A Topography of Executive Functions revealed by functional Magnetic Resonance Imaging.

C. Fassbender[1], K. Murphy[1], J. Foxe[2], G. Wylie[2], D.C Javitt[2], I.H. Robertson[1] and H. Garavan[1].

[1]Department of Psychology and Institute of Neuroscience, Trinity College, Dublin 2, Ireland

[2]Nathan Kline Institute for Psychiatric Research, Orangeburg, New York, USA

Correspondence should be addressed to:

Hugh Garavan, PhD
Department of Psychology,
Trinity College Dublin,
Dublin 2,
Ireland.

Ph: +353-1-608-3910
Fax: +353-1-671-2006
E-mail: Hugh.Garavan@tcd.ie

We used fMRI to study the brain processes involved in the dynamic control of behaviour. The Sustained Attention to Response Task (SART), which allows unpredictable and predictable No-go events to be contrasted, was imaged using a mixed (block and event-related) fMRI design to examine tonic and phasic processes involved in response inhibition, error detection, conflict monitoring and sustained attention. A network of regions, including right ventral prefrontal cortex (PFC), left dorsolateral PFC and right inferior parietal cortex, was activated for successful unpredictable inhibitions, while rostral anterior cingulate was implicated in error processing and the pre-SMA in conflict monitoring. Furthermore, the pattern of correlations between left dorsolateral PFC, implicated in task-set maintenance, and the pre-SMA were indicative of a tight coupling between prefrontally mediated control and conflict levels monitored more posteriorly. The results reveal that the executive control of behaviour can be separated into distinct functions performed by discrete cortical regions.

The control over routine, everyday behaviour involves a number of complex executive processes, including the maintenance of current goals, allocation of attentional resources, performance monitoring, inhibition of irrelevant stimuli or responses, detection of errors and the subsequent adjustment of behaviour. Understanding how the brain instantiates these processes and brings them to bear on current task demands in a smooth and dynamic manner remains one of the challenges of cognitive neuroscience as well as a critical challenge for understanding and ultimately preventing human error.

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An essential part of the performance of any task is the maintenance of "task-set", that is, a representation of task goals held in memory against which one can evaluate and monitor one's performance. This function has been attributed to the prefrontal cortex (PFC) [1], particularly dorsolateral prefrontal cortex (DLPFC) [2-4]. The detection of errors is one of the clearest examples of performance monitoring. Rabbitt [5] noted that subjects adjusted their behaviour and performed more conservatively following an error. A number of electrophysiological studies have detected a characteristic ERP component, the error-related negativity (ERN), present after participants make an error [6]. The source of the ERN is thought to be fronto-centrally located, consistent with an error-processing role that has been associated with the anterior cingulate cortex (ACC) [7-11]. However, it has been suggested that error detection may not be the sole trigger for performance amendment, but that the detection of conflict as caused by the simultaneous engagement of conflicting responses may be sufficient [3,12,13]. Monitoring of response conflict is also thought to be performed by ACC [14-16] so some controversy exists as to whether ACC is monitoring performance with respect to errors specifically, or more general response

conflicts. Recent data suggest that the two processes might be dissociated along the midline with rostral ACC involved in error detection *per se* and caudal ACC/ pre-SMA being central to conflict monitoring [8,9](H. G., Ross, T. J., Kaufman, J. & Stein, E. A., unpublished observations).

Inhibition is central to the control and regulation of behavior and impulses [17,18]. Problems with inhibitory control have been implicated in clinical syndromes such as Tourette's [19], OCD [20], schizophrenia [21] and ADHD [22-24] and in age-related cognitive decline [25,26]. Prefrontal cortical activity has been identified for no-go events in monkeys [27] and Iverson and Mishkin [28] identified the prefrontal inferior convexity with inhibition in primates using the Go/No-go paradigm.

Functional brain imaging, while also implicating posterior brain areas, has confirmed the importance of PFC in inhibitory control. Bilateral, but predominately left hemisphere activation has been observed in block-design Go/No-go paradigms [29,30]. A possible limitation of block-design studies, however, is that tonic processes, such as task "set" [31], as well as error-related processes are included in task activation maps. The inclusion of errors in activation maps has been demonstrated to substantially contaminate them and to confound between-condition contrasts (K. M., Nielson, K. A. & H. G., unpublished observations). Event-related fMRI designs are therefore more appropriate for studying discrete cognitive processes such as response inhibition as they can identify areas activated phasically at the actual moment of successful inhibition. Previous event-related designs have identified the right inferior frontal cortex (IFC) [18,32], right DLPFC and right

inferior parietal lobule (IPL) [4,16,18] in response inhibition. However, event-related paradigms also have limitations, in that they often compare No-go with Go activation, which may not be optimal due to the different stimuli typically used for Go and No-go events and the additional motor component involved in Go responses. The present study utilized a Go/No-go task in which random unpredictable No-go events could be compared with identical, yet predictable No-go events, allowing us to confirm that the inhibitory-related activation could be attributed to the inhibitory processes *per se* rather than to the perceptual or motor demands of the No-go event.

