

Dissociable Neural Effects of Task Order Control and Task Set Maintenance during Dual-task Processing

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Abstract

■ The functional relevance of the lateral prefrontal cortex (IPFC) for the ability to process two tasks simultaneously has been debated extensively in previous studies that employed functional magnetic resonance imaging (fMRI) to investigate the neural correlates of dual-task processing. In the present fMRI study, we shed new light on this debate by directly comparing the IPFC activity changes for two cognitive functions commonly associated with dual-task performance: task order control and task set maintenance. We manipulated both functions in a 2×2 integrated parametric design. The fMRI data revealed a functional–neuroanatomical dissociation for the IPFC. Regions surrounding the inferior frontal sulcus and the middle frontal gyrus were ex-

clusively associated with task order control but not with increased demands on task set maintenance during dual-task processing. The only IPFC region associated with task set maintenance was located in the left anterior insula. Outside the IPFC, we found dissociable regions for task order control and task set maintenance bilaterally in the premotor cortices with more rostral premotor activity for task order control and more caudal premotor activity for task set maintenance. In addition, task order control activated the intraparietal sulci bilaterally. Our data clearly suggest that task order control is a separable cognitive mechanism in dual-task situations that is related to activity changes in the IPFC and that can be dissociated from task set maintenance. ■

INTRODUCTION

The simultaneous processing of multiple behaviorally relevant information streams by the human brain is essential for dealing with the demanding environment surrounding us. Although it seems to most of us as if we process multiple task requirements in a strictly parallel fashion, usually severe performance costs emerge from the simultaneous performance of two tasks compared to single-task performance. These dual-task costs are characterized by increased processing times and error rates, indicating serious capacity constraints of the cognitive system (e.g., Baddeley, 1998; Pashler, 1994; Kahneman, 1973). To date, it is relatively unknown how the human brain regulates the cognitive processes involved in task situations affected by these capacity constraints.

Recently, a number of neuroimaging studies started to investigate the neural correlates of the performance costs in dual-task situations using functional magnetic resonance imaging (fMRI). These studies provided evidence that the lateral prefrontal cortex (IPFC) plays a central role in dual-task processing (Erickson et al., 2005; Herath, Klingberg, Young, Amunts, & Roland, 2001; D'Esposito et al., 1995). In a series of own studies (Stelzel, Schumacher, Schubert, & D'Esposito, 2006;

Schubert & Szameitat, 2003; Szameitat, Schubert, Müller, & von Cramon, 2002), we also localized dual-task-related brain regions by contrasting blood oxygenation level dependent (BOLD) fMRI activity in dual-task blocks with activity in single-task blocks, thereby employing the method of cognitive subtraction (Friston et al., 1996). The most consistently activated dual-task-related regions were located in regions around the inferior frontal sulcus (IFS) and in regions of the middle frontal gyrus (MFG; Stelzel et al., 2006; Schubert & Szameitat, 2003; Szameitat et al., 2002). Using easy choice-reaction time (RT) tasks as component tasks, our studies further specified the findings of earlier studies (D'Esposito et al., 1995) and avoided methodological problems of studies with more complex component tasks, which failed to detect such dual-task-related BOLD signal changes in the IPFC (see Szameitat et al., 2002 for discussion).

Although the finding of greater IPFC activity suggests an association of the IPFC with dual-task performance, it remains an open question which specific cognitive mechanisms are associated with the dual-task-related activity in the IPFC. Because of the applied subtraction method, a comparison of BOLD signal changes between dual-task blocks and single-task blocks may reflect any cognitive difference between these types of blocks. In order to understand the functionality of the IPFC for dual-task processing in more detail, the underlying cognitive mechanisms need to be specified and compared directly

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above, suggesting an involvement of these regions in interference control.

Task Set Maintenance

The attribution of dual-task-related LPFC activity to task order control processes was recently objected to by other authors (Erickson et al., 2005; Jiang et al., 2004). Jiang et al. (2004) noted that the demands to maintain additional task set components in working memory might have caused the additional LPFC activity in dual-task compared to single-task situations.

It is commonly assumed that the components of a task set, including the stimulus and response sets, the task rules, and the task context, have to be maintained in an active state of working memory when behavioral tasks are performed (Miller, 2000; Cowan, 1999). We call this task set maintenance (Logan & Gordon, 2001; Meiran, 1996; Rogers & Monsell, 1995). Importantly, the demands on task set maintenance depend on the size of the task set, for example, the number of task set components to be held in an active processing state for the duration of a task block. Compared to single-task situations, task set size is increased in dual tasks, including larger stimulus and response sets as well as a higher number of stimulus–response (S–R) mapping rules (Jiang et al., 2004; Duncan, 1977). Accordingly, it is plausible that the processing requirements in the neural substrate associated with task set maintenance are increased in dual-task compared to single-task situations.

Indeed, task set maintenance has been associated with neural activity in various regions of the lateral frontal cortex, including the LPFC. For example, task-set-specific activity in the LPFC has been shown in pretask preparation intervals (Brass & von Cramon, 2004; Sakai & Passingham, 2003; Wallis & Miller, 2003). Lateral PFC activity was also found in numerous working memory studies that manipulated the size of the stimulus set to be maintained (Zarahn, Aguirre, & D'Esposito, 1999; Goldman-Rakic, 1987; Fuster & Alexander, 1971) or the number of active working memory items in the *n*-back paradigm (Braver et al., 1997; Schumacher et al., 1996; Cohen et al., 1994). In addition, the maintenance of task set components has also been associated with more posterior lateral frontal regions located in the premotor cortex. For example, a number of recent studies found increased activity in the premotor cortex and in the LPFC when manipulating the number of S–R mapping rules comprising the task set of simple choice reaction tasks (Marois, Larson, Chun, & Shima, 2006; Erickson et al., 2005; Schumacher et al., 2003). In addition, activity in regions of the lateral premotor cortex has been associated with the maintenance and preparation of response sets (van Eimeren et al., 2006; Grafton, Fagg, & Arbib, 1998).

Not surprisingly, the exact location of activity related to task set maintenance varies depending on the specific

set size manipulations applied (D'Esposito et al., 1998). Just like for the studies on interference control, there is a large overlap of regions related to task set maintenance and the dual-task-related regions discussed above. Thus, increased demands on task set maintenance due to a larger task set size in dual tasks compared to single-task situations might indeed be a factor causing additional neural activity in the LPFC and other brain regions when participants perform two tasks simultaneously. Accordingly, not only task order control but also task set maintenance may be associated with the additional dual-task-related LPFC activity.

The Rationale of the Present Study

From the study of Szameitat et al. (2002), we know that task order control is one specific cognitive mechanism underlying dual-task-related LPFC activity. We do not know yet whether increased demands on task set maintenance are likewise responsible for activity changes in the LPFC in dual-task situations. If so, the question of interest would be whether those regions overlap with the brain regions associated with task order control during dual-task processing or whether they are dissociable from those regions. In the present study, we used fMRI to answer this question. We orthogonally manipulated the difficulty of both functions in different versions of the same dual-task paradigm in a parametric fMRI design. According to the method of parametric manipulation, the neuroanatomical correlates of a specific cognitive process can be localized by manipulating the difficulty of that process (Braver et al., 1997). Using an integrated experimental design for the manipulation of the two functions, we are able to disentangle brain regions in the LPFC that are sensitive to the difficulty manipulation of task order control or of task set maintenance, respectively. In addition, we can identify brain regions that are sensitive to the difficulty manipulation of both functions. If present, such common activations would reflect an overlapping localization of both functions (but see Caplan & Moo, 2004; Sarter, Berntson, & Caccioppo, 1996; and the Discussion section).

