically, across all languages some types of stress and phoneme arrangements are more common than others and infants at 8-10 months begin to distinguish between high and low frequency phonological patterns of their language. The neural correlates of this developmental change remain unknown yet critical to our ability to leverage infants’ linguistic environment for better learning and to predict impairments of language acquisition. Thus, our goal was to investigate infants’ cortical response to phonotactic frequencies of their native language, how this response relates to infants’ verbal abilities, and how it varies from adults.

Hypotheses & Predictions. Prior neuroimaging research suggests that children’s cortical response is strongest to those aspects of language that are being actively acquired at the age of testing (Knoll, Friederici et al., 2012). We therefore hypothesized a developmental difference in cortical response to phonotactic frequency between infants and adults. We predicted that infants about to begin producing their first word should show greater left hemisphere response to high than low frequency phonological patterns of their native language. In contrast, proficient adult speakers should show greater left hemisphere response to low frequency phonological patterns, potentially signaling new learning demands. To test these predictions we used fNIRS imaging to test infants and adults as they listened to high and low frequency nonwords.

Methods. 17 nine-month-old infants and 13 adult participants (M(SD) = 24.27(3.80) years) passively listened to nonwords in English, their native language, during fNIRS imaging (TechEN CW6). The nonwords varied in frequency of stress pattern and phonotactic properties of the English language. Half the experimental blocks had nonwords with HIGH frequency linguistic patterns and the other half the blocks nonwords with LOW frequency linguistic patterns. We used a customized configuration of 28 channels in infants and 40 channels in adults covering frontal, temporal and parietal regions, bilaterally.

Results & Discussion. Both adults and 9 month old infants can tell a difference between high and low frequency phonological properties of their language. Remarkably, their neural response differs. Consistent with our hypotheses and predictions, infants’ left hemisphere showed significant response to high frequency nonwords (Fig. 1a, p < 0.05). Infants with better verbal ability had even stronger left hemisphere activation to high frequency condition. Conversely, adults’ left hemisphere responded to low frequency nonwords (Fig. 1b). Taken together, the findings suggest that by 9 months, infants’ left hemisphere becomes increasingly sensitive to high frequency properties of infants’ language, which likely relates to and prepares them for speaking their first words at around 12 months. Further learning is likely supported by a shift in sensitivity to more novel and less frequent patterns of one’s language.
Resting state fNIRS with awake infants and children

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Resting state analyses continue to be an area of interest in the fNIRS community due to their ease of use and ability to answer general questions about brain function that might not be tied to a particular task. These abilities are of particular interest to developmental neuroscience in order to index the maturing brain. However, doing resting state analyses with infants and children pose unique challenges due to the high degree of motion in these participants and their inability to comply with task instructions. Most prior resting state studies in these age groups have tested participants while they were sleeping, thus reducing motion artifact, although potentially also altering functional connectivity. We ask the question if it is possible to also do resting state functional connectivity analyses in awake babies and children, avoiding the problems inherent in trying to get infants and young children to sleep in a lab setting.

We present resting state data from two cohorts of children, an infant cohort and a child cohort. The participants in the infant cohort were 5-months-old (N=44) or 7-months-old (N=40) at the time of testing, and were recorded with simultaneous motion monitoring via accelerometer. The NIRS cap recorded brain activity over the frontal, temporal, and parietal cortices using a Hitachi ETG-400 NIRS system. The participants in the child cohort were 36-months-old (N=50) and recordings were over the bilateral temporal, frontal, and parietal cortices using a UCL 38-channel system. In both cohorts, data was recorded in awake participants during a 2-minute video of moving infant toys. Data was processed using wavelet motion correction and strict criteria for motion artifact rejection. Functional connectivity was assessed as correlations between pairs of channels in the 0.02-0.2 Hz frequency range (Figure 1).

Both local correlations and interhemispheric correlations between homologous regions were found. In conclusion, we show that it is possible to do resting state functional connectivity analyses with awake infants and children.

![Figure 1. Group mean results. Correlated channels (r>0.5) at 5 months, 7 months, and 36 months](image-url)
Differential activation during mental state reasoning in the right temporoparietal junction
Kimberly A. Brink, Lindsay C. Bowman, Xiaosu Hu, Henry M. Wellman

Theory of Mind (ToM) is the ability to reason about others’ mental states (e.g., thoughts, beliefs, desires and emotions). This ability is a critical component of social development that provides the foundation for children’s interactions with others and their social relationships across the lifespan. Research in adulthood has identified a set of brain structures associated with ToM reasoning tasks: a “ToM network” including the right temporoparietal junction (TPJ), MPFC and PC (Saxe, 2009). However, ToM reasoning in early childhood differs greatly from ToM reasoning in adulthood, emerging at about 3 years of age and increasing in complexity over early childhood (Wellman & Liu, 2004). Children’s ToM progresses such that, developmentally, children first demonstrate an ability to reason about others’ desires before they are able to reason about others’ beliefs. This progression has been hypothesized to be determined in part by maturation of structures in the ToM network (Bowman, Kovelman, Hu, & Wellman, 2015). Does activation in the ToM network vary according to ToM understanding? Will children demonstrate distinct activation patterns when reasoning about different mental states?

