The neural implementation of task rule activation in the task-cuing paradigm: An event-related fMRI study

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ABSTRACT

To isolate the neural correlates for task rule activation from those related to general task preparation, the effect of a cue explicitly specifying the S–R correspondences (rule-cue) was contrasted with the effects of a cue specifying only the task to performed (task-cue). While the task-cue provides merely information about the type of task, the rule-cue is explicit about both the task type and the task rule (i.e., the set of S–R correspondences). The rule-cue was expected to activate the task rule more efficiently in the preparation period (prior to target presentation); by contrast, in the task-cue condition, part of the task rule activation was expected to be postponed into the task execution period (following the presentation of the target). In an event-related fMRI experiment, we found the right anterior and middle parts of the middle frontal and superior frontal gyri, the right inferior frontal junction, the pre-SMA, as well as the right superior and inferior parietal lobes to show larger activation elicited by the rule-cue than by the task-cue prior to target presentation. Conversely, the results revealed larger activations in these regions in the task-cue than in the rule-cue condition during the task execution period. In summary, this study identified some of the neural correlates of task rule activation and showed that these are a subset of the general task preparation network.

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Introduction

The ability to flexibly activate appropriate task rules in situations with changing task contexts represents an important prerequisite for successful goal-directed behavior. According to Miller and Cohen (2001) rule knowledge is processed in the prefrontal working memory and it contains knowledge about the stimuli, the behavioral responses, and the context of the situations in which a particular rule has to be applied. Presumably, the activation of such rule representations is part of a more general mechanism of task preparation (Gollwitzer and Sheeran, 2006; Monsell, 2003; Rubinstein et al., 2001), which includes the prior activation of neural modules necessary for behavior and starts long before the manifestation of the overt behavior (Brass and von Cramon, 2002, 2004; Gruber et al., 2006; Luks et al., 2002; MacDonald et al., 2000; Sohn et al., 2000).

The neural mechanisms of task rule activation in changing task contexts are still not clear, although there are a number of studies that have investigated the neural basis of the broader mechanisms of task preparation. These studies showed cortical regions including the lateral prefrontal cortex (LPFC), the medial frontal cortex (MeFC), pre-

motor regions, and parietal regions to be part of a network that comes into play when participants prepare for an upcoming sensory-motor task. The present study is aimed at investigating whether regions specific to the mechanisms of task rule activation can be found.

To start with, studies concerned with understanding the neural mechanisms of task preparation have often used the task-cuing paradigm in combination with an event-related fMRI design (Brass and von Cramon, 2002, 2004; Gruber et al., 2006; Luks et al., 2002; Sohn et al., 2000). In the task-cuing paradigm, participants are required to rapidly switch between two different tasks, which leads to ongoing changes of the relevant task representations including the corresponding rule knowledge. The current task can either be the same or different to the preceding task, which is referred to as repetition or switch condition, respectively. Prior to the onset of the target, a task-cue is presented that indicates the upcoming task, thus permitting preparation for the task to be performed next and making it possible to temporally dissociate task preparation from task execution (e.g., Meiran, 1996). Using the task-cuing paradigm, participants' performance (reaction times (RT) and switch costs) has been shown to benefit from a prolonged cue-target interval (CTI), which points to their ability for efficient task preparation (Meiran, 2000; Rogers and Monsell, 1995).

Earlier neuroimaging studies investigated preparation-related activity by analyzing the fMRI activity during very long CTIs (e.g., up

to 12.5 s) and, therefore, their findings may have been compromised by memory load confounds (Luks et al., 2002; MacDonald et al., 2000; Sohn et al., 2000); in particular, the cue-related activity in these studies may have been related to the maintenance, rather than to the preparation of the task sets. More recent studies isolated task preparation-related activity by measuring neural activity separately for cue-only trials, cue-target trials, and null-events in the task-cuing paradigm (Brass and von Cramon, 2002, 2004). On cue-only trials, there is no target following the cue; by contrast, on cue-target trials, a target is presented that requires the execution of the task; and null-events represent a baseline condition without any cue and target information. Because participants do not know in advance whether or not a target will follow the cue, they have to prepare for task execution on every type of trial, that is, on both cue-only and cue-target trials (see also Corbetta et al., 2000; Weissman et al., 2005). This allows for measurement of preparation-related activity during the processing of cue-only trials (but see Lavric et al., 2008, for effects of cue-only trials on the degree of task preparation). Brass and von Cramon (2002) contrasted activation on cue-only trial and null-event trials and found a fronto-parietal network to be related to task preparation. In particular, this network included regions in the dorsolateral prefrontal cortex (DLPFC), for example, near the inferior frontal junction point (IFJ), regions surrounding the intraparietal sulcus (IPS), in the dorsal premotor cortex, and in the pre-supplementary motor area (pre-SMA) of the medial frontal gyrus.

Although these findings provided a number of valuable insights into the functional neuroanatomy of task preparation, they are not unequivocal regarding the neural correlates of task rule activation. This is so because a task-cuing paradigm such as that used by Brass and von Cramon (2002) does not permit the mechanisms of activating the specific task rules to be distinguished from rather general task preparation (see also Ruge et al., 2009). The presentation of the cue informed participants about the task they had to perform later upon the presentation of the target. If the time was sufficient and the participants intended to do so, they could either activate the current task rule or, alternatively, they could wait with the activation of the task rule until the presentation of the imperative stimulus. Thus, depending on participants' strategy, either to prepare the task rule early upon the presentation of the cue or only later upon the presentation of the target, the point in time when the task rule was activated was not sufficiently controlled.