Critical to the implementation of these executive functions is the capacity to maintain an appropriate attentional state. While attention is a term which encompasses a number of separable yet interacting set of processes with very different utilities, [33] sustained attention can be thought of as the maintenance of endogenous attentional focus, usually to detect infrequent targets, over a given period of time, and hence is critical in the successful completion of many experimental paradigms as well as everyday tasks. Positron emission tomography (PET) [33-35] (Manly, T. et al, unpublished observations) and lesion studies [36] have implicated right prefrontal and right parietal areas in this process.

The Present Study

The control over everyday behaviour is underpinned by complex executive functions and errors in this control are revealed in absentminded action slips in normal - but particularly in frontally-damaged - brains. The Sustained Attention to Response Task (SART) [37] has been shown to both predict the likelihood of such real life errors in normal and brain

damaged individuals, but also to be particularly sensitive to the presence of frontally-impacting traumatic injury. In the Random SART the digits 1 to 9 are presented in random order and subjects respond with a mouse click to each digit except 3 to which they must withhold their response. In the Fixed SART the digits are presented in a repeating, ascending order (1, 2, 3,…, 8, 9, 1, 2….). This task facilitates the investigation of a number of executive functions. Activation has been observed in the right DLPFC and right superior parietal lobe (SPL) when performing the SART (Manly et al, unpublished observations) and this right hemisphere fronto-parietal network has been implicated in sustained attention [33-36]. Error processing, believed to implicate ACC [7,8,10], can be investigated as commission errors are common in the Random SART. As it is a Go/No-go paradigm, inhibition of prepotent motor responses can be examined. In addition the SART involves simultaneous activation of competing response tendencies resulting in response conflict. Consequently, a mixed design (block and event-related) was utilized in order to identify tonically activated areas, presumably including those reflecting the sustained attentional demands of the task, and areas that were active phasically, for error and conflict related processes and for both successful and unsuccessful attempts to inhibit responding. Finally, given the dynamics between response conflict and top-down attentional control that have been proposed [1,3,4,13,14] individual differences among participants were examined in order to evaluate whether or not there was evidence of a relationship between the two processes in the implementation of cognitive control.

By studying the dynamic tonic-phasic processes of executive subcomponents of response inhibition, error monitoring, conflict monitoring and sustained attention in the SART, we

hoped to uncover a possible dynamic set of processes involved in executive control over routine behaviour.

RESULTS

Performance Results

Three subjects were excluded from analysis due to excessive movement. The remaining eighteen subjects (five male, mean age 26.5, range 19-37) had significantly more correct withholds in the Fixed (90.2% ± 9.8%) than in the Random SART (71.47%± 16%; $t(17) = 6.06$, $p \leq 0.001$). There were comparable numbers of errors of omission in the two conditions (7.28± 9.22 in the Fixed and 6.83± 9.68 in the Random SART, $t(17) = 0.17$, $p \leq 0.86$). Reaction times are presented in Figure 1. Although the commission errors in the Random SART followed a typical pattern for commission errors in Go/No-go tasks in that they were significantly faster than response times for Gos ($t(16) = 4.121$, $p \leq 0.001$) this was not the case for errors of commission in the Fixed SART in which commission errors and Go response times did not differ ($t(15) = 0.350$, $p \leq 0.731$).

Insert Figure 1. here

Block Activation

A number of regions, visual, motor and frontoparietal were tonically activated during task performance (see Table 1). A subset of these areas were significantly more active for Random compared with Fixed SART and included pre-SMA, left and right putamen, left

insula/ inferior frontal gyrus (IFG), left precuneus, left parahippocampal gyrus and left supramarginal gyrus. No area showed significantly greater activation for the Fixed SART (see Figure 2A).

Insert Table 1. and Figure 2. here

Correct Inhibition Activation

Two distinct networks were seen to underlie correct inhibitions in the Fixed and Random conditions (see Table 2). The right ventral frontal cortex, right IPL, left DLPFC and the left putamen were significantly more active during correct inhibitions in the Random condition than in the Fixed condition, whereas the left IFG , right angular gyrus, left insula, and left middle frontal gyrus showed significantly greater activation during correct inhibitions in the Fixed Condition. No area was significantly activated for correct inhibitions in both the Fixed and Random SART suggesting that distinct networks were responsible for withholding a response in the two conditions (see Figure 2).

Insert Table 2. and Figure 3. here

Commission Error Activation

Errors of commission produced widespread cortical activity with the highest concentration along the medial wall (see Table 3). All regions, bar two, showed

significantly greater activation for Fixed errors relative to Random errors. These two exceptions, located in the ACC and the left IPL showed no significant difference in activation between the Fixed and Random SART (the IPL had greater activation for the Fixed SART but just missed significance at $p \leq 0.06$).

