Cerebral Hemodynamics Measured by Near-Infrared Spectroscopy at Rest and During Motor Activation

Maria Angela Franceschini, Sergio Fantini

Bioengineering Center, Department of Electrical Engineering and Computer Science, Tufts University, 4 Colby Street, Medford, MA 02155, USA

mari@eecs.tufts.edu

Vlad Toronov, Mattia E. Filiaci, Enrico Gratton

Laboratory for Fluorescence Dynamics, Department of Physics, University of Illinois at Urbana-Champaign, 1110 West Green Street, Urbana, IL 61801, USA

Abstract: Near-infrared spectroscopy and imaging are powerful tools to detect and continuously monitor the cerebral hemodynamic and oxygenation changes induced by brain activity. However, in addition to the focal neuronal-activation-induced hemodynamic signals, near-infrared methods are also sensitive to the cerebral hemodynamic fluctuations of systemic origin associated, for instance, with the arterial pulse, respiration, and heart rate fluctuations. We have used near-infrared spectroscopy to non-invasively measure the cerebral hemodynamics in a human subject at rest. We have observed hemoglobin oscillations at the heart rate (~1 Hz), respiratory rate (~0.2 Hz), and at lower frequencies that are associated with heart rate fluctuations and vasomotion activity. With near-infrared imaging, we have measured the spatial maps of temporal changes in the cerebral oxy- and deoxy- hemoglobin concentrations during motor activity (hand tapping). We have found a more localized activation-induced response in the deoxy-hemoglobin map with respect to the oxy-hemoglobin map. This result can be explained by the observed synchronization between the sequence of tapping/rest periods and several systemic physiological oscillation such as the arterial pulse, respiration, and heart rate fluctuations.

OCIS codes: (170.0170) Medical optics and biotechnology; (170.3880) Medical and biological imaging; (170.0110) Imaging systems; (170.1470) Blood/tissue constituent monitoring

1. Introduction

The high sensitivity of near-infrared tissue spectroscopy to changes in the hemoglobin concentration (changes as small as 0.05-0.10 μM in tissues can be detected) affords the optical detection of small cerebral hemodynamic fluctuations. It has been shown that functional activity associated with motor or visual stimulation induces hemodynamic and oxygenation changes that can be detected with non-invasive optical methods [1-8]. Even under rest conditions, one can detect significant fluctuations in the optical signals from the brain, which may have an amplitude comparable with that of the signals evoked by functional activity [9]. The systemic arterial pulse oscillations (~1 Hz) are very evident and easy to recognize in optical signals [10-12]. Oscillations at the breathing frequency (0.2-0.3 Hz) are due to respiratory sinus arrhythmia and venous blood pooling during inspiration. Even though the general pattern of these oscillations is systemic, their amplitude and the corresponding saturation changes are local because of the spatial dependence of the tissue vascularization and oxygen consumption [13,14]. Vasomotion Traube-Hering and Mayer waves are caused by cyclic increases and decreases in arterial blood pressure and heart rate occurring at frequencies lower than the respiratory rate, in the range 0.05-

0.10 Hz. In the same frequency range, spontaneous fluctuations originated by local vasomotion can also occur [15]. Slower hemoglobin waves (frequency < 0.05 Hz) are associated with thermoregulation. Finally, aperiodic influences, including metabolic demand, can also contribute to changes in the optical signals.

We have used near-infrared spectroscopy to measure the cerebral hemodynamics in human subjects at rest and during motor stimulation (hand tapping). By measuring the optical signal at two wavelengths (758 and 830 nm), we have monitored the temporal changes of the cerebral concentrations of oxy-hemoglobin and deoxy-hemoglobin. The spatially resolved data acquired during motor activity shows a stronger localization of the deoxy-hemoglobin response with respect to the oxy-hemoglobin response. We discuss how a synchronization of the systemic hemodynamics with a periodic stimulation may explain this result.

