Posterior parietal cortex is implicated in continuous switching between verbal fluency tasks: an fMRI study with clinical implications

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Summary
We investigated whether posterior parietal cortex controls attentional switching when the tasks involve neither spatial nor visual cognition. Normal volunteers were scanned using functional MRI (fMRI). In all conditions, subjects were required to covertly produce words in verbal fluency tasks. They did so at a rate of one every 2 s (with eyes closed) in response to an auditory beep. In the non-switching (NS) trials, subjects responded with a series of items from a prespecified semantic category (SC) (e.g. fruits or cars) and from overlearned sequences (OSs) (days of the week, months of the year or letters of the alphabet). Instructions as to which category items should be drawn from on a given run of trials were presented over fMRI-compatible earphones prior to each run. In the switching (S) trials, subjects produced a series of word triads from three SCs: for example, fruits, cars and furniture (e.g. pear, Mercedes, table...); and from three OSs: days of the week, months of the year and letters of the alphabet (e.g. Monday, January, A...). This design is factorial, with the factors verbal class (SC or OSs) and switching conditions (S or NS). Increases in neural activity (P < 0.05, corrected for multiple comparisons) were observed only in superior posterior parietal cortex bilaterally as a main effect of the S conditions compared with the NS conditions. When SC fluency was compared with OS fluency, significant activations were found in anterior cingulate cortex bilaterally, the left inferior frontal gyrus, the middle frontal gyrus bilaterally, frontal operculum bilaterally and in the cerebellar vermis. These results support the hypothesis that superior posterior parietal cortex is a supramodal area implicated in task switching, even when no visual or spatial component is implicated in the tasks. Task switching, frequently used to examine ‘frontal’ executive functions, may also be clinically relevant to the assessment of patients with superior posterior parietal lesions.

Keywords: Broca’s area; frontal cortex; functional neuroimaging; task switching

Abbreviations: fMRI = functional MRI; NS = no switching; OS = overlearned sequence; S = switching; SC = semantic category; SPM = statistical parametric map; WM = working memory

Introduction
Having to divide one’s time between the performance of two (or more) tasks is a ubiquitous aspect of everyday life, as is coping with unheralded changes. The skills required to deal with such situations are particularly susceptible to disruption by brain damage and it is thus not surprising that clinical neuroscientists have attempted to bring simplified models of multi-tasking under experimental control and to elucidate the brain regions implicated therein. Progress towards this goal has, however, been slow. In part, this is due to the large range of conceptually distinct capacities and operations that have been studied in different task paradigms (Shallice, 1988). It accordingly may be necessary to distinguish between (at least) three types of task change: (i) shift of sorting criterion; (ii) dual-task performance; and (iii) alternating task demands.

Typical examples of type (i), shift of sorting criterion, include the Colour Form Sorting Test (Weigl, 1941) and the...
Wisconsin Card Sorting Test (Berg, 1948). In such tests, stimuli that differ in two or more dimensions (e.g. colour, shape and number) must first be categorized according to one dimension (e.g. colour) and then according to another (e.g. shape). The ability to switch from one sorting criterion to another is particularly impaired after prefrontal lesions (Rylander, 1939; Milner, 1963). More recently, Konishi and colleagues have shown with functional MRI (fMRI) that shifting cognitive sets on the Wisconsin Card Sorting Test reliably activates the inferior frontal gyri bilaterally (Konishi et al., 1998; see also Nagahama et al., 1999, 2001).

Type (ii) studies of dual-task performance can be conducted with virtually any two tasks. The demand characteristic of dual-task experiments is that the tasks should be performed concurrently. Since most cognitive tasks are sufficiently demanding that they cannot literally be performed simultaneously (although they may be presented simultaneously), dual-task experiments typically involve participants dividing their attention between the tasks as they switch from one to the other. Precisely how and when participants concentrate upon one task or the other may be exogenously or endogenously driven. Dual-task performance thus draws strongly upon working memory (WM) and the ‘executive’ or ‘supervisory’ functions that control input to and output from WM (Shallice, 1988; Baddeley, 1990). Prefrontal lesions give rise to particularly severe impairments in situations that require the supervisory attentional system to ‘manage’ the performance of concurrent tasks (Shallice, 1988).

Only partially similar conclusions have been drawn from the performance of healthy subjects in functional neuroimaging experiments. In studies by Bunge and colleagues, subjects performed a sentence reading and a verbal short term memory task either separately or concurrently while fMRI scans were collected (Bunge et al., 2000). Dual-task performance did not implicate any new areas (relative to performance on the individual tasks), although bilateral prefrontal regions were more highly activated when the tasks were undertaken concurrently. On the basis of comparable fMRI studies of dual-task performance, Adcock and colleagues concluded that there are no areas ‘dedicated to a general executive system’ involved in managing concurrent tasks (Adcock et al., 2000). Smith and colleagues likewise found no prefrontal regions that were active only during performance of a dual task in young subjects who performed the tasks well (Smith et al., 2001). In contrast, more elderly subjects did show activations of prefrontal cortex during the dual task that were not seen in the individual component tasks.

In type (iii) studies of alternating task demands, two or more tasks are performed in an explicitly alternating sequence. Psychophysical studies of normal subjects have shown that there is a reaction time cost to performing two tasks in strict alternation (ABABAB... compared with either task in isolation (Jersild, 1927). More recently, these ‘switch costs’ have been measured in ‘alternating runs’ paradigms with trial sequences such as AABBAABB... (Rogers and Monsell, 1995). Paradigms with alternating trials (ABAB) or alternating runs (AABBAA) have not been extensively deployed with patients who have suffered brain damage. Gurd and colleagues did however find that a patient with Pick’s disease [and marked bilateral frontal hypoperfusion on single photon emission CT (SPECT)] showed severe impairment on alternating verbal fluency tasks (Gurd et al., 1990). Rogers and colleagues studied performance on alternating runs in patients with focal damage to frontal cortex, and in patients with mild, early-stage Parkinson’s disease (Rogers et al., 1998). The patients with frontal damage showed time costs associated with switches only when there was the possibility of confusion over which task should be performed on a given trial. The patients with Parkinson’s disease showed no greater time costs of switching than normal controls (although their error rates increased over time).

