

# Contributions of the Prefrontal Cortex and Basal Ganglia to Set Shifting

Susan M. Ravizza and Michael A. Ciranni

## Abstract

■ Impairments of set shifting have been associated with damage to both the prefrontal cortex (PFC) and to the basal ganglia. The purpose of these experiments was to determine whether damage to the PFC was associated with shifting impairments per se or whether any switching deficits could be attributed to a reduction of working memory capacity. In contrast, shifting impairments were expected for Parkinson patients regardless of memory load, given that these patients seem to have no cognitive deficits other than when having to shift set. To vary working memory demands, a cue to the relevant dimension (letter or shape)

in an odd-man-out task was presented or withheld. Pathology to prefrontal areas associated with normal aging was not linked to shifting deficits when working memory load was reduced in a comparison of older and younger adults (Experiment 1). In contrast, set-shifting abilities were still impaired for stroke patients with prefrontal damage regardless of working memory demands (Experiment 2). Parkinson patients were relatively unimpaired on this task (Experiment 2), but began to display shifting deficits when response competition was present in the display (Experiment 3). ■

## INTRODUCTION

People are faster when they can execute the same task repeatedly than when they must stop performing one task to begin another (Mayr & Keele, 2000; Meiran, 1996; Rogers & Monsell, 1995; Allport, Styles, & Hsieh, 1994). Costs to response speed when switching tasks are thought to reflect the reconfiguration of stimulus or response sets associated with each task (Meiran, 2000). As switching between tasks requires that goals or responses be altered to fit the rules of a new situation, set shifting has been claimed to be a process of executive control (Rogers et al., 1998)—the ability to plan and direct goal-oriented behavior. Accordingly, impairments of set shifting have been displayed by those with damage to the prefrontal cortex (PFC, Rogers et al., 1998; Owen et al., 1993; Robinson, Heaton, Lehman, & Stilson, 1980), an area considered to be the site of executive systems (Burgess & Shallice, 1996; Luria, 1966). Moreover, set-shifting tasks have been associated with increased activation of the PFC in imaging studies (Rogers, Andrews, Grasby, Brooks, & Robbins, 2000; Konishi et al., 1998).

Deterioration of frontal regions as a function of age has also been linked to deficits in task switching (Keys & White, 2000; Kramer, Hahn, & Gopher, 1999; Robbins et al., 1998). Normal aging processes affect frontal lobe functioning to a greater degree than other areas of the cortex (Raz et al., 1997; Azari, Rapoport, Salerno, &

Grady, 1992; Ivy, MacLeod, Petit, & Markus, 1992), which may result in diminished performance on tasks relying on these neural areas. In addition to slower processing speeds in general (see Salthouse, 1985, for a review), set-shifting impairments have been reported for older adults (Keys & White, 2000; Kramer et al., 1999; Robbins et al., 1998). Of course, older adults are typically used as a control group in studies demonstrating set-shifting impairments for prefrontal patients. This suggests that prefrontal patients must have a more severe deficit than those who have difficulty switching tasks because of age. However, the extent of the set-shifting deficit for aging individuals in comparison to prefrontal patients has not been tested.

In addition to executive control deficits, damage to prefrontal areas has been associated with reduced working memory capacity (Goldman-Rakic, 1992; Petrides, 1991; Janowsky, Shimamura, & Squire, 1989; Milner, Petrides, & Smith, 1985). Thus, the ability to keep plans and goals in mind as well as the ability to implement these goals depends upon an intact PFC. In the case of switching tasks, the relative importance of a normal working memory capacity to shifting efficiency has not been assessed. Perhaps prefrontal patients and older adults perform more poorly on set-shifting tasks because of the greater demand placed on working memory when a task switch occurs. All of the tasks in which prefrontal patients display set-shifting impairments also place demands on working memory. For example, tests of discrimination learning and the Wisconsin Card Sorting

Task (WCST) rely on the ability to remember one's errors over time in order to determine the correct sorting rule. Furthermore, Rogers et al. (1998) reported that prefrontal patients displayed a shifting deficit only when the task required participants to remember an arbitrary association between the color of the cue and the rule for responding. When word cues were used instead of colors, prefrontal patients performed as well as controls. Moreover, one study of set shifting and aging has suggested that older adults may not have a switching deficit per se, but that declining working memory functions may underlie their poor performance on shifting tasks (Kray & Lindenberger, 2000).

Interestingly, impairments in set shifting have not been exclusively linked to dysfunction of the PFC. Patients with damage to subcortical areas including the basal ganglia and cerebellum have been shown to be impaired when having to shift attention (Hayes, Davidson, Keele, & Rafal, 1998; Courchesne et al., 1994; Owen et al., 1993; Akshoomoff & Courchesne, 1992; Brown & Marsden, 1988). In the case of cerebellar damage, switching deficits may occur only when motor demands are high (Ravizza & Ivry, 2001). However, patients with basal ganglia dysfunction due to Parkinson's disease exhibit shifting impairments even when motor demands are reduced or the task does not require rapid responses (Ravizza & Ivry, 2001; Downes, Roberts, Sahakian, & Evenden, 1988; Taylor, Saint-Cyr, & Lang, 1986). Basal ganglia damage has been linked to impaired performance on a number of switching tasks that assess both the accuracy (Owen et al., 1993; Downes et al., 1989; Gotham, Brown, & Marsden, 1988; Taylor et al., 1986) and speed of set shifting (Hayes et al., 1998; Brown & Marsden, 1988).

Although damage to the PFC has been associated with deficits in memory tasks, cognitive deficits in Parkinson's disease appear to be restricted to those tasks where the rules of responding alternate from trial to trial. Parkinson patients are unimpaired at tasks that do not require shifting set such as mental rotation (Duncombe, Bradshaw, Iansek, & Phillips, 1994), recall and recognition (Russ & Seger, 1995; Taylor et al., 1986), strategic planning (Morris, Downes, Sahakian, & Evenden, 1988), and orienting of spatial attention (Rafal, Posner, Walker, & Friedrich, 1984). It is more likely, then, that patients with Parkinson's disease have a pure shifting deficit that is unrelated to working memory demands or other cognitive processes.

One goal of these experiments was to determine whether patients with damage to the PFC are impaired at task switching even if working memory demands are low. Toward this end, we used an odd-man-out task where participants responded to the locations of dissimilar targets by pressing buttons that were in the same spatial configuration as the stimuli on the screen thereby creating an intuitive stimulus-response mapping that could be easily recalled. The odd-man-out could be

present on one of two dimensions (letter or shape) that could vary from trial to trial. Cues that indicated the relevant dimension were straightforward (words or icons) and did not require participants to remember an arbitrary association between cue and stimulus properties. We also varied working memory demands in our task by withholding the cue in some conditions. Without the cue, the task becomes more difficult as one has to remember which dimensions and locations have been searched as well as being able to shift between dimensions. In this way, we can assess the interaction of set shifting and working memory demands for each group of participants. We also examined the extent of shifting impairments for two types of PFC pathology—that due to normal aging and that due to stroke/tumor resection.

