

191 W-AM

Cortically Constrained Spectral Imaging of Lorazepam Modulation of Spontaneous Activity

Jyrki Ahveninen¹, Fa-Hsuan Lin¹, Reetta Kivisaari², Taina Autti², Matti Hämäläinen¹, S. Stufflebeam¹, John W Belliveau¹, Seppo Kähkönen^{3,4,5}

¹MGH/MIT/Harvard Medical School - Athinoula A. Martinos Center for Biomedical Imaging, Boston, MA, USA, ²Department of Radiology, Helsinki University Central Hospital, FINLAND

³Cognitive Brain Research Unit, Department of Psychology, University of Helsinki, FINLAND

⁴BioMag Laboratory, Engineering Centre, Helsinki University Central Hospital, Helsinki, FINLAND, ⁵Helsinki Brain Research Centre, Helsinki, FINLAND

Background

Neuropharmacological studies of spontaneous brain oscillations are complicated by MEG/EEG source-localization difficulties. A non-invasive method to estimate MEG power sources directly on the cortical surface utilizing anatomical MRI constraints was recently described [1]. We use this method, combining a cortically constrained minimum norm estimate [2] and spectral analysis employing complex Morlet wavelets [3], to localize the cortical effects of the GABA-A-agonist benzodiazepine *lorazepam* on spontaneous brain oscillations.

Methods

To localize cortical effects of lorazepam (30 micrograms/kg *i.v.*) on spontaneous brain rhythms, healthy subjects were measured with 306-channel MEG in a double-blind, randomized, placebo-controlled (saline), crossover design. For anatomically-realistic source modeling, wavelet-transformed MEG data was combined with high-resolution MRI to constrain the current locations to the cortical surfaces [1], after which the individual data were spatially normalized to a cortical surface-based coordinate system [4] for the calculation of group statistical parametric maps of drug effects. Additionally, we identified two regions-of-interest (ROI) per hemisphere, the calcarine sulcus and the parieto-occipital sulcus, using an automatic cortical parcellation algorithm [5], to confirm the group effects of lorazepam.

Results

According to our cortically-constrained MEG source estimates, lorazepam decreased alpha activity in and around the parieto-occipital sulcus and in the calcarine sulcus of the occipital lobe (**Figure 1**). The group statistics, calculated in the spherical standard space, were supported by ROI analysis (two-way Friedman ANOVA), suggesting that lorazepam reduced the eyes-closed/eyes-open ratio of alpha-band power in the right ($\chi^2=8.3$, $P<0.05$) and left medial occipital ($\chi^2=9.5$, $P<0.05$).

Discussion

The decrease of alpha activity by the GABA-A-agonist lorazepam is consistent with previous observations. However, few prior studies have modeled human pharmacodynamics utilizing MEG source localization, guided by the subjects' individual anatomy. The group analysis in spherically-registered standard space [4], showing cortical drug effects as group statistics, indicated the strongest alpha attenuation in the upper banks of the calcarine sulcus, and in and around the occipital sulcus. Our anatomically-constrained spectral imaging may provide a powerful tool for human neuropharmacology.

Acknowledgements

Supported by the NIH Grants R01 HD040712, R01 NS037462, and P41 RR14075, the National Center for Research Resources, the MIND institute, and the Academy of Finland.

References

1. Lin & al. (2004) *Neuroimage* **23**:582-95.
2. Dale & al. (2000) *Neuron* **26**:55-67.
3. Tallon-Baudry & Bertrand (1999) *Trends Cogn Sci* **3**:151-162.
4. Fischl & al. (1999) *Hum Brain Mapp* **8**:272-84.
5. Fischl & al. (2004) *Cereb Cortex* **14**:11-22.

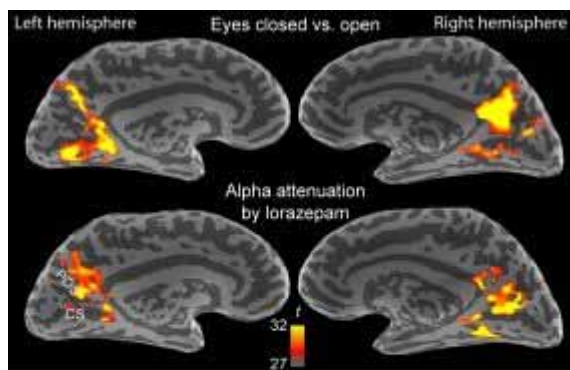


Figure 1. Group SPMs, shown on the medial inflated cortical surfaces of one subject. **(Top)** The main contrast of alpha band-power between eyes closed vs. open. **(Bottom)** The cortical sources of maximal alpha band-power attenuation by lorazepam. (Abbreviations: CS, calcarine sulcus; POS, parieto-occipital sulcus).