

Neural Activation During Response Competition

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Abstract

■ The flanker task, introduced by Eriksen and Eriksen [Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, 16, 143–149], provides a means to selectively manipulate the presence or absence of response competition while keeping other task demands constant. We measured brain activity using functional magnetic resonance imaging (fMRI) during performance of the flanker task. In accordance with previous behavioral studies, trials in which the flanking stimuli indicated a different response than the central stimulus were performed significantly more slowly than trials in which all the stimuli indicated the same response. This

reaction time effect was accompanied by increases in activity in four regions: the right ventrolateral prefrontal cortex, the supplementary motor area, the left superior parietal lobe, and the left anterior parietal cortex. The increases were not due to changes in stimulus complexity or the need to overcome previously learned associations between stimuli and responses. Correspondences between this study and other experiments manipulating response interference suggest that the frontal foci may be related to response inhibition processes whereas the posterior foci may be related to the activation of representations of the inappropriate responses. ■

INTRODUCTION

The successful performance of any task requires filtering out inappropriate actions and selecting actions that are consistent with current goals. The flanker task, introduced by Eriksen and Eriksen (1974), provides a well-controlled method for examining the neural systems that resolve the conflict among response options. In the task, a central target stimulus is presented simultaneously with two distractor stimuli (flankers) and participants are instructed to respond according to the target and ignore the flankers. These task demands require participants to select the relevant information in a display and inhibit the surrounding irrelevant information in order to make the correct response. The effect of the irrelevant information can be assessed by comparing reaction times on trials in which the flankers indicate the same response as the target (congruent trials) to trials in which they indicate a conflicting response (incongruent trials).

The flanker task has some distinguishing properties in relation to other tasks that bring about conflict between competing responses. The Wisconsin Card Sorting Task

(WCST), which requires individuals to change the stimulus dimension (e.g., shape or color) to which they respond, and the Stroop task, which requires that they name the color of a printed word while ignoring its meaning, induce response interference by creating uncertainty about the relevant stimulus information. In both tasks, participants must inhibit responses that were previously linked to the stimuli. In contrast, the flanker task uses a stimulus–response (S–R) mapping that is constant throughout the experiment.

This property relates to an important difference between the flanker task and both the Stroop and the WCST: In the flanker task, participants must choose the relevant object in the display rather than the relevant rule to apply to generate the response. Thus, visuospatial attention may be used to gate the appropriate information on to the response selection processes. Such a process is not applicable for the Stroop and WCST tasks because the relevant and irrelevant information are typically integral parts of the same stimulus. Spatial attention, however, is not the only means by which interference is resolved in the flanker

task. The magnitude of flanker interference, though dependent on the distance between the target and the flankers, is also determined by whether the flankers indicate the same or a different response (see Cohen & Shoup, 1995; Cohen, Ivry, Rafal, & Kohn, 1995). Thus, it is the congruency of response indicated by the flankers and not their physical similarity to the target that is critical for interference. This finding suggests that flanker effects are not strictly dependent on the inability to perceptually filter out the irrelevant information.

The flanker task has been administered to people across the life span of human development. Children (Ridderinkhoff, van der Molen, Band, & Bashore, 1997) and older adults (Tipper, 1991), relative to young adults, show exaggerated flanker effects—greater increases in reaction time when the flankers conflict with the target than when the target and flankers indicate the same response. The standard interpretation of such findings is that the ability to inhibit irrelevant information is affected by age on both ends of the developmental spectrum (Roberts, Hager, & Heron, 1994; West, 1996). Further, there is reason to believe that the frontal lobes may play a critical role in developmental differences in the ability to inhibit irrelevant information because the frontal lobes appear to be the last cortical region to mature in childhood (e.g., Huttenlocher & Dabholkar, 1967; Yakovlev & Lecours, 1967) and also the cortical region of greatest vulnerability in normal old age (e.g., Raz et al., 1997).

Despite its widespread use in behavioral studies, little imaging work has examined neural activation during the flanker task. Botvinick, Nystrom, Fissell, Carter, and Cohen (1999) used an event-related design to isolate the neural systems associated with conflict monitoring during the flanker task. They evaluated their imaging data to test a hypothesis that flankers exert more influence on selection mechanisms following congruent trials than following incongruent trials (Gratton, Coles, & Donchin, 1992). Building on this proposal, Botvinick et al. (1999) sought brain regions that increased activation on incongruent trials that followed congruent trials. Only the anterior cingulate cortex demonstrated this pattern of activity. The right inferior parietal lobe and the left anterior insula showed significant changes during incongruent trials compared to congruent trials, but these changes were not modulated by the congruency of the previous trial.

Two aspects of the flanker task used by Botvinick et al. (1999) are critical for the interpretation of their results. First, unlike the present study, which uses color stimuli, the S–R mapping in the Botvinick et al. study was highly compatible: The stimuli were arrows pointing in the direction of the correct response. The compatibility of the mappings may introduce additional forms of interference during incongruent trials, as evidenced by data from Stroop tasks (see Virzi & Egeth, 1985). The magni-