It has to be noted that other methodological approaches have been proposed to compare the localization of brain regions associated with two or more different cognitive functions. For example, several authors have used a meta-analysis approach (Turkeltaub, Eden, Jones, & Zeffiro, 2002; Fox, Parsons, & Lancaster, 1998) to compare the activation foci of two or more cognitive functions detected in other neuroimaging studies (Derrfuss et al., 2005; Wager & Smith, 2003). Despite the valuable effort that meta-analyses take to combine the results of multiple experimental studies from different laboratories, the comparison of specific cognitive functions based on such an approach may be highly confounded. This is because even after an

elaborate selection of studies, there are still multiple potential differences between the specific studies included for data processing in the meta-analysis. These differences concern the specific experimental design, the magnetic field strength and other scanner peculiarities, the methods of data processing, and so forth. This makes an accurate comparison of the localization of different cognitive functions difficult.

Contrary to the meta-analysis approach, the present parametric approach allows us to exclude such caveats because two cognitive mechanisms are manipulated in an integrated experimental paradigm performed by one group of participants. This design allows comparing the neural effects of the two distinguished functions directly and gives the opportunity to make unequivocal conclusions about their localization relative to each other. In particular, we manipulated task order control difficulty by comparing dual-task blocks with random and fixed temporal order (task order) of the component tasks as proposed in the Szameitat et al. (2002) study. Additionally, we manipulated the demands on task set maintenance via the task set size of the component tasks (set size) in a dual-task situation. In detail, we compared dual-task blocks with four S–R mappings per component task with dual-task blocks with two S–R mappings per component task. Using a 2×2 factorial design, we determined regions sensitive to either of both factors and regions sensitive to both factors, that is, the conjunction (Nichols, Brett, Andersson, Wager, & Poline, 2005; Price & Friston, 1997), with a whole brain random effects analysis. A possible dissociation of both factors would have important implications for the understanding of the neural and cognitive mechanisms involved in dual-task processing. In addition, the results of this experiment contribute essentially to the discussion about the extent to which different types of cognitive control mechanisms employ the same or different neural substrate within the IPFC (Duncan & Owen, 2000).

METHODS

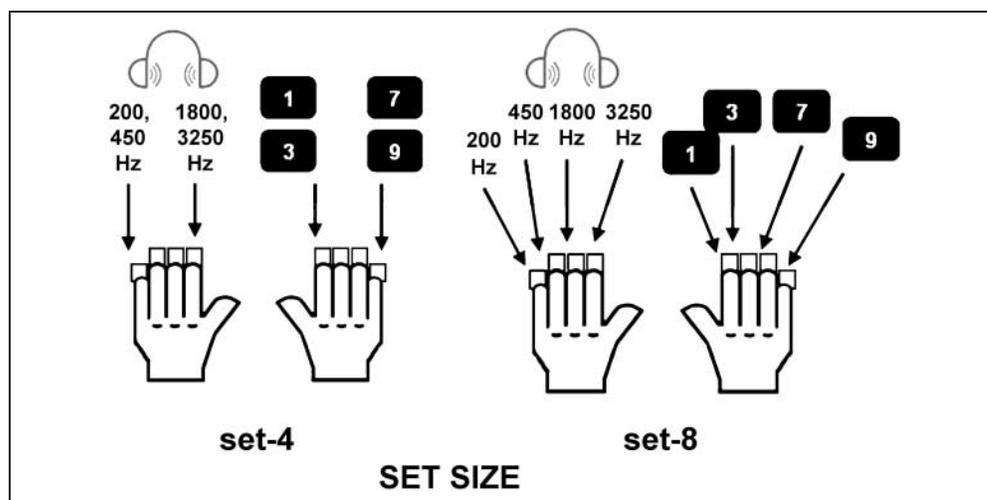
Participants

Thirteen healthy right-handed volunteers with normal or corrected-to-normal vision participated in the experiment (8 women, ages 21–29 years) after obtaining informed consent according to the Declaration of Helsinki. Participants were paid 10 Euros per hour.

Behavioral Procedure

Participants performed four types of dual tasks in different blocks. In each trial, we presented a visual and an auditory stimulus with an SOA of 250 msec between them. The visual stimulus was one of four centrally presented digits (1, 3, 7, or 9), projected onto a screen that the participants viewed through a mirror mounted on the head of the radio-frequency coil in the MRI scanner. The auditory stimulus was one of four tones with a frequency of 200, 450, 1800, or 3250 Hz, presented via headphones (see Figure 1). A dual-task trial started with the presentation of a fixation cross for 850 msec, followed by the presentation of the first stimulus for 250 msec which was followed directly by the second stimulus for 250 msec. Next, the fixation cross was presented for another 2250 msec. During this time, participants responded to both stimuli.¹ Participants were instructed to respond as fast and accurate as possible on both stimuli. Importantly, they were instructed to respond on the two stimuli in the order of their presentation. They performed manual responses using two response boxes with four buttons each (4 left, 4 right), both positioned on their abdomen. Participants responded with the left hand for the auditory stimuli and with the right hand for the visual stimuli (see Set Size Manipulation section for details). Before the next trial, a blank screen appeared for 400 msec.

Figure 1. Set size manipulation. Stimulus–response mappings for the set-4 and set-8 conditions. Participants responded with their left hand on one of four tones and with their right hand on one of four centrally presented digits. The presentation order of the stimuli was either fixed or random within one block (SOA = 250 msec). Using a 2×2 factorial design, four types of dual-task blocks were realized: DT fixed/set-4, DT fixed/set-8, DT random/set-4, DT random/set-8.



Design of Measurement

The total duration of a dual-task trial was 4 sec. Each block consisted of eight trials. An instruction screen was presented for 6 sec before the beginning of each block and a fixation period followed each block with a duration of 6 sec. Each block type was presented twice per run. One fMRI run lasted 7 min 26 sec (223 scans). We collected three runs for each participant. The presentation order of the blocks was counterbalanced across participants with the restriction that the different set size conditions (see below) alternated and fixation blocks were presented as the first and last blocks in each run. All participants performed one training session outside the scanner to practice the corresponding single and dual tasks.

Task Order Manipulation: Fixed- vs. Random-order Blocks

In *fixed-order* blocks (half of the blocks), the presentation order of the two stimuli remained constant during a block (e.g., the stimuli were always presented in the order visual–auditory or auditory–visual across the whole block of dual-task trials). In *random-order* blocks (i.e., the other half of the blocks), the presentation order changed pseudorandomly within a block so that participants did not know whether the next trial would be a visual–auditory or an auditory–visual trial. Both presentation orders were presented four times within each random-order block with balanced transitions of the presentation orders.

