The modulation of 7.0T spontaneous blood-oxygenation-level-dependent (BOLD) signal by the behavioral state

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Introduction. Spontaneous BOLD signal fluctuations, in the absence of specific cognitive tasks, are increasingly being used to identify spatial regions of functional connectivity [1]. This approach is especially promising in clinical scenarios where inadequate patient compliance prevents the administration of many tasks or stimuli. However, limited quantitative evidence is available on how spontaneous activity is modulated by behavioral state [2,3]. It was recently shown that in visual cortex (VC), both coherence and amplitude of spontaneous signal exhibited an inverse correlation with wakefulness [3]. Here, we examine the dependence of spontaneous BOLD signal on behavioral state in another highly studied brain region, the motor cortex (MC), by performing BOLD for varying degrees of wakefulness and motor performance. Data were acquired at 7.0T and high spatial resolution. The findings demonstrate how MC spontaneous activity is dependent on behavioral state, with implications for both spontaneous and evoked BOLD experiments discussed.

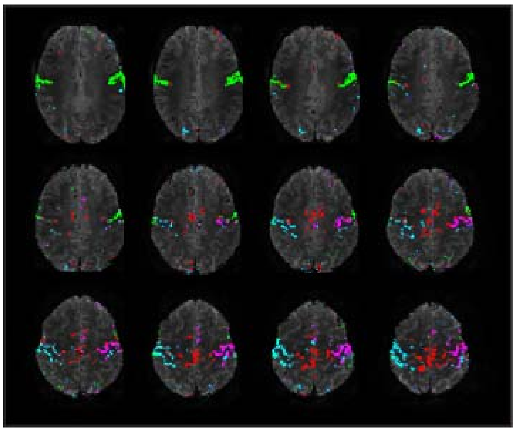

Fig. 1. 7.0T motor sub-networks.

Methods. All volunteers (n=7; age=25.6±4.2 yrs) provided informed consent and we scanned at 7.0T (Philips). *Experiment.* Four separate behavioral states were studied for each volunteer, during which cardiac and respiratory rate were recorded: (1) awake with eyes closed (EC), (2) eyes open resting (EO), (3) eyes open with constant right hand fist clench (EO-F), and (4) eyes open 6s/6s off/on (frequency=0.083 Hz) right-handed finger tapping (EO-T). For each condition, a BOLD scan was performed with RF volume coil transmit and 16-channel head coil receive; scan parameters: gradient echo EPI, FOV=216x192 mm^2, slices=33, SENSE=3.0, TR/TE=3000/25 ms, spatial resolution=1.6x1.6x1.6 mm^3, time points=100. Prior to the BOLD scans, a whole brain B_0 map was acquired which was used for 3rd order Image Based Shimming after brain extraction using BET [4]. *Pre-processing.* All images were corrected for motion, baseline drift and were coregistered using FSL routines [5]; retrospective correction for cardiac and respiratory motion was applied [6]. No spatial smoothing was applied. *Processing.* First, to characterize evoked responses, BOLD finger tapping data were high-pass filtered (removing<0.083 Hz) and evoked activation maps (z>5.0) and corresponding timecourses recorded. Second, all data were variance-normalized and a 50-component and 30-component ICA decomposition was performed [7]. The 50-component decomposition was used for assessing MC sub-network detectability at 7.0T and the 30-component analysis for MC mask generation. Specifically, a mask was generated for voxels showing coherence in primary MC for all behavioral states. The choice of the appropriate independent component was guided by the Juelich Histological Atlas of the MC. The evoked mask was subtracted from this MC mask and a new 'other' mask was generated which corresponded to regions of MC that were not involved in evoked activity. Third, all data were low-pass filtered at 0.067 Hz to remove contributions from the 0.083 Hz evoked activity in EO-T condition and to allow for uniform pre-processing in all data. Fourth, coherence, (measured as Pearson correlation coefficient, r) and amplitude (measured as std over time) of the spontaneous signal were calculated by comparing low-pass filtered timecourses from the evoked mask to those from the 'other' mask for each behavioral state. The same evoked mask and other mask was used for all behavioral states for each subject.

