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Recherche empirique d'un substrat neuronal aux processus cognitifs impliqués dans différentes tâches de flexibilité

Empirical search for neural correlates of cognitive subcomponents in different shifting tasks

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Résumé

Certaines théories concernant les fonctions exécutives proposent que des processus de mise à jour, de flexibilité mentale et d'inhibition puissent être distingués l'un de l'autre, mais qu'ils partagent cependant un mécanisme cognitif de base (Miyake *et al.*, 2000). Dans une étude récente en neuroimagerie par tomographie à émission de positons (TEP), une analyse en conjonction de plusieurs tâches représentatives des processus exécutifs décrits par Miyake (2000) a démontré qu'il existe effectivement une activation commune à ces différents processus, localisée bilatéralement dans des régions proches du sillon intrapariétal . Cependant, on peut poser la question d'une similarité ou d'une diversité de composantes cognitives pour différentes tâches associées à même processus exécutif. La présente étude décrit une analyse empirique des données d'activation cérébrale obtenues lors des trois tâches de flexibilité *(« shifting »)* incluses dans la publication de Collette *et al.* Les trois tâches (opérations arithmétiques, catégorisation verbale et catégorisation visuelle) étaient réalisées par le même groupe de sujets au cours d'une même session. Durant l'épreuve arithmétique, un nombre était présenté et le participant devait alterner, d'un essai à l'autre, entre une opération d'addition et de soustraction. La tâche de catégorisation verbale consistait en la présentation d'une paire chiffre/lettre sur un écran et, selon l'endroit de présentation, les participants devaient effectuer un jugement soit sur le chiffre (pair/impair) soit sur la lettre (consonne/voyelle). Finalement, dans l'épreuve de catégorisation visuelle, il s'agissait d'effectuer un jugement sur les aspects locaux ou globaux de figures de Navon, en fonction de la présentation de la figure en traits pleins ou pointillés. Ces trois tâches, bien que mettant toutes en jeu des processus de flexibilité, différaient selon plusieurs aspects, tels que le caractère prédictible (opérations arithmétiques, catégorisation verbale) ou non (catégorisation visuelle) de l'épreuve, la source endogène (opérations arithmétiques) ou exogène (catégorisation verbale et visuelle) du contrôle attentionnel requis, ou la présence d'un indice conditionnel (catégorisation verbale et visuelle) pour engager le processus de flexibilité. Une analyse en conjonction des trois tâches de flexibilité confirme l'engagement commun d'une région située dans le fond du sillon intrapariétal à droite, une activation probablement liée à la mise en œuvre d'un processus attentionnel de base commun à plusieurs fonctions exécutives. En raison de la disparité des tâches expérimentales, l'examen empirique des analyses de soustraction et d'interaction a été centré sur des composantes cognitives présentes dans deux des tâches mais pas dans la troisième. On a pu observer une activation commune du versant médial du sillon intrapariétal gauche caractéristique des deux épreuves requérant une association conditionnelle entre un indice externe et la tâche de flexibilité. Cette étude montre donc le corrélat neuronal (une activation pariétale supérieure) d'une composante cognitive (l'association conditionnelle entre un indice et une consigne) qui est partie prenante de certaines tâches de flexibilité mentale, mais qui n'est toutefois pas spécifique à ce type d'épreuve cognitive.

Mots clés : flexibilité • association conditionnelle • neuro-imagerie

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Abstract

We aimed to contrast cognitive subcomponents in three different shifting tasks combined in a single positron emission tomography study. The three tasks differed according to various aspects, such as their predictability and their (endogenous or exogenous) cueing. A conjunction analysis reproduced a previously reported common activation in the middle portion of the right intraparietal sulcus (IPS), related to attentional processes involved in many executive tasks. We then used simple subtractions/interaction analyses and plots of parameter estimates, looking for brain activation that could empirically be related to a specific cognitive subcomponent intervening in only two of the three tasks. Predictable cued shifting between stimuli for verbal categorization and unpredictable exogenously cued shifting between local and global features of Navon figures (but not the endogenously controlled arithmetic task) recruited the medial bank of the left IPS, involved when shifting between stimuli was conditional upon external cue-target association. The empirical study is consistent with hypothesis-driven reports and shows consistent neural correlate of a non-specific but useful cue-target association that intervenes in different shifting tasks.

Key words: shifting • cueing • conditional association • brain imaging

The shifting process refers to cognitive flexibility, namely the ability to displace the attentional focus from one stimulus, response or cognitive process to another to achieve a currently relevant goal. The difference in reaction times between trials in which subjects have to repeat the same task (task-repeat trials) and trials in which they have to shift from one task to another (task-shift trials) constitutes the task-shift cost [1]. Many theoretical frameworks have been applied to shifting, and various cognitive processes may explain the shift cost, such as task-set inertia (transient carry-over of task-set activation, inhibition or interference resolution from trial to trial), exogenous task-set activation generated by a cue (associative retrieval), and endogenous (top-down) control operations [2, 3].

In the functional neuroimaging literature, shifting processes have been related to activation in the superior parietal lobule [4-6], in the intraparietal sulcus [7-9], and in the inferior parietal cortex [10]. For example, superior parietal activation is specific to spatial shifts of attention *versus* the maintenance of attention at a single spatial location [11, 12]. But the superior parietal cortex is also recruited bilaterally when subjects have to shift between three semantic categories in a fluency task, compared to a non-shifting task [13], and activation in this area was observed during non-spatial cued shifting [14]. These results support the hypothesis that the superior parietal cortex is a supramodal area involved in task shifting, even when no visual or spatial component is involved in the tasks [15]. Other subregions in the frontal cortex have been assumed to respond to specific components of shifting [9]. In particular, the left inferior frontal junction has been claimed to be involved in resistance to interference from the irrelevant task set during the processing of the relevant task set [16]. Different shifting tasks have rarely been contrasted in the same experiment [9]. Nevertheless, in a factorial design, timing (fixed/random) and task order (predictable or not) were shown to differentially influence brain activation during task shifting [17]. For example, anticipating task order activated the right hippocampus, the anterior medial prefrontal and the posterior cingulate cortex, while unpredictable task order was associated with bilateral intraparietal activation.