Set Size Manipulation: Set-4 vs. Set-8 Blocks

Set size was manipulated blockwise by varying the number of relevant S–R mappings between four (set-4 blocks) and eight (set-8 blocks). We varied the number of S–R mappings via the number of relevant motor responses. Note that previous studies have shown that differences in stimulus probabilities between conditions may also be related to IPFC activity (Casey et al., 2001). To avoid this potential confound, we kept the number of stimuli constant across conditions in the present experiment. In both component tasks, two of the respective four sensory stimuli were mapped onto the same motor response in the set-4 condition while they were mapped onto four different motor responses in the set-8 condition (see Figure 1 for details). This, effectively, increased the overall task set size by doubling the amount of relevant motor responses and, accordingly, the number of relevant S–R mappings in the set-8 compared to the set-4 blocks.

By combining the two factors task order and set size in a 2×2 factorial design, we realized four different dual-task (DT) conditions in the present experiment: DT

fixed/set-4, DT fixed/set-8, DT random/set-4, DT random/set-8.

Fixation

Additionally, we included two fixation blocks per run, in which the participants were instructed to fixate a centrally presented fixation cross for 32 sec to get a baseline measure of brain activation.

fMRI Procedure

All images were acquired with a 3-Tesla Signa LX MR scanner (General Electric Company, USA) equipped with a fast gradient system for echo-planar imaging. We used a standard radio-frequency head coil and an air-filled cushion to restrict head motion comfortably. Functional images were acquired using a whole-brain, one-shot, gradient-echo echo-planar sequence (TR = 2000 msec, TE = 30 msec, matrix size = 64×64 , FOV = 24 cm, flip angle = 90°). Each functional volume consisted of 23 axial slices with 4 mm thickness and a 1-mm gap between. We also acquired a structural T1-weighted 3-D scan at the end of the experiment, using a spoiled Gradient Recalled Acquisition in the Steady State (GRASS) sequence (matrix size 256×256 , slice thickness: 1.0 mm, flip angle: 30°). These data were used for the normalization of the functional data to the Montreal Neurological Institute (MNI) atlas space.

fMRI Data Analyses

All analyses were carried out with SPM2 (www.fil.ion.ucl.ac.uk/spm/spm2.html). First, each participant's functional dataset was motion corrected and spatially normalized into the standard MNI atlas space. Then, we smoothed the data with an 8-mm full-width half-maximum Gaussian kernel and high-pass filtered during analysis. We then applied the general linear model for serially autocorrelated data (Friston et al., 1995) using covariates for the four different task types, the fixation blocks, the instructions, and the movement parameters. For each individual participant, we derived voxelwise parameter estimates for each covariate and calculated contrast images for the main effects of each dual-task condition versus fixation.

Random Effects Group Analysis (Whole Brain)

For the group analysis, the individual contrast images were entered into a repeated measures analysis of variance (ANOVA) with replication across participants. The levels were defined as DT fixed/set-4, DT fixed/set-8, DT random/set-4, and DT random/set-8. We then calculated the contrasts for the main effects of task order

[(DT random/set-4 + DT random/set-8) – (DT fixed/set-4 + DT fixed/set-8)], and set size [(DT fixed/set-8 + DT random/set-8) – (DT fixed/set-4 + DT random/set-4)] and the respective interactions for these group data. We used a statistical threshold of $p < .001$, uncorrected for multiple comparisons. That way we could identify whether there was any activity for either function in the IPFC or other relevant brain regions at a rather lenient criterion. Additionally, we performed a conjunction analysis ($p < .01$, uncorrected) to determine which voxels were activated in both contrasts (Nichols et al., 2005; Price & Friston, 1997). In general, a conjunction analysis tests voxels for a conjoint effect of two or more functional contrasts. Here, we tested the conjunction hypothesis of common effects of task order and set size against the conjunction null hypothesis (Nichols et al., 2005), in this case: (not task order) or (not set size).

Regions-of-Interest Analyses

In order to further illustrate the effects of the different dual-task conditions in the IPFC, we performed a region-of-interest (ROI) analysis in those IPFC regions that were found to be associated with task order and/or set size in the whole-brain random effects analysis. Using MarSBAR (<http://marsbar.sourceforge.net/>), we extracted the parameter estimates from the time series of every individual participant for all four dual-task conditions. We applied spherical masks with a diameter of 8 mm centered at the peak voxels of the corresponding statistical group contrasts for task order and set size, respectively. For the voxels covered by these masks, we then compared the mean parameter estimates across conditions with paired t tests. That way, we applied a more liberal statistical criterion than in the whole-brain analysis for detecting possible set size and task order effects in the IPFC. In addition, we used two further ROIs from an independent study where a related manipulation of task order control was applied (Szameitat, Lepsien, von Cramon, Sterr, & Schubert, 2006). For the IPFC activity peaks from the task order control contrast of that study, we created additional spherical masks of 8 mm in diameter and extracted the parameter estimates for the four dual-task conditions in the present study to further validate the present findings.

RESULTS

Behavioral Data

The analysis of the behavioral data indicated that the difficulty manipulations for task order control and task set maintenance effectively influenced the performance of participants in the scanner session. Mean RTs and accuracies for all dual-task conditions are shown in Figure 2. All data points are averaged RTs across the

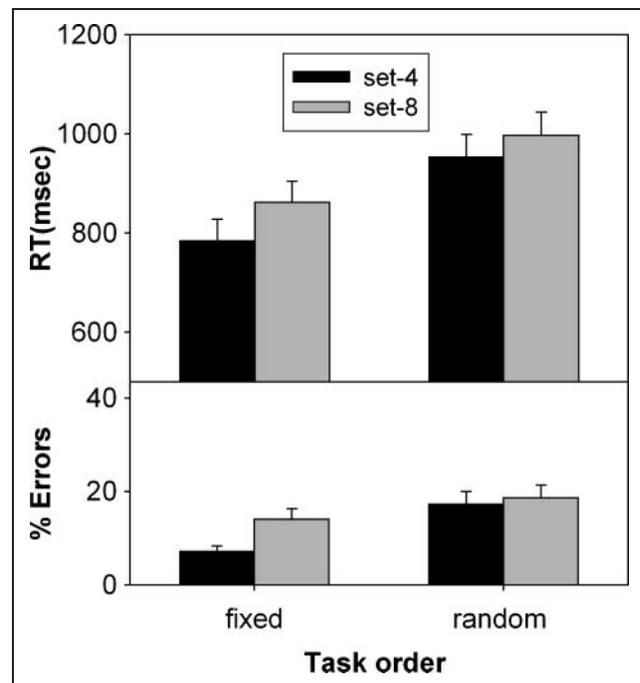


Figure 2. Behavioral data for the four dual-task conditions. RTs and error rates are averaged for Task 1 and Task 2 irrespective of the presentation order (e.g., visual–auditory or auditory–visual). Error bars denote the standard error.

two component tasks, that is, the mean RT for the respective visual and auditory tasks independent of presentation order. A two-factorial ANOVA with repeated measures (factors task order and set size) was performed for the mean RTs. It revealed a reliable effect of task order [$F(1, 12) = 124.77$, $MSE = 2429.35$, $p < .001$], with RTs in the random-order conditions ($M = 975$ msec) being slower than in the fixed-order conditions ($M = 823$ msec). In addition, there was a significant effect of set size [$F(1, 12) = 14.26$, $MSE = 3237.14$, $p < .01$], reflecting an increase of RTs in the set-8 ($M = 929$ msec) compared to the set-4 conditions ($M = 869$ msec). There was no interaction between the two factors ($p > .11$). The same pattern was found for the error rates. There were significant effects of task order [$F(1, 12) = 16.18$, $MSE = 0.0043$, $p < .01$] and set size [$F(1, 12) = 8.96$, $MSE = 0.0023$, $p < .05$], but no significant interaction of both factors, $p > .10$.

