ELSEVIER

Neuropsychologia 42 (2004) 1910–1916

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

# The functional neuroanatomical correlates of response variability: evidence from a response inhibition task

Mark A. Bellgrove [a,b,*], Robert Hester [a], Hugh Garavan [a,c]

[a] *Department of Psychology, Institute of Neuroscience, Trinity College Dublin, Dublin 2, Ireland*
[b] *Department of Psychiatry, Trinity College Dublin, Dublin 2, Ireland*
[c] *Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee, WI, USA*

Received 23 February 2004; received in revised form 12 May 2004; accepted 18 May 2004

**Abstract**

Intra-individual performance variability may be an important index of the efficiency with which executive control processes are implemented, Lesion studies suggest that damage to the frontal lobes is accompanied by an increase in such variability. Here we sought for the first time to investigate how the functional neuroanatomy of executive control is modulated by performance variability in healthy subjects by using an event-related functional magnetic resonance imaging (ER-fMRI) design and a Go/No-go response inhibition paradigm. Behavioural results revealed that individual differences in Go response time variability were a strong predictor of inhibitory success and that differences in mean Go response time could not account for this effect. Task-related brain activation was positively correlated with intra-individual variability within a distributed inhibitory network consisting of bilateral middle frontal areas and right inferior parietal and thalamic regions. Both the behavioural and fMRI data are consistent with the interpretation that those subjects with relatively higher intra-individual variability activate inhibitory regions to a greater extent, perhaps reflecting a greater requirement for top-down executive control in this group, a finding that may be relevant to disorders of executive/attentional control.


*Keywords:* fMRI; Intra-individual variability; Response inhibition

## 1. Introduction

In recent times there has been increased interest in the study of intra-individual performance variability as a marker of brain pathology (Stuss, Murphy, Binns, & Alexander, 2003). It has been argued that performance variability, rather than reflecting uninteresting random noise, may tell us something about how efficiently cognitive control is instantiated within the brain. This line of reasoning has considerable face validity given that disorders of frontal and putatively frontal pathology such as Traumatic Brain Injury (TBI; Stuss et al., 1989), schizophrenia and attention deficit hyperactivity disorder (ADHD; Castellanos & Tannock, 2002; Loo et al., 2003) all share performance variability as a ubiquitous and unifying feature. However, given the potential relevance of performance variability for clinical disorders (both neurological and neuropsychiatric) and clinical practice, its brain-behaviour basis remains poorly defined.

The use of intra-individual performance variability as a legitimate dependent measure has a long history within studies of normal cognition in young and older adults (Anstey, 1999; Fozard, Vercryssen, Reynolds, Hancock, & Quilter, 1994; Jensen, 1992; West, Murphy, Armilio, Craik, & Stuss, 2002), where it has been used as an index of information processing efficiency, and also within studies of neurological populations (Loo et al., 2003; Stuss et al., 1989, 2003) (see Stuss et al., 2003 for a review of the history of using variability as a dependent measure within cognitive studies). Intra-individual performance variability seems most applicable, however, to studies of executive control. This assertion is supported by observations that variability indexes the demand for top-down executive control in healthy subjects (West et al., 2002) and that impaired top-down regulation of attention is accompanied by increased variability in TBI (Stuss et al., 1999). Further, patients with right frontal damage experience difficulties with sustaining attention (Wilkins, Shallice, & McCarthy, 1987) and this capacity for sustained attention itself is correlated with intra-individual variability (Manly, Davison, Heutink, Galloway, & Robertson, 2000). In the first direct examination of the effect of focal frontal (versus non-frontal) lesions on performance variability, Stuss and colleagues reported that patients with damage to either the dorsolateral prefrontal cortex (right

* Corresponding author. Tel.: +353 1 608 3913; fax: +353 1 671 2006.
*E-mail address:* bellgrom@tcd.ie (M.A. Bellgrove).