Studies of the differential activation of brain regions during task switching have used a variety of traditional psychophysical paradigms. Dove and colleagues presented repeated trials of a visual task with manual response before reversing which hand should respond to which visual stimulus (Dove et al., 2000). Left and right prefrontal cortex was more highly activated on trials in which the hand of response was switched, as was a region within the left intraparietal sulcus. However, these same regions were activated, albeit less strongly, during simple task repetition. A similar result was obtained by Sohn and colleagues: task switching activated prefrontal cortex and posterior parietal cortex (PPC) more strongly than when the two tasks were simply repeated (Sohn et al., 2000). Kimberg and colleagues used a task switching design based closely on that of Rogers and Monsell (1995) in an event-related fMRI study (Kimberg et al., 2000). The stimulus materials were presented visually (letters and numbers) in different spatial positions (Kimberg et al., 2000). In contrast with the studies described previously, the results showed a small region in the left superior parietal lobule that was specific to the switch trials. It would seem, then, that some forms of multi-tasking do not depend upon prefrontal cortex. Smith and colleagues write ‘there is no special switching area in prefrontal cortex’, but their own experiment involves dual-task performance, not alternating task demands. Furthermore, those studies in which subjects have been requested to alternate between tasks (task switching) have typically presented switching and non-switching trials within the same experimental block of trials: the results were then analysed with event-related fMRI techniques (Dove et al., 2000; Kimberg et al., 2000; Pollmann, 2001). Whether the findings of such studies generalize to conditions in which non-switching and switching trials are separated into different blocks is unclear. There is, however, increasing evidence that some types of switching might draw significantly upon parietal cortex. For example, posterior parietal cortex is implicated in the switching of attention between different spatial locales (Posner and Petersen, 1990; Corbetta et al., 1995; Vandenberghhe et al., 2001) and between global and local aspects of hierarchically organized visual stimul
(Fink et al., 1997). Non-spatial shifting of selective attention between distinct visual attributes of a stimulus (shape versus colour) also involves parietal cortex (Le et al., 1998). Hence the parietal activations reported by Dove and colleagues, Sohn and colleagues, and Kimberg and colleagues may not have been due to switching per se, but rather to the visual or visuo-spatial nature of the tasks studied (Dove et al., 2000; Kimberg et al., 2000; Sohn et al., 2000): in the study by Dove and colleagues, the appropriate response (to a visual stimulus) was switched between the left and right hands (Dove et al., 2000). In the study by Sohn and colleagues, the participants classified letters as consonants or vowels and digits as odd or even by pressing the appropriate one of two buttons. In the study of Kimberg and colleagues, subjects responded to visual stimuli with the left or right hand (Kimberg et al., 2000). All these experiments thus involved visual processing and some degree of spatial attention.

To examine the hypothesis that parietal cortex is implicated in the control of switching per se, we must investigate task alternation in a paradigm that has no explicit spatial or visual components. Problem solving demands [as incorporated in type (i) card-sorting tests] should be minimized. Furthermore, the switching task should be constrained with respect to demands on WM. The neural circuits that underlie the verbal components of short-term WM are reasonably well established and should accordingly be detectable if differentially implicated in the different conditions of the current experiment (Warrington et al., 1971; Paulesu et al., 1993). The experiment that follows meets the requirements of minimal problem solving and constrained demand on WM by using verbal fluency tasks. We compare producing a series of words from a single superordinate class with producing a series of word triads from three distinct classes, and hence study switching between those classes.

Materials and methods

Subjects

Eleven healthy, right-handed volunteers (six male and five female; mean age 32 years, standard deviation 3.8 years) with no history of neurological or psychiatric illness were studied. The investigation was approved by the ethics committee of the University Hospital, Heinrich Heine University, Düsseldorf. Informed consent was obtained prior to participation.

Experimental design

Two verbal fluency tasks were used (factor 1: verbal class). In semantic category (SC) fluency, subjects were asked to covertly produce a series of words from a single predefined SC (e.g. fruits, cars or furniture), and in overlearned sequence (OSs) fluency, subjects were asked to covertly produce words from a single known ordered list (days of the week, months of the year or letters of the alphabet). The contrast between these two tasks enables us to image the brain regions implicated in the greater semantic search requirements of the category fluency task. We then contrasted these single specification trials with alternation trials (factor 2: switching). Here the subject must produce either sequences of triads of words from three semantic categories (fruits, cars and furniture) or triads from three OSs (days of the week, months of the year and letters of the alphabet). The comparison of these alternating trials with the single specification trials should isolate those brain regions implicated in switching between verbal categories. The use of two types of verbal fluency task allows us to investigate whether the same brain regions are involved in switching, irrespective of the precise verbal task employed. The experimental design was thus factorial: factor 1 is verbal class SC fluency versus OS fluency; and factor 2 is switching [single specification fluency (no switching, NS) versus alternating specification fluency (switching, S)]. A low-level baseline task was also employed, in which subjects were requested to relax and visualize the night sky. All tasks were performed with closed eyes.

Auditory task instructions were presented at the start of each block of trials using a digital playback system consisting of a PC, an audio amplifier and a magnetically shielded transducer system. The acoustic stimulation system terminated in tightly occlusive headphones allowing unimpeded conduction of the stimulus with good suppression of ambient scanner noise by ~20 decibels. In all conditions except the low-level baseline, subjects covertly produced words according to the task instructions, at a rate of one every 2 s, as cued by an auditory beep. Each task lasted 30 s.

