

Functional Specialization within the Medial Frontal Gyrus for Perceptual Go/No-Go Decisions Based on “What,” “When,” and “Where” Related Information: An fMRI Study

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Abstract

■ Cortical systems engaged during executive and volitional functions receive and integrate input from multiple systems. However, these integration processes are not well understood. In particular, it is not known whether these input pathways converge or remain segregated at the executive levels of cortical information processing. If unilateral information streams are conserved within structures that serve high-level executive functions, then the functional organization within these structures would predictably be similarly organized. If, however, unilateral input information streams are integrated within executive-related structures, then activity patterns will not necessarily reflect lower organizations. In this study, subjects were imaged during the performance of a “perceptual go/no-go” task for which instructions were based on spatial (“where”), temporal (“when”), or object (“what”) stimulus features known to engage unilateral processing streams, and

the expected hemispheric biases were observed for early processing areas. For example, activity within the inferior and middle occipital gyri, and the middle temporal gyrus, during the what and when tasks, was biased toward the left hemisphere, and toward the right hemisphere during the “where” task. We discover a similar lateralization within the medial frontal gyrus, a region associated with high-level executive functions and decision-related processes. This lateralization was observed regardless of whether the response was executed or imagined, and was demonstrated in multiple sensory modalities. Although active during the go/no-go task, the cingulate gyrus did not show a similar lateralization. These findings further differentiate the organizations and functions of the medial frontal and cingulate executive regions, and suggest that the executive mechanisms operative within the medial frontal gyrus preserve fundamental aspects of input processing streams. ■

INTRODUCTION

Specializations within the right hemisphere of the cerebral cortex for processing spatial (“where”)-related information are well documented. For example, lesions within the right posterior parietal lobe are sufficient to disrupt several aspects of visuospatial behavior including space perception (Irving-Bell, Small, & Cowey, 1999), spatial cue recognition (Losier & Klein, 2001), spatial attention (Miniussi, Rao, & Nobre, 2002), orientation (Warrington, 1982), judgments of geometrical shapes (Umiltà, Bagnara, & Simion, 1978), programming of exploratory eye movements (Sava, Liotti, & Rizzolatti, 1998), and stylus maze performance (De Renzi, Faglioni, & Previdi, 1977). Spatial neglect, the inability to attend to stimuli presented in the contralesional hemispace, is also more frequent, severe, and long-lasting following right parietal lobe lesions (De Renzi, 1977; Arrigoni & De Renzi, 1964). This right-hemispheric bias for spatial processing has also been shown for auditory and tactile spatial systems within both parietal (Brodmann’s Area

[BA] 40) and dorsolateral prefrontal (BA 9 and BA 46) cortices (Coghill, Gilron, & Iadarola, 2001).

In contrast, left hemisphere systems are specialized for processing temporal (“when”) and object (“what”)-related information. Language production, for example, is predominantly located within the left hemisphere, and lesions of the left hemisphere result in both Broca’s and Wernicke’s aphasia (see Davidson & Hughdahl, 1995). Temporal-related musical perturbations have also been shown to selectively activate the left hemisphere of the temporal and parietal lobes (Samson, Ehrle, & Baulac, 2001; Hofman, Klein, & Arlazoroff, 1993), even though nontemporal components of music such as pitch perception preferentially activate the right hemisphere (Warrier & Zatorre, 2004; Zatorre, 2001; Alcock, Wade, Anslow, & Passingham, 2000).

Left hemisphere pathways are also specialized for processing of object (“what”)-related information. For example, a lesion restricted to the left occipito-temporal area may be sufficient to produce visual object agnosia (McCarthy & Warrington, 1990). However, the identification of objects shown with either unusual perspectives, or familiar features such as a known face,

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has been reported to enlist processes within the right hemisphere (Sergent, Ohta, & MacDonald, 1992; Warington, 1982). Nonetheless, other features of object recognition such as naming (Hirsch, Rodriguez-Moreno, & Kim, 2001; Atchley & Atchley, 1998; Phelps, Hyder, Blamire, & Shulman, 1997; Sergent et al., 1992), discrimination (Georgopoulos, 2000), and construction (Georgopoulos, 2000), (“what”) preferentially activate regions within the left hemisphere.

If high-level executive systems that converge multiple inputs respect the organization of these input processing streams, then these hemispheric asymmetries for spatial, temporal, and object information would also be preserved within structures that mediate executive-related functions. For example, the right-hemispheric bias seen in the early visual areas and parietal lobe for spatial (“where”-based) information would predictably be retained within frontal regions serving executive-related tasks. Conversely, the left hemisphere would be expected to predominate for executive tasks based on “when” and “what” information. In this study, we test this hypothesis using functional magnetic resonance imaging (fMRI) and a new perceptual go/no-go task.

The conventional go/no-go task is a response-selection task that requires either the execution of a response, or the inhibition of a response, depending on instructions relating to sequential presentations of letters (Schumacher, Elston, & D’Esposito, 2003; Konishi et al., 1999; Aminoff & Goodin, 1997). Go/no-go tasks have been used as probes for cognitive processes such as decision making, and are shown to reliably activate the primary motor cortex, the supplementary motor cor-

tex, and the dorsolateral prefrontal structures (Durstun, Thomas, Worden, Yang, & Casey, 2002; Watanabe et al., 2002; Konishi et al., 1999; Humberstone et al., 1997; Grafton, Mazziotta, Woods, & Phelps, 1992).

In this study, the “go” or “no-go” choice was based on a perceptual decision using a simple discrimination of the type that might be made in suprathreshold psychophysical tasks (Salzman & Newsome, 1994). These tasks were based on stimulus features such as shape, color (“what”), location (“where”), or temporal properties (“when”). Thereby, a go/no-go task was guided by three different categories of input information (Figure 1). For example, in the case of the “where” experiments using visual stimuli (Column 1), the subject indicated when a filled circle appeared in the upper left and lower right quadrants of a screen (go) but gave no response (no-go) when the circle appeared in other quadrants. In the case of the “when” experiments (Column 3), subjects indicated when a circle appeared after a short time interval (go) but not after a long one (no-go). In the case of the “what” experiments (Column 6), the subject indicated if the shape was a square, or a diamond, (go), but gave no response (no-go) when the shape was a triangle, or a circle (no-go).

Similar tasks were performed using tactile and auditory stimuli where possible (Figure 1, Columns 2, 4, and 5). For the tactile stimulation, the “where” condition was replicated by tapping subjects in one of four previously demarcated quadrants on the undersurface of their foot and instructing them to respond only if they felt a tap on their 1st (toe) or 4th (heel) quadrants but not the middle quadrants (Column 2). For the “when”

Figure 1. This figure shows the stimuli, instructions, and sensory modalities tested in this study. Columns represent the three experimental conditions (“where,” “when,” and “what”) on which the decisions were based; subcolumns represent the sensory modalities (visual, tactile, and auditory) through which cues for these experimental conditions were delivered. Rows represent the stimuli for the go and no-go instructions. For each experimental condition, the upper two images represent images to which subjects responded with a “go” response, and the lower two images represent images to which subjects responded with a “no-go” response.

| STIMULI, TASKS, MODALITY, AND DECISION TYPES | | | | | | |
|--|--------------------------------|---------|--------------------------------|---------|----------|---------------------------|
| Decision | “WHERE” SPATIAL LOCATION | | “WHEN” TEMPORAL INTERVAL | | | “WHAT” OBJECT SHAPE |
| | Visual | Tactile | Visual | Tactile | Auditory | Visual |
| go | | | | | | |
| | | | | | | |
| no-go | | | | | | |
| | | | | | | |

condition, subjects were instructed to respond if the tap on the foot preceded the previous stimulus by a “short” (1 sec) interstimulus interval (ISI) but not a long (3 sec) one (Column 4). Auditory stimuli were employed for the “when” task only. Subjects were instructed to tap if a tone of fixed frequency (440 Hz, 500 msec) preceded the previous tone by a “short” (1 sec) ISI but not a long (3 sec) one (Column 5). To test for response-specific effects, visual tasks were also replicated using an imagery (imagine tap [go]/imagine no tap [no-go]) response. Stimuli and instruction details are provided in the Methods section.