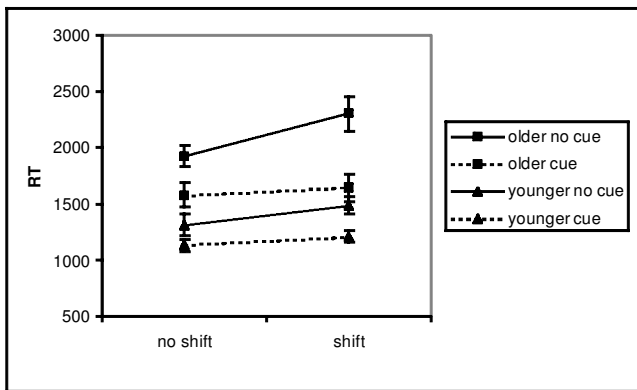
The first experiment compared the performance of older and younger individuals on our set-shifting task while varying working memory load. Prefrontal and Parkinson patients were tested on this same task in Experiment 2 to assess the contribution of these areas to set-shifting abilities. The third experiment determines the effects of cue strength on shifting difficulty for both the older and neurologically impaired groups.

## EXPERIMENT 1

The effects of age on set-shifting performance for otherwise healthy individuals were assessed under varying working memory demands in this first experiment. As stated previously, the PFC is affected most by the aging process and deficits in the ability to shift set have been reported for older adults (Kramer et al., 1999; Robbins et al., 1998). Controversy exists as to whether working memory problems are at the root of this apparent shifting deficit (Kray & Lindenberger, 2000), however. If older adults are impaired at shifting tasks only when working memory demands are high, then any shifting impairments shown by the older group in the uncued condition should be remedied by the presentation of a cue. Given the general slowing of response speed with age, the older group is predicted to perform more slowly than younger adults.

## Results and Discussion

The effects of cueing and age on shift cost (the difference in reaction time, RT, between shift and no-shift trials) were examined first. The RTs of the older and younger groups were subjected to a 2 (cue)  $\times$  2 (shift) repeated measures ANOVA using group as a between-subjects factor. As expected, a main effect of group,  $F(1,16) = 21.3, p < .01$ , indicated that older participants were slower than the younger adults at the task (see Figure 1). RTs were also slower when participants did not have a cue,  $F(1,16) = 95.68, p < .01$ , or when the target shifted dimension,  $F(1,16) = 54.82, p < .01$ .



**Figure 1.** RTs in the shifting and cueing conditions for older and younger participants in Experiment 1.

However, shift cost was reduced when a cue was present [Shift  $\times$  Cue:  $F(1,16) = 25.13, p < .01$ ]. This result is in accordance with previous set-shifting studies (Mayr & Keele, 2000; Meiran, 1996; Rogers & Monsell, 1995) finding that shift costs become smaller when participants are able to execute part of the switch in advance. Most importantly, a significant three-way interaction of shifting, cueing, and group,  $F(1,16) = 7.55, p < .05$ , indicated that the switch costs of the older participants decreased to a greater degree than the younger group. Remarkably, older adults' shift costs were actually 15 msec lower than younger adults in the cued condition. Thus, the older group showed no shifting deficit when a cue was presented, although they were impaired when the cue was withheld.

To determine whether it was easier to shift to either the letter or shape dimension, RTs were analyzed by means of a repeated measures ANOVA with the relevant dimension (letter or shape), presence of a shift, and cue condition as within-subjects factors and group as a between-subjects factor. Given that the four-way interaction was significant,  $F(1,16) = 7.79, p < .05$ , separate Cue  $\times$  Shift  $\times$  Dimension repeated measures ANOVAs were performed for each group. In addition to the effects of shifting and cueing as reported above, a main effect of stimulus dimension,  $F(1,9) = 5.4, p < .05$ , was obtained indicating that participants in the younger group were faster at detecting odd-men-out on the letter dimension than the shape dimension. Surprisingly, this was not the case for the older adults who were just as fast responding to either dimension. Given that the older adults showed more benefits from the cue in terms of overall speed and switching costs, it might be that they were less influenced by the greater "pop-out" effect from the letters. As the task was solvable without the cue, younger participants may have been more likely to use a bottom-up strategy while older adults may have used more controlled processes even in the uncued conditions.

A marginally significant interaction of Cue  $\times$  Dimension was found for the younger group,  $F(1,9) = 4.05,$

$p = .075$ , but shifting did not interact with stimulus dimension,  $F(1,9) = .47, p > .1$ . Thus, the cue was more helpful when shape was the relevant dimension for younger participants. However, switching was not disproportionately affected by the dimension of the previously relevant task set—it was just as difficult to shift from letter to shape than from shape to letter. In contrast, a three-way interaction of Dimension  $\times$  Cueing  $\times$  Shifting was obtained,  $F(1,7) = .47, p < .05$ , for older participants where the cue reduced the cost of switching to shapes more than the cost of switching to the letter dimension. Although it was manifest in different ways by younger and older participants, it appears to be the case that cues were more helpful in processing the shape dimension than the letter dimension for both groups.

The average percentage of errors was about 2% and there was no difference in error rate between groups.

## Conclusions

The process of aging in otherwise healthy individuals does not appear to disrupt the ability to switch between tasks. When given a cue to direct attention to the relevant dimension, older participants were able to switch between processing letters and shapes just as quickly as the younger group. However, shifting difficulty increased disproportionately for older participants when not given any guidance in the task. By withholding the cue, participants were required to devise a strategy for searching the display and had to remember where they had already looked. This process could only become more difficult when the target shifted dimensions. Thus, PFC pathology associated with normal aging does not affect switching abilities per se although it may affect working memory capacity or general problem-solving abilities.

## EXPERIMENT 2

Damage to the PFC due to the removal of tumors or stroke has also been associated with impairments of set shifting (Rogers et al., 1998; Owen et al., 1993; Robinson et al., 1980). However, the locus of set-shifting computations has not been narrowed down to a restricted area of the PFC. Indeed, both the dorsolateral and ventrolateral PFC have been associated with set-shifting abilities in neuropsychological and neuroimaging studies (Konishi et al., 1998; Rogers et al., 1998, 2000; Owen et al., 1993), and no definitive laterality effects have been demonstrated. Therefore, patients with left- or right-hemisphere lesions to either dorsolateral or ventrolateral areas were included in the following experiments.

Shifting costs for older adults vanished when working memory demands were minimized, and it may be that patients with damage to the PFC will show similar benefits. Patients with PFC lesions are known to have working memory impairments that are more severe than

older controls (Janowsky et al., 1989; Milner et al., 1985). In fact, for the seven PFC patients that had been given the digit span subtest of the WAIS in our group, six scored well below the mean of the control subjects (see Methods section). It is predicted that shifting costs in the cued condition will be reduced to a greater degree for PFC patients than for the older controls tested in Experiment 1. In contrast, Parkinson patients are not expected to be disproportionately affected by working memory demands and their shift costs should remain higher than controls even when a cue is presented.

## Results and Discussion

Separate 2 (cue) × 2 (shift) repeated measures ANOVAs were run comparing the RTs of each patient group to that of the older controls tested in Experiment 1.

