

The Roles of Timing and Task Order during Task Switching

Jean-Claude Dreher,* Etienne Koechlin,† Syed Omar Ali,‡ and Jordan Grafman*

*Cognitive Neuroscience Section, National Institute of Neurological Disorder and Stroke, National Institutes of Health, Bethesda, Maryland 20892; †INSERM U483, Université Paris VI, 75005 Paris, France; and ‡Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, Maryland

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The neural bases of the different processes involved in task switching remain poorly identified. Whether distinct brain regions are involved according to the overall structure of the task sequence and the predictability of task timing during task switching is unknown. To address this question, we used functional magnetic resonance imaging and a 2×2 factorial design varying timing (fixed/random) and task order (predictable/unpredictable). We hypothesized that predictable task order should activate brain regions involved in long-term memory retrieval because retrieving which task has to be performed constitutes the essential part of what subjects can do to prepare before stimulus presentation. When examining the “pure” main effects of task order/timing predictability/unpredictability, we found that anticipating task order activated the right hippocampus, the anterior medial prefrontal cortex, and the posterior cingulate cortex, while anticipating task onset timing activated the left middle and superior frontal gyrus. Furthermore, task order unpredictability activated the intraparietal cortex bilaterally while random relative to fixed timing activated the right cerebellum. Interactions between task order and timing were found in a network, which included the left frontopolar cortex and the lateral prefrontal cortex bilaterally. Specifically, the left frontopolar cortex was more activated when both timing and task order were predictable, while the lateral prefrontal cortices were more activated when both task order and timing were unpredictable. These results indicate a hierarchic organization of the prefrontal cortex along a posterior-anterior axis as the task becomes more endogenously guided. Finally, we found no evidence for specific brain regions involved in task switching because a bilateral prefronto-parietal network, which was activated in task switching relative to performing each task separately, was no longer activated relative to a control condition, which required subjects to maintain two tasks in memory without switching between them.

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INTRODUCTION

The ability to constantly switch between various tasks is crucial for the flexibility of behavior. This capacity was investigated in a pioneering study in which each stimulus was a potential input for two possible tasks (Jersild, 1927). A significant increase of response times (RTs) was reported when comparing a block of trials in which subjects alternated between two tasks and a “pure task” block in which subjects repeatedly performed the same task. The RT difference between “pure” and alternating blocks, named the *alternation cost*, disappeared when two distinct set of stimuli were used for each task (Allport *et al.*, 1994; Jersild, 1927; Spector and Biederman, 1976). A problem with interpreting the cause of the alternation cost is that the working memory load is higher in the alternation block, which requires subjects to maintain two tasks in memory, as compared to the pure task block in which subjects hold in mind only one task. To avoid this confound, Rogers and Monsell (1995) introduced a new measure, the *task switch cost*, defined as the RT difference between the switch and the repeat trials when alternating between two tasks.

The nature of the switch cost remains unclear. Manipulation of distinct aspects of preparation during task switching have led to two not mutually exclusive theories with regard to the task switch cost. Manipulating the response–stimulus interval revealed that the switch cost is reduced when more preparation time is given between blocks of predictable switches (Meiran *et al.*, 2000; Rogers and Monsell, 1995), suggesting that the switch cost is at least in part a measure of the duration of a control process needed for task set reconfiguration, a process induced only for switch trials. On the other hand, manipulating the foreknowledge of the next task to be performed does not reduce the switch cost (Sohn and Carlson, 2000), suggesting that the switch cost also depends upon the persistent activation of a previous task set (Allport and Wylie, 2000; Allport *et al.*, 1994). Indeed, if the switch cost reflects only the duration of a control process, it should be reduced with

foreknowledge. The switch cost, thus, seems to result both from reconfiguration processes and from the carryover of persisting task-set interference (Meiran *et al.*, 2000; Monsell *et al.*, 2000).

The fact that foreknowledge of the next task to be performed reduces RTs for both the switch and the repeat trials (Sohn and Carlson, 2000) indicates that preparation has a general effect on RTs and is not restricted to the switch trials. The overall structure of the task sequence is important because subjects adopt different strategies according to the predictability of the experimental condition (Gopher *et al.*, 2000; Strayer and Kramer, 1994). When task order is predictable, routine preparation for the whole sequence of tasks is possible. In contrast, when task order is unpredictable, subjects can apply the relevant stimulus-response mapping only subsequent to stimulus presentation. The relations between the predictability of task order and timing and the specific role of timing during task switching are still poorly understood. In particular, whether task timing predictability and task order predictability are independent preparatory processes and whether RTs are reduced for fixed relative to random task timing are unknown.

These behavioral problems concerning task order and timing predictability during task switching led us to question whether distinct brain regions are influenced by these two aspects of preparation. Although the influence of the foreknowledge of the next task to be performed on brain activation has recently been investigated (Sohn *et al.*, 2000), it concerns only a transient aspect of preparation during task switching. This event-related fMRI study found a specific activation of the right ventrolateral PFC (BA 45) during the preparatory period before predictable switch relative to repeat trials (Sohn *et al.*, 2000). However, this study could not investigate whether specific brain regions are involved in a general preparatory state for an entire block of trials. Other fMRI studies of task switching have neglected the importance of timing and of the overall structure of the task sequences. One study, which used unpredictable task order, reported nonspecific activation of a bilateral dorso-lateral prefronto-parietal network for infrequent reversals between two task sets as compared to when the same task set was simply repeated (Dove *et al.*, 2000). Another fMRI study, which used a predictable task order, reported a superior parietal cortex activation for switch as compared to repeat trials (Kimberg *et al.*, 2000). It is difficult to establish the respective influence of timing and task order predictability on these results because these two factors were not manipulated.

To test whether specific brain regions are involved in a general preparatory state for an entire block of trials, we used a block design that enabled us to investigate brain regions that are not event specific. We also examined whether the ability to predict task timing in-

volves specific brain regions. To address these two questions, we conducted a fMRI experiment using a 2×2 factorial design varying timing (fixed relative to random) and task order (predictable relative to unpredictable). This design permitted us to determine whether distinct brain regions are activated by general preparatory processes involved in timing and task order predictability during task switching. Subjects had to switch between two letter discrimination tasks. Two different conditions were used to control for the processes required to perform each task separately (baseline condition) and for the increased memory load required to actively maintain two task sets without switching between them (control condition). This allowed us to test whether task switching activates specific brain regions beyond those involved in maintaining two tasks in memory without switching between them.

We hypothesized that predictable task order would activate brain regions, such as the hippocampus, involved in long-term memory retrieval. This hypothesis was based on the fact that retrieving which task has to be performed next constitutes the essential part of what subjects can do to prepare before stimulus presentation (Mayr and Klieg, 2000). We also tested whether a mediolateral dissociation would be present in the prefrontal cortex according to task order predictability. Indeed, a recent fMRI study investigating the effect of task order predictability during branching tasks (complex backward matching tasks) combining switching processes and maintenance of information during a delay found a dissociation along a lateromedial axis in the anterior prefrontal cortex (Koechlin *et al.*, 2000). The anterior medial PFC was more activated when subjects performed cued sequences of branching tasks in predictable order, whereas bilateral frontopolar cortices were activated when the tasks were performed in an unpredictable order. However, whether a similar dissociation is present when subjects simply need to switch between tasks, without the need to remember previous stimuli during a delay period is unknown. Finally, we investigated whether the task order and timing factors, confounded in previous studies, would interact in specific brain regions (i.e., whether brain regions involved with task order predictability/unpredictability depend upon the timing factor).

MATERIALS AND METHODS

Subjects

Eight subjects (mean age = 25 years; range 20–31 years) with at least a high school education were recruited following procedures approved by the Institutional Review Board. All subjects were native speakers of English and strongly right-handed, as measured by

the Edinburgh handedness inventory (mean score = 90.5). Informed consent was obtained from each subject. One or 2 days before the MR session, subjects participated in a behavioral testing session during which they were trained to perform each of the tasks and were required to attain an overall accuracy score greater than 90% to participate in the fMRI experiment.