For the present study, we used what we refer to as a rule-cue, which differs from the task-cue in earlier neuroimaging studies because it conveys information not only about the task (e.g., classify color), but also about the S–R rule to be applied (e.g. red → press left button, yellow → press right button; see also Logan and Bundesen, 2003). Thus, while a task-cue (the sort of cue used in earlier studies) conveys only general information about which task to perform, the rule-cue provides also specific information about task rules, that is, the stimulus–response (S–R) mapping, on the upcoming trial (task-and-rule information). By administering the rule-cue randomly mixed with task-cues, we aimed to trigger processes related to the activation of the specific task rules during task processing.

In particular, participants were presented with either a color or a gender discrimination task, with the particular task specified by the presentation of a cue before the target stimulus. In the rule-cue condition (Fig. 1, left panel), we displayed the Chinese symbols "颜色" (for color) or "性别" (for gender) to indicate the upcoming task, and also the specific instructions of its S–R mapping rule. For example, if the task was gender discrimination, the symbols "男" (for male) and "女" (for female) were presented above the corresponding response keys (e.g., "male" was shown above the left key and "female" above the right key).

In the task-cue condition, we also used the symbols "颜色" (color) and "性别" (gender) to indicate the next task, whereas there was no specific information about the task rule (see Fig. 2). Instead, only non-informative words "按 键" (press key) were presented below the task-cues, in order to make the cue display similar to that in the rule-cue condition.

Similar to Brass and von Cramon (2002), we presented cue-only trials (Fig. 1, right panel), null-events, and cue-target trials (Fig. 1, left panel). While an analysis of the cue-only trials allows for detection of preparation-related activation that is elicited by the cues (rule-cues and, respectively, task-cues), target-related processes are revealed by contrasting activity between cue-target and cue-only trials (e.g., Brass and von Cramon, 2002; Weissman et al., 2005). Because the activation on cue-target trials consists of activation related to cue- and to target-processing, subtracting the cue-related activation from the activation on cue-target trials will leave the target-related activation only.

The distinction between rule-cues and task-cues permits rule-related neural activity to be analyzed in the following manner. First of all, we expected a significant performance benefit from the presentation of rule-cues compared to task-cues and we expected rule-cues to evoke stronger cue-related activation than task-cues, specifically on cue-only trials. The reason for the latter hypothesis is that, in the rule-cue condition, the cue provides explicit rule information and this information may be activated by the cue presentation. In contrast, in the task-cue condition, participants may postpone at least part of the rule activation processes until later, for example, up to the time where the target is expected to appear. And even if activation of the rule is not postponed, it may be less effective because the cue provides no explicit information as to the precise task rule. Consequently, rule-related activation should be manifest during the preparation period on cue-only trials in terms of an increased amount of activity in the rule-cue, compared to the task-cue, condition.

The converse pattern (of activation in rule-cue and task-cue conditions) may be expected when considering the rule-related activation that emerges after target presentation on cue-target trials, that is, during task execution. It is reasonable to assume that, if participants failed to activate the (complete) task rule right upon cue presentation, they must activate the necessary S–R mapping rule following target presentation (Gruber et al., 2006). This would be consistent with Gruber et al. (2006) who analyzed the neural activity under conditions of short versus long cue-target intervals (CTIs) in a task-cuing paradigm. While the time for preparing the upcoming task was sufficient after cue presentation with long CTIs, it was insufficient with short CTIs. The latter led to the postponement of (at least parts of) the preparation processes until after target presentation, as indicated by an increased amount of neural activity in preparation-related brain regions under conditions of short compared to long CTIs (Gruber et al., 2006; see also Brass and von Cramon, 2002). In analogy to these findings, we expected postponed rule activation in the task-cue condition compared to the rule-cue condition. This should lead to greater activation in rule-related brain regions under task-cue, compared to the rule-cue, conditions upon target presentation on cue-target trials.

In summary, we expected stronger neural activity related to task rule activation in the rule-cue compared to the task-cue condition during the preparation period, and stronger activity in rule activation-related regions during task execution in the task-cue compared to the rule-cue condition. The common neural substrate in these two comparisons thus represents those brain regions that are important for the process of task rule activation in either the task preparation or the task execution period; this should be revealed by means of a conjunction analysis of the corresponding contrasts.

Method

Fifteen right-handed, healthy students of Peking University (recruited by advertisement in the campus Bulletin Board System)

Cue-target trial

Cue-only trial

Cue : 1200 ms

性别

Target: 600 ms

性别

Time interval:
1000 - 1800ms

time

性别(Gender)

男(male)   女 (female)