In that context, we reanalyzed shifting data obtained in a previous study that explored the neural substrates common to the executive processes of shifting, updating and inhibition [18]. In the Collette *et al.* study, increased activity common to all executive processes was observed in the right intraparietal sulcus and the left superior parietal gyrus, and a conjunction analysis of the three shifting tasks revealed bilateral activation in the parietal cortices. The three shifting tasks, studied with positron emission tomography (PET) in the same subjects, were designed to engage different cognitive processes. They differed according to various conditions, such as the predictability of shifting, and endogenous attentional control *versus* exogenous cueing. In our new analysis, all scans were entered in a single design matrix, and we performed within-task comparisons (individual shifting task *versus* reference conditions), we looked for differences between shifting processes using interaction analyses and we plotted parameter estimates.

The aim of this new analysis was to tease out the neural correlates of cognitive processes involved in the shifting tasks:

– predictable and endogenously controlled shifting between two arithmetic operations was involved when subjects alternately performed addition and subtraction while hearing numbers spoken aloud;

– predictable shifting between two verbal categorization tasks was conditional on a spatial cue when subjects had to categorize either the number or the letter in pairs successively displayed in four quadrants of a screen, depending on the position (in the upper or lower row);

– unpredictable shifting between visual targets was conditional on a visual cue when volunteers had to categorize the global or local features of Navon figures, according to an unpredictable plain or dotted line display.

We first performed a conjunction analysis on the three shifting tasks, and we anticipated parietal activation, which has been found to be associated with executive and attentional tasks [18, 19]. In our empirical comparison of the three shifting tasks, we searched for the neural correlates of a cognitive subcomponent intervening in two but not in the third shifting task. Activation in the superior parietal cortex was anticipated in the two shifting tasks requiring association between an exogenous cue and the stimulus to be processed, independently of the type of cue or stimulus [20, 21]. Although the intervention of higher control regions in predictability/unpredictability is complex, the literature would relate ventromedial prefrontal activation to task order predictability, and intraparietal sulcus recruitment to task unpredictability [17].

Method

Participants

Twelve right-handed European volunteers (age range from 18 to 34 years) gave their written informed consent to take part in the study on shifting, which was approved by the University of Liège Ethics Committee. None had any past history of relevant medical problems or used any centrally acting medication. All subjects received financial compensation for their participation.

The shifting experiments

In the first condition, subjects had to perform arithmetic operations. In the second and third conditions, subjects had to perform verbal and visual categorizations, respectively. The tasks in question were adapted from Miyake *et al.* (2000), as previously described [18]. All tasks began 10 seconds before the emission scan (see below) and lasted for at least 120 seconds. In the first (arithmetic operations) and third (visual categorization) shifting experiments, responses were collected by recording subjects' responses *via* a digital-to-analog tape recorder connected to a microphone in order to assess *a posteriori* responses accuracy; response latencies (time between the onset of the stimulus and the onset of the subject's response) were also recorded *via* a second microphone connected to E-Prime beta software (Psychology Software Tools, Inc.). In the verbal categorization task, accuracy of response and response times were recorded by key-presses.

Endogenous shifting between arithmetic operations *(figure 1)*

The material consisted of numbers ranging from 10 to 99. Auditory stimuli were created using Praat 3.8.6.1 software [22]. They were presented auditorily *via* earphones and subjects responded aloud. The interval between two auditory presentations in the arithmetic tasks was fixed to 3,000 milliseconds. In the first *control task*, subjects were instructed to add 3 to each number presented, while in the second *control task*, subjects were asked to subtract 3 from each number. In the *shifting task*, subjects had to alternate between adding and subtracting 3 to or from

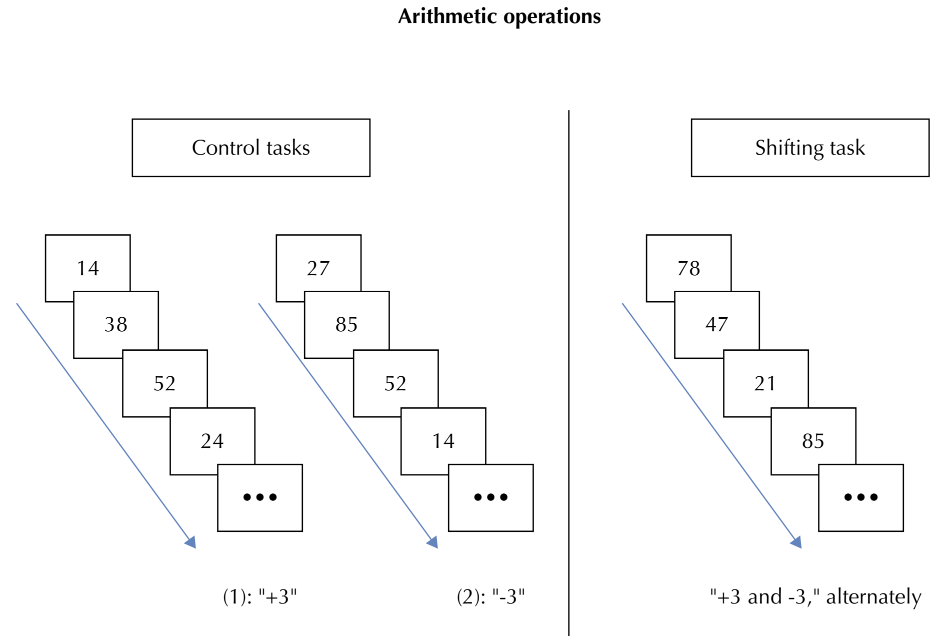

Figure 1. Illustration of stimuli and tasks 1.

each number presented. Thus, the control tasks required the continuous performance of similar arithmetic operations, whereas the experimental tasks required continuous shifting between two types of cognitive operations (addition and subtraction). Forty trials were presented in each task.