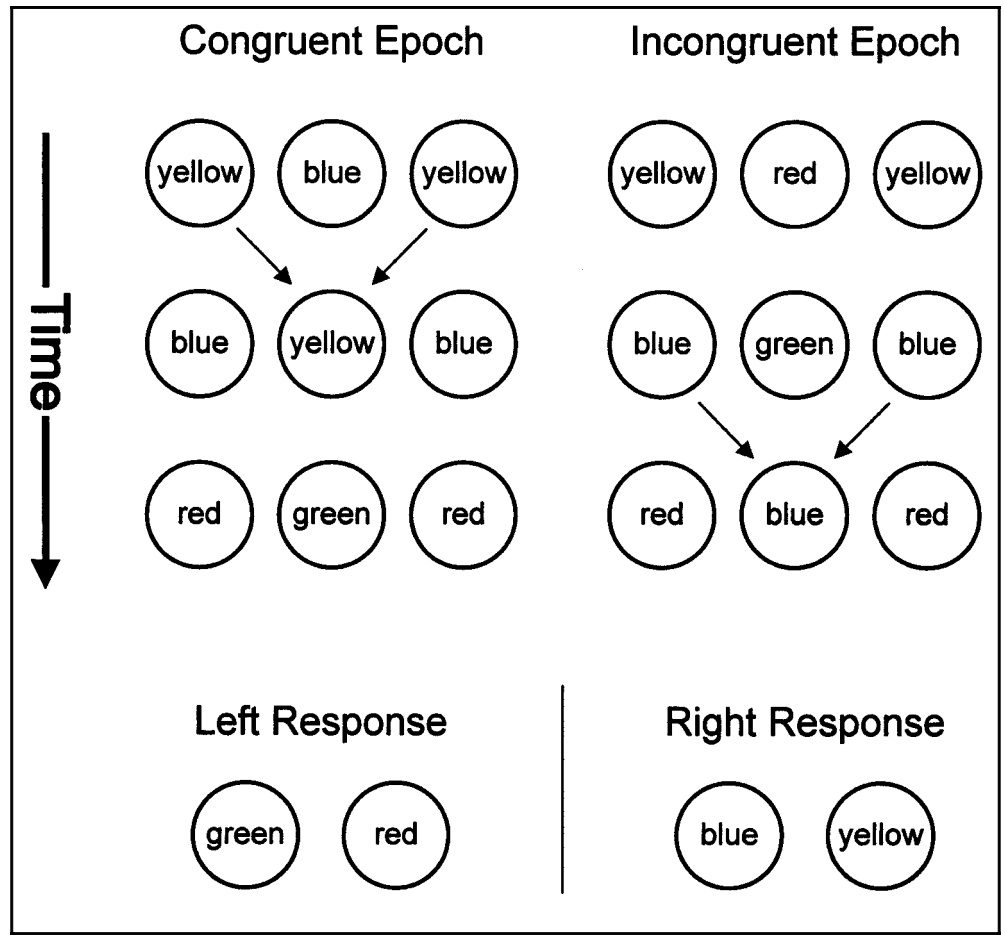
tude of the flanker effect averaged 267 msec for the eight participants included in the Botvinick et al. study, which is much larger than what is observed in flanker studies that use stimuli that are not compatible with responses (i.e., studies using colors or letters to indicate keypresses). For example, in the Gratton et al. (1992) experiments, reaction times for incongruent and congruent trials differed by between 40 and 60 msec (see also, Cohen & Shoup, 1995; Shaffer & Laberge, 1979; Eriksen & Eriksen, 1974).

Second, the researchers used only two possible stimuli in their task. Note that under these conditions congruent trials differ from incongruent trials not only in terms of response conflict but also in terms of visual complexity. That is, on congruent trials all of the stimuli are physically identical (e.g., <<<<< calls for a left key response), so there is no perceptual conflict among stimuli. In contrast, the incongruent trials, (e.g., >><>> calls for a left key response) require considerably more effort to parse the visual display. This property may have important consequences that are unrelated to the suppression of irrelevant information. For example, experimental participants know that visually simple (i.e., homogeneous) displays do not involve interference whereas the complex (i.e., heterogeneous) displays do. With the small number of stimuli, consecutive displays are identical for half of the incongruent trials that follow incongruent trials, whereas incongruent trials that follow congruent trials are never stimulus repetitions. There is good reason to believe that exact stimulus repetitions may represent a special case in which the selection processes may be largely skipped leaving less opportunity for interference (Pashler & Baylis, 1991).

In the present study, we focus on identifying the neural systems that resolve response conflict under conditions of constant S–R compatibility and visual complexity. On each trial, participants saw three colored circles arranged horizontally, and their task was to respond based on the color of the center circle (see Figure 1). To rule out visual complexity as a source of activation increases, four possible target colors were mapped to two possible responses. On congruent trials, the two flankers, which were always the same color, and the target were different colors that indicated the same response, whereas on incongruent trials the flankers and target were different colors that indicated different responses. Consequently, visual complexity was constant across all trials: Every display consisted of a central target that differed in color from the flankers, which were of the same color.

Because stimulus complexity and S–R compatibility are constant across congruent and incongruent trials, the flanker task provides a means for identifying the neural structures that come online during conflict among competing response codes that are presumably represented in working memory. Under these condi-

Figure 1. Sample trial stimuli for the two types of epochs, congruent and incongruent, with the S-R mappings shown at the bottom. The congruent and incongruent epochs are shown in separate columns, although during the experiment the transition from one epoch to the other occurred without the participants' awareness. Examples of "primed" trials, in which the flanker on trial $n-1$ one becomes the target on trial n are depicted graphically by the arrows.



tions, three basic cognitive operations are likely to occur: response code activation, response selection, and response inhibition. Response code activation involves instantiating the representations of all possible responses indicated by the stimuli (see Rafal et al., 1996). During incongruent trials, two codes are activated (i.e., the code for the target response and the code for the flanker response), whereas during congruent trials only one is activated, given that both the target and flankers indicate the same overt response. Response code selection determines which of the activated response codes is most desirable or appropriate. This operation may necessarily involve the third process, response inhibition, which suppresses the unselected codes.

The presence of this third process, response code inhibition, may leave traces that might be detected behaviorally by measuring residual inhibition on trials in which the flanker color of the previous trial has become the target color. That is, if flankers are actively inhibited, then they should be responded to more slowly when they become targets on subsequent trials. This phenomenon is termed negative priming (Tipper, 1985), and it provides a means for determining whether the flankers are processed dif-

ferently on congruent and incongruent trials. If inhibitory mechanisms are more active on incongruent trials, then negative priming should be stronger following these trials. Behavioral studies have suggested that negative priming is expressed only when irrelevant information is present (Moore, 1994), suggesting that these inhibitory processes may be specific to systems that are active when multiple potential targets are presented.