Cue : 1200 ms

性别

No target: 600 ms

Time interval:
1000 - 1800ms

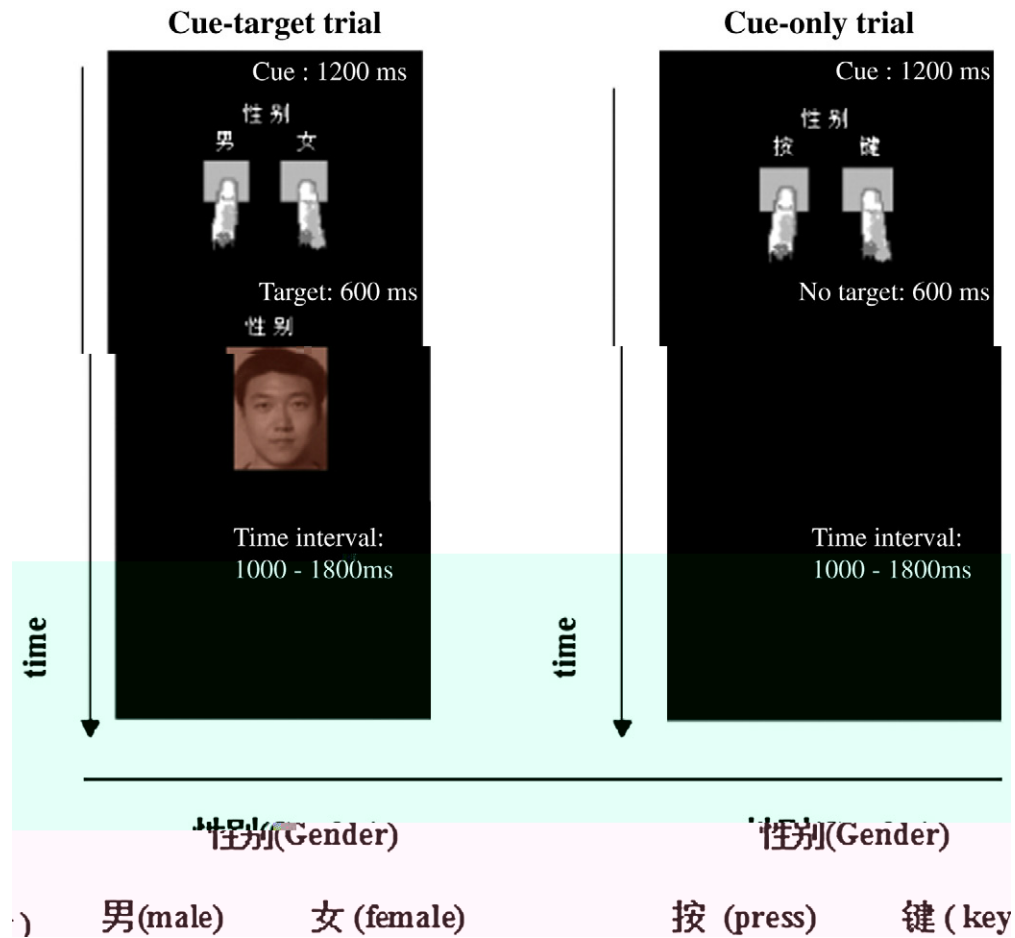time

性别(Gender)

按 (press)   键 (key

Fig. 1. Illustration of the task situation. Upper part: Left panel shows a cue-target trial (example for the gender discrimination task). Right panel shows a cue-only trial (example for gender discrimination task). The lower part of the figure represents the cue displays and their English translation. The cue could either be a rule-cue (left) or a task-cue (right) (for details see Fig. 2).
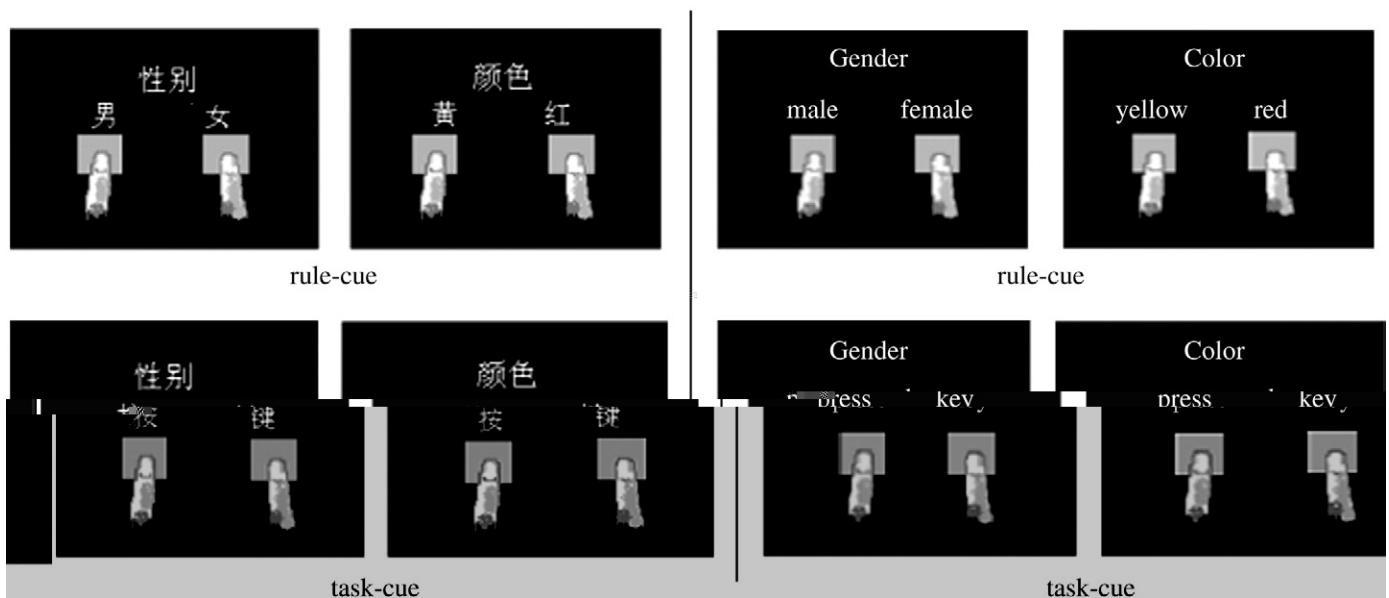
性别
男   女