0028-3932/$ – see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2004.05.007

or left) or the superior medial frontal, but not the inferior medial frontal, cortex, exhibited increased intra-individual variability on an executive function task requiring feature discrimination and integration (Stuss et al., 2003). The work of Stuss and colleagues provides important first insights that focal frontal brain damage, rather than brain damage per se, is a cause of increased intra-individual variability.

In our own programme of research aimed at investigating the functional neuroanatomy of executive control we have employed a response inhibition paradigm, of the Go/No-go type, in which participants are presented with a letter stream (e.g., X Y X Y) and are required to respond to letter alternations but to withhold their response to non-alternations within this stream (e.g., the fourth letter in the sequence X Y X X). Using this task we have identified structures involved in response inhibition, error detection, and error correction. Inhibitory control appears dependent upon activity within right prefrontal and parietal areas (Garavan, Ross, Murphy, Roche, & Stein, 2002; Garavan, Ross, & Stein, 1999).

In this study we examined for the first time, the functional neuroanatomical correlates of response variability, as observed within our event-related functional magnetic resonance imaging (ER-fMRI) studies of response inhibition. Since the present study, relative to most other imaging studies had a large sample size ($n = 42$) it allowed us to examine these individual differences using correlational analyses (see also Gray, Chabris, & Braver, 2003; Hester, Fassbender, & Garavan, 2004 for examinations of individual differences within fMRI designs). If intra-individual variability is a marker of executive control, then we hypothesised that variability would be consequential for both inhibitory performance (behavioural) and task-related brain activation (fMRI). We therefore predicted that individual differences in intra-individual response variability would be associated with distinct patterns of task-related brain activity within the above defined response inhibition networks.

## 2. Materials and methods

### 2.1. Participants and task design

Forty-two right-handed subjects (29 females, mean age 31, range: 18–46), reporting no history of neurological or psychological impairment, completed a Go/No-go task after providing written informed consent. The task presented the letters X and Y serially in an alternating pattern at 1 Hz and subjects were required to make a button press response to each letter. Responses and response speed (ms) were recorded. Responses were to be withheld to No-go stimuli: these occurred when the alternation was interrupted (e.g., the fourth letter in the sequence X Y X X). The data set for the present study comprised data from 3 separate studies (Garavan, Ross, Kaufman, & Stein, 2003; Garavan et al., 2002; Hester, Murphy, et al., 2004). The trial duration was held at 1 Hz across all three studies, however stimuli durations varied between 600 and 900 ms, and the inter-trial interval varied between 400 and 100 ms across the three studies. While some other variations in the design of these tasks existed, only instances of successful inhibition during the aforementioned design were considered, with the assumption made that the event-related analysis would minimise the influence of unrelated task variance. Indeed, we have recently demonstrated that activation differences between the three tasks can be attributed to the expected variability given the robustness of the sample sizes in each of the three studies, rather than to task-specific variance (Murphy & Garavan, 2004). All participants performed four task-blocks with the ratio of Go:No-Go trials being 13.7:1 across tasks.

We employed an event-related fMRI design to identify the functional areas activated during successful withholds and errors of commission. The event-related design allowed the No-go trials to be distributed unpredictably throughout the stimuli stream. During fMRI scanning, subjects were presented with between 896 and 1180 Go-stimuli (across four blocks) and between 52 and 80 No-go stimuli. This ratio resulted in an average interval of 13.7 s between successive No-go trials across the three studies.