We utilized functional Near Infrared Spectroscopy (fNIRS) to compare activation patterns in one structure of the ToM network, the right TPJ. Specifically, we assessed whether activation differed when children reasoned about others’ beliefs compared to desires. 15 children, aged 7 to 9 years, performed a series of tasks (based on those in Bowman et al., 2015) where they made judgments about characters with differing desires (Diverse-Desires) or differing beliefs (Diverse-Beliefs) concerning a series of objects. As a control, they also made judgments about differing physical events (Diverse-Physical). In each trial, for each of the three conditions (Diverse-Desires, Diverse-Beliefs, Diverse-Physical), participants heard a female voice describe either (a) a boy and girl with diverse desires (e.g., the boy likes apples but the girl likes grapes), (b) a boy and girl with diverse beliefs (e.g., the boy thinks the box has apples but the girl thinks the box has grapes), or (c) two bins that each held different things (e.g., the red bin holds apples but the blue bin holds grapes). An item from the trial was then displayed and children received a target question in which they had to identify which character liked the object (Diverse-Desires), which character was correct about the object (Diverse-Beliefs), or where the object belonged (Diverse-Physical). Trials were presented in a block design by condition. Trials were presented in three runs of 10 experimental blocks (26 s per block). All three conditions were designed to have the same perceptual and linguistic structure, so that the only difference between conditions was the content of the questions and type of mental state reasoning.

Results showed greater activation in the right TPJ when children reasoned about beliefs compared to when children reasoned about desires or physical events. This study adds to the growing literature demonstrating that the right TPJ becomes increasingly selective for ToM reasoning as children mature and ToM develops.
Robustness of the general linear model to noise misspecification in fNIRS

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Rational: A General Linear Model (GLM) is generally used in order to investigate the hemodynamic response associated with specific neurocognitive events. Inference on the estimated response is carried out in order to assess its significance [1]. However, fNIRS residual noise rarely conform to the time-dependency statistical assumptions, due to the presence of different sources of nuisances, which may lead to wrong inference [2]. This study focuses on the relevance of the actual noise sampling distribution on statistical inference.

Methods: For a given ∆[Hb] channel, the GLM reads: \( y = X \beta + e \) with \( y \) being the \( L \) dimensional ∆[Hb] time course, \( X \) being the experimental design matrix consisting of \( p \) response covariates and \( \beta \) the unknown regression coefficients. \( e \) is the model noise and is supposed to be i.i.d and normally distributed. Under this assumption, the GLM can be solved simply using a maximum likelihood estimator for \( \beta \). For a given regression coefficient \( \hat{\beta}_i \) and under the null hypothesis (H0),

\[
t_i = \frac{\sqrt{(L-p)\hat{\beta}_i}}{\sqrt{\text{var} \hat{\beta}_i}} \]

should follow a student’s t distribution with \( L - p \) degree of freedom. In order to measure the robustness of this statistics with regard to the presence of temporal correlation in the data, we simulated 1000 white Gaussian, AR(1) or 1/f artificial time series (sampling frequency 5Hz, \( L = 2048 \)). We also simulated 1000 surrogate fNIRS data obtained using a time-frequency bootstrap of real ∆[HbO] time series obtained at rest on healthy subjects. To accommodate variability of the hemodynamic response, taking full benefit of the excellent temporal resolution offered by fNIRS data, the hemodynamic response function was modelled by a finite impulse response set of \( p = 176 \) basis. We simulated a stimulus sequence with 25 random onsets which was convoluted with the basis functions to form the design matrix. For each simulated dataset, we computed the corresponding t values under H0 and compared their distributions with the expected student’s t probability density function.

Results: Fig.1 shows that the normalized histograms of \( t_{25} \) (usually corresponding to the peak of a canonical HRF) were representative of the student’s t probability density function with 1872 degree of freedom. The statistical thresholds for H0 rejection at 95% (black dashed lines) were respectively at 1.35 for white Gaussian, AR(1) and 1/f dataset and at 1.05 for the real fNIRS dataset and were therefore close to the theoretical threshold at 1.65 (green vertical line). Conclusion: The estimator introduced in this study was shown to be essentially insensitive to the true noise structure of fNIRS data and will not increase the false positives detection rate. We intend to validate the robustness of different other estimators (e.g., generalized least square and maximum a posteriori under Bayesian formalism).

![Figure 1: Normalized histograms of \( t_{25} \) for the different noise sampling distributions together with the theoretical student’s t probability density function with 1872 degree of freedom (in green). Vertical lines represents the statistical thresholds for H0 rejection at 95% of significance classically used for inference.](image)

References: [1]: Tak et al; Statistical analysis of fNIRS data: a comprehensive review; Neuroimage 85. 2014
A model of hemoglobin phase of oxygenation and deoxygenation (hPod) in spontaneous neurovascular and metabolic activity

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Dynamic interaction among the neuro-vascular activity, blood flow and metabolism produces spontaneous low-frequency changes in oxy- and deoxy-hemoglobin (Hb) concentrations in the cerebral tissue, which can be measured by using fNIRS. Relative phase differences between oxy- and deoxy-Hb changes have been observed in adults (Hoshi & Tamura 1997; Obrig et al. 2000) and in infants (Taga et al. 2000). The phase difference exhibits developmental changes from an in-phase to anti-phase pattern in the first half of the first year of life (Taga et al. 2014) and is referred to as hemoglobin phase of oxygenation and deoxygenation (hPod) as an index of the neurovascular and metabolic development of the brain (Watanabe et al. submitted). Intermediate values of hPod between in- and anti-phase can result from the superposition of signals from arterioles, capillaries and venules (Fantini 2002; Boas et al. 2008). Detailed mechanisms that link neural activity to the hemodynamic and metabolic processes are incorporated in a recent modeling study (Kim & Ress 2016). In the present study, a dynamical system model for the spontaneous changes in the neuro-vascular and metabolic process is constructed. A previously proposed model for the hemodynamic and metabolic process (Diamond et al. 2009) is coupled with a neural dynamics model. Differential equations are numerically solved and the developmental changes in hPod values measured using fNIRS are simulated through exploration of parameter space. The result indicates that the developmental change in hPod value from in-phase to anti-phase can be accounted for by the development of the neurovascular coupling and capillary formation.

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