### PFC Patients and Older Controls

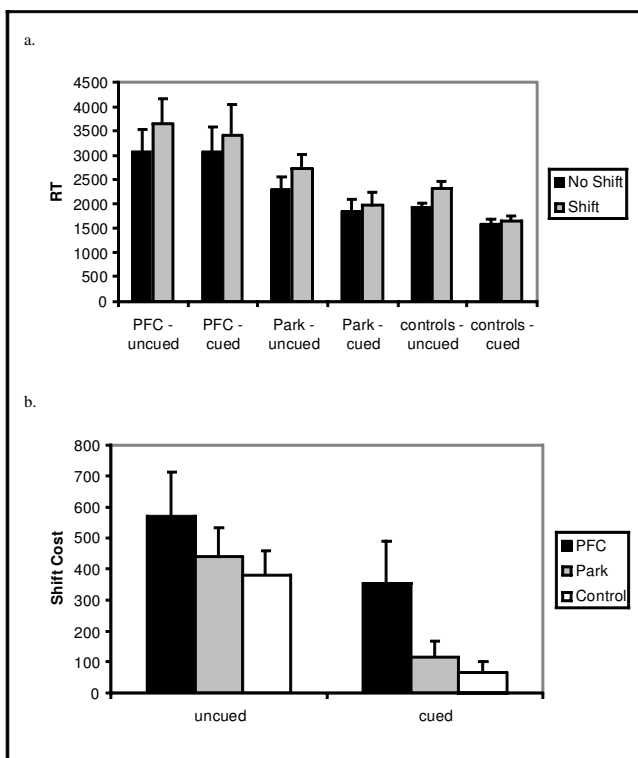
As in Experiment 1, main effects of cueing,  $F(1,13) = 18.83, p < .01$ , and shifting,  $F(1,13) = 30.68, p < .01$ , were obtained as well as a significant interaction of the two,  $F(1,13) = 12.52, p < .01$  (see Figure 2a and b). Shifting costs were reduced by the presentation of a cue, however, the lack of a three-way interaction (Group × Shift × Cue) indicated that PFC patients did not find a greater reduction in switch cost from the cue than controls subjects. PFC patients were slower than the

control group in all conditions and the marginally significant interaction of Shifting × Group indicated that their shift costs were higher as well—even in the cued conditions,  $F(1,13) = 3.77, p = .074$ . Thus, the presentation of a cue did not make the switching impairments of the prefrontal patients disappear. These patients still had difficulty in shifting set even when working memory demands were quite low. Problems with executive control occur over and above a reduction of working memory capacity.

Interestingly, PFC patients did not respond more quickly when given a cue [Cue × Group:  $F(1,13) = 7.46, p < .05$ . Indeed, patients' RTs were the same in the no-switch trials regardless of whether a cue was present or absent. One reason for this may be that the patients took longer to process the cue than controls. In examining the results, this does not appear to be due to any potential language difficulties of the left-hemisphere patients. In fact, one right-hemisphere patient showed no effect of the cue and was actually 300 msec slower in the cued conditions than the uncued conditions. However, it may be that the ability to apply the information given in the cue is generally slower and so the patients do not show any benefits of the cue in overall speed. Although prefrontal patients were able to utilize the cue to reduce shifting costs, their difficulty in processing cue information may have slowed RTs in both shift and no-shift trials of the cued conditions.

Alternatively, PFC patients may be using different strategies than control subjects in solving the task. Given that the task is solvable without the cue, patients may be more likely to use the cue in cases where the target switches dimension. Rather than using the cue in all conditions, they may be trying to solve the problem at first by simply scanning the display and searching for the target in a bottom-up fashion. When this proves more difficult in the case of a task switch, they use the cue to remind them of the other potential dimension. If this were the case, any benefits of the cue to shift cost would be reduced as the patients would not be implementing cue information on every trial. In the next experiment, the task will be altered to become unsolvable without the cue to minimize potential differences in strategy.

The effects of target dimension on RT were assessed by use of a 2 (cue) × 2 (shift) × 2 (dimension) repeated measures ANOVA with group as the between-subjects factor. As in Experiment 1, a significant four-way interaction was obtained,  $F(1,13) = 4.67, p = .05$ , and so a separate analysis was run for the PFC patients. The results for the older control subjects are summarized in the Results and Discussion section of Experiment 1. A marginal effect of target dimension was obtained,  $F(1,6) = 4.78, p = .071$ , for prefrontal patients, but none of the other interactions were significant. Similar to the younger participants in Experiment 1, prefrontal patients tended to be faster responding to letters than shapes. This may be further evidence, then, that PFC



**Figure 2.** The effects of cueing on (a) RT and (b) shift cost for older controls, PFC, and Parkinson patients in Experiment 2.

patients were processing the stimuli at times in a bottom-up fashion rather than in a controlled way. Both younger participants and PFC patients were influenced by the greater “pop-out” effect of the letters and showed less effects of the cue than older control subjects. In the case of the younger group, however, potential ceiling effects made it difficult to determine whether cue effects were really reduced compared to the older group. In contrast, the data for the prefrontal patients show a clear reduction in cue effects and a greater influence of target dimension.

Error rate did not differ between groups.

### *Parkinson Patients and Older Controls*

Parkinson patients performed remarkably well on this test of set shifting (see Figure 2a and b). They were not significantly slower than the older control group and there were no differences in shift costs or cueing effects between groups. This result is contrary to other tasks finding set-shifting impairments for Parkinson’s disease patients tested on their normal medication schedules (Hayes et al., 1998; Owen et al., 1993). One difference between our shifting task and those used by others is that the stimuli dictate only one possible response. For instance, in the task used by Hayes et al. (1998), both the color and shape dimension had a response associated with it and participants determined which dimension to respond to based on the cue. Although stimuli are present on both dimensions in our odd-man-out task, a target is displayed on only one of the dimensions. Thus, the difficulty in searching the display increases with the presentation of both letters and shapes, but there is no response competition between the two dimensions. Perhaps shifting difficulty will only occur when more than one response is potentially specified by the stimulus display. The next experiment will determine whether Parkinson patients will show greater shifting costs than controls when two odd-men-out are presented.

In contrast to the comparison of older controls and PFC patients, a four-way interaction of Group  $\times$  Target Dimension  $\times$  Cue  $\times$  Shift was not obtained in comparing the controls to the Parkinson patients. Parkinson patients responded to target dimension in the same manner as older controls—they were not faster at detecting targets on the letter dimension and shift costs were equivalent when shifting to either dimension. Thus, Parkinson patients displayed a great degree of top-down processing and were not as influenced by the dominance of the letters over the shapes in the display. As in Experiment 1, the significant interaction of target dimension, cueing, and shifting indicated that the cue was more helpful in switching to shape than to letter,  $F(1,12) = 6.63, p < .05$ .

Parkinson patients made slightly more errors than older controls,  $t(12) = -2.15, p = .053$ , but, overall,

the error rate was very small (Parkinson patients: 3% vs. older controls: 2%).

