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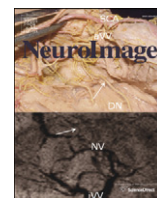
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Domain-general involvement of the posterior frontolateral cortex in time-based resource-sharing in working memory: An fMRI study

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ABSTRACT

Working memory is often defined in cognitive psychology as a system devoted to the simultaneous processing and maintenance of information. In line with the time-based resource-sharing model of working memory (TBRS; Barrouillet and Camos, 2015; Barrouillet et al., 2004), there is accumulating evidence that, when memory items have to be maintained while performing a concurrent activity, memory performance depends on the cognitive load of this activity, independently of the domain involved. The present study used fMRI to identify regions in the brain that are sensitive to variations in cognitive load in a domain-general way. More precisely, we aimed at identifying brain areas that activate during maintenance of memory items as a direct function of the cognitive load induced by both verbal and spatial concurrent tasks. Results show that the right IFJ and bilateral SPL/IPS are the only areas showing an increased involvement as cognitive load increases and do so in a domain general manner. When correlating the fMRI signal with the approximated cognitive load as defined by the TBRS model, it was shown that the main focus of the cognitive load-related activation is located in the right IFJ. The present findings indicate that the IFJ makes domain-general contributions to time-based resource-sharing in working memory and allowed us to generate the novel hypothesis by which the IFJ might be the neural basis for the process of rapid switching. We argue that the IFJ might be a crucial part of a central attentional bottleneck in the brain because of its inability to upload more than one task rule at once.

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Introduction

The ability of storing information, while doing something else, is one of the core abilities of the human mind making it possible for humans to flexibly adapt to an ever-changing environment. In cognitive psychology, the limited-capacity system underpinning human's ability to mentally maintain information in an active and accessible state, while concurrently and selectively processing some additional information, is referred to as *working memory* (WM; Baddeley and Hitch, 1974). A model of WM that has focused explicitly on the dual functioning of WM, i.e., the combination of processing and storage, is the time-based resource-sharing model (TBRS; Barrouillet et al., 2004, 2007, 2011). According to this model, the dual functioning of WM is achieved through a mechanism of time-based sharing of domain-general resources between processing and storage. The model assumes that processing and

storage both require attention which constitutes a pool of limited domain-general resources that needs to be shared (see also Kiyonaga and Egner, 2014a, 2014b, for a similar assumption). When attention is focused on the memory traces of to-be-recalled information, they receive activation, but this activation decays over time as soon as the focus of attention is switched away (Cowan, 1995, 1999; Towse and Hitch, 1995). Their complete loss would be avoided by a rapid and covert retrieval from memory through attentional focusing, i.e., refreshing. From this, it follows that memory performance in tasks requiring both processing and storage will be a function of the proportion of time during which processing activities occupy attention in such a way that the refreshing of decaying memory traces is impeded. This proportion of time is called cognitive load.

This conception of cognitive load and its predicted effect on memory performance have been tested extensively using computer-paced complex span tasks in adults (e.g., Barrouillet et al., 2004, 2007, 2011; see Barrouillet and Camos, 2012, 2015, for reviews). These tasks require participants to maintain some information while performing a concurrent processing activity at a pace that is pre-defined by the experimenter. Using such tasks, Barrouillet and colleagues systematically varied the cognitive load of processing and showed that recall performance was a direct function of the cognitive load involved in concurrent processing, a

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relation observed in both the verbal (e.g., Barrouillet et al., 2004, 2007, 2011) and the visuo-spatial domain of WM (Vergauwe et al., 2009). Moreover, a direct trade-off between cognitive load and memory performance has been demonstrated, even when storage and processing pertain to different domains (Vergauwe et al., 2010, 2012).

From all this, it is clear that cognitive load plays a crucial role in determining memory performance when processing and storage are performed together. According to the TBRS model, this relationship between the cognitive load of processing and memory performance reflects sharing of attentional resources at the central level of WM. Importantly, this sharing of attention is not conceived as a continuous sharing of resources but rather as an alternation with the focus of attention switching from one function to the other. The crucial process for this alternation is the process of rapid switching. Rapid switching from processing to storage is assumed to occur during short pauses that would be made available while concurrent processing is running.

Without the process of rapid switching, the TBRS model would no longer predict an effect of cognitive load on memory performance. Suppose individuals do not switch their attention during processing. Then, their attention would continuously stay on the processing component of the task and memory traces would suffer from time-based decay without any attempt to refresh them. As a result, memory performance would not be affected by the proportion of time during which attention is occupied by processing activities (i.e., cognitive load), but by the raw duration of these activities because, without the crucial process of rapid switching, no attempt is made to use the available time to refresh items while processing is running. This is in sharp contrast with the large body of research showing a clear effect of cognitive load on recall performance (e.g., Barrouillet et al., 2004, 2007, 2011; Vergauwe et al., 2009, 2010, 2012). Thus, within the TBRS model, the process of rapid switching is crucial to the effect of cognitive load on memory performance.

The goal of the present study was to advance our understanding of WM by addressing the effect of cognitive load on memory performance using a neuroimaging approach. A crucial first question to tackle is whether there are regions in the brain that are sensitive to cognitive load involved in concurrent processing. Identifying brain areas where activity is varying as a direct function of cognitive load can be seen as a first step towards identifying the neural bases of time-based resource-sharing in WM. According to the TBRS model, the mechanism of time-based resource-sharing is supposed to operate in a domain-general way. The present neuroimaging approach is ideally suited to test this assumption in a very straightforward way. If there is indeed a domain-general component in the process of rapid switching, then an overlap between the effect of cognitive load in the verbal and the visuo-spatial domain should be observed at the neural level. More precisely, we should be able to observe brain areas that are recruited as a direct function of increased cognitive load, regardless of the domain involved. Moreover, if the cognitive load effect is indeed closely related to the process of rapid switching, as assumed by the TBRS model, then one would expect to find cognitive load-related activity in regions that are typically involved in switching-related processes.

Switching processes have mostly been studied using the task-switching paradigm which requires subjects to switch frequently among a small set of simple tasks (see Monsell, 2003; Vandierendonck et al., 2010, for a review on the task switching literature). Task switching has been related to a fronto-parietal network (see Kim et al., 2012, for a meta-analysis). In the frontal cortex, one of the regions that have been most consistently observed in neuroimaging studies of task switching is the Inferior Frontal Junction (IFJ; Brass et al., 2005; Brass and von Cramon, 2002, 2004a, 2004b; Derrfuss et al., 2005; Dove et al., 2000; Sylvester et al., 2003). The IFJ is situated at the junction of the precentral sulcus and the inferior frontal sulcus and, as such, anatomically perfectly suited for task switching and task management because it is located at the border of the premotor and prefrontal cortices (Brass and von Cramon, 2002). Interestingly, the meta-analysis of Kim et al. (2012)

suggests that the IFJ contributes to task switching in a domain-general way. Based on the crucial involvement of the IFJ in task switching, we hypothesized that the IFJ would be among the brain regions playing a crucial role in rapid switching and as such, showing activity as a direct function of cognitive load of concurrent processing in a complex span task, regardless of the domain involved.

To test this, we created two computer-paced WM tasks that combined storage and processing demands, a verbal and a spatial one. In the verbal task, memory for letters was combined with a processing task involving lexical decisions. In the spatial task, memory for locations was combined with a processing task involving mirror judgments. In both tasks, we manipulated the cognitive load of processing in two different ways by manipulating either the number of items to be processed or their difficulty. Cognitive load was manipulated in two different ways in order to exclude alternative accounts of our findings. For example, if only the number of items were manipulated, one could account for our findings in terms of representation-based interference with more processing items resulting in more interference rather than increased cognitive load. The other way around, if only the difficulty of items were manipulated, one could account for our findings in terms of task complexity or task difficulty rather than time-based cognitive load as defined by the TBRS model. This setup enabled us to investigate which areas are sensitive to manipulations of cognitive load independently of the domain involved (verbal vs. spatial) by means of conjunction analysis.

Moreover, using the TBRS model, we computed the cognitive load on a trial-by-trial basis and used this as the input for a model-based fMRI analysis. This approach relates the brain signal directly to cognitive load as a theory-based parameter and enabled us to investigate which brain areas are recruited as a direct function of increased cognitive load.