All subjects were pre-trained on all tasks. This training was to ensure that the experimental results reflected task performance per se, rather than the effects of learning novel tasks. Several days before scanning, subjects were made familiar with the stimulus categories, and told not to learn to produce SC items in a fixed sequence. One day before scanning, subjects practised the tasks out loud to ensure that they understood the task demands. Immediately prior to scanning, a final practice session was recorded on tape in order to assess error rates. Subjects accordingly received three practice sessions. In each session, subjects practised two repeats of each of the four experimental conditions. In the practice sessions and in the actual experiment, the categories within a NS condition (e.g. cars or fruit;…; days or letters…) were sequenced pseudo-randomly. In the S conditions, the categories and their order of production (e.g. days, months, letters, or months, letters, days) were also assigned pseudo-randomly. Subjects were instructed to produce the OSs in their canonical order (e.g. ABCD,…, or, in switching trials, A, Monday, January, then B, Tuesday, February…). We considered that the amount and timing of practice given would not be sufficient to routinize performance and thereby significantly reduce the neuronal activations in the real experiment (Raichle et al., 1994).
MRI acquisition

MRI scanning was performed on a Magneton Vision 1.5 tesla scanner. Anatomical images were obtained using a high-resolution, T1-weighted MP-RAGE (magnetization-prepared, rapid acquisition gradient echo) pulse sequence with the following parameters: TR (repetition time) = 11.4 ms; TE (echo time) = 4.4 ms; flip angle = 15°; field-of-view (FOV) = 230 mm; matrix = 200 × 256; 128 sagittal slices with 1.25 mm slice thickness. EPI (echo planar imaging) was performed with a gradient booster system; the standard radio frequency head coil was used for transmission of radio frequency and signal reception. Pulse sequence parameters were as follows: gradient echo EPI; TE = 66 ms; TR = 5 s; slice thickness = 4.0 mm; inter-slice gap = 0.3 mm; 32 slices. The blocked design fMRI paradigm, which was preceded by three dummy scans to allow the MR signal to reach a steady state, comprised eight repetitions of a 45 s baseline state and a 30 s activation state (two repeats of each of the four experimental conditions). The baseline consisted of 30 s (six images) without presentation of auditory task instructions and 15 s (three images) with presentation of auditory task instructions. During the activation state, six whole-brain images were acquired (30 s). Each volunteer performed all five runs (each run comprising the eight blocks mentioned above) of the experiment during the complete measurement procedure.

Image processing

All calculations and image manipulations were performed on SPARC Ultra 10 workstations (SUN Microsystems Computers, Palo Alto, CA, USA) using MATLAB (The Mathworks Inc., Natick, Mass., USA) and Statistical Parametric Mapping software, SPM (Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk). SPM99 was used for image realignment, image normalization, smoothing, and to create statistical maps of significant relative regional BOLD (blood oxygenation level dependent) response changes (Friston et al., 1995a, b).

The first three images of each time series (123 images), during which the MRI signal reaches a steady state, were discarded. The remaining 120 volume images of each time series were automatically realigned to the first image (corresponding to the fourth acquired image of the time series) to correct for head movement between scans. Image sets of the four conditions and the baseline were then co-registered to the 3D anatomical data set using MPItool (MPItool, Max-Planck Institute for Neurological Research, Cologne, Germany) and SPM. The AC (anterior commissure) and PC (posterior commissure) points were identified, and transformed into a standard stereotactic space (Talairach and Tournoux, 1988), using the intercommissural line as the reference plane for the transformation. This spatial transformation uses linear proportions and a non-linear sampling algorithm (Friston et al., 1995a) and a representative brain from the Montreal Neurological Institute series as a template. Data were thereafter expressed in terms of standard stereotactic coordinates in the x-, y- and z-axes (as defined in Table 1). The resulting pixel size in standard stereotactic space was 2 mm with an interplane distance of 0.4 mm. Transformed functional data sets from each subject were smoothed with a Gaussian kernel of 6 mm for single-subject analysis, and of 10 mm (full-width half maximum) for the group analysis to meet the statistical requirements of the theory of Gaussian fields presupported by the ‘General Linear Model’ employed in SPM and to compensate for normal variation in individual brain size, shape and sulcal/gyral anatomy across subjects. Voxels that had values >0.8 of the

<table>
<thead>
<tr>
<th>Region</th>
<th>Side</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z score</th>
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<tr>
<td>S &gt; NS</td>
<td>Superior posterior parietal cortex&lt;sup&gt;1&lt;/sup&gt;</td>
<td>L</td>
<td>−16</td>
<td>−68</td>
<td>60</td>
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<td></td>
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<td>R</td>
<td>28</td>
<td>−64</td>
<td>58</td>
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<tr>
<td>SC &gt; OS</td>
<td>Anterior cingulate cortex&lt;sup&gt;2&lt;/sup&gt;</td>
<td>L</td>
<td>−4</td>
<td>18</td>
<td>40</td>
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<td></td>
<td></td>
<td>R</td>
<td>8</td>
<td>20</td>
<td>34</td>
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<td></td>
<td>Middle frontal gyrus&lt;sup&gt;3&lt;/sup&gt;</td>
<td>L</td>
<td>−32</td>
<td>38</td>
<td>28</td>
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<td>R</td>
<td>34</td>
<td>46</td>
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<td></td>
<td>Frontal operculum&lt;sup&gt;4&lt;/sup&gt;</td>
<td>L</td>
<td>−36</td>
<td>22</td>
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<td></td>
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<td>R</td>
<td>38</td>
<td>26</td>
<td>−10</td>
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<tr>
<td></td>
<td>Inferior frontal gyrus&lt;sup&gt;5&lt;/sup&gt;</td>
<td>L</td>
<td>−36</td>
<td>4</td>
<td>28</td>
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<td></td>
<td>Cerebellar vermis&lt;sup&gt;6&lt;/sup&gt;</td>
<td>M</td>
<td>8</td>
<td>−80</td>
<td>−42</td>
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<tr>
<td>SC,NS &gt; OS,NS &gt; SC,S &gt; OS,S</td>
<td>Inferior frontal cortex</td>
<td>L</td>
<td>−24</td>
<td>38</td>
<td>−18</td>
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</table>