## **EXPERIMENT 3**

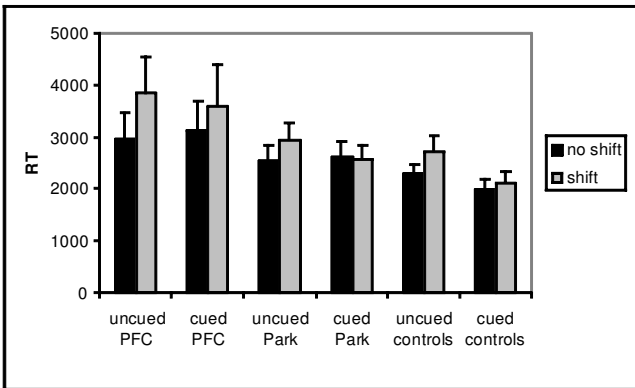
PFC patients were impaired at shifting set even when working memory demands were reduced by the presentation of a cue. However, the fact that these patients were not generally faster when given a cue made it difficult to determine whether set-shifting abilities were really impaired or whether the cue was being used ineffectively. If these patients were not using the cue on some trials, working memory load was not being manipulated effectively. Experiment 3 controlled for strategy use by requiring participants to use the cue on each trial. By presenting odd-men-out on both dimensions, we were able to determine whether set-shifting costs in Experiment 2 remained higher than controls because of poor problem-solving strategies or because these patients have set-shifting deficits per se. Moreover, cues were changed to be iconic so that any potential language difficulties would not interfere with cue processing.

In contrast to the PFC patients, Parkinson patients had very little difficulty with this task. Their performance was equal to that of the older controls except for a slight increase in error rate. It may be that Parkinson patients only experience difficulty when set shifting also involves selecting between two competing responses. Experiment 3 addressed this issue by examining the performance of these patients when two odd objects are presented at the same location versus different locations.

## **Results and Discussion**

### *Cued Versus Uncued–Unambiguous Conditions*

The conditions where one odd object was presented (unambiguous conditions) were examined to see whether the results of Experiment 2 would be replicated. The unambiguous conditions are exactly the same as those discussed in Experiment 2 except for the presentation of iconic rather than word cues. Thus, the condition where two odd objects were presented (ambiguous condition) was not examined in this section. The RTs for each patient group were submitted to a 2 (cue)  $\times$  2 (shift)  $\times$  2 (group) repeated measures ANOVA that compared their performance to that of a new set of controls subjects. The results for the unambiguous conditions were very similar to the results reported in Experiment 2. Prefrontal patients were slower than controls and the marginal Cue  $\times$  Group interaction,  $F(1,15) = 4.49, p = .051$ , indicated that they were not faster when given a cue (see Figure 3). As before, both groups showed similar reductions in shift costs when a cue was presented. Parkinson patients again showed no impairments in speed or shifting costs in this experiment.

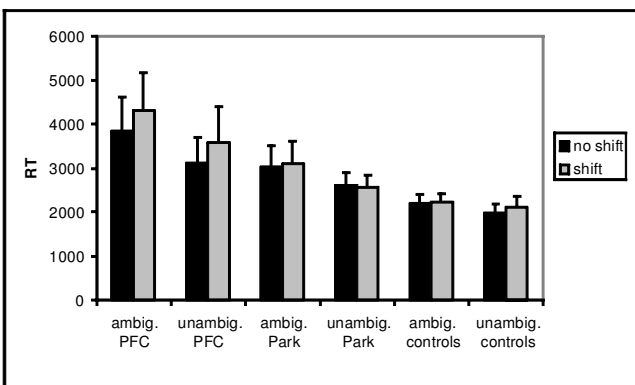


**Figure 3.** RTs in the unambiguous conditions (cued vs. uncued) for older controls, PFC, and Parkinson patients in Experiment 3.

*Cued Conditions—Ambiguous Versus Unambiguous*

Performance in both cued conditions were contrasted to assess the effects of the number of potential targets (ambiguity). Separate 2 (ambiguity) × 2 (shift) × 2 (group) repeated measures ANOVAs were run comparing the RTs of each patient group to that of the control group (see Figure 4). A main effect for ambiguity in both group comparisons indicated that responses were slowed when two targets were presented instead of one [PFC vs. controls:  $F(1,15) = 15.07, p < .01$ ; Parkinson patients vs. controls:  $F(1,15) = 4.50, p = .051$ ]. However, RTs for prefrontal patients were slowed to a greater degree than for control subjects [Ambiguity × Group:  $F(1,15) = 5.8, p < .05$ ]. Thus, increasing the general difficulty of the task by adding another odd-man-out was more detrimental to the PFC patients than for either the Parkinson patients or controls subjects.

A significant Shift × Group interaction,  $F(1,15) = 4.79, p < .05$ , together with the lack of a three-way interaction with ambiguity confirmed that the prefrontal groups' shifting cost was higher than that of the control group even when strategy use was controlled for by making cue processing mandatory. Given that the cue had to be processed on every trial in order to

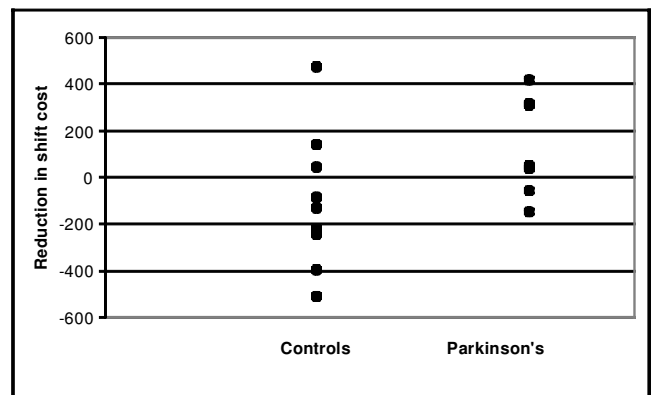


**Figure 4.** RTs in the cued conditions (ambiguous vs. unambiguous) for older controls, PFC, and Parkinson patients in Experiment 3.

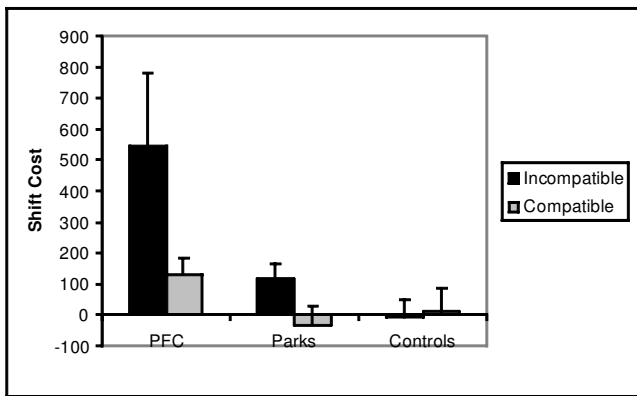
do the task, we know that the shifting impairments displayed by these patients are not due to ineffective strategies in using the cue. Although shifting costs for controls tended to decrease in the ambiguous condition, costs for prefrontal patients did not show a reliable pattern so that the interaction of Shift × Ambiguity was not significant. Aside from the main effects of group and shifting, no other differences were significant. Thus, damage to the PFC results in set-shifting difficulty over and above any reduction of working memory capacity.

In contrast, the three-way interaction of Group × Shift × Ambiguity approached significance in comparing Parkinson patients to controls,  $F(1,15) = 3.84, p = .069$ . As stated previously, shifting costs tended to decrease for controls when two odd-men-out were presented, but they tended to increase for the Parkinson patients. Although there was variability in the effects of the number of targets on shifting costs among both the control and Parkinson group, 70% of the control subjects showed a decrement in shifting costs whereas only 29% of the Parkinson patients did (see Figure 5). Thus, shifting became difficult for Parkinson patients only when response competition was present in the stimulus set.