Stimuli and Task Parameters

Subjects responded to visually presented single letters (vowels or consonants, lower or upper case, red or green) by pressing response buttons held in each hand. There were eight conditions (24 trials each), each cued by a distinct written instruction, consisting of two conditions used for baseline (Task A, vowel–consonant discrimination; Task B, case discrimination), four task switching conditions (obtained by crossing the task order and timing factors), and two conditions used for controlling memory load (Union task, A or B).

In the *vowel–consonant discrimination* condition, subjects had to press the right button if the letter was a vowel and the left button if the letter was a consonant. In the *case discrimination* condition, subjects had to press the right button if the letter was in upper case and the left button if the letter was in lower case. For both conditions, the color of the letters was irrelevant and changed every three letters. The *baseline* was composed of the mean of these two discrimination tasks $[(A + B)/2]$ (i.e., the two single tasks averaged together).

In the *task switching* conditions, subjects had to perform one of the two discrimination tasks according to the color of the letter. Red letters indicated the vowel–consonant discrimination task and green letters indicated the case discrimination task. In the *fixed timing* conditions, the stimuli appeared every 2.5 s, whereas in the *random timing* conditions, the timing between two stimuli was pseudo-randomized ($2.5\text{ s} \pm 260, \pm 390, \pm 510\text{ ms}$). In the *Predictable* conditions, subjects switched from one task to the other on every second trial, while in the *unpredictable* conditions the switch was pseudo-randomized. Manipulation of task order/timing predictability/unpredictability thus created four task switching conditions referred to as FP, FU, RP, RU, where the first letter stands for the timing factor (Fixed versus Random) and the second letter stands for the task order factor (Predictable versus Unpredictable). Stimulus duration was 500 ms in all conditions. Across each task switching condition, the numbers of switches (11), vowels/consonants (12 of each), red/green letters (12 of each), and left/right responses (12 of each) were consistently maintained.

In addition, the mean of the following two *Union* tasks was used to control for memory load of the two

tasks. In the first Union task, subjects had to press the right button if the letter was a vowel or was in upper case (and if both were true) and the left button otherwise, the stimuli appearing every 2.5 s. In the second Union task, the timing between two stimuli was pseudo-random (every $2.5\text{ s} \pm 260, \pm 390, \pm 510\text{ ms}$). In both conditions, the color of the letter was irrelevant and changed pseudo-randomly.

The letters used in the different conditions were taken among the following set of letters (which were upper or lower cases, red or green): c, d, f, h, k, m, p, r, t, v, a, e, i, o, u, y. Both the baseline and the task switching conditions were constructed by pseudo-randomly choosing among this set of letters that were equated for the number of vowels/consonants, upper/lower case letters, red/green letters, and left/right responses. These constraints were violated for the Union conditions to keep an equal number of left/right responses (there were more consonants than vowels and more lower case than upper case letters).

fMRI Methods

High-resolution structural images were obtained using a standard 1.5 GE whole-body signa scanner with an RF coil. For each subject, six time series of 180 whole-brain images (4 first images removed) were obtained with a gradient-echo, echo-planar scanning sequence (TR 3 s, TE 40 ms, flip angle 90°; FOV 24 cm, acquisition matrix 64×64 , 22 axial slices, thickness 6 mm). Each run was pseudo-randomly ordered according to a latin square design so that each condition appeared only once at different serial positions within a run and that baseline/control and switch conditions alternated. The order of runs was also counterbalanced across subjects. Using SPM96 with modified memory-mapping procedures, for each subject, the series of functional images for the six runs was realigned using a bilinear interpolation method, normalized to the Montreal Neurological Institute template, smoothed with a Gaussian filter (10-mm FWHM kernel), and finally scaled across scans. Then, the data from all subjects were pooled together and statistical parametric maps were computed from local MR signals using linear multiple regression with conditions, modeled as two temporal basis functions, and runs as covariates (fixed effect model) (Friston *et al.*, 1991). Only regions formed by more than 12 adjacent active voxels (voxel size = 4 mm^3) were reported ($Z > 4.3$; $P < 0.05$, corrected for multiple comparisons). We acknowledge that the results reported with this fixed effect model concern the specific group of subjects that we tested and may not be applicable to the general population, as would have been the case with a random effect model.

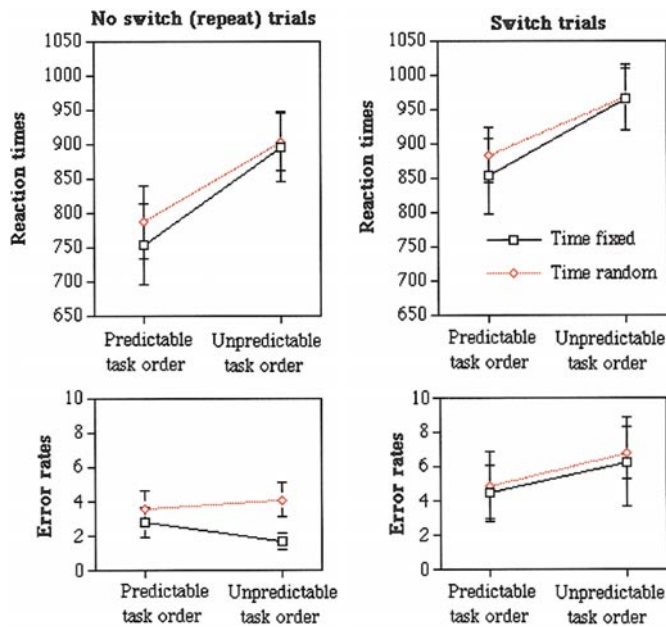


FIG. 1. Mean reaction time and error rates for the repeat and switch trials averaged across subjects in the various task switching conditions.

RESULTS

Behavioral Performance

Behavioral data for the different task switching conditions were analyzed with a three-factor repeated-measures ANOVA which included *switch* (no switch versus switch trials), *task order* (predictable versus unpredictable), and *timing* (fixed versus random) as factors (Fig. 1). RTs that were associated with errors or that were longer than 1800 ms were excluded from the analysis. As expected, RTs showed a main effect of *switch*; i.e., there was a significant RT increase in switch relative to repeat trials (switch cost) [$F_{(1,7)} = 32.2, P < 0.001$]. Furthermore, there was a main effect of *task order*; i.e., performance was significantly better when the order of the tasks was anticipated in the predictable compared to unpredictable task order conditions [RTs = 818 ms (MSE 142.9) versus 932.2 ms (MSE 130.1), $F_{(1,7)} = 14.4, P < 0.01$; 3.9% (MSE 3.4) of errors versus 4.7% (MSE 3.1), $F_{(1,7)} = 5.7, P < 0.05$]. Finally, no main effect of *timing* was found: fixed timing, compared to random timing, did not significantly reduce the error rate [3.8% (MSE 3.4) versus 4.8% (MSE 3.3), $F_{(1,7)} = 2.0, P = 0.19$] nor the RTs [865.6 ms (MSE 138.1) versus 884.6 ms (MSE 123.8), $F_{(1,7)} = 2.2, P = 0.18$]. No interaction reached statistical significance. The mean RTs of the individual tasks used for baseline and control were vowel/consonant, 717.3 ms (MSE 100.1); case discrimination, 656.5 ms (MSE 89.8); first Union, 778 ms (MSE 115.2); and second Union, 747.1 ms (MSE 79.2).

It is possible that the different time lags between stimuli in the random timing conditions induce different types of behavior (e.g., subjects may be more prepared with long than with short interstimuli intervals) that may not be observed by directly comparing the fixed to the random timing conditions. To better understand the contribution of the various time lags in random timing, we thus performed an additional three-factor repeated-measures ANOVA for only the two random timing switching conditions, which included *task order* (predictable versus unpredictable), *time lag* (five intervals of 408 ms from 1480 to 3520 ms), and *switch* (no switch versus switch trials). As before, we found a main effect of *switch* [$F_{(1,7)} = 15.3, P < 0.01$] and a main effect of *task order* [$F_{(1,7)} = 9.5, P < 0.05$]. There was a trend toward a reduction of RTs with *time lag* [$F_{(4,28)} = 2.2, P = 0.09$] (this trend became significant [$F_{(4,56)} = 3.2, P < 0.05$] in another analysis adding seven pilot subjects). No interactions were found between these factors. Error rates did not show any significant main effect or interactions.