Insert Table 3. and Figure 4. here

Relationship between Tonic and Phasic Activation

We were interested in the interactions between tonic and phasic activation levels and, particularly between areas that might reflect the dynamic between the maintenance of task-set information and levels of response conflict. The tonically activated left DLPFC region is a probable area for subserving the task-set maintenance role [2,4,38,39] while the activated midline areas, particularly the ACC and pre-SMA, were likely to have subserved the conflict monitoring role [8,14]. Tonic left DLPFC activation correlated positively with tonic pre-SMA activation ($r = 0.7$, $p \leq 0.001$). For correct inhibitions, phasic activity within this left DLPFC region correlated positively with phasic pre-SMA activation in both the Fixed and Random SART ($r = 0.5$, $p \leq 0.03$; $r = 0.49$, $p \leq 0.04$, respectively). For errors of commission phasic left DLPFC activity correlated highly with the same pre-SMA region in the Random SART ($r = 0.92$, $p \leq 0.001$). An inverse relationship between these two areas was observed in just one circumstance: Tonic left DLPFC activation during the Random SART correlated negatively with phasic pre-SMA

activation for random commissions ($r = -.55$, $p \leq 0.02$, for the pre-SMA region defined by the tonic activation map; $r = -.62$, $p \leq 0.01$, with one statistical outlier excluded from the regression for the pre-SMA region defined by the phasic commission error activation map). For just one of these particular comparisons was a significant correlation found between the left DLPFC and ACC: Phasic activation in the ACC for correct inhibitions in the Fixed and Random SART correlated with tonic left DLPFC activation ($r = 0.59$, $p \leq 0.01$, $r = 0.69$, $p \leq 0.001$, respectively).

DISCUSSION

The results have revealed a topography of dynamic interactions between executive functions. By utilizing a mixed design separate fronto-parietal networks were identified for phasic, event-related processes such as response inhibition and tonic, task-related processes such as sustained attention. The examination of tonic and phasic activation and the relationships between discrete frontal regions also aided in the identification of separable error-related processes, located in the rostral ACC, and conflict monitoring processes which were associated with the more dorsal ACC extending into the pre-SMA. Correlational analyses have revealed that these discrete areas are functionally inter-related and, consequently, that the executive control of behaviour is accomplished through the coordinated involvement of these areas in task performance.

Neural network underlying response inhibition.

Two separate networks were activated for correct inhibitions in the Fixed and Random

SART. Correct inhibitions to unpredictable No-go events in the Random SART activated the right ventral PFC, right IPL, left putamen and the left DLPFC. The involvement of prefrontal and parietal areas in response inhibition is consistent with previous investigations [16,18,32,40,41]. A role in inhibitory processes has been attributed to the right IPL based on Go/NoGo tasks [10,16,18,30], Stroop tasks [42], material-independent flanker tasks (Hazeltine, E., Bunge, S. A. & Gabrielli, J. D. E., unpublished observations), Stop paradigm tasks [30] and the Simon task [42]. Ventral prefrontal activation has also been consistently observed [18,28]. Right IPL activation was also observed in the Fixed SART when participants made an error of commission. This activation may reflect a late attempt to inhibit an already initiated response. Alternatively, this activation could reflect an arousal response to an unexpected error in such a simple task as the Fixed SART. Right inferior frontal involvement in inhibition was noted irrespective of which hand was used to respond [32] and across different types of inhibitory tasks [40]. Menon and colleagues [10] also found bilateral, but in particular, right hemisphere activation of the inferior frontal sulcus for inhibitory events.

Whereas others have identified response inhibition with the right DLPFC [10,18,43] the present study has observed activation in this region of the left hemisphere. While one reason for this disparity may be the relatively high verbal demands of the present task, another possibility is that observed differences may be due to the use of a consistent stimulus-response mapping in this experiment (i.e., subjects always inhibited to the number 3), whereas others [4,18,43] have utilized variable stimulus-response mappings (i. e., the appropriate response must be chosen for different contexts as it is not unambiguously

determined by the stimulus). Variable mapping between the stimulus and the appropriate response may require more "selection," a function which has been attributed to right DLPFC [4,44] and hence may not have been observed in this task. The PFC has been implicated in the top down orientation of attention towards salient information over competing or distracting information [45]. The present results are consistent with an anterior network focusing attention in the case of highly meaningful, infrequent stimuli with high levels of behavioral importance or acting to facilitate certain responses while inhibiting other irrelevant ones.

In contrast, a mainly left-lateralized network of areas was observed for correct inhibitions to predictable No-go events in the Fixed SART. The distinctiveness of these networks was reflected in different response times for the Random and Fixed SART. Commission errors in the Random SART were significantly faster than Go response times, a common reaction time finding in Go/No-go tasks suggestive of insufficient time to inhibit the prepotent Go response [46]. Conversely, No-go error response times in the Fixed SART were not significantly different than Go response times, suggesting that errors may have been due to an inattentive default Go response. Therefore, the network of brain regions activated for Random correct inhibitions can be interpreted as being specifically related to response inhibition.

Tonically Activated Executive Functions

A number of areas were activated over the whole block. One particular area of note, the left DLPFC, has previously been implicated in maintenance of representations [2,3,11]. This

same area was observed in a Go/NoGo study [4] after subjects adjusted their behaviour following commission errors and was interpreted as being involved in maintaining/re-establishing task set. Consistent with this functional attribution, Brass and colleagues [39] have recently shown this area to be active during task preparation. Consequently, this left DLPF area, which was significantly active for both the Fixed and the Random SART, was likely to have been involved in the maintenance of the task set or goals.