RESULTS

Seven cortical regions met all statistical criteria which included a cluster of at least 5 contiguous voxels each at $p < .0005$ in all individual subjects within the same anatomical region: middle and inferior occipital gyri, middle temporal gyrus, medial frontal gyrus, inferior parietal lobule, cingulate gyrus, and cerebellum. The anatomical areas, Brodmann’s areas, and average coordinates are shown for the average laterality indices determined for each condition (“when,” “where,” and “what”) in Table 1.

Laterality

In the go/no-go “where” conditions (Table 1 and Figure 2), the middle occipital, inferior occipital, middle temporal, and medial frontal gyri were associated with positive (right hemisphere dominant) laterality quotients, and (except in the case of the middle occipital gyrus, for which the “when” condition was neutral) negative (left hemisphere dominant) quotients for both the “when” and the “what” conditions. In the inferior parietal, cingulate gyrus, and

cerebellum, however, this pattern of right- and left-hemispheric bias was not observed (Figure 2). When the decision (go/no-go) was removed from the task (control conditions, see Methods for details), the right lateralization for “where” tasks, and the relatively left lateralization for “what” and “when” tasks were retained in the middle occipital gyrus (ANOVA, $F = 4.28$, $p = .024$), but was no longer statistically significant in the inferior occipital ($F = 1.33$, $p = .28$), middle temporal ($F = 0.56$, $p = .61$), and medial frontal areas ($F = 0.51$, $p = .60$). This finding suggests a role for some sensory association areas in aspects of the go/no-go task, and indicates that the processing of go/no-go decisions is not restricted to the machinery of the frontal lobe.

The “when” condition was the only condition for which the task required consideration of both the previous and the current stimulus, and therefore may have involved a higher working memory load. To compare responses for each condition, the accuracy (percent correct) and speed of response (reaction time) were measured for each condition, in order to test whether these response measures were different across the “where,” “when,” and “what” conditions. The proportion of correct responses for the “where” (.65), “when” (.70), and “what” (.80) conditions were not significantly different from each other ($F = 0.4$, $p = .6$, $df = 2$), and similarly, the reaction times for the “where” (445 msec), “when” (566 msec), and “what” (466 msec) were not significantly different from each other ($F = 3.5$, $df = 2$, $p = .09$). Stratification based on response accuracy also did not reveal any differences in reaction times ($F = 0.9$, $df = 2$, $p = .5$) between correct and incorrect responses. When average reaction times were regressed on the proportion of correct responses for each condition, no significant relationship between the two variables was observed, indicating that variation

Table 1. Anatomical Area, Brodmann’s Area, Average Talairach Coordinates and Laterality Indices for all visual conditions (Figure 1)

| Anatomical Area | Brodmann’s Area | Average Coordinates* | | | Laterality Indices | | |
|--------------------|-----------------|----------------------|-----|-----|-----------------------|----------------------|----------------------|
| | | x | y | z | Where (Mean ± SEM) | When (Mean ± SEM) | What (Mean ± SEM) |
| Middle Occipital | 19 | ±38 | +78 | +4 | +30 ± 11 | +1 ± 21 | -25 ± 23 |
| Inferior Occipital | 18 | ±38 | -78 | -4 | +32 ± 11 | -21 ± 19 | -21 ± 19 |
| Middle Temporal | 21,39 | ±50 | -48 | -1 | +51 ± 11 | -29 ± 16 | -17 ± 20 |
| Medial Frontal | 6 | ±8 | +11 | +55 | +9 ± 8 | -22 ± 9 | -38 ± 14 |
| Inferior Parietal | 40 | ±55 | +12 | +15 | +8 ± 6 | +25 ± 15 | -2 ± 12 |
| Cingulate | 24 | ±50 | +20 | +40 | -17 ± 12 | -3 ± 5 | -1 ± 5 |
| Cerebellum | - | ±25 | -55 | -12 | +17 ± 8 | +13 ± 10 | +4 ± 2 |

*+ = Right Hemisphere; - = left hemisphere.

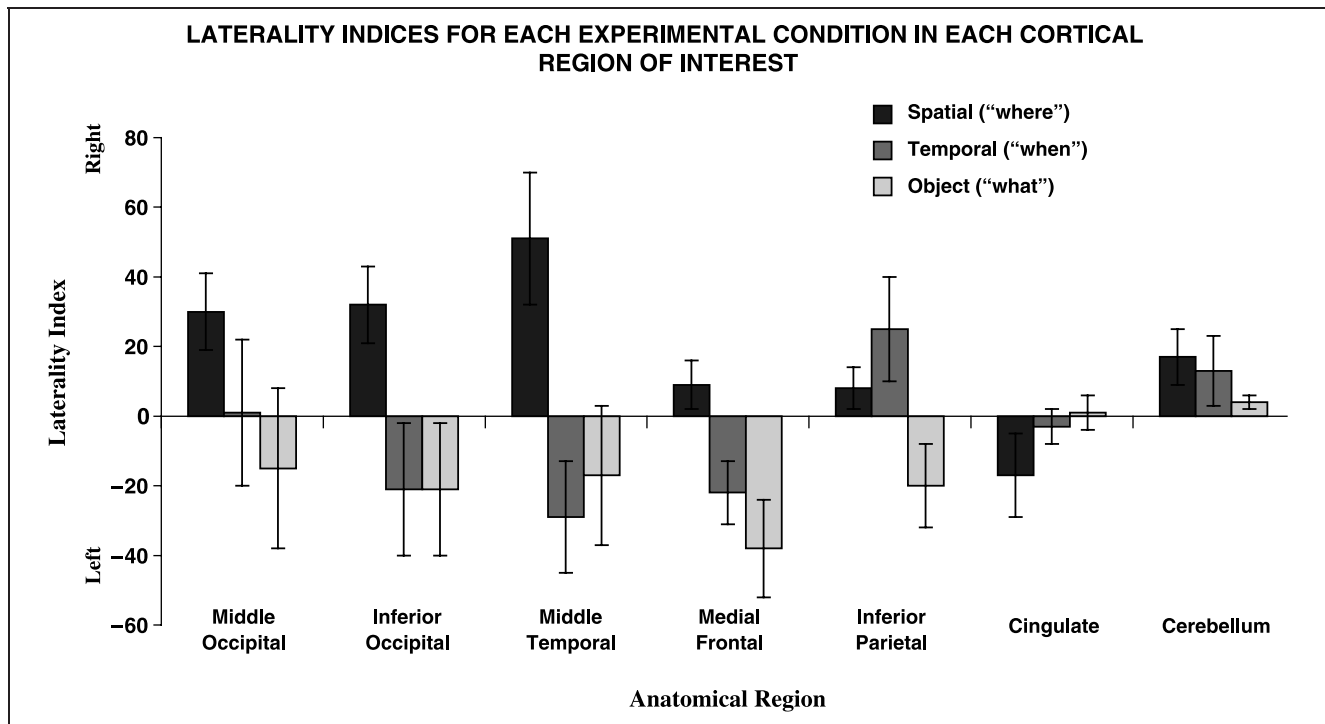


Figure 2. This figure shows the laterality index (*y*-axis) for each of the three conditions (“where,” “when,” and “what”) for each of the seven cortical regions (*x*-axis) consistently activated by all subjects. Bars represent the mean (\pm SEM) laterality indices for each condition. A positive laterality index represents right-hemispheric activity, whereas a negative laterality index represents left-hemispheric activity, based on the formula: $(\text{Right hemisphere volume} - \text{Left hemisphere volume}) / (\text{Right hemisphere volume} + \text{Left hemisphere volume}) \times 100$. ANOVA across “where,” “when,” and “what” conditions for each area: middle occipital, $p = .045$; inferior occipital, $p = .008$; middle temporal, $p = .001$; medial frontal, $p = .001$, indicating laterality differences across the three conditions. There were no significant differences found for the inferior parietal, cingulate gyrus, and cerebellum.

in response times is not a function of accuracy ($r = .007$, $b = 3.4$, $p = .71$). Thus, there is no evidence to support differences between conditions based on performance measures.

To rule out that threshold effects could account for these laterality observations, the volumes of activity were calculated over a range of statistical criteria for all subjects. Figure 3 shows the average laterality quotient as a function of threshold levels. Note that irrespective of the absolute value of the index, the average “where” condition is shifted to the right of the corresponding “when” and “what” conditions, and the laterality effect is demonstrated over a wide range of conventional levels of statistical stringency.