2. Instrumentation and methods

We used the intensity data collected by a frequency-domain tissue spectrometer [16,17] (Model No. 96208, ISS, Inc., Champaign, IL). This instrument employs sixteen intensity-modulated laser diodes (eight emitting at 758 nm and eight at 830 nm) and two heterodyned photomultiplier tube detectors. All of the laser diodes and optical detectors are coupled to optical fibers. The source fibers are multimode silica fibers, 400 μm in core diameter, whereas the detector fibers are fiber bundles with an internal diameter of 3 mm. We have designed a helmet that can be comfortably secured on the head of the subject, and that keeps the source and detector optical fibers in contact with the skin. The sixteen source fibers (eight at 758 nm, and eight at 830 nm) and the two detector fibers were placed on the head according to the arrangement shown in Fig. 1. We have used a source-detector separation of 3.0 cm. The sixteen laser diodes are electronically multiplexed at a rate of 100 Hz (10 ms on-time per diode) to time-share the two parallel detectors. Consequently, the acquisition time for the whole series of 32 source-detector pairs is 160 ms. The average optical power delivered by each source fiber is a few mW.

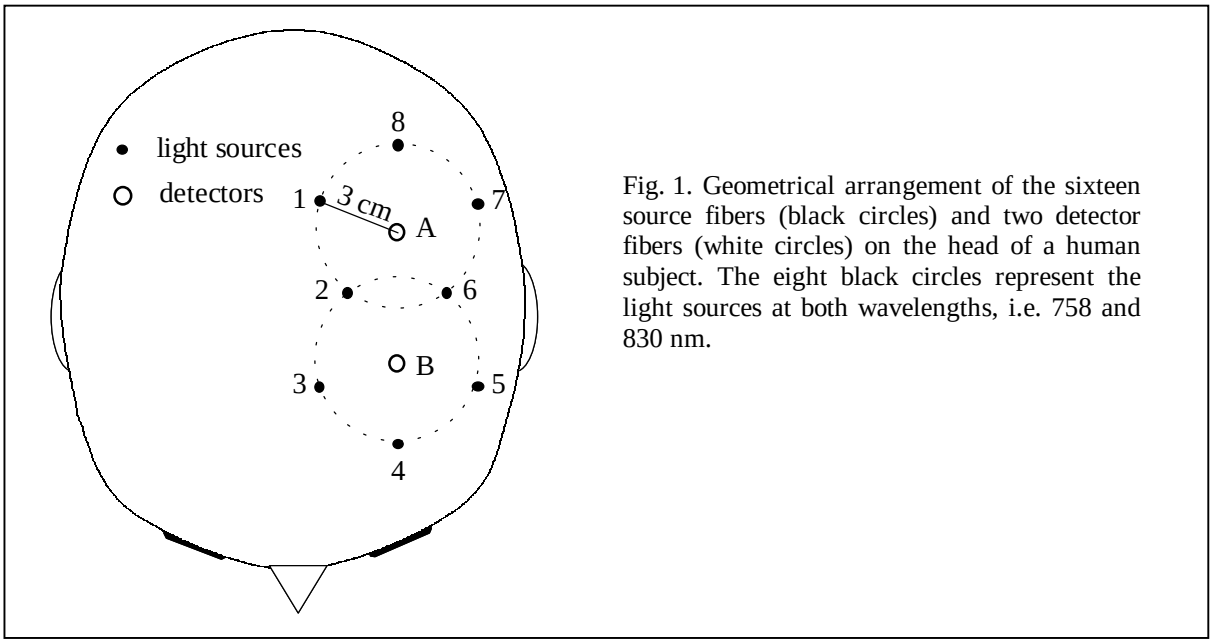

Fig. 1. Geometrical arrangement of the sixteen source fibers (black circles) and two detector fibers (white circles) on the head of a human subject. The eight black circles represent the light sources at both wavelengths, i.e. 758 and 830 nm.

In addition to the near-infrared spectrometer, we have used a pulse oximeter (Nellcor, N-200) to monitor the arterial pulse, the heart rate and the arterial saturation, and a strain gauge to monitor the respiration (Sleepmate/Newlife Technologies, Resp-EZ). The pulse oximeter was attached to a toe of the subject, while the strain gauge was placed around the chest. These monitoring devices were used simultaneously with the near-infrared tissue spectrometer, and their data outputs were recorded on a file together with the optical data.

The subject was a healthy 20-year old, right-handed, male volunteer. The measurement protocol consisted of an initial baseline measurement (10 min long) during which the subject was lying down comfortably in a dark and quiet room, without moving. After the baseline acquisition, we asked the subject to tap with his right hand for a period of 10 s followed by 17 s of rest. The 27-s long tapping/rest sequence was repeated ten times.