To insure that the control condition did not involve switching processes, we directly compared the control and the switching conditions. RTs were significantly slower in the task switching conditions averaged together (mean = 875.0 ms, MSE = 129.9 ms) than in the control condition (mean = 763.2 ms, MSE = 96.1 ms) [$F_{(1,7)} = 34.8, P < 0.001$], indicating that the switching conditions demanded cognitive processes additional to those needed for the union of two tasks. Furthermore, subjects did maintain two task sets simultaneously in memory in the control condition because if subjects coded the control condition as a single stimulus-re-

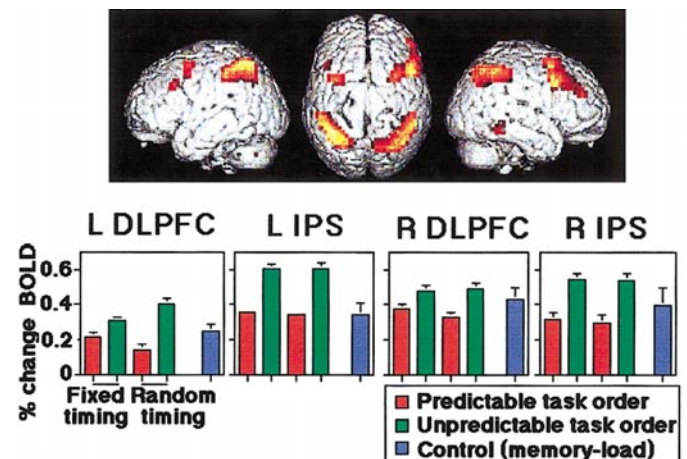


FIG. 2. (Top) Data for brain regions commonly activated by each task switching condition relative to baseline were overlaid onto a 3D-rendered brain. (Bottom) Percentage of signal change relative to baseline for each task switching condition and for the control (memory load) condition at the peak of activation of bilateral DLPFC and intraparietal sulcus regions. Error bars indicate standard error. The Z values and stereotactic coordinates for the regional maxima are listed in Table 1.

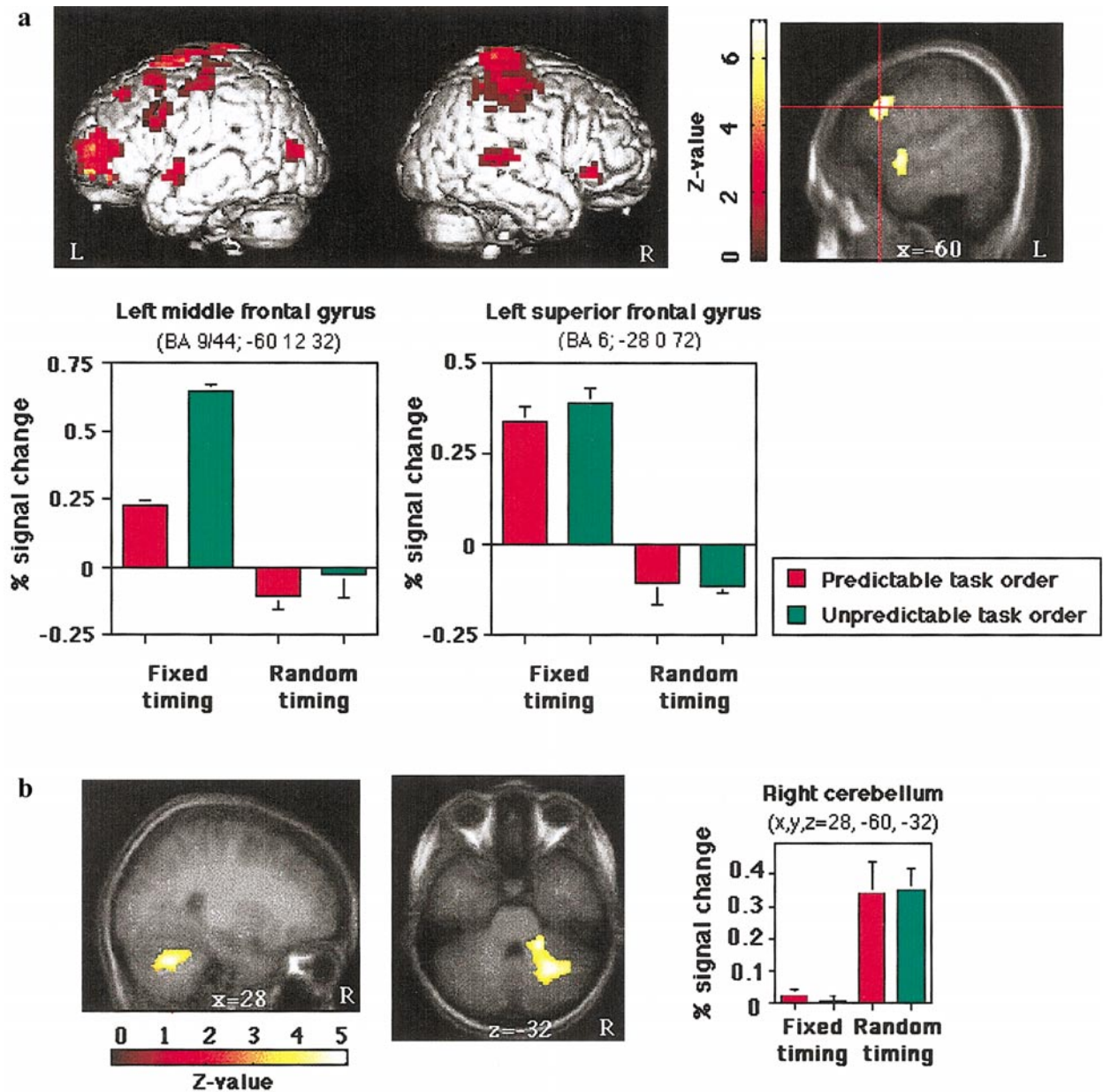


FIG. 3. (a) (Top left) Brain regions significantly activated by the main effect of timing predictability (fixed–random timing conditions; i.e., (FP + FU) – (RP + RU)) were overlaid onto a 3D rendered brain ($Z > 4.3$, $P < 0.05$, corrected). (Top right) Activation in left middle frontal gyrus was superimposed on a mean structural MRI sagittal slice averaged across subjects. (Bottom) A “pure” main effect of task timing predictability was found in the left middle and superior frontal gyrus. Percentage of signal change relative to baseline for each task switching condition in the left middle frontal gyrus (Talairach coordinates: xyz = -60 12 32) and superior frontal gyrus (Talairach coordinates: xyz = -28 0 72). (b) (Left) Main effect of timing unpredictability (random–fixed timing conditions; i.e., (RP + RU) – (FP + FU)) superimposed on normalized MRI slices averaged across subjects activated the right cerebellar hemisphere ($Z > 4.3$, $P < 0.05$, corrected). A threshold of $Z > 3.09$, $P < 0.001$, uncorrected, was used for display purposes. (Right) Percentage of signal change relative to baseline at the peak of activation of the main effect of timing unpredictability for each task switching condition in the right cerebellar hemisphere (Talairach coordinates: xyz = 28 -60 -32).

sponse mapping, they should have directly associated the lower case consonants to a left motor response and other letters to a right button press. However, RTs were not significantly faster for lower cases consonants than for other letters (vowels and upper case consonants) [$F_{(1,7)} = 0.95$, $P = 0.4$].

fMRI

Brain regions commonly activated by each task switching condition. We first identified common brain regions activated by each task switching condition relative to the simple baseline condition. This was