The pre-SMA region was seen to be significantly more active for the Random over the Fixed SART. Given this region's involvement in motor preparation [47,48], it may be that the increased need for motor preparation in the Random SART, that is the need to be primed to withhold a response, may be responsible for this activation pattern. However this region and more inferior midline regions within the ACC have also been implicated in conflict monitoring [8,14,16,43] and it is reasonable to assume that the Random SART would generate greater amounts of tonic conflict than the Fixed SART. This latter interpretation is consistent with the pattern of correlations, discussed below, between the left DPFC and the pre-SMA.

Finally, right parietal and prefrontal areas were anticipated to be tonically active given their established role in sustained attention [33-36]. Activation was observed in the left IPL and bilateral superior lobules (extending into the IPL in the right hemisphere) and the right IFG in both conditions. Curiously, deactivation was also seen in the right SPL for the Fixed SART.

Conflict Monitoring and Error Processing

Some controversy exists as to whether the ACC is involved in error processing *per se*, or rather conflict monitoring [7,8,11,14,49]. Carter and colleagues observed activation in the ACC not only during error trials but also during trials involving high amounts of response conflict [14]. Other evidence suggests that the more rostral region of the ACC may be involved in error detection and the more caudal ACC extending into the pre-SMA may be involved in response conflict [8,9] (H.G., Ross, L. L., Kaufman, J. & Stein, E. A., unpublished observations). In the present study a rostral ACC region and left IPL were the only two areas to show similar activation for errors in the Fixed and the Random SART. The medial parietal lobes (precuneus) have previously been implicated in error processing [10] and the left parietal lobe has also been considered to be a contributor to the P_E (error positivity) [9], a component of error trial ERPs which is thought to reflect error processing. The fact that these two areas alone were seen to be activated for both Fixed and Random errors in this study lends credence to the notion that they are specifically involved in error processing. Conversely, an area in the pre-SMA displayed significantly greater tonic activation for the Random SART. Together, these findings suggest that the more rostral area of the ACC is an error processing area and that the more caudal ACC area extending into the pre-SMA serves a response conflict monitoring function [7-10,16].

PFC and Midline Interactions

Barch and colleagues [15] predicted a correlation between DLPFC and ACC, under the assumption that conflict monitored by the ACC triggers recruitment of top-down

attentional resources from the DLPFC. In the present study, this relationship was seen between DLPFC and pre-SMA. A positive correlation was also seen between phasic activation of left DLPFC and phasic pre-SMA for Fixed and Random correct inhibitions and was especially high for Random errors of commission. We would expect to see this pattern if cognitive control is enacted by the detection of high levels of conflict by pre-SMA triggering a rise in top-down control exercised by left DLPFC akin to the model suggested by Botvinick and colleagues [13]. In effect, those subjects who showed the greatest midline (response-conflict) activation also showed the greatest left DLPFC (top-down control) activation. Consistent with this interpretation, individuals who displayed poor tonic levels of top-down control showed increased levels of phasic conflict, monitored by pre-SMA, on error trials. This relationship also supports existing models [12,14,16] which posit that cognitive control is achieved by the PFC maintaining representations of task-relevant information and suppressing competing or distracting, task-irrelevant information, thus reducing response conflict as monitored by the ACC, or as in this task, the more caudal part of the ACC extending into the pre-SMA region. Together, these correlations add strong support to the concept of a reciprocal relationship between these two regions [1], the pre-SMA monitoring for conflict and feeding back to DLPFC which maintains task set and allocates attentional resources. These conclusions are based on inter-individual correlations between activated brain areas. In order to investigate the temporal dynamic in which conflict and control interact, within-subject, time-series correlations between areas using the superior temporal resolution of electrophysiological recording could prove very illuminating.

Interestingly, the inter-regional correlations that have been reported above were not seen between DLPFC and rostral ACC. However, in the Fixed and Random SART, phasic left DLPFC activation did correlate with phasic ACC activation for correct trials only. That this relationship was not observed for incorrect trials, trials in which conflict should have been higher, suggests that the ACC-DLPFC correlation may not reflect a conflict-related prefrontal-midline interaction. Instead, one conjecture, in need of further corroborating evidence, is that the ACC activation may reflect emotional, reward-related processes, the magnitude of which are related to the strength of the task goals, represented in the DLPFC. In total, these results suggest that midline regions and DLPFC work cooperatively in order to complete the task successfully, constantly working in parallel to monitor conflict, maintain task goals and enforce control.

In summary, the comparison of correct inhibitions to unpredictable No-go events with inhibitions to predictable No-go events revealed a discrete number of prefrontal and parietal brain regions implicated in inhibitory control. The rostral area of the ACC and the left parietal lobe displayed a role in error processing, whereas the more dorsal part of the ACC and the pre-SMA appeared to play a role in conflict monitoring. Guided by previous research, we suggest that the parietal and right prefrontal areas were involved in sustained attention while the left DLPFC actively maintained the task set. These results reveal a neuroanatomical fractionation of those executive functions critical for smooth behavioural control. Furthermore, the inter-regional correlations revealed that these discrete cortical areas work together in effecting this control.

METHODS

Subjects

7 male and 14 females with ages ranging from 19 to 37 and a mean age of 26.4 participated in this experiment. All participants were right-handed, were free of neurological disorders, psychiatric problems or head trauma and were not under any medication. Written consent was obtained from each participant and they were paid for their participation.

Sustained Attention to Response Task (SART).

