

# Neural Evidence for Representation-Specific Response Selection

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## Abstract

■ Response selection is the mental process of choosing representations for appropriate motor behaviors given particular environmental stimuli and one's current task situation and goals. Many cognitive theories of response selection postulate a unitary process. That is, one central response-selection mechanism chooses appropriate responses in most, if not all, task situations. However, neuroscience research shows that neural processing is often localized based on the type of information processed. Our current experiments investigate whether response selection is unitary or stimulus specific by manipulating response-selection difficulty in two functional magnetic resonance imaging experiments using spatial and nonspatial stimuli. The same participants were used in both experiments.

We found spatial response selection involves the right prefrontal cortex, the bilateral premotor cortex, and the dorsal parietal cortical regions (precuneus and superior parietal lobule). Nonspatial response selection, conversely, involves the left prefrontal cortex and the more ventral posterior cortical regions (left middle temporal gyrus, left inferior parietal lobule, and right extrastriate cortex). Our brain activation data suggest a cognitive model for response selection in which different brain networks mediate the choice of appropriate responses for different types of stimuli. This model is consistent with behavioral research suggesting that response-selection processing may be more flexible and adaptive than originally proposed. ■

## INTRODUCTION

Selecting appropriate responses to current environmental stimuli is a critical process carried out by all of us countless times every day. Despite its ubiquity, much is unknown about the required neural processing. Some results suggest a dorsal prefrontal–parietal network of brain regions underlying response selection, whereas others implicate the ventral prefrontal and temporal cortices.

Evidence for the fronto-parietal network comes mainly from neuroimaging studies requiring spatial processing. In one of the first neuroimaging studies investigating response selection, Deiber et al. (1991) reported activity in the superior parietal cortex related to conditional joystick movements to the frequency of a tone. Three other neuroimaging studies varied the stimulus–response (S–R) compatibility of the S–R pairs, a manipulation that has been shown to affect response selection (Kornblum, Hasbroucq, & Osman, 1990; Sternberg, 1969). In these studies, on some trials participants made a compatible button press to the location of a stimulus cue (e.g., press the left button when the cue appears on the left) and on other trials they made an incompatible button press to the stimulus cue (e.g.,

press the left button when the cue appears on the right; Schumacher & D'Esposito, 2002; Dassonville et al., 2001; Iacoboni, Woods, & Mazziotta, 1996; Deiber et al., 1991). Two of these studies reported activation related to response selection in premotor and parietal cortices (Dassonville et al., 2001; Iacoboni et al., 1996) and the other, using a more sensitive region-of-interest analysis, reported response-selection activity in these regions as well as the dorsal prefrontal cortex (Schumacher & D'Esposito, 2002).

Further evidence that the dorsal prefrontal cortex is involved in response selection comes from Rowe, Toni, Josephs, Frackowiak, and Passingham (2000). They reported brain activity in this region related to the selection of the appropriate response to spatial targets held in working memory. These neuroimaging data suggest that several regions in the prefrontal cortex (i.e., dorsal and premotor) and regions in the parietal cortex mediate the selection of responses as we carry out behaviors to achieve our goals.

Research with neuropsychological patients and non-human primates also implicates some of these brain regions in response selection. For example, patients with prefrontal and premotor lesions have difficulty choosing appropriate responses to their current situations (Decary & Richer, 1995; Fuster, 1995; Passingham, 1993). And in a clinical setting, they often forget their goals, perseverate on obsolete responses, or otherwise

fail in their decision-making processes when examined with tests such as the Wisconsin Card Sorting Task or the Tower of London (Kolb & Wishaw, 1990). Similarly, regions in the frontal and parietal cortices of nonhuman primates, especially premotor and parietal, have been implicated in the selection of responses to environmental stimuli (Wise, Boussaoud, Johnson, & Caminiti, 1997; Passingham, 1993).

Thus, current research suggests that response selection in humans involves a fronto-parietal brain network. However, most of this research involves tasks requiring spatial processing—either when representing the stimuli, the responses, or both.<sup>1</sup> For example, three of the four neuroimaging studies involved S–R compatibility, where the manipulation involves an incongruity between the spatial position of the stimulus and response. Therefore, it is possible that the response-selection process implicated by these studies is specific to spatial material.

A recent study involving spatial and nonspatial tasks adds additional support for the idea that response selection may be mediated by separate brain systems based on the type of stimulus represented (Toni, Rushworth, & Passingham, 2001). Toni et al. had participants either reach and grasp an object or perform an arbitrary hand gesture based on the shape of a visually presented stimulus. They reported more activity in dorsal brain regions for the spatial reaching task, and more activity in ventral brain regions for the visual association task. Furthermore, several studies implicate a fronto-temporal brain network for the learning of nonspatial tasks (Toni, Ramnani, Josephs, Ashburner, & Passingham, 2001; Toni, Rowe, Stephan, & Passingham, 2002; Passingham & Toni, 2001; Raichle et al., 1994). These results suggest that response selection may be representation specific, with a fronto-parietal network mediating spatial response selection, and a fronto-temporal network mediating nonspatial response selection.

The neuroscience research thus far has focused on identifying the neural substrate for response selection. Much is still unknown about the nature of the processing in these regions. From cognitive psychology, conversely, there are many theories describing the nature of response selection, although little about the brain mechanisms underlying it.