### 2.2. fMRI parameters

Scanning for two of the studies (Garavan et al., 2002, 2003) was conducted using contiguous 7 mm sagittal slices covering the entire brain from a 1.5 T GE Signa scanner using a blipped gradient-echo, echo-planar pulse sequence (TR = 2000 ms; TE = 40 ms; FOV = 240 mm; 64 mm × 64 mm matrix; 3.75 mm × 3.75 mm in-plane resolution). High resolution spoiled GRASS anatomic images (TR = 24 ms; TE = 5 ms, flip angle = 45°; FOV = 240 mm, thickness = 1.0 mm with no gap, matrix size = 256 × 256 × 124) were acquired prior to functional imaging to allow for subsequent activation localisation and spatial normalisation. Foam padding was used to limit head movements within the coil. Stimuli were back-projected onto a screen at the subject's feet and were viewed with the aid of prism glasses attached to the inside of the radio-frequency head-coil.

Scanning for the third study (Hester, Murphy, et al. 2004) was conducted using a 1.5 T Siemens VISION scanner in which foam padding was used to restrict head movements. Contiguous 5 mm sagittal slices covering the entire brain were collected using a single-shot, $T^2$* weighted echo planar imaging sequence (TR = 2000 ms; TE = 50 ms; FOV = 256 mm; 64 mm × 64 mm matrix size in-plane resolution). High-resolution T1-weighted structural MPRAGE images (FOV = 256 mm, isotropic 1 mm voxels) were acquired following functional imaging to allow subsequent activation localisation and spatial normalisation. Stimuli were delivered using an IFIS-SA stimulus-delivery system (MRI Devices Corp., Waukesha, Wisconsin), which was equipped with a head-coil-mounted 640 × 480 LCD panel. This shielded LCD screen was mounted on the head-coil, directly in the subjects' line of vision.

### 2.3. fMRI analysis

All analyses were conducted using AFNI software (Cox, 1996). Following image reconstruction, the time-series data were time-shifted using Fourier interpolation to remove differences in slice acquisition times, and motion-corrected using 3D volume registration (least-squares alignment of three translational and three rotational parameters). Activation outside the brain was also removed using edge detection techniques. No subjects showed significant residual motion, thus allowing all 42 to be included.

Separate haemodynamic response functions at 2-s temporal resolution were calculated using deconvolution techniques for successful response inhibition (STOPS) and errors of commission (ERRORS). We have previously reported on the functional neuroanatomy of errors of commission (Hester, Fassbender, et al., 2004), however this was not addressed in the present study. Although the stimulus stream was presented at 1 Hz, all events of interest were time-locked to the beginning of the 2-s whole-brain volume acquisition. A multiple regression analysis was used to derive estimates for the time-point parameters of the haemodynamic response functions by estimating the signal contributed by each individual event type to the overall time series. Thus, in the present analysis the regression estimated the signal contributed by the STOP events over and above that accounted for by the ongoing task (Go trials). The haemodynamic response functions were then modelled voxelwise with a gamma-variate function using non-linear regression (Garavan et al., 1999; Ward et al., 1998). An area-under-the-curve measure of the gamma-variate model was expressed as a percentage of the tonic baseline activity and served as the activation measure for the event-related responses. The activation map for STOPS therefore represents the activation during successful No-go events that is significantly greater than during the ongoing Go trials.

One-sample *t*-tests against the null hypothesis of zero event-related activation changes (i.e., no change relative to tonic task-related activity) were performed voxel-by-voxel on the percentage area-under-the-curve measure for STOPS for the 42 subjects. Significant voxels passed a voxelwise statistical threshold ($t(41) = 4.309$, $P < 0.0001$) and were required to be part of a larger 91 μl cluster of contiguous significant voxels. Thresholding was determined through Monte Carlo simulations and resulted in a 1% probability of a cluster surviving due to chance. The mean activation for clusters in the combined subjects map was calculated for the purposes of an ROI analysis in which activation measures were correlated with performance variability (see below).