A modified version of the SART[37], which consists of a series of numbers from 1 to 9, which are presented in a random and unpredictable (Random SART) or sequential and predictable (Fixed SART) order was employed. Subjects responded by mouse click to every number except the number 3. Each digit was presented for 250 msecs. In order to minimize response time differences between the Random and Fixed SART a visual response cue of 50 msecs duration with a post-stimulus onset time of 100 msecs, (parameters based on Manly, 2000 [50]), was utilized. This response cue, a thickening of the post-stimulus mask, appeared as a "visual blip". Subjects were instructed to respond during this response cue and were trained before entering the scanner. The duration of the entire post-stimulus mask varied, (461, 572, 683, 794, 906 or 1017 msec) in order to sample different points in the haemodynamic curve as the No-go stimulus (the number 3) consistently fell after every ninth digit in the Fixed SART. Post-stimulus duration changed after each full cycle (digits 1 through 9 in the Fixed SART and after each set of

nine random digits in the Random SART). A distinct cue to indicate the onset of the next digit was presented during the final 400 msec of all post-stimulus periods.

Stimuli were presented and responses recorded using E-prime (Psychology Software Tools Inc.) in blocks of 90 to 92 seconds, which alternated with 30 second rest periods. Five blocks of Fixed SART comprised one run and five blocks of Random SART comprised a second run and run order was counterbalanced across subjects. There were 36 No-gos in the Fixed and 34 No-gos in the Random SART of the 326 stimuli in each condition.

fMRI scanning

Scanning was performed on a 1.5 T Siemens scanner [in which foam padding was used to restrict head movements]. 202 T_1-weighted saggittal slices were acquired for each subject (slice thickness = 1 mm, field of view = 256 mm). Functional images were single-shot, T2* weighted, echo planar imaging sequences. 22 axial slices (5 mm slice thickness) were acquired for each subject (TR = 2000 msec, TE = 50 msec, flip-angle = 90º, 64 mm x 64 mm matrix size, field of view = 256 mm). 305 volumes were scanned for each run (Fixed and Random SART).

Image analysis

Data were analyzed using AFNI [51] software. Images were time-shifted using Fourier interpolation [to correct for differences in slice acquisition time], edge-detected by removing any activation outside the brain and 3D motion corrected. Images or individual

subjects that displayed excessive motion were excluded from further analysis as were the first three images in each run. A mixed regression analysis was employed whereby tonic, task-related activation was calculated as a percentage change score using rest as baseline and separate impulse response functions (IRF) were calculated for correct inhibitions and commission errors. A non-linear regression program determined the best-fitting gamma-variate function for these IRFs [52,53]. The area under the curve of this gamma-variate function was expressed as a percentage of the area under the baseline (i.e., tonic activation level, having first removed variance associated with tonic, task-related activation levels). These percentage area (event-related activation) and percentage change maps (block activation) were then warped into standard Talairach space [54] and spatially blurred using a 3 mm isotropic rms Gaussian blur.

Separate t-tests against the null hypothesis of no percentage activation change were then performed for each condition (Random and Fixed tonic activation, Random and Fixed correct inhibitions and Random and Fixed errors of commission) with a voxel-wise threshold of $p \leq 0.001$ and a cluster-size criterion of 126 μl of contiguous significant voxels. These thresholds, determined by Monte Carlo simulations resulted in a 0.05 probability of a significant cluster being seen by chance. Fixed and Random tonic activation maps were then combined (OR maps) and mean activation calculated for the resulting functionally defined regions of interest by condition. A similar procedure was employed for the Fixed and Random event-related activation maps. Event-related clusters of activation were analyzed with 2 (correct inhibitions and errors of commission) by 2 (Fixed and Random SART) ANOVAs while tonic activation differences between the

SART conditions were tested with paired t-tests.

Inter-individual correlations between activated brain regions were performed to determine the degree to which areas underlying executive functions interacted with one another.

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FIGURE CAPTIONS

Figure 1.

GO event reaction times and commission error reaction times for the Fixed (F) and Random (R) SART.

Figure 2.

Tonic functional activation associated with the Random (red) and both Random and Fixed (green) SART. Areas that were activated for the Random over the Fixed SART included the pre-SMA, left precuneus and right medial inferior frontal gyrus. Areas that were activated tonically in the Fixed and Random SART included left dorsolateral prefrontal cortex, bilateral inferior parietal cortex and visual areas (bilateral cuneus and left lateral occipital gyrii are shown).

Figure 3.

Functional activation associated with correct inhibitions for Fixed (blue) and Random (red) SART. Correct inhibitions to unpredictable No-go events (in the Random SART) activated right ventral frontal cortex, right inferior parietal cortex and left dorsolateral prefrontal cortex. Correct inhibitions to predictable No-go events (in the Fixed SART) activated left middle frontal gyrus, left inferior frontal gyrus and left insula.

Figure 4.

Functional activation associated with errors of commission for Fixed (blue) and both Fixed and Random (green) SART. Commission errors to predictable No-go events in the

Fixed SART activated the anterior cingulate extending into pre-SMA, medial superior frontal gyrus, bilateral inferior parietal lobe, right precuneus, left inferior frontal gyrus and right superior gyrus extending into middle frontal gyrus. Only two areas, a more rostral area of the ACC and the left inferior parietal lobe, were activated for errors irrespective of condition.