One prominent psychological theory is that response selection is a unitary central process (Pashler, 1984, 1994; Welford, 1959). Under this hypothesis, there is one response-selection process and it selects appropriate responses for a wide variety of tasks and modalities. Some evidence for this theory comes from studies of multiple-task performance using the psychological refractory period (PRP) procedure. In these studies, participants perform two tasks separated by a stimulus onset asynchrony (SOA). Mean reaction times (RTs) for the primary task are typically not affected much by

SOA, but mean RTs for the secondary task typically show a PRP effect, that is, they increase as SOA decreases (Pashler, 1994). This increase in RT has been interpreted to reflect the delay in processing of a central response-selection stage. Response-selection processing for the secondary task is suspended during response selection for the primary one. The PRP effect occurs in a wide variety of tasks including: choice reaction, memory retrieval, memory scanning, and mental rotation tasks, as well as when both tasks share perceptual and response modalities and when they do not (Meyer & Kieras, 1997; Pashler, 1990, 1994). These data suggest that response selection may indeed be a central process one not tied to particular tasks or modalities.

Recent research however, leads us to question this hypothesis. Meyer and his colleagues propose that the delay in the PRP procedure is caused to a large extent by strategies participants adopt in an attempt to adhere to experimental instructions. They showed that people have a profound ability to select responses for multiple tasks simultaneously. Participants may develop this ability with increased practice (Schumacher et al., 1999) or with training that emphasizes flexible processing for the tasks (Schumacher et al., 2001; Meyer et al., 1995). In fact, Schumacher et al. (2001) showed that dual-task interference may disappear entirely when participants perform under task instructions that encourage independent processing (Hazeltine, Teague, & Ivry, 2002).

If the delay in processing for the secondary task reflects a strategic rather than a structural mechanism, and it can be overcome entirely under certain task situations, then response selection may not be a unitary central process. Rather, distinct response-selection processing may proceed for each task, perhaps depending on the type of stimuli and responses required. If this is true, then distinct brain regions may mediate response selection for tasks involving different types of stimuli. We tested this hypothesis in two separate functional magnetic resonance imaging (fMRI) experiments.

Rather than testing this hypothesis in a dual-task situation, where additional central control processes may obscure response selection, our current experiments address this issue by manipulating response-selection difficulty with different experimental factors and different types of visual stimuli (i.e., spatial and nonspatial).

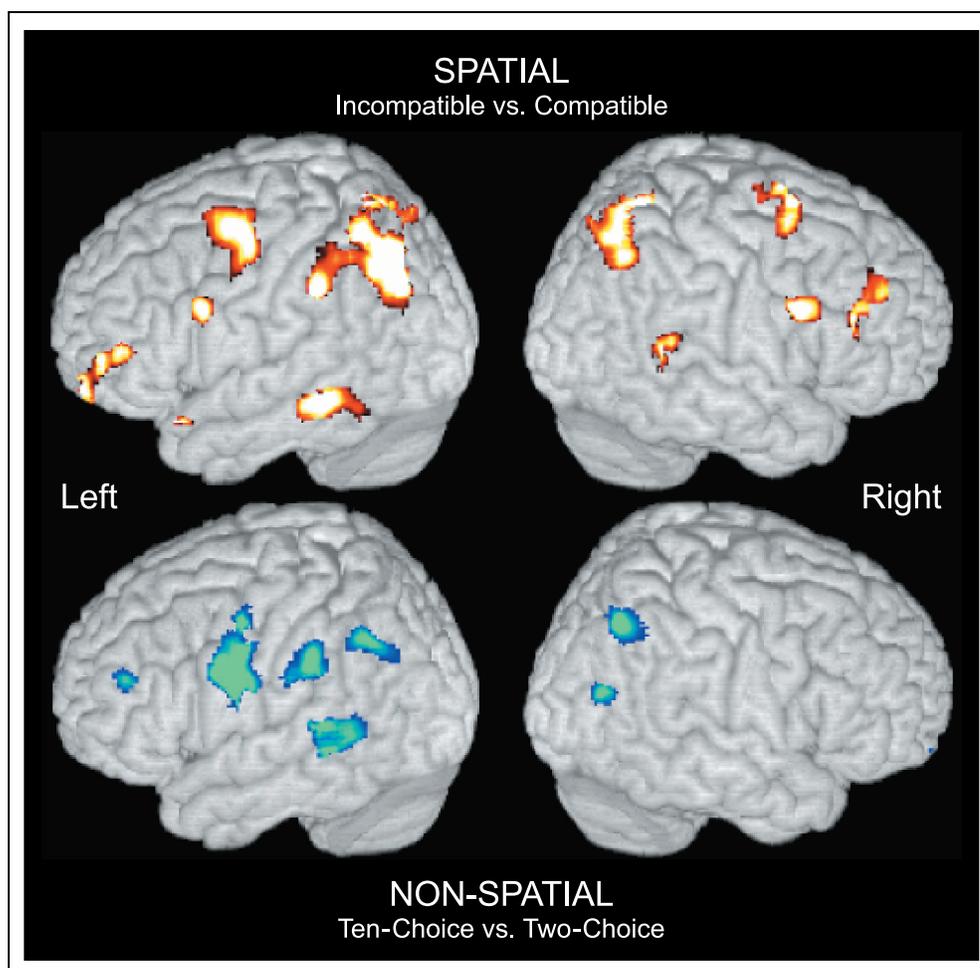
We manipulated response-selection difficulty in two ways using spatial material in Experiment 1. Participants made keypresses based on the location of a visually presented cue. We varied the numerosity of the S–R pairs by manipulating the number of possible stimulus locations across blocks of trials. Additionally, we varied S–R compatibility across blocks by requiring participants to make either a compatible or incompatible keypress to the cue location.