It is important to mention that these findings replicate the results of a pilot study, where another group of participants performed the same tasks with a higher number of trials per condition outside the scanner. Here, task order [$F(1, 11) = 24.39$, $MSE = 11,302.31$, $p < .001$] and set size [$F(1, 11) = 32.59$, $MSE = 5720.11$, $p < .001$] also revealed additive effects [$F(1, 11) = 0.69$, $MSE = 1954.65$, $p > .42$]. Note that the finding of additive effects represents an important precondition for the unequivocal interpretation of any conjunction effects in the fMRI data (for more details, see the Discussion section).

fMRI Data

Regions sensitive to the manipulations of task order, set size, and the conjunction of both contrasts in the whole-brain random effects analysis are listed in Table 1 and shown in Figure 3. Note that the statistical thresholds are lowered in Figure 3 ($p < .005$, uncorrected) compared to Table 1 ($p < .001$, uncorrected) to illustrate the overall pattern of activation. In the following, we describe the effects of the corresponding contrasts in detail.

Task Order-related Regions

Task order-related regions are presented in red–yellow colored scale in Figure 3. When comparing the BOLD signal changes in random-order and fixed-order blocks, we found bilateral activation foci in the IPFC. In the right hemisphere, there were two IPFC activation foci, one of them located along the IFS, the other located ventrally to the IFS in posterior regions of the IFG. The latter activation peak was close to the inferior frontal junction region (IFJ; Brass, Derrfuss, Forstmann, & von Cramon, 2005) adjacent to the precentral sulcus. In the left hemisphere, we found two activation foci for task order, both located in anterior regions of the MFG. In addition to the IPFC regions, we found one activation focus in the right dorsal premotor cortex (PMd) in regions surrounding the precentral sulcus and two further peaks in regions posterior to the left precentral sulcus; one in the ventral premotor cortex (PMv) and one in the PMd more laterally. Moreover, increasing demands on task order control activated the inferior parietal lobe bilaterally along the horizontal segment of the intraparietal sulcus (IPS), as well as the left precuneus and the right superior temporal sulcus.

Set Size-related Regions

Set size-related regions are illustrated in a green-colored scale in Figure 3. Most importantly, we did not find any significantly activated voxels for the set size contrast in regions surrounding the IFS or in regions of the MFG in the IPFC. The only set size-related IPFC activity was located in the left anterior insula. Furthermore, we found four activation peaks in the premotor cortex in regions surrounding the precentral sulcus. In particular, there was one activation focus in the right PMd, two in the left PMd, and one in the left lateral PMv. Outside the frontal cortex, we found set size-related activity in regions of the post-central gyrus, close to the IPS, and in the left cerebellum.

Interestingly, no region showed interaction effects of both factors.

Conjunction Analysis

The findings of the conjunction analysis are presented in a blue-colored scale in Figure 3. We found several

regions that were activated by both factors as indicated by the subsequent conjunction analysis. For the frontal cortex, most of these conjunction regions were located in the premotor cortex, at the transition between the task order- and the set size-related regions. The right PMd conjunction cluster was located along the precentral sulcus. In addition, we found one left-lateralized PMd peak right in the middle of the respective task order and set size regions and two further peaks located more laterally in the left premotor cortex. Additionally, we found one conjunction cluster in the left anterior insula and one in the right caudate nucleus.

Regions-of-Interest Analyses

Taken together, these results indicate that activity changes in regions along the IFS and the MFG are only associated with increasing demands on task order control but not with increasing demands on task set maintenance in dual-task situations. To ensure that the lack of set size effects in the IPFC cannot be attributed to a potential type II error, we performed a series of subsequent ROI analyses to further validate this finding.

In the first ROI analysis, we used spherical masks located around the IPFC peak voxels for the task order group contrast (i.e., the contrast of random-order and fixed-order blocks). Note that the set size contrast is orthogonal to the task order contrast where the ROIs were determined from (Friston, Rotshtein, Geng, Sterzer, & Henson, 2006). In Figure 4, we present the ROI data of all four dual-task conditions separately. In a first step, we performed pairwise comparisons of the set size conditions to further test the lack of set size-sensitive IPFC regions as indicated by the whole-brain analysis. Neither in fixed-order blocks (all p s $> .16$) nor in random-order blocks (all p s $> .34$) did we detect any effects of set size in the analyzed IPFC ROIs. Thus, this ROI analysis confirms that the lack of set size effects in the analyzed IPFC ROIs cannot be explained by a potential type II error.

