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Running Head: Task-switching and fMRI

Domain-independent neural underpinning of task-switching: an fMRI investigation

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Abstract

The ability to shift between different tasks according to internal or external demands, which is at the core of our behavioral flexibility, has been generally linked to the functionality of left fronto-parietal regions. Traditionally, the left and right hemispheres have also been associated with verbal and spatial processing, respectively. We therefore investigated with functional MRI whether the processes engaged during task-switching interact in the brain with the domain of the tasks to be switched, that is, verbal or spatial. Importantly, physical stimuli were exactly the same and participants' performance was matched between the two domains. The fMRI results showed a clearly left-lateralized involvement of fronto-parietal regions when contrasting task-switching vs. single task blocks in the context of verbal rules. A more bilateral pattern, especially in the prefrontal cortex, was instead observed for switching between spatial tasks. Moreover, while a conjunction analysis showed that the core regions involved in task-switching, independently of the switching context, were localized both in left inferior prefrontal and parietal cortices and in bilateral supplementary motor area, a direct analysis of functional lateralization revealed that hemispheric asymmetries in the frontal lobes were more biased toward the left side for the verbal domain than for the spatial one and vice versa. Overall, these findings highlight the role of left fronto-parietal regions in task-switching, above and beyond the specific task requirements, but also show that hemispheric asymmetries may be modulated by the more specific nature of the tasks to be performed during task-switching.

Keywords: task-switching, left prefrontal cortex, hemispheric asymmetries, conjunction analysis, executive functions.

Introduction

Executive functions are a set of high-level cognitive operations aimed at controlling other lower-level processes towards a goal. There is consensus in the literature that the implementation of these superior processes in the brain involves the prefrontal cortex (e.g., Barbey et al., 2012; D’Esposito, 2007; Luria, 1966; Yuan and Raz, 2014) and more broadly fronto-parietal networks (Dosenbach et al., 2007; Fassbender et al., 2004; Woolgar et al., 2011). What is less understood is the role of hemispheric asymmetries in executive functions.

While hemispheric asymmetries have indeed been extensively documented for other functions, such as right hemispheric dominance for visuo-spatial attention (Boulinguez, Ferrous, Graumer, 2003; Corbetta and Shulman, 2011; Weintraub and Mesulam, 1987) and left hemispheric dominance for semantic and verbal processing (Corballis, 2009; Fairhall and Caramazza, 2013; Thompson-Schill et al., 1997), the relationship between executive functions and hemispheric asymmetries remains under-investigated and poorly understood (see Vallesi, 2012, for a review).

Certain executive functions preferentially involve the prefrontal cortex in one hemisphere with respect to the other. Among these, in the present study we will focus on task-switching, the capacity to flexibly shift among different task rules from one trial to another in response to changing environmental or endogenous demands. This complex capacity involves many components (e.g., Monsell, 2003; Shallice et al., 2008). Among other cognitive processes, task-switching conceivably requires resource-demanding controlled operations (cf. Logan and Bundesen, 2003) such as set-shifting, that is, the capacity to reconfigure a task-set if different from that used in the previous trial (Rogers and Monsell, 1995). Performance on this type of task is indeed characterized by a general worsening on repeat trials when intermixed with switch trials as compared to trials in single-task blocks, namely the mixing costs (Rubin and Meiran, 2005; Koch et al., 2005), and on rule switch trials with respect to repeat ones in task-switching blocks, namely the switching costs (Rogers and Monsell, 1995).

From a neuro-functional point of view, task-switching preferentially engages left prefrontal and posterior parietal regions, as it has been demonstrated by converging neuroimaging (e.g., Badre and Wagner, 2006; Gurd et al., 2002; Kim et al., 2011; Muhle-Karbe et al., 2014) and neuropsychological evidence (e.g., Aron et al., 2004; Keele and Rafal, 2000; Mecklinger et al., 1999; Rogers et al., 1998; Shallice et al., 2008; Stablum et al., 1994). However, the precise localization as well as connectivity pattern within the left hemisphere during task-switching depends on the type of switch involved (e.g., Kim et al., 2012; Philipp et al., 2013; Stelzel et al., 2011). On the other hand, task-switching does not seem to be generally associated with right prefrontal involvement (e.g., Brass and von Cramon, 2004; Hedden and Gabrieli, 2010).

In a recent study (Kim et al., 2011), for instance, although different types of switching were found to involve progressively more rostral (both medial and lateral) prefrontal regions as a function of the rule abstractness (i.e., stimulus-, response- and set-switching), common nodes of activation for all the different switching conditions were found in the inferior frontal junction and posterior parietal cortex at the border with the superior occipital cortex, both in the left hemisphere.

In the present study, we aimed at understanding how brain lateralization involved in task-switching may be modulated by the nature of the task to be performed. In task-switching blocks, participants had to switch either between two spatial tasks or between two verbal ones. In single task control blocks participants only performed one task at a time. Both spatial and verbal tasks were administering physically identical stimuli. The spatial tasks consisted in judging how visually presented words were oriented in either roll or pitch dimensions. Processing of spatial information is usually more right-lateralized in the brain (Dupont et al., 1998; Logie et al., 2011; Marshall and Fink, 2001; Jansen et al., 2004; Orban et al., 1997; but see Cubelli et al., 2011). The verbal tasks consisted in judging the female/male status or proper/common noun status of the presented words. Thus, the verbal task involved mainly left lateralized cognitive activities such as word reading and grammar processing (e.g., Buchweitz et al., 2009; Petersson and Hagoort, 2012; Semenza, 2006).

Our main goal was to identify which regions are involved in task-switching independently of the strongly lateralized specific tasks to be performed. Task-switching blocks were contrasted to single task ones in order to control for both more basic sensorimotor processes and possible general lateralization patterns within each task, which were not specific to task-switching. A prediction based on the previous literature was that left inferior prefrontal and parietal regions would be commonly activated during different types of task-switching (e.g., Kim et al., 2011).