We manipulated response-selection difficulty using nonspatial material in Experiment 2. Participants made keypresses based on the identity of a centrally pre-





**Figure 2.** Extent of activity for cortical regions from Table 1 superimposed on a spatially normalized brain. Voxels with activity greater than  $p < .01$  contiguous to peak activity are shown. Regions more active in the spatial-incompatible than in the spatial-compatible task are shown in warm colors (top). Regions more active in the nonspatial ten-choice than in the nonspatial two-choice task are shown in cool colors (bottom).



monotonic increase was tested across subjects by fitting a regression line to the activation data from each region for each participant. The number of participants with regression lines with positive slopes was tested against the null hypothesis with a binomial test. Figure 3 (and Table 1) shows the cortical regions with reliable monotonic increases ( $p < .05$ , one-tailed for all regions). As shown in Figure 3, the regions mediating spatial and nonspatial are largely distinct: spatial response selection involving the right prefrontal cortex, the bilateral premotor cortex, and the dorsal parietal cortical regions (precuneus and superior parietal lobule) and nonspatial response selection involving the left prefrontal cortex and the more ventral posterior cortical regions (left middle temporal gyrus, left inferior parietal lobule, and right extrastriate cortex).

All regions showing monotonic increases in activation related to spatial response selection also showed a reliable interaction ( $p < .001$ , in all cases) between the effects on activation of task (spatial and nonspatial) and difficulty (the contrast levels from Table 1 and Figure 2). This strengthens our conclusion that these regions mediate spatial but not nonspatial response selection.

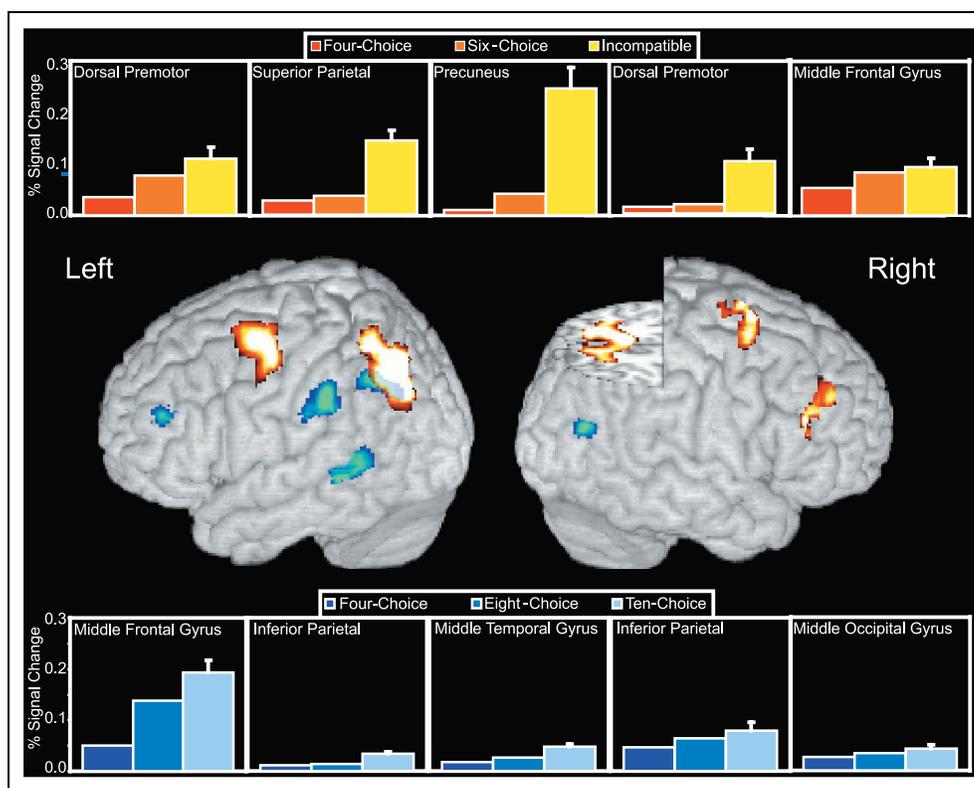
None of the regions showing monotonic increases in activation related to nonspatial response selection

showed a similar interaction. This may reflect a lack of power for this test, or it may indicate that the spatial and nonspatial tasks share some underlying processes, which one might expect given that the stimuli for the nonspatial task had to be localized to particular spatial positions. In either case, this lack of an interaction effect does not indicate an overlap in response-selection processing because no monotonic increases in activation with response-selection difficulty occurred in these nonspatial regions for the spatial task.

## DISCUSSION

The 4-choice spatial-incompatible task produced more activity than the 4-choice spatial-compatible one in the parietal, temporal, and prefrontal cortices. The nonspatial ten-choice task also produced more activity than the two-choice one in parietal, temporal, premotor, and prefrontal brain regions. However, as shown in Figure 2, the regions activated by these two comparisons are largely distinct. Furthermore, the brain regions implicated for spatial and nonspatial response selection, as shown by the monotonicity analysis (Figure 3), are strikingly different. Therefore, we conclude that brain mechanisms for response selection are stimulus specific.

**Figure 3.** Extent of activity for subset of cortical regions from Table 1 showing response-selection related monotonic increases in activity superimposed on a spatially normalized brain. Regions related to spatial response selection are shown in warm colors. Regions related to nonspatial response selection are shown in cool colors. From the left to right hemispheres, the bar graphs show the corresponding monotonic increases in percent signal change for these regions. The standard error is shown for the contrast from which the region was identified.