TABLE 1

Foci of Activations in the Different Statistical Contrasts

Anatomical structure (Brodmann's area)	Common task switching conditions vs baseline				Main effect of regular timing				Main effect of predictable task order				Main effect of unpredictable task order			
	Talairach coordinates				Talairach coordinates				Talairach coordinates				Talairach coordinates			
	x	y	z	Z value	x	y	z	Z value	x	y	z	Z value	x	y	z	Z value
Frontal																
L sFG (BA 6)	-28	4	56	7.56	-28	0	72	7.04								
L mFG (BA 8/9/44)	-40	20	32	7.18	-60	12	32	6.21					-44	16	32	5.79
R mFG (BA 8/9/46)	48	16	40	7.77												
	60	28	32	6.47												
R iFG (BA 44/45)													36	24	20	6.21
L fronto-polar ex (BA 10/46)					-36	60	-4	7.17								
Anterior medial PFC (BA 10)									0	64	8	4.45*				
L Somato-motor area (BA 4)					-48	-20	64	5.52					-28	-16	60	5.16
R Somato-motor area (BA 4)					28	-24	76	6.71					20	-16	68	6.21
Parietal																
L IPS (BA 7/40)	-36	-56	52	8.36									-32	-56	48	6.10
R IPS (BA 7/40)	36	-60	44	8.05									40	-48	48	5.74
L Pr. Somatosens. cx (BA 1)					-24	-32	80	6.08								
R Pr. Somatosens. cx (BA 1)					20	-28	80	5.91								
Cerebellum																
L lat. cerebellar hemisphere	-28	-68	-40	6.72									-32	-68	-36	4.88
Vermis	0	-68	-32	5.80												
Gyrus temporal																
L iTG (BA 20)													-52	-28	-12	6.64
R iTG (BA 37)	52	-56	-4	7.54									52	-56	-4	7.54
L sTG (BA 22)					-60	0	-4	5.92								
R sTG (BA 22)					68	-40	8	6.07								
Insula																
L INS													-20	24	-4	5.59
R INS													28	28	4	5.37
R Operculum					40	28	0	5.15								
L m occip. gyrus (BA 18/19)					-40	-80	12	5.58					-28	-88	4	6.19
R m occip. gyrus (BA 18/19)													28	-84	-8	5.38
R Hippocampus									28	-20	-8	6.03*				
Post. cingulate cx. (BA/30)									0	-48	16	4.64*				

Note. The coordinates are given within the framework of the standardized stereotaxic brain atlas of Talairach and Tournoux (1988). All areas were significant at $P < 0.00001$ (uncorrected for multiple comparisons), *except $P < 0.001$. L, Left; R, Right; sFG, superior Frontal Gyrus; mFG, middle Frontal Gyrus; IPS, Intraparietal Sulcus; INS, insula; iTG, inferior Temporal Gyrus; sTG, superior Temporal Gyrus; Somatosens.cx., Somatosensory cortex; occip. gyrus, occipital gyrus.

done by selecting the voxels activated in all task switching conditions averaged together relative to baseline ($Z > 4.3$, $P < 0.05$, corrected) which were also activated in each individual task switching condition compared separately to baseline ($Z > 2.33$, $P < 0.01$, uncorrected) (a logical mask was used for this comparison). Activation was found in the middle and superior frontal gyri bilaterally, the intraparietal sulcus (IPS) bilaterally, the right inferior temporal gyrus (iTG) (BA 37), and the cerebellum (Fig. 2; Table 1).

To control for the higher working memory load necessary to keep both task sets active during the task switching conditions, we examined, as described previously, the voxels commonly activated by each task switching condition relative to the control condition,

which required subjects to maintain two task sets in memory without switching between them. None of the brain regions mentioned above (DLPFC, IPS, iTG, cerebellum) were significantly activated in this comparison ($Z < 1.7$, $P > 0.05$, uncorrected). Furthermore, all these brain regions were significantly activated in the control condition relative to baseline ($Z > 4.3$, $P < 0.05$, corrected), indicating that they were not specifically activated during task switching (Fig. 2).

Brain regions involved in the main effects of timing and task order predictability/unpredictability. The main effect of *task timing predictability* on regional brain activation was computed by subtracting the two task switching conditions with random timing from the

two with fixed timing [(FP + FU) – (RP + RU)]. The results revealed activation of the left frontopolar cortex (BA 10/46), left middle and superior frontal gyrus (BA 6/8/9/44), bilateral sensorimotor cortices, right operculum, left medial occipital gyrus (BA 18/19), and bilateral superior temporal gyrus (BA 22) ($Z > 4.3$, $P < 0.05$, corrected) (Fig. 3a). Conversely, the main effect of *timing unpredictability* revealed activation only in the right cerebellar lobule (Larsell VI) ($Z > 4.3$, $P < 0.05$, corrected) (Fig. 3b).

The main effect of *task order predictability* on regional brain activation was computed by subtracting the two task switching conditions with unpredictable order from the two with predictable order. The results revealed significant activation of the anterior medial prefrontal cortex (BA 10), right hippocampus, and posterior cingulate gyrus (BA 30) ($Z > 3.09$, $P < 0.001$, uncorrected) (Fig. 4). Conversely, brain regions activated by the main effect of *task order unpredictability*, obtained by subtracting the two task switching conditions with predictable order from the two with unpredictable order ($Z > 4.3$, $P < 0.05$, corrected), activated a network consisting of a large right inferior frontal gyrus region (BA 45), the left middle frontal gyrus (BA 9), the somatomotor area (BA 4), the IPS region, the insula, the inferior temporal gyrus (BA 20/37), the occipital gyrus (BA 18/19), and the left cerebellum (Fig. 5). Subthreshold activation was also obtained in the anterior putamen bilaterally ($Z > 3.09$, $P < 0.001$, uncorrected).

Brain regions involved in the interactions between timing and task order. The main effect analysis did not allow us to determine whether the brain regions involved in the main effects of task timing/order predictability/unpredictability were also activated in the interactions between task order and timing. To assess the degree of independence of brain areas involved in these aspects of the tasks, we identified brain regions involved in the interactions between task order and timing. The interaction representing the modulatory effect of fixed timing on the activity associated with predictable task order [(FP – RP) – (FU – RU)] resulted in activation of the left frontopolar cortex, the middle frontal gyrus bilaterally (BA 9/46) (in a region more inferior to the one commonly activated by each task switching condition), the motor cortex bilaterally, the anterior cingulate cortex (BA 24), the middle temporal gyrus bilaterally, and the pre-SMA ($Z > 4.3$, $P < 0.05$, corrected) (Fig. 6a, Table 2). The converse interaction [(FU – RU) – (FP – RP)], representing the modulatory effect of fixed timing on the activity associated with unpredictable task order, did not activate any brain region at this threshold ($Z > 4.3$, $P < 0.05$, corrected).

We then examined whether the brain regions previously reported to be involved with task timing/order

predictability/unpredictability were also activated with the interactions between task order and timing. First, we tested whether the brain regions involved with task timing predictability share the same neural substrate as those found with interactions between task order and timing. To do this, we selected the brain regions activated with fixed relative to random timing ($Z > 4.3$, $P < 0.05$, corrected) that were also activated by the interactions between timing and task order effects ($Z > 2.33$, $P < 0.01$) (logical mask). Only the left frontopolar cortex was activated in this comparison ($xyz = -40\ 56\ 12$; $Z = 6.7$), showing that this brain region is not involved in the “pure” main effect of timing predictability but that its activation depends upon whether task order is also predictable (Fig. 6b). No brain regions were significantly activated when we similarly tested whether there were brain regions involved with task order predictability masked with those showing interactions between task order and timing, suggesting that the medial PFC, the right hippocampus, and the posterior cingulate cortex are all involved in a “pure” main effect of task order predictability. The brain regions involved with task order unpredictability ($Z > 4.3$, $P < 0.05$, corrected) masked with the brain regions showing interactions between task order and timing ($Z > 2.33$, $P < 0.01$) revealed activation in most of the brain regions found with task order unpredictability: the right inferior frontal gyrus (BA 45) and the left middle frontal gyrus (BA 9/46), the inferior temporal gyrus (BA 20/37) and the occipital gyrus (BA 18/19) (Fig. 6c), except for the intraparietal sulcus region and the somatomotor area (BA 4). These two latter brain regions thus show a “true” main effect of task order unpredictability. No cerebellar region was activated when the main effect of timing unpredictability ($Z > 4.3$, $P < 0.05$, corrected) was masked with the brain regions activated in the interactions between task order and timing ($Z > 2.33$, $P < 0.01$), indicating that the right cerebellum shows a “true” main effect of timing unpredictability.