Response competition was also assessed by examining shift costs when the targets on both dimensions were displayed in the same location (compatible) or different (incompatible) locations (see Figure 6). A 2 (group) × 2 (shift) × 2 (response compatibility) repeated measures ANOVA was run comparing each patient group to the control group. A marginally significant three-way interaction,  $F(1,15) = 3.43, p = .084$ , was obtained in comparing the PFC and control subjects. Whereas controls subjects' shift costs were equivalent regardless of the location of the two odd-men-out, prefrontal patients' shift costs tended to be smaller when targets were at compatible locations. Parkinson patients displayed this same pattern of results, but the three-way interaction was not significant.



**Figure 5.** Reduction in shift cost from the unambiguous condition to the ambiguous condition for older controls and Parkinson patients in Experiment 3.



**Figure 6.** Shift costs when the location of both odd objects was compatible or incompatible in Experiment 3.

Error rate ranged from 4% to 5% and did not differ between groups. Given that this experiment included one Parkinson patient who had undergone a pallidotomy procedure, we excluded this participant and ran all the statistical tests again. None of the results were changed by excluding this participant.

## GENERAL DISCUSSION

Shifting deficits have been associated with damage to both the PFC and to the basal ganglia. The purpose of these experiments was to determine whether damage to the PFC was associated with shifting impairments per se or whether any switching deficits could be attributed to a reduction of working memory capacity. On the other hand, shifting impairments were expected for Parkinson patients regardless of memory load given that these patients seem to have no cognitive deficits other than when having to shift set.

Although the older control group showed a marked decrease in shift costs when given a cue, PFC patients' shifting impairments did not vanish when working memory demands were reduced. Even when strategy use was controlled for in Experiment 3, shifting costs remained high for prefrontal patients. It may be argued that prefrontal patients' difficulty with goal-directed planning prevented them from utilizing the information presented in the cue. There was evidence that prefrontal patients took longer in processing the cue given that they were not faster in general when a cue was presented. However, prefrontal patients did show a decrease in shift costs in the cued conditions demonstrating that even if cue processing was slower it had similar effects in reducing shift costs. Thus, prefrontal patients' shifting impairments do not seem to be due to differences in the speed of extracting information from the cue or applying that information to the task. These experiments, then, constitute the first evidence that damage to the PFC results in set-shifting impairments over and above any reduction in working memory capacity.

In contrast, general deterioration of the prefrontal lobes as a function of aging is not associated with deficits in shifting set. Indeed, once working memory demands were attenuated, older adults' switching costs were on par with those of younger adults. The fact that the cue had a much greater effect on shift costs and that target dimension had less of an effect on response speed for older adults is in line with the finding that adults shift more attentional resources in response to cues than younger adults (Hartley, Kieley, & Slabach, 1990). Furthermore, older adults were not slower to utilize information contained in the cue. Unlike the prefrontal patients, older controls were much faster in the cued conditions than the uncued conditions.

Surprisingly, Parkinson patients were mostly unimpaired at this set-shifting task although these same patients showed difficulty with the WCST (see Methods section). Indeed, Parkinson patients began to show switching difficulties only when response competition was present in the stimulus display. Shifting may have become more difficult when two odd-men-out were presented in the ambiguous condition as it was harder to ignore the irrelevant dimension. In fact, response times for all groups became slower in this condition. Perhaps, Parkinson patients have a less severe deficit than prefrontal patients and will be impaired at shifting set only when the difficulty level is sufficiently high.

Although we were unable to measure this directly with our paradigm, it may be that the basal ganglia and PFC contribute in different ways to shifting tasks. Meiran (2000) has suggested several components necessary to task switching including the ability to switch between stimulus as well as response sets. Given the basal ganglia's role in motor coordination, this area may be more involved in switching between response sets than stimulus sets. It may seem strange that separate response sets would occur for each dimension in our task since the requirements for responding to targets were the same regardless of whether the odd-man-out was a letter or a shape. Nevertheless, it may be that separate response schemas are associated with each dimension even if the rules for responding are the same. For example, participants may have to recall a stimulus-specific rule such as "Press the key that spatially corresponds to the odd letter (shape)" rather than a more general rule that would apply both dimensions. The ability to shift from one response set to another may be more difficult if the response rules for the irrelevant dimension are being activated when odd-men-out appear on both dimensions.

Ravizza and Ivry (2001) found shifting impairments for Parkinson patients despite targets being presented singly rather than simultaneously. Although response competition should not occur for singly presented items, the stimuli were presented in a rapid, continuous stream with the next stimulus sometimes appearing before a response had been made. In such a case, response competition may still have been present in the display

**Table 1.** Participant Characteristics

	<i>Age</i>	<i>Education</i>	<i>Digit Span Subtest of WAIS</i>	<i>Number of Categories Sorted (WCST)</i>
Control ( <i>n</i> = 13)	68	14.4	11.08 ( <i>n</i> = 12)	5.2 ( <i>n</i> = 10)
Parkinson ( <i>n</i> = 9)	68	15.3	10.14 ( <i>n</i> = 7)	3 ( <i>n</i> = 6)
Frontal ( <i>n</i> = 8)	70	13.4	7.29 ( <i>n</i> = 7)	3.3 ( <i>n</i> = 4)

and, therefore, account for the shifting deficits found in those experiments. Thus, Parkinson patients may have a deficit in switching between response sets while prefrontal patients experience difficulty in shifting between both stimulus and response sets.

Alternatively, testing Parkinson patients while medicated may obscure differences between groups. Hayes et al. (1998) found that shifting deficits increased when Parkinson patients were unmedicated although they were still impaired at shifting regardless of the medication state. Moreover, medication may preferentially restore dopaminergic function to basal ganglia–dorsolateral PFC loops while other basal ganglia–cortical connections may suffer from an “overdosage” effect (Swainson et al., 2000; Gotham et al., 1988). Swainson et al. (2000) suggest that medicated Parkinson patients will be more impaired at tasks that rely on intact basal ganglia–orbito-frontal connections such as learning stimulus–reinforcement associations. Although shifting set requires learning these associations, difficulty in learning can be manipulated independently from the ability to shift per se. Medicated Parkinson patients may only show shifting impairments in tasks that require many trials of learning stimulus associations such as the WCST and discrimination learning tasks.

These experiments suggest that both the dorsolateral PFC and the basal ganglia are involved in the ability to shift set. Impairments of set shifting for PFC patients do not appear to be a result of their reduced working memory capacity, but derive from their difficulty in

reconfiguring stimulus and response sets. The lack of an impairment for Parkinson patients suggests that they either have a less severe deficit than the PFC patients or that our task did not tap the process that the basal ganglia is contributing to set shifting. It may be that the basal ganglia is involved in shifting response rather than stimulus sets or is indirectly contributing to shifting tasks because of its role in learning stimulus–reward associations over time.