Table 1

Tonic Activations for Fixed and Random SART

ROI (Brodmann Area)	Hemisphere	Volume (μl)	Talairach coordinates x (RL)	y (AP)	z (IS)
Precentral gyrus/MFG (6/9)	L	1148	-43	0	32
(4)	L	936	-40	-18	49
Precentral gyrus (6)	R	280	46	0	28
Medial IFG (6/32)	B[b]	1022	-2	-1	49
Frontal operculum (47)	L[b]	691	-43	8	1
Occipital lobe (Cuneus) (17/18/19)	B[†]	15668	-3	-67	6
Inferior occipital gyrus (17/18/19)	R	5762	31	-80	-5
(17/18)	L	3853	-30	-89	-5
Lateral occipital gyrus (19)	L	2692	-42	-64	-8
Superior parietal lobule (7/31)	R	592	28	-53	42
(7)	R[†]	153	18	-53	62
(7/40)	L	629	-30	-46	40
Precuneus (7)	L[b†]	1079	-12	-46	47
Inferior parietal lobule (7)	L	610	-33	-61	48
Paracentral lobule (4)	R[b†]	385	5	-27	43
Supramarginal gyrus (40)	L[b]	181	-42	-39	30
Lingual gyrus	L[†]	289	-24	-38	-11
Insula (41/42)	R[b†]	824	39	-21	10
Putamen	R[b]	762	22	0	7
	L[b]	5238	-21	-8	7
Optic tract	L[b]	519	-12	-8	-10
Lateral ventrical	L	159	-21	-43	14
Cerebellum	R	300	6	-55	-20

Note: IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus; L, Left; R, Right; B, Bilateral.

[a] signifies that activation was significantly greater in the Fixed than the Random SART.

[b] signifies that activation was significantly greater in the Random than the Fixed SART.

[†]: signifies a deactivation in the Fixed SART

Table 2

Event-Related Activations for Fixed and Random SART

ROI (Brodmann Area)	Hemisphere	Volume (μl)	Talairach coordinates x (RL)	y (AP)	z (IS)
Activations for Correct Inhibitions					
IFG (45/47)	L [a]	340	-52	16	3
MFG (6)	L [a]	162	-39	8	42
Postcentral gyrus/ Insula (40)	L [a]	253	-47	-23	18
Angular gyrus (39)	R [a]	264	44	-61	31
IFG (10)	R [b]	131	35	49	2
IFG/ MFG (9)	L [b]	136	-42	24	35
Inferior parietal lobule (40)	R [b]	244	36	-48	44
Putamen/ Internal capsule	L [b]	193	-22	11	8
Activations for Commission Errors					
SFG (6)	L [a]	140	-14	3	49
Medial SFG (8)	R [a]	214	9	31	45
(6/32)	B [a]	847	1	6	50
Medial SFG/ Cingulate gyrus (32/24)	B	847	3	20	31
Medial SFG/ MFG (10/9)	R [a]	308	18	44	25
SFG/ MFG (10)	R [a]	152	23	54	21
IFG (47)	L [a]	333	-46	21	2
IFG/ Insula (47/13)	R [a]	935	44	14	0
(45)	L [a]	148	-38	22	10
(45)	L [a]	194	-31	29	9
Insula/ Frontal operculum	R [a]	151	29	10	18
Angular Gyrus (22)	R [a]	184	50	-52	9
Middle temporal gyrus (19/37)	R [a]	133	38	-54	0
Inferior parietal lobule (40)	R [a]	767	52	-44	38
(40)	L	353	-56	-45	27
(7)	L [a]	138	-31	-52	37
Precuneus (7/31)	R [a]	449	12	-44	34
Insula (47)	L [a]	134	-42	9	-4

Note: Abbreviations and diacritics are as for Table 1.

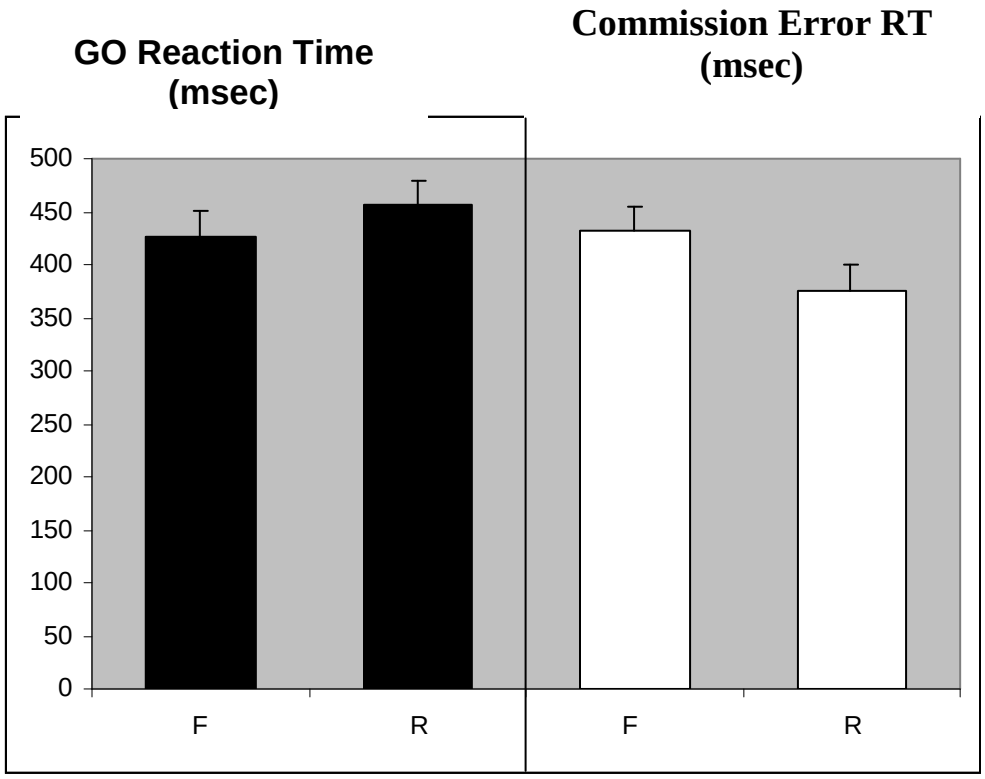
GO Reaction Time
(msec)
Commission Error RT
(msec)
500
450
400
350
300
250
200
150
100
50
0
F
R
F
R