Activity Clusters in the Medial Frontal Gyrus

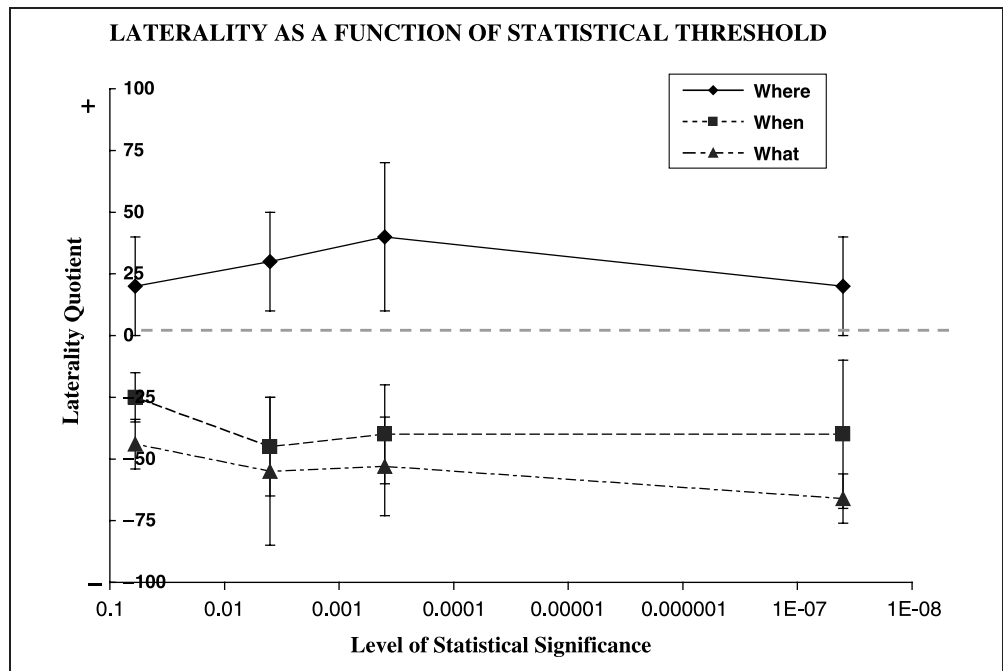
The activity patterns are shown for each subject (Figure 4, yellow) relative to the hemisphere bisection line indicated by the vertical white line. Center-of-mass locations (mm from the bisection line, *x* dimension) are shown for each subject and experimental condition (right columns). Note that these measurements are made on the actual acquisition grid (T2* images) with an in-plane spatial resolution of 1.5×1.5 mm, and therefore do not include errors associated with registra-

tion processes. The right hemisphere (R) was assigned positive values, and the left hemisphere (L) negative values. Average distances across all subjects are shown in the schematic at the bottom. The average coordinates are: $x = +4.8 \pm 1.5$ mm, $y = +10.5 \pm 3.5$ mm, $z = +50$ mm (“where”); $x = -3 \pm 1.5$ mm, $y = +11 \pm 3.5$ mm, $z = +50$ mm (“when”); $x = -5 \pm 0.8$ mm, $y = +11.3 \pm 3.1$ mm, $z = +50$ mm (“what”). The “where” and “when” conditions were significantly spatially separated in the *x* dimension ($p = .02$), and the “where” and “what” conditions were also significantly separated ($p = .0001$). These measured distances are illustrated on the Human Brain Atlas (Talairach & Tournoux, 1988). Because this analysis measures horizontal in-plane distances, rather than in flat space, it therefore discounts tissue that folds out of the plane in the hemispheric fissure, hence the effects reported here are likely to be underestimated.

Signal Amplitudes within the Medial Frontal Region

Signal amplitudes provide an alternative response measure by examining voxel by voxel variations in the signal changes during the task epochs relative to rest epochs. Figure 5 illustrates the average signal intensity change

Figure 3. This figure presents the relationship between statistical thresholds (x -axis) and average laterality indices (y -axis), for all 10 subjects where + = right-hemispheric activity and - = left-hemispheric activity. The x -axis represents the log of the statistical threshold. The figure demonstrates that as statistical cutoffs are changed, the main lateralization effect is retained: in each case, the “where” condition is shifted to the right (i.e., has a higher laterality index) of the “when” and “what” conditions. The error bars represent the standard error of the mean (SE).



from baseline to activation epochs across all voxels in the 10×10 voxel grid for each subject (see Methods). Each bar represents the average of 2000 signals ($100 \text{ voxels} \times 2 \text{ test-baseline/activity comparisons}$ per condition for each of 10 subjects). The “where” condition shows the highest signal change in the right hemisphere ($t = 3.2, p = .0009$), whereas both the “when” ($t = 6.3, p = 4.3E-8$) and the “what” ($t = 1.9, p = .03$) conditions show the highest signal change in the left hemisphere.

Multiple Output Responses (Executed and Imagined)

To rule out the possibility that the centroid shifts observed in this study were an effect of the specific motor response used (in this case, a finger thumb tap where left and right hands were alternated throughout), all experimental conditions were repeated using a non-motor (imagined tap) response (Figure 1). The subject was instructed to employ an “internal” cognitive response. Figure 6A shows the laterality index for each experimental condition and output response. Because the 10 subjects who participated in these tasks were different from the 10 subjects in the previous experiments, the executed motor task (left) was replicated to confirm previous findings and to enable within-subject comparisons. Note the right hemisphere laterality index (LI) for “where” conditions. For the executed task, activity elicited by the “where” decision was biased toward the right hemisphere (LI = $+10 \pm 6$), whereas activity elicited by the “when” (LI: -22 ± 6) and “what” (LI: -44 ± 13) tasks were significantly

biased toward the left hemisphere. Laterality indices for the imagined tasks were consistent with tasks in which the tapping was physically executed: Activity elicited by the “where” decision was biased toward the right hemisphere (LI = $+11 \pm 6$), whereas activity elicited by the “when” (LI: -53 ± 21) and “what” (LI: -22 ± 7) tasks were significantly biased toward the left hemisphere.

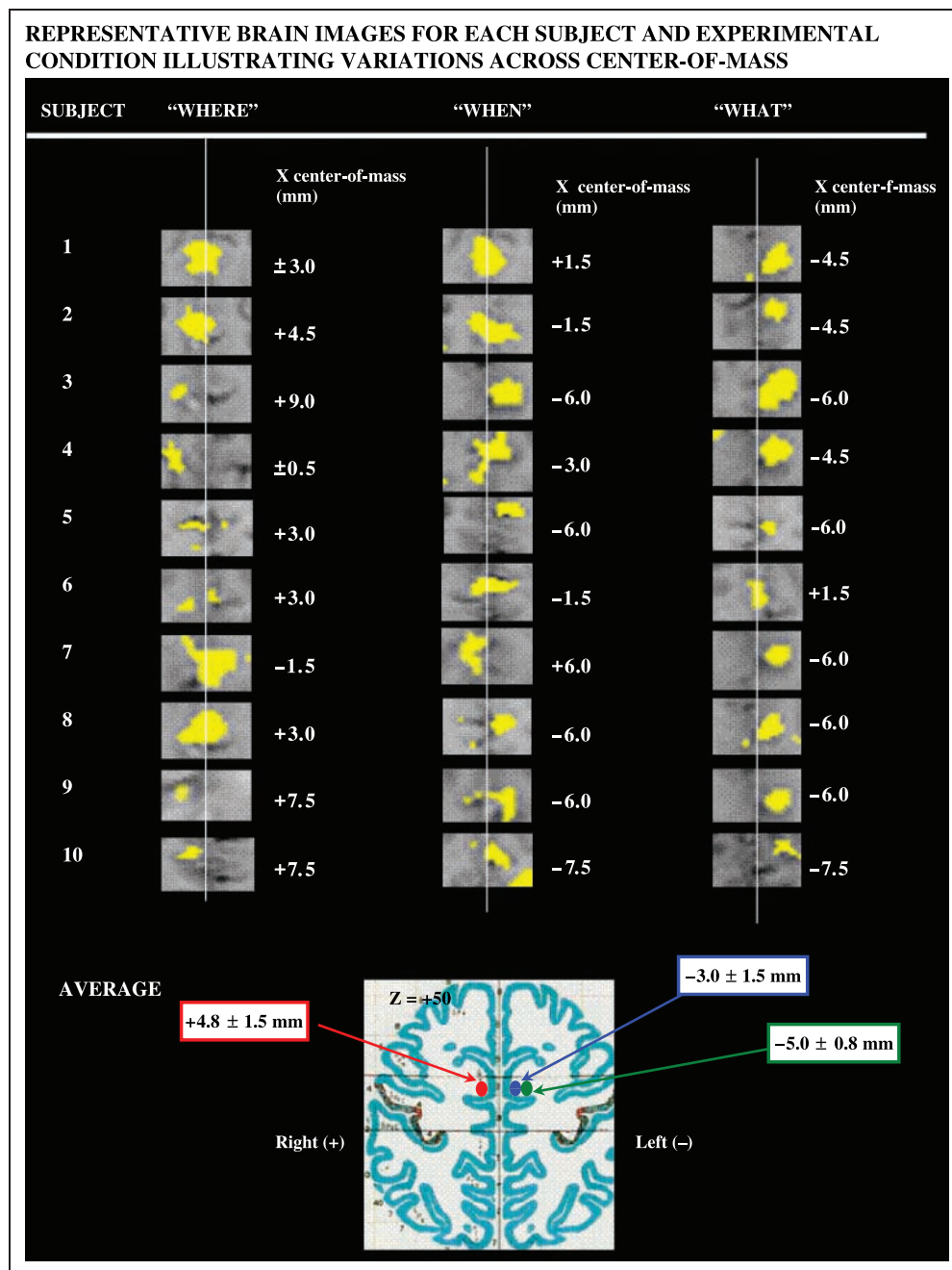
Multiple Sensory Modalities (Visual, Auditory, Tactile)