Relationship between Behavioral Performance and Brain Activation

Finally, we examined whether specific brain regions, among those commonly activated in all task switching conditions, correlate with the corresponding response time. The RT alternation cost, defined as the difference between the RT averaged across all task switching conditions and the RT in the baseline, negatively correlated with the bilateral DLPFC (BA 9/46) ($xyz = -40\ 20\ 32$, $r = -0.77$; $P < .05$, two-tailed; $xyz = 60\ 28\ 32$, $r = -0.87$; $P < 0.01$, two-tailed) (Fig. 7). We also investigated which brain regions correlate with the task switch cost (RTs difference between switch and repeat trials of the task switching conditions) and found that it negatively correlated with the left

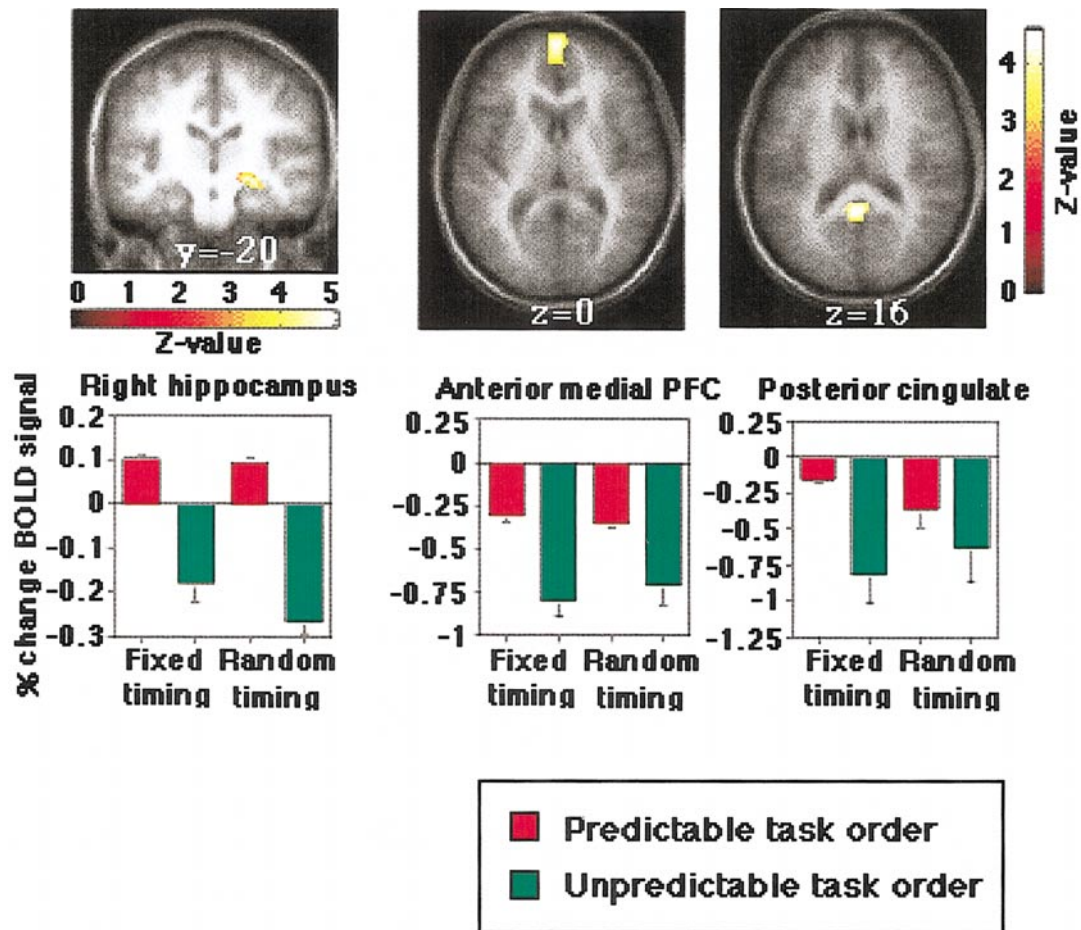


FIG. 4. (Top) Main effect of task order predictability (i.e., predictable–unpredictable task order conditions; (FP + RP) – (FU + RU)) superimposed on normalized structural MRI slices averaged across subjects ($Z > 3.09$, $P < 0.001$, uncorrected). Activation was found in right hippocampus, anterior medial PFC (BA 10), and posterior cingulate cortex (BA 30). The Z value scale on the right of the figure applies for both anterior medial PFC and posterior cingulate. (Bottom) Percentage of signal change relative to baseline for each task switching condition in those brain regions.

frontopolar cortex ($xyz = -40\ 56\ 8$, $r = -0.83$; $P < 0.01$; two-tailed) (Fig. 6b, right).

DISCUSSION

The results of our study demonstrate that a bilateral prefronto-parietal network was commonly activated by each task switching condition compared to a simple baseline, but not compared to a control condition that required subjects simply to keep in mind two task sets without switching between them (Fig. 2). This network is thus not specific for task switching per se. Moreover, switching between two tasks does not require the recruitment of additional brain regions beyond those involved in simply maintaining two task sets. A similar brain activation pattern was previously reported for dual tasks (Adcock *et al.*, 2000; Bunge *et al.*, 2000), indicating that a range of tasks requiring executive processes tend to recruit a nonspecific prefronto-parietal network.

Although no specific brain region was differentially activated by task switching, subjects with greater activation in the DLPFC (BA 9/46) showed a reduction in the response time alternation cost (Fig. 7). This suggests that the DLPFC has a particular role in mediating top-down control processes and may provide bias signals to posterior brain regions establishing the proper stimulus–response mapping required to perform a given task (Miller and Cohen, 2001; Tomita *et al.*, 1999). Neuropsychological studies have also reported that patients with DLPFC lesions show a task switching deficit (Mecklinger *et al.*, 1999; Rogers *et al.*, 1998). The exact role of the DLPFC in task switching remains to be determined. One hypothesis is that it participates in inhibiting the preceding and currently irrelevant task set in working memory (Arbuthnott and Frank, 2000; Baddeley *et al.*, 1998; Mayr and Keele, 2000). Alternatively, the DLPFC activation may reflect the loading of the task set in working memory. Consistent with this hypothesis, activation of this area