Figure 1

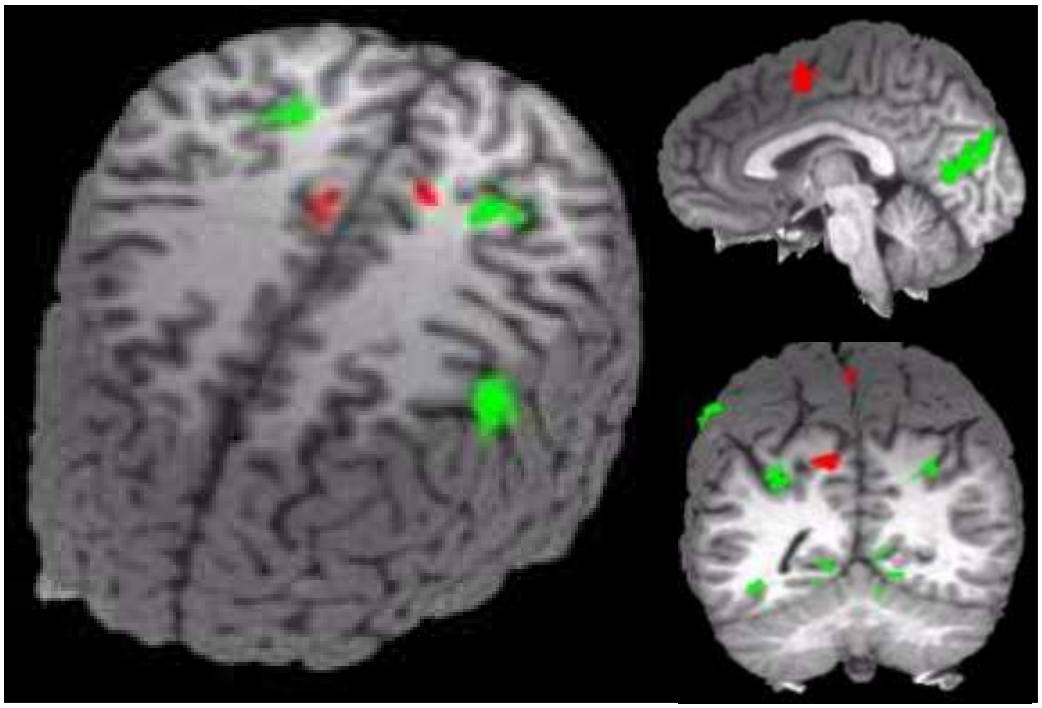

Figure 2

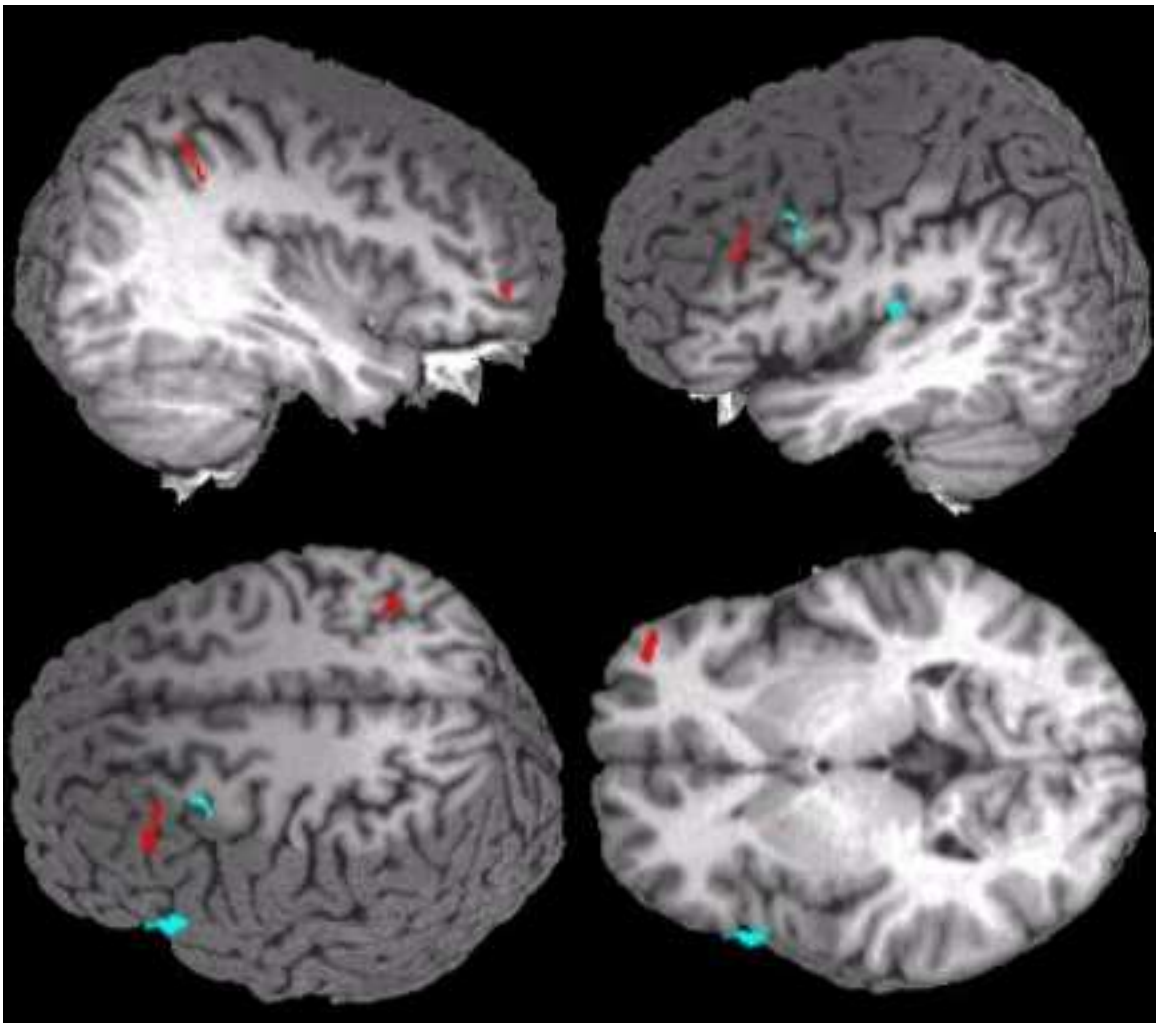