RESULTS

Behavioral Data

Reaction times (Figure 2) during the congruent epochs (534 msec; SD : 56) were significantly faster than reaction times during the incongruent epochs (573 msec; SD : 76), producing a significant effect of congruency [$t(7) = 3.24$; $p < .05$].

We tested for evidence of distinct processes resolving the response conflict following congruent and incongruent trials, as proposed by Gratton et al. (1992). A second analysis was performed after removing the first trial from each epoch. In this analysis, all trials were preceded by trials of the same type (i.e., congruent or incongruent) so that transitions to new processing

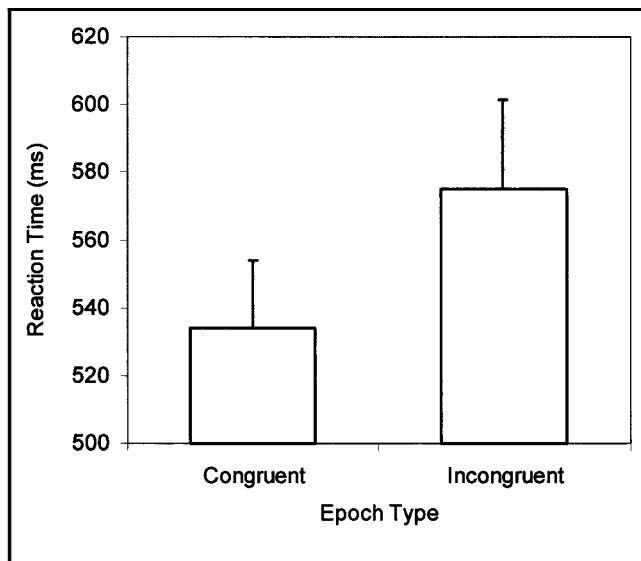


Figure 2. The bars in Figure 2 indicate the mean reaction times for the two epochs with the standard errors of the mean depicted by error bars. Congruent epochs consisted of trials in which the target and flankers indicated the same response; incongruent epochs consisted of trials in which the target indicated a different response than the flanker.

strategies did not contaminate the results. Reaction times for both trial types were highly similar to those obtained in the previous analysis, and the flanker effect was nearly identical [533 (*SD*: 58) vs. 574 (*SD*: 77) msec; $t(7) = 3.47$; $p < .05$].

A final analysis was performed on the behavioral data to specifically test for evidence of increased inhibitory processes during the incongruent epochs. Rather than focus on the relationship between the target and the flankers within a given trial, we instead examined the relationship between the target on the present trial and the flankers on the preceding trial. The reasoning was that inhibitory processes could be detected by evaluating the costs for target colors that were the same as the flanker colors on the previous trial. That is, inhibitory processes should cause these targets to be responded to more slowly than targets that were not present in the previous display. If these inhibition processes were more active during the incongruent epochs then this effect would be larger following the incongruent trials. In short, there should be more negative priming after incongruent trials than after congruent trials.

To measure negative priming, the data were submitted to a two-way ANOVA. The first factor, Congruency, indicated whether the previous trial occurred during a congruent or incongruent epoch, and the second factor, Prime, indicated whether the target was the same color as the flanker on the previous trial or was a color not present on the previous trial. Examples of “primed” trials are depicted by the arrows in Figure 1. The results, shown in Figure 3, indicated no main effect

of Prime [$F < 1$], but the effect of Congruency was significant [$F(1, 7) = 15.54$; $p < .01$; $MSE = 19,208$], presumably reflecting the fact that trials usually followed trials of the same type, and congruent trials were performed more quickly than incongruent trials. Most importantly, the Congruency \times Prime interaction achieved significance [$F(1, 7) = 7.79$; $p < .05$; $MSE = 8,844$], indicating that the effect of negative priming depended on whether the previous trial was congruent or incongruent. Follow-up t tests revealed that primed trials were significantly slower than unprimed trials during the incongruent epochs [37 msec; $t(7) = 2.00$; $p < .05$ (one-tailed)], but the difference (in the opposite direction) between primed and unprimed trials was not significant during the congruent epochs [22 msec; $t(7) = -1.55$; $p > .05$]. As predicted, there was no evidence of any inhibition of the flanker color following congruent trials; the reaction times for the primed trials were nonsignificantly faster than those for the new unprimed target trials. Because the flankers indicate the same response as the target on congruent trials, there is little reason that they should be inhibited, and the behavioral findings are consistent with inhibitory processes being selectively invoked during the epochs of incongruent trials.

Mean accuracy was 94% across participants. Performance during the congruent epochs was more accurate (98%; *SD*: 3%) than during the incongruent epochs (90%; *SD*: 9%) [$t(7) = 2.91$; $p < .05$; $MSE = 0.03$]. Thus,

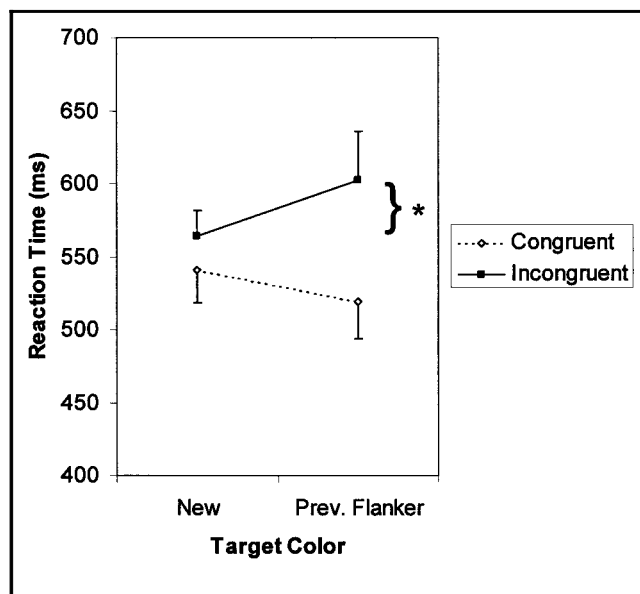


Figure 3. Reaction times are presented as function of whether the previous trial was in the congruent (open diamonds) or incongruent (filled squares) epoch, and whether the target is the same color as the flankers on the previous trial (Prev. Flanker) or a color not present on the previous trials (New). The asterisk indicates a significant difference between the primed and unprimed incongruent trials. The error bars represent standard errors of the mean.