颜色
黄   红

rule-cue

Gender
male   female

Color
yellow   red

rule-cue

性别
按   键

颜色
按   键

task-cue

Gender
press   key

Color
press   key

task-cue

Fig. 2. Illustration of the rule-cue and task-cue displays (left panel) and their English translation (right panel). In the rule-cue and the task-cue conditions, the current task was indicated by the words "颜色" (color) and "性别" (gender), respectively. In the rule-cue condition (upper row), additional information indicated the assignments of the response keys to the stimulus categories male and female in the gender task and yellow and red in the color task.

participated in the study. Six participants were female; participants' ages ranged between 20 and 26 years, and all had normal or corrected-to-normal vision. Prior the fMRI scanning session, they gave informed consent about the investigation according to the Helsinki guidelines and the approval of the Academic Committee of the Department of Psychology, Peking University. Participants were paid 50 yuan (about EUR 5) for their service.

One participant's response error rate was more than 20%. Hence this participant's behavioral and fMRI data were removed from the data set. There was also a loss of the behavioral data from one participant, due to data recording error. Thus, ultimately, 14 participants' image data sets and thirteen participants' behavioral data sets were available for analysis.

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The task to be performed by the participants was either color discrimination or gender discrimination. Each trial began with the presentation of a cue for a fixed duration of 1200 ms, which could either be a rule-cue or a task-cue (Fig. 1). Both cues displayed an instruction for the upcoming task; however, a precise instruction about the required task rule was provided only in the rule-cue condition (for more details, see Fig. 2). On cue-only trials (= 160 trials, of which 80 presented a rule-cue and 80 a task-cue), there was no target following the cue offset, but only a black screen that lasted for 600 ms, and there was no need for participants to make a response (Fig. 1, right panel).

In contrast, on cue-target trials (= 280, of which 140 presented a rule-cue and 140 a task-cue), the cue was followed by a colored face picture that was presented for 600 ms; during this period, the task-cue instruction remained visible on the screen (above the target picture) by presenting the words 'gender' or 'color', so as to reduce participants' working memory load for maintaining the task goal in the two conditions. Importantly, the information presented during the execution period concerned only the task information and not the rule information because the symbols 'press key' and the symbols illustrating the rule information were not presented during the execution period (see Fig. 1, left panel). Participants were to respond to either the color or the gender of the face depicted in the target display, depending on the instruction of cue. Participants made two-alternative forced-choice responses using either their left or right thumbs, with response sets counterbalanced across participants. After the offset of the target picture, a black screen was presented for a variable interval of 1000, 1200, 1400, 1600, or 1800 ms. The next trial could then either be a cue-target or a cue-only trial, that is an 'event trial', or a 'null trial' (= 110) in which there was neither a cue nor a target event. Together with the duration of the null trials, which were of the same duration as the task trials, the interval between two event trials (the interval between the disappearance (offset) of the target in the present trial and the appearance (onset) of the next cue) resulted in 2200 ms on average.

The present study used a 2 × 2 event-related fMRI design. The first factor was cue type: the cue could be either a rule-cue or a task-cue (Figs. 1 and 2). The second factor was task transition: the task was either repeated or switched relative to the preceding trial. Based on the instruction cue presented prior to the target, participants were required to distinguish either the color or the gender of the face pictures. If the current task was different from the preceding one, the current trial was classified as a switch trial; if the current task was identical with the previous one, the current trial was classified as a repetition trial. This factor was examined because rule activation (or retrieval) was hypothesized to differ between task repetition trials and switch trials (Mayr and Kliegl, 2000; Rogers and Monsell, 1995; Monsell, 2003; Rubinstein

et al., 2001). That is, this factor was introduced to examine whether or not preparation for a switched, compared to a repeated, task leads to a modulation of the task rule activation.

Each one of the four conditions (rule / task-cue × task switch / repetition) consisted of 40 cue-only trials and 70 cue-target trials. In sum, there were 440 event trials, the order of which was unpredictable for the participants. In addition, the event trials were randomly intermixed with 110 null trials in which only a black screen was shown. The length of a null trial varied from 2800 ms to 3600 ms, which was similar to the length of the other (task) trials.

For each condition, the cue-related activation can be assessed by measuring the activation on the cue-only trials, whereas target-related activation can be assessed by calculating the contrast between the activation in corresponding cue-target minus cue-only trials.

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On cue-only trials, only a black screen (i.e., no target) was presented after the presentation of the cue and there was need to respond. On cue-target trials, the target stimulus was a colored face picture. In order to create colored face pictures we merged each one of the original black–white face pictures (two males and two females) with same-sized, faded red rectangles (RGB 187- 124-106) and yellow rectangles (RGB 179- 155- 111) with Photoshop software. As a result eight colored face pictures were created, which we used as target stimuli: two yellow male faces, two red male faces, two yellow female faces, and two red female faces (with the same face presented in either red or yellow on different trials). Participants were informed by the cue to respond to either the color or the gender of the face. The stimuli (cue and target stimuli) were located on a black background in the center of the screen and subtended 5 degrees of visual angle.

