Stimulus induced modulation of low frequency fluctuations in BOLD fMRI of the rat

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Introduction: Low frequency fluctuations (LFFs) in T2*-weighted MR images have been observed in humans as well as rats [1, 2, 3]. Although previous studies explore the effect of task/stimulation on functional connectivity (FC) maps created from LFFs (e.g. [4]), the effect of stimulation on LFFs has not been explored. In this study, the amplitude of the LFFs before and during continuous somatosensory stimulation was examined. Stimulation reduced power of LFFs in the corresponding area in the primary somatosensory cortex (SI) as well as the contralateral cortical region 'functionally connected' with the stimulated cortex. This finding suggests that LFFs are altered in response to neural activity.

Methods: Imaging was performed on 9.4T Bruker scanner. The rats (n = 5) were sedated using medetomidine as described in [3]. An electrical stimulation paradigm (left forepaw) was used to detect the slice containing activated pixels in right SI (set of activated voxels is abbreviated as SI_ipsi). The same slice geometry was used for the rest of the scans. Time-series of gradient-echo EPI images were acquired either without stimulation (NoStim) or with continuous stimulation of left forepaw (Stim) with following parameters: TR = 100 ms, TE =20 ms, matrix size = 64x64, in-plane resolution = 300 microns, slice thickness = 1 mm, number of repetitions = 1200-1500. The scans were acquired in one of the following orders for each rat: 1) NoStim-Stim-Stim-NoStim 2) Stim-NoStim-NoStim-Stim. ~30-60s gap was placed between scans after switching the condition in order to avoid transient effects. Thus four RS scans were acquired for each rat, 2 for each condition. The area in contralateral (left) SI showing high connectivity with average time-course of SI_ipsi was detected for each rat by performing cross correlation analysis on NoStim scans (area of 'connected' contralateral cortex is termed as SI_contra). Average time-courses from SI_ipsi and SI_contra were normalized to percentage difference relative to the mean and power spectra were obtained. In addition, power in 0-0.2 Hz range was estimated by computing variance of low-pass filtered time-courses (0-0.2 Hz). Results (power spectra and variances) with the same condition were averaged for each rat, yielding one power spectrum and one variance value for each condition (NoStim and Stim) for each rat. Using manual ROI selection, we obtained spectra and variances for the right caudate-putamen (CP) under both conditions, to serve as a control.

Results and discussion: The short TR used in this study (0.1 s) avoids aliasing of the primary components of physiological rhythms into the low frequency band. High power was observed in all the spectra in 0-0.2 Hz range. Figure 1a shows the zoomed-in power spectra for both conditions for SI_ipsi averaged over all the rats. Stimulus-induced reduction of power in 0-0.2 Hz range is observed. Interestingly, stimulus-induced decrease in power of LFFs is also observed for contralateral (non-stimulated) SI (fig 1b). This reduction of power is reproducible across rats (fig 2). Paired t-test showed significance of stimulus-induced reduction in power of in 0-0.2 Hz range (p-values of 0.012 and 0.016 for NoStim-SI_ipsi vs Stim-SI_ipsi and NoStim-SI_contra vs Stim-SI_contra respectively). CP does not show robust change in power associated with stimulation (p-value = 0.23) (fig 2).

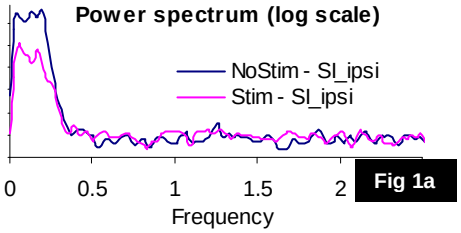


Fig 1a

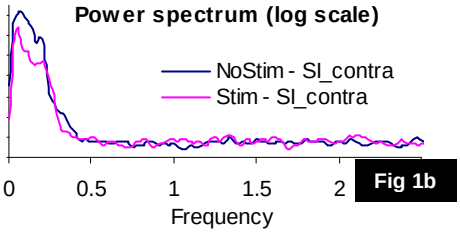
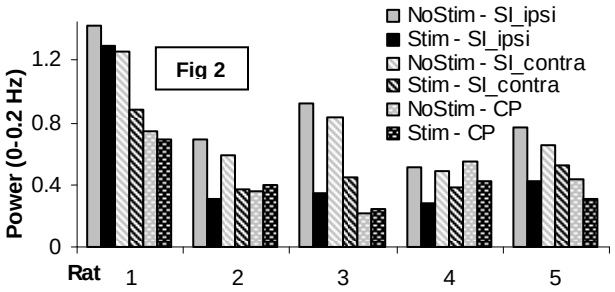


Fig 1b



Consistent with [3], FC maps with seeds placed in SI and CP (non-stimulated datasets) reveal two networks consisting of bilateral SI and bilateral CP respectively (fig 3). SI and CP are not part of the same network, whereas left and right SI form a network. Therefore, our results indicate that stimulation-induced reduction in power is not global and occurs only in the network of which stimulated area is a part. This observation suggests neural modulation of synchronized LFFs. Interestingly, Morgan et al observed reduction in correlation coefficients related with sensory-motor task [4]. That reduction might be caused be reduced power of fluctuations. It should also be noted that stimulus induced reduction in power of ~0.1 Hz oscillations in blood oxygenation and vascular tone (vasomotion) has been observed using other modalities [5, 6]. Recent work has shown that LFFs in the BOLD signal are closely related to neural activity [7]. Our results, combined with these studies, support the theory that LFFs in the BOLD signal are either caused or modulated by neural activity.

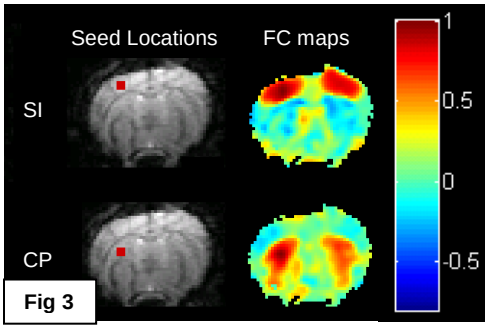


Fig 3

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