Our analysis considers the optical intensity acquired with a source-detector separation of 3.0 cm (20 source-detector pairs). We have translated the changes in the average intensity (with respect to the initial intensity) into changes in the absorption coefficient ($\Delta\mu_a$) using the differential-pathlength-factor (DPF) method [18]. We set the values of the DPF at two wavelengths (λ_1=758 nm and λ_2=830 nm) to 6.53 and 5.86, respectively, from literature data [19]. From the values of $\Delta\mu_a^{\lambda 1}$, and $\Delta\mu_a^{\lambda 2}$ we have obtained the temporal changes in the cerebral oxy-hemoglobin ($\Delta[HbO_2]$) and deoxy-hemoglobin ($\Delta[Hb]$). Since this approach to measuring changes in the cerebral oxy- and deoxy-hemoglobin concentrations relies on tissue homogeneity, we do not expect its results to be quantitatively accurate. However, we believe that the qualitative detection of the changes and their direction (increase vs. decrease) are reliable.

3. Results and discussion

3.1. Baseline cerebral hemodynamics

Under rest conditions, the cerebral concentrations of oxy- and deoxy-hemoglobin show significant oscillations at a number of characteristic frequencies. For example, Fig. 2 shows the power spectra of the optically detected cerebral $\Delta[HbO_2]$ and $\Delta[Hb]$ traces at rest. The comparison of the spectra of cerebral hemoglobin, arterial pulse, respiration wave, and heart rate (all acquired simultaneously with the spectra of cerebral hemoglobin) assigns the origin of most of the peaks in the spectra of $\Delta[HbO_2]$ and $\Delta[Hb]$. In particular, the low frequency (< 0.2 Hz) oscillations are mostly due to fluctuations in the heart rate, while respiration and arterial pulsation give rise to evident features in the hemoglobin spectra at the breathing (0.23 Hz) and heartbeat (1.06 Hz) frequencies, respectively. We observe that the amplitude of the fluctuations of the oxy-hemoglobin at rest is much larger than that of the deoxy-hemoglobin over the whole frequency-band examined. Furthermore, the spectral shape of $\Delta[HbO_2]$ closely matches that of the heart rate, indicating that the heart rate fluctuations have a stronger influence on $[HbO_2]$ than on [Hb].

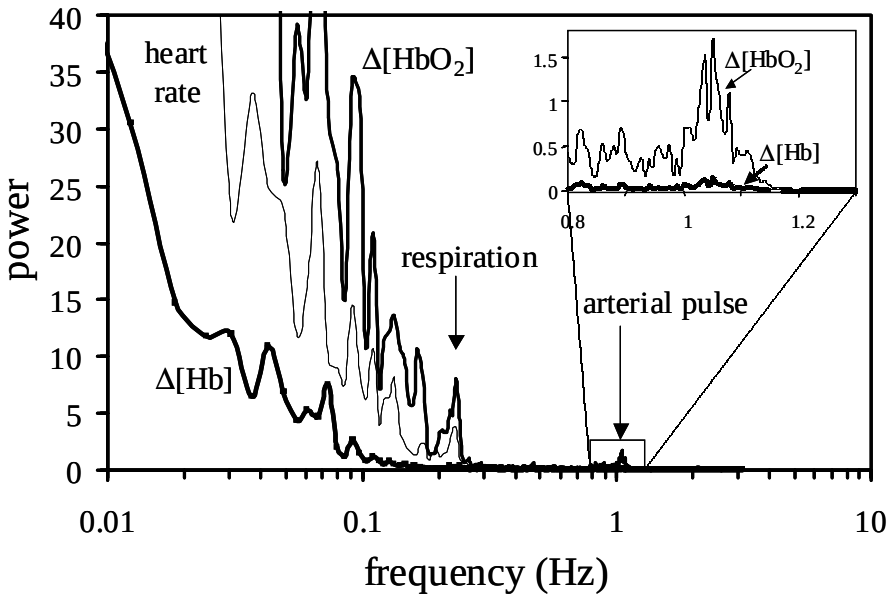

Fig. 2. Power spectra of baseline cerebral $\Delta[HbO_2]$ and $\Delta[Hb]$ (optically measured), and heart rate (measured on a subject's toe by a commercial pulse oximeter). The inset shows a magnified view of the arterial pulsation peak observed in the oxy- and deoxy-hemoglobin concentration spectra.