Participants used their left and right thumbs for response. They were instructed to respond as fast and as accurately as possible. For half the participants, the S–R mapping rule was male-left, female-right and yellow-left, red-right. This was reversed for the other half: female-left, male-right and red-left, yellow-right.

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Imaging was performed with a SIEMENS TRIO 3-Tesla scanner at the Beijing MRI Center for Brain Research. T2*-weighted echo-planar images (EPI) with blood oxygenation level-dependent contrast were acquired (TR = 1500 ms, TE = 30 ms, flip angle = 90°, voxel size = 3.4 × 3.4 × 5 mm^3

Then the image data were modeled by applying a general linear model (Friston et al., 1995). In event-related single-subject analyses, the four cue-only and the four cue-target conditions were modeled as separate volumes (resulting from the factorial combination of the two cue type (rule-cue vs. task-cue) and the types of task transition (task switch vs. task repetition). Additionally, all error trials were selected to form an error trial volume. The resulting nine volumes were convolved with the hemodynamic response function (HRF), and then beta values of these regressors were estimated according to the ordinary least-squares (OLS) method.

For group statistics, one-sample -tests of contrast maps across subjects (random-effects model treating subjects as a random variable) were computed to indicate whether observed differences between conditions were significantly different from zero.

In particular, two main contrasts were calculated: Contrast 1: For cue-only trials, rule-cue minus task-cue trials, intended to isolate extra activation for a rule-cue. Contrast 2: (cue-target trials minus cue-only trials for task-cues) minus (cue-target trials minus cue-only trials for rule-cues), intended to isolate the extra activation related to the target-processing when the cue did not specify the rule. In a subsequent conjunction analysis, SPM5 (Nichols et al., 2005) was used to locate the common task rule-related activation between these two main contrasts. Only those voxels were reported as active which proved to be significant for both contrasts, Contrast 1 AND Contrast 2; that is we tested for a rejection of the conjunction null hypothesis: voxel (not activated in Contrast 1) OR (not activated in Contrast 2).

The way in which the remaining statistical contrasts were calculated is detailed in the Results section. Unless stated otherwise, for one-sample t-tests, we used a statistical threshold of $p < 0.001$, uncorrected, covering at least 10 contiguous voxels. This threshold was commonly used in the studies of rule-related processing and cue-related processing (e g., see Bunge et al., 2003; Crone et al., 2006a,b; Gruber et al., 2006; Wendelken et al., 2008). We also checked all reported activation foci with a small volume correction procedure (10 mm sphere centered at the voxel with local maximum activation). If not otherwise noted, then the reported foci prove significant at a threshold of $p < 0.05$ (small volume corrected on both the voxel and the cluster level). For the conjunction analysis, the statistical threshold was $p < 0.005$, uncorrected, again spanning at least 10 contiguous voxels.

Results

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Fig. 3 presents group means of the RTs (left panel) and error rates (right panel) as a function of task transition, for the two types of cue. Mean RTs and error rates were submitted to a 2×2 repeated-measures ANOVA with the factors task transition and cue

type. RTs were significantly faster in the rule-cue than in the task-cue condition (main effect of cue type, $F(1,12) = 6.71$, $p < 0.05$), which indicates that participants effectively utilized the rule-cue information during the preparation period following cue presentation. The RT advantage for rule-cue compared to the task-cue presentation (i.e., the 'behavioral rule-cue effect') was 17 ms. In addition, RTs were significantly slower for task switch than for task repetition trials (main effect of task transition, $F(1,12) = 12.96$, $p < 0.005$), with switch costs amounting to 25 ms. With mean switch costs of 24 and 27 ms in rule-cue and task-cues conditions, respectively, the interaction effect between cue type and task transition was not significant ($F(1,12) = 0.11$, $p > 0.7$).

The error rate ANOVA revealed a significant main effect of task transition ($F(1,12) = 60.91$, $p < 0.0001$): more errors were made on task switch than on task repetition trials. Additionally, a significant interaction between cue type and task transition was obtained ($F(1,12) = 8.84$, $p < 0.05$). Further analyses with separate t-tests revealed elevated error rates in switch compared to repetition trials in the rule-cue and task-cue conditions (both t's(12)>4.00, both p's<0.005), and larger switch costs (error rate switch–error rate repetition) in the task-cue (error rate = 6.6 %) compared to the rule-cue condition (error rate = 3.8 %) ($t(12) = 2.97$, $p < 0.05$). Thus, as with the RT data, the error data indicated that participants' performance benefited from the presentation of the rule-cue as compared to the task-cue. This benefit was especially pronounced in conditions in which participants had to switch between the tasks as revealed by the increased error rate in the switch compared to the repetition condition.