Predictable cued shifting between verbal categorizations *(figure 2)*

The material consisted of the 64 number-letter pairs. Items were presented on a PC screen in the Arial font (48 points), at a comfortable mean viewing distance of 90 cm from the subject's gaze. Numbers comprised four odd and four even digits, and the letters were four consonants and four vowels. These number-letters pairs were visually presented one at a time in one of the four quadrants of the computer screen. In the first *control task*, number-letter pairs were successively presented in the two upper quadrants of the screen, and the subject had to make an consonant/vowel decision on the letter. In the second *control task*, number-letter pairs were successively presented in the two lower quadrants of the screen and the subjects' task was to make a odd/even decision on the number. In the *shifting task*, number-letter pairs were presented in all four quadrants in a predictable clockwise rotation. Subjects had to process the letter (consonant/vowel) when the pair was presented in the upper quadrants and the number (odd/even) when the pair was presented in the lower quadrants. Thus, the trials within the control tasks required no shifting, whereas half of the trials in the experimental tasks required shifting between the two types of categorization operations (since item pairs were presented in the four quadrants of the screen clockwise). Fifty-six items were presented in each task. The maximum time allowed for each trial was 5,000 milliseconds, and the production of the response triggered the next trial.

Unpredictable cued shifting between visual categorizations *(figure 3)*

The material consisted of geometric figures often called Navon Figures [23] in which the lines of a large "global" figure (*e.g.*, a triangle) are composed of much smaller "local" figures (*e.g.*, squares). The items were 4 cm wide x 4 cm high, presented on a PC screen at a comfortable mean viewing distance of 90 cm from the subject's gaze. The figures were constructed to induce a global precedence effect (namely, the local elements were positioned very closely together and care was taken to ensure that the global identity

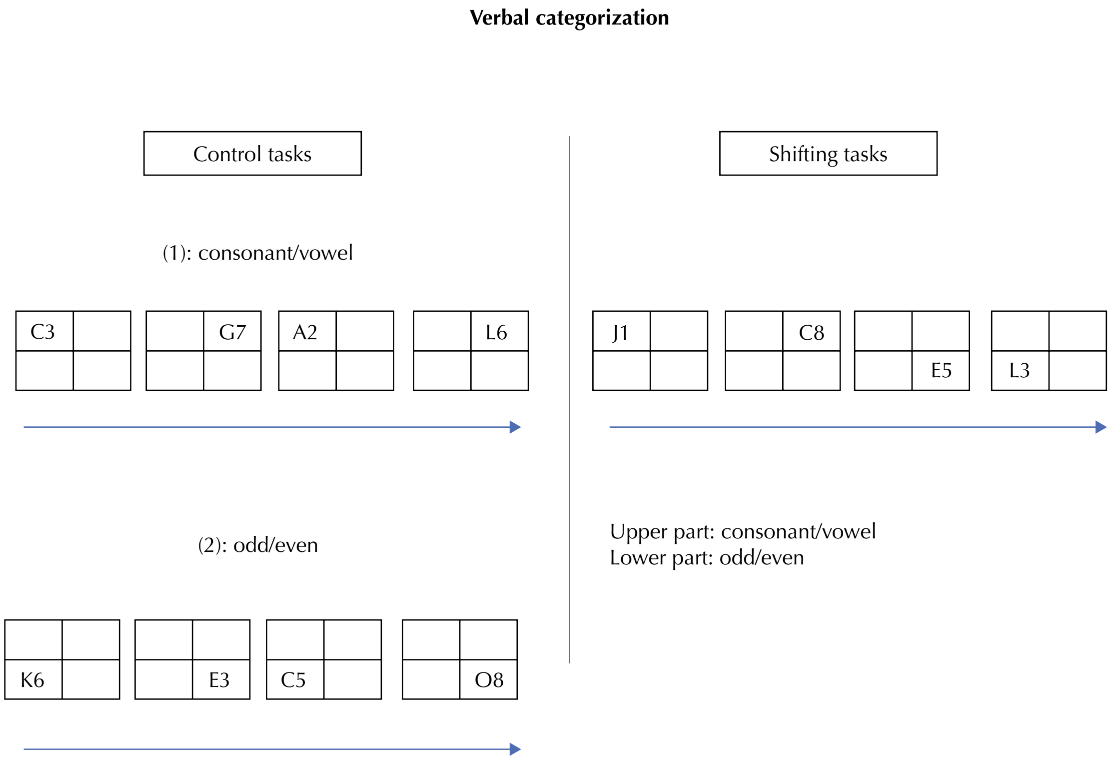

Figure 2. Illustration of stimuli and tasks 2.