To test whether our findings within the medial frontal gyrus were invariant across multiple sensory modalities, “where” and “when” conditions were repeated using analogous auditory (tone) and tactile (touch on foot) cues (Figure 1). Motor responses were employed for these experiments. Figure 6B shows the laterality indices for each sensory modality and each experimental condition. Note that the spatial (“where”) condition was biased toward the right hemisphere irrespective of the sensory modality (visual LI: $+10 \pm 8$, tactile LI: $+10 \pm 8$), whereas the “when” condition was biased toward the left hemisphere (visual LI: -29 ± 9 , tactile LI: -26 ± 8 ; auditory LI: -37 ± 11), suggesting that the lateralization previously documented is not specific to the sensory system.

Medial Frontal Versus Cingulate Activity

Another frontal structure, the cingulate gyrus, was also active during the go/no-go tasks in all conditions (Table 1). However, comparison of the medial frontal

Figure 4. Activity observed within the targeted grid of the medial frontal gyrus is shown (yellow) for each experimental condition (columns) and each subject (rows). Images shown correspond approximately to sectors $\pm a, E, +50$ of the Talairach and Tournoux atlas (1988). The hemispheric midline was determined from the entire anatomical slice prior to the acquisition of functional data, and is indicated by the white line in each column. All data are illustrated on the original T2*-weighted axial images on which they were acquired with a resolution of 1.5×1.5 mm. Following radiological convention, brain right is image left. Note that activity for the “where” condition tends to be shifted to the right of activity for corresponding “when” and “what” conditions. This is confirmed by the center-of-mass locations indicated to the right of the images and by the average distance from the midline (bottom row). The schematic at the bottom shows average centroid locations across all subjects for the “where,” “when,” and “what” condition, on atlas plate $z = +50$ (Talairach & Tournoux, 1988). Note that “where” centroid is located within the right hemisphere and the “when” ($p = .003$) and the “what” ($p = .0001$) conditions centroids are located within the left hemisphere.



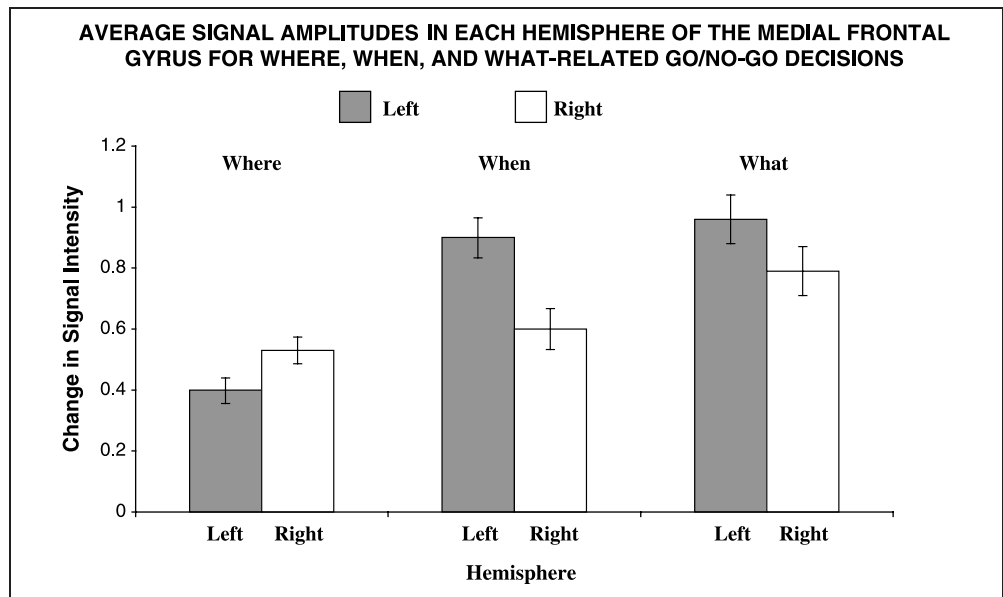
gyrus (BA 6) and the anterior cingulate gyrus (BA 24) revealed different patterns of activity. Whereas the medial frontal region demonstrated hemispheric lateralization with respect to the “where,” “when,” and “what” tasks (ANOVA; $p = .0001$), the cingulate gyrus did not (ANOVA; $p = .67$). This finding was also replicated with signal amplitudes and center-of-mass comparisons. However, although the lateralization effect was not observed in the cingulate gyrus, the overall volumes of activity covaried between the medial frontal and cingulate gyri for the go/no-go and control tasks. Specifically, the volume of activity within both regions was significantly decreased when the go/no-go compo-

nent was removed (control task) (medial frontal gyrus: $p = .009$; cingulate gyrus: $p = .0001$). Thus, overall the two regions appeared to covary, but showed separate internal organizations.

DISCUSSION

Functional specializations based on “what” and “where” distinctions have been previously associated with ventral and dorsal processing “streams,” respectively (Haxby et al., 1991; Mishkin & Ungerleider, 1982). These prior studies were instrumental in the rationale for the studies reported here. Although some dorsal