Table 1. The Four Foci Showing Significantly Greater Activity During the Incongruent Epochs Compared to the Congruent Epochs, Listed with the Stereotactic Coordinates, Peak z Scores, and Volumes (in Voxels)

<i>Region</i>	<i>Brodmann's area</i>	<i>X</i>	<i>Y</i>	<i>Z</i>	<i>z score</i>	<i>Volume</i>
Right inferior prefrontal cortex	44/9	52	12	26	3.92	136
Left supplementary motor cortex	6	-18	0	60	4.11	122
Left superior parietal cortex	7	-24	-34	68	4.14	58
Left inferior anterior parietal cortex	40	-44	-32	44	3.72	56

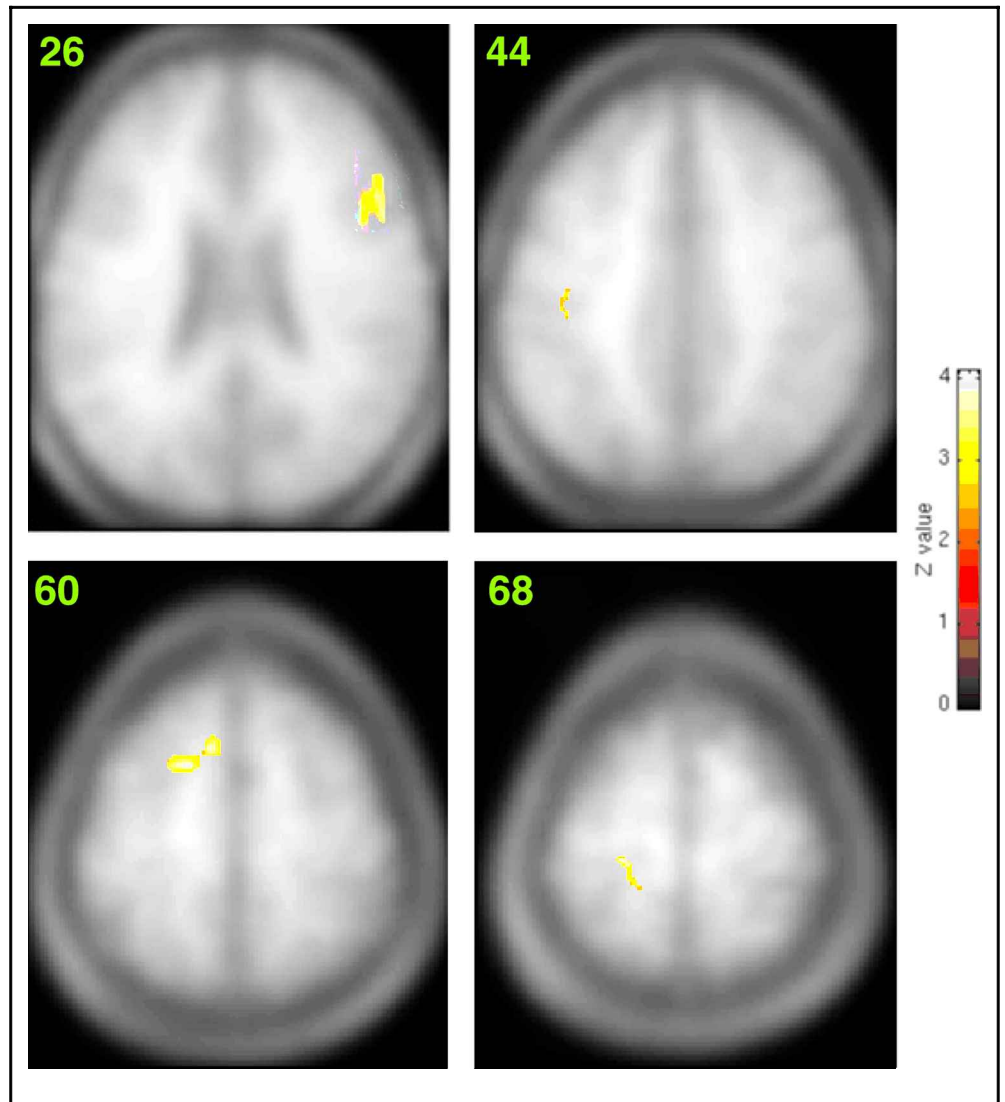
the reaction time effect is not the result of a speed-accuracy tradeoff.

Imaging Data

The comparison of the incongruent epochs to the congruent epochs revealed significant increase in

activation in four regions, the right inferior frontal cortex, the left anterior parietal cortex, the left supplementary motor area (SMA), and the left superior parietal cortex (Table 1 and Figure 4). No regions showed significant increases in neural activity during the congruent epochs relative to the incongruent epochs.

Figure 4. The significantly active foci are projected onto averaged anatomical images for the eight participants. Going clockwise starting with the upper-left image, the slices show foci in the right inferior frontal gyrus (RIFG), the inferior anterior parietal cortex, the SMA and preSMA, and the superior parietal cortex. The relevant z coordinate is portrayed in green in the upper left hand corner of each panel. On the far right, the scale equating color with the z score is shown.



DISCUSSION

Two principal findings emerge from the analysis of the behavioral data. First, participants took longer to respond to incongruent trials than to congruent trials. The 40-msec flanker effect was similar in magnitude to those observed in studies performed outside the MRI scanner using similar stimuli in randomized rather than blocked designs. Second, negative priming occurred during the incongruent epochs, but not during the congruent epochs. That is, the flanker colors appeared to be inhibited only on the incongruent trials.