3.2. Evoked cerebral hemodynamics

During hand tapping, we have found that systemic rhythms such as heartbeat, respiration, and heart rate fluctuations can achieve a significant degree of synchronization with the periodic stimulation/rest sequence. This result is illustrated in Fig. 3 where the heart rate, arterial pulse, and respiration all show peaks at the stimulation fundamental frequency and its harmonics. The spectra of cerebral $\Delta[HbO_2]$ and $\Delta[Hb]$, which are also reported in Fig. 3, show a significant response to motor stimulation when measured at the motor cortex area (continuous lines). However, a measurement about 3 cm away (dashed lines) shows that only $\Delta[HbO_2]$, and not $\Delta[Hb]$, still gives a response at the stimulation frequency. The different spatial features of the responses of oxy-hemoglobin and deoxy-hemoglobin to motor stimulation are further illustrated in Fig. 4. In Fig. 4, we report the traces obtained from a folding average procedure, where the ten stimulation/rest sequences are averaged together to yield an average response. The ten panels of Fig. 4 report the data collected by each of the ten source-detector pairs considered by us, namely 1A, 2A, 6A, 7A, 8A, and 2B, 3B, 4B, 5B, 6B. The locations of the sources and detectors are also illustrated in Fig. 4. A significant deoxy-hemoglobin response (decrease of [Hb] during stimulation) is confined to the area probed by source-detector pairs 2B, 3B, and 6B. By contrast, the oxy-hemoglobin concentration shows a significant stimulation-induced increase over the whole probed area. The largest oxy-hemoglobin response occurs over an area that overlaps with the area showing a deoxy-hemoglobin response. We believe that the de-localized oxy-hemoglobin response can be attributed to the synchronization between systemic fluctuations (heart rate, arterial pulse, respiration) and the motor stimulation sequence. In fact, these systemic fluctuations, and in particular the heart rate (beats/min), affect the cerebral $\Delta[HbO_2]$ to a larger extent that $\Delta[Hb]$ (see Fig. 2).

