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## Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent.

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### Abstract

FMRI studies of response inhibition consistently reveal frontal lobe activation. Localization within the frontal cortex, however, varies across studies and appears dependent on the nature of the task. Activation likelihood estimate (ALE) meta-analysis is a powerful quantitative method of establishing concurrence of activation across functional neuroimaging studies. For this study, ALE was used to investigate concurrent neural correlates of successfully inhibited No-go stimuli across studies of healthy adults performing a Go/No-go task, a paradigm frequently used to measure response inhibition. Due to the potential overlap of neural circuits for response selection and response inhibition, the analysis included only event-related studies contrasting No-go activation with baseline, which allowed for inclusion of all regions that may be critical to visually-guided motor response inhibition, including those involved in response selection. These Go/No-go studies were then divided into two groups: “simple” Go/No-go tasks in which the No-go stimulus was always the same, and “complex” Go/No-go tasks, in which the No-go stimulus changed depending on context, requiring frequent updating of stimulus-response associations in working memory. The simple and complex tasks demonstrated distinct patterns of concurrence, with right dorsolateral prefrontal and inferior parietal circuits recruited under conditions of increased working memory demand. Common to both simple and complex Go/No-go tasks was concurrence in the pre-SMA and the left fusiform gyrus. As the pre-SMA has also been shown to be involved in response selection, the results support the notion that the pre-SMA is critical for selection of appropriate behavior, whether selecting to execute an appropriate response or selecting to inhibit an inappropriate response.

### Keywords

activation likelihood estimate; ALE; pre-SMA; response selection

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## 1. Introduction

Executive function refers to the ability to plan and execute behavior, while constantly updating representations and goals in an always-changing environment. Central to these control functions is the ability to appropriately select actions that are behaviorally advantageous, and conversely to withhold or suppress actions that are either inappropriate in a given behavioral context or unwanted because they interfere with completion of motor and/or cognitive goals. Much emphasis has been placed on the ability to suppress inappropriate and unwanted actions, often referred to as response inhibition, not only because of its importance for control of human behavior, but also because deficient response inhibition has been hypothesized to contribute to several neuropsychiatric disorders. Most notable is attention deficit/hyperactivity disorder (ADHD), in which a leading hypothesis proposes that failure to inhibit impulsive and off-task behavior is a core deficit of the disorder (Barkley, 1997).

Many studies have investigated the neural correlates of response inhibition. Human lesion studies have demonstrated the involvement of the frontal cortex (Drewe et al., 1975; Godefroy & Rousseaux, 1996), with more specific localization in the superior medial (BA6/8) (Drewe et al., 1975; Floden & Stuss, 2006; Picton et al., 2006) and right inferior prefrontal cortices (Aron et al., 2003; Chambers et al., 2006). fMRI studies of response inhibition consistently reveal frontal lobe activation (Blasi et al., 2006; Garavan et al., 1999; Liddle et al., 2001; Mostofsky et al., 2003; Rubia et al., 2001; Wager et al., 2005; Watanabe et al., 2002). Localization within the frontal cortex, however, varies across studies; this variation appears to be task dependent (Mostofsky et al., 2003). Several tasks used to study inhibition during fMRI such as the Wisconsin Card Sorting Task and the Stroop task involve additional cognitive processes necessary to guide response inhibition, including stimulus-response conflict, learning, working memory and shifting attention (Buchsbaum et al., 2005); as all of these processes have been shown to involve various regions of the prefrontal cortex, the degree to which each of these processes are engaged may affect the localization of inhibitory activity.

The Go/No-go task is frequently used during fMRI and the traditional, simple format of this task allows for examination of response inhibition under conditions in which other cognitive/behavioral processes are minimized. The traditional Go/No-go task design involves only two stimuli: a Go stimulus and a No-go stimulus. Participants are instructed to respond rapidly, generally with a button-press, to presentation of Go stimuli only, and response inhibition is measured by the ability to appropriately withhold responding to No-go stimuli. Typically, the task is weighted towards Go stimuli, in order to build up a prepotent tendency to respond, thereby increasing the inhibitory effort necessary to successfully withhold responding to No-go stimuli.

Yet, findings from fMRI studies of the Go/No-go task also differ in localization of inhibitory-associated activation within the frontal cortex. The most likely explanation for this is differences in task-design. While some studies employ a more traditional GNG task design, with a single Go stimulus and single No-go stimulus (Kiehl et al., 2000; Liddle et al., 2001; Mostofsky et al., 2003; Watanabe et al., 2002), others use more complex designs involving multiple Go cues (Fassbender et al., 2004; Garavan et al., 1999; Wager et al., 2005), which increases the number of stimulus-response associations and/or involves frequently updating stimulus-response associations. In either situation, complex designs increase short-term/working memory demands. For instance, in one frequently used version of the task (Garavan et al., 2002; 2003; Hester et al., 2004; Kelly et al., 2004), X's and Y's are alternately presented on the screen, and infrequently there is a two-letter repeat, which is the No-go signal; after presentation of an X, Y becomes the Go signal and X the No-go signal, and vice versa. As there are several processes important to visually-guided Go/No-go tasks, such as stimulus recognition, maintenance and manipulation of stimulus-response associations and response

selection, including selecting not to respond, the degree to which each of these processes is engaged by each task may influence the resulting neural correlates of successful response inhibition.

Meta-analysis offers a viable approach for establishing concurrence across studies. One method of meta-analysis called activation likelihood estimate (ALE) (Turkeltaub et al., 2002), allows for statistically verifiable concurrence across functional neuroimaging studies. This is made possible by standardized coordinate reporting, with most studies reporting in Talairach space (Talairach & Tournoux, 1988). In ALE, foci are plotted as the center of a three-dimensional Gaussian function and pooled to create a new, statistically thresholded whole-brain image, showing regions with the highest “likelihood” of activation, or where the concurrence is highest.

A previous review of response inhibition tasks mapped coordinates reported in several studies (Aron & Poldrack, 2005), including both blocked and event-related Go/No-go tasks as well as Stop-Signal tasks, and suggested a preponderance of activation in the right inferior frontal cortex; however, no statistical methods were used to confirm this observation. Recently, an ALE meta-analysis of Go/No-go tasks was performed (Buchsbaum et al., 2005), reporting a mainly right-lateralized network associated with response inhibition, including the right middle/inferior frontal gyrus (BA46/44), right inferior parietal regions (BA40), and the superior medial frontal gyrus (BA6); however, a wide range of Go/No-go tasks with different cognitive and working memory demands were represented, including a number of tasks with high working memory load that required manipulation of stimulus-response associations on a trial-by-trial basis. Given evidence that the neural correlates of response inhibition may vary depending on task demands (Mostofsky et al., 2003), it may be that concurrence in right-lateralized frontoparietal regions seen in the ALE analysis is reflected in the tasks with high working memory load that necessitate recruitment of these regions to guide response inhibition, but that this network is not critical to tasks of response inhibition that do not require working memory to guide inhibition.