### 2.4. Behavioural analyses

Based upon the work of Stuss et al. (2003) we sought to determine the relationship between intra-individual response variability and other measures of behavioural performance on our Go/No-go task. In addition to calculating the intra-individual coefficient of variation (ICV; Go-RT$_{S.D.}$/Go-RT$_{M}$; thus controlling for differences in mean response times), we also calculated the percentage of No-go trials on which the subject successfully inhibited their response (STOPS%). Successful inhibitions were calculated as percentages since the number of No-go trials differed across the three response-inhibition tasks. Finally, we also calculated the average Pre-STOP RT and the Pre-STOP RT-GO RT difference across subjects to determine the relationship between the RT for the trial immediately preceding a successful withhold and response variability. The Pre-STOP RT-GO RT difference represents the amount of slowing required, relative to one's own Go RT baseline, for successful inhibition.

## 3. Results

### 3.1. Behavioural measures

We conducted analyses on data from the group of 42 participants to determine the relationship between response variability and other measures of behavioural performance. Table 1 presents the results of a partial correlation analysis, adjusting for Experiment, between ICV and performance and demographic variables.

This analysis indicated that greater response variability correlated with poorer inhibitory performance ($r^2 = 0.12$), but not age or Go-RT. After adjusting for mean Go-RT, subjects with higher response variability tended to have slower Go-RT's prior to STOPS (Pre-STOP RT-Go-RT difference: $r^2 = 0.52$).

### 3.2. Event-related activation

#### 3.2.1. Analyses for STOPS

The activation map for STOPS indicated significant activation clusters in 21 regions, including bilateral inferior parietal, middle frontal and insula regions, and right hemispheric activation in the inferior frontal and thalamic areas. Significant clusters were also identified along the midline in both the anterior cingulate and pre-SMA regions (see Table 2 for all regions of interest).

Partial correlation analyses (adjusting for Experiment) examined the relationship between activation in each of the

Table 1
Correlation between intra-individual coefficient of variation (ICV) and demograhic and performance variables

| Variable | ICV |
|---|---|
| Age | −0.13 |
| Go-RT | 0.25 |
| STOPS % | −0.34* |
| Pre-STOP RT | 0.62** |
| Pre-STOP-Go RT difference | 0.72** |

* $P < 0.05$.
** $P < 0.01$.

Table 2
Regions of event-related activation during successful response inhibition (STOPS). Positive values for $x$, $y$, and $z$ coordinates denote, respectively, locations that are right, anterior and superior relative to the anterior commissure. Correlation coefficients are shown for those regions with which activity significantly correlates with the intra-individual coefficient of variation (ICV)

| Structure | BA | HS | Volume (μl) | Centre of mass | | | ICV |
|---|---|---|---|---|---|---|---|
| | | | | $x$ | $y$ | $z$ | |
| Frontal lobe | | | | | | | |
| Middle frontal | 46 | R | 2623 | 37 | 33 | 24 | 0.42 |
| | 6 | R | 680 | 24 | −7 | 49 | |
| | 46 | L | 245 | −45 | 29 | 24 | 0.51 |
| | 9 | L | 180 | −33 | 24 | 29 | |
| Inferior frontal | 9 | R | 128 | 46 | 15 | 21 | 0.44 |
| Precentral | 6 | L | 782 | −26 | −10 | 51 | |
| | 6 | L | 414 | −45 | −4 | 36 | |
| | 44/6 | L | 128 | −51 | 2 | 13 | 0.72 |
| Pre-SMA | 6 | L | 2047 | −1 | −1 | 56 | |
| Anterior cingulate | 32/24 | L | 198 | −10 | 17 | 28 | |
| Parietal lobe | | | | | | | |
| Inferior parietal | 40 | R | 10099 | 48 | −43 | 33 | 0.35 |
| | 40 | L | 1417 | −44 | −43 | 40 | |
| Precuneus | 7 | L | 414 | −19 | −63 | 47 | |
| | 7 | R | 91 | 18 | −64 | 40 | |
| Subcortical | | | | | | | |
| Thalamus | | R | 234 | 6 | −14 | 5 | |
| | | R | 101 | 19 | −8 | 2 | 0.34 |
| Insula | 13 | R | 5801 | 36 | 5 | 14 | |
| | 13 | L | 2118 | −31 | 8 | 5 | |
| Insula/temporal | 13 | L | 326 | −53 | −43 | 19 | |