## METHODS

### Participants

Ten undergraduates at the University of California, Berkeley participated in Experiment 1 for course credit. A total of 13 older adults, 9 patients with a diagnosis of idiopathic Parkinson’s disease, and 8 patients with lesions to the PFC were paid to participate in these experiments (see Table 1). All Parkinson patients were tested while on their normal medication schedules. One of the seven patients in Experiment 3 had undergone a pallidotomy for remediation of his symptoms (see Table 2). Six prefrontal patients exhibited focal lesions to the left while two patients exhibited right-hemisphere damage (see Figure 7). The bottom portion of Figure 7 displays the overlap of PFC patients’ lesions. Patients’ lesions primarily included ventrolateral portions of the inferior frontal gyrus (Brodmann’s area [BA] 44) and ventral portions of the precentral gyrus (BA 6 and 4). Damage extending to the dorsolateral

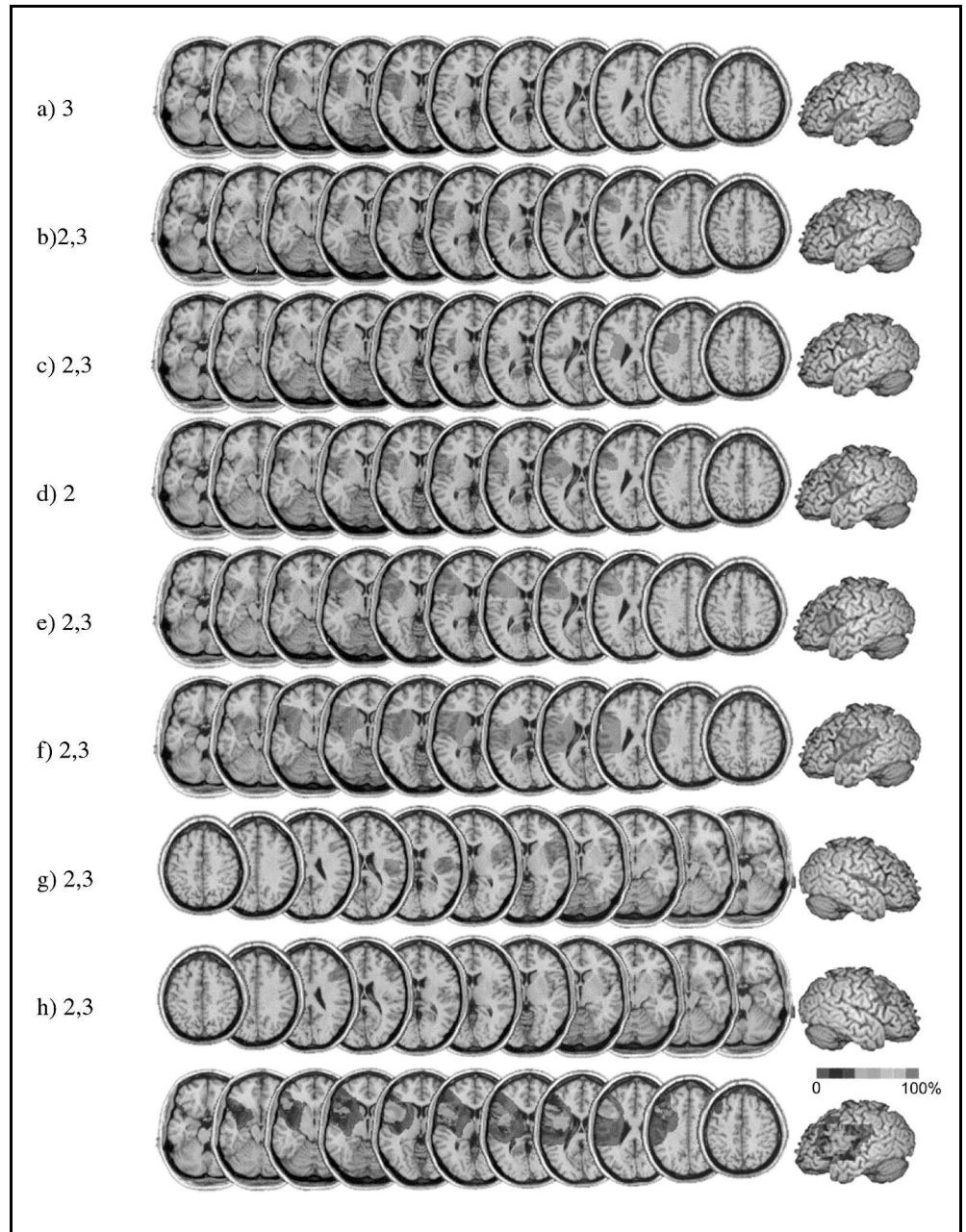
**Table 2.** Disease Duration, Type, and Hoehn & Yahr Scores for Parkinson’s Disease Patients in Experiments 2 and 3

<i>Patient</i>	<i>Years Since Onset</i>	<i>Surgery</i>	<i>Symptoms When Medicated</i>	<i>Hoehn &amp; Yahr Stage</i>	<i>Experiment</i>
1	7		bradykinetic	2 <sup>a</sup>	2 and 3
2	9		bradykinetic	not available	2
3	25		dyskinetic	3 <sup>a</sup>	2 and 3
4	11	pallidotomy	dyskinetic	2	3
5	9		bradykinetic	2	2
6	14		bradykinetic	2 <sup>a</sup>	3
7	14		bradykinetic	2.5	2 and 3
8	>10		bradykinetic	4	3
9	16		bradykinetic	3	2 and 3

<sup>a</sup>Assessment was with the Unified Parkinsonism Rating Scale (UPRS). Hoehn & Yahr scores were estimated from the UPRS.



**Figure 7.** The site of neural damage for PFC patients tested in Experiments 2 and 3. Numbers refer to the experiment in which the patient participated.



PFC (BA 9), frontal eye field (BA 8), and the superior portion of the temporal pole was also observed.

The average age and education level of the elderly control subjects did not significantly differ from either patient group (see Table 1). The WCST is often used to measure executive function and involves the ability to switch between sorting rules (Gotham et al., 1988). Both Parkinson and PFC patients displayed impairments on the WCST and were only able to sort to three categories on average compared to an average of five categories for control subjects. As statistical power was low given that only a subset of each group had been tested on the WCST, the differences between groups approached, but did not reach significance [controls vs.

Parkinson:  $F(1,14) = 4.41, p = .054$ ; controls vs. PFC:  $F(1,12) = 3.08, p = .105$ ].