Additionally, Buchsbaum et al. selected studies employing a range of analytic approaches, including those from block designs and a variety of event-related approaches; this may have impacted their meta-analysis findings. Early fMRI studies of GNG tasks used a block design approach (Rubia et al., 2001; Menon et al., 2001), in which blocks containing both Go and No-go stimuli are contrasted with Go-only blocks. This contrast shows activation related to the inhibitory process; problematically, it is also confounded by issues such as task difficulty, attention, different stimuli and maintenance of stimulus-response associations, and as such is not ideal for isolating regions involved in the inhibitory process.

More recent studies have tended to use an event-related design (Blasi et al., 2006; Garavan et al., 2002; Liddle et al., 2001; Mostofsky et al., 2003; Watanabe et al., 2002), whereby activation associated with successfully inhibited No-go stimuli is contrasted with other portions of the task, generally either the implicit task baseline, which excludes errors and may exclude Go trials, or activation specific to Go stimuli. The “No-go versus Go” contrast is useful in revealing activation that is exclusive to the inhibitory process but makes the assumption that the processes of response selection (Go) and response inhibition (No-go) are independent. This may not be the case; similar to motor response selection, response inhibition is an active process, in which an individual actively selects not to respond, and hence their neural bases may overlap (for review, see Mostofsky & Simmonds, in press). This is particularly highlighted in a recent study of rhesus monkeys (Isoda & Hikosaka, 2007) in which neurons in the rostral portion of the superior medial wall (“pre-SMA”; BA6) were found to be active during the response “switching”, which involved the selection of a new, controlled response and suppression of a habitual response. When activity from these same neurons was recorded during a Go/No-go

task, it was seen that some of these pre-SMA neurons responded to Go stimuli (Go type), some responded to No-go stimuli (No-go type) and some responded to both (Dual type). The data from the response switching experiment was then reanalyzed, and it was shown the No-go and Dual type neurons fired earlier than Go type neurons, suggesting that 1) selection of a response involves first inhibiting other responses and then selecting the new response and that 2) the processes of response inhibition and selection may be distinguished in the temporal domain, rather than the spatial domain.

Further evidence for the link between response inhibition and selection comes from studies of humans. An fMRI conjunction analysis of motor response selection and inhibition tasks identified a frontal network activated in response to all low-frequency stimuli across the tasks, irrespective of whether they involved a execution or inhibition of a motor response (Braver et al., 2001). The commonality between motor response selection and response inhibition is further reflected in the executive deficits associated with ADHD, where impairments in both motor response inhibition (Aron & Poldrack, 2005; Barkley, 1997; Nigg, 1999) and motor response selection/execution (Banaschewski et al., 2004; Ben-Pazi et al., 2003; Rubia et al., 2003) are observed. Thus, the “No-go versus Go” contrast may be masking activation that is critical to the inhibitory process but is also involved in motor response selection.

Along these lines, it is also important to note that the Go/No-go task has been used for several decades as a measure of response inhibition and was not originally designed for use during fMRI; as such, the intermixing of Go and No-go stimuli was not intended to create a functional contrast between two “opposite” events, rather, the presence of Go stimuli was intended to create a prepotent tendency to respond, which then necessitates inhibition with the appearance of a No-go stimulus. Given that both Go and No-go events involve response selection, including selecting to inhibit movement in the case of No-go, it would be best to not treat them as opposite contrasts in an fMRI design; doing so may lead to the erroneous conclusion that certain brain regions are not critical to response inhibition because they are involved in response selection as well.

In the present study, we performed a meta-analysis of Go/No-go tasks, focusing on those studies using an event-related contrast of “No-go versus baseline,” in order to reveal all regions common to successfully inhibited No-go stimuli that may be critical to response inhibition. These Go/No-go studies were then divided into two groups: “simple” Go/No-go tasks in which the No-go stimulus was always the same, and “complex” Go/No-go tasks, in which the No-go stimulus changed depending on context, requiring frequent updating of stimulus-response associations in working memory. While regions recruited to guide response inhibition may vary depending on task design, processes central to response selection are likely common to all Go/No-go tasks as a final common pathway involved in selecting to withhold a response. Hence, our hypothesis was that for the complex tasks only, concurrence would be seen in a right-lateralized network of frontoparietal regions, which are important for guiding behavior under conditions of increased cognitive and working memory load. However, for both simple and complex tasks, we hypothesized that the rostromedial prefrontal cortex (“pre-SMA”, BA6) would show high concurrence across Go/No-go studies due to its involvement in both response selection (Ball et al., 1999; Barber & Carter, 2005) and inhibition (Drewe et al., 1975; Mostofsky et al., 2003; Picton et al., 2006).

## 2. Methods

### 2.1 Study Selection

Studies were selected for the meta-analysis by searching the Pubmed database ([www.pubmed.org](http://www.pubmed.org)) using two keyword searches: “Go/No-go AND fMRI” and “response inhibition AND fMRI.” Selection criteria were applied such that studies 1) employed a Go/

No-go task during fMRI of healthy adults, 2) analyzed the data using a contrast of correctly-rejected No-go trials against the general task baseline and 3) reported the results as three-dimensional coordinates in stereotactic space.

After these criteria were applied, ten studies remained (Garavan et al., 1999; 2002; 2003; Fassbender et al., 2004; Hester et al., 2004; Kelly et al., 2004; Kiehl et al., 2000; Liddle et al., 2001; Mostofsky et al., 2003; Watanabe et al., 2002), shown in Table 1. Of these studies, seven included Go trials in the baseline, and the other three modeled Go trials as separate regressors and excluded them from the baseline (Liddle et al., 2001; Mostofsky et al., 2003; Watanabe et al., 2002). The studies varied in number of participants (11–48), number of foci reported (3–23), type of stimuli (letters, colored objects), number of stimuli (48–1260), proportion of No-go trials (6.8–50%), stimulus duration (200–1100ms) and inter-trial interval (800ms–12s), as well as in statistical thresholds used. Although not all studies mentioned handedness and the hand used to respond, those that did reported that all participants were right-handed and responded with their right hand. These studies were then divided into “simple” tasks in which the No-go stimulus-response association always remained the same, and “complex” tasks in which the No-go stimulus-response association was manipulated based on information in working memory. Of the ten studies, four were classified as simple (Fassbender et al., 2004; Kiehl et al., 2000; Liddle et al., 2001; Watanabe et al., 2002), five were classified as complex (Garavan et al., 1999; 2002; 2003; Hester et al., 2004; Kelly et al., 2004), and one paper (Mostofsky et al., 2003) reported on both a simple and complex task, for a total of five simple and six complex tasks.

## 2.2 ALE meta-analysis

Three separate ALE analyses were run: one for all 11 studies, one for the “simple” studies and one for the “complex” studies. The analyses were based on the original methods designed and described in detail by Turkeltaub et al. (2002). Foci of activation reported in the selected studies for the contrast of No-go versus baseline were plotted and processed using the Brainmap Search&View program v3.1 (Laird, Lancaster & Fox, 2005). Three of the studies included in the analyses reported their coordinates in the standard space of the Montreal Neurological Institute (MNI) (Kiehl et al., 2000; Liddle et al., 2001; Watanabe et al., 2002); these were converted to Talairach space using formulas provided by Matthew Brett (<http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html>). Our parameters were identical to those used by Buchsbaum et al. (2005). Activation foci were plotted as the center of a 3-dimensional Gaussian function with a full-width half-maximum (FWHM) of 15mm. 5000 permutations using the same FWHM and number of foci were generated in order to assess statistical significance, and the ALE map was thresholded at a p-value of  $10^{-3}$ . ALE values were overlaid onto the “colinbrain” anatomical template normalized to Talairach space (Kochunov et al., 2002) using the MRICron software (<http://www.sph.sc.edu/comd/rorden/mricron>).