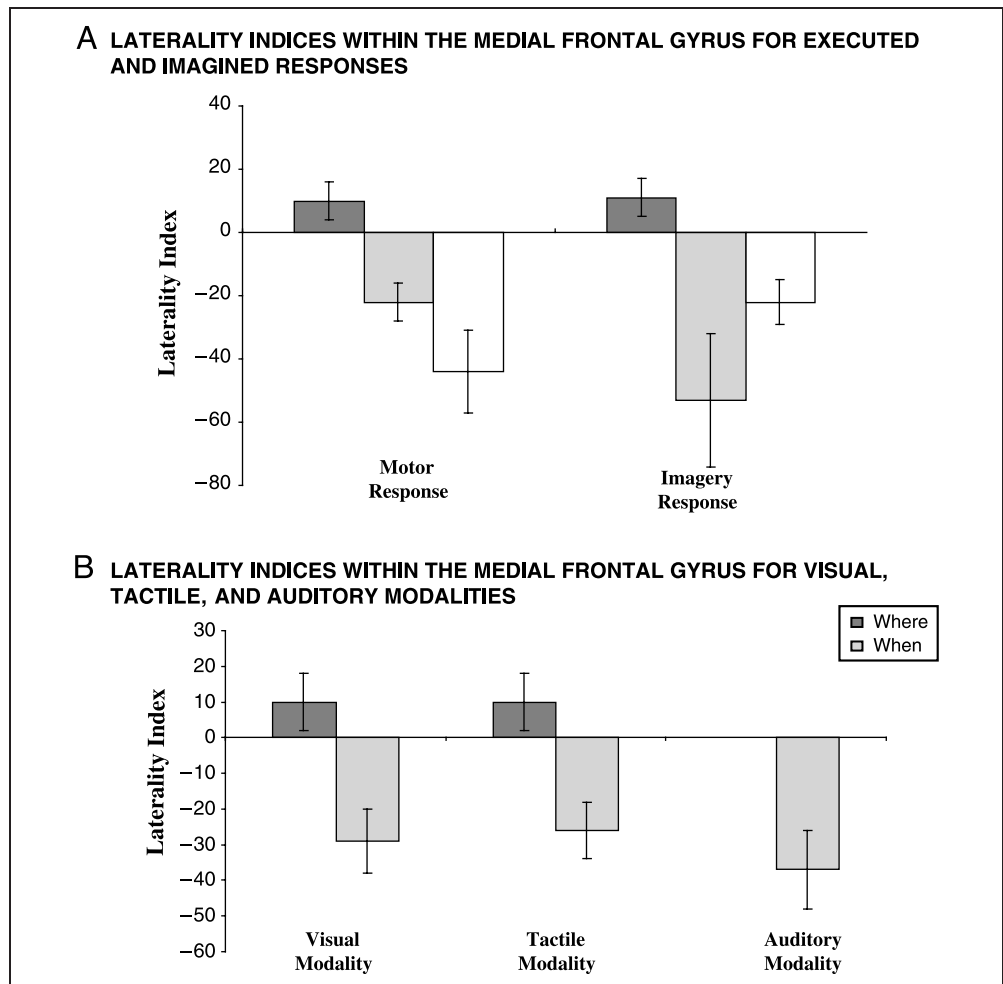
Figure 5. Signal intensity (mean \pm SEM) (*y*-axis) within the medial frontal gyrus for the “where,” “when,” and “what” tasks is shown for 10 subjects ($n = 200$ per subject). Changes in signal intensity are the difference between the average intensity during the stimulation epoch and the average intensity during the baseline epoch. The change in signal intensity during the “where” condition was greater in the right hemisphere than in the left ($t = 3.2, p = .0009$). Conversely, the change in signal intensity during the “when” ($t = 5.2, p = 5E-7$) and “what” conditions ($t = 1.8, p = .03$) was greater in the left hemisphere than in the right.



stream (parietal cortex, area 40) and ventral stream (temporal cortex, areas 21 and 39) areas were active in all conditions (“where,” “when,” and “what”), our

experimental approach did not isolate dorsal and ventral pathways with respect to these features. However, the left and right hemisphere distinctions found in this study

Figure 6. (A) The laterality indices (*y*-axis) for each experimental condition (“where,” “when,” and “what”) and each response (executed motor, imagined motor) (*x*-axis). Note that for both responses, the “where” condition is significantly different from the “when” and the “what” conditions (Motor: $p = .001$; Imagery: $p = .0008$). (B) The laterality indices (*y*-axis) for the “where” and “when” experimental conditions, and the visual, tactile, auditory sensory modalities (*x*-axis). Note that for each sensory modality, the “where” condition is biased toward the right hemisphere, whereas the “when” condition is biased toward the left hemisphere. (Note that the auditory modality was tested using the “when” condition only.) The error bars represent the standard error of the mean (SE).



are consistent with an extension of these pathways within the frontal lobe.

Our findings demonstrate that the cortical processing of perceptual (go/no-go) decisions based on “when” and “what” information predominantly engage the left hemisphere of the medial frontal gyrus, whereas analogous decisions based on “where” information predominantly engage right hemispheric regions of the same structure, reflecting lower-level processing biases. This lateralization effect was observed whether the unit of measure was the volume of activity (Figure 2), center-of-mass (Figure 4), or signal amplitudes (Figure 5). The lateralization was observed regardless of the nature of the response (motor or imagery, Figure 6A), and was preserved when visual cues were replaced by tactile or auditory ones. However, because not all experimental conditions were tested in all sensory modalities, these findings cannot be generalized across all sensory systems (Figure 6B). Finally, this lateralization was robust over a wide range of levels of statistical stringency (Figure 3), confirming that effects are not due to thresholding. Our findings are the first to observe such a functional lateralization within a frontal lobe structure, and suggest that input from some sensory regions is communicated ipsilaterally to frontal regions of the medial wall where some aspects of the basic organizational pattern observed at lower levels of processing are preserved within this executive processing stage.

Medial Frontal Gyrus, BA 6

The active region of the medial frontal gyrus in this study includes the supplementary motor area (SMA) proper (caudal to the vertical plane intersecting the anterior commissure; Picard & Strick, 1996), but not the pre-SMA (rostral to the plane), based on the Talairach and Tournoux's (1988) atlas anatomy (estimated average coordinates: $x = -4.8 \pm 1.5$ mm, $y = +10.5 \pm 3.5$ mm, $z = +50$ mm [“where”]; $x = +3 \pm 1.5$ mm, $y = +11 \pm 3.5$ mm, $z = +50$ [“when”]; $x = +5 \pm 0.8$ mm, $y = +11.3 \pm 3.1$ mm, $z = +50$ mm). This general region has been studied in earlier electrophysiological, lesion, and imaging investigations that have implicated a function in motor planning and imagery, as well as complex nonmotor tasks such as decision making, discrimination, computation, and reasoning (Rodriguez-Moreno, et al., 2001; Erdler et al., 2000; Hirsch, Wildgruber, Erb, Klose, & Grodd, 1997; Tanji, & Mushiake, 1996; Roland, Larsen, Lassen, & Skinhoj, 1980). Our data are also consistent with previous studies that have reported a convergence of sensory information within the frontal lobe for high-level processes related to motor coordination (Eimer & Driver, 2001). Within the medial frontal region, the left hemisphere demonstrated the most robust activity for responses based on object shape/color (“what”) and temporal interval information (“when”), whereas the right hemi-

sphere was comparatively more active when input was based on spatial location (“where”). Although the lateralization was not absolute, the shifts were significant when measured by volume (Figure 2), location (Figure 4), and amplitude (Figure 5).

These observations are consistent with previous studies suggesting that neuronal activity involved with spatial information is partitioned from that involved with object identification (Rao et al., 1995). For example, our findings are consistent with a recent study by Schumacher et al. (2003) who showed using fMRI that spatial response selection involves the right prefrontal cortex, whereas nonspatial response selection involves the left prefrontal cortex and the more ventral posterior cortical regions (left middle temporal gyrus, left inferior parietal lobule, and right extrastriate cortex). Previous studies have also reported lateralization and specialization for spatial and nonspatial processes within the prefrontal cortex (Postle & D'Esposito, 1999; Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; Baker, Frith, Frackowiak, & Dolan, 1996; McCarthy et al., 1996), providing additional evidence for functional organization in the frontal lobe based on hemispheric specialization in systems related to decision making and memory.

Cingulate Gyrus

Although the anterior cingulate gyrus (BA 24), was active during the go/no-go tasks (Table 1, Figure 2), this region did not demonstrate a similar lateralization effect to the medial frontal gyrus, consistent with the notion that these two regions contribute differently to the task. The anterior cingulate cortex (ACC, BA 24) has been previously identified as a component of parallel-distributed attention (Colby, 1991; Mesulam, 1990) and emotional (Devinsky, Morrell, & Vogt, 1995; Vogt, Finch, & Olson, 1992) networks. Animal studies (Rushworth, Hadland, Gaffan, & Passingham, 2003), rapid transcranial magnetic stimulation (rTMS) (Rollnik et al., 2004), and fMRI (Ullsperger & von Cramon, 2003; Garavan, Ross, Murphy, Roche, & Stein, 2002; Casey et al., 1997) have shown that the ACC is involved in error detection and correction, rather than response selection (Swick & Turken, 2002). This is consistent with previous observations that the cingulate gyrus is equally active during “go” and “no-go” trials, whereas the supplementary motor regions are preferentially activated by the “go” decisions (Liddle, Kiehl, & Smith, 2001). Similarly, the anterior cingulate is engaged during attention, particularly when complex control is required; indeed, individuals with attention deficit disorder demonstrate anterior insular activation, presumably compensating for weak cingulo-frontal circuitry (Bush et al., 1999).