clusters from the activation maps for STOPS with ICV. The Pearson coefficients reported in Table 2 indicate that significant correlations (corrected for multiple comparisons), ranging between 0.34 ($r^2 = 0.12$) and 0.72 ($r^2 = 0.52$), were found between the measures of response variability and activation in right inferior parietal and thalamic regions, right inferior frontal and bilateral middle frontal areas. All correlations were positive, indicating that greater response variability related to increased activation in these regions during successful response inhibition.

In the behavioural analyses we observed a significant correlation between inhibitory success (STOPS%) and Pre-STOP RT and the Pre-STOP RT-Go RT difference. This suggests that the more variable subjects were only successful in inhibiting following relatively slow GO trial responding. This is potentially problematic as our previous work with this task has found that RT preceding a successful inhibition is significantly related to the level of STOP activation (Garavan et al., 2003; Hester, Fassbender, et al., in press; Hester, Murphy, et al., 2004) and other work demonstrates speed-activation relationships within fMRI designs (Gray et al., 2003; Rypma, Berger, & D'Esposito, 2002; Rypma & D'Esposito, 1999). In order to discount the possibility that the STOP activation differences, as a function of variability, might be due to subjects with higher variability having slower RT prior to successful inhibitions, we conducted stepwise regression analyses, entering Experiment[1] and Pre-STOP RT-Go RT difference (first step) and ICV (second step) as predictors. Activation level within the above 6 clusters as the dependent measure. This analysis used the Pre-STOP RT-Go RT difference (rather than Pre-STOP RT) since this measure accounts for RT slowing, relative to ones own Go RT baseline. Thus, this analysis allowed us to determine the unique variance in BOLD signal that was accounted for by intra-individual variability. After controlling for the effects of Experiment and Pre-STOP RT-Go RT difference, the association between ICV and brain activation remained significant in three of the aforementioned six clusters [right middle frontal (BA 46): $\Delta r^2 = 0.13$, $P = 0.017$; left middle frontal (BA 46): $\Delta r^2 = 0.18$, $P = 0.003$; left precentral (BA 44/6): $\Delta r^2 = 0.30$, $P = 0.001$] (Fig. 1). The Pre-STOP RT-Go RT difference significantly accounted for activation in the right inferior frontal, right inferior parietal and right thalamic areas, with ICV not adding unique variance.

[1] As in previous analyses we controlled for the effect of Experiment due to the slight timing differences between each of the three experiments from which the data for this study were derived.

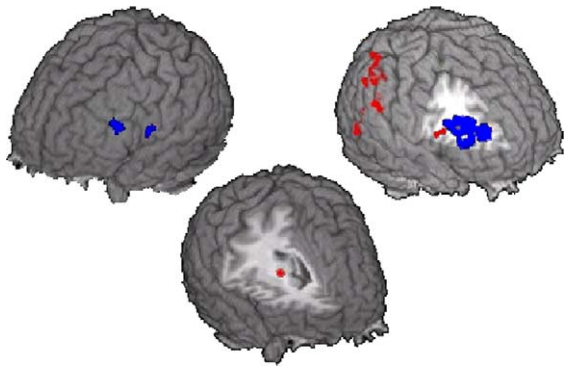

Fig. 1. Functional neuroanatomical correlates of intra-individual response variability. Correlations between variability and task-related activity within blue regions remained significant after adjusting for Pre-STOP RT/Go RT difference, while correlations with red regions did not. (Top left) Areas in blue represent left middle frontal (BA 46) and left precentral (BA 44/6) activations; (top right) blue area represents right middle frontal (BA 46) activation. Red areas represent right inferior frontal (BA 9) and right parietal (BA 40) activations. (Centre bottom) Red area represents right thalamic activation.