## 3. Results

The results from the ALE analysis for all 11 studies can be seen in Figure 1, with the cluster details in Table 2. The analysis demonstrated a primarily right-lateralized network associated with successfully inhibited No-go stimuli, with concurrence seen in the rostral portion of the superior medial wall (pre-SMA; BA6/32), right prefrontal regions (BA9/10/44), left premotor cortex (BA6), bilateral inferior parietal regions (BA40), bilateral occipital regions (BA19/37), bilateral putamen and bilateral insula.

The results from the ALE analyses for the simple and complex studies can be seen in Figure 2, and the cluster details can be seen in Table 2. The analysis of the simple studies demonstrated concurrence in the right pre-SMA (BA6/32), bilateral occipital regions (BA19/37) and the



precuneus (BA7). The analysis of the complex studies demonstrated concurrence in the pre-SMA (BA6/32), right middle/inferior frontal gyrus (BA9/44), bilateral inferior parietal regions (BA40), bilateral putamen, bilateral insula, right middle temporal gyrus (BA22), left fusiform gyrus (BA19/37) and the left middle frontal gyrus (BA46). Although the ALE analyses of the simple and complex studies demonstrated distinct patterns of concurrence, overlap between the two analyses was seen only in the pre-SMA (BA6/32) with a 176mm<sup>3</sup> extent, indicated by the arrows in Figure 2, and in the left fusiform gyrus (BA37) with a 16mm<sup>3</sup> extent.

#### 4. Discussion

Consistent with the previous ALE meta-analysis of Go/No-go tasks (Buchsbaum et al., 2005), concurrence of activation was observed in a predominantly right-lateralized network involving the rostral superior medial wall (“pre-SMA”), right middle/inferior frontal gyrus, bilateral inferior parietal regions, occipital regions, putamen and left premotor cortex. These regions have been implicated in processes of stimulus recognition, maintenance and manipulation of stimulus-response associations and response selection, including selecting not to respond (Braver et al., 2001; Grafton et al., 1992; Law et al., 1997; Liddle et al., 2001; Mostofsky et al., 2003; Rubia et al., 2001), all of which are critical to performance of Go/No-go tasks. However, when the studies were separated into those using “simple” Go/No-go tasks in which stimulus-response associations remained constant and “complex” Go/No-go tasks in which stimulus-response associations had to be manipulated based on information in working memory, concurrence was seen in different networks for the different task types, with the main overlapping region of concurrence in the pre-SMA.

The pre-SMA is localized to the rostral portion of medial Brodmann Area (BA) 6. In contrast with the more posterior “SMA-proper”, which is connected to primary motor regions and the spinal cord, the pre-SMA is mainly connected with prefrontal regions (Picard & Strick, 2001). Although the pre-SMA and SMA-proper are typically distinguished physiologically rather than anatomically, in humans the border is marked as the vertical plane of the anterior commissure. On the inferior side, it borders on the cingulate motor areas; however, as the cingulate motor areas are typically difficult to isolate in human group analyses due to inter-individual anatomical variability (Picard & Strick, 2001), the cingulate sulcus is typically used as the inferior boundary of the pre-SMA. The region revealed by the meta-analysis bordered on the cingulate sulcus, but was almost entirely contained above the cingulate sulcus (see Figure 2), and hence appeared to be principally localized to the pre-SMA.

Findings from electrophysiology, human lesion and functional neuroimaging studies support the crucial role of the pre-SMA in response inhibition. Single-cell recordings in monkeys have demonstrated the involvement of a region analogous to the pre-SMA in response inhibition (Matsuzaka et al., 1992). In humans, electrophysiological activity has been seen in the pre-SMA during a response inhibition task (Ikeda et al., 1999) and direct stimulation of the pre-SMA region inhibited ongoing, habitual motor actions (Ikeda et al., 1993). In the three largest human frontal lesion studies of response inhibition to date, poor inhibitory performance was associated with lesions of the superior medial frontal lobe (Drewe et al., 1975; Floden & Stuss, 2006; Picton et al., 2006). In fMRI studies of response inhibition, pre-SMA activation has been a consistent finding (Bellgrove et al., 2004; Blasi et al., 2006; Braver et al., 2001; Fassbender et al., 2004; Kelly et al., 2004; Kiehl et al., 2000; Liddle et al., 2001; Mostofsky et al., 2003; Rubia et al., 2001). Additional support for the importance of the pre-SMA to response inhibition comes from fMRI activation seen in the pre-SMA during anti-saccade and anti-pointing tasks (Connolly et al., 2000), both involving inhibition of a prepotent response, and a study combining EEG and fMRI in which a decrease in activation in the pre-SMA was observed prior to primary motor cortex activation and motor execution (Ball et al., 1999).

However, in addition to response inhibition, the pre-SMA has also been found to be involved in response selection. In monkeys, this is demonstrated by the presence of both Go type and No-go type neurons within the pre-SMA (Isoda & Hikosaka, 2007). The presence of both of these types of neurons within the pre-SMA indicate that the pre-SMA plays an important role in switching from an automatic, habitual response to a controlled response by suppressing (i.e., inhibiting) the habitual response and boosting selection of the controlled response (Isoda & Hikosaka, 2007). This is very consistent with functions necessary for withholding a response to a No-go stimulus in which one has to switch from execution of a habitual motor (Go) response to inhibition of such a response when the No-go stimulus appears; the same mechanism is applicable to other tasks of response inhibition, including the Stop-Signal task and antisaccade tasks.

In humans, electrophysiological (Ball et al., 1999) and imaging (Ball et al., 1999; Barber and Carter, 2005) studies show the importance of the pre-SMA in motor response preparation and selection. There is also much behavioral evidence indicating that the processes of response selection and inhibition are linked (for review, see Mostofsky & Simmonds, in press), and in Go/No-go tasks, it has been shown that commission errors, which are an indicator of inhibitory performance, correlate with response time variability (Bellgrove et al., 2004; Simmonds et al., in press), a measure of efficient response preparation/selection. The commonality between processes involved in motor response preparation and those central to response inhibition is further reflected in the executive deficits associated with ADHD, where impairments in both response inhibition (Aron & Poldrack, 2005; Barkley, 1997; Nigg, 1999) and motor response preparation/selection (Banaschewski et al., 2004; Ben-Pazi et al., 2003; Rubia et al., 2003; Mostofsky, 2003) are observed. Furthermore, examination of cortical thickness in ADHD revealed significant thinning principally localized to the pre-SMA (Shaw et al., 2006), and children with ADHD showed reduced fMRI activation in this region during a Go/No-go task (Suskauer et al., in press; Tamm et al., 2004), indicating that the pre-SMA may be central to these deficits in response selection and inhibition.