Another important goal was to understand how functional hemispheric asymmetries in task-switching blocks are modulated by the specific task-demands (i.e., spatial or verbal). Assuming that task-switching interacts with the specific domains of the tasks to be switched, we also predicted task-specific activations more biased toward the right and left hemisphere, for the spatial and verbal rules, respectively.

Methods

Participants

Thirty-eight university students voluntarily took part in the experiment. All participants gave informed consent prior to their recruitment. They were reimbursed 25 euros for their time. All had normal or corrected-to-normal visual acuity (MRI-compatible glasses were used when appropriate) and reported having normal colour vision. The study was approved by the Bioethical Committee of the Azienda Ospedaliera di Padova and was conducted according to the guidelines of the Declaration of Helsinki. Data from 4 participants were discarded because of excessive head-movements ($> \pm 3$ mm in any translation direction). We also had to discard data from 3 extra participants because of low compliance with the task instructions (accuracy level < 2.5 standard deviations in some conditions). The final number of included participants was 31. All of them were right-handed (which was an inclusion criterion), as assessed with the Edinburgh Handedness Inventory (average score: 83.4, range: 45-100). There were 24 females and 7 males and their mean age was 23 years (range: 21-30 years).

Apparatus and stimuli.

The stimulus material consisted of 18 proper nouns and 18 common nouns, that were divided into four categories of 9 nouns each according to our experimental manipulation: proper female nouns, common female nouns, proper male nouns and common male nouns. The proper nouns comprised personal names (e.g., “LAURA”) and names of states (e.g., “CILE”, the Italian word for Chile), while the common nouns comprised terms for non-living things (e.g., “MATITA”- “pencil”) and generic terms referring to people (e.g., “PRETE” - “priest”). Each set of words was matched for word length (mean word length: 5 letters) and frequency of use (mean frequency: 81) (Bertinetto et al., 2005; <http://linguistica.sns.it/CoLFIS/Home.htm>). To discourage the strategy of identifying the grammatical gender of the words by simply attending to the ending vowel (i.e., the final vowel “a” that in Italian is almost always diagnostic of the feminine gender, while the vowel “o” indicates the masculine gender), some of the words for each set contained either an ending consonant (e.g., “MAIS”- “corn”) or an ending vowel that is opaque in Italian for grammatical gender (e.g., “LUCA” for a personal male name).

Each word, including the proper names, was presented in lowercase letters with a Calibri bold font and a letter size of 80. We applied to all words both a 3-D effect, in order to add depth to the shape of the words, and a 3-D rotation, in order to manipulate the spatial configuration of the words. That is, each word could assume either a clockwise or an anti-clockwise rotation (i.e., roll) and an upward or a downward rotation (i.e., pitch). For each word, there were 36 possible spatial configurations resulting from the combination of six degrees of roll rotations (350°, 340° and 315° for the clockwise and 10°, 20° and 45° for the anti-clockwise rotation) by six degrees of pitch rotations (330°, 320° and 310° for the upward and 30°, 40° and 50° for the downward rotation). Each word could be filled with one of four colours: red, blue, green or brown. The red and blue colours were associated with the task rules in the task-switching blocks (see procedure for further

details), while the green and brown colours were used in single-task blocks without any task association.

Procedure and task.

Participants were tested inside the MRI scanner. A trial started with the presentation of a 500 ms grey blank screen, which contained a grey frame which was lighter than the background color (see Figure 1). The word stimulus, which was embedded into the frame, was then displayed for 2000 ms. Participants were to respond to the word according to the specific task instructions of each condition as outlined below. After the period of 2000 ms elapsed, the next trial began following a randomly jittered inter-trial interval (taken from a continuous range: 500-4500 ms).

The verbal single-task condition consisted of two subtasks. In the gender-type task, participants had to press the button below the left index finger if the word was a female noun, and the button below the right index finger if the word referred to a male noun. In the name-type task, they had to press the “left” button for a proper name and the “right” button for a common name. The assignment of categories to response keys was counterbalanced across participants for each subtask condition. In the verbal task-switching condition, participants were to switch from one task to another on a trial-by-trial basis according to the colour of the word. Whenever the word was presented in blue, they had to perform the name-task and to decide whether the word referred to a proper name or to a common name. When the word was displayed in red, they had to decide whether it was a female or a male noun. The response keys were the same as those used for the verbal single-task conditions. In order to equalize the perceptual characteristics of the stimuli, the word colours randomly (but meaninglessly) changed between brown and green also in single-task conditions, although in these blocks participants could safely ignore colour information.

The spatial-task procedure was similar to the verbal one. Importantly, it was implemented on exactly the same type of material. In the spatial single-subtasks, participants were requested to classify the words according to either their roll rotation (clockwise or anti-clockwise) or their pitch

rotation (upward or downward) by pressing the left or right buttons with their index fingers. The assignment of categories to response buttons was counterbalanced across participants. In the spatial task-switching blocks, when the colour was blue, the task was to decide whether the word was rotated clockwise or anti-clockwise, whereas when the colour was red the task was to decide whether the word was rotated upward or downward.

Half of the participants started with the verbal-task run, while the other half started with the spatial-task run. Accordingly, the block presentation order in each run was as follows: Single Task 1, Task Switching, Single Task 2, Task Switching for the participants who started with a single task, and Task Switching, Single Task 1, Task Switching, Single Task 2, for those who started with a task-switching block. Each experimental block comprised 25 trials. Moreover, the first task-switching block was preceded by 3 warm-up trials in order to help participants remember the appropriate stimulus-response mapping.

The structure of the spatial task run was exactly the same as the verbal-task one but the task rules concerned now pitch and roll categorization. The relative order of the verbal and spatial tasks was counterbalanced across subjects. Moreover, these two runs were randomly intermixed with another type of executive function task (i.e., monitoring for the presence of a target stimulus) performed within two additional runs, the results of which will be reported elsewhere. Since the order of the different tasks was completely randomized, no systematic order effects were observed.

