Negative BOLD effect on somato-motor inhibitory processing: An fMRI study

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\textbf{A B S T R A C T}

Inhibiting inappropriate behavior and thoughts in the current context is an essential ability for humans, but the neural mechanisms for response inhibitory processing are a matter of continuous debate. The aim of this event-related functional magnetic resonance imaging (fMRI) study was to evaluate the negative blood oxygen level dependent (BOLD) effect on inhibitory processing during go/no-go paradigms. Fifteen subjects performed two different types of somatosensory go/no-go paradigm: (1) button press and (2) count. Go and no-go stimuli were presented with an even probability. We observed a common negative activation during Movement No-go and Count No-go trials in the right SFG, corresponding to BA 8. These findings suggest that the right SFG region was responsible for the negative BOLD effect on inhibitory processing, which was independent of the required response mode. We hypothesized several possible explanations for the deactivation of the SFG during no-go trials.

The go/no-go paradigm is one of the most useful tasks with which to elucidate the neuronal mechanisms of response execution and inhibition. Response execution has been studied in go (target) trials using an index of behavioral performance like reaction time (RT), but it is difficult to study response inhibition in no-go (non-target) trials because of the absence of actual behavioral performance. To investigate response inhibitory processing in human brain, neuroimaging methods such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been used during go/no-go paradigms. These studies have clarified the neural networks associated with inhibitory processing, including the dorsolateral (DLPFC) and ventrolateral (VLPFC) prefrontal cortices, supplementary motor area (SMA), anterior cingulate cortex (ACC), inferior parietal lobule (IPL), insula, and temporoparietal junctions (TPJ) [2,3,5,9,13–15,17,25,26]. The recruitment of neural networks has been reported during not only the pushing a button task of go/no-go paradigms, but also saccade [4], swallowing [29], and counting tasks [18,20].

Recently, the negative blood oxygen level dependent (BOLD) effect has been used to evaluate various neural networks in detail. For instance, some studies reported deactivation in the ipsilateral primary somatosensory corex (SI) after somatosensory stimulation [1,12], the ipsilateral primary motor cortex during unilateral finger movements or low-force grip tasks [11,22,21,27], and nonstimulated areas of the visual cortex on partial visual field stimulation [30]. These negative BOLD effects have been explained by several theories [27]. To our knowledge, however, no studies have examined the neural networks for response inhibitory processing by recording negative BOLD effects during go/no-go paradigms, and the relationship in brain regions between the negative BOLD effect and inhibitory processing has remained unclear. Therefore, the purpose of the present study was to clarify the characteristics of neural networks for response inhibitory processing by using the negative BOLD effect in somatosensory go/no-go paradigms. The results for positive BOLD responses are activations for no-go trials [20].

Fifteen normal subjects (eight females and seven males; mean age 23.6 years, range 19–32 years) participated in this study. All of them were right-handed according to the Edinburgh Inventory [24]. The subjects did not have a previous history of any neurological or psychiatric disorders. Before the experiment, the study's risks and procedures were explained to all participants, and a written informed consent was obtained. The protocol of the present study was approved by the Institutional Ethics Committee of the Gabriele D'Annunzio University, Chieti, Italy.

The subjects performed somatosensory go/no-go paradigms. The electrical stimuli were a current constant square-wave pulse 0.3 ms in duration. Stimulus intensity was set to the threshold to induce a clear twitch of the fingers. Just before recording the fMRI...
The recordings were conducted in two conditions: Movement and Count go/no-go paradigms. In the Movement go/no-go paradigm, the subjects had to respond by pushing a button with their right index finger (contralateral to the stimulated side) as quickly as possible only after the presentation of a go stimulus. In the Count go/no-go paradigm, the subjects had to count the number of go stimuli silently and report the result after the end of recordings. One condition comprised 80 stimuli, which included 40 stimuli for the median nerve and 40 for the ulnar nerve. The practice session consisted of 1 min before the recordings. The order of conditions was randomized in each subject and counterbalanced across all subjects.