## 4. Discussion

The present study is the first to examine the functional neuroanatomical correlates of response variability. Analyses of the behavioural data indicated that response variability was inversely related to inhibitory success and may therefore reflect an important aspect of executive control. Response variability was positively correlated with the degree to which participants slowed prior to a successful inhibition suggesting that the more variable subjects were only successful in inhibiting when responding particularly slowly. Variability was not, however, related to age or mean reaction time (RT) to go-stimuli. In the fMRI analyses, task-related brain activity was positively related to response variability within a distributed neural network including right inferior parietal and thalamic regions and bilateral middle frontal areas. These areas overlap substantially with those previously reported in studies of response inhibition (Garavan et al., 1999, 2002, 2003) and visual sustained attention (Pardo, Fox, & Raichle, 1991; Sturm et al., 1999). Associations between activations in frontal regions and response variability remained significant after controlling for the Pre-STOP RT-Go RT difference, suggesting that these activations relate to executive/inhibitory processes rather than an artefact arising from the operation of speed-accuracy tradeoffs.

We observed a relationship between inhibitory success (%STOPS) and intra-individual variability, such that lower variability was associated with greater inhibitory success. Within tasks of visual sustained attention, lower intra-individual variability has been associated with relatively better sustained attention performance (i.e., fewer commission errors; Manly et al., 2000). While individual differences in mean response speed are related to inhibitory success in our task these cannot fully account for the observed relationship between variability and inhibitory success since our measure of intra-individual variability (i.e., ICV) accounts for differences in mean reaction time. Indeed, preliminary analyses revealed that associations with the ICV were much stronger (both for behavioural and fMRI data) than using the standard deviation alone. Further, in keeping with a number of studies, we did not observe any relationship between mean reaction time and intra-individual variability (Stuss et al., 2003; West et al., 2002). Taken together, these results indicate that intra-individual variability is a strong predictor of inhibitory success. Relatively higher variability, likely due to the reduced efficiency with which top-down attentional control is consistently instantiated in the brain, is associated with lower inhibitory success.

Stuss et al. (2003) demonstrated that intra-individual variability, rather than being a consequence of indiscriminate brain damage per se, is associated with focal damage to the frontal lobes. The present study demonstrates that within a healthy population, individual differences in intra-individual variability predict inhibitory success and are associated with distinct patterns of, predominantly frontal, task-related brain activity.

In our previous work with this task (Garavan et al., 2003; Hester, Fassbender, et al., 2004; Hester, Murphy, et al., 2004) we have observed that slowing prior to successful inhibitions is associated with increased activation within inhibitory networks and others have documented speed-activation relationships (Rypma et al., 2002; Rypma & D'Esposito, 1999). Since performance variability and Pre-STOP slowing correlated highly in this study, we determined whether activation differences reflected the greater slowing of those subjects with relatively higher variability, or whether the patterns of activation reflected true differences in performance variability. The multiple regression analyses proved instructive with activations in middle frontal regions remaining significant after correcting for Pre-STOP slowing. The areas of significant activation are middle frontal areas that we, a priori, would have expected to be critical for response inhibition. These areas have all been reported in our previous studies of response inhibition (Garavan et al., 1999, 2002; Hester, Fassbender, et al., 2004; Hester, Murphy, et al., 2004; Nielson, Langeneker, & Garavan, 2002). Interestingly, we have also noted left prefrontal foci for older participants performing our response inhibition task, suggesting that these areas are additionally recruited by those for whom inhibition is more difficult (Nielson et al., 2002).

