Finding thalamic BOLD correlates to cortical alpha modulation

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Introduction Neural networks often exhibit coherent oscillations, some of which can be observed in EEG and BOLD fMRI signals recorded from the human brain. Combined analysis of these signals may provide unique information about brain function that is not available from electrophysiology or fMRI alone. The alpha (8-12Hz) rhythm, as the hallmark oscillation in human EEG during alert wakefulness, is an important candidate for comparison with spontaneous fluctuations in fMRI signals. Electrophysiology studies of local field potentials (LFP) in animals have reported predominant alpha signals in both the thalamic and cortical parts of the visual system, and observed strong coherence between these signals[1-4]. What remains unknown is 1) whether such thalamo-cortical alpha coherence also exists in the human visual system and 2) (if yes) which part of the visual thalamus, including lateral geniculate nuclei (LGN) and pulvinar nuclei (Pul), interacts with the visual cortex to produce the modulation of the occipital alpha rhythm. To address these questions, we acquired simultaneous EEG-fMRI data from humans and mapped the thalamic and cortical BOLD correlates to the occipital alpha modulation either resulting from opening and closing the eyes, or occurring spontaneously during eyes-closed rest. For comparison, the reference locations of LGN and Pul were independently defined using a functional localizer with visual stimulation and high-resolution anatomical imaging based on gradient echo (GRE) phase contrast, respectively.

Methods On 15 healthy volunteers, we acquired concurrent EEG (32-channel, BrainAmp MR, BrainProducts) and BOLD fMRI (GRE-EPI, rate-2 SENSE, TE/TR=30ms/1.5s, 30 4-mm axial slices, FOV=220×165mm^2, matrix size=64×48) using a GE 3-T Signa scanner with a 16-channel receive-only coil array. Each subject was instructed to 1) rest wakefully with eyes closed for 10 min, 2) rest with multiple cycles of self-paced alternating eyes-closed or eyes-open periods of about 30s each, and 3) perform a fixation task while visual stimulation (full-field checkerboard reversing at 3Hz) was presented using a block design (30s on and 30s off). Anatomical phase images were acquired using a GE 7-T system with a 32-channel receive coil (2D multi-echo GRE, rate-2 SENSE, TE=15.5/30/44.5ms, TR=2s, 90 axial slices with 0.31×0.31mm^2 in-plane resolution, 0.8mm slice thickness and 0.2mm gap).

The EPI images were preprocessed for geometric distortion correction and removal of nuisance variables related to respiratory and cardiac cycles, motion, respiratory volume and heart rate. The BOLD responses to visual stimulation were mapped through general linear model (GLM) analysis. The MR gradient and cardiac pulse artifacts were removed from EEG recordings using a method developed in-house[18]. The occipital alpha modulation was extracted by averaging the alpha power computed from three occipital electrodes with a 2s time window sliding in 1s steps. After convolving with the hemodynamic response function (HRF), the occipital alpha modulation was correlated with the BOLD signals for both the eyes-closed rest and the eyes-open-and-closed task. The anatomical phase images were extracted from the GRE image at 15.5ms TE after phase unwrapping and removing the background phase. Both the functional maps and the anatomical images were normalized to the standard MNI brain space for group analysis.

