Spontaneous BOLD Signal Changes Mimic Task-related Activation in Anesthetized Rats

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Introduction

Electrical forepaw stimulation of anesthetized rats is a commonly used paradigm in rodent functional MRI (fMRI) studies [1]. However, researchers rarely look for signal changes that are uncorrelated with the stimulation. During recent studies, we observed that signal changes comparable in magnitude and duration to those observed during stimulation also occurred in scans where no stimulation was applied. To characterize this phenomenon, fMRI scans with long periods without stimulation were acquired from two groups of rats on separate imaging systems under two different anesthesias, α-chloralose and medetomidine.

Materials and Methods

Two groups of adult Sprague-Dawley rats (200-300g) were imaged. Group 1 was scanned using an 11.7 T Bruker scanner (gradient strength of 60 G/cm, rise time 100 μs) and α-chloralose anesthesia (n = 5). Group 2 was imaged using a 9.4 T Bruker scanner (gradient strength of 20 G/cm, rise time 120 μs) and anesthetized using Medetomedine (n = 4) [2]. For both groups, a single shot spin-echo EPI sequence with TR=1500 ms, TE=30 ms, field of view = 1.92 cm, and matrix size=64x64 was used to acquire three to five slices centered over the primary somatosensensory cortex. Five scans, consisting of 310 images at rest, 30 images during stimulation, and 60 more images at rest, were acquired for each rat. In order to analyze the five test scans, a Matlab program was written that creates a boxcar function with an 'on' period of 30 images which began with the first image in the set for the first iteration and was shifted by 5 images for each of the remaining iterations. The maximum correlation coefficient and time at which this correlation occurred was recorded and mapped for each pixel.

Results and Discussion

All rats showed normal BOLD activation in the primary somatosensory cortex contralateral to the forepaw containing the electrodes during stimulation periods. Rats in group 1 showed strong patterns of signal changes (in the motor cortex, contralateral and ipsilateral SI and SII, and subcortical areas) that were uncorrelated with the stimulus as seen in Figure 1a. The rats in group 2 showed no evidence of uncorrelated BOLD signal changes (Figure 1b). In group 1, the spatial extent of the uncorrelated BOLD signal changes increased over the scanning session. The cause of the unexpected activation in group 1 is not known, but several hypotheses can be suggested. Our first theory was that the rat was learning to associate the sound of the MRI scanner with the electrical stimulation. The data was acquired in an interleaved fashion with multiple scans for other projects, so that each rat underwent approximately 30 scans receiving stimulation. In order to test this theory, a control group of five rats was imaged with the same scans, but with stimulation only during the long baseline scans (approximately 5 scans during stimulation per rat). These rats showed similar patterns of uncorrelated activity, which suggests association is not the cause. Another possibility is peripheral nerve stimulation (PNS) due to the fast switching of the gradients. The gradient set on the 11.7 T system was operating at a slew rate of 400 $Tm^{-1}s^{-1}$ in the direction parallel with the rat's body (Z-axis) for this imaging session, which could likely cause PNS in the long nerves of the forepaw or hindpaw. As a reference point, the threshold PNS value for humans is 15-25 $Tm^{-1}s^{-1}$ [3].

It is interesting that the rats anesthetized with medetomedine show no sign of these random activation patterns. This could be due to altered neurovascular coupling, different levels of cortical activity, or many other factors. During functional studies, the percent signal change in the activated region is typically 2-3% for medetomidine compared to 4-8% for α-chloralose, so it may be more difficult to detect uncorrelated BOLD changes. The medetomidine data was acquired with a lower gradient slew rate of 333 $Tm^{-1}s^{-1}$ in the direction parallel to the rat's body, lower than the slew rate for Group 1 rats but still well above the threshold for stimulation in humans. This work is important for researchers using α-chloralose in fMRI studies, because spurious activations maps may be seen without knowing of the effects presented in this abstract.

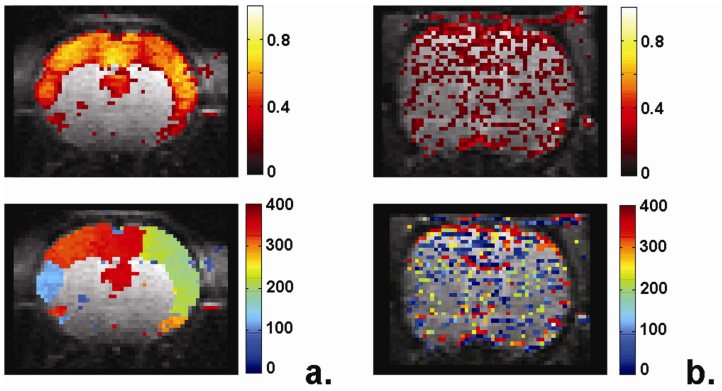

Figure 1: Coronal brain slices showing maximum correlation values (top) and time of maximum correlation (bottom) obtained from association program in rats anesthetized with α-chloralose (a) and medetomidine (b). Stimulation was applied from 310-340 s.

References

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