Other brain regions commonly reported in association with cognitive control and response inhibition include

the orbito-frontal cortex. However, in this study, image quality in the ventral regions of the brain including the orbito-frontal cortex was variable across subjects (verified on the base T2* scans). Thus, failure to observe consistent cortical responses in that area may have been due to imaging rather than experimental factors. Nonetheless, these observations suggest that the medial frontal region plays a significant role in the convergence of information required for the go/no-go task, and this function is differentiated from that of the cingulate gyrus in these tasks.

Medial Wall and Response Selective Functions

Medial wall structures are activated during tasks that require response selection. For example, Grafton et al. (1992) used positron emission tomography (PET) to demonstrate that incorporating a “no-go” contingency into a movement response resulted in a significant increase of cerebral blood flow to the SMA. Humberstone et al. (1997), using fMRI, confirmed an increase in SMA activity during go/no-go tasks. However, in that fMRI study, the anterior portion (pre-supplementary) was more active during the decision component. More recent paradigms have differentiated the “go” components from the “no-go” components of response selection tasks. Liddle et al. (2001) showed that the ACC was active during both “go” and “no-go” trials, whereas the dorsolateral prefrontal cortex was more active during the “no-go” trial, and motor structures (primary motor cortex, supplementary motor area, premotor cortex, and cerebellum) were more active during the “go” trials. These authors concluded that medial wall regions were primarily engaged in monitoring and attending to decisions, whereas the dorsolateral prefrontal sites played a role in response inhibition during the “no-go” component. Similar differentiations have also been reported by Durston et al., (2002), Watanabe et al. (2002), and Konishi et al. (1999). These studies, however, examined motor responses, thereby engaging activity in primary motor structures during the “go” component. In the present study, we employed two different types of output (executed motor and imagined motor) to confirm that the neural correlate was specific to the go/no-go decision processes, rather than the motor response.

Sensory information from visual and temporal cortices is transmitted ipsilaterally to the frontal cortex through a variety of parietal sites (Cipolloni & Pandya, 1999; Goldman-Rakic, 1987), where a dense network of colossal and associational fibers connects homotopic areas (Matsuzaka, Aizawa, & Tanji, 1992). Anterograde tracing has demonstrated that these pathways are predominantly ipsilateral, although interhemispheric connections may be present (McGuire, Bates, & Goldman-Rakic, 1991). These input pathways suggest

a functional organization of decision-making processes observed in this study where the medial frontal gyrus is involved in the gathering of facts for the decision aspects of go/no-go tasks, and the cingulate gyrus is involved in some aspect of cognitive control that does not require compartmentalized input features. Such a functional separation is consistent with both the previously known roles of each region as well as the known connectivity.

METHODS

Imaging

A 1.5-Tesla Magnetic Resonance Scanner with a standard head coil (General Electric, Waukesha, WI) was employed to obtain T2*-weighted images with a gradient-echo pulse sequence (echo time 60 msec, repetition time 4000 msec, flip angle 60°). This sequence is known to be sensitive to variations in magnetic resonance susceptibility due to alteration in the proportion of deoxyhemoglobin in the local vasculature accompanying neuronal activation (Ogawa, Menon, et al., 1993; Ogawa, Tank, et al., 1992). The cubic size of each volume element (voxel) was 10 mm³, where the in-plane resolution was 1.5 × 1.5 mm, and slice thickness was 4.5 mm. This high-resolution acquisition grid enabled similarly precise observations of activity centroids. Twenty-one contiguous slices were acquired parallel to the “AC/PC line,” a standard reference line that intersects the superior edge of the anterior commissure (AC) and the inferior edge of the posterior commissure (PC). This orientation allowed direct comparison of acquired images with the Human Brain Atlas (Talairach & Tournoux, 1988). In each subject, the 21 slices covered the entire cortex. Conventional high-resolution (T1-weighted) images were also acquired along the same plane locations as the T2*-weighted images for anatomical reference. A conventional block design was employed, in which 72 images were acquired during each run which lasted 4 min 48 sec. Ten images were acquired during each of two performance epochs (40 sec), and 10 images were acquired during each baseline epoch (40 sec). The two performance epochs occurred between different baseline epochs.

Analysis

Prior to statistical analysis, all images were reconstructed, aligned, and corrected (in the *x* and *y* dimension) for movement artifacts (Woods, Mazziotta, & Cherry, 1993). A two-dimensional Gaussian filter (approximately 3 mm at half-height) was applied to enhance signal-to-noise characteristics for each voxel. Signal changes during brain activity were identified using a “block design” that compared average signal amplitude acquired during the activity epochs with

average signals acquired during baseline epochs according to a general linear model. An “active” voxel was defined as one in which the average magnetic resonance signal acquired during the stimulation periods was significantly different from the average baseline levels, $p \leq .0005$, corrected for multiple comparisons based on empirically validated false-positive rates obtained using both resting brain and copper sulfate phantoms (Hirsch, Ruge, et al., 2000). This particular analysis procedure was developed to map sensory/motor, language, and visual-sensitive areas for neurosurgical planning using fMRI, and has been validated by conventional mapping techniques such as direct cortical stimulation, somatosensory evoked potentials, and surgical outcome studies (Hirsch, Ruge, et al., 2000; Ruge et al., 1999). An active area was defined for each subject as a cluster of at least 5 contiguous voxels each with a false-positive rate, $p \leq .0005$.

To preserve the highest spatial resolution for each subject, an idiopathic strategy was applied for the first stage of data analysis where each subject was processed separately. A modified “forward transform” method was employed to assign labels to the active individual brain areas for each subject where the brain topology was employed as an index to labels of the Human Brain Atlas (Lancaster et al., 2000). Accordingly, the stages of assignment included identification of the brain slice passing through the AC/PC line and location of respective commissures of the axial view; assignment of an atlas plate to each brain slice; location of the vertical AC/PC plane on all T2*-weighted images of brain slices; location of the central sulcus and confirmation of those landmarks on all T1-weighted images of brain slices; assignment of the anatomical labels, Brodmann’s areas, and atlas sectors for each active cluster; and determination of each active cluster volume on the basis of voxel count.

Laterality Indices

Each individual brain was computationally divided into two hemispheres based on the anatomy as represented by T1 images prior to the acquisition of functional data. The number of active voxels was taken as an estimate of active brain volumes and a laterality index (LI) was based on the comparison of the number of active voxels observed within the two hemispheres (Devlin et al., 2003):

Laterality Index

$$= \frac{(\text{Right Hemisphere Volume} - \text{Left Hemisphere Volume})}{(\text{Right Hemisphere Volume} + \text{Left Hemisphere Volume})} \times 100$$

An index of +100 indicates an absolute right-hemispheric specialization, whereas an index of -100 indi-

cates an absolute left-hemispheric specialization, and an index of 0 indicates equal distributions of activity.

Signal Amplitudes

In the case of the medial frontal gyrus, a fixed grid (10 × 10 voxels; 15 × 15 mm) was located symmetrically around the hemispheric midline, posterior to the perpendicular plane bisecting the anterior commissure, and 50 mm above the AC/PC line for each subject. Average amplitudes for each voxel within the specified grid were determined during all baseline and activation epochs, and the difference between the average signal intensity during the stimulation epoch and the average signal intensity during the initial baseline epoch was calculated for each voxel within that defined grid.

Center of Mass

Centers of mass for activity during each of the three experimental conditions (“what,” “when,” and “where”) were calculated within the grid based on the distance from the hemispheric midline to each voxel. All distances were averaged to determine the center of mass with respect to the lateral dimension.

Subjects

Thirty healthy volunteers participated in this study: 10 subjects performed the primary study using visual cues and motor responses, 10 subjects performed the study testing alternate response modalities (motor vs. imagined response), 10 subjects performed the study testing alternate sensory modalities (visual, auditory, tactile). All basic findings of the primary data (go/no-go motor response using visual cues) were replicated in all studies. All subjects were right handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), and were recruited according to institutional guidelines for informed consent. Mean age was 27.5 years; mean Edinburgh Handedness Quotient was +91. All experimental conditions were randomized both between and within subjects. Response performances were monitored throughout the experimental sessions. For the executed motor response, tapping was monitored visually by the investigator. For the mental imagery response, subjects were questioned after each test run. Trials that were not correctly completed were repeated.