Materials and methods

Participants

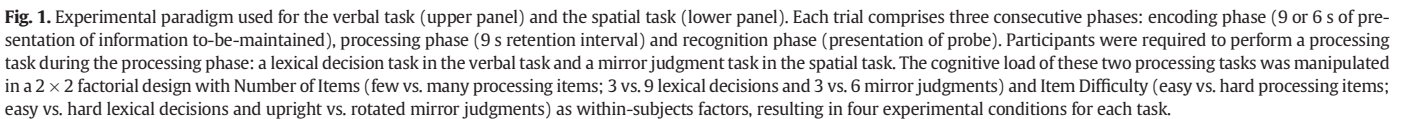
Twenty young adults (12 females, mean age = 21.77) took part in the study. Participants had no history of neurological disorders and reported to be healthy. The study was approved by the Medical Ethical Review Board at the Ghent University hospital and written consent was obtained from all subjects prior to scanning. All participants were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), and were paid €25 for their participation.

Task and design

Two computer-paced WM tasks were administered, a verbal and a spatial one. In the verbal task, storage of 6 letters was combined with a processing task involving lexical decisions. In the spatial task, storage of 4 locations was combined with a processing task involving mirror judgments. For both tasks, each experimental trial was composed of three consecutive phases (see Fig. 1).

In the first phase (i.e., encoding phase), participants viewed the successive presentation of a series of memory items. In the verbal task, participants saw a sequence of 6 upper-case letters centrally displayed on screen at a rate of 1 letter/1.5 s. All consonants of the Dutch alphabet, except for “L”, were used and participants were asked to maintain the letters in order of appearance. In the spatial task, participants were presented with a white box on screen in which 16 squares were displayed randomly (always the same 16 locations, see Fig. 1). Four of these squares were highlighted in red (the other squares remaining white) in a continual sequence on screen (1 red square/1.5 s) and participants were asked to maintain the location of the highlighted squares in order of appearance.

Presentation of the last memory item was immediately followed by the second phase which consisted of a 9-s retention interval prior to recognition. Participants were required to perform a processing task during



Finally, following the 9-s retention interval, a probe was presented in both tasks. For the verbal task, the probe consisted of one single lower

case letter among a series of 5 dashes, with the 5 dashes representing the letters in the other serial positions. Participants had to decide if the probe matched with the letter that was presented in that serial position (i.e., recognition phase). For the spatial task, the probe consisted of one box among a series of 3 dashes representing the locations in the other serial positions of the series to be maintained (see Fig. 1). Participants had to decide whether the probe matched the square that was highlighted in red in that serial position (e.g., in Fig. 1: whether this was the location of the third red square of the series). For both tasks, a total

of 48 series of different memory items was created (4 lists of 12 series). Within each list of 12 series, half of the probes were positive (i.e., 6 series required a 'yes' response), and both positive and negative probes were approximately evenly distributed over the serial positions. The negative probes were as much sampled at random from the other memory items presented in the series as sampled from the memory items not presented in the series. This was done to make sure that participants memorized both item and order information. Responses were to be made as quickly and as accurately as possible by pressing the right key when the probe matched the target item or the left key when probe and target did not match.

Processing tasks and procedure

In the verbal task, participants performed a lexical decision task during the 9-s processing phase. In the spatial task, participants performed a mirror judgment task during the 9-s processing phase.

Lexical decision task

Participants were presented with a display containing two four-letter strings with different lexical status (i.e., one Dutch word and one nonword). One letter string was presented on the left side of the screen, the other on the right side. Words and nonwords were equally often presented on the right and left side and participants had to decide which letter string was a word by pressing as quickly and as accurately as possible the corresponding key: the left button when the letter string constituting a word was located on the left side of the screen, the right button when the letter string constituting a word was located on the right side of the screen.

Item Difficulty was manipulated by using different types of words and non-words. In the easy condition, a high-frequency word was presented together with a random letter string, whereas a low-frequency word was presented together with a pseudo-word in the hard condition. For each trial in the easy condition, word stimuli were sampled randomly without replacement from a pool of 21 high-frequency Dutch words (Mean LogFreqMln = 2.84), selected from the CELEX lexical Database (Baayen et al., 1993), using the WordGen stimulus generation software (Duyck et al., 2004); non-word stimuli were sampled randomly without replacement from a pool of 21 random letter strings constructed using WordGen. The high-frequency words and random letter strings were matched on structure to avoid decisions based on pure visual strategies. For each trial in the hard condition, word stimuli were sampled randomly without replacement from a pool of 21 low-frequency Dutch words (Mean LogFreqMln = .35), selected from the CELEX lexical Database using WordGen; non-word stimuli were sampled randomly without replacement from a pool of 21 pronounceable letter strings (i.e., pseudo-words), created by replacing all the vowels of the 21 low-frequency words with other vowels.

Number of Items was manipulated by the requirement to perform either 3 or 9 lexical decisions within the 9-s delay. In the former condition, the lexical decisions were to be performed at a slow pace of 1 decision each 3 s with the lexical decision display remaining on screen during 2 s, followed by a blank screen of 1 s. In the latter condition, the lexical decisions were to be performed at a fast pace of 1 decision per second with the lexical decision display remaining on screen during 667 ms, followed by a blank screen of 333 ms. All verbal stimuli were presented in white color on a black background.

Mirror judgment task

Four asymmetrical symbols ("?", ":", "£" and "&") were used as stimuli. Symbols were presented in black on a white background (Arial 48 uppercase) and were either normally oriented or mirror-imaged. For each symbol, participants had to decide whether it was normally oriented or mirror-imaged by pressing the appropriate button as quickly and as accurately as possible (right for normal, left for mirror-imaged).

Item Difficulty was manipulated by presenting the symbols either upright (easy items) or rotated by 30, 60, 90, 120, 150 or 180°, clockwise or counter-clockwise (hard items). For each trial in the easy condition, stimuli were sampled randomly without replacement from a pool of 16 images (each of the 4 symbols was represented four times, twice normally oriented and twice mirror-imaged). For each trial in the hard condition, stimuli were sampled randomly without replacement from a pool of 88 images (each of the 4 symbols was represented 22 times, 11 times using the canonical format and 11 times mirror-imaged with the number of 11 due to the 11 different rotations).

Number of Items was manipulated in the mirror judgment task by the requirement to perform either 3 or 6 mirror judgments within the 9-s delay. In the former condition, the mirror judgments were to be performed at a slow pace of 1 judgment each 3 s with the symbol remaining on screen during 2 s, followed by a blank screen of 1 s. In the latter condition, the mirror judgments were to be performed at a fast pace of 1 decision per 1500 ms with the symbol remaining on screen during 1000 ms, followed by a blank screen of 500 ms.

Procedure

Instructions appeared on screen and were paraphrased if needed. In both tasks, each trial started with a fixation cross presented for 500 ms after which the first memory item was presented. After 1500 ms, the first memory item was replaced by the second one which was then replaced by the third one and so on. This resulted in a 9-s encoding phase in the verbal task and a 6-s encoding phase in the spatial task. In all trials, the presentation of the last memory item was followed by the first processing item of the 9-s processing phase. For all trials in all conditions, the 9-s interval was followed by the local recognition display. This probe remained visible till response or till 5000 ms was elapsed. The next trial started after a variable blank inter-trial interval (i.e., ITI) which was jittered in a pseudo logarithmic fashion using steps of 600 ms. Throughout the experiment, the ITI varied randomly between 700–4900 ms (50%), 5500–9700 ms (33.3%) and 10,300–14,500 ms (16.7%) with a mean ITI of 6000 ms, this in order to disentangle the neural signal stemming from the previous trial from the current one.

Each participant performed 96 trials: 48 trials in the verbal task and 48 trials in the spatial task (i.e., for each task 12 trials for each experimental condition: "Few-Easy", "Few-Hard", "Many-Easy" and "Many-Hard"). For each task, the 48 trials were divided into two blocks within which the order of presentation of the trials was random. In each task, the association between the four lists of 12 series memory items and the four experimental conditions was counterbalanced across participants, as was the order of presentation of the four experimental blocks.