Coordinates are in standard stereotaxic space and refer to maximally activated foci as indicated by the highest Z-score within an area of activation associated with the contrasts described. x is the distance in millimetres to the right (+) or left (−) of the midsagittal (interhemispheric) line; y is the distance anterior (+) or posterior (−) to the vertical plane through the anterior commissure; and z is the distance above (+) or below (−) the intercommissural line. R = right, L = left, M = medial. The superscript numbers refer to the labelling of areas of activation illustrated in Figs 1 and 2.
Statistical analysis
Following stereotactic normalization and smoothing, statistical analysis was performed. Low frequency cosine waves modelled and removed subject-specific low frequency drifts in signal. Data were analysed using a Random Effects Model, modelling the different conditions OS–NS, OS–S, SC–NS and SC–S as reference waveforms (i.e. box-car functions convolved with a haemodynamic response function in the context of the general linear model employed by SPM99). We accordingly defined a design matrix comprising contrasts modelling the alternating periods of ‘baseline’ and ‘activation’ using a delayed box-car reference vector that accounted for the delayed cerebral haemodynamic response function. Specific effects were tested by applying appropriate linear contrasts to the parameter estimates for each condition, resulting in a t-statistic for each and every voxel. These t-statistics (transformed to Z-statistics) constitute a statistical parametric map (SPM\(_{z}\)). These SPM\(_{z}\)s were then interpreted by referring to the probabilistic behaviour of Gaussian random fields. Voxels were identified as significant only if they passed a height threshold of \(Z = 4.5\) (\(P < 0.05\), corrected for multiple comparisons) and belonged to a cluster of at least 40 activated voxels (Friston et al., 1995b).

The data were first analysed for the main effects of verbal class (i.e. SC fluency versus OS fluency) and switching (S versus NS). A masking procedure was employed to ensure not only that the activations of experimental interest were positive with respect to the other experimental conditions but also that they were positive with respect to the low-level baseline. Accordingly, S > NS and NS > S were masked with S > baseline and NS > baseline, respectively, to assess whether or not relative increases in neural activity reflected activations of one condition or rather deactivations of the other (relative to baseline). Likewise, SC > OS and OS > SC were masked with SC > baseline and OS > baseline, respectively. Secondly, the data were analysed for the interaction of verbal class by switching.

For the fMRI data group analysis, repeated measures (scans) were collapsed within subject (after having adjusted for both global blood flow by using proportional scaling, and low-frequency physiological drifts by using a high-pass filter of 120 Hz) to give one scan per condition per subject. These conditions were then compared between subjects, thereby effecting a random effects model, allowing extrapolation to the general population. In addition, individual fMRI data were analysed to aid anatomical localization of significant activations from the group analysis. For individual subject analysis, fMRI data were analysed in an identical way to the group data but without collapsing the individual scans. The SPM was thresholded at \(P < 0.001\), uncorrected as we were concerned only with areas showing significant activations in the group analysis.

Localization of activations
The stereotactic coordinates of the pixels of the local maximum significant activations were determined within areas of significant relative activity change associated with the tasks. The anatomical localization of these local maxima was assessed with reference to the standard stereotactic atlas (Talairach and Tournoux, 1988), and validation of this method of localization was obtained by superimposition of the SPM maps on the group mean MRI image calculated after each individual’s MRI image had been stereotactically transformed into the same standard stereotactic space (Friston et al., 1995a).

Results
Neural activations during scanning
Table 1 shows the regions that are differentially activated as a main effect of switching (SC, S > OS, S > SC, NS + OS, NS). Superior posterior parietal cortex is activated bilaterally (\(P < 0.05\), corrected for multiple comparisons). The percentage signal changes in the BOLD signal (relative to the low-level baselines) are, for the local maximum (28, −64, 58) in the right superior posterior parietal cortex (mean ± standard error): OS, NS = −0.047 (± 0.02); SC, NS = −0.071 (± 0.02); OS, NS = 0.156 (± 0.03); SC, S = 0.089 (± 0.02). The comparable values for the local maximum (−16, −68, 60) in left superior posterior parietal cortex are: OS, NS = −0.141 (± 0.02); SC, NS = −0.012 (± 0.03); OS, S = 0.134 (± 0.04); SC, S = 0.178 (± 0.02). No other regions are significantly activated. In the reverse comparison (the main effect of non-switching greater than switching), no significant activation was observed.

Table 1 also shows the main effect of SC fluency (SC, NS + SC, S > OS, NS + OS, S). There are bilateral activations in anterior cingulated cortex, the middle frontal gyrus and the frontal operculum. The inferior frontal gyrus (containing Broca’s area) is significantly activated on the left only. The cerebellar vermis is likewise activated. All these regions are significant at \(P < 0.05\), corrected. The two main effects (S versus NS, and SC fluency versus OS fluency) are shown in Figs 1 and 2, respectively. In the reverse comparison (the main effect of OS fluency > SC fluency), there were no significant activations.

An interaction (\(P < 0.05\), corrected) between SC/OS and NS was observed. This interaction was an augmentation of activation in left inferior frontal cortex due to SC fluency without switching. The percentage signal changes of the local maximum at the locus of interaction (−24, +38, −18) are (mean ± SE): OC, NS = −0.368 (± 0.15); S, NS = 0.643 (± 0.01); OS, S = 0.245 (± 0.14); SC, S = −0.710 (± 0.20).

At \(P < 0.001\) (uncorrected), all 11 subjects showed activation in superior posterior parietal cortex. These activations are bilateral in seven subjects, and unilateral left in four subjects. Activations in superior posterior parietal cortex in a representative single subject are shown in Fig. 3.
We also show (Fig. 4A) plots of the NS and the S conditions each compared with the baseline ($P < 0.05$ corrected). Frontal and prefrontal activations are seen in both plots, with somewhat more extensive activation in the S condition. Bilateral superior parietal activation is seen only in the S condition. Fig. 4B shows the percentage signal changes associated with the left and right supplementary motor area (in both the S and NS conditions) and the left and right superior parietal cortex (in the S condition only). The loci plotted are for the maximally activated voxels in these regions.