For both the simple and complex tasks, concurrence was also seen in the left fusiform gyrus (BA19/37), a visual association region that has reciprocal connections with both posterior parietal and prefrontal areas (Leichnetz, 1990; Pandya & Seltzer, 1982). Thus, activation likelihood in this area may reflect either stimulus classification, with modulatory feedback from higher order regions (Rockland & Pandya, 1979) about the behavioral salience of No-go stimuli necessary to correctly recognize the cues and inhibit the prepotent response.

Within the complex tasks only, and consistent with findings from Buchsbaum et al., concurrence of activation was seen in a right-lateralized set of regions including the middle/inferior frontal gyrus and inferior parietal lobule (BA40), near the temporo-parietal junction. The inferior parietal cortex has extensive reciprocal connections with the prefrontal cortex (Petrides and Pandya, 1984; Rushworth et al., 2005). These circuits appear to be critical for executive control needed to guide goal-directed and stimulus-driven attention (Corbetta & Shulman, 2002). Centrally relevant to the Go/No-go tasks is the importance of these circuits in maintaining representations of stimulus-response associations used to guide response selection (Hester et al., 2007). The concurrence of these regions in the complex tasks, but not in the simple tasks, suggest that these regions may be recruited in a task-dependent manner, under conditions where increased working memory demand necessitate increased recruitment of these regions to guide response inhibition. This is consistent with a study contrasting fMRI activation from two Go/No-go tasks, whereby activation associated with No-go events in right-lateralized frontoparietal regions, mainly in the right DLPFC, was significantly greater during the “complex” Go/No-go task which required manipulation of stimulus-response associations in working memory over the “simple” Go/No-go task in which stimulus-response associations remained constant (Mostofsky et al., 2003).

It has been suggested that the role of posterior cortical regions within this circuit is maintaining representations of stimulus-response associations by integrating cues and motor actions into stimulus-response associations (Garavan et al., 1999; Liu et al., 2004; Rubia et al., 2001). This may explain why activation in right inferior parietal regions has been a very consistent finding across fMRI studies of response inhibition (Bellgrove et al., 2004; Blasi et al., 2006; Fassbender et al., 2004; Garavan et al., 1999; Liddle et al., 2001; Menon et al., 2001; Mostofsky et al., 2003; Rubia et al., 2001; Wager et al., 2005).

The role of the prefrontal cortex in this circuit, on the other hand, appears to be in exercising top-down control to determine which stimulus-response associations need to be accessed in a given context (Curtis & D'Esposito, 2003; Miller & Cohen, 2001). This is particularly relevant for the right DLPFC, which has been noted to play an important role in manipulation of information, such as stimulus-response associations, in working memory. There is strong evidence for a dorsal/ventral dissociation within the prefrontal cortex, whereby ventral prefrontal regions (lateral IFC) are involved in maintenance of information, whereas dorsal prefrontal regions (DLPFC) are involved in manipulation of information in working memory (for review, see Courtney, 2004 and D'Esposito et al., 1998). It has also been shown that the DLPFC is important for representing task set and instructions, both of which are critical to complex Go/No-go tasks (Courtney, 2004). Due to its crucial role in the domain of working memory, it is apparent that this region is necessary to guide response inhibition under conditions of increased working memory demand. However, recruitment of this region under conditions of minimal working memory demands may in fact be counterproductive, as it has been shown that increased response time variability, or inefficient performance, during a simple Go/No-go task is associated with activation of the right prefrontal cortex (Simmonds et al., in press).

There was a notable lack of concurrence in any of the three analyses in the frontal operculum portion of the right inferior frontal gyrus (BA47), which has been emphasized by some studies to be critical to response inhibition (for review, see Aron & Poldrack, 2005). Recruitment of the RIFC is not a universal finding, with many fMRI and lesion studies of response inhibition failing to report involvement of this region (Drewe et al., 1975; Garavan et al., 2003; Godefroy & Rousseaux, 1996; Kiehl et al., 2000; Langenecker & Nielson, 2003; Li et al., 2006; Mostofsky et al., 2003; Picton et al., 2006; Ramautar et al., 2006; Wager et al., 2005; Watanabe et al., 2002). As the RIFC has been shown to be involved in maintenance of working memory (Courtney, 2004), it follows that activation of the RIFC, like the DLPFC, may be task-dependent.

Whether activation in the RIFC is observed in fMRI investigations of response inhibition may also be related to the type of contrast applied. Many of the studies reporting RIFC involvement during Go/No-go tasks used a direct contrast of No-go and Go trials (Braver et al., 2001; Horn et al., 2003; Rubia et al., 2005), presuming that the sole difference between the two trials is response inhibition. However, there may be additional differences between the two trial types. For example, one of these differences is frequency of presentation, as nearly all Go/No-go studies present stimuli at a Go:No-go ratio of at least 3:1. This raises the likelihood that the appearance of No-go stimuli is associated with an oddball effect, which has been found to result in activation in the RIFC for both response selection and inhibition (Braver et al., 2001). Another difference between the two trials is trial difficulty, as the error rates differ between the two trials; there are generally very few omission errors during Go trials but a large number of commission errors during No-go trials. These confounds were addressed by one study (Liddle et al., 2001) which examined both the "No-go versus Go" and "No-go versus baseline" contrasts within the same study and found RIFC activation only for the "No-go versus Go" contrast.



While the present ALE findings are consistent with previous research, there are several notable issues with the ALE method that may reduce the accuracy of the results. In ALE analyses, the only information taken into account is the location of the voxel of peak activation for each reported cluster, and this voxel is treated as the center of a three-dimensional Gaussian function. ALE analyses do not consider the magnitude or extent of activation for each cluster, both of which are typically, although not always, reported in fMRI studies. This may skew the ALE results; for example, one study may report several small clusters in a region, while another reports a large cluster in the same region. While both may have the same magnitude and extent of activation within the region, the study reporting several coordinates will have more power in the ALE analysis.

Another key issue with ALE is that studies are not weighted based on their statistical power. A study with 48 subjects has more statistical power than a study with 11 subjects, and ALE ideally would take this into account to get a better estimate of concurrence across the population. Additionally, studies use different statistical methods and thresholds; while there may be no way of comparing the differences between studies using random or fixed effects analyses, studies using these types of analyses can be weighted by their statistical thresholds, such that those with stricter thresholds carry more weight. It may also be necessary to exclude fixed effects studies, as their results cannot be generalized to the population as a whole, although depending on the number of published studies available to use in the meta-analysis, this may seriously hinder the power of the analysis. While the ALE method has been widely used and validated, it is important that future studies begin to address these concerns to increase the reliability of the method.

## 5. Conclusions

The present study followed up on a previous study (Buchsbaum et al., 2005), which performed an ALE meta-analysis of Go/No-go tasks. Eleven studies were selected and divided into two groups, for which separate meta-analyses were performed: one group of five using “simple” Go/No-go tasks and one group of six using “complex” Go/No-go tasks, which required a high working memory load to guide response inhibition. The simple and complex tasks demonstrated distinct patterns of concurrence, with right-lateralized prefrontal-parietal circuits observed only for the complex tasks, suggesting that these regions are recruited under conditions in which working memory is necessary to guide response inhibition. Common to both simple and complex Go/No-go tasks was concurrence in the pre-SMA, suggesting that recruitment of the pre-SMA is critical to response inhibition, irrespective of task demands. The findings have implications for ADHD, in which deficits are seen for both response inhibition and response selection; in future studies of children with ADHD, the pre-SMA region may serve as a correlate of genetic variation and a marker of effects of pharmacological intervention in investigations of candidate therapies.