This result suggests that different cognitive components were engaged during the two trial types and provides an empirical basis for attributing differences in neural activation to inhibitory processes. Given the small difference between the unprimed trial types (see Figure 3), it is tempting to ascribe the bulk of the difference between congruent and incongruent trials to negative priming. However, findings from other studies using completely randomized trial-orders (e.g., Cohen & Shoup, 1995; Eriksen & Eriksen, 1974) show that negative priming, at least as it is presently understood, is not the dominant source of the reaction time difference. It may be that the blocked structure of the experiment allows inhibitory processes to be selectively engaged during the incongruent trials. Moreover, incongruent trials may be more sensitive to the expression of negative priming (see Moore, 1994). Thus, because a blocked design was used, it cannot be determined from the present design whether the observed behavioral differences result from changes in task operations during the prime or the probe trial.

Neural Activation

Four brain regions exhibited greater activation under conditions of greater response competition: the right inferior frontal cortex, the left anterior parietal lobe, the SMA, and the superior parietal lobe. In the present study, changes in activation associated with incongruent versus congruent epochs can be associated with the error detection processes, because error rates were higher during the incongruent epochs (10% vs. 2%). While we cannot rule out this possibility, it seems unlikely given the high accuracy rates that all of the participants were able to maintain. The difference in the error rates is equivalent to less than 1 error per epoch. Thus, we interpret the observed increases in activation based on their correspondences with neuroimaging results from other tasks involving manipulations of response interference.

Prefrontal Cortex

The largest focus of activation associated with the incongruent epochs was located in the right inferior

frontal gyrus (RIFG). Intriguingly, the selection of task-relevant action has long been thought to be the purview of the prefrontal cortex. Patients with lesions in the prefrontal cortex often demonstrate deficits in producing coherent goal-oriented sequences of actions (Goel & Grafman, 1995; Fuster, 1989). Their behaviors can be fragmented and disorganized, often characterized as highly distractible and excessively influenced by the environment rather than internal goals (Luria, 1966; Lhermitte, Pillon, & Seraru, 1986).

Neuropsychological research has sought to further specify the cognitive consequences of frontal lobe damage through widely used behavioral tests. Tasks such as the Stroop task and the WCST require that prepotent responses be suppressed so that the appropriate actions are executed. Individuals with damage to the prefrontal cortex show deficits in performing these tasks (Stroop: Vendrell et al., 1995; Perret, 1974; WCST: Milner, 1963). Owen et al. (1993) developed a variant of the WCST in which the requirement that a previously relevant dimension be inhibited is dissociated from the requirement that a previously irrelevant dimension receive attention. In their study, frontal patients' deficits were largely restricted to the inhibition of previously relevant dimensions; they demonstrated no difficulty in switching when the previously relevant dimension was no longer present in the display. These behavioral phenomena suggest that the frontal lobes may be specifically involved in the inhibition of previously relevant information rather than a generic selection process.

Several imaging studies have investigated set-shifting, a cognitive component of the WCST. In these tasks, participants must first respond according to one dimension of a stimulus (e.g., its color) and then, on a subsequent trial, respond according to a different dimension of a second stimulus (e.g., its shape). Thus, to perform the task correctly, participants must switch from one set of rules to another. Behavioral studies have shown that the presence of the irrelevant dimension dramatically increases reaction times, but predominantly when it was relevant on a previous trial (Mayr & Keele, 2000). Thus, as in the flanker and Stroop tasks, the set-shifting task requires that the appropriate response be selected from amongst multiple alternatives indicated by a visual display. Neuroimaging studies examining set-shifting (e.g., Konishi et al., 1998; Naga-hama et al., 1996; Berman et al., 1995) have each reported foci of activation in the right prefrontal cortex that are similar to the prefrontal focus reported in the present study.

Response Code Activation, Selection, or Inhibition?

In the set-shifting studies, the relevant and irrelevant information are located in the same region of the visual

field. Thus, the overlap between the foci observed in the present study and the set-shifting experiments suggests that spatial attention is likely not the critical operation that is reflected by the activity in this region. However, three remaining candidate processes, response code activation, response selection, and response inhibition remain viable possible roles for the RIFG. These processes are not differentiable in the present experimental design: Although the behavioral data indicate that inhibition is taking place, they do not rule out the operation of other processes. Therefore, we turn to other neuroimaging studies for clues as to which operation may best characterize the function of this region.

Evidence that the RIFG may play a more generic role in response inhibition has emerged from imaging studies employing a go/no-go task. In this paradigm, participants are presented with a series of stimuli, some of which require a response (go) and others require withholding responses (no-go). Imaging studies have taken advantage of this behavioral phenomenon and new functional magnetic resonance imaging (fMRI) analysis techniques that allow the assessment of activation specifically associated with collections of single, pseudorandomly distributed trials. Several studies have reported foci in the RIFG linked to no-go trials (Garavan, Ross, & Stein, 1999; Konishi et al., 1998; see also Kawashima et al., 1996) that are highly similar to the one observed in the present study. Importantly, selection demands should be equivalent and response code activation should be greater or no different during the go trials compared to the no-go trials, indicating that the operation of the inhibition process may be critical for activating this region.

Konishi, Nakajima, Uchida, Kikyo, et al. (1999) compared the activation associated with set-shifting to the activation associated with no-go trials and found common foci located in the inferior frontal gyrus, predominantly in the right hemisphere. As pointed out by the researchers, one common feature of set-shifting and go/no-go tasks is the need to inhibit latent responses induced by either the no-go stimuli or the irrelevant dimensions of the target stimuli. Other evidence that inhibition may serve as the best characterization of RIFG's function comes from a consideration of the computational requirements of the go/no-go task. Here, the consistent finding in imaging studies using this task is that the RIFG is more active during no-go trials compared to go trials. Moreover, Kawashima et al. (1996) compared activation during a response selection task and a go/no-go task in the same group of participants and found that relative to a control task, only the go/no-go task induced significant increases in the right frontal cortex, including the RIFG. In sum, the strong correspondences between the RIFG focus observed in the present study and those reported in go/no-go and set-shifting studies suggest that response inhibition may

provide the most succinct characterization of this region's function.