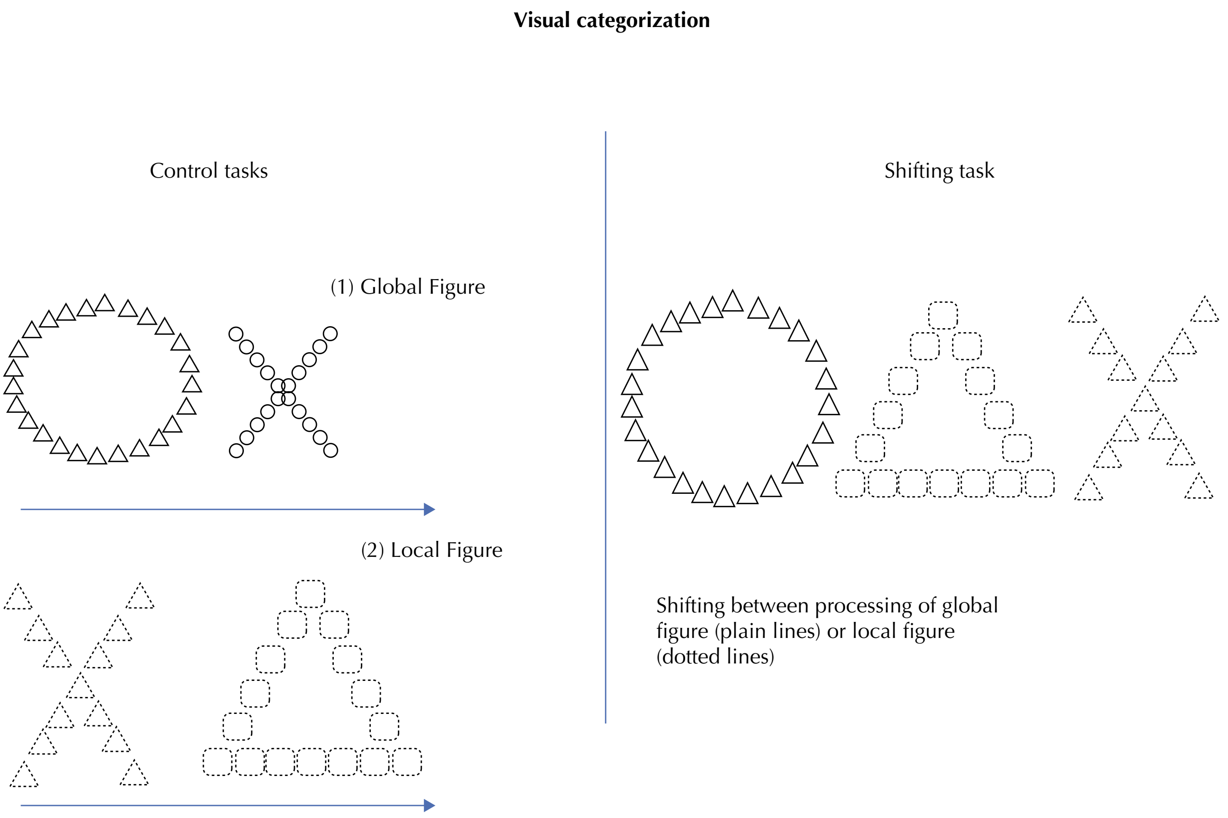

Figure 3. Illustration of stimuli and tasks 3.

constituted a good exemplar of the target figure [24]. Figures were presented one at a time on a visual display. In the first *control task*, exemplars with plain lines were presented and the participants had to say aloud the number of lines in the global figure (*i.e.*, 1 for a circle, 2 for a cross, 3 for a triangle and 4 for a square). In the second *control task*, figures with dotted lines were presented and subjects had to say aloud the number of lines in the local figures. In the *shifting task*, Navon figures with plain or dotted lines were randomly presented. Depending on the kind of lines in which the figure was printed (plain or dotted), participants were instructed to say aloud the number of lines in the global, overall figure (plain) or the local, smaller figures (dotted). Thus, when the lines of the stimuli changed across successive trials, the participants had to shift from examining the local features to the global features and vice versa. Plain *versus* dotted line to determine the level of perceptual processing were selected according to the procedure of Miyake *et al.* (2000) who also slightly modified the visual structure of the figures by using colors to induce local or global processing of information. Forty items were presented in each task. Each item was presented for a maximum duration of 3,000 milliseconds, and the production of the response triggered the next trial. In the experimental condition, half of the trials necessitated a shift between the local and global processing of the figure, and shifting trials were pseudo-randomly presented, with a maximum number of successive shift or non-shift trials fixed at three.

Positron emission tomography scanning

Positron emission tomography (PET) was used as neuroimaging procedure because the first and the third tasks required vocal responses to be recorded, and we did not have access to this technology for MRI at the time of the experiment. PET data were acquired on a Siemens CTI 951 R 16/31 scanner in 3D mode. The subject's head was stabilized by a thermoplastic facemask secured to the head holder (TruScan Imaging), and a venous catheter was inserted in a left antebrachial vein. First, a 20-minute transmission scan was acquired for attenuation correction using three rotating sources of 68Ge. Then, regional cerebral blood flow (rCBF), taken as a marker of local neuronal activity [25], was estimated over twelve emission scans. Each scan consisted of two frames: a 30-second background frame and a 90-second acquisition frame. The slow intravenous water ($H_2{}^{15}O$) infusion began 10 seconds before the second frame. Six mCi (222 MBq) were injected for each scan, in 5 cc saline, over a period of 20 seconds. The infusion was totally automated in order not to disturb the subject during the scanning period. Data were reconstructed using a Hanning filter (cutoff frequency: 0.5 cycle/pixel) and corrected for attenuation and background activity. Each experimental shifting task was carried out twice during the session and each control task was performed once. The order of presentation of the cognitive tasks was randomly assigned, except that no cognitive task was administered twice in succession and no more than two experimental or control tasks were administered successively.

Data analysis

PET data were analyzed using statistical parametric mapping (SPM99; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (MathWorks Inc, Sherborne, MA). For each subject, all scans were realigned together, then normalized to a standard PET template using the same transformations. Finally, the PET images were smoothed using a Gaussian kernel of 16 mm full width at half maximum. Such transformations of the data allow for voxel-by-voxel averaging of data across subjects and for direct cross-reference to the anatomical features in the standard stereotactic space.

The condition and subject (block) effects were estimated according to the general linear model at each voxel, using a random effect analysis. In SPM99, the random effect analysis is a two-step procedure applied to accommodate intra-individual and inter-individual variability of PET data, thus accounting explicitly for subject-by-condition interaction effects. In the first step, areas of significant change were determined at the within-subject level using linear contrasts of condition estimates. For each individual, subtraction contrasts were computed separately. The number of acquisitions is limited with PET and we capitalized on previous neuroimaging reports to compute a single contrast between shifting experiments and their two reference tasks. The resulting estimates (*i.e.*, individual contrast images) fitted the within-subject component of variance. In the second set of analyses, the residual between-subject variance was assessed comparing individual estimates created at the first level (using one sample t-test in SPM). The resulting set of voxel values for each contrast constituted a map of the *t* statistic [SPM(t)], thresholded at $p < 0.001$. Statistical inferences were obtained at the cluster level, at $p < 0.05$, corrected for multiple comparisons. Random effect analyses were used to determine the presence of statistical effects between control and experimental tasks in all subjects. Finally, the subtraction between each matched experimental and control task was entered into a single matrix to perform a conjunction analysis, so we could reproduce data previously published using different executive functions [18]. To ensure that regions were activated in each task, we used individual contrasts as inclusive masks, with a statistical threshold of $p < 0.005$. These random effect analyses were performed presuming that the assumption of variance equivalence (*i.e.*, that the error terms are uncorrelated) was satisfied. Note that similar results were obtained with a fixed effect analysis.

Interaction analyses were performed for each shifting process in opposition to each of the two others. This was done to determine the cerebral areas specific to particular shifting processes. Regions demonstrating interaction effects were determined as follows: cerebral areas with differential activity changes between the executive and control tasks in two conditions were determined, namely (first shifting task – mean of first control tasks) – (second shifting task – mean of second control tasks). A random effect analysis was used (see above). Moreover, we checked whether each region obtained in an interaction was also significantly activated in the random effect analysis (one sample t-test) of the first shifting task (at $p < 0.05$ using small volume correction). When relevant, plots of mean parameter estimates in some representative regions were displayed to illustrate our main results. Subtraction analyses are still widely used in the literature, although different caveats need to be taken into account. Since our shifting tasks were quite different, we concentrated on precise cognitive processes (predictability of a stimulus and conditional cue-target association) that occurred during two but not the other shifting tasks.