A few days before the fMRI session, participants had already performed the task outside the scanner. On the same day of the fMRI session, participants performed another practice session outside the scanner that was similar to the experimental one except for the following changes. Each practice block comprised 10 trials. A feedback message, the word “sbagliato” - “wrong” in red or “bene” - “good” in blue, was presented after response on each trial for a duration of 1500 ms. Stimulus presentation was set to last until a response was detected to allow participants enough time to familiarize themselves with the verbal and spatial features of the words. However, if they failed to achieve 80% of accuracy during the first block of trials, from the second block on stimulus

duration was set to 2000 ms like in the proper experimental session. The practice experiment was automatically interrupted by the program if participants' accuracy was still below 80% after 5 consecutive blocks of trials. All participants met this criterion and were admitted to the subsequent fMRI session.

----Insert Figure 1 about here----

Acquisition and Pre-processing of fMRI data.

Scanning was performed at the Neuroradiology Unit, Azienda Ospedaliera di Padova on a 3T Ingenia Philips whole-body scanner with a 32-channel head-coil. Head movements were minimised through apposite cushioning. Functional volumes were obtained using a whole head T2*-weighted echo-planar image (EPI) sequence (repetition time, TR: 2 sec; echo time, TE: 35 ms; 30 transverse axial slices with ascending acquisition; flip angle: 90; 2.4x2.4x4 mm voxel size; field of view, FOV: 23 cm, acquisition matrix: 84x80; SENSE factor: 2 in anterior-posterior direction). Anatomical images (TR/TE: 8.1/3.7, 180 sagittal slices; flip angle: 8; 1 mm³ voxel size; FOV = 24 cm; acquisition matrix: 240x220) were acquired after the first 2 functional runs. Stimulus presentation and data recording were controlled by E-prime 2 software (Schneider et al., 2002). Visual stimuli were shown within the scanner by means of a mirror mounted on the coil that reflected images from a monitor located at the bottom of the scanner. Finger-press responses were recorded with two MRI-compatible response pads with two buttons each.

The fMRI data pre-processing and statistical analyses were performed using SPM8 (Friston et al., 1995). Functional images were spatially realigned and unwarped to compensate for participants' head movements during the experiment using a 4th degree B-Spline interpolation. For normalization, first a transformation matrix between the mean image of realigned volumes and a standard functional Montreal Neurological Institute (MNI) template (EPI.nii) was generated with a 4th degree B-spline algorithm and applied to re-slice volumes with a 2 mm³ voxel-size. The

functional images were then spatially smoothed with an 8 mm full-width-at-half-maximum Gaussian filter to reduce residual inter-individual anatomical variability.

fMRI statistical analysis.

For each participant, first-level analysis was performed using General Linear Model. The data were modeled using a block design with 4 conditions (spatial and verbal single-task, spatial and verbal task-switching) convolved with a canonical hemodynamic response function. We used blocks instead of single events since the former would better capture activity that is sustained throughout different types of blocks, and since previous evidence showed that left prefrontal cortex is activated, although to a different extent, in both switch and repeat trials (Dove et al., 2000), making an event-related analysis of the difference between these two conditions less sensitive. Moreover, in a preliminary event-related analysis on our dataset, differences among switch and repeat conditions did not survive the chosen level of significance, probably because our design was not optimally conceived for this purpose (e.g., the ITI range and values were generally too short). Estimates of head movements from realignment were included in the matrix as six additional regressors of no interest. Slow signal drifts were removed using a 480 sec high-pass filter. For each participant, four t-contrasts were extracted comprising each of the 4 conditions of interest vs. implicit baseline (single task and task-switching block in the spatial and verbal domains). The SPM second-level (i.e., group) maps were generated with a random-effects model within SPM8 using the individual contrast maps. A ‘full factorial’ ANOVA model was used comprising one factor with 4 levels corresponding to the four types of blocks. From this SPM, we extracted brain regions activated in the task-switching vs. single task blocks, separately for the verbal and spatial domain. The statistical significance was set at cluster-wise $p < 0.05$ corrected for multiple comparisons using False Discovery Rate (individual voxel p-value $< .001$). Moreover, we ran a conjunction analysis to find those voxels which were activated above the chosen statistical threshold for both

domains. The MNI coordinates of the peak voxels within each cluster were used to search the corresponding anatomical areas within the AAL atlas in MRIcron (Rorden et al., 2007).

Statistical Lateralisation Maps.

To statistically assess functional hemispheric asymmetries, the voxel-wise assessment of differences in the BOLD effect size across hemispheres was adopted (Statistical Lateralisation Maps, SLM). Using this approach (Liégeois et al., 2002; also see Berlingeri, Danelli, Bottini, Sberna, & Paulesu, 2013), a direct statistical comparison between the level of activation of each voxel in one hemisphere and its homologue voxel in the opposite hemisphere was computed. For SLM, the output is not represented by a single value (i.e., the lateralization index), but by an anatomical map representing the brain regions that are significantly lateralized at a given statistical threshold. We applied the SLM at the whole-brain level.

Since we had to statistically investigate functional hemispheric asymmetries without biases due to anatomical asymmetries between the two hemispheres, we created a symmetric EPI template by averaging the mean MNI normalized EPI for all subjects and their flipped counterpart (along the y-axis). We re-ran the normalization of all (unflipped) EPIs by using this symmetric template. The functional images were then spatially smoothed with an 8 mm full-width-at-half-maximum Gaussian filter and the first-level analyses were ran again as described above. For this analysis we used, on one side, contrast images with voxel-wise information about the effect size of the difference between task-switching and single task conditions in the verbal and spatial domains, expressed in the neurological convention (i.e. right is right). On the other side, these contrast images were flipped by 180 degrees on the y-axis, so that the left and right hemispheres were reversed, thus conforming the images to the radiological convention (i.e., right is left). The group statistical analyses were ran by directly comparing the neurological and radiological contrast images, that is, by comparing the BOLD signal recorded in the homologous voxels of the two hemispheres. To that aim, we used two second-level t-tests. The first t-test compared the

neurological contrast images (task-switching vs. single task) in the spatial domain and their radiological counterparts. The second t-test compared the neurological contrast images (task-switching vs. single task) in the verbal domain and their radiological counterparts. We extracted second-level contrasts between neurological and radiological contrasts, separately for the spatial and verbal domains. We applied the same correction for multiple comparisons as for the standard analyses (Cluster-level False Discovery Rate correction with $p < .05$, single voxel $p < .001$).