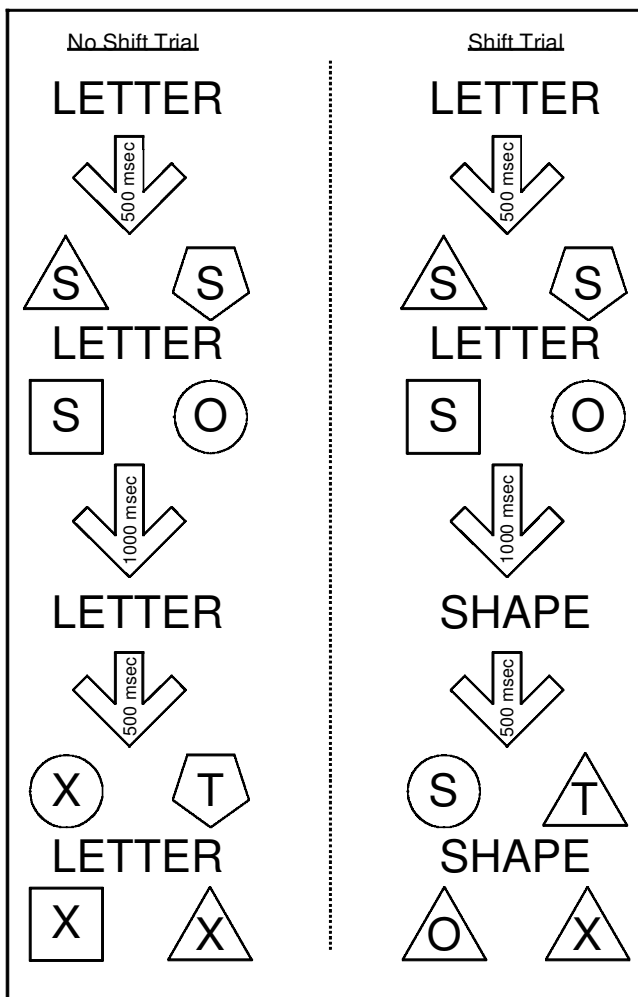
Working memory was disrupted for the PFC patients as indicated by their lower digit spans,  $F(1,17) = 11.37, p < .01$ . In contrast, the digit spans of Parkinson's disease patients were no different than controls and indicated normal working memory capacity. Thus, working memory was only affected by damage to the PFC while poor performance on a task of executive functions was associated with pathology of both the PFC and basal ganglia.

For Experiment 1, 8 older and 10 younger adults were tested on the set-shifting task. Six patients with Parkinson disease and seven with lesions to the PFC were tested on this same task in Experiment 2. Of the PFC

patients, five exhibited focal lesions to the left hemisphere and two to the right hemisphere. Experiment 3 compared the performance of 10 age-matched control subjects, 7 Parkinson disease patients, and 7 patients with a focal lesion to the PFC. There was some overlap between the Parkinson patients who participated in Experiments 2 and 3 (see Table 2). Four of the left-hemisphere and both right-hemisphere PFC patients tested in Experiment 2 participated in Experiment 3 as well. An additional left-hemisphere patient was tested in Experiment 3.

### Stimuli

Stimuli were presented at four locations arranged in a square around a central point (see Figure 8) and consisted of four letters (O, S, T, and X) and four shapes (circle, triangle, square, and pentagon). Letters were presented at each of the four locations in the center of one of the shapes. Shapes were formed by white lines



**Figure 8.** Example of the stimuli used in Experiments 1–3. The left side of the figure displays the sequence of events in the no-shift trials while the right side refers to shift trials.

and the locations of the four stimuli formed the corners of a square.

In Experiments 1 and 2, the cue consisted of the words “letter” or “shape” and was displayed in the center of the screen. The word cue was changed to an iconic cue in Experiment 3 and consisted of four miniature shapes or letters (e.g., “xost”). This was done to ensure that the subset of PFC patients who were aphasic or apraxic would not be at a disadvantage in processing the cues. Cues were always valid and indicated the correct dimension to which the participant should respond. In the uncued condition, a series of five asterisks was displayed in the center of the screen instead of a cue. Both cues and asterisks appeared on the screen 500 msec before the onset of the shapes and letters.

In the first two experiments, the odd-man-out task was composed of only one dimension. If letter was the relevant dimension then three of the letters would be identical and the fourth would be different. The irrelevant dimension would then be composed of shapes that were all different from each other. If shape was the relevant dimension, three identical and one odd shape would be displayed and all the letters would be different. In Experiment 3, odd targets could appear on either one dimension as in the first two experiments (unambiguous condition) or on both dimensions (ambiguous condition). The unambiguous conditions were identical to those employed in Experiments 1 and 2 where the odd object was either on the letter or shape dimension but not both. Stimuli in the unambiguous conditions were preceded either by asterisks or cues. In the ambiguous condition, an odd object was presented on both the relevant and irrelevant dimensions, and subjects in this condition had to use the cue word in order to select the correct target. This resulted in three conditions—cued (ambiguous), cued (unambiguous), and uncued (unambiguous).

Every combination of letter (4), shape (4), location (4), and dimension (2) was presented as the odd-man-out in a random order resulting in a total of 128 trials per block. The three identical letters or shapes on the relevant dimension were chosen at random as well as the location of the three remaining stimuli on the irrelevant dimension. Moreover, the shift from one dimension to another was unpredictable but occurred with a probability of .5.

### Procedure

Participants were first given a practice block of 20 trials of the cued condition in order to become familiar with the demands of the experiment. The instructions were as follows:

On each trial, you will see four shapes at different locations with letters inside of them. Either all the shapes or all the letters will be identical except for

one object. Your task is to choose the odd-man-out—the letter or shape that is different from the other three identical shapes or letters. Push the button on the keypad that corresponds to the location on the screen of the odd object. Before each trial, a word will be displayed on the screen that will tell you if the odd-man-out involves a letter or a shape. Either the letters or the shapes will be important not both. If the odd object is a shape, no letters will be identical, and if the odd object is a letter, no shapes will be identical. Respond as quickly and accurately as possible. Do you have any questions?

Responses were made on the computer keyboard and corresponded to the location of the odd object on the screen. Computer keys that formed a square (i.e., I, O, K, and L or 1, 2, 4, and 5 on the keypad) were used for responding to targets. Stimuli stayed on the screen until the subject responded. The response-to-stimulus interval was 1 sec.

Four test blocks followed the practice block and alternated between the cued and uncued conditions in Experiments 1 and 2. Half the subjects were tested with the cued block first and half with the uncued block first (ABAB or BABA). Before the first uncued block, participants were told that five asterisks would be displayed on the screen to alert them to the upcoming set of objects. In Experiment 3, a practice block of the unambiguous, cued condition was provided for all participants. Subjects then ran through one block each of the of the unambiguous conditions and two blocks of the ambiguous condition. Order was counterbalanced such that only one of the two factors—cueing or ambiguity—could change between blocks. This resulted in two sequences, ABCC or CCBA.

RTs greater than three standard deviations away from the subject's mean RT were discarded from the analysis as well as those RTs made to incorrect targets.

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Reprints requests should be sent to Dr. Susan Ravizza, Department of Psychology, University of Pittsburgh, 640 LRDC, 3939 O'Hara Street, Pittsburgh, PA 15260, USA, or via e-mail: ravizza@pitt.edu.

## REFERENCES

Akshoomoff, N. A., & Courchesne, E. (1992). A new role for the cerebellum in cognitive operations. *Behavioral Neuroscience, 106*, 731–738.

Allport, D. A., Styles, E. A., & Hsieh, S. (1994). Shifting

intentional set: Exploring the dynamic control of tasks. In C. Umiltà & M. Moscovitch (Eds.), *Attention and performance: XV. Conscious and nonconscious information processing* (pp. 421–452). Cambridge: MIT Press.

Azari, N. P., Rapoport, S. I., Salerno, J. A., & Grady, C. L. (1992). Interregional correlations of resting cerebral metabolism in old and young women. *Brain Research, 589*, 279–290.

Brown, R. G., & Marsden, C. D. (1988). Internal versus external cues and the control of attention in Parkinson's disease. *Brain, 111*, 323–345.