Spatial response selection involves a fronto-parietal network including the right middle frontal gyrus, the bilateral dorsal premotor cortex, the left superior parietal lobule, and the precuneus. Whereas, nonspatial response selection involves a different fronto-temporo-parietal network, including the left middle frontal gyrus, the left inferior parietal lobule, the left posterior parietal, the left middle temporal gyrus, and the right middle occipital gyrus. Importantly, because visual stimuli and manual-motor responses were used for both experiments, the specificity identified here is for the type of information processed, not for the modalities of stimulus input or response output. Our results are consistent with other recent evidence for stimulus-dependent response processing (Hazeltine, Bunge, Scanlon, & Gabrieli, 2003).

The spatial/nonspatial dissociation identified here generally conforms to the dorsal/ventral cortical pathways identified for visual information processing (Mishkin, Ungerleider, & Macko, 1983). Under this hypothesis, the dorsal pathway processes spatial information and the ventral one nonspatial visual information. Here we have shown that this dissociation may apply to the selection of appropriate responses to visual stimuli, even when the responses for both tasks are manual. Additionally, we have demonstrated a hemispheric processing bias in the dorsal prefrontal cortex for the selection of responses to different types of stimuli: the right middle frontal gyrus for spatial and left for

nonspatial response selection (Postle & D'Esposito, 2000).

Brain regions from the comparisons shown in Table 1 and Figure 2 that do not show monotonic increases with response-selection difficulty may reflect additional processes required for successful task performance. If our experiments manipulated only two levels of response-selection difficulty, we may have incorrectly concluded that these regions mediated response selection. However, we avoid this error by manipulating response selection parametrically. This technique has been used previously to overcome some of the limitations of cognitive subtraction (Jonides et al., 1997).

### Spatial Response Selection

The fronto-parietal network for spatial response selection identified in Experiment 1 closely replicates previous research (Schumacher & D'Esposito, 2002; Dassonville et al., 2001; Rowe et al., 2000; Iacoboni et al., 1996; Deiber et al., 1991).

Superior parietal (viz., superior parietal lobule and precuneus) cortex has been hypothesized to co-ordinate visual information and the responses to them (Wise et al., 1997; Milner & Goodale, 1995). Similarly, the premotor cortex is hypothesized to program movements based on external cues (Wise et al., 1997; Passingham, 1993). Indeed, Wise et al. postulate that these regions act in concert to synthesize proprioceptive, visual, attentional,

and other information to select and produce appropriate movements. The dorsal prefrontal cortex has been hypothesized to be involved in the control of behavior (Miller, 2000; Fuster, 1995; Shallice, 1988; Baddeley, 1986). This region is active in studies where participants must update, maintain, or otherwise organize their task goals (MacDonald, Cohen, Stenger, & Carter, 2000; Rogers, Andrews, Grasby, Brooks, & Robbins, 2000; Meyer et al., 1998; D'Esposito et al., 1995). Additionally, Rainer, Asaad, and Miller (1998) report that neurons from this region in nonhuman primates are sensitive to task context. They found a modulation of neuronal activity for neurons in the prefrontal cortex based on the task relevance of the stimulus presented on a particular trial.

Reciprocal direct neuronal connections between the superior parietal, dorsal prefrontal, and premotor cortices have been found in nonhuman primates (Passingham, 1993; Petrides & Pandya, 1984; Jones & Powell, 1970) suggesting a model for the neural processing for spatial response selection. The parietal cortex may represent the task-relevant stimulus position, the dorsal premotor cortex may use this information to program a response, and the dorsal prefrontal cortex may modulate activity for that response so that it is appropriate given the participant's task goals, environmental situation, and individual predilections.

### **Nonspatial Response Selection**

Nonspatial response selection, conversely, activates the left dorsal prefrontal cortex and the ventral posterior cortical regions (*viz.*, left middle temporal gyrus, left inferior parietal lobule, and right extrastriate cortex). The known functionality and interconnectivity of these regions suggest a different processing network. Like the superior parietal cortex, the inferior temporal and inferior parietal brain regions project directly to the prefrontal cortex in nonhuman primates (Gaffan & Harrison, 1988; Jones & Powell, 1970). These regions (especially in the left hemisphere) are thought to mediate the processing of visual object information (Milner & Goodale, 1995). Thus, for nonspatial response selection, the left temporal and inferior parietal cortices may represent the task-relevant stimulus and the left dorsal prefrontal cortex may modulate activity in these regions based on the current task goals and situation.

Although the peak of activity in the inferior parietal lobule was slightly inferior to the activity produced by the spatial task, the extent of the activity produced by both tasks overlapped in this region (Figure 3). Thus, activity in this region may reflect the engagement of similar visual processes in both tasks. That is, the co-ordinating of responses to task-relevant visual stimuli (Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Wise et al., 1997; Milner & Goodale, 1995). This interpretation is consistent with a previous study reporting that this region

mediates visual attention processes for both spatial and nonspatial tasks (Wojciulik & Kanwisher, 1999).

Given this view of response selection, it is surprising that we did not find dorsal premotor activity in the nonspatial task. After all, like the spatial task the nonspatial task required manual responses based on external cues. Perhaps the dorsal premotor cortex was involved in nonspatial response selection, but did not produce enough activity to surpass our statistical threshold. To investigate this, we extracted the activity from the nonspatial tasks from the dorsal premotor regions involved in spatial response selection. Activity in the left, but not in the right, dorsal premotor cortex showed a monotonic increase for nonspatial response selection ( $p < .05$ ). This was the only region that showed monotonic activity in both experiments. This result is consistent with hypothesis that the left premotor cortex is involved in manual response selection in general.