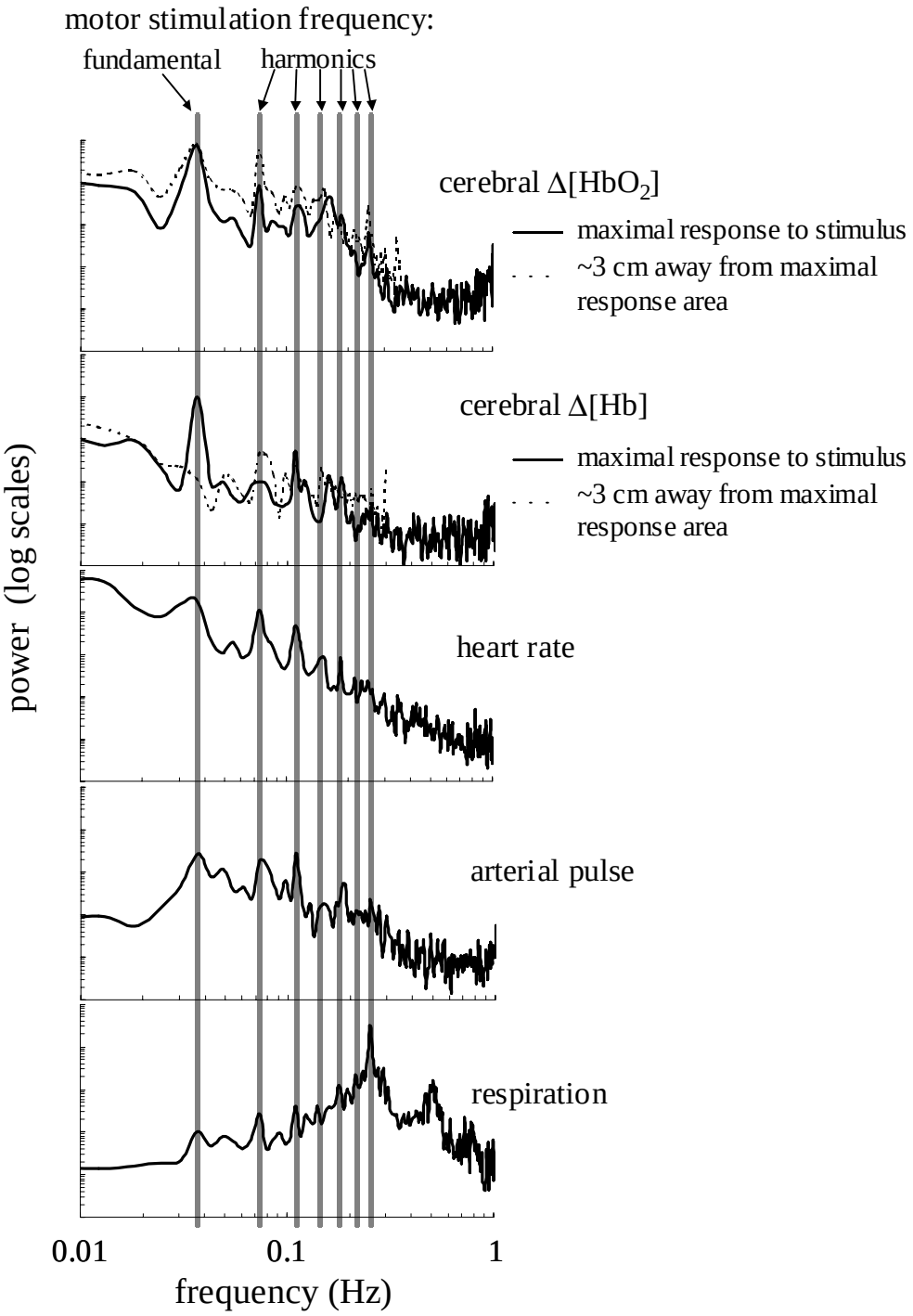

Fig. 3. Power spectra of cerebral $\Delta[HbO_2]$ and $\Delta[Hb]$, heart rate, arterial pulse, and respiration signal, during motor stimulation (hand tapping) at a frequency of 0.037 Hz. The fundamental stimulation frequency (0.037 Hz) and its harmonics are indicated by vertical lines. The continuous lines in the $\Delta[HbO_2]$ and $\Delta[Hb]$ spectra (collected where the deoxy-hemoglobin response to the stimulus was maximal) have been acquired with source-detector pair 6B (see Fig. 1), while the dashed lines correspond to source-detector pair 2A (see Fig. 1).

