NeuroImage xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

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Response control networks are selectively modulated by attention to rare events and memory load regardless of the need for inhibition

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ARTICLE INFO

Article history:
Received 2 March 2015
Accepted 3 July 2015
Available online xxxx

Keywords:
Response inhibition
Response selection
Go/Nogo
Simon
fMRI
Insula

ABSTRACT

Recent evidence has sparked debate about the neural bases of response selection and inhibition. In the current study, we employed two reactive inhibition tasks, the Go/Nogo (GnG) and Simon tasks, to examine questions central to these debates. First, we investigated whether a fronto-cortical-striatal system was sensitive to the need for inhibition per se or the presentation of infrequent stimuli, by manipulating the proportion of trials that do not require inhibition (Go/Compatible trials) relative to trials that require inhibition (Nogo/Incompatible trials). A cortico-subcortical network composed of insula, putamen, and thalamus showed greater activation on salient and infrequent events, regardless of the need for inhibition. Thus, consistent with recent findings, key parts of the fronto-cortical-striatal system are engaged by salient events and do not appear to play a selective role in response inhibition. Second, we examined how the fronto-cortical-striatal system is modulated by working memory demands by varying the number of stimulus-response (SR) mappings. Right inferior parietal lobule showed decreasing activation as the number of SR mappings increased, suggesting that a form of associative memory – rather than working memory – might underlie performance in these tasks. A broad motor planning and control network showed similar trends that were also modulated by the number of motor responses required in each task. Finally, bilateral lingual gyri were more robustly engaged in the Simon task, consistent with the role of this area in shifts of visuo-spatial attention. The current study sheds light on how the fronto-cortical-striatal network is selectively engaged in reactive control tasks and how control is modulated by manipulations of attention and memory load.

Introduction

Inhibitory control is a pervasive cognitive process. It is needed in the context of immediate threats such as stopping entry into the street in the face of an on-coming car, as well as to suppress urges so that we actively choose a more desirable response option over an alternative prepotent response. Not surprisingly, inhibitory control changes dramatically over development with robust individual differences in adulthood, and has been implicated in multiple forms of psychopathology including attention deficit hyperactivity disorder (Aron, 2011; Bhaijiwala et al., 2014) and obsessive-compulsive disorder (Tolin et al., 2014).

A central challenge to studying inhibitory control is that it comes in many flavors. A recent review by Aron provides a useful taxonomy, classifying inhibitory control along two key dimensions (Aron, 2011). The first dimension contrasts global control and selective control. In global inhibitory control tasks (Aron and Verbruggen, 2008), global inhibition of the motor system is required whenever a specific stimulus is presented, while in selective control tasks, the specifics of the stimulus determine the control needed to slow down the system to give enough time for one particular set of response tendencies to win out over another when conflict is detected (for detailed review, see Aron (2011).

The second dimension in Aron's taxonomy contrasts reactive and proactive control (Aron, 2011). In the former case, participants must inhibit a behavior in reaction to a specific stimulus *after* a response has been prepared. This type of control is often studied in a stop-signal paradigm where participants are instructed to stop a previously prepared response when a stop-signal is presented. Proactive control, by contrast, occurs where there is some advance control process that modulates behavior *before* the presentation of a response cue. Proactive control often implicates attentional or working memory processes that

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http://dx.doi.org/10.1016/j.neuroimage.2015.07.026
1053-8119/© 2015 Published by Elsevier Inc.

modulate control in task-appropriate ways. For instance, actively maintaining information in working memory (WM) can have inhibitory consequences, suppressing the influence of potentially distracting information.

Given the challenges of teasing apart different aspects of inhibitory control at the behavioral level, many studies have examined inhibitory control at the neural level. Data from both neurophysiology and fMRI have revealed a fronto-cortical-basal ganglia network critically involved in reactive control. This network includes the inferior frontal cortex (IFC), the pre-supplementary motor area (preSMA), the basal ganglia, and aspects of the motor system including thalamus and motor cortex (Aron et al., 2014a,b; Braver et al., 2001; Garavan et al., 2002, 2003; McNab et al., 2008; Menon et al., 2001; Mostofsky et al., 2003; Rae et al., 2015; Rubia et al., 2003; Simmonds et al., 2008). This same network may play a key role in 'braking' in proactive control tasks (Aron, 2011), but proactive control likely also involves other WM systems including the dorso-lateral prefrontal cortex (DLPFC) (Barber et al., 2013; Hester et al., 2004; McNab et al., 2008).

In the present report, we focus on a recent controversy regarding the neural systems that underlie reactive inhibitory control. A large body of evidence suggests that a fronto-cortical-striatal network is actively involved in inhibitory control, with a specific part of this network – rIFC and preSMA (Rae et al., 2015) – playing a breaking function in reactive tasks. But a recent paper suggests that this fronto-striatal network is also engaged in attentionally-demanding conditions that do not have obvious inhibitory requirements (Erika-Florence et al., 2014). For instance, these researchers found increased activation in the rIFC network in response to infrequent cues across four task variants, even in tasks with no inhibitory demands. These data are consistent with prior studies that also suggested an attentional/WM role for the fronto-striatal network (Erika-Florence et al., 2014; Hampshire, 2015; Hampshire et al., 2010; McNab et al., 2008). More recently, Swick and Chatham have pointed out that tasks need to be designed such that they contain conditions matched for saliency and attentional demands amongst other elements (Swick and Chatham, 2014). Thus, at the heart of this controversy is whether there is a right-lateralized network for inhibitory control or a network involved in a broader class of control operations, including attention to rare events and the modulation of processing via task goals in working memory.