The brain network identified here for nonspatial response selection is consistent with previous research on nonspatial response selection. Raichle et al. (1994) reported that naive performance of a verbal response-selection task activated frontal (both dorsal and ventral) and temporal cortices. Interestingly, they found no evidence for the involvement of the dorsal premotor cortex, even when this region was investigated with a region-of-interest analysis, reinforcing the interpretation that this brain area is involved in manual-motor response selection. Similarly, Schluter, Krams, Rushworth, and Passingham (2001) reported activity in the dorsal prefrontal and inferior parietal of the left hemispheres related to response selection for objects.

Other studies investigating the learning of visuomotor associations also implicate a fronto-temporal brain network (Toni, Ramnani, et al., 2001; Toni, Rushworth et al., 2001; Toni et al., 2002). However, these studies implicate a frontal region more ventral to the one identified here. This is inconsistent with our current results where we found no activity in the ventral prefrontal cortex related to response selection in either experiment. This inconsistency, however, may be due to a difference in the difficulty of the tasks used and the amount of practice the participants received. Based on RTs and error rates, the most difficult response-selection condition in both of our experiments was the incompatible S-R task. As shown in Figure 2, we found activity in the inferior frontal gyrus bilaterally in the spatial-incompatible task. Perhaps, for the other easier conditions, the learning processes mediated by this region had progressed such that no sustained activity remained across the session and therefore no monotonic increases in activity could be found. Consistent with this hypothesis, Toni, Ramnani, et al. (2001) and Toni, Rushworth, et al. (2001) reported activity in the inferior frontal gyrus as participants learned a set of arbitrary S-R mappings, but not when they performed a well-practiced visual-motor task. Nonhuman primates show a similar

involvement of the ventral prefrontal cortex for the performance of novel visuomotor tasks (Murray, Bussey, & Wise, 2000). Additionally, in a previous experiment with this task using more practiced participants, we found no evidence for inferior frontal gyrus activity (Schumacher & D'Esposito, 2002). Taken together, these results suggest that this region plays a role only in the early stages of learning arbitrary S–R mappings. The temporal cortex, on the other hand, has been found to produce sustained activity throughout the performance of a nonspatial visuomotor task (Toni et al., 2002).

It is somewhat surprising that activity in the extrastriate cortex showed a monotonic increase in activity. Each trial included the presentation of only one stimulus; therefore, we expected visual encoding to remain substantially constant across S–R numerosity conditions. Activity here suggests that encoding processes may also have increased with S–R numerosity in this task (Sternberg, 1969). There are at least two possible reasons for this. The first involves stimulus repetitions: They decreased as S–R numerosity increased. Perhaps the higher level of stimulus repetitions in the lower numerosity conditions made encoding the numeral easier on these trials, thereby decreasing the brain activity in regions mediating these processes. Another possibility is that the increased activity in the extrastriate cortex may reflect top-down modulation from anterior response-selection regions (Druzgal & D'Esposito, 2001; Martinez et al., 1999).

Our data suggest a general description of the neural processing underlying response selection. Given one's current task situation and task goals, the dorsal prefrontal cortex (in the left hemisphere for nonspatial and in the right for spatial information) may act to modulate and control response-related activity in the dorsal premotor cortex and posterior stimulus-specific response-selection cortical regions: the ventral temporo-parietal regions for nonspatial and the dorsal parietal regions for spatial information.

Our results cast further doubt on the existence of a unitary central response-selection mechanism. Rather, they suggest that separate response-selection mechanisms exist for different types of tasks. The label “response-selection bottleneck” captures the simplicity of the proposed mechanism of this process in some theories (Pashler, 1994). The involvement of the dorsal prefrontal cortex in both response-selection networks identified here may belie this simplicity. This brain region plays a role in higher-level cognitive processes such as planning, problem solving, and working memory (Miller, 2000; Fuster, 1995; Shallice, 1988; Baddeley, 1986). Given that it is also involved in controlling the selection of appropriate responses to one's current environment, it should come as no surprise that response selection shows some of the same flexibility as these other frontal lobe-mediated cognitive processes. And that response-selection processing would be affected by practice, task goals, and participant predilections,

as suggested by previous investigations with dual-task procedures (Hazelton et al., 2002; Schumacher et al., 1999; Schumacher et al., 2001; Meyer et al., 1995).

## METHODS

### Participants

Ten healthy volunteers (5 females, ages 23–33) participated in Experiment 1. Nine of them (5 females) also participated in Experiment 2. All participants were recruited from the University of California community and gave their informed consent.

### Behavioral Procedure

#### *Experiment 1: Spatial Tasks*

Stimuli were projected onto a screen that the participants viewed through a mirror mounted on the head radio-frequency (RF) coil while lying prone in an MR scanner. Participants made their responses using two response pads (one for each hand) positioned comfortably to the participants' left and right.

Participants performed two-choice reaction tasks in the experiment. For the spatial numerosity task, a fixation stimulus (+) appeared in the center of a fixation display. The display consisted of a horizontal array of six circles, three on either side of the fixation stimulus. The fixation and circles appeared outlined white on a black background. The circles were equidistant from each other and the entire display subtended roughly 10°. This fixation display remained onscreen for 1400 msec, then a filled white circle (i.e., the cue stimulus) replaced one of the display circles for 100 msec. The original fixation display then appeared again and remained onscreen until the next cue stimulus appeared (viz., for 1400 msec). Participants responded during the fixation display. They made a compatible button press with their index, middle, or ring fingers to the location of the stimulus cue. Participants made a left index, middle, or ring finger keypress if the cue appeared in the inner, middle, or outer left position; and a right index, middle, or ring finger keypress if the cue appeared in the inner, middle, or outer right position, respectively.