Stimuli and Instructions

The number of stimuli requiring a “go” response always equaled that the number requiring a “no-go” response; each test-run epoch therefore involved a total of 10 “go” responses, and 10 “no-go” responses. The experimental conditions were presented in separate test epochs, so when performing the motor response sub-

jects used their left hand for one epoch, and their right hand for the other. The order for the use of each hand was randomized across tasks and subjects. Activity present across the use of both hands was included in the analysis, and thus, hand-specific effects are assumed not represented in the data.

Visual Stimuli

All three tasks (“what,” “when,” and “where”) were performed with visual stimuli (Figure 1) which were back-projected onto a gray screen located at the foot of the scanner platform. Subjects viewed the screen through a slanted mirror incorporated into the head coil. Viewing distance (eye to center of screen) was 205 cm. Each stimulus subtended 0.5° of visual angle, and the stimulus field subtended approximately $14^\circ \times 9^\circ$ of visual angle. For the “when” and “what” tasks, all stimuli appeared in the center of the screen; in the case of the “where” task, all quadrants had similar viewing angles, and the four-quadrant area subtended $12^\circ \times 6^\circ$ of visual angle. A fixed crosshair was present during baseline and recovery periods.

Tactile Stimuli

Two tasks (“where” and “when”) were performed with tactile stimulation (Figure 1). Subjects were tapped by the investigator on the center of the undersurface of their foot (right foot for one run, left foot for the other), and were instructed to tap respond using the contralateral hand. “Where”: Subjects were tapped in one of four quadrants (previously demarcated by tactile sensation) on the undersurface of their foot. Subjects were instructed to respond only if they felt a tap on their first (toe) or fourth (heel) quadrants but not the middle two. “When”: Subjects were tapped on the center of the undersurface of their foot, and were instructed to respond if the stimulus preceded the previous stimulus by a short (1 sec) ISI but not a long (3 sec) one. To ensure consistency, a single experimenter performed all tactile stimulations, which were practiced prior to the experiment. All responses were externally verified.

Auditory Stimuli

Auditory stimuli were employed for the “when” (temporal interval discrimination) task only (Figure 1). A tone of fixed frequency (approximately 440 Hz) was presented for 500 msec. Subjects were instructed to tap if the tone preceded the previous tone by a short (1 sec) ISI but not a long (3 sec) one.

Control Conditions

Stimuli were identical to previous conditions. Instead of responding to selected stimuli (go/no-go), subjects re-

sponded to all stimuli with a single “go” response. Thereby both the stimuli and responses were similar to the initial test conditions, with presumably only the decision phase eliminated. For the “where/spatial” condition, subjects were instructed to perform a “go” response irrespective of which quadrant the dot appeared in, whereas in previous experiments they had been instructed to respond if a dot appeared in the top left or bottom right quadrants, but do nothing (“no-go”) if the dot appeared in the top right or bottom left quadrants. For the “when” condition, subjects were instructed to tap irrespective of the temporal interval, and for the “what” condition, subjects were instructed to tap irrespective of the shape or color of the stimulus. All responses were recorded and confirmed that arousal levels were maintained across all conditions. For the “imagined” conditions (Figure 6), subjects were instructed to internally imagine tapping their thumb with their index finger each time a “go” stimulus (as above) appeared, but not when a “no-go” stimulus appeared.

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The data reported in this experiment have been deposited with the fMRI Data Center archive (www.fmridc.org). The accession number is 2-2005-118QT.

REFERENCES

- Alcock, K. J., Wade, D., Anslow, P., & Passingham, R. E. (2000). Pitch and timing abilities in adult left-hemisphere-dysphasic and right-hemisphere-damaged subjects. *Brain and Language*, *75*, 47–65.
- Aminoff, M. J., & Goodin, D. S. (1997). The decision to make a movement: Neurophysiological insights [Review]. *Canadian Journal of Neurological Sciences*, *24*, 181–190.
- Arrigoni, G., & De Renzi, E. (1964). Constructional apraxia and hemispheric locus of lesion. *Cortex*, *1*, 170–197.
- Atchley, R. A., & Atchley, P. (1998). Hemispheric specialization in the detection of subjective objects. *Neuropsychologia*, *36*, 1373–1386.
- Baker, S. C., Frith, C. D., Frackowiak, R. S., & Dolan, R. J. (1996, July–August). Active representation of shape and spatial location in man. *Cerebral Cortex*, *6*, 612–619.
- Bush, G., Frazier, J. A., Rauch, S. L., Seidman, L. J., Whalen, P. J., Jenike, M. A., Rosen, B. R., & Biederman, J. (1999). Anterior cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the Counting Stroop. *Biological Psychiatry*, *5*, 1542–1552.