Interestingly, the association between performance variability and activations in the interior frontal, parietal and thalamic areas did not remain significant after correcting for the Pre-STOP RT-Go RT difference slowing. If slower RT can be taken to reflect a more conservative or controlled response style then the degree to which one has slowed relative to one's baseline response speed may provide an indirect measure of phasically increased attentiveness. When one is paying attention, as indexed by a greater Pre-STOP RT-Go

RT difference, there are increased activations within visual attention areas, such as the right interior frontal, parietal and thalamic regions (Manly et al., 2003; Pardo et al., 1991; Sturm et al., 1999, 2004; Sturm & Willmes, 2001) and performance variability does not explain unique variance in these activations. Equally, however, the relationship between Pre-STOP slowing and performance variability might reflect the operation of a speed-accuracy tradeoff, with more variable subjects adopting a more conservative response criterion in order to successfully inhibit on the No-go trials. Regardless of the exact interpretation for the above relationship, that associations between performance variability and activity within frontal regions remained significant after such corrections suggests that variability may have a functional consequence that is specific to the frontal lobes, with increased activity likely reflecting the increased requirement for executive control. In this regard, our results are consistent with lesion studies of frontal patients (Stuss et al., 2003) and disorders of putative frontal origin, such as Attention Deficit Hyperactivity Disorder (ADHD; Castellanos & Tannock, 2002; Loo et al., 2003), where variability is a hallmark.

In summary, we have identified that intra-individual variability is a strong predictor of inhibitory success, and is related to brain activation within frontal regions. Specifically, higher intra-individual variability within a response inhibition task is associated with increased frontal activation, likely reflecting the greater demand for executive control in order to maintain task performance. Our results support the notion that the performance variability might serve as a marker for executive dysfunction in a range of clinical disorders.

## Acknowledgements

This research was supported by USPHS grant DA14100 and GCRC M01 RR00058. M.A.B. is supported under a grant from the Irish Health Research Board.

## References

Anstey, K. J. (1999). Sensorimotor variables and forced expiratory volume as correlates of speed, accuracy, and variability in reaction time performance in late adulthood. *Aging, Neuropsychology and Cognition*, *6*, 84–95.

Castellanos, F. X., & Tannock, R. (2002). Neuroscience of attention-deficit/hyperactivity disorder: The search for endophenotypes. *Nature Reviews Neuroscience*, *3*(8), 617–628.

Cox, R. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers in Biomedical Research*, *29*, 162–173.

Fozard, J. L., Vercryssen, M., Reynolds, S. L., Hancock, P. A., & Quilter, R. E. (1994). Age differences and changes in reaction time: The Baltimore Longitudinal Study of Aging. *Journal of Gerontology*, *49*(4), P179–P189.

Garavan, H., Ross, T. J., Kaufman, J., & Stein, E. A. (2003). A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage*, *20*(2), 1132–1139.

Garavan, H., Ross, T. J., Murphy, K., Roche, R. A., & Stein, E. A. (2002). Dissociable executive functions in the dynamic control of behavior: Inhibition, error detection, and correction. *Neuroimage*, *17*(4), 1820–1829.

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemisphere dominance for inhibitory control: An Event-related functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America*, *96*, 8301–8306.

Gray, J. R., Chabris, C. F., & Braver, T. S. (2003). Neural mechanisms of general fluid intelligence. *Nature Neuroscience*, *6*(3), 316–322.

Hester, R., Fassbender, C., & Garavan, H. (2004). Individual differences in error processing: A review and meta-analysis of three event-related fMRI studies. *Cerebral Cortex* (in press).

Hester, R., Murphy, K., Foxe, J., Foxe, D., Javitt, D., & Garavan, H. (2004). Predicting success: Patterns of cortical activation and deactivation prior to response inhibition. *Journal of Cognitive Neuroscience*, *16*(5), 776–785.

Jensen, A. R. (1992). The importance of intrainidivual variation in reaction time. *Journal of Personality and Individual Differences*, *13*(8), 869–881.

Loo, S. K., Specter, E., Smolen, A., Hopfer, C., Teale, P. D., & Reite, M. L. (2003). Functional effects of the DAT1 polymorphism on EEG measures in ADHD. *Journal of American Academy of Child Adolescence and Psychiatry*, *42*(8), 986–993.