The numerosity of the possible cue locations varied across blocks. On some blocks, the cue could appear in only the two inner locations; on other blocks, the two inner and two middle positions only; and other blocks one of all six locations. The number of outlined circles in the display indicated the possible cue locations. That is, the stimulus cue only appeared in an outlined circle and on some blocks two or four of the circles in the fixation display were colored gray indicating a smaller S–R numerosity for that block.

The spatial compatibility task was similar to the four-choice spatial numerosity one except the fixation stimulus was an “x” instead of a “+.” Participants made an

incompatible button press to the cue location. That is, they pressed a button with their left middle, left index, right index, or right middle finger if the cue appeared in the middle left, far right, far left, or middle right position, respectively.

Neither of these tasks may solely affect response selection. S–R numerosity may affect encoding and response processing and S–R compatibility may affect processes for dealing with response conflict (Schumacher & D’Esposito, 2002; MacDonald et al., 2000). Therefore, we identify brain regions related to response selection as those that show an effect of S–R compatibility and also show a monotonic increase with S–R numerosity.

Before scanning began, participants performed five practice blocks of 40 trials each. First, they practiced the six-choice S–R numerosity task once and then they practiced the S–R compatibility task four times. Participants were paid US\$ 8 an hour plus a monetary bonus based on their performance. The top three performers, based on their RTs and error rates, received an extra US\$ 20 compensation for their participation.

### *Experiment 2: Nonspatial Tasks*

At the beginning of each trial, a white fixation stimulus (+) appeared in the middle of a black display for 1000 msec. It was replaced by a white numeral between 0 and 9. The numerals subtended roughly 3°. Participants made a left index finger keypress if the presented numeral was a 0, 2, 5, 6, or 9 and right index finger keypress if the numeral was a 1, 3, 4, 7, or 8. The S–R numerosity varied across blocks. On some blocks, only 2 numerals appeared (*viz.*, 2 or 3); on other blocks 4 (*viz.*, 2–5), 8 (*viz.*, 2–8), or 10 (0–9) appeared. A numeral word (e.g., 2, 4, 8, or 10) appeared for 2000 msec before each block indicating the set size for the upcoming block.

Experiment 2 manipulated S–R numerosity using nonspatial material (*i.e.*, numerals) instead of spatial stimuli. Here the number of possible stimuli and responses are constant across conditions only the number of possible S–R pairs (from 2 to 10) varies across conditions. Therefore, brain regions showing a monotonic increase from the two-choice to the ten-choice conditions likely mediate response selection.

Before scanning began, participants performed four practice blocks of 40 trials each of the ten-choice nonspatial task. Participants received monetary compensation as in Experiment 1.

### **fMRI Procedure**

The fMRI scanning session consisted of five fMRI runs for each participant for each experiment. During each run, participants performed blocks of 12 trials of each condition, and fixation baseline condition in which they fixated on a centrally presented cue for 18 sec. Each block was repeated three times in each fMRI run. The

block order was fixed for each participant and randomized across participants.

Imaging was performed using a 4.0-Tesla Varian Inova scanner equipped with a fast gradient system for echo-planar imaging. A standard RF head coil was used with foam padding to restrict head motion comfortably. A gradient-echo, echo-planar sequence (TR = 2000 msec, TE = 28 msec, matrix size = 64 × 64, FOV = 22.4 cm) was used to acquire data sensitive to the blood oxygen level dependent signal. Each functional volume contained 18–5 mm axial slices with a 0.5-mm gap. Each fMRI run was preceded by 20 sec of dummy gradient RF pulses to achieve a steady state of tissue magnetization. For Experiment 1, each run lasted 4 min 54 sec (147 volumes/run). For Experiment 2, each run lasted 5 min 24 sec (162 volumes/run). Two high-resolution structural T1-weighted scans were also acquired. The first collected 18 axial slices in the same plane as the echo-planar images (TR = 200 msec, TE = 5 msec, matrix size = 256 × 256, FOV = 22.4 cm). The second was a 3-D MPFLASH scan (TR = 9 msec, TE = 4.8 msec, TI = 300 msec).

### **fMRI Data Processing**

Data processing and analysis were performed with analysis routines written in Interactive Data Language (Boulder, CO). Before data were analyzed, they were corrected for head-motion artifacts using a six-parameter, rigid-body transformation algorithm (Friston et al., 1995) and the time-series from each voxel was normalized by the mean signal value across the run to remove scaling differences.

Statistical analyses were performed using a modified general linear model (Worsley & Friston, 1995). In this model, for each participant we created a design matrix including covariates for each task condition convolved with an idealized hemodynamic response function. This design matrix also included covariates for the global signal for each run. These covariates were orthogonalized with respect to the other covariates of interest to increase the sensitivity of the general linear model (Desjardins, Kiehl, & Liddle, 2001). Finally, frequencies below 0.005 and above 0.25 Hz were removed from the data (Zarahn, Aguirre, & D’Esposito, 1997).