Error rates during final practice
The last practice session took place immediately before imaging began. During this session, two repeats of each of the four conditions took place. This corresponds in length to one of the five runs of the imaging experiment itself. Errors were categorized as omissions (i.e. the subject failed to produce 15 items in response to the 15 auditory cueing beeps), repetitions (where the subject produced the same item more than once within a 30 s task category) or, during switching conditions, sequencing errors (e.g. Monday, A, January¼ when the required order was A, January, Monday¼). During this last practice session the error rates (sum of all errors made by all the 11 subjects) on two repeats of all four conditions per condition were as follows: SC,NS = 28 (15 omissions and 13 repetitions); SC,S = 60 (60 omissions); OS,NS = 0; OS,S = 19 (18 omissions, one sequence error).

The mean numbers of errors were compared between the four experimental conditions by a two-way ANOVA (Sigma Stat 2.03) with two verbal classes (SC fluency versus OS fluency) and two switching conditions (NS versus S) as factors. There were significantly higher error rates in SC
SC versus OS

Fig. 2 Relative differential increases in neural activity (for the 11 subjects) associated with SC relative to OS. Areas of significant relative increase in neural activity are shown as through-projections onto representations of standard stereotactic space (Talairach and Tournoux, 1988). The local maxima of the areas of significant relative increase \( (p < 0.05, \text{corrected for multiple comparisons}) \) in neural activity are displayed superimposed on transverse and coronal group mean MRI sections to detail the functional anatomy of the activations and their relationship to underlying structural anatomy. Transverse, view from above; coronal, view from the back. The exact coordinates of the local maxima (identified by numbers in boxes) within the areas of activation and their Z statistics are given in Table 1. R = right, L = left, A = anterior. The numbers on the axes refer to coordinates of standard stereotactic space (Talairach and Tournoux, 1988). See Table 1 for brain regions (numbered).

Discussion

The role of the parietal lobes in spatial attention is well established. Posterior superior parietal cortex in particular is implicated in switching attention from one spatial locale to another (Posner and Peterson, 1990). More recently, evidence from both the effects of parietal lesions (Humphreys et al., 1994) and from functional neuroimaging in normal volunteers (Le et al., 1998) has suggested that posterior parietal cortex is also involved when non-spatial shifts of attention are required. In the experiment of Humphreys and colleagues, patients with parietal lesions could only attend to one of two overlapping components of a complex visual stimulus (Humphreys et al., 1994). Le and colleagues found bilateral activation of posterior superior parietal cortex when subjects made ‘rapid, serial shifts in attention between stimulus shape or color’ (Le et al., 1998). In a typical sequence, ‘subjects responded to the first red target independent of shape, then switched to detecting a circle regardless of color’, continuing to alternate at an average rate of once every 3 s. It is important to stress, however, that in these previous studies that implicated parietal cortex in non-spatial switching, attentional shifts were made in response to visual targets (see Introduction).

An extended role for parietal cortex

The current study extended switching paradigms to verbal tasks that had no spatial and no visual component whatsoever. Our tasks and design thus differ considerably from those of Kimberg and colleagues who reported activation of the left...
precuneus (30, −52, 50) specific to switch trials, albeit with visuo-spatial displays (Kimberg et al., 2000). We should also reiterate (see Introduction) that our experimental design ran S (task change) and NS (task repetition) trials in separate blocks. There is evidence from psychophysical studies (Kray and Lindenberger, 2000) that general switch costs, defined as reaction time differences between NS and S blocks (AAAA or BBBB versus ABABAB) can be distinguished from specific switch costs within mixed blocks of non-switching and switching trials (AABBAABB). Although our design did not allow us to collect reaction time differences, the superior parietal activations we report here (Table 1) are (in terms of the distinction made by Kray and Lindenberger, 2000) a reflection of general switch costs. Furthermore, in our experiment particular responses were endogenously determined and switches were likewise endogenously driven, although in both cases their timing was externally cued. That subjects received no external task cue in the S condition (other than the instructions and the timing cue) makes our experiment methodologically quite distinct from previous studies of switching in which the alternation of a given trial is specifically triggered by a stimulus cue. For example, in the study of Dove and colleagues, a switch in response mapping was cued by a change in stimulus colour (Dove et al., 2000). Although tasks performed without external cues (Goldman-Rakic, 1987) typically implicate dorsolateral prefrontal cortex, we found no such activations over and above those found in the NS conditions (Table 1 and Fig. 4). This result does not imply that dorsolateral prefrontal cortex is irrelevant to switching: rather, it shows that the prefrontal activations implicated in verbal fluency tasks are not further augmented (at the level of statistical significance we set) by performing alternating verbal fluency (Fig. 4). If we reduce the threshold for the S > NS contrast to Z = 3.09 (P = 0.001, uncorrected), then there are activations in both left and right prefrontal cortex (−34, 0, 30 and 38, 6, 40, respectively). The activations are close to those reported by Dove and colleagues in an experiment in which responses to visual cues were switched between the index and middle fingers (−44, 5, 37 and 40, 8, 36, respectively) (Dove et al., 2000). The experiment of Dove and colleagues was specifically designed to have low WM load in the switch trials (Dove et al., 2000).

