

Layer Specific Detection of Inhibitory fMRI Response in Somatosensory Cortex through Cortico-cortical Interaction in Rats

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Introduction: There is great interest in using anatomical and functional neuroimaging techniques to understand both the topographical as well as the dynamic organization of cortical functional circuits with high spatial and temporal resolution. For example, fMRI has been used to probe the laminar flow of information [1], as well as the suppressive interaction of consecutive neuronal events in rat primary somatosensory cortices [2]. Laminar-specific cortico-cortical and thalamo-cortical projections were recently traced by manganese-enhanced MRI [3]. In the present work, we use BOLD fMRI to investigate the laminar dependence of cortico-cortical interactions induced by paired bi-lateral somatosensory stimulation in α -chloralose anesthetized rats.

Materials and Methods: Adult male Sprague-Dawley rats ($n = 14$, 356 ± 47 g) were initially anesthetized under isoflurane and orally intubated. Arterial and venous catheters were placed for monitoring of arterial blood gases. After surgery, anesthesia was switched to α -chloralose (80 mg/kg initial bolus followed by 27 mg/kg/h constant infusion) [1]. Arterial blood gases and rectal temperature was monitored and maintained at normal level. fMRI experiments were performed in a horizontal 11.7 T/31 cm magnet (Bruker-Biospin, Billerica, MA) equipped with a 12 cm gradients capable of 1,000 mT/m amplitude within 150 μ s rise-time (Resonance Research Inc, Billerica, MA). A home-built surface coil (1.2 cm ID) was positioned on top of the head over bregma. BOLD fMRI were obtained with a gradient-echo sequence with the following parameters: TE = 10 ms, TR = 31.25 ms, flip angle = 10°, nominal resolution = $200 \times 200 \times 2,000$ mm³, acquisition bandwidth = 12,500 Hz. A pair of needle electrodes was inserted into each forelimb and bilateral forepaw were stimulated by paired electrical stimulation (333 μ s pulses, 2 mA amplitude, 3 Hz) with different inter-stimulus interval (ISI) between one forepaw and the other (Fig. 1). Stimuli were performed synchronized with the scanner and controlled from a PC running Presentation (Neurobehavioral Systems, Inc., Albany, CA). Three ISI values (0, 40, and 100 ms) were utilized. The stimuli consisted of individual epochs containing 6 electrical pulses (~2-s stimulus length), repeated 64 times. Both forepaw regions of primary somatosensory cortex (S1FL) were divided into 10 laminar-specific cortical profiles along the cortical depth in S1. BOLD fMRI intensity profiles were normalized by the amplitude of signal changes in contralateral S1FL cortices (left and right) at 0 ms ISI.

Results and Discussion: Robust BOLD responses to brief (2 s) stimulation of the contralateral forepaw were observed across all cortical layers. These responses were significantly inhibited when the ipsilateral forepaw was stimulated 40 ms in advance (Fig. 1). When compared to the response obtained at 0 ms ISI, the BOLD percent signal change in the S1FL responding to the late stimulus was decreased by 47 % at 40 ms ISI. In closer inspection, MRI intensity profiles in the suppressed S1FL side showed a laminar heterogeneity at 40 ms ISI, with the degree of suppression in layers III to V being stronger than suppression of fMRI changes in layers I-II and in bottom of layer VI (Fig. 2). These results are consistent with the topography of callosal cortico-cortical projections exerting inhibitory action in contralateral S1FL at 40 ms ISI [3, 9]. Our data shows that BOLD fMRI has sufficient spatial and temporal resolution to study cortical circuits, within functional columns and layers.

References: [1] Silva AC & Koretsky AP, PNAS 2002 [2] Ogawa S et al., PNAS 2000 [3] Tucciarone J et al. Neuroimage 2009 [4] Wise SP & Jones EG, J Comp Neurol 1978 [5] Wise SP & Jones EG, J Comp Neurol 1976 [6] Douglas RJ & Martin KA, Annu Rev Neurosci 2004 [7] Logothetis NK, Nature 2008 [8] Paxinos G & Watson C. The Rat Brain in Stereotaxic Coordinates 1986. [9] Silva AC et al., J Neurosci Methods 2008

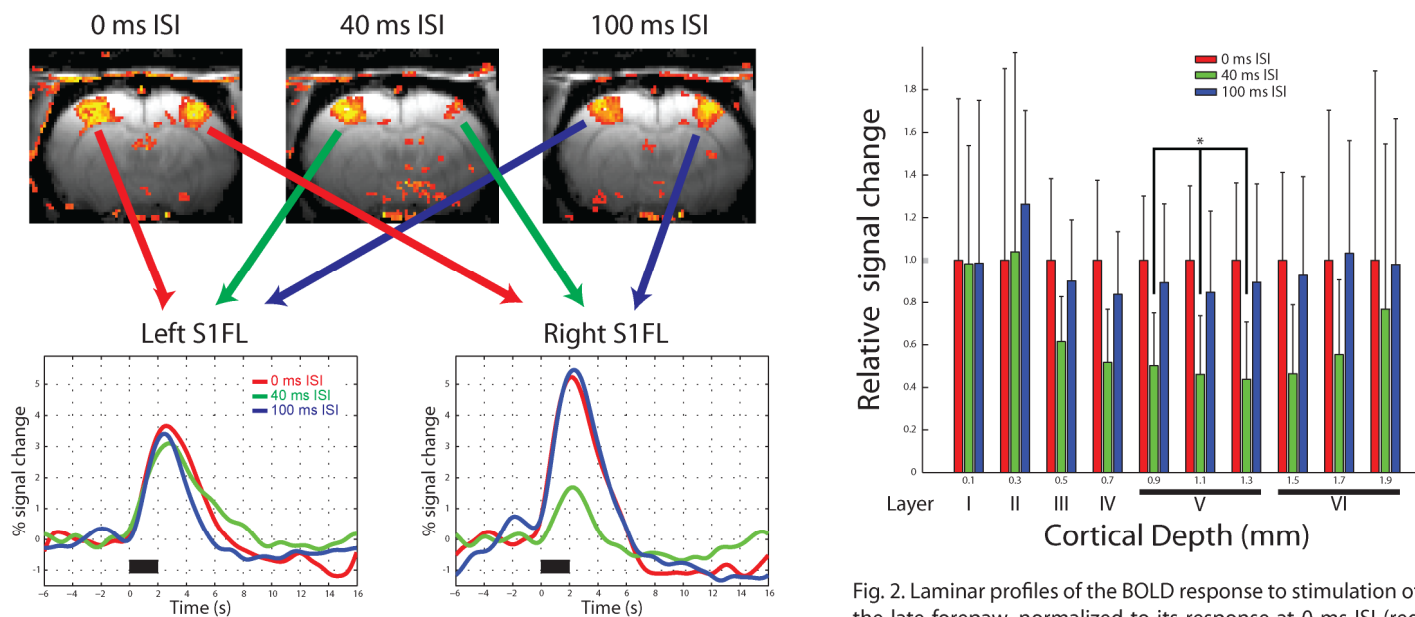


Fig. 2. Laminar profiles of the BOLD response to stimulation of the late forepaw, normalized to its response at 0 ms ISI (red bars).

Fig. 1. Somatosensory activation maps induced by bilateral forepaw stimulation with different ISI in a representative rat ($p < 0.0000001$, top) and their time courses (bottom).