All images were acquired using a 1.5T MR scanner (Magnetom Vision; Siemens, Erlangen, Germany). Blood oxygen level dependent (BOLD) contrast functional images were acquired using T2*-weighted echo planar imaging (EPI) free induction decay (FID) sequences with the following parameters: TR 2000 ms, TE 60 ms, T2*-weighted echo planar imaging (EPI) free induction decay (FID) dependent (BOLD) contrast functional images were acquired using tom Vision; Siemens, Erlangen, Germany). Blood oxygen level of conditions was randomized in each subject and counterbalanced practice session consisted of 1 min before the recordings. The order of conditions was randomized in each subject and counterbalanced across all subjects.

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Conjunction analysis for regions deactivated during Movement No-go and Count No-go, and trends during Movement No-go and Count No-go.

<table>
<thead>
<tr>
<th>Region</th>
<th>Side</th>
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<th>Talairach coordinates</th>
<th>Z-score</th>
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<td></td>
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<td>14 43 44</td>
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Table 1

BA, Brodmann’s area; L, left hemisphere; R, right hemisphere.

It is known that diverse regions of the brain are implicated in response inhibitory processing, including the DLPFC, VLPFC, SMA, ACC, IPL, insula, and TPJ [2,3,5,9,13–15,17,25,26]. Our previous report for positive BOLD activation during somatosensory go/no-go paradigms supported these previous results, identifying the recruitment of neural networks in both Movement No-go and Count No-go trials [20]. However, it should be noted that the region of the SFG, corresponding to BA 8, was outside of the inhibitory neural networks. This notion was also supported by a meta-analysis with data from 17 previous studies of go/no-go paradigms [20,23]. Our previous report using the positive BOLD effect showed that there were some regions that differ in the strength of activation between Movement No-go and Count No-go [20]. Overall, the activation was stronger during Movement No-go than Count No-go in the inhibitory network. Therefore, we assumed that withholding a count response consume less inhibitory resources than withholding a movement response. Indeed, it would be difficult to interpret the deactivated regions neurophysiologically concerning Movement No-go, but our findings suggest the applicability of the BOLD signal as a marker of the neuronal state for inhibitory processing. Of course, there is a possibility that the above hypotheses may interact.

In conclusion, the present findings showed the negative BOLD effect on inhibitory processing during somatosensory go/no-go paradigms. We observed common negative activation during Movement No-go and Count No-go trials in the right SFG, corresponding to BA 8. Our results suggest that the SFG region was responsible for the negative BOLD effect on inhibitory processing, which was independent of the required response mode.

While there is common acceptance that the BOLD effect is correlated with the level of neuronal postsynaptic activity reflected in local field potentials [16,19], it is still a matter of debate about the neurophysiological meaning of negative BOLD effects. In the current study, we considered why a negative BOLD effect concerning inhibitory processing was found in the right SFG. One hypothesis is ‘reciprocal modulation within the prefrontal cortex’. fMRI studies have provided an identification that prefrontal cortical regions are involved in cognitive processing including judgments and preceding attention. For example, judgments of emotion involve such processing, and the activity in the DLPFC and VLPFC increased during emotional–cognitive interaction, while at the same time deactivation was found in the dorsomedial and ventromedial prefrontal cortex, corresponding to SFG/MFG [10,23]. These studies demonstrated the existence of a reciprocal neural network in the lateral and medial prefrontal cortex. In the present study, the deactivation in the SFG might be related to this reciprocal neural network in the prefrontal cortex.

A second hypothesis is ‘deactivation neural networks for inhibitory processing’. In the present study, although a conjunction analysis including Movement No-go and Count No-go revealed deactivation of the right SFG, contrast images by one sample t-tests demonstrated deactivation in inferior and middle temporal gyri, parahippocampal region, ACC, and PCC during Movement No-go (Fig. 2 and Table 1). These results indicate a negative BOLD effect during Movement No-go on not only the right SFG, but also several brain regions, compared to Count No-go. Our previous report using the positive BOLD effect showed that there were some regions that differ in the strength of activation between Movement No-go and Count No-go [20]. Overall, the activation was stronger during Movement No-go than Count No-go in the inhibitory network.
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References