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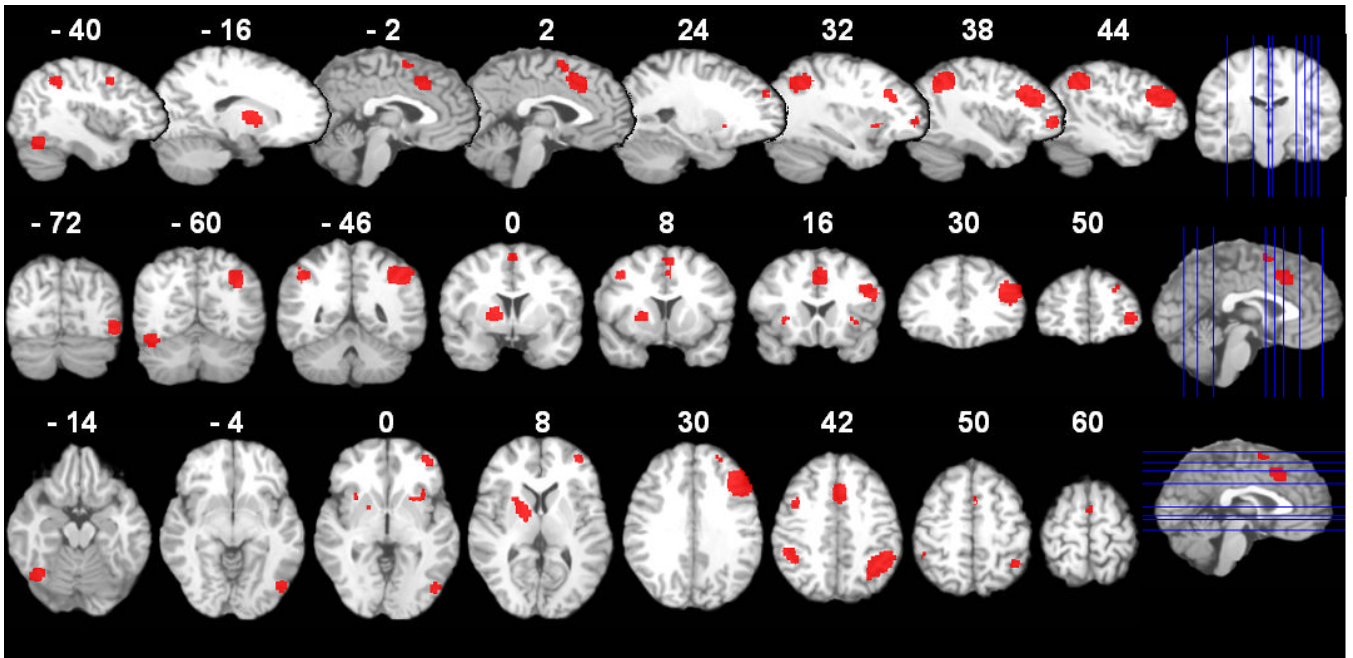
### References

- Aron AR, Poldrack RA. The cognitive neuroscience of response inhibition: relevance for genetic research in attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2005;57(11):1285–92. [PubMed: 15950000]
- Aron AR, Fletcher PC, Bullmore ET, Sahakian BJ, Robbins TW. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nat Neurosci* 2003;6(2):115–6. [PubMed: 12536210]

- Ball T, Schreiber A, Feige B, Wagner M, Lucking CH, Kristeva-Feige R. The role of higher-order motor areas in voluntary movement as revealed by high-resolution EEG and fMRI. *Neuroimage* 1999;10(6): 682–94. [PubMed: 10600414]
- Banaschewski T, Brandeis D, Heinrich H, Albrecht B, Brunner E, Rotherberger A. Questioning inhibitory control as the specific deficit of ADHD—evidence from brain electrical activity. *J Neural Transm* 2004;111(7):841–64. [PubMed: 15206002]
- Barber AD, Carter CS. Cognitive control involved in overcoming prepotent response tendencies and switching between tasks. *Cereb Cortex* 2005;15(7):899–912. [PubMed: 15459082]
- Barkley RA. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull* 1997;121(1):65–94. [PubMed: 9000892]
- Bellgrove MA, Hester R, Garavan H. The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. *Neuropsychologia* 2004;42(14):1910–6. [PubMed: 15381021]
- Ben-Pazi H, Gross-Tsur V, Bergman H, Shalev RS. Abnormal rhythmic motor response in children with attention-deficit-hyperactivity disorder. *Dev Med Child Neurol* 2003;45(11):743–5. [PubMed: 14580129]
- Blasi G, Goldberg TE, Weickert T, Das S, Kohn P, Zolnick B, Bertolino A, Callicott JH, Weinberger DR, Mattay VS. Brain regions underlying response inhibition and interference monitoring and suppression. *Eur J Neurosci* 2006;23(6):1658–64. [PubMed: 16553630]
- Braver TS, Barch DM, Gray JR, Molfese DL, Snyder A. Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. *Cereb Cortex* 2001;11(9):825–36. [PubMed: 11532888]
- Buchsbaum BR, Greer S, Chang WL, Berman KF. Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. *Hum Brain Mapp* 2005;25(1):35–45. [PubMed: 15846821]
- Chambers CD, Bellgrove MA, Stokes MG, Henderson TR, Garavan H, Robertson IH, Mattingley JB. Executive brake failure following deactivation of human frontal lobe. *J Cogn Neurosci* 2006;18(3): 444–55. [PubMed: 16513008]
- Connolly JD, Goodale MA, Desouza JF, Menon RS, Vilis T. A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. *J Neurophysiol* 2000;84(3):1645–55. [PubMed: 10980034]
- Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 2002;3(3):201–215. [PubMed: 11994752]
- Courtney SM. Attention and cognitive control as emergent properties of information representation in working memory. *Cogn Affect Behav Neurosci* 2004;4(4):501–16. [PubMed: 15849893]
- Curtis CE, D'Esposito M. Persistent activity in the prefrontal cortex during working memory. *Trends Cogn Sci* 2003;7(9):415–23. [PubMed: 12963473]
- D'Esposito M, Aquirre GK, Zarahn E, Ballard D, Shin RK, Lease J. Functional MRI studies of spatial and nonspatial working memory. *Brain Res Cogn Brain Res* 1998;7(1):1–13. [PubMed: 9714705]
- Drewe EA. Go – no go learning after frontal lobe lesions in humans. *Cortex* 1975;11(1):8–16. [PubMed: 1149469]
- Fassbender C, Murphy K, Foxe JJ, Wylie GR, Javitt DC, Robertson IH, Garavan H. A topography of executive functions and their interactions revealed by functional magnetic resonance imaging. *Brain Res Cogn Brain Res* 2004;20(2):132–43. [PubMed: 15183386]
- Floden D, Stuss DT. Inhibitory control is slowed in patients with right superior medial frontal damage. *J Cogn Neurosci* 2006;18(11):1843–9. [PubMed: 17069475]
- Garavan H, Ross TJ, Stein EA. Right hemispheric dominance of inhibitory control: an event-related functional MRI study. *Proc Natl Acad Sci U S A* 1999;96(14):8301–6. [PubMed: 10393989]
- Garavan H, Ross TJ, Murphy K, Roche RA, Stein EA. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. *Neuroimage* 2002;17(4):1820–9. [PubMed: 12498755]
- Garavan H, Ross TJ, Kaufman J, Stein EA. A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage* 2003;20(2):1132–9. [PubMed: 14568482]
- Godefroy O, Rousseaux M. Divided and focused attention in patients with lesion of the prefrontal cortex. *Brain Cogn* 1996;30(2):155–74. [PubMed: 8811992]