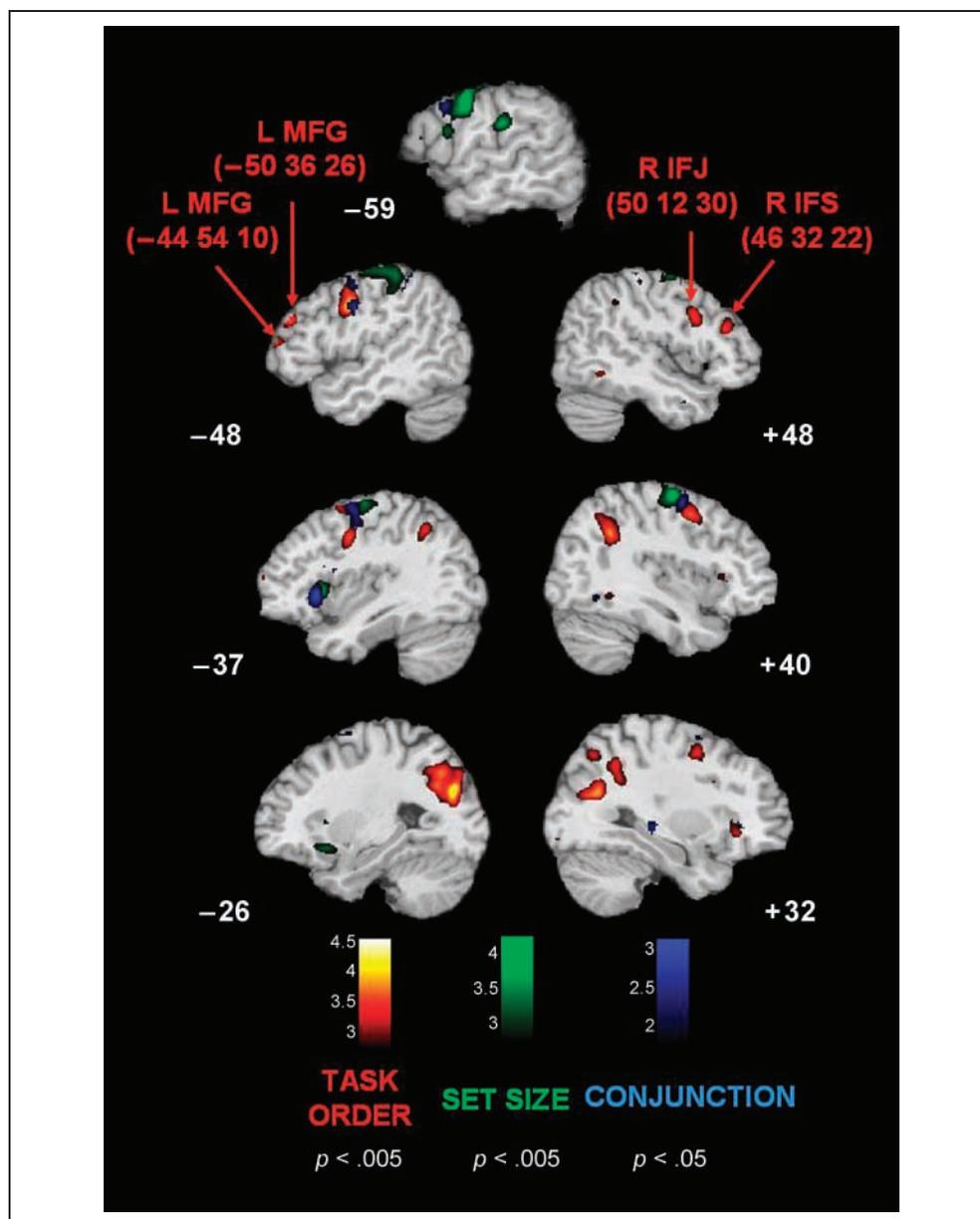
A second post hoc ROI analysis aimed at replicating the dissociation of task order and set size effects in the present fMRI dataset with ROIs obtained in an independent study. For this purpose, we used the IPFC activity peaks from the study of Szameitat et al. (2006), who manipulated task order control in an event-related design. Within the two ROIs of the study of Szameitat et al. (MNI coordinates: left IFS: $x = -35$, $y = 4$, $z = 30$; right MFG: $x = 31$, $y = 3$, $z = 45$; see Discussion section for details), the corresponding ANOVA confirmed selective task order-related effects for the left IFS ($p < .06$) and the right MFG region ($p < .05$) and, most importantly, a lack of any set size effects in these ROIs (both p s $> .38$). Additionally, there was no significant interaction of task order and set size in these regions (both p s $> .10$). Thus, task order and set size can be dissociated even within ROIs from an independent study.

Table 1. MNI Coordinates and Anatomical Location of the Peak Activations for Task Order, Set Size, and the Conjunction Effects in the Group Analysis

Region	Hem	BA	MNI Coordinates			t
			x	y	z	
<i>Task Order (Random vs. Fixed Order)</i>						
Frontal						
Middle frontal G/inferior frontal S	R	46	46	32	22	3.61
Precentral S/inferior frontal G (IFJ)	R	6/9	50	12	30	3.61
Precentral S/middle frontal G	R	6	42	2	48	3.98
Precentral S/middle frontal G	L	6	-40	4	60	3.59
Middle frontal G	L	46	-44	54	10	3.80
Middle frontal G	L	10/46	-50	36	26	3.89
Precentral S/inferior frontal G	L	6/9	-44	0	36	4.54
Other						
Parieto-occipital S/precuneus	L	19	-24	-76	30	4.39
Inferior parietal lobe/intraparietal S	L	40	-34	-52	44	3.43
Inferior parietal lobe/intraparietal S	R	40	38	-52	36	4.10
Superior temporal S	R	39	34	-64	22	3.89
<i>Set Size (Set-8 vs. Set-4)</i>						
Frontal						
Precentral S	R	6	40	-8	60	3.96
Precentral G	L	6	-42	-14	64	4.02
Precentral S/inferior frontal G	L	6/44	-62	6	20	3.84
Precentral G	L	6	-60	4	40	4.24
Insula	L	13	-34	18	4	4.20
Other						
Postcentral G/intraparietal S	L	2/40	-62	-22	26	3.89
Cerebellum	L		-2	-66	-18	3.72
<i>Conjunction (Task Order and Set Size)</i>						
Frontal						
Precentral S/middle frontal G	R	6	40	-2	56	2.66
Precentral G/middle frontal G	L	6	-40	-4	58	2.66
Precentral S	L	6	-54	0	36	3.12
Precentral G	L	6	-54	-2	48	2.69
Insula	L	13/47	-36	22	0	3.14
Other						
Caudate nucleus	R		32	-26	-2	2.50

Hem = hemisphere (L = left, R = right); BA = Brodmann's area; G = gyrus; S = sulcus; IFJ = inferior frontal junction.

Figure 3. Results of the whole-brain random effects analysis in Experiment 1. Red: positive task order-activations (random-order vs. fixed-order blocks); green: positive set size-activations (set-8 vs. set-4); blue: conjunction regions (effects of task order and set size). Coordinates denote the peak voxels of IPFC clusters in MNI space.

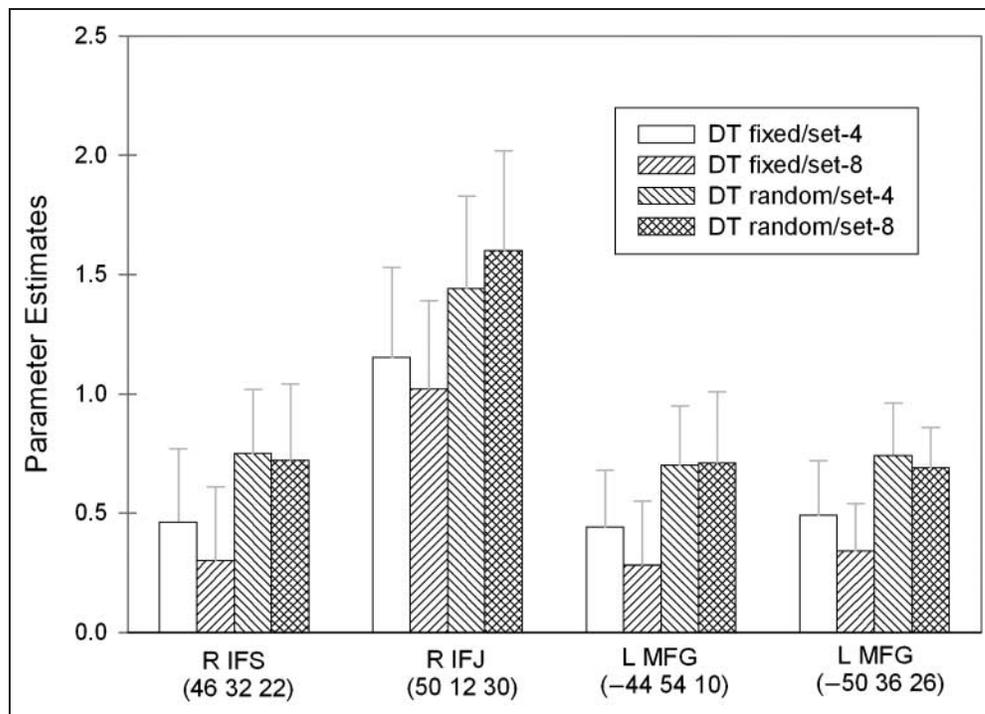


In two further analyses, we tested whether the lack of set size effects in the IPFC may be due to an insufficient strength of the present set size manipulation being associated with the relatively small effect size of this factor in the corresponding behavioral data. For this purpose, we used a split-half method, dividing the group of participants into two groups, which differed with respect to the effect sizes of their behavioral set size effects (i.e., the mean RT differences between the set-8 and the set-4 conditions). In particular, the members of the two groups had either a mean behavioral set size effect below or above the group median ($Md = 40.5$ msec, range = -47 to 142).² We then compared the neural set size effects in the parameter estimates between these groups in the task order ROIs created from the present dataset. As a result, there were no reliable