Two training sessions preceded the experimental trials. The first training session took place outside the scanner. Participants were trained on the recognition tasks and the processing tasks separately before being trained on performing them concurrently. The second training session took place inside the scanner and consisted in training of the processing task alone, followed by 8 trials that combined processing and storage (4 verbal trials and 4 spatial trials).

The participants were tested individually by means of a Pentium III personal computer running the E-prime software (Psychology Software Tools, Inc., Pittsburgh, PA). Stimuli were generated from a computer and back-projected onto a screen located above the subject's neck. Visual images were viewed through a mirror attached to the head-coil. Responses were recorded using two button response boxes which were placed on the participant's left and right upper leg. The right hand was used for the right response box, the left hand for the left response box.

Behavioral analysis

Before testing the effect of Number of Items and Item difficulty on recognition performance in both tasks, we verified whether the cognitive load induced by the processing task varied indeed as a function of these variables. Therefore, for each task, we calculated, for each

individual and for each trial, the approximated cognitive load of the processing task performed during the retention interval. Within the TBRS model, the cognitive load induced by concurrent processing corresponds to the proportion of time during which processing captures attention in such a way that it impedes attentional refreshing of memory traces. On the basis of the TBRS model, this proportion of time can be approximated by the following formula (see Barrouillet et al., 2004): $CL = \Sigma PT/T$ with ΣPT referring to total processing time (i.e., sum of response times of all responses given within a processing phase) and T referring to the total time allowed to perform processing (i.e., duration of processing phase, here 9000 ms).¹ Cognitive load was then analyzed using a three-way repeated-measures ANOVA with Domain (verbal vs. spatial), Number of Items (few vs. many), and Item Difficulty (easy vs. hard) as within-subject factors.

Following Oberauer (2003), recognition rate was scored by calculating the proportion of correct responses upon the probes and correcting it for guessing by the formula $p_c = (p - g)/(1 - g)$ with p referring to the uncorrected proportion of correct responses, p_c referring to the corrected proportion, and g referring to the guessing probability which was $\frac{1}{2}$, reflecting the 50% chance of guessing correctly when choosing between yes and no options in the recognition task. Recognition rate was analyzed using a three-way repeated-measures ANOVA with Domain (verbal vs. spatial), Number of Items (few vs. many), and Item Difficulty (easy vs. hard) as within-subject factors.

fMRI procedure

Functional magnetic resonance imaging was performed with a 3 T scanner (Siemens Trio), using an 8-channel radiofrequency head coil. Subjects were positioned head first and supine in the magnet bore. First, 176 high-resolution anatomical images were acquired using a T1-weighted 3D MPRAGE sequence (TR = 2530 ms, TE = 2.58 ms, image matrix = 256×256 , FOV = 220 mm, flip angle = 7° , slice thickness = 0.90 mm, voxel size = $0.9 \times 0.86 \times 0.86$ mm (resized to $1 \times 1 \times 1$ mm)). Whole brain functional images were collected using a T2*-weighted EPI sequence, sensitive to BOLD contrast (TR = 2000 ms, TE = 35 ms, image matrix = 64×64 , FOV = 224 mm, flip angle = 80° , slice thickness = 3.0 mm, distance factor = 17%, voxel size = $3.5 \times 3.5 \times 3$ mm, 30 axial slices). Slices were acquired from bottom up in interleaved fashion. A varying number of images were acquired per run due to the varying ITI starting upon the participant's response to the probe.

fMRI analysis

Neuroimaging data were preprocessed and analyzed using SPM5 software (<http://www.fil.ion.ucl.ac.uk/spm/software/spm5>) implemented in MATLAB (Mathworks Inc., Sherborn, MA). To account for T1 relaxation effects, the first 4 scans of each EPI series were excluded from the analysis. First, a mean image for all scan volumes was created, to which individual volumes were spatially realigned using rigid body transformation after which they were corrected for differences in slice timing using the first slice as reference. The structural image of each

subject was coregistered with their mean functional image, after which all functional images were normalized to the T1 template in the Montreal Neurological Institute (MNI) space. The images were resampled into $3 \times 3 \times 3$ mm voxels and spatially smoothed using a 9-mm full-width at half maximum Gaussian kernel. A high pass filter of 128 s was applied during fMRI data analysis.

Statistical parametric maps for condition-specific effects were calculated for individual subjects using the general linear model (GLM). Of particular interest in this study were changes in BOLD signal associated with the processing phase of the experimental trials. Both a canonical hemodynamic response function (HRF) and the 1st derivative were modeled on the onset of the first processing item (lexical decision in the verbal task, mirror judgment in the spatial task) to the onset of the probe using a duration of 9 s (i.e., processing phase). Besides the processing phase, we also modeled the encoding phase (using a duration of 9 s for the verbal task and a duration of 6 s for the spatial task) and the recognition phase (using the actual response times as duration) as regressors of no interest. For the processing and recognition phase, we distinguished between the two tasks and the four experimental conditions of Cognitive Load (i.e., Few-Easy, Few-Hard, Many-Easy and Many-Hard). For the encoding phase, we only distinguished between the two tasks because no difference as a function of Cognitive load is to be expected. Six regressors defining head movements were also included so to account for any residual movement-related effect.

We were mainly interested in BOLD signal associated with the 9-s processing phase in the four different experimental conditions of the verbal and the spatial tasks. Therefore, per condition we computed a condition > NULL contrast image for each participant to compare the relevant parameter estimates for the regressors containing the canonical HRF. The resulting contrast images were submitted to a second level group analysis.

At the second level, a full factorial analysis with factors Domain (verbal vs. spatial) $\times$ Number of Items (few vs. many) $\times$ Item Difficulty (easy vs. hard) was performed, treating participants as random effect. First, we wanted, for each task separately, to identify brain areas exhibiting activation change by *both* manipulations of cognitive load. To this end, we first computed the contrasts “many minus few items” and “hard minus easy items” for both tasks separately. Next, for both the verbal and the spatial task, a conjunction analysis was performed on these contrasts (using the “conjunction null method” as implemented in SPM5; see Friston et al., 2005, which entails a logical AND method). Crucially, to test which regions would be sensitive to cognitive load in a domain-independent way, we performed a conjunction analysis that included the following four contrasts: (1) verbal many minus few items, (2) verbal hard minus easy items, (3) spatial many minus few items, and (4) spatial hard minus easy items. This allowed us to identify those brain areas exhibiting activation change by *both* manipulations of cognitive load, regardless of the domain involved in concurrent processing and storage.

Parametric analysis

In addition to the aforementioned conjunction analysis, we adopted a model-driven approach which enabled us to extract the regions that are recruited as a direct function of the increasing cognitive load of concurrent processing. In this model-based fMRI analysis, we correlated for each task the fMRI signal with the computationally determined cognitive load as defined by the TBRS model. Thus, we performed a parametric analysis that uses approximated cognitive load as modulation parameter. For both tasks, this proportion of time was calculated for each participant for each experimental condition on a trial-by-trial basis using the aforementioned formula. Next, we included these values of approximated cognitive load as parametric modulation regressors during the processing phase in a separate GLM for the verbal and the spatial task. This was done so to test for voxels that exhibited an increased BOLD signal with increasing approximated cognitive load

¹ CL is a theoretical notion, derived from the TBRS model and RT is used to approximate CL. However, RT and CL cannot be used interchangeably; one cannot approximate the CL of an experimental condition without knowing, in addition to RT per item, (1) how many items were to be processed per processing phase and (2) the duration of each processing phase. In the TBRS model, CL is conceived as the ratio between the time during which a task occupies attention and the time available for that task. As such, CL is similar to the notion of power which corresponds to the ratio between the amount of work to be done and the time available. CL is not the same as time-on-task. In contrast to the “time-on-task” hypothesis, we have previously shown that (1) spending the same amount of time on a task while having less time available results in poorer memory performance (e.g., Barrouillet et al., 2007; Vergauwe et al., 2010, 2012), and (2) whereas spending more time on a task that requires attention results in poorer memory performance, spending more time on a task that does not require attention to a sizeable extent does not result in poorer memory performance (e.g., Barrouillet et al., 2007).

during the processing phase of the verbal task and during the processing phase of the spatial task.