Results

Behavior

The comparison of each experimental task to the mean of its two control tasks demonstrated slower response times in the three shifting tasks compared to their control tasks [arithmetic operations: $F(1,11) = 17.50$, $p < 0.005$; verbal categorization: $F(1,11) = 17.23$, $p < 0.0001$; visual categorization: $F(1,11) = 50.41$, $p < 0.0001$]. The response times (in milliseconds) in the shifting and (mean of two) control tasks, respectively, were 1404 ± 203 *vs* 1308 ± 199 (arithmetic operations), 641 ± 110 *vs* 529 ± 67 (verbal categorization) and 1042 ± 193 *vs* 711 ± 149 (visual categorization). We did not directly compare response times between the shifting tasks because either verbal or manual responses were obtained, depending on the task. With regard to accuracy of responses, the percentage of errors was lower in the control task than in the shifting task for verbal ($Z = 2.31$, $p < 0.05$) and visual categorization ($Z = 2.36$, $p < 0.05$) while no difference was found between shifting and control arithmetic operations ($Z = 1.07$, n.s.). The percentages of errors in the shifting and control tasks, respectively, were 3.85 ± 1.80 *vs* 3.02 ± 2.74 (arithmetic operations), 2.0 ± 1.43 *vs* 0.82 ± 0.71 (verbal categorization) and 1.67 ± 2.02 *vs* 0.1 ± 0.34 (visual categorization). Note that non-parametric Wilcoxon statistical analyses were used due to the small number of errors in all conditions.

Neuroimaging data

Conjunction of three shifting tasks

The conjunction analysis (using a mask corresponding to each task, with a statistical threshold of *p* corrected < p.005 at voxel-level) confirmed our previous report

[18] but restricted the activation to a right middle IPS region, located near the fundus (coordinates: 30, –53, 38; voxels = 19; Z score = 5.44); the plot of parameter estimates clearly showed IPS involvement in each shifting task *(figure 4)*.

Endogenous shifting between arithmetic operations (experimental task 1)

The principal characteristics of the shifting process involved in this task were predictability, endogenous (intentional) control, and reliance on working memory. The comparison between the experimental task and the mean of the two reference tasks revealed activation in the right middle prefrontal cortex (PFC) and in the right inferior frontal sulcus for all subjects *(table 1*, *figure 4)*. The task is labeled ESAO in *figure 4*.

Right inferior parietal involvement was observed in the interaction analysis with experimental task 2 (predictable cued shifting between stimuli for verbal categorization), suggesting there was preferential activation in the right supramarginal gyrus when arithmetic operations were maintained in working memory during endogenous shifting *(table 1)*.

The interaction contrasting intentional shifting between arithmetic operations and task 3 (unpredictable, exogenous cued shifting between global and local features of visual stimuli) revealed that endogenous (intentional) alternation between arithmetic operations particularly recruited the middle cingulate cortex and confirmed the involvement of right lateral prefrontal regions *(table 1)*.

