LAMINAR DIFFERENCES IN NEURAL ACTIVITY DURING POSITIVE AND NEGATIVE BOLD CONDITIONS

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Target audience: fMRI scientists

Purpose

Positive BOLD responses (PBR) are associated with increased neuronal activity and metabolic activity[1]. However, the origin of the negative BOLD responses (NBR) and their relationship to metabolic and neuronal activity are still elusive. Furthermore, recent work has shown that neurovascular coupling differs for the PBR and NBR and that it also differs across cortical layers[2]. We address the question whether these laminar differences have a neural- or a vascular origin by measuring the laminar electrophysiological responses to stimuli that elicit positive and negative BOLD responses.

Methods

Experiments were performed on four anesthetized non-human primates (*macaca mulatta*). The setup and methods have been described previously[1,4]. Anesthesia was a balanced remifentanil/ mivacurium regimen[1,2]. fMRI data was acquired in a vertical 7T scanner. We used a volume coil to transmit in combination with a custom-built 4-channel phased array. We used an eight-shot EPI with a FOV of 64x48 mm^2 and matrix of 128x128. We acquired 13 slices with a slice thickness of 2 mm, TE/TR 20/750 ms. The neurophysiology data was acquired using laminar electrodes (NeuroNexus Technologies). We used paired electrodes positioned in parallel with a distance of ~1.5 mm (Fig. 1). The electrodes were 16-contact probes on a shank of 3 mm long and 50 µm thick. The electrode-sites were spaced 150 µm apart. The signals were amplified and filtered into a band of 1 Hz to 8 kHz (Alpha-Omega Engineering) and digitized at 20.83 kHz with 16-bit resolution (National Instruments). Data were analyzed using custom routines in MatLab (the MathWorks). PBR and NBR were induced using a rotating checkerboard. Stimuli were varied such that the electrode-sites experienced PBR and NBR stimuli, including the condition where one site experienced a PBR stimulus and the other a NBR stimulus (Fig. 1).

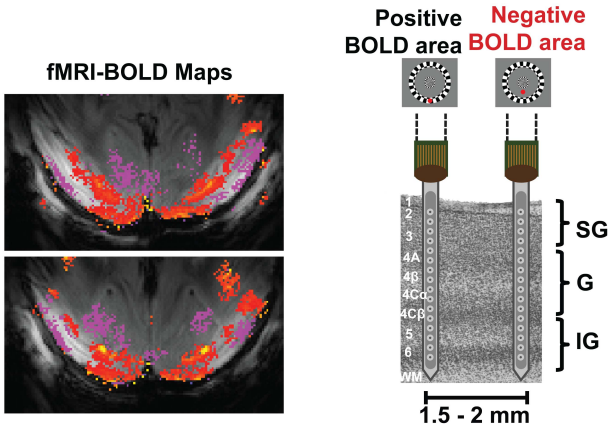

Figure 1. NBR and Neurophysiology Experimental Paradigm

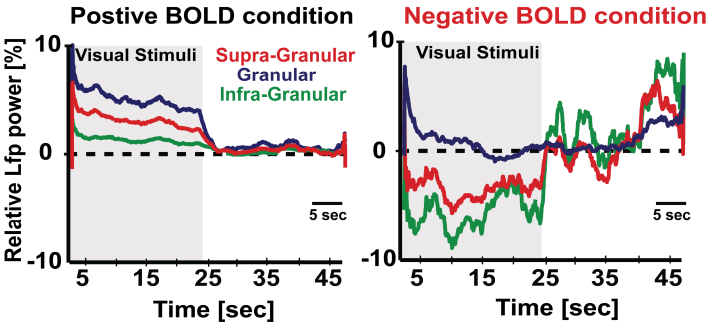

Figure 2. Broad-band LFP results across layers

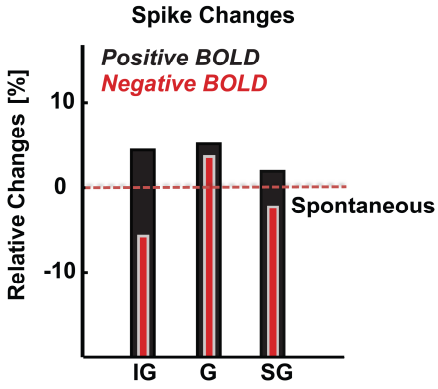

Figure 3. Spike count across layers

Results

Figure 2 shows the average time courses of neural responses during the PBR and NBR conditions in the granular- (middle, G), infragranular (lower, IG) and supragranular (upper, SG) layers of V1. The shaded regions in both conditions denote the presentation of the stimuli. We computed the relative power of the local field potentials (LFP; 0 – 150 Hz) for both PBR and NBR conditions relative to the baseline periods (periods without visual stimulation). Afterwards, we normalized their responses to the baseline power. The PBR power was increased in all layers, presenting quantitative layer-dependent differences. More interestingly, during the NBR, the power in the granular layer increased (10.0±2.5%, p = 0.025), while the power in the supra- and infragranular layers decreased relative to the baseline power (IG= -9.3±1.2%, p = 0.034; SG = -11.2±3.3%, p = 0.029). These effects were also reflected in the number of spikes across layers (Fig. 3), which clearly showed that the PBR condition elicited increased neural activity in all cortical layers, whereas the NBR elicited an inhibitory response in the infragranular and supragranular layers but an excitatory response in the granular layer (G = 5.2±1.1%, p = 0.031; IG = -8.2±2.2%, p = 0.028; SG = -4.5±0.9%, p = 0.041).

Conclusion

Our results confirm that the overall neural activity decreases below the spontaneous activity during NBR[3]. Moreover it shows that there are layer-dependent differences in neural activity during the NBR, with the neural activity increasing in the middle layers. This suggests that the granular layers keep receiving input during the NBR. Furthermore, a significant component of the NBR originates from decreases in neural activity from supra- and infra-granular layers, but our results indicate that the increase in cerebral blood volume observed in the middle cortical layers during the NBR[2] has a neural origin.

References **1.**Logothetis et al., Nature 412:150-157 (2001); **2.**Goense et al., Neuron 76:629-639 (2012); **3.**Shmuel et al., Nat. Neurosci 9:569-577 (2006); **4.**Zaldivar et al., Curr. Biol. 24:1-7 (2014) in press