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Segregating attention from response control when performing a motor inhibition task
Segregating attention from response control

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ABSTRACT

Considerable work has demonstrated that inferior frontal gyrus (IFG), anterior insula cortex (AIC) and the supplementary motor area (SMA) are responsive during inhibitory control tasks. However, there is disagreement as to whether this relates to response selection/ inhibition or attentional processing. The current study investigates this by using a Go/No-go task with a factorial design. We observed that both left IFG and dorsal pre-SMA were responsive to no-go cues irrespective of cue frequency. This suggests a role for both in the inhibition of motor responses. Generalized psychophysiological interaction (gPPI) analyses suggest that inferior frontal gyrus may implement this function through interaction with basal ganglia and by suppressing the visual representation of cues associated with no-go responses. Anterior insula cortex and a more ventral portion of pre-SMA showed greater responsiveness to low frequency relative to higher frequency stimuli, irrespective of response type. This may reflect the hypothesized role of anterior insula cortex in marking low frequency items for additional processing (cf. Menon and Uddin, 2010). Consistent with this, the gPPI analysis revealed significantly greater anterior insula cortex connectivity with visual cortex in response to low relative to high frequency cues.
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Introduction

Response inhibition is considered a core executive function (Friedman and Miyake, 2004) and has been related to measures of task switching ability, executive control and the ability to produce non-stereotyped responses (Friedman and Miyake, 2004). However, the functional properties of the core neural systems involved in response inhibition, particularly the inferior frontal gyrus, anterior insula cortex and dorsomedial frontal cortex (particularly the pre-supplementary motor area [pre-SMA]), remain debated.

Claims have been made that inferior frontal gyrus and adjoining anterior insula cortex (IFG & AIC), particularly on the right, are implicated in inhibitory motor control (e.g. Aron, 2011; Aron et al., 2014; Cai and Leung, 2011; Chikazoe et al., 2009; Dodds et al., 2011). Consistent with this, stopping is impaired after right (Aron et al., 2003; Rieger et al., 2003) and left (Swick et al., 2008) IFG lesions. Moreover, stopping is disrupted after temporary deactivation of right IFG by transcranial magnetic stimulation (Chambers et al., 2007; Chambers et al., 2006). It is argued that the right IFG sends "a Stop command to intercept the Go process, via the basal ganglia" particularly the subthalamic nucleus (Aron, 2011,e56).

Alternatively, it has been argued that IFG and AIC activation during inhibitory control tasks reflects an attention-based response to the stop signal (Sharp et al., 2010). Certainly, it appears that the integrity of inhibitory control is reliant on attention-based reductions of the representation of irrelevant stimuli and monitoring for cues engendering inhibitory control (Verbruggen et al., 2014). Indeed, Criaud and Boulinguez concluded in a recent meta-analysis "that most of the activity typically elicited by no-go signals … is actually driven by the engagement of high attentional or working memory resources" (2013, p. 11). Moreover, a series of studies implicate the right IFG and/or AIC in attention, particularly in response to the detection of salient, behaviorally relevant targets (Bledowski et al., 2004; Corbetta et al., 2008; Corbetta and Shulman, 2002; Hampshire et al., 2010; Kincade et al., 2005; Serences et al., 2005). It is argued that this region is "engaged by the detection of unexpected stimuli" (Sharp et al., 2010, p. 6109). In line with this, Sharp et al. (2010) reported right IFG activity not only when successfully stopping on a Stop task but also when responding to a comparably infrequent "continue" cue that engendered a continuation, rather than a stopping, of the previous triggered response (cf. Chatham et al., 2012). This position has received criticism however (Aron et al., 2014). Aron et al. (2014) argued that the continue trials in the Sharp et al (2010) study included a 'braking' component and thus the IFG activity might

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reflect inhibition. Moreover, Barber et al. (2013) could not find support for a modulatory effect of working memory load on the IFG.

Complicating the issue are suggestions of functional specificity within regions of right IFG and/ or AIC. Thus, Chikazoe et al. (2009) reported that a more inferior region of right IFG showed greater responses during infrequent no-go trials relative to infrequent and frequent go trials. This suggested a role for this more inferior region in inhibition. In contrast, both infrequent no-go trials and infrequent go trials were associated with greater activity in a more superior region of IFG relative to frequent go trials. This suggested a role for this more superior region in attentional processing (Chikazoe et al., 2009); for related studies, see (e.g. Cai and Leung, 2011; Cai et al., 2014; Verbruggen et al., 2010). Indeed, other studies indicating a role of IFG in attentional capture have also reported activity in a more superior region of IFG if the stimulus feature has low behavioral significance (i.e., it has no relationship with target location across trials (e.g. de Fockert et al., 2004)). In contrast, studies where the stimulus has higher behavioral significance (e.g., if the cue indicated an invalid location for the target stimulus), activity was seen in more inferior regions of right IFG (Arrington et al., 2000; Corbetta and Shulman, 2002), perhaps indicative of a more general role for this region in response updating (Levy and Wagner, 2011). Relatedly, Buch et al. (2010) reported that the role of IFG could switch from having facilitatory effects during movement initiation to inhibitory effects on primary motor cortex if the task context required the updating of a response.

With respect to the role of dorsal medial prefrontal cortex (particularly pre-SMA) in response inhibition, there are data indicating that lesions to pre-SMA impair response inhibition (Décary and Richer, 1995; Floden and Stuss, 2006; Picton et al., 2007) and that stimulation of pre-SMA often leads to motor arrest of ongoing movements (see for a review Filevich et al., 2012). On this basis, it has been argued that IFG, AIC and pre-SMA "work together to send a Stop command to intercept the Go process, via the basal ganglia" (p. e56; Aron, 2011). However, while some authors implicate IFG, AIC and pre-SMA in response inhibition (Aron, 2011; Aron and Poldrack, 2006; Chambers et al., 2009), others suggest that *only* pre-SMA is implicated in response inhibition (Sharp et al., 2010; Simmonds et al., 2008), while yet others argue that *neither* IFG, AIC nor pre-SMA are implicated in response inhibition but rather that the response of both to no-go cues reflects the engagement of high attentional or working memory resources (Criaud and Boulinguez, 2013).

