Neurophysiological basis of localized and delocalized fMRI activity patterns

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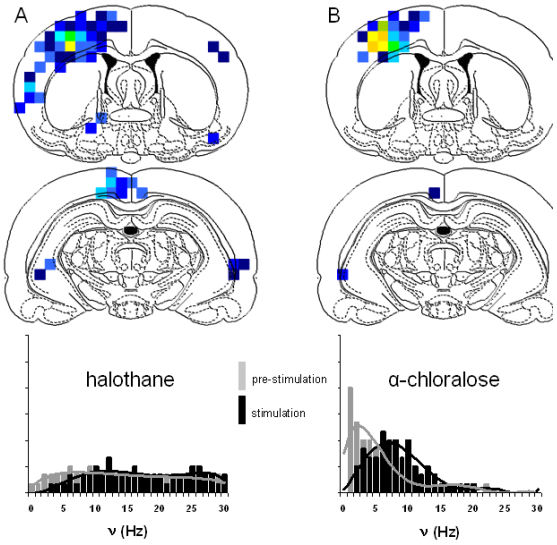
INTRODUCTION

Neuroimaging techniques like fMRI and PET, where incremental signals are generally measured, provide detailed information about locations of activity patterns. While localized activity patterns with sensory stimuli are generally well accepted and the afferent/efferent pathways for these systems have been well studied [1], variations of activity patterns experienced across subjects (for the same paradigm) cannot be fully explained by network- or module-based models [2]. With cognitive stimuli these types of spurious (or nuisance) activation patterns, which are often ignored, become more challenging because the anatomy is less familiar [3]. While some of the result variations mentioned above can be partially addressed by processing (e.g., movement correction, co-registration, spatial normalization) [4], the basic requirement of differencing has limitations because the subtraction of the baseline activity removes an important part of the total activity [5]. Our prior studies have quantitatively revealed that most neurons in the ensemble (in a voxel) contribute differently beforem during, and after the stimulation [6]. Since the ensemble activity of pyramidal neurons in layer 4 depends on sensory (or localized) input by the thalamus and global (or delocalized) input from other cortical regions, delocalized signals from a global workspace may affect localized stimulus-induced responses. To test the hypothesis that delocalized signals, which have been proposed to include subjective contributions [7], can modulate localized signals we conducted fMRI and electrophysiological studies in rats under varied conditions of anesthesia and stimulation.

EXPERIMENTAL

Animal preparation: Sprague-Dawley rats were tracheotomized and artificially ventilated. Intraperitoneal lines were inserted for administration of drugs. An arterial line was used for monitoring physiology (blood pH, pO_2, pCO_2) throughout the experiment. The light baseline activity of halothane (0.7%) was deepened with α-chloralose (46±4 mg/kg/hr). The same forepaw stimulation protocol (2-minute block design; 2 mA; 0.3 ms; 3 Hz) was used for both fMRI and extracellular recordings. fMRI measurements (n=12): All fMRI data were obtained on a modified 7.0T or 9.4T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H resonator/surface coil RF probe. ΔS/S was measured from multiple slices and in some studies and ΔCBF/CBF was also measured to convert to $\Delta CMR_{O2}/CMR_{O2}$ maps with BOLD calibration. Extracellular recordings (n=55): The skull above the forepaw region (4.0 mm lateral and 1.0 mm anterior to bregma) was opened for a tungsten microelectrode (FHC inc, Bowdoinham, ME) which had an impedance of ~2 MΩ. The extracellular signals were filtered (0.01-20 kHz) and amplified (×1000). From the extracellular data we extracted the spiking activity of a neuronal ensemble (ν) as well as the field potentials (FP) that were evoked by the stimulation.

RESULTS AND DISCUSSION



The figure shows the results from the high (A) and low (B) baseline activities, where the two baseline CBF levels varied by ~33%. While the fMRI data from both baselines showed sensory-induced changes in the contralateral primary somatosensory and motor areas, there were increased delocalized activities observed with the (light) halothane anesthesia. These regions were ipsilateral primary somatosensory, contralateral secondary somatosensory, as well as perirhinal and retrosplenial agranular areas (A). In contrast signals from delocalized regions were notably absent with (deep) α-chloralose anesthesia (B). These results were supported by spiking frequency (ν) distributions measured from the most activated foci in the contralateral (and ipsilateral) primary somatosensory area(s). The contralateral distributions with the (deep) α-chloralose anesthesia (B) showed a significant shift from low to high frequency values upon stimulation. The contralateral distribution shift was less noteworthy with (light) halothane anesthesia (A). The distributions for the baselines with halothane and α-chloralose were significantly different, in which the degrees of global inputs assigned to higher frequencies dominated under light anesthesia. The contralateral distributions upon stimulation with halothane and α-chloralose were also significantly different, suggesting that under the light anesthesia level the global inputs dominated whereas local changes were dominated under the deep anesthesia level. Since neuronal populations in different regions of the brain do not function as modules, the resultant fMRI [2] or electrophysiological [8] activity patterns arise from interactions of afferent and efferent connections – the latter of which was modulated by anesthesia in this study. These results provide the initial steps to explore the interactions of localized and delocalized underpinnings of the concept of the global workspace model [7].

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