Nonetheless, our verbal fluency tasks (SC fluency and OS fluency) gave rise to strong superior posterior parietal cortex activations as a main effect when the switching conditions were contrasted with production from a single verbal class (see Table 1). The bilateral coordinates of local maxima within areas of activation that we report (−16, −68, 60; 28, −64, 58) are close to some of the peaks that Le and colleagues reported (−17, −76, 50; 25, −71, 46) when subjects shifted attention between two visual attributes of stimulus displays (Le et al., 1998). Some regions within superior parietal cortex are, it would seem, supramodal areas involved in the control of attentional switching: Its functions in this domain are not restricted to spatial tasks, either visual (Corbetta et al., 1995) or auditory (Bushara et al., 1999; Marshall, 2001), nor to switching tasks with visual input (Sohn et al., 2000). Use of a (sotto voce) verbal response also enabled us to reject the hypothesis that response switching between the hands is a necessary prerequisite for the effect (Dove et al., 2000; Kimberg et al., 2000). Our claim that some regions of parietal cortex play a supramodal role in switching does not preclude

**Fig. 3** Differential increases in neural activity (for Subject 7) associated with S relative to NS for the local maximum (x = −8, y = −66, z = +54, P < 0.05, corrected for multiple comparisons; Z-score = 7.2) after co-registration and superimposition of the individual structural MRI and the SPM maps derived from the fMRI data.
Fig. 4 (A) Relative differential increases in neural activity (for the 11 subjects) associated with NS relative to baseline and S relative to baseline (BL). Areas of significant ($P < 0.05$, corrected) relative increase in neural activity are shown as through-projections onto representations of standard stereotactic space (Talairach and Tournoux, 1988). (B) Percentage signal changes of the local maxima in the left and right supplementary motor area and in left and right superior posterior parietal cortex.
The possibility that other regions within the superior parietal lobe have modality-specific functions (Bushara et al., 1999).

**The role of working memory**

Clearly, both our S and NS tasks draw upon WM: subjects must remember the category or categories from which items are to be selected; they must also remember the items already produced in order not to repeat items within a run. The issue, however, concerns whether verbal WM is differentially involved in S versus NS verbal fluency. It might initially appear that the WM load must be greater in the S conditions (three categories rather than one have to be remembered), but there is another dimension on which WM load will be greater in the NS conditions. The more items that are produced from one category, the greater the WM load to ensure that items are not repeated. That load should be lightened when rather than having to produce, say, 15 items from one category, the subject can produce five items from each of three categories. Total WM load might accordingly be equivalent (although differentially constituted) across the S and NS conditions.

There is a suggestion that this might be so in the findings from the final practice session (with overt responding). In the SC,NS condition, there were 13 repetitions of an item while in the SC,S condition all of the errors were omissions (see Results). Empirically, the basic question can be resolved here by considering whether or not areas known to be implicated in verbal WM are differentially activated in the two relevant conditions.

The principle circuit underlying verbal WM involves inferior parietal cortex (the left supramarginal gyrus) and a range of prefrontal regions (Braver et al., 1997; D'Esposito et al., 2000; Gruber, 2001; Gruber and von Cramon, 2001). These are not the regions maximally associated with task switching in the current experiment. Cohen and colleagues did report that right superior parietal cortex was associated with WM load (in addition to stronger effects in prefrontal cortex and inferior parietal cortex) (Cohen et al., 1997). But their stimuli were visually presented and thus the experiment was not comparable to our study of intrinsic verbal generation (Goldman-Rakic, 1987) without visual, spatial, or indeed any overt stimulus-driven components (other than timing cue). Other experiments have been interpreted as showing that superior parietal cortex is specifically implicated in the maintenance of items in visuo-spatial memory (rather than response selection from WM). The coordinates of the maximally activated voxels reported by Rowe and colleagues for maintenance in spatial WM include 26, −60, 64 and −22, −62, 60 (Rowe et al., 2000). These coordinates are very close to those we report for S > NS (Table 1). Similarly, high memory load in a visual WM task has been associated with bilateral superior parietal activations (−20, −62, 52; 36, −52, 54) among a number of other regions (de Fockert et al., 2001). Again, these coordinates are close to the ones that we have interpreted as implicated in verbal switching. The following qualification is, however, in order.

The experiment conducted by Rowe and colleagues involved remembering the spatial position of three dots; a line was next shown that ran through the location of one of the previously presented dots. The subject then moved a joystick in the direction of the remembered dot that had been indirectly cued by the line. The control task also involved visual presentation and the same movements of the joystick but without any requirement to remember or select spatial locations. This control condition yielded significant activations at superior parietal locations that were very close to those purportedly implicated in maintenance in spatial WM (Rowe et al., 2000). Such congruence raises the strong possibility that the parietal activation observed by Rowe and colleagues is actually associated with having to change (switch) the direction of joystick movement from one trial to the next. This reinterpretation of the results of Rowe and colleagues suggests that the other regions they report as activated in their WM task (prefrontal and inferior parietal) are the ones that are actually implicated in the maintenance of spatial information (Rowe et al., 2000).

In the experiment by de Fockert and colleagues, subjects see and are required to remember a sequence of digits; they then classify famous names as pop stars or politicians while distractor faces are displayed behind the names (de Fockert et al., 2001). Memory for the sequence of digits is then tested. Although high memory load (random digits rather than an ordered sequence such as 1, 2, 3...) is associated with superior parietal activations, it is at least as plausible to interpret those activations as implicated in selective attention to the names rather than in WM per se. This interpretation is fully compatible with the claim of de Fockert and colleagues that a high memory load increases the attentional ‘effort’ required in the control of visual selective attention. It is also apparent that the design adopted by de Fockert and colleagues has a significant switching component: subjects are required to alternate between remembering a digit sequence and performing a judgement task that draws upon semantic (or encyclopaedic) memory (de Fockert et al., 2001).

None of these studies make it plausible that the superior parietal activations we have associated with the main effect of switching are solely due to differential memory load. Most crucially, the left inferior prefrontal activations (BA 47) that Gabrieli and colleagues, and Price associate with ‘the amount, duration and selection demands on semantic knowledge held in WM’ (Gabrieli et al., 1998; Price, 1998) are not found to be a main effect in our S > NS condition.