Results

All the behavioral data are shown in Table I.

Accuracy. Misses were on average 1.1% of trials. Responses outside the 200-2000 ms range were almost absent. Accuracy data were analyzed with a 3x2 repeated measures ANOVA with condition (single-task, repeat and switch trials) and domain (verbal, spatial) as the within-subject factors. There was only a main effect of condition [$F(2,60)=6.2$, $p=.0036$], due to the fact that the accuracy level was higher for single-task trials than for switch trials (Tukey's $p=.0026$), while the other comparisons were not significant (Tukey's $ps \geq .1$).

Response Times (RTs). There was only a main effect of condition [$F(2,60)=359.2$, $p<.0001$], due to the fact that RTs were shorter for single-task trials than for repeat trials, and for repeat than for switch trials (for all comparisons, Tukey's $p<.001$). Importantly, neither the domain main effect ($p=.12$) nor its interaction with condition ($p=.09$) were significant.

----Insert Table I about here----

fMRI results. All fMRI results are reported in Table II. The contrast between task-switching and single task blocks in the spatial domain showed activations in the left inferior parietal cortex, bilateral inferior frontal gyrus (pars triangularis), medial supplementary motor area and posterior

cingulum (Figure 2A). The same contrast in the verbal domain showed activation of the left inferior frontal gyrus (pars triangularis), left inferior parietal cortex and medial (more on the left) supplementary motor area (Figure 2B).

----Insert Table II about here----

----Insert Figure 2 about here----

Finally a conjunction analysis between these two contrasts showed activations of the medial supplementary motor area, left inferior parietal cortex and left inferior frontal gyrus pars triangularis (see Figure 3). Thus, these results showed a generally left-lateralized set of regions (inferior frontal, inferior parietal and supplementary motor area), which was co-activated in task-switching blocks, independently of the domain. Differential activations for switching vs. single task in the spatial and verbal domain were also explored through second-level interaction t-contrasts (weights for the spatial single task, spatial switching, verbal single task, and verbal switching blocks: 1 -1 -1 1 and -1 1 1 -1), but no cluster survived the chosen multiple comparison correction.

----Insert Figure 3 about here----

SLM results. The SLM results (see Table III and Figure 4) showed that hemispheric asymmetries were modulated by the task domain, since there was a mostly right lateralization of activations for the spatial domain and a clearly left lateralization for the verbal one. In particular, the contrast between task-switching and single task in the two hemispheres for the spatial domain produced a right-more-than-left activation in the inferior frontal gyrus (pars triangularis and orbitalis), middle occipito-temporal cortex and hippocampus, and a left-more-than-right activation within the inferior parietal lobule. The contrast between task-switching and single task in the two hemispheres for the verbal domain produced a left-more-than-right activation in the inferior frontal gyrus (pars

triangularis), and superior and inferior parietal lobules (extending to the occipital cortex), with the latter being slightly more lateral and superior than the cluster activated for the spatial domain.

----Insert Table III about here----

----Insert Figure 4 about here----

Discussion

The present study investigated which brain regions were activated in task-switching blocks as a function of task domain. In most of the previous neuroimaging studies on task-switching, the domains among which one has to switch were intermixed among each other within the same blocks, and usually analyzed together by collapsing the domain factor. In the present study the domains of switching were kept separate in different blocks to study their specific contribution to brain activations while avoiding phasic interactions and carry-over effects among the different domains. Tasks concerning more spatial and grammatical class judgments, with classically more right and left hemispheric lateralization, respectively, were employed in both single task and task-switching blocks. This manipulation aimed at understanding how hemispheric asymmetries in support of task-switching performance may interact with hemispheric dominance for more basic functions.

Stimuli were exactly the same and the performance level was matched between the two domains. Therefore, any differential effect which could be found in the present study between task-switching in the spatial and in the verbal domains could not be attributed to any material-specific effect or to different levels of task-difficulty, but it has to be interpreted as a genuine effect of task domain. The only difference between the two task domains was seen in the right inferior frontal gyrus (pars triangularis), which was uniquely activated in spatial switching blocks, although this activation did not significantly differ between the two domains (as tested with interaction contrasts). The left homologous inferior frontal gyrus was instead significantly activated in both domains, although with much wider clusters in the verbal domain. A conjunction analysis showed that the left inferior

prefrontal cortex, the left inferior parietal cortex and the bilateral supplementary motor area were commonly and significantly activated in task-switching blocks in both domains.

The common region involved in task-switching blocks in the left prefrontal cortex was more posterior in the study by Kim and colleagues (Kim et al., 2011, MNI coordinates: -50 1 40; also see Kim et al., 2012, for a meta-analysis) than in ours (MNI coordinates: -44 30 30), although a closer sub-peak belonging to the same cluster was found in our study for the verbal task-switching (MNI: -34 4 56). The specific left prefrontal peak activation in cognitive set-switching in Kim and colleagues' study (Kim et al., 2011, MNI: -42 16 18), which was the most similar to our task-switching conditions among those considered in that study as it implied a shift of the relevant set of stimulus-response rules, was instead slightly closer to that found in our study. The two other types of switches used in Kim and colleagues' study (2011) were a switch between the stimuli to which to pay attention (the number 5 vs. 7) and a switch between two responses of the same type (selecting the higher vs. lower digit in a set), which did not imply a switch between qualitatively different rules.