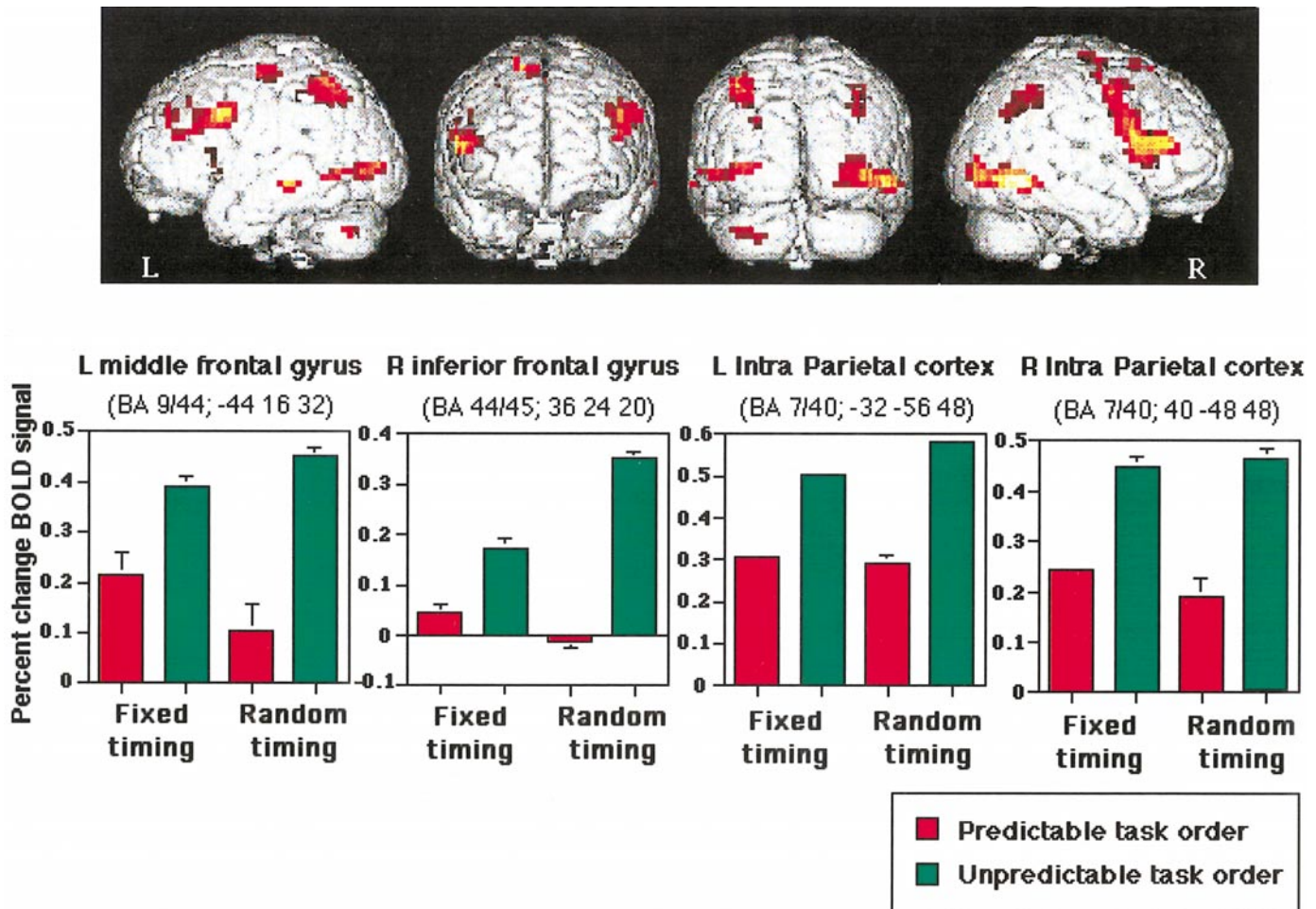


FIG. 5. (Top) Brain regions significantly activated by the main effect of task order unpredictability (i.e., unpredictable–predictable task order (FU + RU) – (FP + RP)) were overlaid onto a 3D rendered brain ($Z > 4.3$, $P < 0.05$, corrected). (Bottom) Percentage of signal change relative to baseline for each task switching condition at the peak of activation of the left middle frontal gyrus (BA 9/44), right inferior frontal gyrus (BA 44/45), and bilateral intraparietal cortex (BA 7/40). Error bars indicate standard error. The Z values and stereotactic coordinates for the regional maxima are listed in Table 1.

increases with the number of dimensions shifted in the Wisconsin Card Sorting Test (Konishi *et al.*, 1998) and overlaps the DLPFC region activated during a working memory task (n-back with card stimuli) (Konishi *et al.*, 1999). Further event-related studies are needed to test these two hypotheses.

Taken together, the behavioral results indicated no interaction between timing and switch cost and confirmed that task order predictability concerns a general preparatory state that is not specific to the switch trials (no interaction between switch cost and task order) (Sohn and Carlson, 2000). Our fMRI findings show that the brain regions involved in the “pure” main effects of timing and task order activate nonoverlapping cortical networks (Figs. 3–5). We discuss in detail the influence of task timing and task order predictability/unpredictability in the following paragraphs.

Timing Predictability/Unpredictability

Our behavioral results showed no reduction of the switch cost with fixed as compared to random timing. This confirms previous behavioral studies showing that the switch cost is not reduced if timing is randomly varied within a block of trials (Meiran *et al.*, 2000; Rogers and Monsell, 1995). Subjects could not prepare to switch when timing was random probably because interval variations were too frequent and unpredictable. It may be noticed that this result may not be generalizable because others have found that the switch cost is reduced as a function of preparation time, even when timing is randomly varied within a block (DeJong, 2000; Meiran, 1996). The differences between paradigms (e.g., shorter interstimuli intervals used in these latter paradigms) may explain this discrepancy. Furthermore, there was no significant im-

provement of RTs and error rates when timing was fixed as compared to random. However, when focusing on the random timing conditions by distinguishing different ranges of time lags between stimuli presentation, we found a trend toward a reduction of the RTs with long as compared to short time lags. This suggests that subjects may have used the probabilistic information conveyed by the passage of time to predict the likelihood of stimuli presentation in the random timing conditions. A similar result has recently been reported in a behavioral task switching experiment (Meiran *et al.*, 2000) and was previously found with simple RTs (Niemi and Naatanen, 1981). Since our study used a block design, we cannot specify which brain regions were involved in long as compared to short time lags in the random timing conditions.

Although no significant RT and error rate reductions were found with fixed relative to random timing, several active brain regions were found in this comparison, suggesting that neuronal changes may not always be associated with detectable behavioral modifications. In particular, in the prefrontal cortex, the “pure” main effect of timing predictability (fixed relative to random timing) principally activated the left middle frontal gyrus (BA 9/44) and the left superior frontal gyrus (BA 6) (Fig. 3a). These brain regions may implement timing estimation or synchronization of the response to regular visual stimuli (Rubia *et al.*, 1998). It is unlikely that this activation merely reflects motor preparation because direct comparison between fixed and irregular finger movements paced by visual timing stimuli did not activate these areas (Lutz *et al.*, 2000). Furthermore, the left premotor cortex (BA 6/44) was activated when subjects voluntarily oriented their attention to time (Coull and Nobre, 1998), suggesting that implicit parameters such as timing predictability may involve similar frontal regions in a range of higher-level cognition paradigms.

In contrast, timing unpredictability (random relative to fixed timing) activated the right cerebellum (Fig. 3b), consistent with its role as an internal timing system (Ivry, 1996) and involvement in preparatory functions (Courchesne and Allen, 1997). This latter theory proposes that the fundamental purpose of the cerebellum is to predict internal conditions needed for a particular mental or motor operation: “At one extreme, if the sequence is random and thus constantly changing, cerebellar activation will be sustained at a relatively constant magnitude for the duration of the task as the cerebellum attempts (yet fails) to discern a meaningful and predictive pattern” (Courchesne and Allen, 1997).

Task Order Predictability/Unpredictability

Reduced response times on both switch and repeat trials during the predictable task order conditions indicated that task order predictability had a general

effect concerning all trial types. Thus, brain regions activated with task order predictability, and in particular the anterior medial PFC (Fig. 4, middle), concern a general preparatory state that is not specific to switch trials. In contrast, a recent event-related fMRI study has reported a specific activation of the right ventrolateral PFC (BA 45) just before predictable switch relative to repeat trials (Sohn *et al.*, 2000). This suggests that distinct frontal regions are involved in a preparatory state concerning the overall structure of the task sequences and in transient aspects of preparation during task switching. A similar distinction has been made in the memory retrieval literature between a retrieval state and a retrieval of events (Duzel *et al.*, 1999; Lepage *et al.*, 2000).

