

## Coupling between resting cerebral perfusion and EEG power

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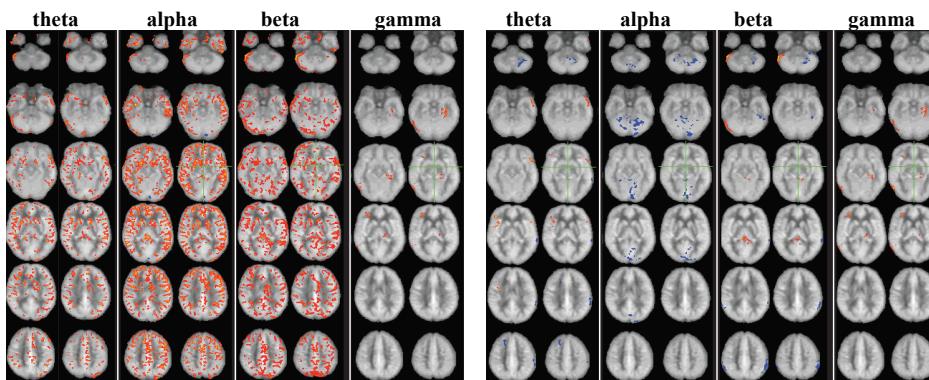
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**Introduction:** Since the cellular mechanism underlying the electroencephalography (EEG) signal requires the metabolism of glucose and an abundant supply of oxygen, the measured EEG signal is assumed to be closely related to the underlying spatio-temporal pattern of metabolism and perfusion, but the relationship between EEG and metabolic/haemodynamic activity has not yet been fully established. Recent studies have uncovered a strong association between spontaneous fluctuations in cerebral blood flow and blood oxygen level dependent (BOLD) signal and EEG activity<sup>1</sup>, and between arteriolar diameter changes and evoked neural responses,<sup>2</sup> indicative of a tight neurovascular coupling between spontaneous fluctuations in electrical and haemodynamic activity. However, one general observation from various EEG-fMRI studies is that peak EEG power values in lower (theta: 4-7 Hz) and middle (alpha, 8-13 Hz) frequencies are negatively coupled to the BOLD signal,<sup>3</sup> although both positive and negative associations have been reported between alpha power and baseline human rCBF or cerebral glucose metabolism (GluM) as measured by positron emission tomography (PET).<sup>4-5</sup> In this study we examine the relationship between resting EEG power fluctuations in low, medium, and high frequency bands and resting cerebral perfusion using whole brain ASL in a group of healthy adults.

**Methods:** The subject group consisted of 12 healthy right-handed volunteers (6 female, age range 25-38) with no history of neurological or psychiatric illness. Resting-state EEG data were acquired outside the MRI scanner from 60 scalp electrodes during an eyes closed rest condition. Data were sampled at 500 Hz, and bandpass filtered from 0.1 to 250 Hz. EEG processing was performed using BrainVision Analyzer (Brain Products, Munich, Germany). The Global Spectral Power (GSP) was calculated as the root mean square across all Fast Fourier-transformed (Hanning window: 10%, zero padded, resolution 0.25 Hz) scalp channels. For the subsequent EEG-ASL correlation analysis the EEG data were log-transformed, and the peak log-transformed band power was calculated for the theta (4-7 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-48 Hz) bands. MR imaging was performed with a 3.0 T GE HD.xt MRI scanner (GE Healthcare, Milwaukee, WI, USA), using an 8-channel receive-only head coil. Cerebral perfusion images were collected during an eyes closed rest condition with a background-suppressed, pulsed continuous arterial spin labelling (pCASL) sequence, using a 3D stack of spirals fast spin echo readout.<sup>6</sup> 32 axial slices were collected with TR=5.5 s, TE=25 ms, FOV= 24 cm, and an effective in-plane resolution of 1.9x1.9mm<sup>2</sup>. The MRI and EEG were acquired in different measurement sessions, either consecutively (n=6) or on a different day (n=6). The relationship between perfusion and maximum GSP was tested for each frequency band by fitting a multiple linear regression model onto the perfusion values at each intracerebral voxel, using the permutation-based methods implemented in the Cambridge Brain Analysis (CamBA) software.<sup>7</sup>

**Results:** Highly significant positive correlations (across subjects) emerged between perfusion and EEG power in low (theta: 4-7 Hz), middle (alpha: 8-13 Hz), and high (beta: 13-30 and gamma: 30-48 Hz) frequency bands across a widespread network including both cortical and sub-cortical regions. The average whole-brain perfusion was also significantly correlated to the peak EEG power in the theta, alpha, and beta bands ( $p<0.05$ , 2-tailed) and showed a strong trend towards a correlation with peak power in the gamma band ( $p=0.08$ , 2-tailed). The strong positive correlations between perfusion and EEG power remained when age and gender were included as covariates in the regression model. When the whole-brain perfusion was included as a covariate, positive correlations remained between peak gamma power and perfusion in frontal, thalamic, and parahippocampal regions and negative correlations emerged between peak alpha power and perfusion in cerebellar and occipital regions.

**Figure 1:** Perfusion images from the EEG-ASL correlation analysis, with clusters demonstrating a significant positive correlation between perfusion and peak EEG power overlaid in red and clusters demonstrating a significant inverse correlation overlaid in blue. Left: absolute perfusion vs EEG power (not covarying for whole brain perfusion). Right: relative perfusion vs EEG power (covarying for whole-brain perfusion).  $p < 0.005$ , FWE corrected.



**Discussion:** The positive correlation seen between perfusion and peak EEG power is consistent with data from previous animal studies demonstrating a positive association between spontaneous fluctuations in EEG amplitude and cerebral blood flow.<sup>1-2</sup> These results are also consistent with the observed inverse correlations between alpha power and BOLD, if subjects with higher resting perfusion show a smaller change in perfusion (and smaller BOLD signal). The basis for the discrepancy between these results and

those from some PET studies reporting inverse correlations between perfusion or metabolism and alpha power<sup>4,8</sup> remains unclear, but may be related to the method or reference region used for PET calibration as an alternative to arterial sampling. Future studies incorporating simultaneous EEG-ASL/BOLD both at rest and during a task may be able to further elucidate the neurovascular coupling between electrical and haemodynamic activity.

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