Lateralization

Frontal activation was lateralized to the right hemisphere, despite the fact that both the stimuli and responses were symmetric with respect to the body's primary axis (e.g., the flanking stimuli were presented to both visual hemifields, and equal numbers of right- and left-hand responses were made in both the congruent and incongruent epochs). The predominance of right-sided activation is shared by the no-go studies (e.g., Garavan et al., 1999; Konishi et al., 1998; Kawashima et al., 1996), suggesting a specialized role for the right prefrontal lobe in the resolution of response competition.

Activation in the RIFG without corresponding activation in the LIFG has been reported in a wide range of studies that potentially share a requirement for inhibitory processes. Fink et al. (1999) report a similar focus of activation linked to a mismatch between intentions, proprioception, and visual feedback during the performance of hand movements. The focus in the RIFG was the only one in their study whose activation depended on an interaction between the veridicality of the feedback and the phase relationship of the hand movements. This condition caused the highest degree of psychological conflict according to a postexperimental interview, consistent with the notion that it required the greatest contribution from inhibitory processes to squelch the tendency to move in a compatible manner to the visual feedback.

Other studies indicate that selection among verbal responses may result in an activation of a homologous region in the left ventral prefrontal cortex. For example, Thompson-Schill and colleagues (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Thompson-Schill, D'Esposito, & Kan, 1999; see also Desmond, Gabrieli, & Glover, 1998) examined frontal activity during a word-generation task. They found that a region in the left inferior frontal cortex, located in a region closely mirroring the foci described above, was sensitive to the number of competing response alternatives that confronted participants. Further evidence for a homologous left-hemisphere region that inhibits conflicting verbal information comes from imaging studies of working memory tasks involving letters performed by D'Esposito, Postle, Jonides, and Smith (1998) and Jonides, Smith, Marshuetz, Koeppe, and Reuter-Lorenz (1998). These researchers identified regions that became more active during a mnemonic search task when the letter probe was an item that was not in the present set but had appeared in a recent set. Significant increases were observed in the left inferior frontal cortex for trials with nontarget probes that had recently been targets compared to trials with nontarget probes that had not recently been targets. The former trial-type likely in-

volves more response conflict relative to the latter, because the nontarget probe was previously associated with a positive response. Thus, this frontal site may embody the verbal analog to the one identified in the present study. A very similar focus was reported by Taylor, Kornblum, Lauber, Minoshima, and Koeppel (1997) as being specifically related to selecting the correct verbal response during the Stroop task.

The left and right ventral regions may be necessary to inhibit inappropriate options when multiple responses are evoked by the stimuli. In keeping with the classical conception of hemispheric functional asymmetry, the left hemisphere structure may be most critical when the task involves linguistic processing and the right hemisphere structure most critical when the responses are coded with coordinates in egocentric space.

Neuropsychological Studies

Patient studies have also emphasized the role of the frontal lobes in the performance of the flanker task. Rafal et al. (1996) tested a group of patients with prefrontal lesions on a lateralized version of the flanker task and found reduced congruency effects when the flanker appeared in the visual hemifield that was contralateral to the side of the injury. Rafal et al. contend that the prefrontal cortex houses a response code that is activated by the flanking stimuli (i.e., the response code activation hypothesis). The present findings are consistent with this proposal, although we have argued based on correspondences with other studies that the increase reflects the engagement of inhibitory processes.

In this regard, it is useful to consider the laterality of the prefrontal focus. Whereas the activation observed in the present study is restricted to the right hemisphere, Rafal et al. (1996) tested individuals with both left- and right-hemisphere damage, with the majority (7 of 10) having lesions in the left-hemisphere. However, on average, the right-hemisphere patients show a similar pattern of flanker effects to the left hemisphere patients, with slightly larger costs for incongruent flankers. Error rates were less than 5% when averaged across participants, but they were not reported for individual patients. In isolation, the data from the right hemisphere patients are only weakly supportive of either the response-code activation or the response-code inhibition hypothesis.

Left Anterior Parietal Cortex

The left anterior parietal lobe (BA 40) also increased activity during the incongruent epochs. Highly similar parietal foci have been reported during the performance of set-switching (Konishi et al., 1998: $-45 -36 -48$; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1999: $-41 -32 -41$; Nagahama et al., 1996: $-40 -54 -40$; Berma et al., 1995: $-38 -44 -40$) and go/no-go tasks

(Garavan et al., 1999: $-44 -39 -40$), reinforcing the proposition that flanker, go/no-go, and set-shifting tasks engage a common set of processes.

Increased activation during set-shifting tasks is consistent with the response code activation, response code selection, and response code inhibition hypotheses. However, comparing go trials and no-go trials in the go/no-go task provides a means to dissociate these processes. In the Garavan et al. (1999) study the left anterior parietal lobe shows significantly greater activation during no-go stimuli trials, whereas in the Konishi et al. (1998) study the activity is associated with go trials. Consideration of the specific tasks employed by these researchers provides some potential explanations for these apparently discrepant results. In the Garavan et al. experiment, the same stimuli were used for go and (less frequently) no-go trials and the appropriate response was determined by the context in which this stimulus occurred. In contrast, the Konishi et al. experiment used stimuli on no-go trials that were not mapped to any overt response. Thus, it is reasonable to assume that the no-go trials in the Garavan et al. experiment activated brain structures housing specific response codes more strongly than the no-go trials in the Konishi et al. experiment.

The anterior parietal lobe, particularly in the left cerebral hemisphere, has been identified in studies using a wide variety of motor tasks, including motor sequence learning (Hazeltine et al., 1997; Grafton et al., 1995; Jenkins et al., 1994), motor preparation (Dieber et al., 1996), and motor imagery (Decety et al., 1994). Like the present experiment, all of these studies involve comparisons between conditions that are equivalent in terms of the number of overt movements. Thus, the activation presumably reflects the representation of action codes that is independent of actual execution. For this reason, the response code activation explanation seems to provide the most likely account for the recruitment of this brain region. We propose that the increases observed during the incongruent epochs result from the activation of the competing response codes by the flanking stimuli. During the epochs of congruent stimuli, the response codes activated by the flankers overlap with those of the targets.