We have found a functional organization of the prefrontal cortex along a mediolateral axis on the basis of task order predictability. The main effect of predictable task order activated the anterior medial PFC (Fig. 4, middle) while task order unpredictability activated the right inferior frontal gyrus (BA 45) and the left middle frontal gyrus (BA 9) (Fig. 5). The anterior medial PFC activation may reflect monitoring of the match between the actual and the expected stimulus color (Luu *et al.*, 2000; Schacter *et al.*, 1997). A similar dissociation along a lateromedial axis has recently been reported in the anterior prefrontal cortex during complex backward matching tasks combining switching processes and maintenance of information during a delay (Koechlin *et al.*, 2000). The anterior medial PFC was more activated when subjects performed cued sequences of branching tasks in predictable order, whereas bilateral frontopolar cortices were activated when the tasks were performed in an unpredictable order (Koechlin *et al.*, 2000). In our current task switching study, we show that temporary maintenance of information is not necessary to evoke activation in the anterior medial prefrontal cortex and additionally report a posterior/anterior dissociation according to task order predictability (Fig. 4, middle and Fig. 5).

Task order predictability also activated the right hippocampus and the posterior cingulate gyrus. As mentioned in the Introduction, it has been proposed that retrieving which task has to be performed constitutes the essential part of what subjects can do to prepare before stimulus presentation (Mayr and Kliegel, 2000). The hippocampal formation targets the medial PFC in monkeys (Barbas and Blatt, 1995; Carmichael and Price, 1995) and is linked to the medial extension of the mid-DLPFC via the cingulum bundle (Morris *et al.*, 1999). There is evidence that the hippocampus is involved in remembering the sequential order of events (Lisman, 1999; Schacter *et al.*, 1997; Schacter and Wagner, 1999) and the posterior cingulate cortex has been found activated during various memory retrieval tasks (Fletcher *et al.*, 1995; Maguire and Mummery, 1999; Mummery *et al.*, 1998). The asymmetric, right

sided activation of the hippocampus could be attributed to the nonverbal aspects of the retrieved memory (Dimsdale *et al.*, 1964; Scoville and Milner, 1957; Smith, 1989). It appears that all of the brain regions that showed more activation with predictable compared to unpredictable task order were actually deactivated relative to baseline (for the unpredictable task order conditions). This is consistent with numerous studies that have reported deactivation of these brain regions relative to baseline in a variety of goal-directed paradigms (Binder *et al.*, 1999; Raichle *et al.*, 2001).

When considering the “pure” main effect of task order unpredictability, the intraparietal cortex was activated bilaterally (Fig. 5), although the stimuli were similar in all conditions. As attention to the color of the stimuli was required in the unpredictable task order conditions to identify which task to perform, activation in these brain regions might reflect selective attention related to the attribute of the stimuli associated with the task (i.e., the color). In contrast, when the task order was predictable, less attention to the color was required. Lateral intraparietal neurons, although believed not to be involved in nonspatial attributes such as color, do respond to cue color if the tasks require constant changes of the association between cue color and motor responses (Toth and Assad, 2002). Thus, our results extend classical findings on the role of the intraparietal cortex in selective attention (Corbetta *et al.*, 1991; Culham and Kanwisher, 2001; Kanwisher and Wojciulik, 2000). In a similar fashion, the inferior temporal cortex activations (BA 20 and BA 37) that we found with task order unpredictability are likely to reflect increased attention to the color of the letters necessary to know which task to perform. This is compatible with the fact that the inferior temporal cortex, which associates color with form, is the final stage of color information processing (Zeki and Marini, 1998).

Finally, it may be argued that brain regions activated with task order unpredictability may be due to an increase in task difficulty as reflected in the slower RTs and increased error rates in unpredictable as compared to predictable task order. This possibility cannot be totally excluded for brain regions activated with task order unpredictability that are also activated in the contrast comparing common brain regions activated by all task switching conditions relative to baseline (as the intraparietal cortex). However, among the brain regions activated by task order unpredictability, brain regions that are not activated in common by all switching conditions averaged together relative to baseline (e.g., the right inferior frontal gyrus) are unlikely to be activated due to task difficulty alone. Indeed, if these brain regions were activated due to task difficulty, they should also be activated in the contrast comparing brain regions commonly activated by all task switching averaged together relative to baseline

(because task switching conditions are clearly more difficult than the baseline in terms of RTs).

Thus, although the task difficulty interpretation is difficult to rule out for certain brain regions activated with task order unpredictability, we interpret activation of these brain regions as reflecting attention to the color of the stimuli to determine which task to perform. This interpretation is consistent with a recent review that proposed two distinct but interacting brain networks: the right temporoparietal cortex–inferior frontal cortex for stimulus driven control and the intraparietal cortex–frontal eye field for top-down control (Corbetta and Shulman, 2002). This distinction nicely maps onto the distinctive roles of two networks of brain regions that we found in our study: the network found with task order unpredictability that responds to the color of the stimuli (which included a large region of the right inferior frontal; Fig. 5) and the network commonly activated by all task switching conditions relative to baseline (Fig. 2) that is involved in goal-directed stimulus–response selection (top-down control).

Interactions between Task Order and Timing

Dissociating the roles of the frontopolar cortex and of the lateral PFC. Although no interaction between the task order and the timing factors were present at the behavioral level, interactions were found at the neuronal level. Except for the left frontopolar cortex, which was activated when predicting task order and timing in combination, all the brain regions that show an interaction between timing and task order were more activated with the combination of unpredictable task order and random timing (the DLPFC bilaterally (BA 9/46) in a region more inferior to the one commonly activated by each task switching condition, the anterior cingulate (BA 24), the pre-SMA, the bilateral motor cortex, and the right inferior temporal gyrus) (Fig. 6a). Furthermore, among the brain regions involved in the main effect of task order unpredictability (Fig. 5), the intraparietal cortex did not show interaction between timing and task order, while interactions appear in the right inferior frontal gyrus and the left middle frontal gyrus (Fig. 6c). Thus, interactions between the timing and the task order factors distinguish the functions played by the intraparietal cortex and by the lateral PFC.

When considering the pattern of activation found in the prefrontal cortex, our results show a dissociation between the left frontopolar cortex, activated when anticipating task order and timing in combination (Fig. 6b), and the lateral PFC, activated when both task order and timing were unpredictable (Fig. 6c). The activation found in the frontopolar cortex is consistent with the behavioral correlation since the more prepared that subjects were, the more they activated the left frontopolar cortex and reduced the task switch cost