For all whole brain contrasts including the conjunction analyses contrast maps, we corrected for multiple comparisons using the program AlphaSim (afni.nimh.nih.gov/afni/doc/manual/AlphaSim, Ward, 2000). The program determined that, when using a threshold of $Z > 3.1$ ($p > .001$, uncorrected) at the individual voxel level, clusters should consist of at least 24 contiguous voxels to be considered corrected for multiple comparisons on a $p < .05$ level. For the purpose of assigning neuro-anatomic and cytoarchitectonic labels using the Talairach Daemon, the maxima coordinates were converted from MNI to Talairach coordinate space using the formulas provided by Matthew Brett (<http://www.mrc-bu.cam.ac.uk/Imaging/mnispace.html>). All coordinates reported here use the MNI coordinate space.

Regions of interest analysis

Using the MARSBAR toolbox for SPM5 (Brett et al., 2002), a region of interest (ROI) analysis was performed. More specifically, we examined the pattern of activation in the left and right IFJ. Importantly, these ROIs were defined independently from the aforementioned analyses by using the coordinates for the IFJ as reported in the meta-analysis of Derrfuss et al. (2005). The coordinates were converted into MNI coordinates using GingerALE. Two spherical ROIs (radius = 10 mm) were centered at $x = \pm 42$, $y = 9$, $z = 29$. For these regions, we extracted the mean percent signal change (PSC) for each subject for each task and for each experimental condition. For each trial, percent signal change was the mean value measured in the time window between 4 and 14 s after the onset of the processing phase. These were submitted to a three-way repeated-measures ANOVA with Domain (verbal vs. spatial), Number of Items (few vs. many) and Item Difficulty (easy vs. hard) as within-subject factors.

Results

Behavioral results

To ascertain that participants paid sufficient attention to the processing tasks during the experimental series, mean percentages of correct responses were calculated. Two participants exhibited a percentage of less than 80% on the mirror judgment task and their data were not included in the analyses of the experimental trials.²

The cognitive load of the verbal task was found to be higher than the cognitive load of the spatial task, $F(1,17) = 11.16$, $p < .01$. Importantly, as can be seen in Fig. 2, the cognitive load induced by the hard items was significantly higher than the cognitive load induced by easy items, $F(1,17) = 357.37$, $p < .001$. Similarly, cognitive load was higher when more items were to be processed, $F(1,17) = 4373.65$, $p < .001$. This effect was larger in the verbal domain, $F(1,17) = 265.03$, $p < .001$. No other interaction reached significance (all $ps > .07$).

Concerning recognition performance, the verbal task resulted in higher recognition performance than the spatial recognition task, $F(1,17) = 9.53$, $p < .01$. Furthermore, as we predicted, performing more judgments during retention resulted in lower recognition

performance, $F(1,17) = 15.85$, $p < .001$ (.73 vs. .80), and performing harder judgments during retention also resulted in lower recognition performance, $F(1,17) = 5.68$, $p < .05$ (.74 vs. .79). As can be seen in Fig. 2, there were no significant two-way or three-way interactions between the variables Domain, Number of Items and Item Difficulty, all $ps > .15$. These behavioral findings are in line with previous findings within the TBRS framework (e.g., Barrouillet et al., 2004, 2007; Vergauwe et al., 2009, 2010).

Imaging results

Whole-brain analysis of the verbal task

Results of the “many > few items” contrast and the “hard > easy items” contrast for the verbal task are reported in the supplementary material (Table S1 and Fig. S1). The conjunction analysis for the verbal task revealed multiple activation clusters sensitive to both manipulations of cognitive load (see Fig. 3). Frontal activation was observed in both the right IFJ and the left IFJ. An additional frontal activation cluster comprised the right superior frontal gyrus and the right cingulate gyrus. Parietal activation clusters were found in the right Superior Parietal Lobule (SPL) extending into the right angular gyrus, and in the left SPL extending into the left precuneus. Finally, significant responses were also observed in the bilateral insulae and the left Middle Occipital Gyrus (MOG) along with the left inferior temporal gyrus (ITG). Coordinates of the activated regions are reported in Table 1.

Whole-brain analysis of the spatial task

Results of the “many > few items” contrast and the “hard > easy items” contrast for the spatial task are reported in the supplementary material (Table S2 and Fig. S1). The conjunction analysis for the spatial task revealed multiple activation clusters sensitive to both manipulations of cognitive load (see Fig. 3). Frontal activation was observed in the right IFJ and the right Inferior Frontal Gyrus. An additional frontal activation cluster comprised the right Middle and Medial frontal gyri. Parietal activation clusters were found in the left SPL extending into the left intraparietal sulcus (IPS), and in the right SPL extending into the right precuneus and the right Inferior Temporal Gyrus (ITG). Finally, significant responses were also observed in the left MOG along with the left ITG. Coordinates of the activated regions are reported in Table 2.

Conjunction analysis including both tasks

The conjunction analysis including the contrasts “verbal many > verbal few items”, “verbal hard > verbal easy items”, “spatial many > spatial few items” and “spatial hard > spatial easy items”, revealed multiple activation clusters sensitive to both manipulations of cognitive load, regardless of the domain involved in processing and storage. As can be seen in Fig. 3, frontal activation was observed in the right IFJ. Parietal activation clusters were found in the left SPL extending into the left IPS and in the right SPL extending into the right IPS and the right Angular Gyrus. Finally, significant responses were also observed in the left MOG along with the left ITG. Coordinates of the activated regions are reported in Table 3. Thus, as we expected, the IFJ was among the brain regions showing activity as a function of cognitive load, regardless of the domain involved.

One could argue, however, that the use of cluster-extent based thresholding as a precursor to conjunction analysis might complicate the interpretation of the results of the conjunction analysis. Indeed, cluster-extent based thresholding detects statistically significant clusters on the basis of the number of contiguous voxels whose statistic values exceed a threshold; this does not mean that every voxel in the cluster displays the significant effect (Woo et al., 2014). As a result, one cannot be certain that the overlapping clusters of voxels identified in the conjunction analysis using cluster-extent thresholding entail any voxels that showed significant effects in their respective initial contrast. One solution to this is to employ a voxel-based correction, such as false discovery rate (FDR) correction for multiple comparisons, in the

² In working memory tasks that combine processing and storage components to examine the effect of processing on memory performance, researchers typically require accuracy on the processing task to be very high to ensure that participants are attending to the processing task. If accuracy on the processing task falls below a certain level (typically 80% in TBRS studies; e.g., Barrouillet et al., 2004, 2007; Vergauwe et al., 2010, 2012), the entire data set for that participant is discarded (see Conway et al., 2005, for a methodological review on working memory span tasks). The rationale is that, if a participant does not reach 80% of correct responses, he or she might be ignoring the processing task to some extent and might, as a consequence, engage less in rapid switching between processing and storage. Applying this performance-based exclusion rule in the current study, the data of two participants were discarded from the dataset; they had an accuracy of 73% and 79% in the mirror task. Highly similar behavioral and imaging results were obtained when we included these two participants in the dataset.