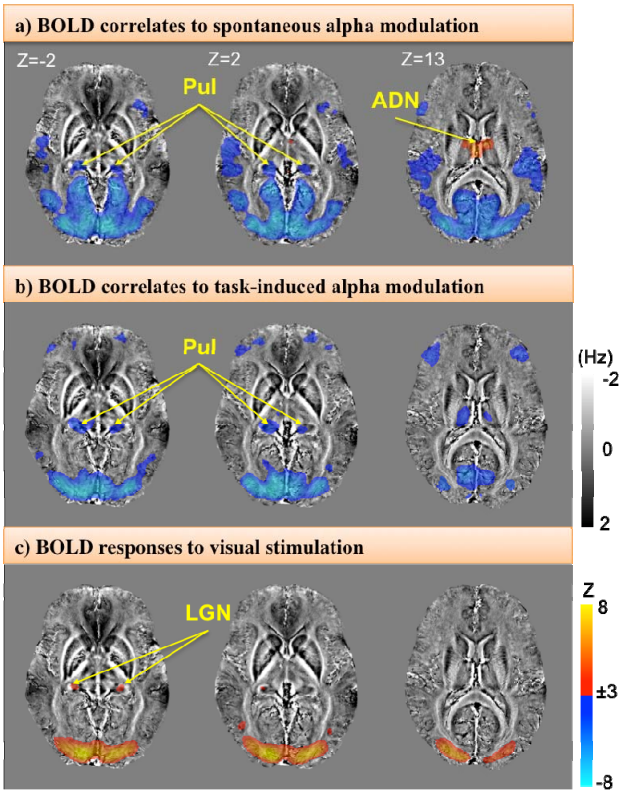

Figure 1. Group-level (n=15) maps showing the BOLD correlates to the occipital alpha modulation occurring spontaneously at rest (a) or reacting to eyes open and closure (b), and the fMRI activations with visual stimulation (c) displayed over high-resolution phase images.

Results The BOLD signals from the visual thalamus, located at the lateral and posterior part of the thalamus, were negatively correlated with the occipital alpha power fluctuation that occurred either spontaneously at rest (Fig. 1.a) or in response to opening and closing eyes (Fig. 1.b). Judged from the anatomical phase images, these areas with negative BOLD-alpha correlation coincided with two bilateral regions showing negative phase (lower intensity in the underlay images) indicative of a focal paramagnetic susceptibility shift. Compared to the LGN localized with visual stimulation (Fig. 1.c), the alpha-correlated regions appeared larger and more medial, extending away from the juncture of the optic tract and radiation. Comparison with these anatomical and functional references suggested that the negative thalamic BOLD correlates of the occipital alpha EEG were not specific to LGN but included more medial and anterior regions attributed to Pul. In the resting state, the BOLD signals at the anterior dorsal nuclei (ADN) were positively correlated with the occipital alpha modulation. However, no BOLD signal correlation was found between the ADN and the visual cortex (or any other sensory and motor cortices), where the cortical BOLD signals were correlated with alpha. Instead, the BOLD signals from the ADN were positively correlated with those from the cerebellum and the cingulate cortex (data not shown).

Discussion Previous EEG-fMRI and EEG-PET studies have reported positive[5-10], negative[9,11-12] or near-zero[13] correlations between the BOLD (as well as regional blood flow and glucose metabolism) signals in the thalamus and the alpha-power signal over the cortex. This inconsistency arises in part from the structural and functional heterogeneity of the thalamus. Sub-divisions of the thalamus not only have distinct appearances in histology[14] and susceptibility-weighted phase MRI[15], but also connect with different parts[16] of the cortex and serve distinct functions.

In this study, we report that both negative and positive BOLD correlates to the occipital alpha modulation exist in the thalamus, but at separate sub-regions. The negative correlations occur at the visual thalamus (including Pul), which is structurally and functionally connected with the entire visual cortex; the positive correlations occur at the anterior-dorsal part of the thalamus, where there is neither structural nor functional connectivity specifically with the visual cortex. The finding regarding the Pul agrees with previous animal electrophysiology studies that found the alpha rhythms from Pul to be coherent with those from the visual cortex, and account for a significant degree of intra-cortical coherence in spontaneous alpha oscillations[2]. The positive BOLD-alpha correlation seen in the ADN cannot be simply taken as the basis of the interpretation that the ADN is the thalamic pacemaker of cortical alpha rhythms[5-10]. .

References 1. *Lopes da Silva et al. 1973*; 2. *Lopes da Silva, 1980*; 3. *Chatila et al. 1993;* 4. *Lorincz et al. 2009*. 5. *Danos et al. 2001;* 6. *de Munck et al. 2007;* 7. *Feige et al. 2005;* 8. *Goldman et al., 2002;* 9. *Moosman et al. 2003;* 10. *Sadato et al. 1998;* 11. *Larson et al. 1998;* 12. *Lindgren et al. 1999.* 13. *Laufs et al. 2003.* 14. Morel et al. 1997; 15. *Duyn et al. 2007*; 16. *Behrens et al. 2003*; 17. *Klimesch et al. 2007*. 18. *Liu et al. 2012.*