Since the pars triangularis of the left inferior prefrontal cortex generally involved in task-switching in our study coincides with Broca's area, it would be useful to test in future studies how specific linguistic demands in task-switching (e.g., sub-vocal rule reiteration, both in verbal and in spatial tasks) may influence its recruitment and specific localization.

The peak of the left posterior parietal activation was more posterior and inferior in the study by Kim and colleagues (Kim et al., 2011; MNI: -31 -74 29) than our main peak within the same region (MNI: -48 -46 54). Again, a left posterior parietal peak specific for cognitive set switching in Kim and colleagues' study (Kim et al., 2011, MNI: -32 -61 54) was instead much closer to ours.

Differences in task requirements may have influenced the specific localization within the frontal and parietal lobes in our study and in Kim and colleagues' one (2011), suggesting that many other factors (besides the spatial-verbal task context dichotomy) should be taken into consideration to understand the heterogeneity of activations within each hemisphere. For instance, it seems that

simpler types of switches (e.g., stimulus- or response-related) are associated with activations in more posterior left prefrontal regions than more complex switches.

Despite these discrepancies, the present study confirms that the task-switching system has a general left hemispheric distribution above and beyond the specific task requirements. Such a claim is also corroborated by other fMRI studies that, unlike our experiment, did not employ either spatial or verbal tasks. For instance, Philipp and colleagues (2013) had their participants to switch between color vs. form categories or between hand vs. foot responses. Confirming the left hemispheric involvement, they found that switching between stimulus categorizations was associated with activation of the left inferior frontal gyrus and the intraparietal sulcus, whereas switching between response modalities led to activation of the left intraparietal sulcus and the supramarginal gyrus. A possible exception to this left lateralization pattern is represented by the study by Braver and colleagues (2003), which reported sustained activations (assessed with block-analyses) in right anterior frontal regions during task-switching between size and semantic judgment tasks, which might have involved cognitive estimation and monitoring, operations which are typically right lateralized (e.g., Vallesi, 2012).

Although left fronto-parietal regions were co-activated in the current study using a task-switching paradigm with an fMRI block-design, recent literature has shown that the role of the left parietal cortex in task-switching with respect to that of its prefrontal counterpart may not be so subordinate as previously thought. While our study used the cue and target information presented within the same stimulus, a recent task-switching study which used temporally separated cues and targets showed, through a multivariate pattern classification to event-related fMRI data, that the left intraparietal sulcus efficiently encoded task rules, earlier than prefrontal cortex, and during a cue-phase, that is before the relevant target stimulus appeared (Bode and Haynes, 2009).

The supplementary motor area was also activated in association with task-switching blocks for both cognitive domains. This region has been repeatedly reported in previous neuroimaging (e.g., Dove et al., 2000) and Transcranial Magnetic Stimulation (Rushworth et al., 2002) literature on

task-switching, with the latter suggesting a critical role for this region in transiently selecting between specific response sets rather than in switching per se. In a previous event-related neuroimaging study adopting cue-target types of paradigms (Chiu & Yantis, 2009), this region was activated after the target presentation, independently of the type of task, thus confirming that it has a role in the implementation of the correct stimulus-response mappings. Our findings corroborate those of this previous study by confirming that the role played by this region in task-switching is domain-general and does not depend on the specific task context.

Importantly, there seems to be no all-or-none functional asymmetry across domains but a more nuanced left-more-than-right gradient of recruitment in the prefrontal cortex, since direct comparisons between task-switching in the two domains, after controlling for more basic domain-specific processes involved in the baseline single tasks, did not show any significant difference which could survive multiple comparison corrections, not even in the right prefrontal region which appeared uniquely in the spatial contrast (i.e., task-switching vs. single-task blocks).

Although we could not find regions that were uniquely activated for spatial and verbal task-switching when we directly contrasted these two types of tasks, we assessed hemispheric asymmetries “within each domain” by directly contrasting the left and right hemispheres through Statistical Lateralization Maps (Liégeois et al., 2002). We observed that task-switching-related activations were statistically more left lateralized for the verbal domain in inferior frontal cortex, inferior and superior parietal lobules (extending to the occipital cortex), and more right lateralized for the spatial domain in inferior frontal cortex, middle occipito-temporal gyri and the hippocampus (with the exception of a left inferior parietal cluster). These results clearly show that, despite common left fronto-parietal nodes of activations in task-switching across domains, there is a certain degree of hemispheric specificity in switching-related executive functions within domain, which is driven by the nature of the task rules between which one has to switch. This is consistent with a classical view that the right hemisphere is relatively more specialized in spatial processing and the left one in linguistic processing (e.g., Corballis, 2009; Hickok, Say, Bellugi, & Klima, 1996), but in

this case extending these domain-specific asymmetries to higher level executive functions involved in sustained task-switching.

The inferior prefrontal domain-dependent asymmetric activations were more ventrally located than the region commonly activated in domain-general task-switching (see conjunction analysis), although both were mostly located within the pars triangularis. These results suggest gradients of organization in the lateral prefrontal cortex along the ventro-dorsal dimension, from the processing of more domain-specific (“what”) information ventrally in each domain-relevant hemisphere, to more domain-general executive functioning more dorsally in the process-specific hemisphere (also see O’Reilly, 2010, for a similar view). The specific connectivity patterns between inferior ventrolateral prefrontal cortex in the two hemispheres and more posterior visual regions could be on the basis of this domain-specificity. For instance it has been demonstrated that the integrity of the left and right inferior frontal-occipital fasciculus, a bundle of white matter fibers connecting the inferior prefrontal cortex and the ventral visual cortex within each hemisphere, predicts language processing (Catani et al., 2007) or age-related face perception abilities (Thomas et al., 2008), respectively.