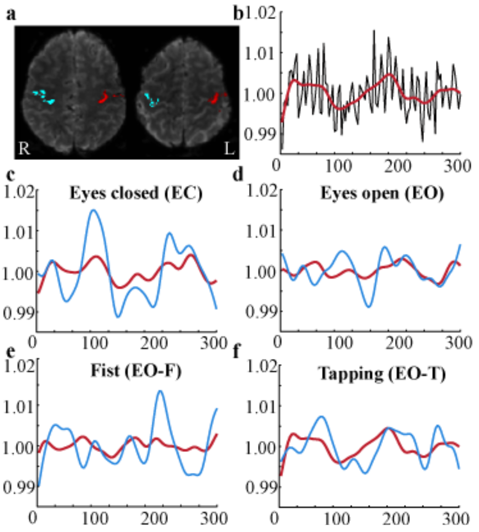

Fig. 2. Behavioral state analysis approach.

Results. Fig. 1 shows four motor sub-networks (green, blue, purple, red) from the 50-component ICA decomposition for a single subject. MC is clearly visible and sub-networks within the MC can be discerned on an individual subject basis. Such robust detectability is likely due to a combination of higher SNR and higher physiological noise to thermal noise ratio at 7.0T, relative to 1.5T-3.0T. Fig. 2a shows two slices, from a representative subject, containing the evoked mask (red) and other mask (blue) which were used for the correlation and amplitude analysis. Fig. 2b (signal vs. time) shows the EO-T timecourse (black); high frequency finger tapping, which was subsequently removed by low-pass filtering (red) is clearly visible. Fig. 2c-f shows representative evoked mask (red) and other mask (blue) timecourses (signal vs. time) for a representative subject for each behavioral condition. The EC task contains the highest coherence, with the other three behavioral states showing reductions in coherence. Fig. 3 shows group results (* denotes P<0.05 compared with EC). During EC, coherence is highest; coherence is lower, but not significantly reduced for EO (P=0.15), whereas coherence is significantly reduced relative to EC for both EO-F (P=0.04) and EO-T (P=0.01). A similar, yet less robust trend, is found for the amplitude analysis (Fig. 3b). For the amplitude comparison, only EO-T is significantly different (P=0.01) from EC amplitude.

Discussion. Reduction in coherence of eyes open tasks, and the reduction in amplitude of EO-T, relative to the eyes closed condition, supports the proposition that spontaneous activity in MC is influenced by behavioral state. Similar findings have been observed in VC using BOLD [3] as well as EEG [8] and reveals that spontaneous fluctuations are suppressed during task performance, relative to EC. We find only a small reduction in amplitude during the eyes open conditions, suggesting that coherence in MC may be more sensitive to behavioral state than amplitude. Evoked fMRI analyses may benefit by incorporating adjustments in spontaneous activity between task and baseline; methods for accounting for such effects have been proposed [9]. Finally, we investigated different approaches for generating the MC mask, which included atlas-guided ROIs and masks derived from different z-score thresholds. We found similar results regardless of MC mask choice, however observed dissimilar trends when masks from different functional networks were compared (e.g. coherence between MC and VC for different behavioral states). Understanding how inter-network coherences are influenced by behavioral state may therefore be of interest. In conclusion, (1) we exploit the high SNR available at 7.0T to demonstrate that cortical sub-networks can be identified in MC on an individual subject basis and (2) spontaneous activity in MC, as quantified by coherence and amplitude, is dependent on the behavioral state.

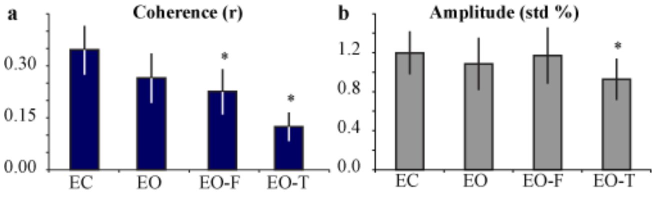

Fig. 3. Group (n=7) coherence and amplitude results.

References. [1] Fox MD et al. Nat Rev Neurosci (2007);8. [2] Hampson M et al. Hum. Brain Mapp (2002);15. [3] Bianciardi M et al. Neuroimage (2009);45. [4] Smith SM. HBM (2002);17. [5] Jenkinson M et al. Neuroimage (2002);17. [6] Glover GH et al. MRM (2000);44 [7] Beckmann CF and Smith SM. IEEE (2004);23. [8] Buzsaki G and Draguhn A. Science (2004);304. [9] de Zwart et al. MRM (2008);59.

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