Burgess, P. W., & Shallice, T. (1996). Response suppression, initiation, and strategy use following frontal lobe lesions. *Neuropsychologia, 34*, 263–272.

Courchesne, E., Townsend, J., Akshoomoff, N. A., Saitoh, O., Yeung-Courchesne, R., Lincoln, A. J., James, H. E., Haas, R. H., Schreibman, L., & Lau, L. (1994). Impairment in shifting attention in autistic and cerebellar patients. *Behavioral Neuroscience, 108*, 848–865.

Downes, J. J., Roberts, A. C., Sahakian, B. J., & Evenden, J. L. (1989). Impaired extra-dimensional shift performance in medicated and unmedicated Parkinson's disease: Evidence for a specific attentional dysfunction. *Neuropsychologia, 27*, 1329–1343.

Duncombe, M. E., Bradshaw, J. L., Iansek, R., & Phillips, J. G. (1994). Parkinsonian patients without dementia or depression do not suffer from bradyphrenia as indexed by performance in mental rotation tasks with and without advance information. *Neuropsychologia, 32*, 1383–1396.

Goldman-Rakic, P. S. (1992). Working memory and the mind. *Scientific American, 267*, 111–117.

Gotham, A.-M., Brown, R. G., & Marsden, C. D. (1988). "Frontal" cognitive functions in patients with Parkinson's disease "on" and "off" levodopa. *Brain, 111*, 299–321.

Hartley, A. A., Kieley, J., & Slabach, E. H. (1990). Age differences and similarities in the effects of cues and prompts. *Journal of Experimental Psychology, Human Perception and Performance, 16*, 523–537.

Hayes, A., Davidson, M. C., Keele, S. W., & Rafal, R. D. (1998). Toward a functional analysis of the basal ganglia. *Journal of Cognitive Neuroscience, 10*, 178–198.

Ivy, G. O., MacLeod, C. M., Petit, T. L., & Markus, E. J. (1992). A physiological framework for perceptual and cognitive changes in aging. In F. M. Craik & T. A. Salthouse (Eds.), *Handbook of Aging and Cognition* (pp. 273–314). Hillsdale, NJ: Erlbaum.

Janowsky, J. S., Shimamura, A. P., & Squire, L. R. (1989). Source memory impairments in patients with frontal lobe lesions. *Neuropsychologia, 27*, 1043–1056.

Keys, B. A., & White, D. A. (2000). Exploring the relationship between age, executive abilities, and psychomotor speed. *Journal of the International Neuropsychological Society, 6*, 76–82.

Konishi, S., Nakajima, K., Uchida, I., Kameyama, M., Nakahara, K., Sekihara, K., & Miyashita, Y. (1998). Transient activation of inferior prefrontal cortex during cognitive set shifting. *Nature Neuroscience, 1*, 80–84.

Kramer, A. F., Hahn, S., & Gopher, D. (1999). Task coordination and aging: Explorations of executive control processes in the task switching paradigm. *Acta Psychologica, 101*, 339–378.

Kray, J., & Lindenberger, U. (2000). Adult age differences in task switching. *Psychology and Aging, 15*, 126–147.

Luria, A. R. (1966). *Higher cortical functions in man*. New York: Basic Books.

Mayr, U., & Keele, S. W. (2000). Changing internal constraints on action: The role of backward inhibition. *Journal of Experimental Psychology, General, 129*, 4–26.

- Meiran, N. (1996). Reconfiguration of processing mode prior to task performance. *Journal of Experimental Psychology, Learning, Memory, and Cognition*, *22*, 1423–1442.
- Meiran, N. (2000). The reconfiguration of the stimulus task-set and the response task-set during task switching. In S. Monsell & J. Driver (Eds.), *Attention and performance: XVIII. Control of cognitive processes* (pp. 377–400). Cambridge: MIT Press.
- Milner, B., Petrides, M., & Smith, M. L. (1985). Frontal lobes and the temporal organization of memory. *Human Neurobiology*, *4*, 137–142.
- Morris, R. G., Downes, J. J., Sahakian, B. J., & Evenden, J. L. (1988). Planning and spatial working memory in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *51*, 757–766.
- Owen, A. M., Roberts, A. C., Hodges, J. R., Summers, B. A., Polkey, C. E., & Robbins, T. W. (1993). Contrasting mechanisms of impaired attentional set-shifting in patients with frontal lobe damage or Parkinson's disease. *Brain*, *116*, 1159–1175.
- Petrides, M. (1991). Functional specialization within the dorsolateral frontal cortex for serial order memory. *Proceedings of the Royal Society of London*, *B246*, 299–306.
- Rafal, R. D., Posner, M. I., Walker, J. A., & Friedrich, F. J. (1984). Cognition and the basal ganglia. *Brain*, *107*, 1083–1094.
- Ravizza, S. M., & Ivry, R. B. (2001). Comparison of the basal ganglia and cerebellum in shifting attention. *Journal of Cognitive Neuroscience*, *13*, 285–297.
- Raz, N., Gunning, F. M., Head, D., Dupuis, J. H., McQuain, J., Briggs, S. D., Loken, W. J., Thornton, A. E., & Acker, J. D. (1997). Selective aging of the human cerebral cortex observed in vivo: Differential vulnerability of the prefrontal gray matter. *Cerebral Cortex*, *7*, 268–282.
- Robbins, T. W., James, M., Owen, A. M., Sahakian, B. J., Lawrence, A. D., McInnes, L., & Rabbitt, P. M. A. (1998). A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. *Journal of the International Neuropsychological Society*, *4*, 474–490.
- Robinson, A. L., Heaton, R. K., Lehman, R. A., & Stilson, D. W. (1980). The utility of the Wisconsin Card Sorting Test in detecting and localizing frontal lobe lesions. *Journal of Consulting and Clinical Psychology*, *48*, 605–614.
- 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.
- Rogers, R. D., & Monsell, S. (1995). Costs of a predictable switch between simple cognitive tasks. *Journal of Experimental Psychology, General*, *124*, 207–231.
- Rogers, R. D., Sahakian, B. J., Hodges, J. R., Polkey, C. E., Kennard, C., & Robbins, T. W. (1998). Dissociating executive mechanisms of task control following frontal lobe damage and Parkinson's disease. *Brain*, *121*, 815–842.
- Russ, M. O., & Seger, L. (1995). The effect of task complexity on reaction times in memory scanning and visual discrimination in Parkinson's disease. *Neuropsychologia*, *33*, 561–575.
- Salthouse, T. A. (1985). Speed of behavior and its implications for cognition. In J. E. Birren & K. Warner Schaie (Eds.), *Handbook of the psychology of aging* (2nd ed.) (pp. 400–426). New York: Van Nostrand Reinhold.
- Swainson, R., Rogers, R. D., Sahakian, B. J., Summers, B. A., Polkey, C. E., & Robbins, T. W. (2000). Probabilistic learning and reversal deficits in patients with Parkinson's disease or frontal or temporal lobe lesions: Possible adverse effects of dopaminergic medication. *Neuropsychologia*, *38*, 596–612.
- Taylor, A. E., Saint-Cyr, J. A., & Lang, A. E. (1986). Frontal lobe dysfunction in Parkinson's disease. *Brain*, *109*, 845–883.