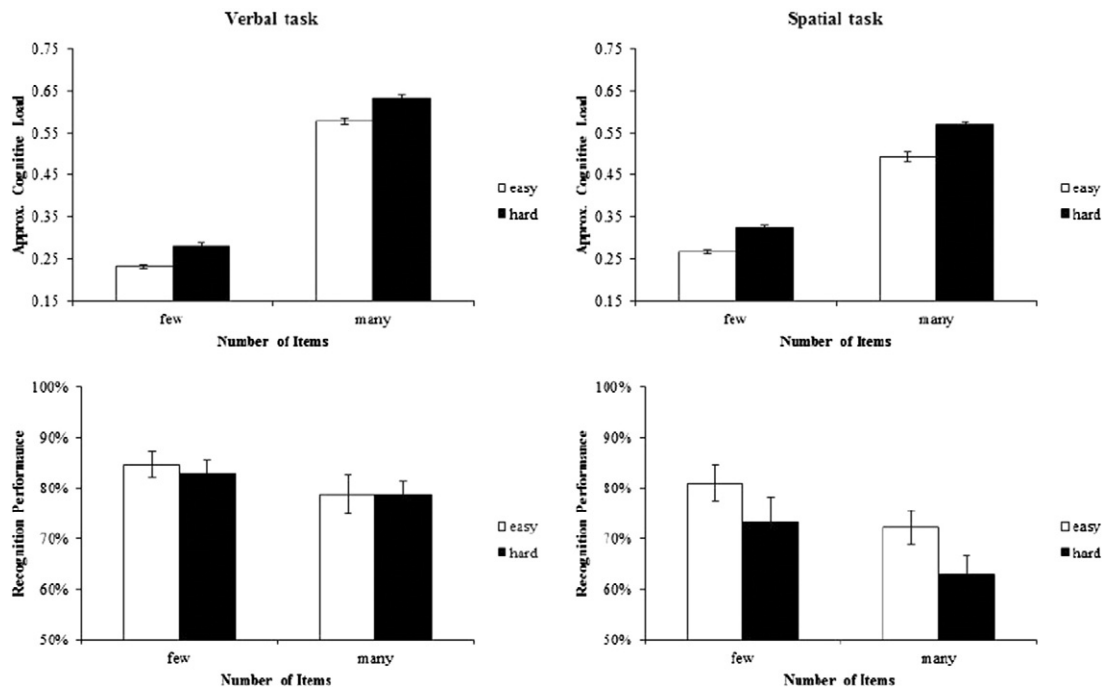


Fig. 2. Behavioral data for the verbal task (left panel) and the spatial task (right panel). Cognitive load (upper panel) and recognition rates (lower panel) are shown as a function of Number of Items (few vs. many) and Item Difficulty (easy vs. hard). Error bars represent standard error.

basic analyses prior to conjunction.³ Applying FDR correction with a significance level of $p < .05$ to the whole-brain analyses of the verbal task and the spatial task resulted in highly similar patterns of activation clusters. Importantly, as can be seen in Table S3 and Fig. S2, activations identified in the FDR-corrected conjunction analysis including both tasks were also highly similar to the activations identified in the conjunction analysis using cluster-extent based thresholding; the IFJ was again found to be among the brain regions showing activity as a function of cognitive load, regardless of the domain involved.

Model-based analysis

Results of the parametric analyses are reported in the supplementary material (Fig. S3). For the verbal task, the model-based analysis revealed only one region that shows a direct relationship with cognitive load, namely the right IFJ. For the spatial task, several regions showed a statistically reliable increase in activity related to cognitive load. Frontal regions include the right IFJ along with the right Inferior Frontal Gyrus, and the bilateral Middle Frontal Gyri. Parietal activation clusters were found in the left SPL and in the right SPL extending into the precuneus. Also, significant responses were observed in the left IPS. For displaying purpose, we overlaid both activation maps and, as can be seen in Fig. 4, there was only one brain region with overlapping activity as a direct function of cognitive load, regardless of the domain involved in the task, namely the right IFJ.

Regions-of-interest analysis

For right IFJ activation, a repeated measures ANOVA with Domain (verbal vs. spatial), Number of Items (few vs. many) and Item Difficulty (easy vs. hard) showed an increase in activation when the number of items to be processed was increased, $F(1,17) = 47.55$, $p < .001$, and when the difficulty of these processing items increased, $F(1,17) = 125.26$, $p < .001$. These variables interacted, $F(1,17) = 14.60$, $p < .001$; as can be seen in Fig. 5, activation was particularly high when there were many difficult items to be processed. Such interaction was not observed in the behavioral data. We did not have predictions concerning

interaction effects and, to the best of our knowledge, there is no obvious theoretical explanation for the difference between the behavioral and brain data. A potential explanation is that the behavioral and brain measures differ in their sensitivity to the CL involved in processing. More importantly, in line with the idea of domain-independent activation in the right IFJ, there was no effect of the domain of the task on right IFJ activation, $F < 1$, and none of the interactions with Domain reached significance (all $ps > .20$).

The same repeated measures ANOVA was performed for the left IFJ. This showed a significant effect of the number of items to be processed, $F(1,17) = 18.06$, $p < .001$, and of the difficulty of these processing items, $F(1,17) = 22.57$, $p < .001$. In contrast to the right IFJ, a significant effect of the domain of the task was revealed for the left IFJ, $F(1,17) = 12.61$, $p < .001$. While Domain interacted with Item Difficulty, $F(1,17) = 7.94$, $p < .05$, it did not interact significantly with Number of Items, $F(1,17) = 1.82$, $p = .19$. More precisely, as can be seen in Fig. 4, increasing the number of items leads to an increase in activation in the left IFJ for both the verbal task, $F(1,17) = 16.86$, $p < .001$, and the spatial task, $F(1,17) = 7.65$, $p < .05$. Increasing the difficulty of the items, however, leads to increased left IFJ activation in the verbal task, $F(1,17) = 38.79$, $p < .001$, but not in the spatial task, $F(1,17) = 1.92$, $p = .18$. Furthermore, Number of Items and Item Difficulty interacted, $F(1,17) = 19.67$, $p < .001$, but the triple interaction did not reach significance, $F(1,17) = 2.39$, $p = .14$.

For the sake of completeness, the fitted event-related time courses were calculated for both the RIFJ and LIFJ. Both time courses show similar results to the percent signal change analysis (see Fig. S4): the right IFJ, but not the left IFJ, is recruited as a direct function of increased cognitive load, regardless of the domain involved.

Discussion

WM is critical to almost all human cognitive behavior. The goal of the present research was to advance our understanding of dynamic WM functioning involved in concurrent processing and storage by investigating the brain circuits underlying the cognitive load effect. The novelty of our research lies in (1) the theory-driven nature of our approach, (2) the use of tasks that have both processing and storage requirements,

³ We would like to thank an anonymous reviewer for this thoughtful suggestion.

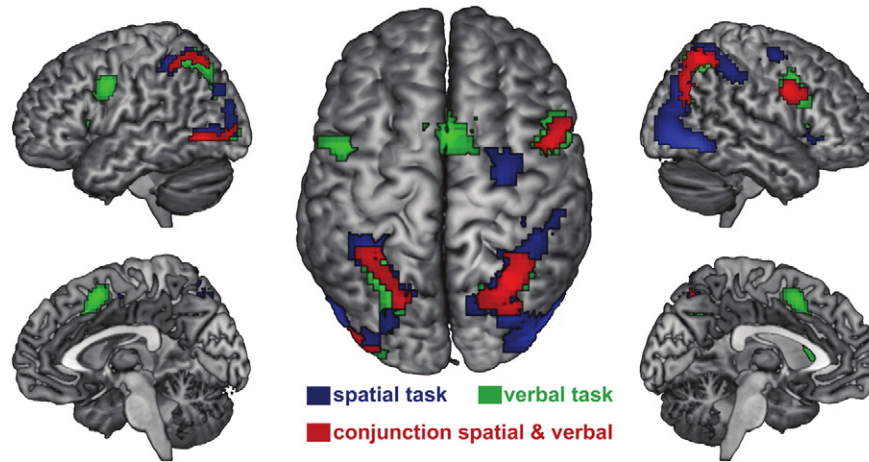


Fig. 3. Whole brain results depicted for the different conjunction analyses. Blue activation map: results of conjunction analysis of “spatial hard items > easy items” & “spatial many > few items”. Green activation map: results of conjunction analysis of “verbal hard items > easy items” & “verbal many > few items”. Red activation map: results of conjunction analysis of “spatial hard > easy items” & “spatial many > few items” & “verbal many > verbal few items” & “verbal hard > verbal easy items”. Statistical maps are cluster corrected on $p < .001$, $k > 24$.

and (3) the manipulation of the cognitive load of verbal and spatial processing components. This approach allowed us to demonstrate that, across different analysis techniques, the IFJ showed activation as a direct function of the cognitive load involved in concurrent processing, regardless of the domain involved in these activities and independently from the specific manipulations of cognitive load. The current findings provide new insights in (1) the nature of the resources involved in time-based resource-sharing in WM, (2) the way the WM system deals with the dual demands of tasks that combine processing and storage components, and (3) the role of the IFJ in WM and cognitive control. In what follows, these points will be discussed in turn. Finally, we will briefly discuss other regions identified in the conjunction analysis including both tasks.