- Grafton ST, Mazziotta JC, Woods RP, Phelps ME. Human functional anatomy of visually guided finger movements. *Brain* 1992;115(2):565–87. [PubMed: 1606482]
- Hester RL, Murphy K, Foxe JJ, Foxe DM, Javitt DC, Garavan H. Predicting success: patterns of cortical activation and deactivation prior to response inhibition. *J Cogn Neurosci* 2004;16(5):776–85. [PubMed: 15200705]
- Hester R, D'Esposito M, Cole MW, Garavan H. Neural mechanisms for response selection: comparing selection of responses and items from working memory. *Neuroimage* 2007;34(1):446–54. [PubMed: 17071112]
- Horn NR, Dolan M, Elliott R, Deakin JF, Woodruff PW. Response inhibition and impulsivity: an fMRI study. *Neuropsychologia* 2003;41(14):1959–66. [PubMed: 14572528]
- Ikeda A, Luders HO, Burgess RC, Shibasaki H. Movement-related potentials associated with single and repetitive movements recorded from human supplementary motor area. *Electroencephalogr Clin Neurophysiol* 1993;89(4):269–77. [PubMed: 7688691]
- Ikeda A, Yazawa S, Kunieda T, Ohara S, Terada K, Mikuni N, Nagamine T, Taki W, Kimura J, Shibasaki H. Cognitive motor control in human pre-supplementary motor area studied by subdural recording of discrimination/selection-related potentials. *Brain* 1999;122(5):915–31. [PubMed: 10355676]
- Kelly AM, Hester R, Murphy K, Javitt DC, Foxe JJ, Garavan H. Prefrontal-subcortical dissociations underlying inhibitory control revealed by event-related fMRI. *Eur J Neurosci* 2004;19(11):3105–12. [PubMed: 15182319]
- Kiehl KA, Liddle PF, Hopfinger JB. Error processing and the rostral anterior cingulate: an event-related fMRI study. *Psychophysiology* 2000;37(2):216–23. [PubMed: 10731771]
- Kuchonov P, Lancaster J, Thompson P, Toga AW, Brewer P, Hardies J, Fox P. An optimized individual target brain in the Talairach coordinate system. *Neuroimage* 2002;17(2):922–7. [PubMed: 12377166]
- Laird AR, Lancaster JL, Fox PT. BrainMap: The social evolution of a human brain mapping database. *Neuroinformatics* 2005;3(1):65–78. [PubMed: 15897617]
- Langenecker SA, Nielson KA. Frontal recruitment during response inhibition in older adults replicated with fMRI. *Neuroimage* 2003;20(2):1384–92. [PubMed: 14568507]
- Law I, Svarer C, Holm S, Paulson OB. The activation pattern in normal humans during suppression, imagination and performance of saccadic eye movements. *Acta Physiol Scand* 1997;161(3):419–34. [PubMed: 9401596]
- Leichnetz GR. Preoccipital cortex receives differential input from the frontal eye field and projects to the pretectal olivary nucleus and other visuomotor related structures in the rhesus monkey. *Vis Neurosci* 1990;5:123–33. [PubMed: 2177637]
- Li CS, Huang C, Constable RT, Sinha R. Imaging response inhibition in a stop-signal task: neural correlates independent of signal monitoring and post-response processing. *J Neurosci* 2006;26(1):186–92. [PubMed: 16399686]
- Liddle PF, Kiehl KA, Smith AM. Event-related fMRI study of response inhibition. *Hum Brain Mapp* 2001;12(2):100–9. [PubMed: 11169874]
- Liu X, Banich MT, Jacobson BL, Tanabe JL. Common and distinct neural substrates of attentional control in an integrated Simon and spatial Stroop task as assessed by event-related fMRI. *Neuroimage* 2004;22(3):1097–106. [PubMed: 15219581]
- Matsuzaka Y, Aizawa H, Tanji J. A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: neuronal activity during a learned motor task. *J Neurophysiol* 1992;68(3):653–62. [PubMed: 1432040]
- Menon V, Adelman NE, White CD, Glover GH, Reiss AL. Error-related brain activation during a Go/NoGo response inhibition task. *Hum Brain Mapp* 2001;12(3):131–43. [PubMed: 11170305]
- Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci* 2001;24:167–202. [PubMed: 11283309]
- Mostofsky SH, Schafer JG, Abrams MT, Goldberg MC, Flower AA, Boyce A, Courtney SM, Calhoun VD, Kraut MA, Denckla MB, Pekar JJ. fMRI evidence that the neural basis of response inhibition is task-dependent. *Brain Res Cogn Brain Res* 2003;17(2):419–430. [PubMed: 12880912]
- Mostofsky SH, Simmonds DJ. Response inhibition and response selection: two sides of the same coin. *J Cogn Neurosci*. in press