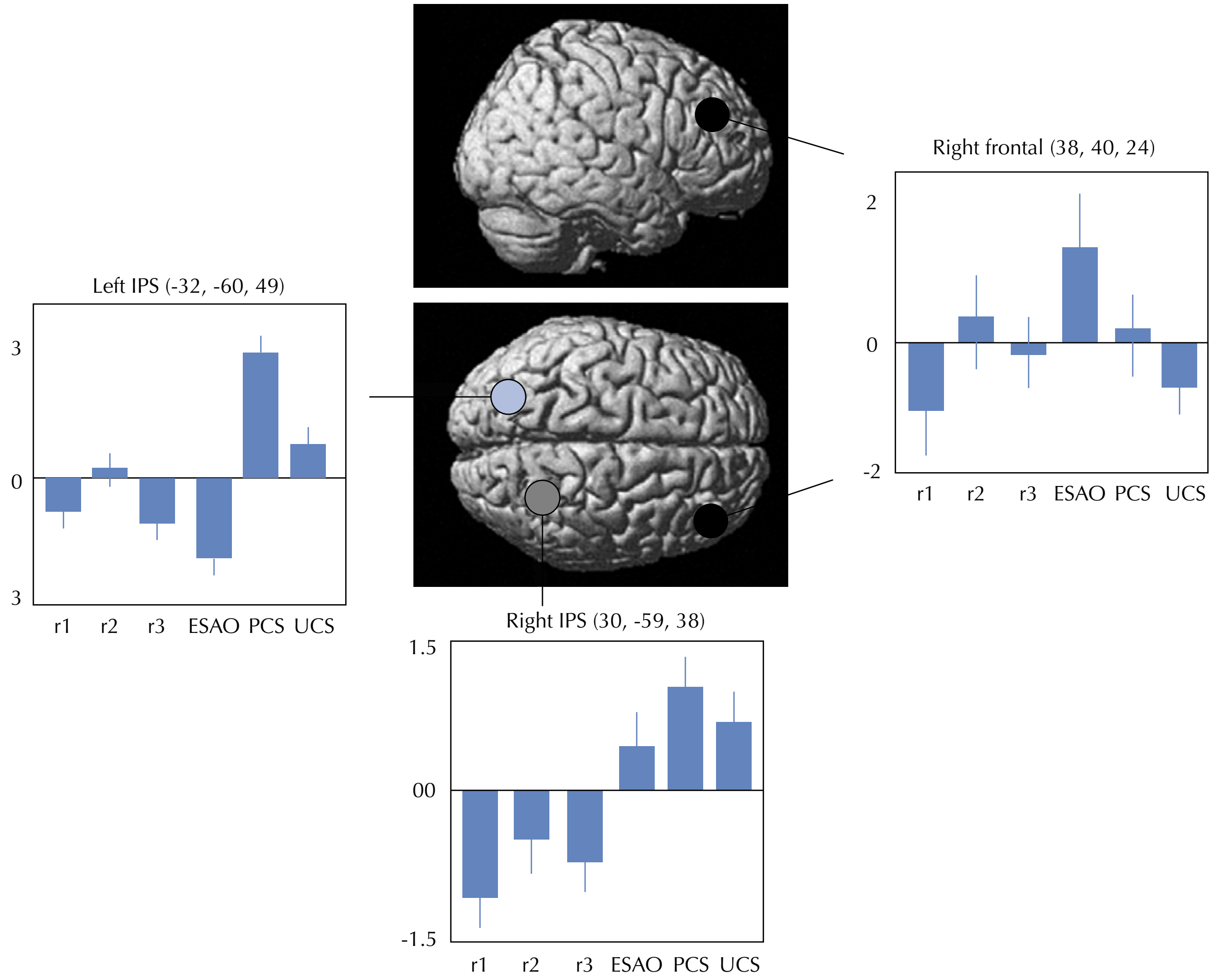

Figure 4. Overview of main activations in our shifting tasks. Activation in the first task is shown in black, activation common to the second and third tasks is in blue, and activation common to all tasks is in grey. The plots correspond to the size of parameter estimates (and 90% confidence interval) in control and experimental tasks; (r1, r2, r3) correspond respectively to the mean of two reference tasks for endogenous shifting between arithmetic operations (ESAO), predictable cued shifting between verbal categorization (PCS) and unpredictable cued shifting between global and local components of visual stimuli (UCS).

Table 1. Endogenous shifting between arithmetic operations

	Voxels	x	y	z	Z score
Subtraction, cluster p < 0.05 corrected					
R. middle frontal gyrus (BA 9)	287	38	40	24	4.25
R. inferior frontal sulcus	“	38	36	11	3.41
Subtraction, p < 0.001 uncorrected (seen in the conjunction analysis, voxel p < 0.005 corrected)					
R. intraparietal sulcus	52	30	– 54	36	3.13
Interaction with predictable cued shifting between stimuli for verbal categorization, cluster p < 0.05 corrected					
R. supramarginal gyrus	120	51	– 35	48	3.85
Interaction with unpredictable cued shifting between global/local features, cluster p < 0.05 corrected					
R. inferior frontal (BA 47)	915	38	41	– 2	4.48
	“	38	34	26	3.84
R. cingulate cortex	135	10	2	35	4.36

R: right; BA: Brodmann’s area; x, y and z (in mm) are coordinates in the standard stereotactical space.

Predictable cued shifting between stimuli for verbal categorization (experimental task 2)

In this classical experiment, subjects had to categorize a number or a letter of a pair, conditional on the pair’s location in the upper or lower row. The main characteristics of the shifting process involved in this task were predictability and exogenous cueing (by stimulus location). The subtraction analysis between experimental and reference conditions showed bilateral activation in the IPS *(table 2)*.

The interaction with task 1 (endogenous predictable shifting between operations) specifically demonstrated an activation in the medial bank of the left IPS. Importantly, *figure 4* shows a plot of activities for each task, confirming that the medial bank of the left IPS was involved in predictable cued shifting between stimuli for verbal categorization (PCS in *figure 4*) and also in unpredictable exogenous cued shifting between global and local feature processing (UCS in *figure 4*; see also subtraction results in *table 3*).

There was no significant activation for the interaction with cued shifting between global and local feature proces-

Table 2. Predictable cued shifting between stimuli for verbal categorization

	Voxels	x	y	z	Z score
Subtraction, cluster p < 0.05 corrected					
R. intraparietal sulcus	203	26	– 60	44	4.07
L. intraparietal sulcus	166	– 26	– 60	38	3.65
Interaction with endogenous shifting between arithmetic operations, cluster p < 0.05 corrected					
R. superior occipital (BA 19)	228	24	–78	31	3.72
L. intraparietal sulcus	141	–32	–60	49	3.75
Interaction with unpredictable cued shifting between global and local features					
Nil					

R: right; L: left; BA: Brodmann’s area; x, y and z (in mm) are coordinates in the standard stereotactical space.

Table 3. Unpredictable cued shifting between global and local feature processing

	Voxels	x	y	z	Z score
Subtraction, cluster p < 0.05 corrected					
L. posterior intraparietal sulcus	1191	– 28	– 66	36	4.69
L. intraparietal sulcus	"	– 28	– 60	51	4.01
R. precuneus (BA 7)	"	8	– 72	46	3.78
R. inferior temporal gyrus (BA 37)	187	62	– 66	– 7	4.46
Interaction with endogenous shifting between arithmetic operations, cluster p < 0.05 corrected					
Nil					
Interaction with predictable cued shifting between stimuli for verbal categorization, cluster p < 0.05 corrected					
Nil					

R: right; L: left; BA: Brodmann's area; x, y and z (in mm) are coordinates in the standard stereotactical space.

sing, suggesting that similar cognitive components are recruited in both tasks, and that (un)predictability does not determine specific activation in this experiment.

Unpredictable cued shifting between global and local feature processing (experimental task 3)

For this experiment using Navon's figures, task characteristics were unpredictability and exogenous cued by visual stimulus. The subtraction analysis between experimental and control conditions showed an activation in the left posterior IPS (extending into the left superior parietal gyrus) and precuneus activation *(table 3, figure 4)*.

The interaction with endogenous predictable shifting between arithmetic operations did not provide statistically significant results (although the plots in *figure 4* showed activation of the medial bank of the left IPS in task 3, and not in task 1).

The interaction with exogenous predictable cued shifting between stimuli for verbal categorization did not provide significant result.

Discussion

The aim of our experimental design was to directly compare three shifting tasks that were randomly performed during the same session by the same subjects. The tasks were derived from an earlier cognitive study suggesting that they are associated with a common shifting factor [26]. In particular, we investigated a global shift cost in tasks 2 and 3, since repeated trials alternated with shifting trials in a same scan, and the PET method did not allow us to specifically study activation during shifting compared to repeated trials. A conjunction analysis of the three shifting tasks demonstrated right IPS activation, using a masking procedure to retain only the activation observed in each task. More interestingly, different types of processes characterized our three shifting tasks. Endogenous displacement of the attentional focus occurred between responses in our first task (arithmetic operations), while shifting of attention between cues and stimuli was required in the two other tasks (verbal and visual categorization). More specifically, shifting was conditional on the presence of cue-target association in the latter two tasks. Subtraction and interaction analyses and plots of parameter estimates demonstrated local differences in brain activation between individual shifting tasks, in both prefrontal and parietal regions, but we concentrated on cognitive processes involved in all task or required by two but not by the other shifting task.