differences in the IPFC activity between the two groups in any of the four ROIs in the IPFC (all p s $> .36$). Even more striking, for the six participants with large behavioral effects (i.e., effect sizes above the median), there was no sign for significant activity changes in regions of the IFS and MFG at all as can be seen in Figure 5, where the six individual t -maps are overlaid onto a single brain ($p > .001$). Importantly, three of the six participants with large effect sizes showed behavioral set size effects that were even stronger than their respective task order effects (mean difference between set size and task order effect sizes = 10 msec; $SEM = 1.8$ msec), still they did not show any reliable IPFC activity associated with the set size manipulation.

Taken together, these post hoc analyses show that the lack of set size effects in the IPFC is a reliable finding in

Figure 4. ROI analysis in the four reliable activation foci for task order in the IPFC. Shown are the parameter estimates for all four dual-task conditions. Error bars denote the standard errors. No significant effects were found in the comparison of set-4 and set-8 conditions.



the present study that cannot be ascribed to a potential type II error or to an insufficient effect size of the corresponding set size manipulation.

DISCUSSION

In this study, we investigated the activity changes in the IPFC associated with task order control and task set maintenance during dual-task processing. This is of considerable interest for the debate about which cognitive mechanisms are associated with dual-task-related activity in the IPFC when contrasting BOLD signal changes in dual-task and single-task situations (Stelzel et al., 2006; Erickson et al., 2005; Schubert & Szameitat, 2003; Szameitat et al., 2002; Herath et al., 2001). Whereas we suggested that the dual-task-specific activity in the IPFC is associated with task order control (Schubert & Szameitat, 2003; Szameitat et al., 2002), other authors proposed that this activity reflects different demands on task set maintenance in dual-task blocks compared to single-task blocks (Erickson et al., 2005; Jiang et al., 2004).

As a most important result, we found cortical activity in the IFS and the MFG to be associated with task order control but not with differences in task set maintenance during dual-task processing. Task set maintenance, by contrast, was associated with bilateral activity changes in the premotor cortex and in the left anterior insular cortex. This neuroanatomical dissociation strongly contradicts the assumption that the neural activity in the IPFC during dual-task processing is simply related to the requirement to maintain the task sets of two tasks simultaneously (Jiang et al., 2004 and others). Instead, the pres-

ent findings suggest that task order control represents a dissociable cognitive mechanism, which is associated with the IPFC during dual-task processing.

Cognitive and Neural Mechanisms of Task Order Control

The finding of activity changes related to task order control in regions surrounding the IFS and in the MFG is consistent with one of our previous studies where we also used a parametric approach in order to localize dual-task-relevant brain regions (Szameitat et al., 2002). These and the present findings suggest that IPFC activity

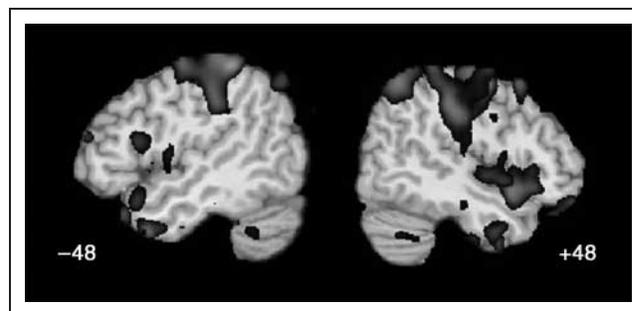


Figure 5. Individual t maps for the set size-contrast of six participants overlaid onto the same brain ($p < .001$). These six participants showed behavioral set size effects higher than the group median (Md = 40.5 msec, range = -47 to 142 msec), similar in size to the respective task order effects. Even for these participants with high set size effects, no evidence for dorsal IPFC activity in the set size-contrast can be observed.

in dual-task situations is related to processes that are needed to manage and to control the temporal processing order of two competing task streams (Meyer & Kieras, 1997; De Jong, 1995).

A number of authors in cognitive psychology proposed that task order control is required in dual-task situations whenever two task streams compete for access to a processing bottleneck (Sigman & Dehaene, 2006; Luria & Meiran, 2003; Meyer & Kieras, 1997; De Jong, 1995). According to these conceptions, task order control represents a general phenomenon which is not limited to random-order dual-task situations, but which is essential for bottleneck processing in fixed-order dual-task situations as well. In both situations (random and fixed order), task order control includes the planning and coordination of the appropriate sequence of actions in two tasks prior to stimulus presentation and the on-line control of the serial processing of the component tasks at the bottleneck itself. Recently, Sigman and Dehaene (2006) proposed a computational model for PRP situations where the serial processing of the two tasks at the bottleneck originates from several executive mechanisms. A task setting mechanism is involved in the planning and coordination of the appropriate action sequence and an attentional switching mechanism enables the task processes in the second task to proceed after the first task has passed the bottleneck. Although the task setting mechanism seems particularly demanding in the random-order dual-task blocks of the present study, the model suggests further that the switching mechanism should be involved in fixed- and random-order dual-task blocks. Note that this is similar to the assumptions of Luria and Meiran (2003), and see also Meyer & Kieras (1997) for a production-rule-based computational model proposing active mechanisms of executive control in dual tasks. Thus, task order control seems to be involved in fixed-order dual-task situations as well and may explain the observation of dual-task-related IPFC activity in other dual-task imaging studies with a fixed temporal order of the component tasks such as the studies by Schubert and Szameitat (2003) or D'Esposito et al. (1995).

The assumption that task order control is not only associated with the specific operationalization of this mechanism as applied in the present study is supported by the findings of a recent event-related fMRI study of our own group (Szameitat et al., 2006). This study showed that IPFC activity is associated with manipulations of task order control located at the micro-level within a dual-task trial. In detail, Szameitat et al. (2006) compared the BOLD signal changes in so-called same-order and so-called different-order dual-task trials, which were presented in the same blocks of dual-task trials. While in same-order trials the processing order of the two component tasks in a given trial n (e.g., visual then auditory task) was identical to trial $n - 1$, the order of the two component tasks was reversed between trial n and $n - 1$ in different-order trials. According to the

assumption that mechanisms of task order control may rely on the episodic trace of the task order in the previous trial, task order control difficulty was expected to be increased in different-order compared to same-order trials (Luria & Meiran, 2003; De Jong, 1995). As expected, the processing times and the error rates were elevated in different- compared to same-order dual-task trials and, even more importantly, these differences were associated with two activation peaks in the IPFC. These were located in the right MFG and along the left IFS, close to the task order control regions in the IPFC found in the present study. In addition, when using these IPFC activity peaks for an ROI analysis in the present dataset, we found the same dissociation of task order control and task set maintenance effects as for the IPFC regions obtained from the present study (see Results section).