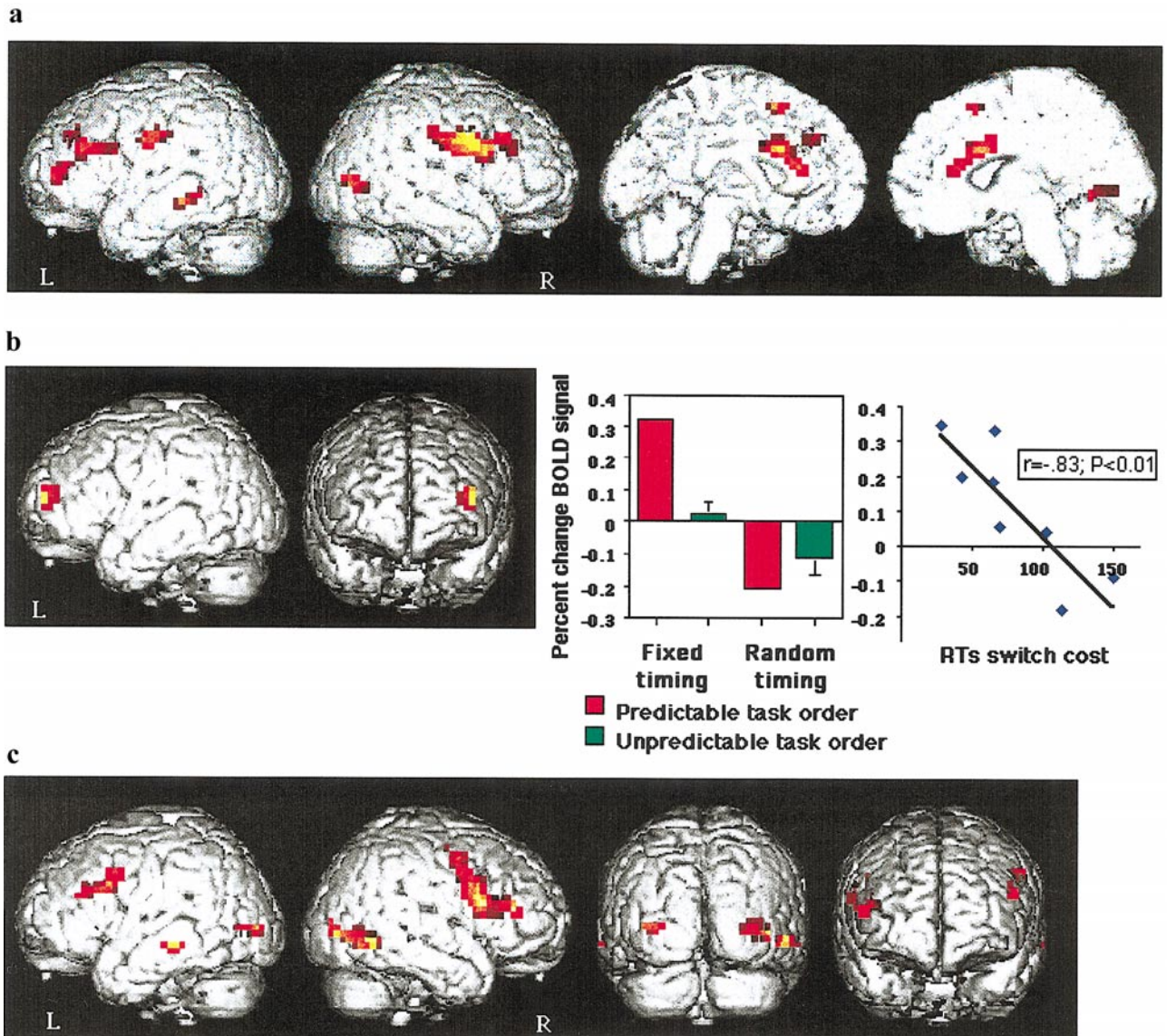


FIG. 6. (a). Brain regions significantly activated by the interactions between task order and timing [(FP + RU) - (FU + RP)] were overlaid onto a 3D rendered brain ($Z > 4.3$, $P < 0.05$, corrected). (b). (Left) Left frontopolar cortex activation found when the main effect of timing predictability [(FP + FU) - (RP + RU)] was masked by the brain regions involved in the interactions between task order and timing. (Middle) Percentage of signal change relative to baseline for each task switching condition at the peak of activation of the left frontopolar cortex (Talairach coordinates: $xyz = -40\ 56\ 12$). (Right) Negative correlation between activation in the left frontopolar cortex and switch cost (RTs difference between switch and repeat trials) ($xyz = -40\ 56\ 8$, $r = -0.83$; $P < 0.01$). Data for each subject are shown in blue. For each subject, the mean signal intensity based on the peak of activation observed in the group analysis was identified. (c). Brain regions significantly activated when the main effect of task order unpredictability [(FU + RU) - (FP + RP)] was masked by the brain regions showing interactions between task order and timing and subsequently overlaid onto a 3D rendered brain.

(Fig. 6b). The frontopolar activation is likely to reflect retrieval and/or preparation of the task to perform that is sensitive to timing predictability. Studies of long-term memory retrieval and problem solving have shown that the frontopolar cortex participates in episodic retrieval (Duzel *et al.*, 1999; Lepage *et al.*, 2000; Schacter *et al.*, 1997) and is activated with anticipation of the consequences of one course of action on a subsequent one (Baker *et al.*, 1996). The dissociation be-

tween the frontopolar cortex and the lateral PFC is also consistent with a recent review of neuroimaging studies on episodic memory retrieval that support a frontopolar cortex activation with evaluation of internally generated information and a lateral PFC activation with evaluation of externally presented information (Christoff and Gabrieli, 2000). Finally, our frontopolar activation may also be considered to reflect the knowledge of the time and the rule which needs to

TABLE 2
Interactions between Task Order and Timing

Anatomical structure (Brodmann's area)	Interactions between task order and timing			Z value
	Talairach coordinates			
	x	y	z	
Frontal cx				
Right PM/Motor cx (BA 4/6)	52	−8	28	6.5
Left Motor cx (BA 4)	−44	−12	32	6.1
Right mFG (BA 9/46)	40	28	28	6.5
Left mFG (BA 9/46)	−36	28	24	5.8
Left fronto-polar cx (BA 10)	−28	48	8	5.2
Pre-SMA	−4	12	56	4.9
Cingulate cx				
Anterior cingulate (BA 24)	4	28	16	5.4
Gyrus Temporal				
Right mTG (BA 19/37)	40	−72	4	5.7
Left mTG (BA 37)	−52	−36	−8	4.8

Note. mFG, medial Frontal Gyrus; mTG, middle Temporal Gyrus; PM, Premotor cortex. $P < 0.00001$ (uncorrected for multiple comparisons).

be applied next while performing a current task, as is the case with frontopolar cortex activation found when subjects perform an ongoing task while monitoring an "intention task" (Burgess *et al.*, 2001) or perform a task while keeping in mind a subgoal (Koechlin *et al.*, 1999).

CONCLUSIONS

Our study provides novel evidence that there are no specific brain regions for task switching. Rather, we have dissociated the neural basis of distinct processes involved in task switching by demonstrating that timing and task order predictability/unpredictability are mediated by different brain regions. In particular, within the prefrontal cortex, the left middle/superior

frontal gyrus is involved in predicting task timing, while the anterior medial prefrontal cortex is involved in task order predictability, possibly monitoring the match between the actual and the expected color of the stimuli. Furthermore, the anterior prefrontal cortex, including the anterior medial prefrontal cortex and the left frontopolar cortex, were more related to endogenous control processes, being activated when knowing which task was going to occur, while the lateral PFC (and specially the right inferior frontal gyrus) was more involved with cognitive control processes in relation to external events. This suggests a hierarchic organization of the prefrontal cortex along a posterior-anterior axis as the task becomes more endogenously guided. These results extend previous functional divisions of the prefrontal cortex reported in working memory paradigms, distinguishing the type of information processing (maintenance vs manipulation) (Owen, 1997) or the domain of processed information (spatial vs object) (Goldman-Rakic, 1996; Ungerleider *et al.*, 1998), to the subcomponents of task switching. Finally, bilateral intraparietal and lateral PFC cortices were differently related to task order unpredictability, the intraparietal cortex reflecting selective attention to the color of the stimuli, independently of the timing factor, while the lateral PFC was more activated with the combined unpredictability of task order and timing.

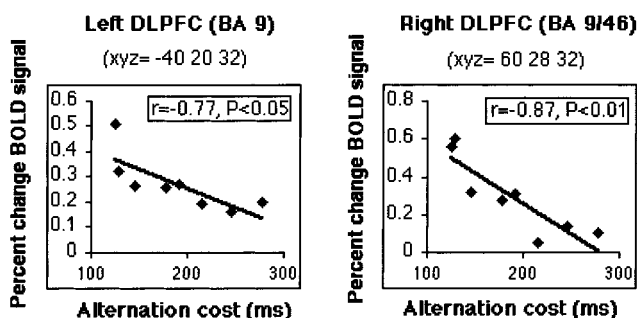


FIG. 7. Negative correlation between activation in bilateral DLPFC (BA 9/46) and the response time alternation cost ($xyz = -40\ 20\ 32$, $r = -0.77$; $P < 0.05$, two-tailed; $xyz = 60\ 28\ 32$, $r = -0.87$; $P < 0.01$, two-tailed). The alternation cost is calculated by subtracting the RTs obtained in the baseline condition from the RTs averaged across all task switching conditions. Data for each subject are shown by filled diamonds. For each subject, the mean signal intensity was identified in all task switching conditions relative to baseline based on the peak of activation observed in the group analysis.

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