Two studies have examined performance on the flanker task of individuals with damage to the parietal lobe. As with the frontal studies, the laterality of the lesions complicates the interpretation of these studies with regard to the present results. First, Cohen et al. (1995) tested two parietal patients on the flanker task and determined that they showed similar costs to controls for incongruent trials. One of the individuals had extensive lesions primarily involving the left parietal and temporal lobes; the other had extensive lesions in the right hemisphere involving parietal, temporal, and frontal cortex, including the RIFG. The principal finding was that both patients showed normal

flanker effects, although the left-hemisphere patient produced extremely slow reaction times, well over 1800 msec in the fastest condition, and high error rates. This general difficulty may reflect a deficit in the ability to transduce the visual stimuli into the appropriate response codes. A later experiment by Ro, Cohen, Ivry, and Rafal (1998) used a larger group of patients with more focal lesions and determined that an intact temporal–parietal junction, which is posterior to the region identified in the present study, was necessary to observe normal flanker effects. However, only one patient with left hemisphere damage was included in the critical group, and this individual showed normal flanker effects.

Superior Parietal and Supplementary Motor Cortices

In contrast to the strong correspondences obtained for the inferior frontal and inferior parietal foci, there have been few reports of superior parietal activity associated with related tasks. Neither Garavan et al. (1999) nor Kawashima et al. (1996) reported activation in area 7 during the go/no-go task (Konishi et al., 1998 did not scan this region of the brain during their experiment). The set-shifting experiments (e.g., Konishi et al., 1998; Nagahama et al., 1996; Berman et al., 1995) did not observe increases in superior parietal cortex, although in some cases it is unclear whether data were collected from this portion of the brain. Finally, imaging studies of the Stroop task also do not report foci in the superior parietal lobe (Bush et al., 1998; Taylor et al., 1997; Bench et al., 1993).

One aspect of the flanker task that differentiates it from the go/no-go, set-shifting, and Stroop tasks is that the irrelevant information is presented in a distinct location from the relevant information. Given that neuroimaging and neurophysiological work has linked the superior parietal region to spatial attention, it seems reasonable to suggest that the increases in activation observed during the incongruent epochs may result from greater demands placed on visual attention during these trials. When the flanking stimuli indicate a different response than the target, attentional mechanisms may facilitate performance by limiting the input from inappropriate regions of the visual field to the selection processes.

Like the activation observed in the superior parietal region, the activation detected in the SMA does not correspond to foci typically reported in the set-shifting or Stroop tasks. However, in many of the relevant studies it is not clear that the SMA fell within the scanner's field of view during the experiment. The SMA is associated with motor planning, and thus the observed increases may reflect the activation of the competing response codes by the incongruent flankers (but see Diamond [1990] for evidence that the SMA may

be necessary for response inhibition). The focus observed here appears near the border of the SMA and preSMA and extends laterally into premotor regions (see Figure 3). Both these structures are strongly linked with motor planning, and their activation would fit nicely with the response-code activation hypothesis. Garavan et al. (1999) proposed that the preSMA is critical for response inhibition whereas the SMA proper plays a role in response execution. The present results are not inconsistent with this framework, except that the amount of actual execution is constant across the congruent and incongruent epochs. It is possible that the anterior portion of the activation in the preSMA reflects response inhibition and the posterior portion reflects response code activation.

Anterior Cingulate Cortex

One interesting null result is the lack of activation in the anterior cingulate. Some neuropsychological research has suggested that the right prefrontal cortex is important for performance on the Stroop task (Vendrell et al., 1995). However, the dominant finding in the neuroimaging literature is that the anterior cingulate is critical for resolving Stroop interference (Bush et al., 1998; Bench et al., 1993; Pardo et al., 1990), although activity in the lateral regions of the cortex has also been observed (Taylor et al., 1997).

There are several candidate reasons for the failure to observe significant increases in that region in the present study using the flanker task. The present study may have lacked sufficient power to detect the changes in this region given that only eight participants were tested. Nonetheless, highly significant changes were observed in several brain regions with this design. Moreover, a re-analysis of the data with a lower probability threshold ($p < .05$) did not reveal activation in this region. Taylor et al. (1997) has suggested that the anterior cingulate activation often observed in the Stroop task is not related to selection per se, but instead relates to generic anticipatory processes that come on-line when response conflict is expected (cf. Murtha, Chertkow, Beauregard, Dixon, & Evans, 1996). Since participants reported that they did not perceive the blocked structure of the congruent and incongruent trials, this hypothesis could explain why no such activation was observed in the present experiment.

In this regard, it is useful to consider Botvinick et al. (1999), who report that the anterior cingulate is only active during the flanker task when an incongruent trial follows a congruent trial. Given that only 1 in 12 of the incongruent trials followed congruent trials in the present study, our ability to detect regions that respond in this way were severely limited. Following this logic, the neural structures identified in the present study may comprise a complementary system to the one described by Botvinick et al. The anterior cingulate may come on-

line when a change in response conflict is detected and the circuit composed of the RIFG and parietal areas may resolve this conflict. The behavioral data from the present study provides some preliminary evidence that distinct sets of inhibitory processes are in operation. In sum, the null result in the anterior cingulate may stem from the greater predictability of interference during the epoch experimental design.