Manly, T., Davison, B., Heutink, J., Galloway, M., & Robertson, I. (2000). Not enough time or not enough attention? Speed, error and self-maintained control in the Sustained Attention to Response Test (SART). *Clinical Neuropsychological Assessment*, *3*, 167–177.

Manly, T., Owen, A. M., McAvenue, L., Datta, A., Lewis, G. H., & Scott, S. K. et al., (2003). Enhancing the sensitivity of a sustained attention task to frontal damage: Convergent clinical and functional imaging evidence. *Neurocase*, *9*(4), 340–349.

Murphy, K., & Garavan, H. (2004). An investigation into the number of subjects required for an event-related fMRI study. *Neuroimage*, *22*(2), 879–885.

Nielson, K. A., Langeneker, S. A., & Garavan, H. (2002). Differences in the functional neuroanatomy of inhibitory control across the adult lifespan. *Psychology and Aging*, *17*(1), 56–71.

Pardo, J. V., Fox, P. T., & Raichle, M. E. (1991). Localisation of a human system for sustained attention by positron emission tomography. *Nature*, *349*, 61–64.

Rypma, B., Berger, J. S., & D'Esposito, M. (2002). The influence of working-memory demand and subject performance on prefrontal cortical activity. *Journal of Cognitive Neuroscience*, *14*(5), 721–731.

Rypma, B., & D'Esposito, M. (1999). The roles of prefrontal brain regions in components of working memory: Effects of memory load and individual differences. *Proceedings of the National Academy of Sciences of the United States of America*, *96*(11), 6558–6563.

Sturm, W., de Simone, A., Krause, B. J., Specht, K., Hesselmann, V., & Radermacher, I. et al., (1999). Functional anatomy of intrinsic alertness: Evidence for a fronto-parietal-thalamic-brainstem network in the right hemisphere. *Neuropsychologia*, *37*(7), 797–805.

Sturm, W., Longoni, F., Fimm, B., Dietrich, T., Weis, S., & Kemna, S. et al., (2004). Network for auditory intrinsic alertness: A PET study. *Neuropsychologia*, *42*(5), 563–568.

Sturm, W., & Willmes, K. (2001). On the functional neuroanatomy of intrinsic and phasic alertness. *Neuroimage*, *14*, S76–S84.

Stuss, D. T., Murphy, K. J., Binns, M. A., & Alexander, M. P. (2003). Staying on the job: The frontal lobes control individual performance variability. *Brain*, *126*(Pt 11), 2363–2380.

Stuss, D. T., Stethem, L. L., Hugenholtz, H., Picton, T., Pivik, J., & Richard, M. T. (1989). Reaction time after head injury: Fatigue, divided and focused attention, and consistency of performance. *Journal of Neurology Neurosurgery and Psychiatry*, *52*(6), 742–748.

Stuss, D. T., Toth, J. P., Franchi, D., Alexander, M. P., Tipper, S., & Craik, F. I. M. (1999). Dissociation of attentional processes in patients with focal frontal and posterior lesions. *Neuropsychologia*, *37*, 1005–1027.

Ward, B., Garavan, H., Ross, T. J., Bloom, A., Cox, R., & Stein, E. A. (1998). *Nonlinear regression for fMRI time series analysis*. Paper presented at the 4th International Conference on Functional Mapping of the Human Brain, Montreal, Canada.

West, R., Murphy, K. J., Armilio, M. L., Craik, F. I., & Stuss, D. T. (2002). Lapses of intention and performance variability reveal age-related increases in fluctuations of executive control. *Brain and Cognition*, *49*(3), 402–419.

Wilkins, A. J., Shallice, T., & McCarthy, R. (1987). Frontal lesions and sustained attention. *Neuropsychologia*, *25*(2), 359–365.