Figure 3.

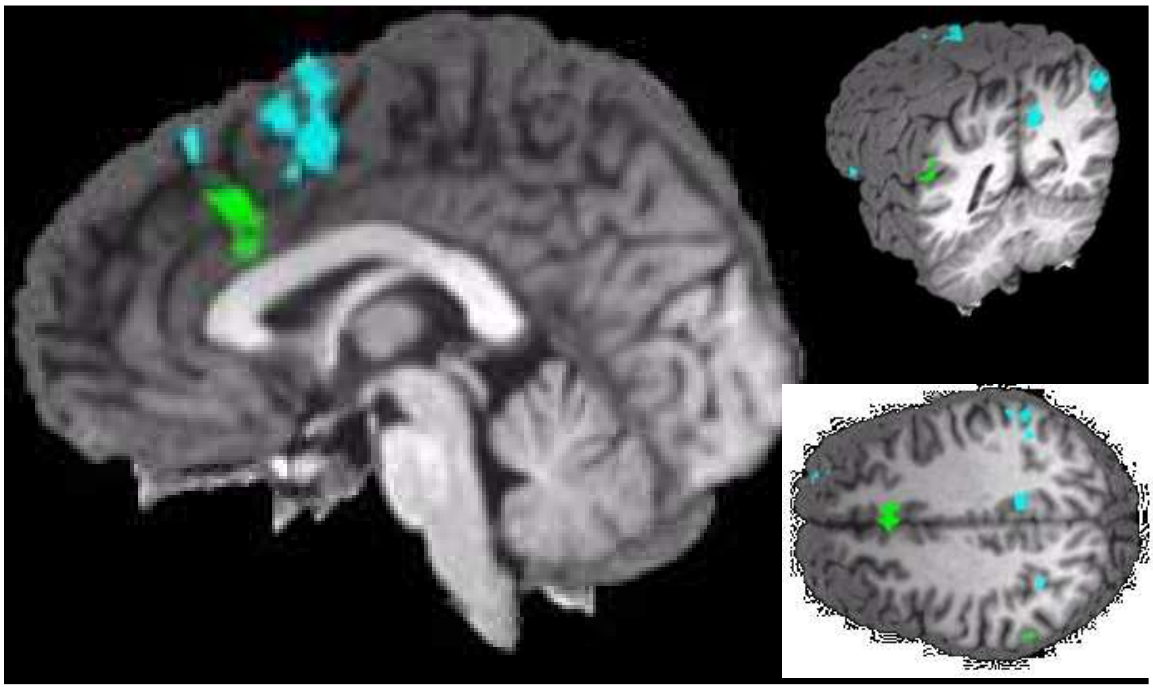

Figure 4.