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To identify the cue-related activation, we calculated the main effect for the cue-only trials separately for the rule-cue and task-cue conditions by fitting the empirical fMRI data to the hemodynamic response function (HRF) described above. The resulting beta values are presented in Fig. 4. Both the presentation of rule-cues and of task-cues elicited neural activations in a large cortical network, with foci in the MeFC, bilateral regions of the LPFC near the IFJ, and the dorsal and the lateral premotor cortex. Additionally, the medial and lateral parietal lobe, the posterior cingulate cortex (PCC), and the thalamus showed significant activation. Finally, there was bilateral activation in the occipital cortex. In addition to these activation foci which were similar for the two types of cue, two small clusters were activated by the rule-cue in the right and left anterior prefrontal cortex (aPFC). Note that, with a more liberal statistical threshold of $p < .005$, these two clusters also showed activation under task-cue conditions.

In summary, the two types of cue activated highly overlapping brain networks, that is, the preparation processes associated with rule-cues and task-cues are mediated by similar brain regions.
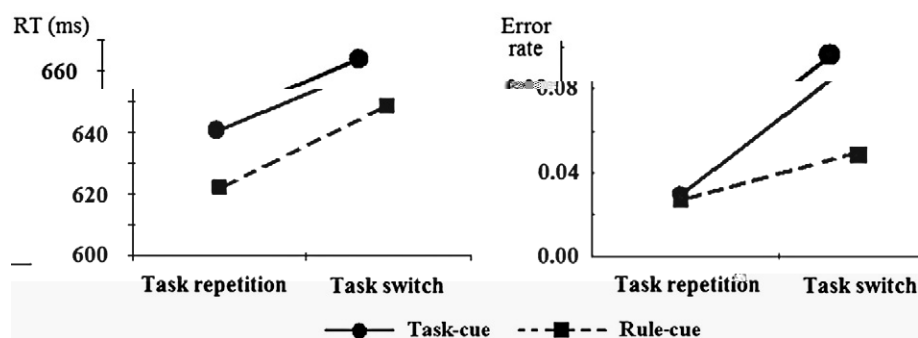
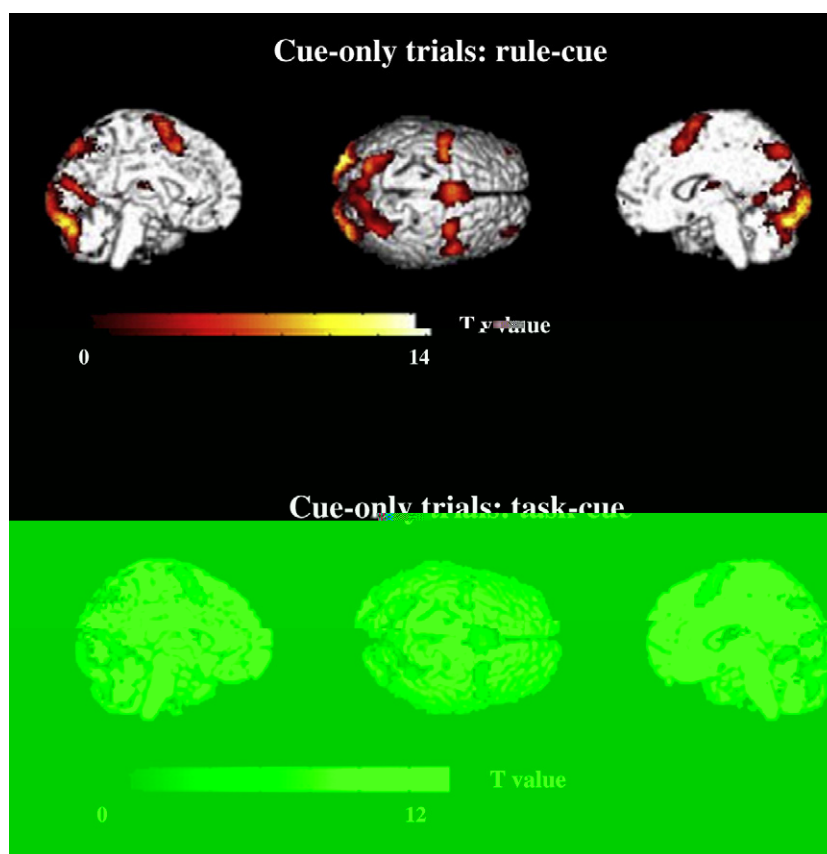**Fig. 3.** Reaction time (RT) and error rates as function of task transition and cue type.

Fig. 4. Illustration of the brain activation elicited by the presentation of the cue in cue-only trials in the rule-cue condition (top) and in the task-cue condition (below). The resulting cue-related activation across the two cue conditions is associated with the general mechanism of task preparation.

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As outlined in the Introduction, we expected stronger activation on rule-cue compared to task-cue trials during the preparation period, and, additionally, we assumed these regions to be associated with task rule activation. To examine for this, we calculated a whole-brain contrast of the activation in the rule-cue versus the task-cue condition specifically for cue-only trials. The results of this analysis are presented in Fig. 5 and Table 1.

Stronger activation was found for the rule-cue compared to the task-cue condition in the anterior part of the superior frontal gyrus (SFG), that is, the right aPFC, bilaterally in the premotor cortex, and in regions of the MedFC; the latter regions extended from anterior portions in the pre-SMA to posterior portions of the pre-SMA/SMA region. In addition, we found increased activation in the right superior parietal lobe (SPL) and the left precuneus. Finally, activation foci were found bilaterally in the occipital cortex (e.g., in the lingual gyrus and the fusiform gyrus) (see Fig. 5a and Table 1).