Conjunction of activation for three shifting tasks

The fundus of the right IPS was activated in all three shifting tasks, but the conjunction analysis did not show any prefrontal area common to the three tasks. This result was previously reported in a conjunction analysis of executive tasks which tapped updating, shifting and inhibition processes [18]. Previous neuroimaging studies also showed a more systematic activation of parietal than prefrontal areas in various shifting tasks [27, 28]. In the literature, the intraparietal sulcus has been found to be more activated for unpredictable than for predictable shifting tasks; however, it is also recruited to maintain two tasks in memory without shifting between them [17]. Accordingly, the intraparietal sulcus is classically assumed to play a role in selective attention [19, 29, 30], principally in the right hemisphere [31], and selective attention may act as a common denominator in many executive processes [31]. More specifically, Miyake *et al.* (2000) proposed that a primary characteristic of all executive tasks is the necessity to select some information and to inhibit other information. In keeping with this hypothesis, an activation very close to our right intraparietal focus (coordinates: 35, –53, 40) was observed when subjects alternately shifted between shape and color detection for centrally presented stimuli [5]: selecting the target stimulus feature while suppressing the other feature was the task requirement in this study. In summary, the common activation that we observed in the middle part of the right IPS could be related to amodal selective attention to behaviorally relevant information and to the suppression of irrelevant stimuli [18].

Predictable shifting between verbal categorizations conditional on spatial cues

In this task, subjects had to shift between two different kinds of stimuli to be categorized, and the predictable shift was cued by the location of the stimuli. The task was mixed, since shifting was both predictable and dependent on a cued association. This shifting task clearly relied on combined attention to the visual stimulus and its location. Activation occurred bilaterally in the middle/posterior part of the IPS, centered on the fundus of the sulcus, but extending to the superior parietal lobule.

The intraparietal sulcus (coordinates: 27, –59, 50) had previously been shown to be recruited for shifts of visuospatial attention [32], and there were predictable shifts of visual attention between the superior and inferior quadrants of the screen in our task. Such an activation might be driven by the spatial characteristic of the cue in this shifting task. More interestingly, the superior parietal cortex (coordinates: 21, –61, 50, close to the medial bank of the IPS activated in our task) had been found to be recruited for shifting attention between predictable positions and also for directing attention to a conjunction of features [20]. Importantly, activation in the medial bank of the IPS (coordinates: –36, –56, 52) was previously observed when subjects had to shift between feature discrimination according to different colors [17], or when shifting between color or motion dimension was cued by a letter [14]. Similarly, the main characteristic of our second experimental task was that predictable shifting between visual items to be verbally categorized was conditionally associated with a cue (the location of the pair of items in the upper or lower row).

In summary, predictable cued shifting between visual stimuli to be verbally categorized essentially recruited parietal regions centered around the middle/posterior IPS. The relative influences of the shifting task or the spatial attention to the cue on the IPS activation cannot be disentangled. There was no significant prefrontal activation for this task during our PET acquisition (possibly related to lack of power in the experiment). The most superior activation, near the medial bank of the left IPS, appeared to be preferentially recruited for shifting between the associations of a cue and a target to process (*i.e.*, feature association between upper row and number or between lower row and letter), a binding process not required for endogenous shifting between arithmetic operations. There was no significant interaction when cued shifting between types of verbal categorization was compared to cued shifting between global and local components of a figure, suggesting that both tasks required similar shifts of attention between cue and target associations.

Unpredictable cued shifting between global and local components of visual stimuli

In this task, unpredictable shifting between different components of the stimulus was conditional upon a visual cue within the stimulus itself. This experiment should require particular attention to be paid to the stimulus, thus eliciting parietal activation.

Activation in the fundus of the left IPS was similar to that observed in the second experimental task, and it had previously been reported in a meta-analysis of neuroimaging studies dedicated to shifting tasks [9]. This region probably subserves the selection of information (as discussed for the right IPS activation common to the three shifting tasks) during stimulus-driven shifts of attention [33]. As previously suggested [10], precuneus activation might also be related to high attentional demands, linked to shifting rate in our experiment. Indeed, the number of shifts between the global and local levels of Navon figures had previously been associated with activation in the precuneus [24, 34].

Left superior parietal activation (coordinates: –24, –57, 57) had previously been observed for shifting of spatial attention [11]. In our study, a plot of activity showed that the medial bank of the left intraparietal sulcus, near the superior parietal gyrus, was involved in conditional shifting between stimuli to be categorized (for both verbal and visual categorization), but not in endogenous alternating shifting between arithmetic tasks. In the present task, conditional shifting depended on an association of features (*i.e.*, plain line and global figure or dotted line and local figure).

In summary, the task was characterized by shifts of attention to cue and target associations, related to left medial IPS activation, as in experiment 2. Although the IPS activation was close to that previously reported for the main effect of unpredictable order task [17], there was no significant difference between unpredictable and predictable conditions in our experiment.

Conclusion

This combined study of three shifting experiments allowed us to confirm that various cognitive processes required for different shifting tasks have different cerebral correlates [3, 16]. A common cognitive process, activating the middle portion of the right IPS, might be related to selective attention to and inhibition of information. This process is not linked to individual strategies and is probably recruited in most executive and attentional tasks [18, 19]. The novel finding was the demonstration that specific processes involved in shifting tasks are related to activation in specific cerebral areas. More precisely, the medial bank of the left

IPS was particularly involved when shifting between the stimuli to be processed was conditional upon a specific cue. This region appears to be particularly important when association or conjunction of information is required for a shifting task [20, 21, 35], and its activation has also been reported during cue-related, switching-specific preparatory processes [36]. ■