### **Random Effects Analysis of fMRI Data**

Each participant’s brain was normalized to the Montreal Neurological Institute reference brain using SPM99. Statistical parametric maps of  $\beta$ -values for specific conditions of interest were calculated for each participant. These data were spatially smoothed with a 10-mm full-width half-maximum gaussian kernel to account for between-subject anatomical variability and then analyzed using one-sample across-participants *t* tests. Significance levels were set at  $p < .001$  for all brain activation analyses. This somewhat lenient statistical criterion was

used to identify all potential regions mediating response selection. An even more lenient threshold was also investigated ( $p < .05$ , uncorrected). The extent of the regions identified in Table 1 increased, but no additional reasonable regions were identified. These potential regions were then tested further for monotonic increases in activity with our parametric manipulation of response-selection difficulty.

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## Note

1. Studies of the Stroop task, whose different versions affect response-selection difficulty, are not included here because a large part of that task involves dealing with conflicting and highly overlearned prepotent responses and thus may not specifically isolate response selection.

## REFERENCES

- Baddeley, A. (1986). *Working memory*. New York: Oxford University Press.
- Bunge, S. A., Hazeltine, E., Scanlon, M. D., Rosen, A. C., & Gabrieli, J. D. (2002). Dissociable contributions of prefrontal and parietal cortices to response selection. *Neuroimage*, *17*, 1562–1571.
- Dassonville, P., Lewis, S. M., Zhu, X. H., Ugurbil, K., Kim, S. G., & Ashe, J. (2001). The effect of stimulus–response compatibility on cortical motor activation. *Neuroimage*, *13*, 1–14.
- Decary, A., & Richer, F. (1995). Response selection deficits in frontal excisions. *Neuropsychologia*, *33*, 1243–1253.
- Deiber, M., Passingham, R. E., Colebatch, J., Friston, K., Nixon, P., & Frackowiak, R. S. J. (1991). Cortical areas and the selection of movement—A study with positron emission tomography. *Experimental Brain Research*, *84*, 393–402.
- Desjardins, A. E., Kiehl, K. A., & Liddle, P. F. (2001). Removal of confounding effects of global signal in functional MRI analyses. *Neuroimage*, *13*, 751–758.
- D'Esposito, M., Detre, J. A., Alsop, D. C., Shin, R. K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature*, *378*, 279–281.
- Druzgal, T. J., & D'Esposito, M. (2001). Activity in fusiform face area modulated as a function of working memory load. *Cognitive Brain Research*, *10*, 355–364.
- Friston, K. J., Ashburner, J., Frith, C. D., Poline, J.-B., Heather, J. D., & Frackowiak, R. S. J. (1995). Spatial registration and normalization of images. *Human Brain Mapping*, *2*, 165–189.
- Fuster, J. M. (1995). *Memory in the cerebral cortex*. Cambridge: MIT Press.
- Gaffan, D., & Harrison, S. (1988). Inferotemporal–frontal disconnection and fornix transection in visuomotor conditional learning by monkeys. *Behavioural Brain Research*, *31*, 149–163.
- Hazeltine, E., Bunge, S. A., Scanlon, M. D., & Gabrieli, J. D. (2003). Material-dependent and material-independent selection processes in the frontal and parietal lobes: An event-related fMRI investigation of response competition. *Neuropsychologia*, *41*, 1208–1217.
- Hazeltine, E., Teague, D., & Ivry, R. B. (2002). Simultaneous dual-task performance reveals parallel response selection after practice. *Journal of Experimental Psychology: Human Perception and Performance*, *28*, 527–545.
- Iacoboni, M., Woods, R. P., & Mazziotta, J. C. (1996). Brain–behavior relationships: Evidence from practice effects in spatial stimulus–response compatibility. *Journal of Neurophysiology*, *76*, 321–331.
- Jones, E. G., & Powell, T. P. (1970). An anatomical study of converging sensory pathways within the cerebral cortex of the monkey. *Brain*, *93*, 793–820.
- Jonides, J., Schumacher, E. H., Smith, E. E., Lauber, E. J., Awh, E., Minoshima, S., & Koeppe, R. (1997). Verbal working memory load affects regional brain activation as measured by PET. *Journal of Cognitive Neuroscience*, *9*, 462–475.
- Kolb, B., & Whishaw, I. (1990). *Fundamentals of human neuropsychology*. New York: W. H. Freeman.
- Kornblum, S., Hasbroucq, T., & Osman, A. (1990). Dimensional overlap: Cognitive basis for stimulus–response compatibility—a model and taxonomy. *Psychological Review*, *97*, 253–270.
- MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science*, *288*, 1835–1838.
- Martinez, A., Anllo-Vento, L., Sereno, M. I., Frank, L. R., Buxton, R. B., Dubowitz, D. J., Wong, E. C., Hinrichs, H., Heinze, H. J., & Hillyard, S. A. (1999). Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nature Neuroscience*, *2*, 364–369.
- Meyer, D. E., Evans, J. E., Lauber, E. J., Gmeindl, L., Rubinstein, J., Junck, L., & Koeppe, R. A. (1998). The role of dorsolateral prefrontal cortex for executive cognitive processes in task switching. *Cognitive Neuroscience Society Abstracts*, *5*, 106.
- Meyer, D. E., & Kieras, D. E. (1997). A computational theory of executive cognitive processes and multiple-task performance: Part 1. Basic mechanisms. *Psychological Review*, *104*, 3–65.
- Meyer, D. E., Kieras, D. E., Lauber, E., Schumacher, E. H., Glass, J., Zurbruggen, E., Gmeindl, L., & Apfelblat, D. (1995). Adaptive executive control: Flexible multiple-task performance without pervasive immutable response-selection bottlenecks. *Acta Psychologica*, *90*, 163–190.
- Miller, E. K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews*, *1*, 59–65.
- Milner, A. D., & Goodale, M. A. (1995). *The visual brain in action*. New York: Oxford University Press.
- Mishkin, M., Ungerleider, L. G., & Macko, K. A. (1983). Object vision and spatial vision: Two cortical pathways. *Trends in Neurosciences*, *6*, 414–417.
- Murray, E. A., Bussey, T. J., & Wise, S. P. (2000). Role of prefrontal cortex in a network for arbitrary visuomotor mapping. *Experimental Brain Research*, *133*, 114–129.
- Pashler, H. (1984). Processing stages in overlapping tasks—Evidence for a central bottleneck. *Journal of Experimental Psychology: Human Perception and Performance*, *10*, 358–377.
- Pashler, H. (1990). Do response modality effects support