The inhibition and attention accounts make contrasting predictions with respect to stimulus frequency. Within the inhibition view, it can be argued that systems necessary for inhibitory control (IFG, AIC and/or pre-SMA) should be engaged by no-go stimuli irrespective of the frequency of these stimuli (c.f. Criaud and Boulinguez, 2013). It has alternatively, but relatedly, been argued that they will only be engaged under conditions of low no-go stimulus frequency; i.e., their function is to over-ride the prepotent go response engendered by the presence of frequent go stimuli (e.g. Casey et al., 1997). The attention-based accounts, in contrast, predict that stimulus frequency (whether a go or no-go cue) should affect activity (c.f. Sharp et al., 2010 p. 6109). In other words, regions will respond to go stimuli when they are rare (and no-go stimuli are common) *and* no-go stimuli when they are rare (and go stimuli are common).

Previous studies attempting to disentangle the role(s) of IFG and AIC in inhibition or attention have frequently involved contrast approaches; i.e., is there significant IFG and/ or AIC activity for rare no-go trials relative to rare go trials (Cai et al., 2012; Chikazoe et al., 2009; Sharp et al., 2010). While interesting, it is perhaps also useful to approach the issue with a factorial design. This will not only allow for the identification of regions showing activity for no-go trials relative to go trials independent of no-go frequency but also for frequent items relative to infrequent items irrespective of response type and any regions showing a significant trial type by frequency interaction. Importantly, in such a design, rare go stimuli are not presented within a context that additionally contains rare no-go stimuli, thereby eliminating the automatic brake effect rare stimuli can trigger if some of them require a stop (Bissett and Logan, 2014). One previous study implemented such a factorial design (Braver et al., 2001), and observed IFG recruitment during low frequency no-go cues. However, their analysis did not assess IFG involvement during high-frequency no-go cues.

Recent work has begun to examine functional connectivity within the inhibition network. Duann et al. (2009) reported positive psychophysiological interactions (PPIs) between right IFG and pre-SMA and negative PPIs between pre-SMA and caudate for successful stop trials compared to unsuccessful stop trials. On the basis of these data, they argued that IFG responds to a stop signal and expedites the stop process in the pre-SMA, the primary site of motor response inhibition. However, other connectivity studies have not suggested a primary role for pre-SMA. Thus, Dambacher et al. (2014) observed an inter-correlated core network, including IFG/ AIC, pre-SMA and SMA proper and basal ganglia, during response inhibition. Similarly, Jahfari et al. (2012) observed effective connectivity between both right IFG and pre-SMA and caudate during performance of a Stop task. Finally, Behan et al. (2015) reported positive connectivity between a region of right IFG and motor cortex during successful motor inhibition (interestingly, they also reported negative connectivity between another region of right IFG and bilateral ventral striatum during reward anticipation for successful compared to unsuccessful no-go trials). It should be noted that one study reported positive PPIs between the AIC/ IFG and the subthalamic nucleus during infrequent versus frequent trials in a Stop-Signal Task [SST] irrespective of whether the infrequent cue was a stop or a go signal (Erika-Florence et al., 2014). This would suggest that connectivity between AIC/ IFG and the subthalamic nucleus reflected attentional demands rather than response inhibition. However, these previous connectivity studies also involved contrast approaches, rather than factorial designs. For this reason, we applied the method of generalized psychophysiological interactions (gPPI, McLaren et al., 2012), which allows for data analysis involving more than two levels.

In short, we implemented a factorial Go/No-go design, with trials separated into blocks containing 75% go cues/ 25% no-go cues or blocks containing 75% no-go cues/ 25% go cues. We analyzed our data in two ways. Firstly, we assessed which brain regions were differentially activated as a function of task condition. We predicted: (i) if IFG, AIC and/ or pre-SMA play a role in inhibition and inhibitory demands are not a function of no-go frequency, then either or all of these regions should show greater responsiveness to no-go stimuli than go stimuli irrespective of no-go stimulus frequency; (ii) if IFG, AIC and/ or pre-SMA play a role in inhibition, and if the over-riding of a prepotent response is important for their activation (cf. Casey et al., 1997), then activity within either or all of these regions should be greatest when responding to no-go cues when these are infrequent (i.e., in 75% go/ 25% no-go cue blocks); or (iii) if instead, or additionally, responsiveness of IFG, AIC and/ or pre-SMA is driven by the engagement of "high attentional resources" cf. (Criaud and Boulinguez, 2013), then activity within either or all of these regions should be larger when processing *both* no-go and go cues during blocks when these are infrequent (i.e., to no-go cues in 75% go/ 25% no-go cue blocks and go cues in 75% no-go/ 25% go cue blocks). Secondly, we analyzed our data using generalized context-dependent psychophysiological interactions (gPPIs, McLaren et al., 2012). We predicted: (i) if IFG or AIC interrupts the go process via basal ganglia (cf. Aron, 2011; Aron et al., 2014), it should show negative connectivity with striatum particularly during no-go trials; and (ii) if IFC, or AIC is engaged in attentional processes it should show positive connectivity with temporal and visual cortices (Pantazatos et al., 2012).

Materials and methods

Participants

Twenty-two healthy adult volunteers were recruited from the community through newspaper ads and fliers (54.50% female; average age