The nature of WM resources: domain-general time-based resource-sharing

In line with the TBRS assumption that time-based resource-sharing operates in a domain-general way, we observed neural overlap between the cognitive load effect in the verbal and the spatial domains of WM. Indeed, we observed the right IFJ being recruited as a direct function of increased cognitive load, regardless of the domain involved. By showing neural overlap between the effect of cognitive load in the verbal and the visuo-spatial domain of WM, the present study is the first to provide neuroscientific evidence for the idea that there is a domain-general component to time-based resource-sharing in WM. We know of only one study that aimed at identifying brain regions making domain-general contributions to WM performance using tasks that combine

memory and processing demands. In this study of [Chein et al. \(2011\)](#), lateral prefrontal, anterior cingulate, and parietal cortices were found to be involved in both verbal and spatial WM. Our study confirms their finding of there being brain regions playing a crucial role in WM in a domain-general way.⁴

The current results suggest that the domain-general nature of cognitive load-dependent IFJ activation is limited to the right IFJ. Indeed, only the right IFJ survived the whole-brain conjunction analysis, was revealed in the parametric analyses and was shown in the ROI analysis to be recruited as a function of increased cognitive load, regardless of the domain involved. This might suggest that the right IFJ solely plays a domain-independent role in WM. This contrasts with a study of [Morimoto et al. \(2008\)](#) who demonstrated a verbal /nonverbal hemispheric specialization in the IFJ suggesting that the cognitive control processes in tasks involving verbal material are associated with left IFJ activation whereas cognitive control processes in tasks involving non-verbal material are associated with right IFJ activation.

While the conjunction of the spatial task in our study only revealed the right IFJ, the conjunction of the verbal task revealed bilateral IFJ. Similarly, the ROI analysis showed that the right IFJ activation was not influenced by the domain involved in any way while the left IFJ activation seemed more specifically sensitive to manipulations of cognitive load in the verbal task. This might suggest that both verbal and spatial

Table 1
Activation clusters for the conjunction analysis in the verbal task (MNI coordinates).

Cortical area	Voxels	Hem.	BA	x	y	z	Z
Inferior frontal gyrus	289 ^a	R	9	45	9	30	5.90
Superior parietal lobule	422	R	7	36	−57	51	5.90
Angular gyrus		R	39	30	−66	36	5.09
Superior frontal gyrus	265	R	6	6	9	54	5.63
Cingulate gyrus		R	32	9	18	42	5.09
Superior parietal lobule	334	L	7	−27	−54	45	5.62
Precuneus		L	7	−27	−66	39	4.85
Inferior frontal junction	169 ^a	L	9	−45	3	33	5.43
Insula	49	L	13	−30	18	12	4.65
Inferior temporal gyrus	97	L	37	−48	−69	−3	4.64
Middle occipital gyrus		L	18	−27	−93	−3	3.64
Middle occipital gyrus		L	19	−45	−87	0	3.49
Insula	49	R	13	33	21	9	4.31

^a Denotes cluster containing the Inferior Frontal Junction.

⁴ One could argue that subjects might verbally recode the spatial memoranda rather than maintaining them in visuo-spatial WM. Two observations in the current study go against this verbal recoding hypothesis. First, in line with previous studies (e.g., [Vergauwe et al., 2010, 2012](#)), we observed lower memory performance for spatial locations than for verbal letters. The mean recognition rate was lower in the spatial task than in the verbal task, even though participants were only required to maintain 4 locations in the spatial task, compared to 6 letters in the verbal task. If people were verbally recoding the locations, it is unclear why they would not be able to maintain as many labels that are referring to spatial locations as labels that are referring to letters. Second, verbal recoding of visually presented material has been associated with the left Broca area (44; e.g., [Henson et al., 2000](#)). If, like we assume, participants were verbally recoding the visually presented letters but not the visually presented locations, then one would expect to see, during the encoding phase, increased activation levels in the left Broca area in the verbal task, relative to the spatial task. To test this, we created a ROI using the coordinates reported in the Henson et al. study. A spherical ROI (radius = 10 mm) was centered at $x = -57$, $y = 22$, $z = 14$. We extracted the mean PSC for each subject and for each task. For each trial, PSC was the mean value measured in the time window between 4 and 8 s after the onset of the encoding phase. In line with what we expected, activation levels in the left Broca area were higher during the verbal encoding phase, compared to the spatial encoding phase (.10 vs. −.03). Together, these findings contrast sharply with the verbal recoding hypothesis. Finally, while verbal recoding of non-verbal material can never be ruled out completely, this does not jeopardize the current conclusion of domain-general involvement of the IFJ in working memory. Indeed, even if spatial locations were verbally recoded and maintained in verbal WM, resource-sharing and rapid switching would have been necessary between processing and storage across verbal and visuo-spatial WM.

Table 2
Activation clusters for the conjunction analysis in the spatial task (MNI coordinates).

Cortical area	Voxels	Hem.	BA	x	y	z	Z
Inferior temporal gyrus	1223	R	19	45	−63	−9	>7
Precuneus		R	19	33	−72	33	5.70
Superior parietal lobule		R	7	30	−63	57	5.66
Inferior temporal gyrus	219	L		−51	−72	−3	5.49
Middle occipital gyrus		L	19	−42	−87	0	4.33
Middle occipital gyrus		L	19	−39	−90	18	4.00
Inferior parietal sulcus	223	L	40	−36	−45	51	4.98
Superior parietal lobule		L	7	−21	−66	48	4.46
Superior parietal lobule		L	7	−27	−57	60	3.57
Middle frontal gyrus	107	R	6	27	−9	57	4.72
Medial frontal gyrus		R	6	21		3	54
Inferior frontal gyrus	102 ^a	R	9	48		3	33
Inferior frontal gyrus	63	R	47	36		27	−3
Precuneus	40	L	7	−24	−72	33	3.82
Precuneus		L	19	−27	−81	33	3.68

^a Denotes cluster containing the Inferior Frontal Junction.

tasks recruited the right IFJ and that only the verbal task additionally recruited the left IFJ on top of that. This specific pattern is reminiscent of the recently observed behavioral asymmetry between the maintenance of verbal and spatial information suggesting that while spatial information can solely rely on domain-general attentional maintenance, verbal information can also rely on a domain-specific maintenance mechanism independent from attention (Vergauwe et al., 2014). It might be possible that the right IFJ is involved in domain-general rapid switching of attention between processing and storage and is thus revealed in both tasks, whereas the left IFJ might be more closely related to verbal WM. This might also explain why, in our more sensitive model-based analysis, only the right IFJ was revealed in both tasks.

Recently, Zanto et al. (2010) reported that top-down modulation of motion elicits bilateral IFJ connectivity while top-down modulation of color preferentially engages right IFJ connectivity. Thus, like in our study, only the right IFJ was recruited across different types of information. However, one should not forget that the current design has only 12 trials in each of the 8 experimental conditions. While this seems be enough to identify domain-general contributions of the IFJ, which was our main goal here, this might not be sufficient to study hemispheric domain-specific differences in detail. As such, the significance of hemispheric differences in our study remains uncertain. Hemispheric differences in the lateralization of the involvement of the IFJ in cognitive control merit additional research in the future.

Coping with the dual demands of WM tasks: rapid switching

Our study is the first to manipulate the cognitive load of concurrent processing, a parameter shown to be one of the main determinants of working memory performance (e.g., Barrouillet et al., 2004, 2007, 2011). We observed that the IFJ is highly sensitive to cognitive load, independently of the domain of WM involved. This suggests that the IFJ might be crucial for the time-based interplay between processing and storage at its most central, domain-general level. In other words, the IFJ might be the neural basis of the process that enables the cognitive system to cope with concurrent processing and storage. We suggest that our approach of searching for brain areas that are sensitive to cognitive load manipulation might result in capturing some of the “mechanics” of WM by capturing the brain regions that are involved in the critical process of rapid switching between processing and storage, a feature that is crucial for WM dual functioning.

From the present findings, we derive the novel hypothesis by which the IFJ is the neural basis of the central process of rapid switching in WM. One might argue, that, to conclude for the IFJ being crucial for rapid switching, it is important to know how this region behaves in the absence of any storage requirements. If the same pattern of activity would be found without a concurrent memory load, one could argue

Table 3
Activation clusters for the conjunction analysis including both tasks (MNI coordinates).