In sum, converging empirical findings and theoretical assumptions from cognitive psychology and neuroimaging research suggest that task order control represents a rather generalized phenomenon, being involved in the serial processing in different types of dual-task situations with different degrees of difficulty.

In addition to the task order control regions in anterior and middle portions of the IFS and in the MFG, we found further IPFC activity in posterior portions of the IFG (MNI coordinates: $x = 50, y = 12, z = 30$) close to the so-called IFJ. This region was found to be associated with certain aspects of dual-task processing in other parametric fMRI studies as well (Jiang, 2004; Herath et al., 2001).

For example, Jiang (2004; see also Jiang et al., 2004) manipulated the temporal overlap (SOA) and the amount of perceptual interference between two visually presented stimuli. In particular, the shape and color stimuli for the two component tasks were presented with short (100 msec) and long (1500 msec) SOAs in a PRP situation. Interestingly, the observed SOA effect in the IFG (MNI coordinates: $x = 48, y = 14, z = 37$) was exclusively found for conditions with both stimuli presented in the periphery of a circular display, thus requiring the simultaneous allocation of attention in space. Accordingly, Jiang concluded that this region is related to the resolution of perceptual interference rather than to the resolution of cognitive (i.e., bottleneck) interference in dual tasks.

However, specific perceptual interference might not be the only factor associated with IFG activation in dual tasks. For example, Herath et al. (2001) found a similar activation focus (MNI coordinates: $x = 46, y = 5, z = 29$) when comparing BOLD signal changes between SOA conditions with different perceptual modalities. In that study, participants performed two simple manual reaction tasks employing the presentation of a visual and a somatosensory stimulus in short succession. The finding of an SOA-related activation in the right IFG in that study excludes the possibility that exclusively perceptual

interference resolution is related to the right posterior IFG region. In addition, it is not very likely that interference at a cognitive level is associated with the IFG activity in that study either, as it has been argued previously that simple detection tasks do not require response selection and, therefore, do not interfere at a cognitive level of processing (Schubert, 1999). Consequently, Herath et al. associated this region with the processing of interference at a motor level.

In the present study, we found posterior IFG activity in the comparison of random-order and fixed-order dual-task blocks that were matched regarding perceptual and motor interference. Instead, the two types of blocks differed specifically with respect to the control of cognitive interference involved in dual-task processing (Sigman & Dehaene, 2006; Luria & Meiran, 2003). Thus, the findings of these three studies suggest that control mechanisms for interference at various levels (e.g., perceptual, motor, and/or cognitive) may be associated with the neural substrate in the right posterior IFG.

The conclusion about the role of the IPFC in task order control in dual tasks is consistent with the idea that the IPFC exerts cognitive control in interference situations by biasing task processing in posterior task-relevant regions (Hopfinger, Buonocore, & Mangun, 2000; Miller, 2000). In dual-task situations, the regulation of the processing order of two task streams may result from biasing signals of the IPFC to posterior brain regions associated with the processing of the component tasks. These biasing signals may cause the fast and alternating activation or suppression of neural processing in posterior brain regions associated with Task 1 and Task 2, which results in the serial scheduling of the competing processes in two tasks. Note that a similar neural mechanism had recently been shown for interference processing in situations requiring the sequential (i.e., not simultaneous) processing of two different tasks (Yeung, Nystrom, Aronson, & Cohen, 2006; Egner & Hirsch, 2005). Future studies employing effective connectivity measures in combination with the present operationalization of task order control may further elucidate these top-down mechanisms for dual-task situations.

Such a connectivity approach might also shed further light on the specific contribution of the parietal cortex to the mechanisms of task order control. The finding of parietal activity along the horizontal segment of the IPS and in the left precuneus converges with findings of other studies suggesting a role of the parietal cortex in the spatial coordination and control of motor sequences (Schubert, von Cramon, Niendorf, Pollmann, & Bublak, 1998; Andersen, Essick, & Siegel, 1987; see Culham & Kanwisher, 2001 for a comprehensive review). As participants had to switch between left-right and right-left response sequences in random-order blocks but not in fixed-order blocks, this may be a plausible account for the parietal activity changes. However, a further specification of the interactions of these parietal regions with

the IPFC during dual-task processing would be of great importance for the understanding of the neural dynamics during dual-task processing.

Task Set Maintenance

Localization of Task Set Maintenance

The assumption that task order control represents a dissociable dual-task mechanism in the IPFC is strongly supported by the finding that the manipulation of task set maintenance (set size) did not affect the activity changes in IPFC regions except for the anterior insular cortex.

With respect to this lack of set size effects in the dorsal regions of the IPFC, one might argue that the present set size manipulation was probably not strong enough to elicit activity changes in the IPFC. However, in our view, this seems not to be a plausible assumption because a number of additional findings show the reliability of the lack of set size effects in the IPFC. First, the findings of the ROI analyses indicated an almost identical size of the parameter estimates for the set-4 and the set-8 conditions in IPFC regions sensitive for task order control. Note that an ROI analysis allows testing for the emergence of set size effects with a more relaxed criterion of statistical significance than the whole-brain analysis because only two *t* tests are conducted across the aggregated parameter estimates of prespecified voxels of interest. Second, in order to test the potential emergence of set size-related activity changes under conditions of stronger behavioral set size effects, we assessed the IPFC activity changes for those participants exposing the strongest set size effects in the behavioral measures (i.e., RTs). However, even when analyzing the fMRI signals for these specific participants, we could not detect any reliable activity changes in those IPFC regions that were relevant for task order control. Of course, we cannot exclude the possibility that a far stronger set size manipulation might evoke activity changes in dorsal parts of the IPFC (see Schumacher et al., 2003). However, in that case, set size might cause dorsal IPFC activity because of the recruitment of additional strategic mnemonic processes to deal with supracapacity memory load (Rypma, Berger, & D'Esposito, 2002).

Finally, we point out that the present manipulation of set size did affect the neural processing in certain regions of the IPFC (i.e., the anterior insular cortex), as well as in regions of the premotor cortex outside the IPFC. Accordingly, the present type of set size manipulation was strong enough to elicit significant activity changes in certain cortical brain regions which are dissociable from regions relevant for task order control. Thus, we are confident that lateral premotor and anterior insular regions, but not regions in the dorsal IPFC, are relevant for task set maintenance during dual-task processing in the present study.