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References

1. Rogers RD, Monsell S. The costs of a predictable switch between simple cognitivet asks. *J Exp Psychol Gen* 1995 ; 124 : 207-31.
2. Monsell S. Task switching. *Trends Cogn Sci* 2003 ; 7 : 134-40.
3. Aron AR, Monsell S, Sahakian BJ, *et al.* A componential analysis of task-switching deficits associated with lesions of left and right frontal cortex. *Brain* 2004 ; 127 : 1561-73.
4. Corbetta M, Miezin FM, Shulman GL, *et al.* A PET study of visuospatial attention. *J Neurosci* 1993 ; 13 : 1202-26.
5. Le TH, Pardo JV, Hu X. 4 T-fMRI study of nonspatial shifting of selective attention: cerebellar and parietal contributions. *J Neurophysiol* 1998 ; 79 : 1535-48.
6. Kimberg DY, Aguirre GK, D'Esposito M. Modulation of task-related neural activity in task-switching: an fMRI study. *Brain Res Cogn Brain Res* 2000 ; 10 : 189-96.
7. Dove A, Pollmann S, Schubert T, *et al.* Prefrontal cortex activation in task switching: an event-related fMRI study. *Brain Res Cogn Brain Res* 2000 ; 9 : 103-9.
8. Nagahama Y, Okada T, Katsumi Y, *et al.* Dissociable mechanisms of attentional control within the human prefrontal cortex. *Cereb Cortex* 2001 ; 11 : 85-92.
9. Wager TD, Jonides J, Reading S. Neuroimaging studies of shifting attention: a meta-analysis. *Neuroimage* 2004 ; 22 : 1679-93.
10. Barber AD, Carter CS. Cognitive control involved in overcoming prepotent response tendencies and switching between tasks. *Cereb Cortex* 2005 ; 15 : 899-912.
11. Vandenberghe R, Gitelman DR, Parrish TB, *et al.* Functional specificity of superior parietal mediation of spatial shifting. *Neuroimage* 2001 ; 14 : 661-73.
12. Yantis S, Schwarzbach J, Serences JT, *et al.* Transient neural activity in human parietal cortex during spatial attention shifts. *Nat Neurosci* 2002 ; 5 : 995-1002.
13. Gurd JM, Amunts K, Weiss PH, *et al.* Posterior parietal cortex is implicated in continuous switching between verbal fluency tasks: an fMRI study with clinical implications. *Brain* 2002 ; 125 : 1024-38.
14. Liston C, Matalon S, Hare TA, *et al.* Anterior cingulate and posterior parietal cortices are sensitive to dissociable forms of conflict in a task-switching paradigm. *Neuron* 2006 ; 50 : 643-53.
15. Braver TS, Reynolds JR, Donaldson DI. Neural mechanisms of transient and sustained cognitive control during task switching. *Neuron* 2003 ; 39 : 713-26.
16. Brass M, von Cramon DY. Decomposing components of task preparation with functional magnetic resonance imaging. *J Cogn Neurosci* 2004 ; 16 : 609-20.
17. Dreher JC, Koechlin E, Ali SO, *et al.* The roles of timing and task order during task switching. *Neuroimage* 2002 ; 17 : 95-109.
18. Collette F, Van der Linden M, Laureys S, *et al.* Exploring the unity and diversity of the neural substrates of executive functioning. *Hum Brain Mapp* 2005 ; 25 : 409-23.
19. Kanwisher N, Wojciulik E. Visual attention: insights from brain imaging. *Nat Rev Neurosci* 2000 ; 1 : 91-100.
20. Corbetta M, Shulman GL, Miezin FM, *et al.* Superior parietal cortex activation during spatial attention shifts and visual feature conjunction. *Science* 1995 ; 270 : 802-5.
21. Wolpert DM, Goodbody SJ, Husain M. Maintaining internal representations: the role of the human superior parietal lobe. *Nat Neurosci* 1998 ; 1 : 529-33.
22. Boersma P, Weenink D. Praat - A system for doing phonetics by computer (Computer Software): The Netherland: Institute of Phonetic Sciences, University of Amsterdam, 2003.
23. Navon D. Forest before trees: the precedence of global features in visual perception. *Cognit Psychol* 1977 ; 9 : 353-83.
24. Wilkinson DT, Halligan PW, Marshall JC, *et al.* Switching between the forest and the trees: brain systems involved in local/global changed-level judgments. *Neuroimage* 2001 ; 13 : 56-67.
25. Jueptner M, Weiller C. Review: does measurement of regional cerebral blood flow reflect synaptic activity? Implications for PET and fMRI. *Neuroimage* 1995 ; 2 : 148-56.
26. Miyake A, Friedman NP, Emerson MJ, *et al.* The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. *Cognit Psychol* 2000 ; 41 : 49-100.
27. Collette F, Hogge M, Salmon E, *et al.* Exploration of the neural substrates of executive functioning by functional neuroimaging. *Neuroscience* 2006 ; 139 : 209-21.
28. Collette F, Van der Linden M. Brain imaging of the central executive component of working memory. *Neurosci Biobehav Rev* 2002 ; 26 : 105-25.
29. Culham JC, Kanwisher NG. Neuroimaging of cognitive functions in human parietal cortex. *Curr Opin Neurobiol* 2001 ; 11 : 157-63.
30. Hopfinger JB, Buonocore MH, Mangun GR. The neural mechanisms of top-down attentional control. *Nat Neurosci* 2000 ; 3 : 284-91.
31. Coull JT, Frith CD. Differential activation of right superior parietal cortex and intraparietal sulcus by spatial and nonspatial attention. *Neuroimage* 1998 ; 8 : 176-87.
32. Beauchamp MS, Petit L, Ellmore TM, *et al.* A parametric fMRI study of overt and covert shifts of visuospatial attention. *Neuroimage* 2001 ; 14 : 310-21.
33. Sohn MH, Ursu S, Anderson JR, *et al.* Inaugural article: the role of prefrontal cortex and posterior parietal cortex in task switching. *Proc Natl Acad Sci USA* 2000 ; 97 : 13448-53.
34. Fink GR, Halligan PW, Marshall JC, *et al.* Neural mechanisms involved in the processing of global and local aspects of hierarchically organized visual stimuli. *Brain* 1997 ; 120 : 1779-91.
35. Deiber MP, Passingham RE, Colebatch JG, *et al.* Cortical areas and the selection of movement: a study with positron emission tomography. *Exp Brain Res* 1991 ; 84 : 393-402.
36. Slagter HA, Weissman DH, Giesbrecht B, *et al.* Brain regions activated by endogenous preparatory set shifting as revealed by fMRI. *Cognitive, affective & behavioral neuroscience* 2006 ; 6 : 175-89.