Reducing the error: Regional effects of HRF basis functions on EEG-microstate informed fMRI

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Introduction: Microstates are stable topographic configurations for around 100 ms derived from neuronal signals captured by EEG[1]. The time course of such states have been successfully used in fMRI analysis to identify resting-state networks[1,2] and topographic mapping of the thalamic nuclei[3]. In such analyses, microstate fluctuations are convolved with the canonical HRF and used as a parametric predictor in the GLM. However, it is unclear to whether the classical canonical HRF is the best approach to study the association between microstates and hemodynamic response. In the present work, we aimed to compare two sets of HRFs for microstate-informed resting-state fMRI analysis: the standard canonical HRF (CA), and the HRFs extended by the two derivatives (CA+). We tested the hypothesis that the extended model CA+ including the temporal and dispersion derivatives that account for inter-subject and regional variability (+/- 1 second) in the BOLD signal may have a positive effect on residual reduction in microstate-informed fMRI analysis on distinct brain regions.

Methods: We reanalyzed a data-set already published in our previous study[4]. Fourteen healthy subjects (6f/8m, mean age 26±2.7 years) underwent simultaneous EEG/fMRI in a no-task condition with eyes closed and not falling asleep (resting state). All subjects were measured in the morning and had no caffeine, nicotine or alcohol 10 hours prior to the experiment. They had no history of neurological or psychiatric disease and were free from illegal drugs or psychoactive medication. MRI data were acquired with a 3T Siemens Magnetom Trio, functional data using a EPI sequence (252 volumes, 32 slices, 3x3x3 mm3, gap thickness 0.75 mm, matrix size 64x64, FOV 192x192 mm2, TR/TE 1980ms/30ms. EEG data were acquired with a 96 channel MR compatible system (Brain Products, Gilching, Germany). Preprocessing of fMRI data included slice-time and motion correction, co-registration to anatomical data, normalization to standard Talairach space, and smoothing (8 mm FWHM). EEG preprocessing included RF-artifact correction using averaged artifact subtraction and ballistocardiogram correction by ICA. EEG time courses were then downsampled to 100Hz, and filtered between 1-20Hz and epochs exhibiting artifacts (eyes, muscles) were removed. The EEG was then subjected to a Topographic Time-Frequency Decomposition algorithm[5] that decomposed the EEG into 6 classes of transient states of synchronized oscillations. For each subject, the BOLD response was predicted by using 2 different HRF models on the 48 microstate timecourses (total GLMs per subject: 2 models x 6 classes x 8 frequency bands). The first model involved microstate time series convolved with the canonical HRF (CA), while the second model (CA+) involved microstate time series convolved with three basis functions (the canonical HRF and two derivatives). We also included head motion parameters and dummy regressors corresponding to periods where EEG microstates were not calculated due to artifacts. All GLMs were performed in SPM8. We subtracted residual images (mean square error) from both models (CA – CA+) showing the difference of the two models with the magnitude proportional to the advantage of CA+ over the CA and created a median image for each subject. For nonparametric group analysis (SnPM8) the one-sample t-test was performed on the residual differences images (14 images) to test against the null hypothesis of zero difference between models.

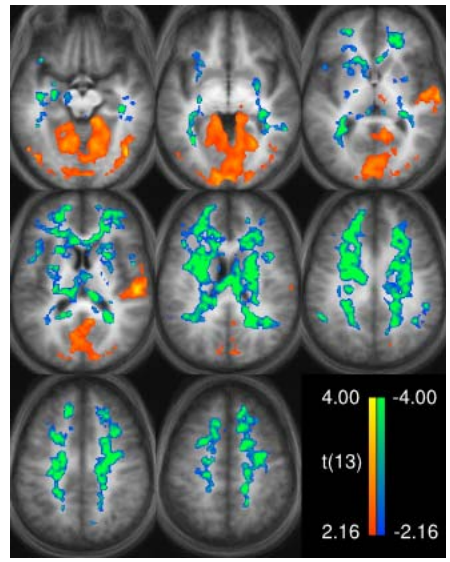

Fig. 1: t-Maps ($p < .05$, uncorr., df=13) show residual differences in favor for CA+ in visual and right auditory regions (red) across subjects (N=14). Negative effects occur mainly in white matter.

Results: We have found that the model with the canonical HRF and its temporal and dispersion derivatives (CA+) shows significantly lower residuals in visual and right auditory areas across subjects. Global mean residual difference of the significant voxels of the visual and right auditory cortex across all subjects was 0.01 (SD=0.02), while mean local maxima in the selected areas across subjects were 0.13 (SD=0.12).

Discussion: The results suggest that EEG-microstate-informed fMRI analysis can benefit by extending the classical canonical HRF model in order to elucidate comprehensive association between microstates and hemodynamic response and to reduce residual error of the BOLD response estimates. Albeit the global mean residual difference along entire visual and right auditory areas and along subjects is very small, mean local maximum values show significant large differences in specific voxels, suggesting that residual reduction is more likely to be regionally observed at the subject level, and to a lesser degree as a group level effect. These findings provide further support that the canonical HRF may be insufficient to explain variation of BOLD responses across brain regions and subjects. However, further investigation is needed to reduce residuals by using more flexible HRF models.

References: 1) Van de Ville D, et al. PNAS. 2010;107(42):18179–18184. 2) Britz, J, et al. Neuroimage. 2010;52(4):1162–1170. 3) Schwab, S, et al. Proc. Intl. Soc. Mag. Reson. Med. 2013; 21:3246. 4) Jann, K, et al. PLoS One. 2010;5(9):e12945. 5) Koenig, T, et al. Neuroimage. 2001;14(2):383–390.