During task execution on cue-target trials, we expected stronger activation in the task-cue, compared to the rule-cue, condition in cortical regions that are associated with the activation of the task rules; this is because of the expected postponement of the rule activation under task-cue conditions. To determine the corresponding activation foci, we contrasted the target-related activation during the execution period in the task-cue and rule-cue conditions. For this purpose, we calculated the contrast: cue-target–cue-only trials separately for the task-cue and rule-cue conditions, so as to derive the corresponding task execution-related activations in both types of trial. Subsequently, we calculated the second-order contrast, task-cue (cue-target minus cue-only trials)–rule-cue (cue-target minus cue-only trials), to compare the target-related activation between the task-cue and rule-cue conditions.

This analysis revealed stronger target-related activity in the task-cue compared to the rule-cue condition in most regions that had proved to be rule-related during the preparation period in the above analysis (see Cue-related activation section). In particular, these regions were the right anterior part of the SFG (i.e., aPFC), the right pre-motor cortex, the MeFC (i.e., pre-SMA), the right SPL, and the bilateral lingual and fusiform gyri. In addition to these regions, activity was found in the LPFC, with peak activation in the right posterior MFG that extended into the IFJ (see Fig. 5b and Table 1).

Subsequently, we performed a conjunction analysis in order to identify the regions commonly associated with task rule activation during the preparation and the execution period (see Fig. 5c and Table 2). This analysis was calculated across the contrasts rule-cue minus task-cue of the cue-related activation in the preparation period, and task-cue minus rule-cue of the target-related activation in the execution period (see the two analyses above).

This analysis revealed common activation foci in the right LPFC extending from anterior to posterior portions of the LPFC regions near the IFJ and in anterior and more posterior medial regions of the SFG (pre-SMA/SMA) and the MeFG. Furthermore, the two contrasts exhibited common activity in the right SPL extending into inferior parts of the parietal cortex (IPL), as well as common activation foci in the bilateral lingual gyrus (see Fig. 5c and Table 2). Note that there are some regions that showed activation in the conjunction analysis but not in both of the two single contrasts (. <0.001, for clusters of 10 contiguous voxels); e.g., the right inferior frontal junction (Fig. 5a), and the middle part of the dorsolateral prefrontal cortex (Figs. 5a and b). However, these regions showed significant activation foci in the two single contrasts of 5a and 5b, when using a more liberal threshold of . <0.005.

We propose that these regions, which proved to be activated in the conjunction analysis, are associated with processes of task rule
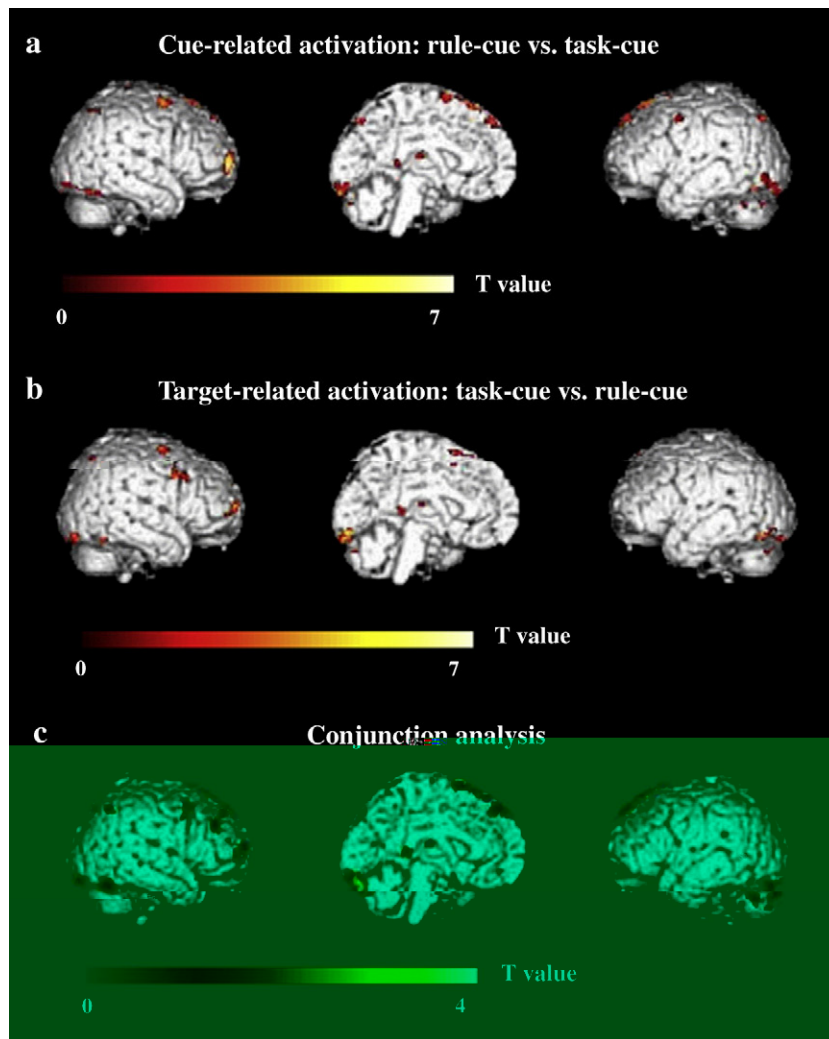
Fig. 5. Cortical activation associated with rule activation in the task-cuing paradigm. (a) Significant activation in the comparison of rule-cue versus task-cue for cue-only trials. (b) Brain regions which show increased target-related activation in the comparison of task-cue versus rule-cue trials (for details see text). Note that target-related activation is observed when contrasting activation in cue-target minus cue-only trials. (c) The brain regions which are observed in the conjunction analysis across the contrasts illustrated in a and b. In the conjunction analysis, we used a criterion of <0.005. Note that there are some regions that showed activation in c but not in a or b (thresholded with <0.001, for clusters of ten contiguous voxels); e.g. the right inferior frontal junction (a), and the middle part of the dorsolateral prefrontal cortex (a and b). However, these regions showed significant activation in the single contrasts of a and b, when using a more liberal threshold of <0.005. For further details, see Tables 1 and 2.