There is, however, one study of a ‘self-ordered’ verbal WM task that did find activation of medial superior parietal cortex, in addition to prefrontal and inferior parietal activations (Petrides et al., 1993). Subjects were required to say aloud numbers between one and 10 in a random order without repeating the same number (experimental condition). In the control task, they counted aloud from one to 10 in that order. The Talairach coordinates reported for this midline superior
parietal activation in the experimental condition minus the
control task are $-1, -69, 47$ for the maximally activated voxel
in this region. The (bilateral) activations we report for S > NS
(Table 1) are more lateral and more superior than those
reported by Petrides and colleagues (Petrides et al., 1993).
Whether it is plausible to regard the midline superior parietal
activation in their experiment as reflecting having to ‘switch’
implicitly from the OSs (1, 2, 3, 4...) to less ‘automatic’
continuations (2, 7, 1, 5...) remains to be determined.
Whatever the answer to this issue, we do not find in our S
condition (relative to the NS condition) any significant
activation of the other regions (Brodmann areas 9, 24, 40 and
46) that are implicated in verbal WM in the experiment of
Petrides and colleagues (Petrides et al., 1993). We accord-
ingly suggest that, in our experiment, the superior parietal
regions activated are indeed associated with task switching.
The group activations we report for switching are superior (z-
axis) to any of the parietal activations seen in a representative
sample of (non-spatial) WM experiments (e.g. Table 1 of
Schumacher et al., 1996; Tables 1 and 3 of Becker et al.,
1999; Honey et al., 2000).

Further evidence that equivalent WM loads are implicated
in both the S and NS trials of our experiment can be obtained
by examining these conditions in relation to the baseline
activations (Fig. 4). When contrasted with the baseline, there
are significant ($P < 0.05$ corrected) activations in the
supplementary motor area in both the S > baseline and the
NS > baseline conditions. This region has been associated
with high load in WM (de Fockert et al., 2001); the
coordinates reported ($-4, 4, 60$) are close to one of those
found in our experiment ($-6, 12, 52; 4, 10, 52$). Similarly,
Paulesu and colleagues report the supplementary motor area
as one of the regions implicated in verbal WM (Paulesu et al.,
1993). One of the coordinates they list ($-6, 6, 56$) is again
close to the activation we find.

The design of the current study cannot conclusively rule
out the possibility that a higher WM load is associated with
switching. One way in which memory load could be reduced
would be to use explicit cues to indicate (in an event-related
design) which category of item (S or NS) should be produced
in a given trial. The disadvantage of such a design, however,
is that it would remove much of the endogenously driven
response that we set out to investigate (Goldman-Rakic,
1987).

**Subject compliance**
The verbal fluency tasks and the experimental design
deployed here were well chosen to avoid visual and spatial
aspects of task switching. However, the fact that responses
were made covertly has the obvious consequence that no
explicit behavioural record exists of how (or indeed if) our
subjects were performing the tasks they had been set (and had
practised outside the scanning environment). Verbal tasks,
including fluency, can of course be readily performed aloud
with PET (Price, 1998), but it is generally accepted that with
fMRI a better signal can be obtained with covert (sotto voce)
responding (Yetkin et al., 1995). Nonetheless, many func-
tional neuroimaging studies of verbal fluency have already
been reported using either PET or fMRI and can provide an
external check on the validity of our results. The relevant
question is: are the results reported in Table 1 concerning
verbal fluency consistent with prior lesion studies and with
the normal functional neuroanatomy as observed in PET and
fMRI experiments? A positive answer to this question is
cri|cal to our claim that superior parietal cortex is implicated
in a type of verbal task alternation that would previously have
been regarded as a function of prefrontal cortex. Although
positive evidence from the pattern of activations in the NS
conditions does not necessarily imply that the subjects also
followed the task instructions during the S conditions, it must
prima facie make it more likely that they did. Likewise, the
fact that the activations we report for the S conditions are in
areas that are already known to be implicated in visuo-spatial
attentional shifts must increase confidence in the idea that our
subjects were indeed switching between the requisite sub-
tasks. It is, moreover, clear from the error rates of the final
practice session before scanning (in which the tasks were
performed out loud) that substantial error costs did arise in the
S conditions (see Results).

**Validity of the main effect of SC fluency**
SC fluency can be impaired after penetrating missile injury to
frontal, temporal and parietal regions of the left hemisphere
(Newcombe, 1969). But in patients who are not aphasic,
lesions of prefrontal cortex have a particularly deleterious
effect upon verbal fluency (Owen et al., 1990; Baldo and
Shimamura, 1998). Although deficits are produced by lesions
of either hemisphere, left prefrontal lesions give rise to the
more severe impairment (Baldo and Shimamura, 1998).
Preservation of so-called ‘automatic speech’ (including the
kinds of OS used in this study) has been reported in the
context of severe aphasic impairment on language and speech
tasks that are less "prepared" (Albert et al., 1981). Clearly, SC
fluency maximizes the demand on search mechanisms within
the internal lexicon, while ‘automatic speech’ (OS) tasks
minimize that information processing load when a fixed,
prespecified sequence of items can be ‘automatically’ articu-
lated. By contrast, tasks such as SC fluency are paradigm
elements of ‘intrinsic generation’ (Goldman-Rakic, 1987).
That is, sequences of discrete responses that meet the criteria
must be made in the absence of any external guidance other
than the instructional set itself and without the possibility of
pre-preparing particular responses. Evidence from both
monkeys and man suggests that such task demands draw
heavily upon the dorsolateral prefrontal cortex (Goldman-
Rakic, 1987). Bilateral activation of the middle frontal gyrus
shown in Table 1, when SC fluency is contrasted with OS
fluency, is thus consistent with what is known from lesion
studies about the functions of these areas.
There is also previous evidence from functional neuroimaging that strong activation of dorsolateral prefrontal cortex is associated with SC fluency. This result has been found in normal volunteers (Frith et al., 1991), and in patients with temporal lobe epilepsy (Lehéricy et al., 2000). In some studies, the stronger activations are found bilaterally in the inferior frontal gyrus (Pihlajamäki et al., 2000). Similar prefrontal activations are seen when subjects perform verbal fluency tasks in which the items are specified by a particular first letter (Phelps et al., 1997; Schlösser et al., 1998; Pujol et al., 1999). More generally, dorsolateral cortex is implicated in the selection of responses from memory rather than the maintenance of responses within WM (Rowe et al., 2000). By contrast, automatic speech (our OS fluency) does not significantly activate dorsolateral prefrontal cortex (Wildgruber et al., 1996; Brookheimer et al., 2000), although it does activate Broca’s area on the left (Wildgruber et al., 1996; Brookheimer et al., 2000). Likewise, Broca’s area is activated by initial letter fluency tasks (Hinke et al., 1993; Mummery et al., 1996). That Broca’s area is more highly activated in SC fluency than in OS fluency (Table 1) is consistent with the former task, imposing a greater load on the strategic control of phonological processing (Fiez, 1997). This region is also implicated in WM (de Fockert et al., 2001): verbal fluency tasks place some load on WM given the requirement that subjects do not repeat previously produced items. We found no significant activations specific to OS fluency (relative to SC fluency); hence our data do not support the claim that automatic speech is the prerogative of the right hemisphere (Ryding et al., 1987).