Here, we examine this controversy using two different reactive control tasks – one task that requires global reactive control – the GnG task – and one that requires selective reactive control – the Simon task. By studying tasks along the global-to-selective control dimension,[1] we hope to tap a range of tasks relevant to daily life that may have broad implications for populations with deficits in inhibitory control.

We examined two central questions about how the role of fronto-cortical-striatal system may differ during selective versus global reactive control. First, is the fronto-cortical-striatal system sensitive to the need for inhibition per se or the need for control on rare, attentionally-demanding trials? To address this question, we varied the response frequency of trials that do not require motoric inhibition (Go trials). In a frequent condition, participants completed a block of GnG trials with many Go trials and few Nogo trials. We contrasted performance in this condition with a block of trials with frequent Nogo trials and few Go trials. If fronto-cortical-striatal networks are sensitive to the inhibitory demands of the task, we expected to see greater activation on trials that require inhibition than during trials that do not require inhibition. By contrast, if fronto-cortical-striatal networks are sensitive to the need for control during rare, attentionally-demanding events, we expected to see greater activation during infrequent trials, regardless of whether these trials occurred during a frequent Go block or a frequent Nogo block. An important question is whether such effects generalize across tasks. Thus, the same participants completed a Simon task where the frequencies of Compatible and Incompatible trials were manipulated across blocks in an analogous fashion.

The second question we examined was whether activation of the fronto-cortical-striatal system is modulated by the need for inhibition per se or by the WM demands of the task. To examine this issue, we varied the memory load, while holding attentional demands constant (i.e., equal numbers of Go/Compatible and Nogo/Incompatible trials). In particular, we changed the number of stimulus-response (SR) mappings that participants had to maintain in both the GnG and Simon tasks. Previous studies have demonstrated that WM maintenance has a particular neural signature – activation increases as the WM load increases (Pessoa et al., 2002; Pessoa and Ungerleider, 2004; Todd and Marois, 2004). Thus, if WM is critically involved in these tasks, we would expect to see an increase in activation as the load increases within WM-specific regions of the fronto-cortical-striatal network. Data from several studies are consistent with this hypothesis. For instance, an increase in activation was observed within middle frontal gyrus, left middle temporal gyrus, thalamus, and rostral and dorsal ACC/preSMA as the memory load was increased in a GnG task (Hester et al., 2004).

Materials and methods

Participants

Twenty right-handed native English-speaking participants (age range 25±4 years; 9 women) took part in the experiment. All of them were students at the University of Iowa. All participants had normal or corrected vision. All participants signed an informed consent form approved by the Ethics Committee at the University of Iowa.

Procedure

The experimental paradigms were created using E-prime version 2.0 and were run on an HP computer (Windows 7). Participants were instructed that they would be given a set of response mappings that would be indicated before the start of each block. There were no practice trials, but participants were shown the sequence of events for a couple of trials to make sure they knew what they were going to do in the scanner.

In the GnG task, observers were asked to press a button when they saw a Go stimulus and withhold their response when they saw a Nogo stimulus (see Fig. 1B). In the Simon task, participants were asked to press the left button for one set of colors and the right button for a second set of colors (see Fig. 1C). On half the trials, stimuli were presented in the compatible hemifield (i.e., the color associated with a left button press was presented in the left hemifield), while on the other half of trials, stimuli were presented in the incompatible hemifield (i.e., the color associated with a left button press was presented in the right hemifield).

Stimuli were all the same shape and varied in color. The colors were equally distributed in CIELAB 1976 color space, a perceptually uniform color space and color-appearance model developed by the Commission Internationale de l'E´clairage. The shape was chosen from Drucker and Aguirre (Drucker and Aguirre, 2009). Colors used for the GnG task were separated by 30 degrees in color space from those colors used in the Simon task (see Fig. 1A). Within a task, the colors associated with specific responses (i.e., Go color and Nogo color) were chosen by going around the color wheel in a clockwise direction. The chosen colors were separated by 60 degrees in color space such that directly adjacent colors were associated with different response types. This prevents participants from adopting any sort of color category response strategy. Participants indicated the response for each trial using left and right

[1] Note that although the GnG and Simon tasks differ along this key dimension, these tasks can be conceptualized in other ways as well. For instance, the Simon task is often discussed as a 'resistance to interference' task. Critically, these different conceptualizations are not mutually exclusive.

Please cite this article as: Wijeakumar, S., et al., Response control networks are selectively modulated by attention to rare events and memory load regardless of the need for inhibition, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.07.026