- Casey, B. J., Trainor, R., Giedd, J., Vauss, Y., Vaituzis, C. K., Hamburger, S., Kozuch, P., & Rapoport, J. L. (1997). The role of the anterior cingulate in automatic and controlled processes: A developmental neuroanatomical study. *Developmental Psychobiology*, *30*, 61–69.
- Cipolloni, P. B., & Pandya, D. N. (1999). Cortical connections of the frontoparietal opercular areas in the rhesus monkey. *Journal of Comparative Neurology*, *403*, 431–458.
- Coghill, R. C., Gilron, I., & Iadarola, M. J. (2001). Hemispheric lateralization of somatosensory processing. *Journal of Neurophysiology*, *85*, 2602–2612.
- Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science*, *279*, 1347–1351.
- Davidson, R. J., & Hugdahl, K. (1995). *Hemispheric asymmetry*. Cambridge: MIT Press.
- De Renzi, E., Faglioni, P., & Previdi, P. (1977). Spatial memory and hemispheric locus of lesion. *Cortex*, *13*, 424–433.
- Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour [Review]. *Brain*, *118*, 279–306.
- Devlin, J. T., Raley, J., Tunbridge, E., Lanary, K., Floyer-Lea, A., Narain, C., Cohen, I., Behrens, T., Jezzard, P., Matthews, P. M., & Moore, D. R. (2003). Functional asymmetry for auditory processing in human primary auditory cortex. *Journal of Neuroscience*, *23*, 11516–11522.
- Durston, S., Thomas, K. M., Worden, M. S., Yang, Y., & Casey, B. J. (2002). The effect of preceding context on inhibition: An event-related fMRI study. *Neuroimage*, *16*, 449–453.
- Eimer, M., & Driver, J. (2001). Cross-modal links in endogenous and exogenous spatial attention: Evidence from event-related brain potential studies. *Neuroscience and Biobehavioral Reviews*, *25*, 497–511.
- Erdler, M., Beisteiner, R., Mayer, D., Kaindl, T., Edward, V., Windischberger, C., Lindinger, G., & Deecke, L. (2000). Supplementary motor area activation preceding voluntary movement is detectable with a whole-scalp magnetoencephalography system. *Neuroimage*, *11*, 697–707.
- 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*, *7*, 1820–1829.
- Georgopoulos, A. P. (2000). Neural aspects of cognitive motor control. *Current Opinion in Neurobiology*, *10*, 238–241.
- Goldman-Rakic, P. S. (1987). Circuitry of the frontal association cortex and its relevance to dementia [Review]. *Archives of Gerontology and Geriatrics*, *6*, 299–309.
- Grafton, S. T., Mazziotta, J. C., Woods, R. P., & Phelps, M. E. (1992). Human functional anatomy of visually guided finger movements. *Brain*, *115*, 565–587.
- Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., Herscovitch, P., Schapiro, M. B., & Rapoport, S. I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proceedings of the National Academy of Sciences, U.S.A.*, *88*, 1621–1625.
- Hirsch, J., Rodriguez-Moreno, D., & Kim, K. H. S. (2001). Interconnected large-scale systems for three fundamental cognitive tasks revealed by functional MRI. *Journal of Cognitive Neuroscience*, *13*, 1–16.
- Hirsch, J., Ruge, M. I., Kim, K. H. S., Correa, D. D., Victor, J. D., Welkin, N. R., Labar, D. R., Krol, G., Bilsky, M. G., Souweidane, M. M., DeAngelis, L. M., & Gutin, P. H. (2000). An integrated fMRI procedure for preoperative mapping of cortical areas associated with tactile, motor, language, and visual functions. *Neurosurgery*, *47*, 711–722.
- Hofman, S., Klein, C., & Arlazoroff, A. (1993). Common hemisphericity of language and music in a musician. A case report. *Journal of Communication Disorders*, *26*, 73–82.
- Humberstone, M., Sawle, G. V., Clare, S., Hykin, J., Coxon, R., Bowtell, R., Macdonald, I. A., & Morris, P. G. (1997). Functional magnetic resonance imaging of single motor events reveals human presupplementary motor area. *Annual Neurology*, *42*, 632–637.
- Irving-Bell, L., Small, M., & Cowey, A. (1999). A distortion of perceived space in patients with right-hemisphere lesions and visual hemineglect. *Neuropsychologia*, *37*, 919–925.
- Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain*, *122*, 981–991.
- Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nickerson, D., Mikiten, S. A., & Fox, P. T. (2000). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping*, *10*, 120–131.
- Liddle, P. F., Kiehl, K. A., & Smith, A. M. (2001). Event-related fMRI study of response inhibition. *Human Brain Mapping*, *12*, 100–109.
- Losier, B. J., & Klein, R. M. (2001). A review of the evidence for a disengage deficit following parietal lobe damage. *Neuroscience and Biobehavioral Reviews*, *25*, 1–13.
- Matsuzaka, Y., Aizawa, H., & Tanji, J. (1992). A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: Neuronal activity during a learned motor task. *Journal of Neurophysiology*, *68*, 653–662.
- McCarthy, G., Puce, A., Constable, R. T., Krystal, J. H., Gore, J. C., & Goldman-Rakic, P. (1996). Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cerebral Cortex*, *6*, 600–611.
- McCarthy, R., & Warrington, E. K. (1990). The dissolution of semantics. *Nature*, *343*, 599.
- McGuire, P. K., Bates, J. B., & Goldman-Rakic, P. (1991). Interhemispheric integration: I. Symmetry and convergence of the corticocortical connections of the left principal sulcus (PS) and the left and the right supplementary motor area in the rhesus monkey. *Cerebral Cortex*, *1*, 390–407.
- Mesulam, M. M. (1990). Large-scale neurocognitive networks and distributed processing for attention, language, and memory [Review]. *Annals of Neurology*, *28*, 597–613.
- Miniussi, C., Rao, A., & Nobre, A. C. (2002). Watching where you look: Modulation of visual processing of foveal stimuli by spatial attention. *Neuropsychologia*, *40*, 2448–2460.
- Mishkin, M., & Ungerleider, L. G. (1982). Contribution of striate inputs to the visuospatial functions of parieto-preoccipital cortex in monkeys. *Behavioural Brain Research*, *6*, 57–77.
- Ogawa, S., Menon, R. S., Tank, D. W., Kim, S. G., Merkle, H., Ellermann, J. M., & Ugurbil, K. (1993). Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging. A comparison of signal characteristics with a biophysical model. *Biophysical Journal*, *64*, 803–812.
- Ogawa, S., Tank, D. W., Menon, R., Ellermann, J. M., Kim, S. G., Merkle, H., & Ugurbil, K. (1992). Intrinsic signal changes accompanying sensory stimulation: Functional brain

- mapping with magnetic resonance imaging. *Proceedings of the National Academy of Sciences, U.S.A.*, 89, 5951–5955.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9, 97–113.
- Phelps, E. A., Hyder, F., Blamire, A. M., & Shulman, R. G. (1997). fMRI of the prefrontal cortex during overt verbal fluency. *NeuroReport*, 8, 561–565.
- Picard, N., & Strick, P. L. (1996). Motor areas of the medial wall: A review of their location and functional activation. *Cerebral Cortex*, 6, 342–353.
- Rao, S. M., Binder, J. R., Hammeke, T. A., Bandettini, P. A., Bobholz, J. A., Frost, J. A., Myklebust, B. M., Jacobson, R. D., & Hyde, J. S. (1995). Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging. *Neurology*, 45, 919–924.
- Roland, P. E., Larsen, B., Lassen, N. A., & Skinhoj, E. (1980). Supplementary motor area and other cortical areas in the organization of voluntary movements in man. *Journal of Neurophysiology*, 43, 118–136.
- Ruge, M. I., Victor, J., Hosain, S., Correa, D. D., Relkin, N. R., Tabar, V., Brennan, C., Gutin, P. H., & Hirsch, J. (1999). Concordance between functional magnetic resonance imaging and intraoperative language mapping. *Stereotactic and Functional Neurosurgery*, 72, 95–102.
- Rushworth, M. F., Hadland, K. A., Gaffan, D., & Passingham, R. E. (2003). The effect of cingulate cortex lesions on task switching and working memory. *Journal of Cognitive Neuroscience*, 15, 338–353.
- Salzman, C. D., & Newsome, W. T. (1994). Neural mechanisms for forming a perceptual decision. *Science*, 264, 231–237.
- Samson, S., Ehrle, N., & Baulac, M. (2001). Cerebral substrates for musical temporal processes. *Annals of New York Academy of Sciences*, 930, 166–178.
- Sava, D., Liotti, M., & Rizzolatti, G. (1988). Right hemisphere superiority for programming oculomotion: Evidence from simple reaction time experiments. *Neuropsychologia*, 26, 201–211.
- Schumacher, E. H., Elston, P. A., & D'Esposito, M. (2003). Neural evidence for representation-specific response selection. *Journal of Cognitive Neuroscience*, 15, 1111–1121.
- Sergent, J., Ohta, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing. A positron emission tomography study. *Brain*, 115, 15–36.
- Swick, D., & Turken, A. U. (2002). Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex [Review]. *Proceedings of the National Academy of Sciences, U.S.A.*, 99, 16354–16359. Epub 2002, November 27. Acad Sci USA. 1998, February 3;95, 811–817.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme Medical.
- Tanji, J., & Mushiake, H. (1996). Comparison of neuronal activity in the supplementary motor area and primary motor cortex. *Brain Research, Cognitive Brain Research*, 3, 143–150.
- Ullsperger, M., & von Cramon, D. Y. (2003, May 15). Error monitoring using external feedback: Specific roles of the habenular complex, the reward system, and the cingulate motor area revealed by functional magnetic resonance imaging. *Journal of Neuroscience*, 23, 4308–4314.
- Umiltà, C., Bagnara, S., & Simion, F. (1978). Laterality effects for simple and complex geometrical figures, and nonsense patterns. *Neuropsychologia*, 16, 43–49.
- Vogt, B. A., Finch, D. M., & Olson, C. R. (1992). Functional heterogeneity in cingulate cortex: The anterior executive and posterior evaluative regions [Review]. *Cerebral Cortex*, 2, 435–443.
- Warrier, C. M., & Zatorre, R. J. (2004, July). Right temporal cortex is critical for utilization of melodic contextual cues in a pitch constancy task. *Brain*, 127, 1616–1625. Epub 2004 May 05.
- Warrington, E. K. (1982). Neuropsychological studies of object recognition. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, 298, 15–33.
- Watanabe, J., Sugiura, M., Sato, K., Sato, Y., Maeda, Y., Matsue, Y., Fukuda, H., & Kawashima, R. (2002). The human prefrontal and parietal association cortices are involved in NO-GO performances: An event-related fMRI study. *Neuroimage*, 17, 1207–1216.
- Wildgruber, D., Erb, M., Klose, U., & Grodd, W. (1997). Sequential activation of supplementary motor area and primary motor cortex during self-paced finger movement in human evaluated by functional MRI. *Neuroscience Letters*, 227, 161–164.
- Woods, R. P., Mazziotta, J. C., & Cherry, S. R. (1983). MRI-PET registration with automated algorithm. *Journal of Computer Assisted Tomography*, 17, 536–546.
- Zatorre, R. J. (2001). Neural specializations for tonal processing [Review]. *Annals of the New York Academy of Sciences*, 930, 193–210.