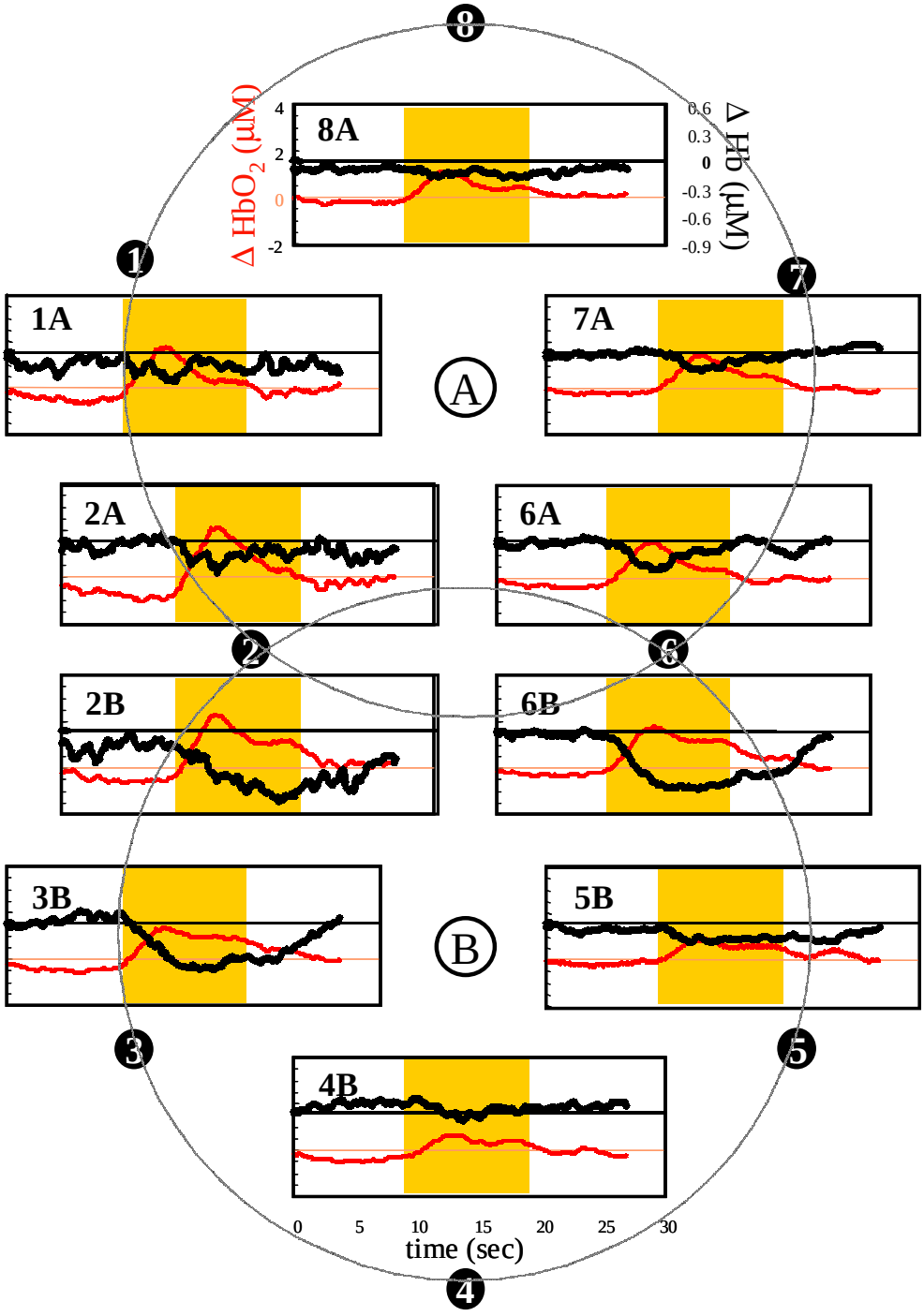

Fig. 4. Results of the folding average analysis of the $\Delta[HbO_2]$ (thin lines)and $\Delta[Hb]$ (thick lines) temporal traces measured on the motor cortex contralateral to the tapping hand. The left and right y-axes labels (shown in the top panel) are the same for all the panels. The shaded areas represent the tapping periods. The black numbered circles represent the source locations (as in Fig. 1), and the two white circles labeled A and B represent the detector locations (as in Fig. 1).

4. Conclusion

Cerebral hemodynamics is affected by systemic physiological rhythms, such as heartbeat and respiration, and by temporal fluctuations in the heart rate (beats/min). Some of these systemic rhythms and fluctuations may synchronize with a sequence of motor task/rest periods in a motor stimulation protocol. Under these synchronization conditions, the apparent cerebral hemodynamic response to motor stimulation will consist of two components, one of systemic and one of focal origin. Because in addition to the arterial pulsation, there are indications that also other systemic fluctuations have a stronger effect on the oxy- than on the deoxy-hemoglobin concentration (see Fig. 2), the systemic component may determine a de-localized oxy-hemoglobin cerebral map during motor stimulation. In this article, we have reported one such case, where the activation-induced decrease in cerebral [Hb] is significantly more localized than the corresponding increase in cerebral [HbO_2] (see Fig. 4).

Acknowledgments

This research is supported in part by the US National Institutes of Health Grant No. CA57032.