- multiprocessor models of divided attention? *Journal of Experimental Psychology: Human Perception and Performance*, *16*, 826–842.
- Pashler, H. (1994). Dual-task interference in simple tasks—Data and theory. *Psychological Bulletin*, *116*, 220–244.
- Passingham, R. E. (1993). *The frontal lobes and voluntary action*. Oxford: Oxford Psychology Series.
- Passingham, R. E., & Toni, I. (2001). Contrasting the dorsal and ventral visual systems: Guidance of movement versus decision making. *Neuroimage*, *14*, S125–S131.
- Petrides, M., & Pandya, D. N. (1984). Projections to the frontal cortex from the posterior parietal region in the rhesus monkey. *Journal of Comparative Neurology*, *228*, 105–116.
- Postle, B. R., & D'Esposito, M. (2000). Evaluating models of the topographical organization of working memory function in frontal cortex with event-related fMRI. *Psychobiology*, *28*, 132–145.
- Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A. M., Pardo, J. V., Fox, P. T., & Petersen, S. E. (1994). Practice-related changes in human brain functional anatomy during nonmotor learning. *Cerebral Cortex*, *4*, 8–26.
- Rainer, G., Asaad, W. F., & Miller, E. K. (1998). Selective representation of relevant information by neurons in the primate prefrontal cortex. *Nature*, *393*, 577–579.
- Rogers, R. D., Andrews, T. C., Grasby, P. M., Brooks, D. J., & Robbins, T. W. (2000). Contrasting cortical and subcortical activations produced by attentional-set shifting and reversal learning in humans. *Journal of Cognitive Neuroscience*, *12*, 142–162.
- Rowe, J. B., Toni, I., Josephs, O., Frackowiak, R. S. J., & Passingham, R. E. (2000). The prefrontal cortex: Response selection or maintenance within working memory? *Science*, *288*, 1656–1660.
- Schluter, N. D., Krams, M., Rushworth, M. F., & Passingham, R. E. (2001). Cerebral dominance for action in the human brain: The selection of actions. *Neuropsychologia*, *39*, 105–113.
- Schumacher, E. H., & D'Esposito, M. (2002). Neural implementation of response selection in humans as revealed by localized effects of stimulus–response compatibility on brain activation. *Human Brain Mapping*, *17*, 193–201.
- Schumacher, E. H., Lauber, E. J., Glass, J., Zurbruggen, E., Gmeindl, L., Kieras, D. E., & Meyer, D. E. (1999). Concurrent response-selection processing in dual-task performance: Evidence for adaptive executive control of task scheduling. *Journal of Experimental Psychology: Human Perception and Performance*, *25*, 791–814.
- Schumacher, E. H., Seymour, T. L., Glass, J. M., Fencsik, D. E., Lauber, E. J., Kieras, D. E., & Meyer, D. E. (2001). Virtually perfect time sharing in dual-task performance: Uncorking the central cognitive bottleneck. *Psychological Science*, *12*, 101–108.
- Shallice, T. (1988). *From neuropsychology to mental structure*. New York: Cambridge University Press.
- Sternberg, S. (1969). The discovery of processing stages: Extensions of Donders' method. *Acta Psychologica*, *30*, 276–315.
- Toni, I., Ramnani, N., Josephs, O., Ashburner, J., & Passingham, R. E. (2001). Learning arbitrary visuomotor associations: Temporal dynamic of brain activity. *Neuroimage*, *14*, 1048–1057.
- Toni, I., Rowe, J., Stephan, K. E., & Passingham, R. E. (2002). Changes of cortico-striatal effective connectivity during visuomotor learning. *Cerebral Cortex*, *12*, 1040–1047.
- Toni, I., Rushworth, M. F., & Passingham, R. E. (2001). Neural correlates of visuomotor associations. Spatial rules compared with arbitrary rules. *Experimental Brain Research*, *141*, 359–369.
- Welford, A. T. (1959). Evidence of a single-channel decision mechanism limiting performance in a serial reaction task. *Quarterly Journal of Experimental Psychology*, *11*, 193–210.
- Wise, S. P., Boussaoud, D., Johnson, P. B., & Caminiti, R. (1997). Premotor and parietal cortex: Corticocortical connectivity and combinatorial computations. *Annual Review of Neuroscience*, *20*, 25–42.
- Wojciulik, E., & Kanwisher, N. (1999). The generality of parietal involvement in visual attention. *Neuron*, *23*, 747–764.
- Worsley, K. J., & Friston, K. J. (1995). Analysis of fMRI time-series revisited—again. *Neuroimage*, *2*, 173–182.
- Zarahn, E., Aguirre, G. K., & D'Esposito, M. (1997). Empirical analyses of BOLD fMRI statistics: I. Spatially unsmoothed data collected under null-hypothesis conditions. *Neuroimage*, *5*, 179–197.