The right lateralization of middle occipito-temporal gyri for the spatial domain is compatible with findings that show their role in spatial processing (e.g., Renier et al., 2010), especially with low spatial frequencies (Peyrin, Baciú, Segebarth, & Marendaz, 2004). The right hippocampus is involved in encoding and processing of spatial relationships (see Burgess, Maguire & O’Keefe, 2002, for a review).

Despite the classically accepted role of the right inferior parietal cortex in spatial attention (e.g., Mort et al., 2003; Vallar & Perani, 1986), it is interesting to note that, when switching between different tasks, the lateralization analysis showed a left-more-than-right pattern in this region in both spatial and verbal domains, although slightly different subdivisions within the left inferior parietal lobule were asymmetrically more active depending on the specific domain of switching (i.e., the left-ward functional asymmetry was more ventral for spatial tasks than for verbal ones).

The present study did not produce significant results when the conditions in the switching blocks (i.e., switch and repeat) were analysed as events rather than block-wise. Previous work adopting more suitable event-related designs was able to demonstrate that another parietal region, the medial superior parietal lobule, shows a domain-independent role in switching between different perceptual, mnemonic, and rule representations (Chiu & Yantis, 2009). Reanalysing those data with a multivoxel pattern analysis approach, a more recent study demonstrated that activations of different neuronal populations within this region were able to predict the domain towards which switching is occurring on a trial-by-trial basis (Esterman, Chiu, Tamber-Rosenau, & Yantis, 2009). Activation in this region did not emerge in any of our contrasts. Among other factors, this may depend on the fact that its role in task-switching is transient and therefore a block-design is unable to detect its activation profile.

In conclusion, our study shows that fronto-parietal regions in the left hemisphere together with the bilateral supplementary motor area are generally associated with task-switching – an executive function which conceivably underlies our flexible behavior. This finding can be taken as evidence of an abstract executive function implemented in a set of left-lateralized regions which are insensitive to the context in which task-switching occurs. Hemispheric asymmetries and intra-hemispheric activations within each region are however modulated by the more specific nature of the tasks to be performed during task-switching, suggesting that the neural implementation of this overarching function is more complex than what a simplistic left-hemispheric view would predict.

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Tables

Table I. Mean error percentage and RTs (and standard error of the mean) for the different task-switching conditions and domains.

	Single	Repeat	Switch
<i>Errors (%)</i>			
Spatial task	3.1 (0.8)	4.3 (0.9)	4.5 (0.7)
Verbal task	2.2 (0.4)	3.6 (0.7)	5.2 (0.8)
<i>RTs (ms)</i>			
Spatial task	803 (27)	991 (34)	1185 (35)
Verbal task	810 (25)	1053 (29)	1220 (32)

Table II. Significant cluster activations in SPM analyses.

Anatomical Localization	MNI coordinates			Peak p-corr. (FDR)	Peak equivalent Z-value	Voxels per Cluster
	x	y	z			
Task switching vs. single task (Spatial)						
L. Inf. Parietal	-38	-48	-4	<0.0001	5.33	850
2 nd peak L. Inf. Parietal	-48	-46	54		4.5	
3 rd peak L. Sup. Parietal	-34	-64	54		3.26	
L. Suppl. Motor Area	-4	12	52	0.047	4.58	259
2 nd peak R. Suppl Motor Area	4	18	50		3.85	
3 rd peak L. Sup Medial Frontal	-6	24	40		3.21	
R. Inf. Frontal (pars triangul.)	44	38	26	0.047	4.49	198
R. Mid. Cingulum (approx.)	6	-28	28	0.047	4.34	198
2 nd peak L. Mid Cingulum	-4	-24	26		4.02	
L. Inf. Frontal (pars triangul.)	-44	30	30	0.047	4.31	233
Task switching vs. single task (Verbal)						
L. Inf. Frontal (pars triangul.)	-46	30	28	<0.0001	5.17	1528
2 nd peak L. Inf. Frontal (pars operc.)	-42	8	26		4.17	
3 rd peak L. mid Frontal	-34	4	56		4.09	
L. Suppl. Motor Area	-6	12	52	0.001	4.89	628
2 nd peak L. Suppl Motor Area	-6	20	46		4.3	
L. Inf. Parietal	-48	-46	56	<0.0001	4.87	1172
2 nd peak L. Inf. Parietal	-40	-48	42		4.17	
3 rd peak L. Inf. Parietal	-30	-74	50		4.1	
Task switching vs. single task (Conjunction)						
L. Suppl. Motor Area	-4	12	52	0.042	4.58	254
2 nd peak R. Suppl. Motor Area	4	18	50		3.85	
L. Inf. Parietal	-48	-46	54	0.005	4.5	519
2 nd peak L. Inf. Parietal	-40	-48	42		4.17	
3 rd peak L. Inf. Parietal	-32	-56	44		3.7	
L. Inf. Frontal (pars triangul.)	-44	30	30	0.042	4.31	226

Table III. Significant cluster activations in Statistical Lateralisation Map analyses (see text for details).

Anatomical Localization	MNI coordinates			Peak p-corr. (FDR)	Peak equivalent Z-value	Voxels per Cluster
	x	y	z			
Unflipped vs. Flipped contrasts (Spatial)						
R. Inf. Frontal (pars triangul.)	42	20	6	<0.0001	4.97	431
2 nd peak R. Inf. Frontal (pars orb.)	30	28	-20		4.15	
3 rd peak R. Inf. Frontal (pars orb.)	38	30	-4		4.08	
R. Mid. Occipital	38	-72	30	<0.0001	4.49	304
2 nd peak R. Mid. Temporal	42	-66	24		4.21	
3 rd peak R. Mid. Occipital	50	-68	28		3.95	
L. Inf. Parietal	-36	-46	44	<0.0001	4.02	141
2 nd peak L. Inf. Parietal	-28	-48	42		3.4	
3 rd peak L. Inf. Parietal	-40	-50	58		3.36	
R. Hippocampus	22	-10	-16	0.041	3.91	52
Unflipped vs. Flipped contrasts (Verbal)						
L. Inf. Parietal	-44	-50	54	0.001	4.71	113
2 nd peak L. Sup. Parietal	-30	-52	66		3.6	
L. Inf. Frontal (pars triangul.)	-44	40	4	0.042	4.34	50
L. Sup. Parietal	-26	-70	42	<0.0001	3.92	172
2 nd L. Mid. Occipital	-24	-58	42		3.61	
3 rd peak L. Sup. Occipital	-24	-78	36		3.54	

Figure captions

Figure 1. (A) Schematic representation of events in a trial. (B) Examples of stimulus material. The top figure displays a common noun (“miele”, “honey” in English), which was rotated in an anti-clockwise and downward manner. The bottom figure shows a proper name (“Laura”) with clockwise and upward rotations. The colours of the words (red versus blue) instructed participants about the specific task to be performed in task-switching conditions (see the main text for further details).

