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Review

Differentiating functions of the lateral and medial prefrontal cortex in motor response inhibition

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ABSTRACT

The right inferior frontal gyrus is generally considered a critical region for motor response inhibition. Recent studies, however, suggest that the role of this cortical area in response inhibition may be overstated and that the contributions of other aspects of the prefrontal cortex are often overlooked. The current study used optical imaging to identify regions of the prefrontal cortex beyond the right inferior frontal gyrus which may serve to support motor response inhibition. Forty-three right-handed healthy adults completed a manual Go/No-Go task while evoked oxygenation of the prefrontal cortex was measured using 16-channel functional near-infrared spectroscopy. During motor response inhibition, the right inferior frontal gyrus, and to a lesser extent the homologous contralateral region, showed increased activation relative to a baseline task. Conversely, the medial prefrontal cortex was significantly deactivated, and the extent of reduced activity in this region was associated with fewer errors on the response inhibition task. These findings suggest a more substantial role of the left inferior frontal gyrus in response inhibition and possibly a distinct function of the middle frontal gyrus subserving error detection on manual motor control tasks.

Contents

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Introduction

The prefrontal cortex (PFC) is a complex brain region that is thought to subserve a number of higher-order cognitive abilities (Miller and Cohen, 2001). Response inhibition represents perhaps one of the most extensively studied of these abilities, particularly with respect to motor control. The Go/No-Go paradigm has frequently been used to measure motor response inhibition across a variety of response modalities, including the hand, eye, and foot (Van't Ent and Apkarian, 1999). In general, this paradigm asks respondents to provide a specific motor response to a target stimulus (termed the *Go* stimulus) but to withhold this response to a non-target stimulus (known as the No-Go stimulus). Regardless of response modality, the Go/No-Go paradigm has been found to reliably activate the right inferior frontal gyrus (right IFG) under conditions of motor response inhibition (Chikazoe et al., 2007). Accordingly, Aron et al. (2004) concluded that this region, in coordination with the basal ganglia and perhaps other subcortical regions, is critical to response inhibition based on their analysis of neuroimaging and human lesion-mapping studies.

A recent meta-analysis of functional neuroimaging studies, however, suggests a different perspective on the prominence of the right IFG in response inhibition. Swick et al. (2011) examined 47 neuroimaging studies that employed a Go/No-Go paradigm and quantitatively synthesized their results using an activation-likelihood-estimation approach. This study revealed significant areas of right-hemisphere activation extending from the right IFG and middle frontal gyrus to the insular cortex and inferior parietal lobule. Significant foci of activation were also identified in the left superior, middle, and inferior frontal gyri. Therefore, in contrast to the widely reported finding of primarily right IFG activation on the Go/No-Go task, the anticipated dominance of this region in supporting response inhibition was not strongly implicated in this meta-analytic review. Notable limitations of this meta-analysis, however, were there it included a variety of Go/No-Go tasks which varied in their relative proportions of Go versus No-Go stimuli, which could impact the relative potency of a motor response and its associated functional activation (Nieuwenhuis et al., 2003). Also, given that most studies included in this meta-analysis comprised functional magnetic resonance imaging (fMRI) contrasts of a condition requiring a motor response (Go) with one that does not (No-Go), it is difficult to disentangle those areas of PFC activation related to the execution of a motor response (e.g., manually pressing a button on a Go trial) versus response inhibition (e.g., withholding a manual button press on a No-Go trial) when these two specific conditions are contrasted (Hester et al., 2004b).