The finding of lateral premotor activity for task set maintenance is consistent with the functional significance of this region in the mapping of arbitrary sensorimotor associations (Kurata, Tsuji, Naraki, Seino, & Abe, 2000; Wise & Murray, 2000) and attentional and motor preparation (Simon et al., 2002; Di Pellegrino & Wise, 1993). Picard and Strick (2001) showed in their review paper that the caudal part of the PMd is associated with movement-related tasks, whereas the rostral PMd has rather cognitive functions that are associated with attentional preparation. Accordingly, the finding of activity associated with task set maintenance in the caudal PMd may reflect task demands when participants maintain a number of task-relevant motor responses in an active state. In contrast, the rostral PMd activity associated with task order control seems to be related to rather attentional aspects of task preparation which is especially required when participants need to arrange and rearrange a specific order of motor responses.

Critically, there is one open issue concerning the present effects of task set maintenance which needs to be discussed in more detail. This issue concerns the question to what extent the location of regions related to task set maintenance is determined by the specific type of set size manipulation applied. In the present study, we varied the number of S–R mappings to be maintained by increasing the number of motor responses relevant for the single component tasks. At the same time, we kept constant the stimulus probabilities between the set-4 and set-8 blocks (Casey et al., 2001).

Importantly, a large number of neuroimaging studies that found set size effects in the LPFC used classical working memory paradigms and manipulated the number of sensory items to be maintained during a delay period (see Introduction section; Zarahn et al., 1999; Goldman-Rakic, 1987; Fuster & Alexander, 1971). Consistent with these studies, Schumacher et al. (2003) also found increased activity in the middle portion of the left MFG when manipulating the number of S–R mapping rules by manipulating the number of relevant sensory stimuli in simple choice reaction tasks (Experiment 2). In contrast, Cavina-Pratesi et al. (2006) compared activity changes for choice reaction tasks with two motor responses with simple reaction tasks with only one response, keeping the stimulus probabilities constant across conditions. In this fMRI study, no LPFC activity was found at all and the only lateral frontal activity peak was located in dorsal premotor cortex. This is consistent with our results as we also kept constant the stimulus probabilities across set size conditions and manipulated the number of motor responses.

Accordingly, the issue whether set size is manipulated either by varying the number of motor responses (Cavina-Pratesi et al., 2006) or by manipulating the number of sensory items (Schumacher et al., 2003) seems to be decisive for the specific localization of set size effects in neuroimaging studies.

Active Maintenance or Automatic Retrieval?

A further important issue which needs consideration is the question to which extent the observed set size effects are related to the active maintenance of task set components in working memory. Alternatively, one may argue that the respective S–R rules are not maintained in an active working memory state but that the RT performance of participants is controlled by the direct retrieval of proceduralized S–R rules from long-term memory. Such retrieval of S–R rules from long-term memory may result from extended practice of the arbitrary S–R mappings, resulting in an automatized retrieval of the motor response upon the presentation of the corresponding stimulus (Frith & Done, 1986).

However, several observations contradict the assumption of an automatic retrieval of the relevant S–R information from long-term memory in the present study. First, we found reliable behavioral effects of the set size manipulation on the RT and error data in this experiment. These behavioral set size effects certainly imply that decisional processes were actually operating during the processing of the choice RT tasks which vary with the number of response alternatives (Hick, 1952). Most working memory models (Cowan, 1999; Baddeley, 1998) would agree that decisional processes are drawing on working memory resources (e.g., require working memory processing capacity). In addition, Mowbray and Rhoades (1959; see also Seibel, 1963) showed that participants needed more than 3000 trial repetitions to develop S–R representations which can be retrieved directly from long-term memory as indicated by the disappearance of the numerosity effect on choice RTs. However, this amount of practice is far more than in the present study, where participants performed 324 trial repetitions per S–R rule including the training session. Moreover, recent studies have shown that after an amount of practice similar to that in the present study, the processing of a choice RT task still interferes with the processing of another capacity-demanding working memory task (Liefoghe, Vandierendonck, Muylaert, Verbruggen, & Vanneste, 2005; Szmalec, Vandierendonck, & Kemps, 2005).

Therefore, the assumption of an automatic retrieval of the S–R rules from long-term memory seems not to be a plausible account to explain the observed pattern of regions related to task set maintenance. On the contrary, we suggest that the observed set size effects originate from the demands to actively maintain the task set components in working memory, which vary in numerosity between the different conditions.

Conjunction Effects

In addition to the dissociable regions related to task order control and to task set maintenance, we also found overlapping regions for both functions in the

lateral premotor cortex. These conjunction regions were located at the transition between regions for task order control and task set maintenance, respectively. According to Sarter et al. (1996), such an overlap may suggest (a) a common cognitive process that serves both functions, (b) a common neural substrate that serves both functions based, however, on distinct neural transformation processes, or (c) a diffuse localization of the two functions at a granular level, only dissociable at a more fine-grained spatial resolution. The present findings suggest at least that the first alternative is not very likely because the behavioral data showed additive effects of the present task order and set size manipulations on RT and error data. According to the additive factor method (Sternberg, 1969), additive effects are predicted when two factors affect separate cognitive processes. Therefore, the present behavioral data are consistent with the assumption that the task order and the set size manipulations affected different cognitive processes. However, one must be cautious with that conclusion because inferences based on the logic of the additive factor method are necessarily true for the reversed type of inferences only (see Prinz, 1972). In any case, the present findings do not suggest that a process common to both functions is associated with the overlapping regions in the lateral premotor cortex. In our view, a conclusive interpretation of the observed conjunction regions in terms of multifunctionality (b) or of a diffuse localization of two functions (c) requires additional support by higher resolved magnetic resonance techniques.

Conclusions

The present study addressed the question of the functional relevance of the LPFC for the simultaneous processing of two task streams. We investigated BOLD signal changes in the LPFC for two cognitive functions commonly associated with dual-task performance: task order control and task set maintenance. We showed that a fronto-parietal network is associated with the control of the processing order of two tasks and that there is only little overlap with regions sensitive to increased demands on task set maintenance during dual-task processing. These results support the conclusion that not all types of cognitive control mechanisms are located in overlapping regions within the LPFC (see also Hester, Murphy, & Garavan, 2004). Instead, we showed that the specific localization of different cognitive control mechanisms can be distinguished using appropriate experimental designs.

Acknowledgments

This work is part of the PhD of C. S. and was supervised by T. S. The work was supported by a grant of the DFG (Deutsche Forschungsgemeinschaft) to T. S. and by a grant of the Sonnenfeld-Stiftung to C. S. We thank André Szameitat for help-

ful discussions concerning the design of the experiment, Rainer Kniesche and Ingo Graul for technical assistance, Raymond A. Mar for proofreading the English, and two anonymous reviewers for helpful comments on earlier versions of this manuscript.

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Notes

- Note that our pilot studies indicated that the overall distribution of Task 2 response times was positively skewed with a mean of 1139 msec and a range up to 2768 msec including error trials in the first session. Thus, a response maximum of 2250 msec in the scanner session with a corresponding ITI of 1250 msec ensured that most participants could successfully perform the rather difficult random-order dual tasks in the majority of the trials.
- Set size effects in the error rates did not differ significantly between the two groups [$t(11) = -1.08, p = .304$]. However, participants with larger RT differences had also numerically increased set size effects in the error rates (5.56% vs. 2.68%, respectively).

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