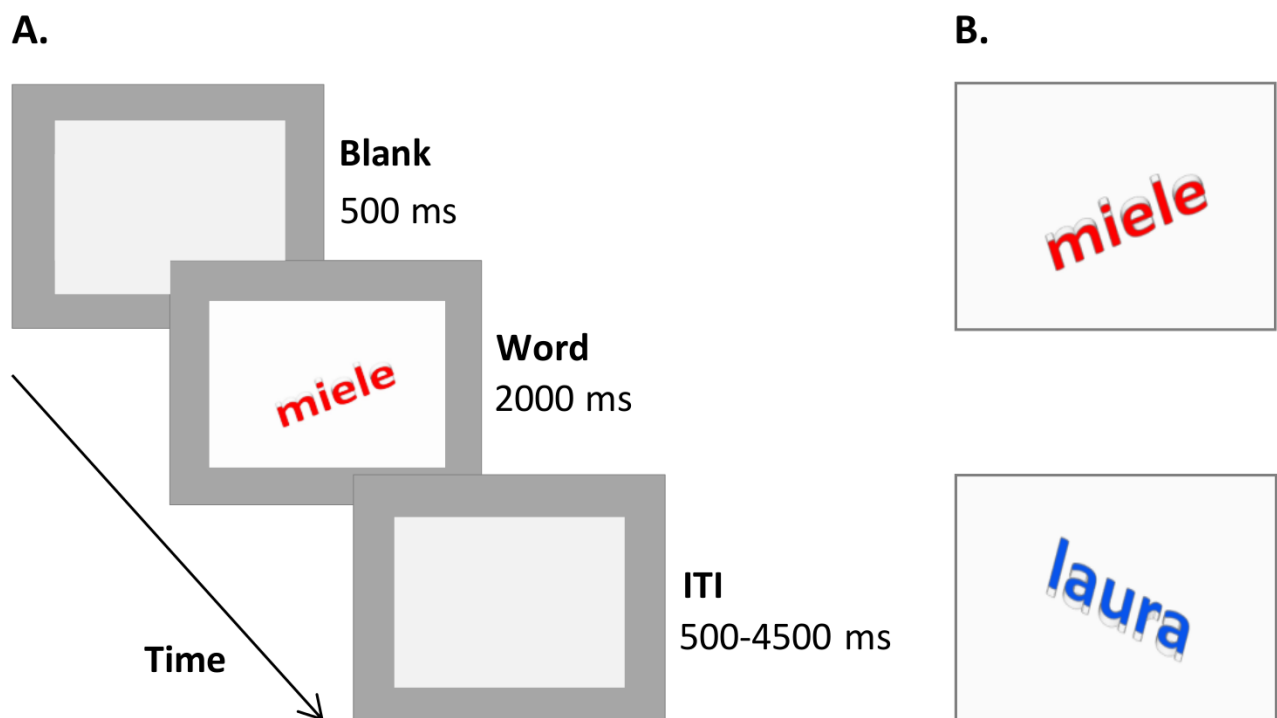


Figure 2. Brain activations obtained with the contrast: task-switching vs. single task blocks with the spatial rules (A) and with the contrast: task-switching vs. single task blocks with the verbal rules (B). Only clusters which survived a False Discovery Rate multiple comparison correction of $p = .05$ at the cluster level are shown. The fMRI activations are shown superimposed to an MNI rendered brain available in SPM8 displayed in lateral and top-down views (neurological convention: left is left). L and R indicate left and right hemisphere, respectively.

