Measuring connectivity in sensory cortex using an fMRI adaptation paradigm

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Introduction

fMRI adaptation paradigms have been used successfully to probe neural activity on a millisecond timescale. For example, if two visual stimuli are presented in quick succession, the response to the second stimulus is reduced[1]. There is a strong body of evidence that this effect is neuronal rather than vascular in nature but the neural mechanism underlying the phenomenon is under debate[2,3]. It is apparent that different mechanisms might be at work at different time-scales and processing levels. In primary sensory systems it seems that short-term adaptation effects are due to reduced excitability of neurons or synaptic depression. Here, we investigate whether this approach can be developed to measure 'connectivity' between two sensory regions. If region A is functionally connected to region B then activating A will inhibit region B, thereby reducing excitability in region B. A second pulse to region B will show a reduction in signal, and the magnitude of this reduction will be a measure of the connection strength. Varying the timing between stimuli can probe the timing of this connection on the millisecond scale. We test this hypothesis in the somatosensory system.

Methods

6 subjects (3 male, 3 female) took part in the experiment which was approved by the University research ethics committee.

Procedure&Task: Vibrotactile stimuli were positioned on the pads of digits 2 and 4 of the right hand. Paired pulses were delivered to the two digits in either order with intervals of 50, 200 or 400ms. Hence there were 6 conditions in total. Pulse frequency was 30 Hz, duration was 500ms and time between the paired pulses was 10s. 30 trials of each condition were presented over 2 runs. A task was introduced to motivate subjects to attend to the stimuli. The amplitude of the first pulse was either the same, higher (+12%) or lower (-12%) and subjects were asked to respond with a button box held in their left hand as to which pulse felt stronger. Two further fMRI runs were used to localise the digit representations with alternate stimulation of each digit for 4s with 8s rest.

MRI methods: All scanning was performed on a 3 T Siemens Trio system. High resolution EPI with prospective motion correction was used with scan parameters: TR 2s, TE 35ms, matrix 64x64, in-plane resolution 2mm, slice thickness 2mm, 28 slices covering the somatosensory cortex. A 1mm isotropic structural MPRAGE image was also collected.

Analysis: Data from each subject was analysed individually using BrainVoyager. Slice-time correction and high-pass temporal filtering was used but no spatial smoothing. The localizer scans were analysed to determine regions of interest for digit 2 and 4 in the primary sensory cortex. Within these regions the amplitude of the BOLD response for six double pulse conditions were recorded by fitting a general linear model.

Results and Discussion

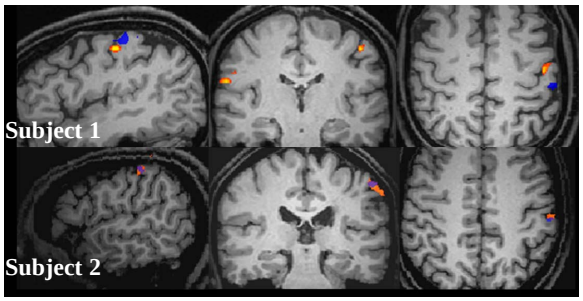

Figure 1 Regions of interest in two example subjects. Digit 2 in red, digit 4 in blue. Note the separation of regions in subject 1 and the overlap in subject 2.

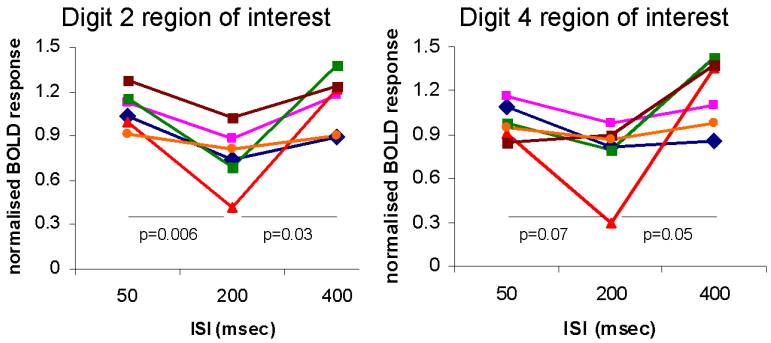

Figure 2. BOLD responses of individual subjects in digit 2 and digit 4 regions of interest for the case where digit 2 is pulsed first.

Pulse order: digit 2 followed by digit 4.

The graphs show clear suppression of response at ISI = 200ms compared to 50ms and 400ms in all subjects in both digit regions of interest when digit 2 was pulsed first. The significance was tested with a two-tailed paired t-test and p values are shown on figure 2. When digit 2 is pulsed first this will inhibit digit 4 region and the expected supression is seen. Supression in digit 2 region is less expected as the pulse to region 4 *follows* it. Supression could be due to overlap between digit regions and/or reciprocal connections between the regions. We suggest that supression is not seen at 50ms because this is too short a duration for lateral inhibition to take place. Likewise by 400ms it appears that the inhibitory influence has passed.

Pulse order: digit 4 followed by digit 2.

In this case supression was weaker in both regions, which could be due to weaker connections from digit 4 to digit 2 than the opposite direction.

This work is important as it demonstrates a method of directly measuring the influence and timing of interactions between sensory regions. Future work will compare measurements between different digit pairs: closer digits should show a stronger, earlier suppression as the relative connectivity is greater and the distances are shorter.

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References

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