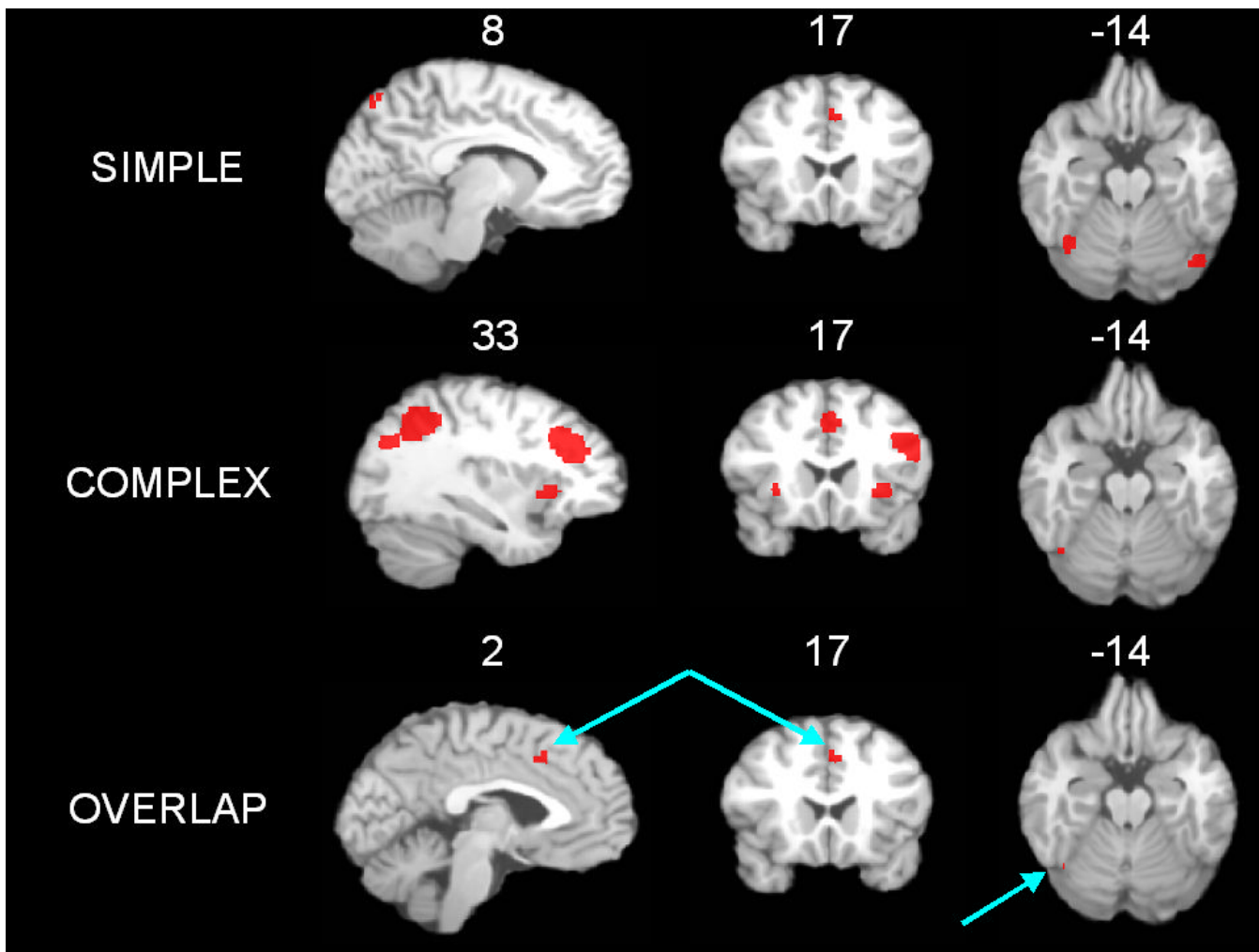
- Nigg JT. The ADHD response-inhibition deficit as measured by the stop task: replication with DSM-IV combined type, extension and qualification. *J Abnorm Child Psychol* 1999;27(5):393–402. [PubMed: 10582840]
- Pandya DN, Seltzer B. Intrinsic connections and architectonics of posterior parietal cortex in the rhesus monkey. *J Comp Neurol* 1982;204(2):196–210. [PubMed: 6276450]
- Petrides M, Pandya DN. Projections to the frontal cortex from the posterior parietal region in the rhesus monkey. *J Comp Neurol* 1984;228(1):105–16. [PubMed: 6480903]
- Picard N, Strick PL. Imaging the premotor areas. *Curr Opin Neurobiol* 2001;11(6):663–72. [PubMed: 11741015]
- Picton TW, Stuss DT, Alexander MP, Shallice T, Binns MA, Gillingham S. Effects of focal frontal lesions on response inhibition. *Cereb Cortex*. 2006
- Ramautar JR, Slagter HA, Kok A, Ridderinkhof KR. Probability effects in the stop-signal paradigm: the insula and the significance of failed inhibition. *Brain Res* 2006;1105(1):143–54. [PubMed: 16616048]
- Rockland KS, Pandya DN. Laminar origins and terminations of cortical connections of the occipital lobe in the rhesus monkey. *Brain Res* 1979;179(1):3–20. [PubMed: 116716]
- Rubia K, Noorloos J, Smith A, Gunning B, Sergeant J. Motor timing deficits in community and clinical boys with hyperactive behavior: the effect of methylphenidate on motor timing. *J Abnorm Child Psychol* 2003;31(3):301–13. [PubMed: 12774863]
- Rubia K, Russell T, Overmeyer S, Brammer MJ, Bullmore ET, Sharma T, Simmons A, Williams SC, Giampietro V, Andrew CM, Taylor E. Mapping motor inhibition: conjunctive brain activations across different versions of Go/No-go and stop tasks. *Neuroimage* 2001;13(2):250–61. [PubMed: 11162266]
- Rubia K, Lee F, Cleare AJ, Tunstall N, Fu CH, Brammer M, McGuire P. Tryptophan depletion reduces right inferior prefrontal activation during response inhibition in fast, event-related fMRI. *Psychopharmacology (Berl)* 2005;179(4):791–803. [PubMed: 15887056]
- Rushworth MF, Behrens TE, Johansen-Berg H. Connection patterns distinguish 3 regions of human parietal cortex. *Cereb Cortex*. November 28;2005 2005 online publication
- Shaw P, Lerch J, Greenstein D, Sharp W, Clasen L, Evans A, Giedd J, Castellanos FX, Rapoport J. Longitudinal mapping of cortical thickness and clinical outcome in children and adolescents with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 2006;63(5):540–9. [PubMed: 16651511]
- Simmonds DJ, Fotedar SG, Suskauer SJ, Pekar JJ, Denckla MB, Mostofsky SH. Functional brain correlates of response time variability in children. *Neuropsychologia*, E-pub January 21:2007. in press
- Suskauer SJ, Simmonds DJ, Fotedar SG, Blankner JG, Pekar JJ, Denckla MB, Mostofsky SH. FMRI evidence for abnormalities in response selection in ADHD: difference in activation associated with response inhibition but not habitual motor response. *J Cogn Neurosci*. in press
- Talairach, J.; Tournoux, P. Thieme Medical Publisher, Inc.; New York: 1988. Co-planar stereotaxic atlas of the human brain..
- Tamm L, Menon V, Ringel J, Reiss AL. Event-related FMRI evidence of frontotemporal involvement in aberrant response inhibition and task switching in attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2004;43(11):1430–40. [PubMed: 15502603]
- Turkeltaub PE, Eden GF, Jones KM, Zeffiro TA. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage* 2002;16(3):765–80. [PubMed: 12169260]
- Wager TD, Sylvester CY, Lacey SC, Nee DE, Franklin M, Jonides C. Common and unique components of response inhibition revealed by fMRI. *Neuroimage* 2005;27(2):323–40. [PubMed: 16019232]
- Watanabe J, Sugiura M, Sato K, Sato Y, Maeda Y, Matsue Y, Fukuda H, Kawashima R. The human prefrontal and parietal association cortices are involved in NO-GO performances: an event-related fMRI study. *Neuroimage* 2002;17(3):1207–1216. [PubMed: 12414261]



**Figure 1.**

Results of the ALE meta-analysis across all of the 11 Go/No-go studies. Images are shown in neurological orientation, such that the left side of the image corresponds to the left side of the brain. Representative slices in sagittal (top), coronal (middle) and axial (bottom) views are shown with Talairach planar coordinates above each slice, and the location of these slices can be seen in orthogonal views to the right of the figure. The analysis demonstrated a primarily right-lateralized network associated with successfully inhibited No-go stimuli, with concurrence seen in the rostral portion of the superior medial wall (pre-SMA; BA6/32), right prefrontal regions (BA9/10/44), left premotor cortex (BA6), bilateral inferior parietal regions (BA40), bilateral occipital regions (BA19/37), bilateral putamen and bilateral insula.