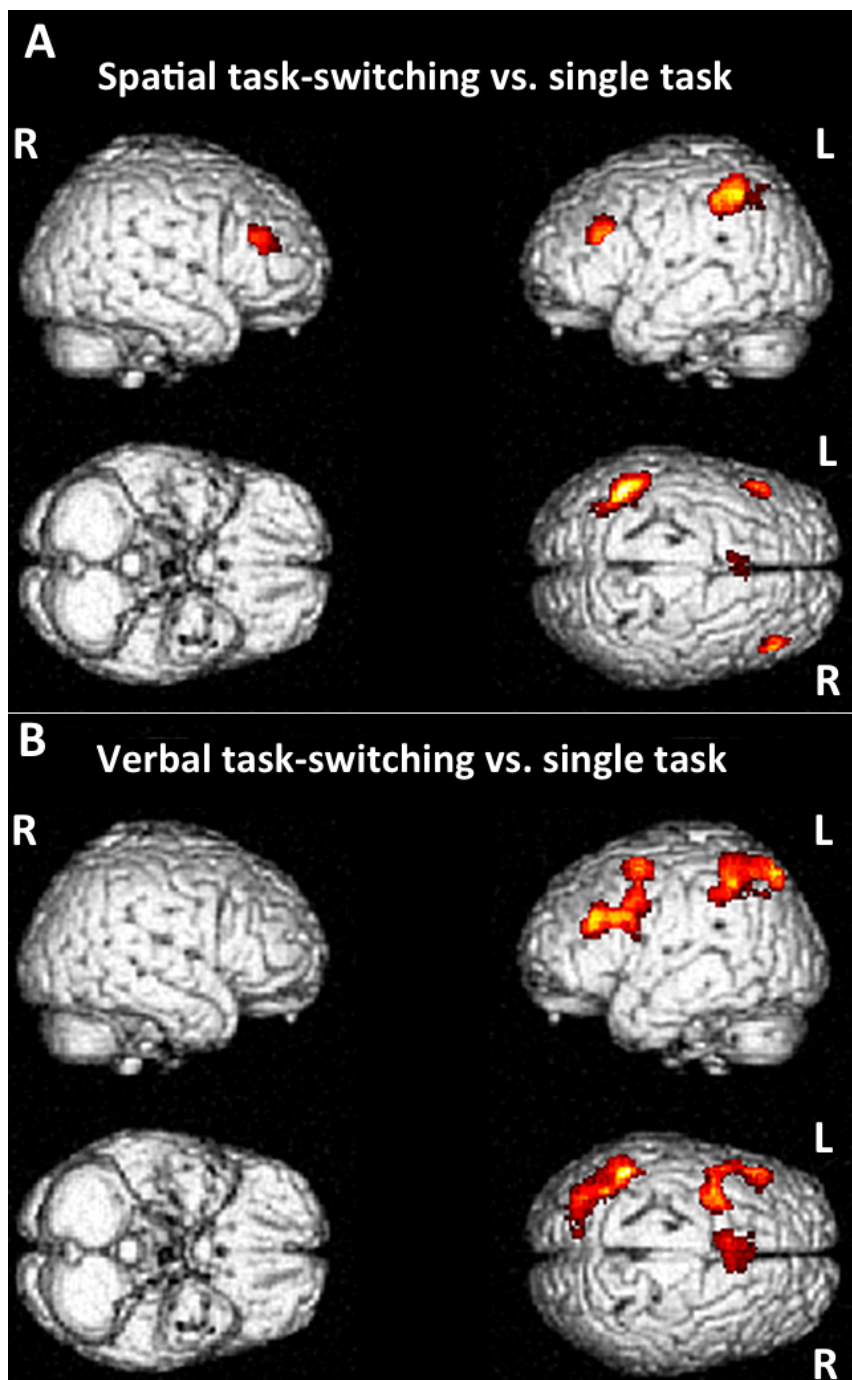


Figure 3. Common activations across switch types (i.e., spatial and verbal) compared with the single-task blocks, as shown by a conjunction analysis. Only clusters which survived a False Discovery Rate multiple comparison correction of $p = .05$ at the cluster level are shown. L and R indicate left and right hemisphere, respectively.

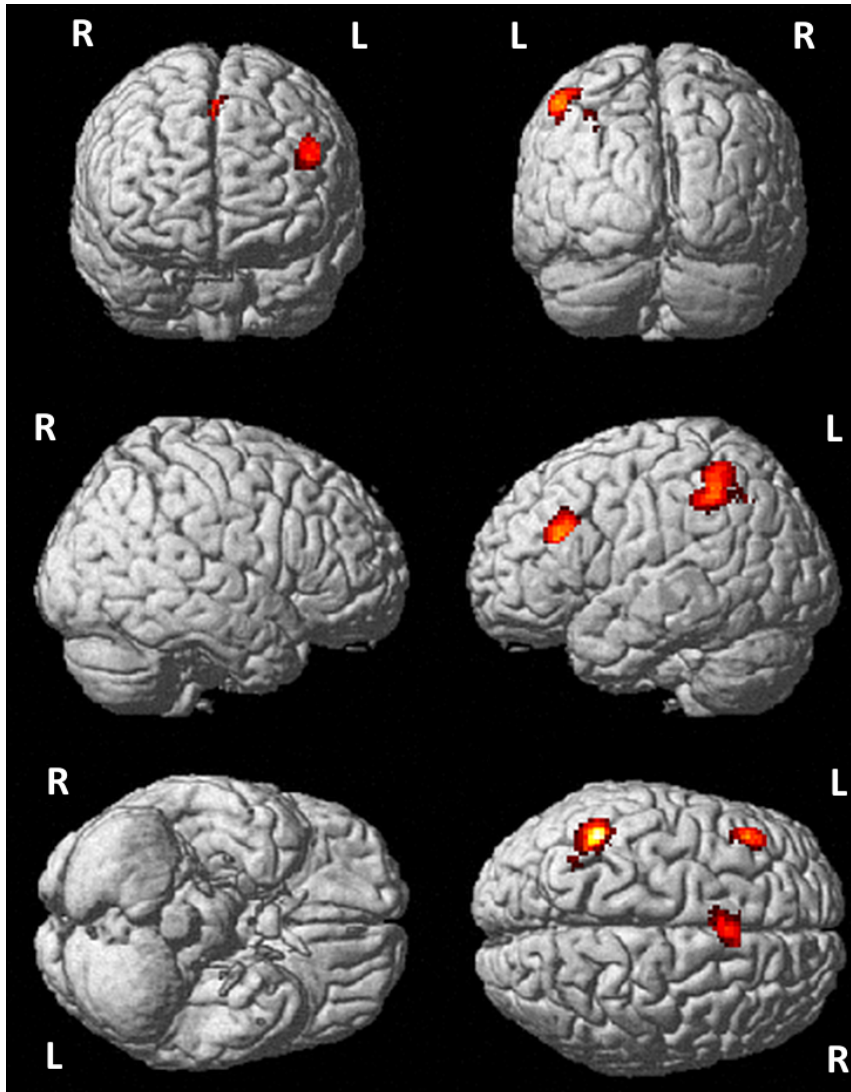


Figure 4. Results of the statistical lateralisation maps of the contrast between task-switching and single task blocks in the spatial (A) and verbal (B) domains. Only clusters which survived a False Discovery Rate multiple comparison correction of $p = .05$ at the cluster level are shown. L and R indicate left and right hemisphere, respectively.