References

1. A. Villringer, J. Planck, C. Hock, L. Schleinkofer, and U. Dirnagl, "Near Infrared Spectroscopy (NIRS): A New Tool to Study Hemodynamic Changes During Activation of Brain Function in Human Adults," Neurosci. Lett. **154**, 101-104 (1993).
2. A. Maki, Y. Yamashita, Y. Ito, E. Watanabe, Y. Mayanagi, and H. Koizumi, "Spatial and Temporal Analysis of Human Motor Activity Using Noninvasive NIR Topography," Med. Phys. **22**, 1997-2005 (1995).
3. G. Gratton, M. Fabiani, D. Friedman, M. A. Franceschini, S. Fantini, P. M. Corballis, and E. Gratton, "Rapid Changes of Optical Parameters in the Human Brain During a Tapping Task," J. Cognitive Neuroscience **7**, 446-456 (1995).
4. H. Obrig, C. Hirth, J. G. Junge-Hülsing, C. Döge, T. Wolf, U. Dirnagl, and A. Villringer, "Cerebral Oxygenation Changes in Response to Motor Stimulation," J Appl. Physiol. **81**, 1174-1183 (1996).
5. T. Kato, A. Kamei, S. Takashima, and T. Ozaki, "Human Visual Cortical Function During Photic Stimulation Monitoring by Means of Near-Infrared Spectroscopy," J Cereb. Blood Flow Metab. **13**, 516-520 (1993).
6. J. H. Meek, C. E. Elwell, M. J. Khan, J. Romaya, J. S. Wyatt, D. T. Delpy, and S. Zeki, "Regional Changes in Cerebral Haemodynamics as a Result of a Visual Stimulus Measured by Near Infrared Spectroscopy," Proc. R. Soc. Lond. B Biol. Sci. **261**, 351-356 (1995).
7. H. R. Heekeren, H. Obrig, H. Wenzel, R. Eberle, J. Ruben, K. Villringer, R. Kurth and A. Villringer, "Cerebral Haemoglobin Oxygenation During Substained Visual Stimulation – a Near-Infrared Spectroscopy Study," Philos. Trans. R. Soc. Lond. B Biol. Sci. **352**, 743-750 (1997).
8. M. A. Franceschini, V. Toronov, M. E. Filiaci, E. Gratton, and S. Fantini, "On-Line Optical Imaging of the Human Brain with 160-ms Temporal Resolution," Opt. Express **6**, 49-57 (2000)

9. Y. Hoshi, and M. Tamura, “Fluctuations in the Cerebral Oxygenation State During the Resting Period in Functional Mapping Studies of the Human Brain,” Med. Biol. Eng. Comput. **35**, 328-330 (1997).

10. M. A. Franceschini, S. Fantini, and E. Gratton, “LEDs in Frequency Domain Spectroscopy of Tissues,” Proc. SPIE **2135**, 300-306 (1994).

11. G. Gratton, and P. M. Corballis, “Removing the Heart from the Brain: Compensation for the Pulse Artifact in the Photon Migration Signal,” Psychophysiology **32**, 292-299 (1995).

12. C. Nolte, M. Kohl, U. Scholz, M. Weih, and A. Villringer, “Characterization of the Pulse Signal over the Human Head by Near Infrared Spectroscopy,” Adv. Exp. Med. Biol. **454**, 115-123 (1998).

13. C. E. Elwell, H. Owen-Reece, M. Cope, A. D. Edwards, J. S. Wyatt, E. O. R. Reynolds, and D. T. Delpy, “Measurement of Changes in Cerebral Haemodynamic During Inspiration and Expiration Using Near Infrared Spectroscopy,” Adv. Exp. Med. Biol. **388**, 619-626 (1994).

14. M. Wolf, G. Duc, M. Keel, and P. Niederer, “Continuous Noninvasive Measurement of Cerebral Arterial and Venous Oxygen Saturation at the Bedside in Mechanically Ventilated Neonates,” Crit. Care Med. **9**, 1579-1582 (1997).

15. A. G. Hudetz, B. B. Biswal, H. Shen, K. K. Lauer, and J. P. Kampine, “Spontaneous Fluctuations in Cerebral Oxygen Supply. An Introduction,” Adv. Exp. Med. Biol. **454**, 551-559 (1998).

16. S. Fantini, M. A. Franceschini, J. S. Maier, S. A. Walker, B. Barbieri, and E. Gratton, “Frequency-Domain Multichannel Optical Detector for Non-Invasive Tissue Spectroscopy and Oximetry,” Opt. Eng. **34**, 32-42 (1995).

17. M. A. Franceschini, D. Wallace, B. Barbieri, S. Fantini, W. W. Mantulin, S. Pratesi, G. P. Donzelli, and E. Gratton, “Optical Study of the Skeletal Muscle During Exercise with a Second Generation Frequency-Domain Tissue Oximeter,” Proc. SPIE **2979**, 807-814 (1997).

18. M. Cope and D. T. Delpy, “System for Long-Term Measurement of Cerebral Blood and Tissue Oxygenation on Newborn Infants by Near Infrared Transillumination,” Med. Biol. Eng. Comput. **26**, 289-294 (1988).

19. A. Duncan, J. H. Meek, M. Clemence, C. E. Elwell, L. Tyszczuk, M. Cope, and D. T. Delpy, “Optical Pathlenght Measurements on Adult Head, Calf and Forearm and the Head of the Newborn Infant Using Phase Resolved Optical Spectroscopy,” Phys. Med. Biol. **40**, 295-304 (1995).