Although fMRI has been used most frequently in prior studies of response inhibition, investigations based on other neuroimaging modalities may help to elucidate the relative contributions of distinct regions of the PFC to motor response inhibition. Functional near-infrared spectroscopy (fNIRS) is an optical brain imaging technique which measures relative changes in the concentrations of oxygenated (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) based on the differential absorption and backscattering of infrared light in cortical tissue (for a review, see Irani et al., 2007). An important advantage of using fNIRS to advance our understanding of the role of the PFC in response inhibition is that it can generate distinct biological measures of cortical activation (i.e., oxy- and deoxy-Hb) which may convey information unique to that provided by the fMRI blood-oxygen level dependent signal (Steinbrink et al., 2006; Strangman et al., 2002). Importantly, fNIRS can supply these measures of cortical activation with high levels of temporal and spatial precision within the PFC, which may be crucial for unravelling the complexities of how functioning of this region may support response inhibition.

Only a small number of studies have employed fNIRS to investigate activation of the PFC under conditions of response inhibition using Go/No-Go tasks. These studies have revealed bilateral activation in the most anterior aspect of the IFG bilaterally (Herrmann et al., 2005), but also more dominant right IFG activation (Tsujii et al., 2011) during response inhibition. Similarly, Nishimura et al. (2011) detected significant activation within the left anterior IFG associated with response inhibition as well as an area of deactivation within the medial PFC (a finding which was not observed in a schizophrenia comparison group). Recently, Wriessnegger et al. (2012) used fNIRS to measure activation of the medial PFC and sensorimotor areas for 11 participants who completed finger and foot versions of a Go/No-Go task. They found significant activation of the medial PFC as well as deactivation of the corresponding sensorimotor cortex during motor response inhibition. Taken together, these findings suggest that activation of the homologous left IFG may also support response inhibition, whereas deactivation of specific prefrontal and sensorimotor cortical regions may also be implicated in some as yet unknown manner.

Although previous research using fNIRS to study response inhibition has revealed meaningful information about the potential roles of the left IFG and medial PFC in these processes, this research is limited in a number of ways. First, these investigations tended to utilize very brief activation periods (and sometimes only one activation period per condition) for their response inhibition tasks, thereby limiting the statistical power of these research designs. Second, nearly all prior fNIRS studies on this topic used probes that were limited in their spatial extent, and therefore, only one study simultaneously measured activation within medial and lateral portions of the PFC (including the IFG) (Nishimura et al., 2011). Given preliminary evidence from separate studies showing increased bilateral IFG activity in conjunction with reduced medial PFC activity during motor response inhibition, understanding the relative engagement and disengagement of these regions in a single study is potentially important. Third, the majority of this fNIRS research is based on considerably small samples of adults, limiting the extent to which meaningful conclusions can be drawn from any single study. Fourth, little research has examined the relationship between accuracy on response inhibition tasks and the extent of activation in specific neural regions. For example, research suggests that deactivation in midline areas (insula, medial PFC) prior to the inhibition of a motor response may be predictive of subsequent success in withholding that response (Hester et al., 2004b). Investigating the interaction between performance accuracy and cortical activation may elucidate whether discrete areas of the PFC function to support distinct response inhibition processes.

The present study accordingly set out to investigate several important unanswered questions regarding the role of inferior-lateral and medial areas of the PFC in motor response inhibition. First, we examined whether the homologous region in the left IFG is also recruited for motor response inhibition, contrary to previous claims of predominantly right IFG involvement (Aron et al., 2004). Second, we investigated whether the medial PFC shows significant deactivation associated with motor response inhibition, a finding which has been reported in only a small number of studies (Nishimura et al., 2011; Wriessnegger et al., 2012). To understand the potential interaction between behavioral performance and cortical activation, we also explored the relationship between accuracy on the Go/No-Go task and activation within inferior-lateral and medial aspects of the PFC.

Material and Methods

Participants

Forty-four right-handed healthy adults participated in this study. Participants were recruited from the University of Toronto Scarborough undergraduate research participant pool and the surrounding community. From this original sample, one participant was excluded due to problems with fNIRS signal acquisition during the experiment. In total, fNIRS data for seven men and 36 women with a mean age of 24.8 years (*SD* = 11.3) were included in our analyses. All individuals