**Figure 2.** Results of the ALE analyses for the five “Simple” (top) and six “Complex” (middle) Go/No-go studies, and the overlap between the two types of studies (bottom). Images are shown in neurological orientation, such that the left side of the image corresponds to the left side of the brain. Representative slices in sagittal (left), coronal (middle) and axial (right) views are shown with Talairach planar coordinates above each slice. The ALE analyses of the “Simple” and “Complex” studies demonstrated distinct patterns of concurrence, with a right-lateralized prefrontal (BA9/44) / parietal (BA40) network seen only in the analysis of the complex tasks. Concurrence between the two analyses was localized to the pre-SMA (BA6/32, 176mm<sup>3</sup> extent) and the left fusiform gyrus (BA37, 16mm<sup>3</sup> extent), indicated by the arrows in the figure.

Table 1

Studies included in the ALE meta-analysis.

|                                       | Region                                | Hem                      | BA      | x   | y   | z   | Vol (mm <sup>3</sup> ) | ALE ( $\times 10^{-3}$ ) |
|---------------------------------------|---------------------------------------|--------------------------|---------|-----|-----|-----|------------------------|--------------------------|
| ALL                                   | Middle / inferior frontal gyrus       | R                        | 9 / 44  | 40  | 30  | 26  | 7464                   | 9.21                     |
|                                       | Inferior parietal lobule              | R                        | 40      | 38  | -50 | 42  | 6808                   | 8.14                     |
|                                       | Superior medial wall (pre-SMA)        | B                        | 6 / 32  | 2   | 18  | 40  | 3712                   | 7.95                     |
|                                       | Putamen / insula                      | L                        |         | -16 | 0   | 8   | 2624                   | 6.03                     |
|                                       | Inferior parietal lobule              | L                        | 40      | -44 | -42 | 42  | 1784                   | 5.88                     |
|                                       | Fusiform gyrus / posterior cerebellum | L                        | 19 / 37 | -40 | -60 | -14 | 1376                   | 5.99                     |
|                                       | Middle occipital gyrus                | R                        | 19      | 44  | -72 | -4  | 1032                   | 4.67                     |
|                                       | Middle frontal gyrus                  | R                        | 10      | 36  | 50  | 4   | 1016                   | 5.19                     |
|                                       | Middle frontal gyrus                  | L                        | 6       | -40 | 8   | 42  | 368                    | 4.35                     |
|                                       | Putamen / insula                      | R                        | 0       | 32  | 16  | 0   | 280                    | 4.12                     |
|                                       | Superior frontal gyrus                | R                        | 9       | 24  | 50  | 30  | 128                    | 4.07                     |
|                                       | Simple                                | Inferior occipital gyrus | R       | 19  | 46  | -70 | -6                     | 2648                     |
| Fusiform gyrus / posterior cerebellum |                                       | L                        | 19 / 37 | -38 | -60 | -18 | 488                    | 3.07                     |
| Superior medial wall (pre-SMA)        |                                       | R                        | 6 / 32  | 4   | 14  | 40  | 232                    | 2.90                     |
| Precuneus                             |                                       | R                        | 7       | 8   | -74 | 50  | 144                    | 2.62                     |
| Complex                               | Middle / inferior frontal gyrus       | R                        | 9 / 44  | 40  | 30  | 26  | 9400                   | 9.20                     |
|                                       | Inferior parietal lobule              | R                        | 40      | 36  | -54 | 40  | 6856                   | 6.54                     |
|                                       | Inferior parietal lobule              | L                        | 40      | -44 | -42 | 42  | 2720                   | 5.79                     |
|                                       | Putamen                               | L                        |         | -16 | 0   | 6   | 1472                   | 4.87                     |
|                                       | Putamen / insula                      | R                        |         | 32  | 16  | 0   | 1360                   | 4.12                     |
|                                       | Superior medial wall (pre-SMA)        | B                        | 6 / 32  | 2   | 18  | 40  | 1336                   | 5.32                     |
|                                       | Middle temporal gyrus                 | R                        | 22      | 54  | -36 | 2   | 472                    | 3.74                     |
|                                       | Fusiform gyrus                        | L                        | 19 / 37 | -42 | -60 | -12 | 240                    | 3.74                     |
|                                       | Middle frontal gyrus                  | L                        | 46      | -40 | 40  | 20  | 160                    | 3.40                     |
|                                       | Insula                                | L                        |         | -30 | 14  | 2   | 144                    | 3.60                     |

**Table 2**  
Results from ALE meta-analysis. Foci are reported in Talairach coordinates. 'BA' = Brodmann's area.

|                | Year | Author            | Participants   | Foci | Go stimuli   | No-go stimuli  |
|----------------|------|-------------------|----------------|------|--|--|
| <i>Simple</i>  | 2000 | Kiehl et al.      | 14 (7M, 7F)    | 8    | "X"  | "K"  |
|                | 2001 | Liddle et al.     | 16 (9M, 7F)    | 19   | "X"  | "A"  |
|                | 2002 | Watanabe et al.   | 11 (9M, 2F)    | 5    | Red or blue square   | Red or blue square   |
|                | 2003 | Mostofsky et al.  | 48 (24M, 24F)  | 3    | Green spaceship  | Red spaceship  |
|                | 2004 | Fassbender et al. | 21 (7M, 14F)   | 21   | All numbers except for "3"   | "3"  |
|                |      | TOTAL             | 110 (56M, 54F) | 56   |  |  |
| <i>Complex</i> | 1999 | Garavan et al.    | 14 (8M, 6F)    | 14   | "X" preceded by "Y" or "Y" preceded by "X"   | "X" preceded by "X" or "Y" preceded by "Y"                   |
|                | 2002 | Garavan et al.    | 14 (4M, 10F)   | 16   | "X" preceded by "Y" or "Y" preceded by "X"   | "X" preceded by "X" or "Y" preceded by "Y"                   |
|                | 2003 | Garavan et al.    | 16 (6M, 10F)   | 7    | "X" preceded by "Y" or "Y" preceded by "X"   | "X" preceded by "X" or "Y" preceded by "Y"                   |
|                | 2003 | Mostofsky et al.  | 28 (13M, 15F)  | 3    | Green spaceships and red spaceships preceded by an even number of green spaceships | Red spaceships preceded by an odd number of green spaceships |
|                | 2004 | Hester et al.     | 15 (5M, 10F)   | 21   | "X" preceded by "Y" or "Y" preceded by "X"   | "X" preceded by "X" or "Y" preceded by "Y"                   |
|                | 2004 | Kelly et al.      | 15 (5M, 10F)   | 23   | "X" preceded by "Y" or "Y" preceded by "X"   | "X" preceded by "X" or "Y" preceded by "Y"                   |
|                |      | TOTAL             | 102 (41M, 61F) | 84   |  |  |