Cortical area	Voxels	Hem.	BA	x	y	z	Z
Angular gyrus	328	R	39	30	−66	33	4.94
Superior parietal lobule		R	7	33	−60	57	4.83
Inferior parietal sulcus		R	40	36	−48	48	3.75
Inferior temporal gyrus	70	L	37	−48	−69	−3	4.64
Middle occipital gyrus		L	19	−45	−87	0	3.49
Middle occipital gyrus		L	19	−33	−90	3	3.22
Inferior frontal gyrus	101 ^a	R	9	48		3	33
Inferior parietal sulcus	95	L	40	−36	−48	48	4.21
Superior parietal lobule		L	7	−21	−69	48	4.16
Superior parietal lobule		L	7	−30	−57	57	3.53

^a Denotes cluster containing the Inferior Frontal Junction.

that the IFJ is reflecting task difficulty rather than being involved in rapid switching between processing and storage. However, several findings suggest that, without a concurrent memory load, the IFJ would not be found to vary as a function of the cognitive load of processing. Studies that compared single- and dual-task situations localized dual-task activations in the vicinity of the inferior frontal sulcus (Schubert and Szameitat, 2003; Stelzel et al., 2006; Szameitat et al., 2002). In the same way, Tombu et al. (2011) showed that the IFJ is more activated on dual-task trials than on single-task trials. Importantly, comparing blocked and mixed presentation of trials, Crone et al. (2006) found no activation in the fronto-lateral cortex when presenting a single task in a block. This situation is very similar to our processing task without a concurrent memory load in that only one task set is needed. Thus, we would not expect the activity of the IFJ to increase as a function of cognitive load when the processing tasks were to be performed without a concurrent memory load because, in that situation, no switching between task sets is needed.

While further research will be needed including all necessary control conditions to allow a firm conclusion as to the role of the IFJ in rapid switching, the current data can be used to perform two additional tests of the rapid switching hypothesis.⁵ First, we can compare the IFJ responses observed during the processing phase with the IFJ responses during the encoding phase. In contrast to the processing phase, no rapid switching between processing and storage is needed during encoding and thus, if the IFJ is specifically involved in rapid switching, one would expect the IFJ to show increased activation during the processing phase, relative to the encoding phase. To test this, we extracted mean PSC for the encoding phase and the processing phase from the R IFJ (described in the ROI analysis). In an attempt to efficiently separate R IFJ responses from the encoding phase and the processing phase, PSC for the encoding phase was the mean value measured in the time window between 4 and 8 s after the onset of the encoding phase (i.e., aiming at including only the first four seconds of the encoding phase that had a 6-s duration in the spatial task and a 9-s duration in the verbal task) and PSC for the processing phase was the mean value measured in the time window between 7 and 13 s after the onset of the processing phase (i.e., aiming at including only the last 6 s of the processing phase that had a 9-s duration in both tasks). This analysis confirmed higher activation levels during the processing phase (averaged across the four levels of cognitive load), relative to the encoding phase, in both the verbal and the spatial tasks, $t(17) = 2.52$, $p < .05$, and $t(17) = 3.51$, $p < .01$, respectively.

A second test consists in examining the IFJ responses during the recognition phase as a function of the experimental condition of the task performed during the processing phase. The idea is that, if the increase in IFJ activation as a function of the cognitive load during the processing phase is specifically due to rapid switching between processing and storage, then IFJ activation should not show a similar pattern during the recognition phase where there is presumably no need to switch

⁵ We would like to thank an anonymous reviewer for this thoughtful suggestion.

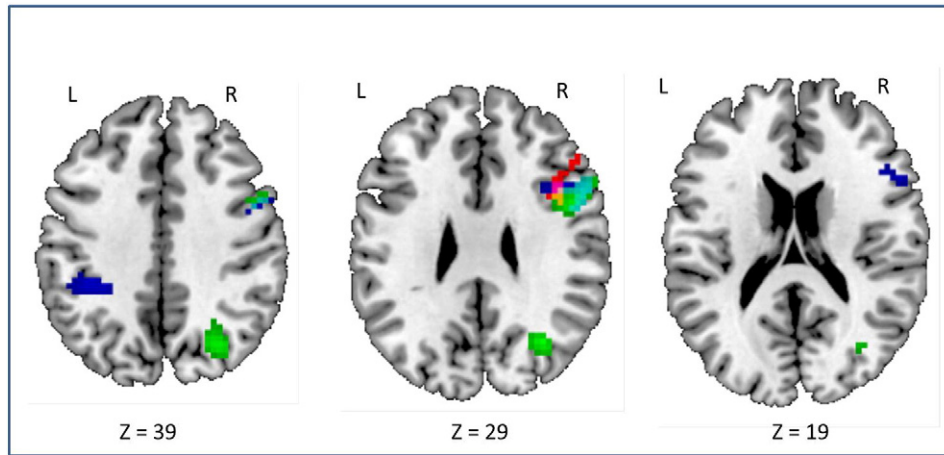


Fig. 4. Results of the conjunction analysis and the model-based analyses. The various colors are depicting different effects. In green are shown the regions that were active in the conjunction analysis including both the verbal and the spatial task. In red is shown the region with activity change as a function of cognitive load in the verbal task revealed by the model-based analysis. In blue are shown the regions with activity change as a function of cognitive load in the spatial task revealed by the model-based analysis. Overlap in regions between both model-based analyses is shown in purple; overlap between these regions and those of the conjunction analysis is shown in yellow. Slices are shown with their MNI Z coordinate value ($z = 39$, $z = 29$, and $z = 19$) and with left/right indicators. Statistical maps are cluster corrected on $p < .001$, $k > 24$.

between storage and processing. To test this, PSC for the recognition phase was the mean value measured in the time window between 4 and 6 s after the onset of the probe (i.e., aiming at including a 2-s response window). Remember, during the processing phase, the R IFJ showed an increase in activation when the number of items to be processed was increased and when the difficulty of these processing items increased. These factors interacted with each other but not with the domain of the task. Using the same repeated measures ANOVA to analyze the activation levels of the R IFJ during the recognition phase showed no significant effects of Domain, Number of Items and Item Difficulty, nor were there any significant interactions between these variables. Even though these results can only be interpreted with caution because of the lack of temporal jitter between the different phases, they do seem to be consistent with a specific role of the IFJ in rapid switching between processing and storage.

Thus, the current study provides us with a novel hypothesis proposing the IFJ as the neural basis of rapid switching.

The role of the IFJ in WM and cognitive control: Uploading relevant rule information

As we mentioned before, studies have shown the IFJ to be crucially involved in cognitive control and, more specifically, in task switching (Brass and von Cramon, 2002, 2004a, 2004b; Brass et al., 2005; Derrfuss et al., 2005; Dove et al., 2000; Kim et al., 2012; Sylvester et al., 2003). Studies have also observed the IFJ to be involved in interference control and updating (e.g., Braver et al., 1997; de Fockert et al., 2004; Derrfuss et al., 2004, 2005; Mead et al., 2002; Roth et al., 2009; Sylvester et al., 2003). The overlap of these different cognitive functions in the IFJ has so far been explained as reflecting common operations of