An alternative hypothesis relates to the nature of the interference. In many cases in which anterior cingulate activation is observed, including the Stroop studies and the flanker task used by Botvinick et al. (1999), the irrelevant stimulus dimension is highly congruent with the inappropriate response. The magnitude of Stroop interference is contingent on which stimulus dimension is relevant and how participants produce their responses (Virzi & Egeth, 1985), suggesting that previously learned associations between the stimuli and the responses may play a critical role in this form of interference. In contrast, the present experiment used stimulus features that were not inherently congruent with the responses. This lack of natural compatibility also tends to be the case in the imaged versions of the set-shifting (e.g., Konishi, Nakajima, Uchida, Kikyo, et al., 1999; Konishi et al., 1998; Nagahama et al., 1996; Berman et al., 1995) and go/no-go tasks (e.g., Garavan et al., 1999; Konishi, Nakajima, Uchida, Sekihara, et al., 1999). There have been reports of increased activity in the anterior cingulate during tasks without obvious S–R compatibility, but in at least some of these cases (e.g., Carter et al., 1998), the activation is associated with responses that are made less frequently to a given stimulus.

In the Stroop task, the competition may exist between a well-learned response and one more reliant on working memory processes. That is, with high S–R compatibility, working memory processes may not be engaged to translate the stimuli into the appropriate actions. When the competing response originates from outside working memory systems, the cingulate may be necessary to gate signals from the appropriate structures to the motor output systems (Paus, Petrides, Evans, & Meyer, 1993; see also Turken & Swick, 1999). In contrast, in the flanker (and set-shifting) tasks, the competition is often restricted to equivalently arbitrary mappings. Thus, a speculative explanation for the pattern of results across these studies is that interference among competing rules within working memory may predominantly engage systems within the RIFG.

Summary

The flanker task uses a single set of S–R mapping instructions and manipulates competition without changing the compatibility between stimuli and responses. These properties make it ideally suited to isolate the neural structures associated with response competition. However, even in this case, the success-

ful resolution of response competition undoubtedly involves multiple processes. The relationship between the results of the present study and those from other imaging experiments suggests that the left anterior parietal lobe may support representations of the potential responses and that the right inferior prefrontal cortex may be critical for the inhibition of actions that are not selected.

METHODS

Task

Eight right-handed participants (five female; mean age 21.0 years; range: 18–24) performed the flanker task and two other experimental tasks inside the GE 1.5-T MRI system. All of the participants provided informed consent before beginning the experiment according to the protocols established by Stanford University's Internal Review Board. Before performing the task in the scanner, participants practiced one run in a separate session to familiarize them with the task. The practice runs were identical to the experimental runs in every way except that congruent and incongruent trials were presented in a random order.

A run of trials consisted of 120 trials, each lasting 1.44 sec. A trial consisted of 1 sec of stimulus presentation followed by 0.44 sec of a fixation cross. The stimulus presentation consisted of three circles presented along the horizontal meridian. Each circle subtended approximately 1.0° of visual angle and was separated from its nearest neighbors by approximately 0.4° , edge to edge. The circles could be one of four colors: red, green, blue, or yellow. If the center circle was red or green, participants were to respond by pressing the leftmost button on the response board; if the center circle was blue or yellow, they were to respond by pressing the rightmost button. Unbeknownst to participants, the trials were organized into ten 12-trial epochs. There were two types of epochs, depicted in Figure 1. In the congruent epochs, the flanking circles differed in color from the center circle but indicated the same response (e.g., a red circle flanked by green), and in the incongruent epochs, the center circles were flanked by circles indicating a different response (e.g., a red circle flanked by blue).

Participants were told to respond as quickly and accurately as possible to the center circle in the display while ignoring the flanking stimuli. Responses to red or green targets were made with a keypress by the left hand and responses to blue or yellow targets were made with a keypress by the right hand. Participants were told that if they made any mistakes they should not correct them but should instead prepare for the next trial. No feedback was provided during the experiment, but participants were interviewed after performing the experiment. They were asked (1) if they used any special strategies during the experiment and (2) if they ever noticed the task change in any way. Five of

the participants reported noticing that on some trials the flankers indicated the same response as the target and on others it did not, but none reported being aware of the blocked nature of the congruent and incongruent stimuli.

Imaging

Sixteen sagittal slices (11.2 cm FOV, 7-mm slice thickness, 0-mm skip) were imaged at a 0° angle to the parasagittal fissure. T1-weighted spin-echo structural images were first collected for the inplane slices. Functional data were acquired every 2.88 sec using a T2*-weighted gradient-echo spiral pulse sequence (Glover & Lai, 1998) with parameters of TR = 1.44 sec, TE = 40 msec, flip angle = 80°, and two spiral interleaves. A total of 60 images were collected during the 172.8-sec scan. A custom quadrature receive-only birdcage head coil was used. Head motion was minimized using a bite-bar formed from the participant's dental impression; residual motion was corrected using an automated registration algorithm (Woods, Cherry, & Mazziotta, 1992).

Data Analysis

Data were analyzed using SPM96 (Wellcome Department of Cognitive Neurology, London) implemented in MATLAB (Mathworks, Sherborn, MA). Following reconstruction and motion correction using AIR (Woods et al., 1992), all images were normalized into a standard stereotactic space (Talairach & Tournoux, 1988) by aligning each image to a normalized template using a 12-parameter affine transformation. Normalized images were then smoothed using an 8-mm FWHM Gaussian kernel.

Data were analyzed using a mixed-effects general linear model treating subjects as a random effect. Adjusted mean images for the congruent and incongruent epochs were first created for each participant from the smoothed images. These images were computed by convolving the boxcar function reflecting the congruent versus incongruent epochs with an approximate hemodynamic response function. A high pass temporal filter of 69.12 sec (2.4 cycles) was applied to the image data to remove low-frequency changes in activation. Activations in each voxel were normalized by proportional scaling. The resulting adjusted mean images were then submitted to a random effects one-way ANOVA with 7 degrees of freedom using one image for each participant in each of the two conditions. Foci were reported for significant differences between the two conditions at a .005 probability level (uncorrected) across 50 contiguous voxels. An uncorrected height threshold was used because of the relatively low power of the random effects analysis, and a relatively large spatial extent threshold was used in order to emphasize larger regions that were significant at the relatively liberal height threshold.

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