The frontal operculum forms part of a semantic network common to words and pictures (Vandenberghe et al., 1996). In particular, it has been conjectured to play a role in the strategic control and on-line retrieval of semantic information (Demb et al., 1995; Fiez, 1997; Poldrack et al., 1999). These functions are consistent with our finding of greater activation of the frontal operculum during SC fluency (relative to OS fluency). Activations in the anterior cingulate cortex (Table 1) during SC fluency are consistent with the role this structure plays in attention to the selection of responses: SC fluency draws more heavily than does OS fluency on the suppression of inappropriate responses and the facilitation of within-category responses (Paus et al., 1993; Thompson-Schill et al., 1997). Relatively little will be required of such control functions when an OS is produced. Cerebellar activation has already been demonstrated during subvocal recitation of OSs (Ackermann et al., 1998). That we find greater activation for SC fluency (relative to OS fluency) suggests that the effect is not due solely to articulatory planning (Table 1).

**Interpretation of the interaction term**

The significant interaction shown in Table 1 suggests that left inferior frontal cortex is most strongly activated when a greater number of different members of a particular SC must be produced during a run: in one interpretation, the activation is associated with the SC, NS condition and hence, in the paced design we employed, must involve producing three times the numbers of items from a given individual category than that obtained when subjects switch between items from three different categories. The activation is thus consistent with the known semantic role of this region (Fiez, 1997). Prefrontal activation is also consistent with the deployment of supervisory control to prevent repetition of items (Burgess and Shallice, 1994). The logic of the interaction makes it equally correct (descriptively) to associate the BOLD signal change with a relative deactivation during the SC,S condition (i.e. when fewer items need to be produced from each specific category). This latter description is fully compatible with our preferred formulation that the interaction reflects increased activation in left inferior frontal cortex when more items from a given semantic class must be produced without repetitions (SC, NS condition). Nonetheless, given that these BOLD signal changes are all relative, the two interpretations are, as it were, two sides of the same coin. An interpretation in terms of semantic retrieval load is compatible with a further aspect of the crossover interaction: that OS,S provokes a larger (more positive) BOLD signal change than OS,NS suggests that an augmented retrieval load is implicated in this activation. Retrieval load should be comparatively low when the ‘automatic’ production of a single OS drawn from one category (e.g. days of the week) is required. Load should increase when alternating retrieval from three distinct OSs is required. Here the subject must keep in mind three categories (days, months and letters). Finally, we note that the switch-specific effects are larger (in addition to being qualitatively different) in the SC condition as compared with the OS condition. This finding is again compatible with the involvement of left inferior prefrontal cortex in semantic load in WM (Gabrieli et al., 1998; Price, 1998).

**Conclusions and clinical implications**

The internal consistency of our data and their congruence with the results of earlier studies of verbal fluency lead us to presume that our volunteers were indeed heeding the instructions and performing the tasks as requested. The apparent validity of the main effect of SC fluency (relative to OS fluency) thus increases confidence that the main effect of switching is likewise reliable and valid. Furthermore, there is little or no evidence to suggest that verbal WM is differentially involved in the main effects of switching in our study (although WM does seem to be implicated in the interaction). The involvement of superior posterior parietal cortex in switching between SCs and between OSs clearly implies a far more multi- or supra-modal role for this region than was hitherto suspected. Attentional shifts do not need to involve visual and/or spatial factors, either at input or output (Corbetta et al., 1995; Fink et al., 1999; Jäncke et al., 2000), in order to implicate parietal cortex.

Some forms of task switching unquestionably draw upon frontal cortex and the relevant tests are typically incorporated...
into the clinical examination of patients with suspected frontal involvement (see Introduction). Our current results strongly suggest that superior posterior parietal cortex also participates in switching between verbal tasks that have no visual or spatial component. The implications for clinical practice are that a wider range of distinct switching tasks should be employed when examining putative behavioural impairments, and that it should not be assumed that only patients with frontal lesions will experience difficulties in shifting between tasks. Likewise, it should not be assumed that patients with superior posterior parietal lesions will only experience difficulties in shifting spatial attention. The human frontal lobe can be recruited by diverse cognitive demands (Duncan and Owen, 2000), and it is likely that a similar conclusion holds for the parietal lobe. The particular switching tasks we deployed here (alternating task demands) are highly repetitive and do not require any kind of problem solving. They thereby differ from the ‘frontal’ tasks typically employed in clinical practice (see Introduction). Relatively intact prefrontal cortex (and its connections with the parietal lobe) may be a prerequisite for ensuring that sufficient WM capacity and executive control (Shallice, 1988) is available to allow verbal fluency tasks, including switching fluency, to be performed correctly (Gurd et al., 1990; Gurd, 1995). Nonetheless, our evidence supports the claim that superior posterior parietal cortex plays a dominant role in alternating between categories in verbal fluency.

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