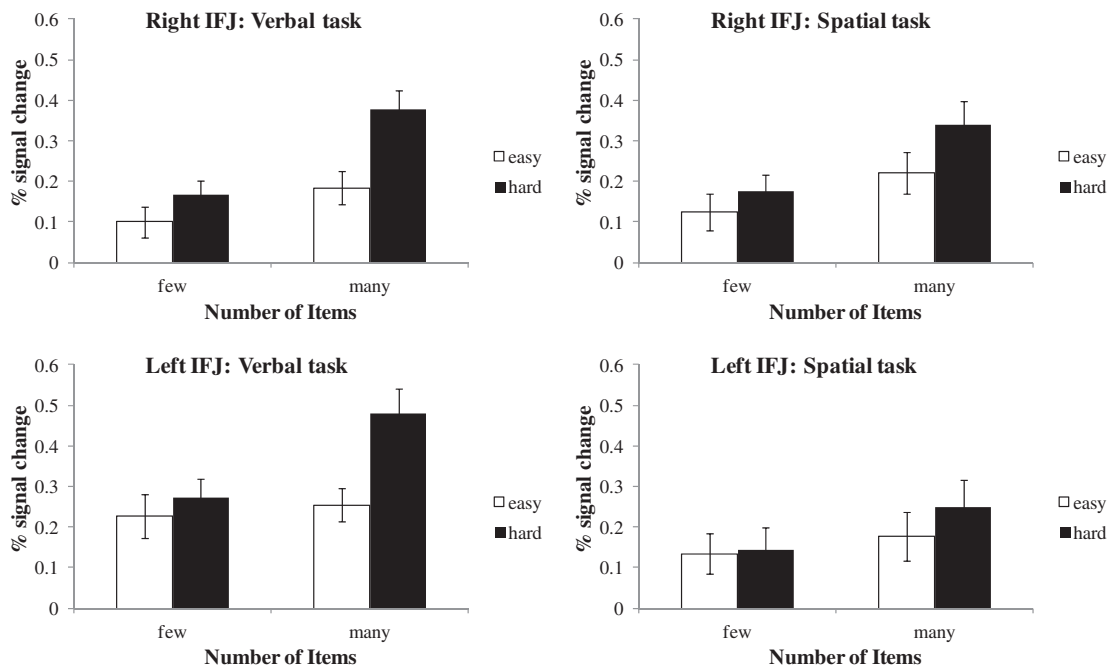


Fig. 5. ROI results. Percent signal change extracted for the right IFJ (upper panel) and left IFJ (lower panel) for the processing phase. Percent signal change is shown as a function of the Domain of the task (verbal task in left panels vs. spatial task in right panels), Number of items (few vs. many) and Item difficulty (easy vs. hard). Error bars represent standard error.

cognitive control such as task set reconfiguration and updating of general task representations (Derrfuss et al., 2004).

What is the specific process that is involved in task set configuration and subserved by the IFJ that makes this brain area so highly sensitive to variations in cognitive load? We propose that the IFJ is involved in mentally selecting relevant representations for the next (cognitive) action and, more specifically, in the process of uploading the relevant rule information for the next step serving ongoing cognition and action. This is crucial to rapid switching between processing and storage; the WM task used in the present study requires participants to recurrently switch between different rules (e.g., letters need to be stored versus letter strings need to be judged in the verbal task) and thus, to continuously upload the relevant rule information so to cope with the dual demands of the task. As the cognitive load of processing increases, one needs to alternate more often between the different rules because increasing the number of items to be processed or their difficulty calls for more rapid switching between processing and storage. This implies an increase in the need to upload the relevant rule information during the processing phase, explaining why IFJ activation was found to be a direct function of cognitive load. In the same way, in the case of task switching, participants have to switch constantly between two tasks resulting in a continuous need to upload the appropriate task rule. Similarly, in a Stroop task, one has to resolve competition either between two responses or between two stimuli. This requires inhibiting the irrelevant representation and enforcing the relevant one by continuously uploading the appropriate rule information for immediate (cognitive) action. Accordingly, Monsell et al., (2001) showed that an important component of the well-known Stroop interference effect is the competition between task rules resulting in the continuous need to upload the non-dominant task rule (naming the color of the ink) to overcome the stronger, dominant task rule of reading the word when it appears. In line with this, Hartstra et al. (2011) found the IFJ to be crucially involved in a task requiring continuous uploading of new rule information by introducing new stimulus–response mappings on every trial.

Recently, Zanto et al., (2010, 2011) showed that the IFJ acts as a control region that mediates the causal connection between top-down modulation in the service of attentional goals and subsequent WM performance. They proposed that updating relevant task representations may occur via goal-directed biasing of neural activity in distal cortical regions and found that this neural biasing optimizes WM performance. While the observations of Zanto et al. (2011) were made during the encoding period, the current results indicate that the IFJ might be involved in similar top-down modulation required for switching between processing and storage during the retention phase of the current task.

Interestingly, the IFJ has also been referred to as a neural basis of a central, amodal bottleneck in information processing by Dux and colleagues (Dux et al., 2006, 2009; see also Tombu et al., 2011). We suggest that this description is compatible with the more functional description provided by Derrfuss et al. (2004) in terms of task set configuration if one assumes that the central bottleneck arises from the inability of the IFJ to update two task set configurations at once. In fact, a recent study of Tombu et al. (2011) concludes that the IFJ is part of a unified attentional bottleneck for perception and action in the brain. Moreover, the authors proposed that the IFJ is involved in a neural central processing unit critical for flexible task implementations. It seems that evidence is converging to a capacity limit in WM, and more broadly, in the human information processing system, in implementing more than one task at the same time because of the IFJ being unable to upload more than one task rule at once. It goes without saying that the idea of IFJ reflecting a central attentional bottleneck in the brain is entirely in line with the TBRS model that postulates such a central bottleneck to constrain the way in which processing and storage can be performed concurrently, resulting in the well-known behavioral effect of cognitive load of processing on memory performance.

Other regions identified in the conjunction analysis

The conjunction analysis was less specific than the model-based analysis in that, in addition to the right IFJ, it identified parietal and occipito-temporal activations. It is worth noting that the pattern of regions observed in the conjunction analysis is highly consistent with the fronto-parietal cognitive control network observed by Sundermann and Pfeiderer (2012) who identified the IFJ as a critical hub within that network. The parietal activations observed in the current study overlapped with those of previous studies that showed increased parietal involvement as task difficulty increases (Crittenden and Duncan, 2014) and as the number of verbal items held in WM that require manipulation increases (Chamod and Petrides, 2010). In a recent meta-analysis focusing on fMRI studies investigating WM (Rottschy et al., 2012), a network of brain regions is revealed that is commonly activated in a wide variety of WM tasks. This network partially included the parietal activation observed in the current study, revealing its importance in WM functioning.

More specifically, the SPL is typically associated with attention and executive functioning (e.g., Ciaramelli et al., 2008; Osaka et al., 2007; Wager and Smith, 2003) and SPL activation has been proposed to reflect the focusing and switching of attention in the light of executive control (Osaka and Osaka, 2007; Osaka et al., 2007). As such, the bilateral SPL activation revealed by the conjunction analysis might reflect SPL involvement in the allocation of attentional resources that is called upon more when there are more items to be processed but also when judging these items becomes harder, regardless of whether the items are verbal or spatial in nature. Interestingly, the parietal activations also included more inferior parietal activations close to the intraparietal sulcus (IPS). Previous research has shown that the IPS is closely associated with capacity-limited WM maintenance (Cowan et al., 2011; Todd and Marois, 2004; Xu and Chun, 2006). Our results of greater IPS activation with increased cognitive load seems consistent with the idea of the IPS being part of a broader parietal lobe basis of one's current focus of attention (Cowan, 1995; Cowan et al., 2011).

The interpretation that we offer for the occipito-temporal activation cluster is that it is related to the specific processing tasks used in our study. This cluster of activation corresponds to the visual word form area (VWFA), an area specialized in visual word processing (McCandliss et al., 2003). Interestingly, it has been shown that low-frequency words require more visual processing than frequently encountered words, resulting in more VWFA activation (e.g., Keller et al., 2001). Also, it has been shown that pseudowords induce higher activations of the VWFA than random letter strings (Cohen et al., 2002; Price et al., 1996). Thus, we think that the observed left MOG activation reflects visual word processing specific to the lexical decision task used as processing task in the verbal WM task. A study by Reinke et al. (2008) showed that the VWFA plays a general role in processing abstract stimuli instead of a specific role in processing words and letter strings. In this study, it was shown that VWFA activity did not differ for words and meaningful symbols like the ones we used (e.g., £, &). The role of the VWFA in extracting information from abstract visual stimuli such as letters and symbols might explain why it was observed in the spatial task too.

Conclusions

The results of the present study suggest that there are neural correlates for the mechanism of time-based resource-sharing in WM. In line with the domain-general assumption of the TBRS model, we observed neural overlap between the cognitive load effect in the verbal and the spatial domains of WM. Across different types of analyses, our results suggest that only one brain area, the right IFJ, was sensitive to cognitive load regardless of the domain involved. The present findings indicate that the IFJ makes domain-general contributions to WM functioning and allowed us to generate the novel hypothesis by which the IFJ

might be the neural basis for the process of rapid switching in WM. More specifically, we argue that the IFJ might be a crucial part of a central attentional bottleneck in the brain because of its inability to upload more than one task rule at once.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2015.04.059>.

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