activation either during the preparation period or later, during the execution period subsequent to target presentation.

Although the aim of the present study was to understand the neural correlates of task rule activation, the adopted paradigm allows us also to investigate the processes genuine to task-switching situations in which participants alternate between different task rules. Therefore, we also examined whether the rule activation in the preparation period is modulated by the need to prepare for a task switch, compared to a repetition. For this analysis, the switch-related activity on cue-only trials (collapsed across cue types) was examined by calculating the contrast: cue-only (switch–repetition). This contrast revealed cortical activation to be increased only in the medial SFG (pre-SMA) for the preparation for a task switch versus a repetition, as is illustrated in Fig. 6. In an additional ROI analysis, we aimed to test whether the need to process a rule-cue or a task-cue leads to any additional modulations of the neural activity in this switch-related region during the preparation period. In order to decrease the second-order error of overlooking a

possible modulation effect of the switch-related activity, we selected an ROI that depended on the particular switch-repetition contrast; according to Kriegeskorte et al. (2009), this way of ROI selection increases the probability of finding any effects related to the depending contrast (i.e., in the present case, the switch-repetition contrast). In more detail, we defined an ROI consisting of 11 active voxels surrounding the local-peak voxel in the contrast: cue-only (switch–repetition), and for this ROI, we extracted the beta values individually for each participant in the rule-cue and task-cue conditions dependent on the task transition (switch vs. repetition). The data are presented in Fig. 6. A 2×2 repeated-measures ANOVA of the beta values revealed significant main effects of the factors task transition ($F(1,13) = 5.07$, <0.05) and cue type ($F(1,13) = 17.82$, <0.001), but no significant interaction ($F(1,13) < 1$). The non-significance of the interaction means that the need to prepare for a task switch (compared to a less demanding task repetition) affects the activation in the medial SFG on cue-only trials to the same degree in the rule-cue and the task-cue condition. In other words, the need to process a rule-cue or a task-cue does not modulate the switch-related activation in the medial SFG during the preparation period.

Discussion

The present study investigated the functional neuroanatomy of task rule activation as a component process of general task preparation. In order to modulate the degree of task rule activation, we adopted the task-cueing paradigm and presented either rule-cues or task-cues to enable participants to prepare for the upcoming task. The rule-cues provided explicit information not only about the type of task to be performed, but also the specific S–R rule to be applied. We expected that, when the task was indicated by a rule-cue, the corresponding task rule should be activated, upon cue presentation, to a higher degree of 'preparedness' compared to when the task was indicated by a task-cue, which (relative to rule-cues) presents only nonspecific information about the type of task to be performed next. This hypothesis was supported by a behavioral performance advantage in terms of both RTs and error rates deriving from the presentation of a rule-cue as compared to a task-cue.

The present paradigm permits task rule-related brain regions to be identified by analyzing the effects of rule-cues and task-cues on brain activity separately for the preparation and execution periods of the task. In the preparation period, rule-activation-related regions should be activated more strongly following the presentation of rule-cues as compared to task-cues. Conversely, for the execution period, rule-related activation would be expected specifically upon target presentation if task rules were not activated sufficiently during the preparation period.

In line with these predictions, the conjunction analysis revealed similar fronto-parietal networks of activation foci in the corresponding contrasts, that is, the contrast of rule-cue minus task-cue for cue-only trials (preparation period) and the contrast comparing target-related activation on task-cue versus rule-cue trials (execution period). The common activation foci in these two contrasts included the anterior and middle parts of the right MFG and SFG, the posterior region of the MFG near the IFJ, regions in the medial SFG extending from anterior to posterior portions of the pre-SMA, as well tocontrgre07(foci)-206(isSPL)-21.3pos-2.863i

suggest that this strongly depends on the amount of explicit task information provided by the cue. If the cue contains information about both the type of task and the specific task rules (and if there is sufficient time until the onset of the target), the level of preparedness for the upcoming task will be superior to conditions in which the cue does not provide any explicit rule information. Restated, even when the time to prepare would be sufficient as such, participants may not retrieve or pre-activate task parameters as fully or completely when presented with a task-cue as when presented with a rule-cue. Rather, a considerable part of the task preparation, in particular, the retrieval and activation of the specific task rule information, appears to be deferred until the presentation of the target.

A recent study by Verbruggen et al. (2007) revealed a pronounced tendency of participants to defer part of the task preparation until target presentation under conditions in which the task-cue remained available (as was the case in the present study), as compared to situations in which the task-cue was removed, during the preparation interval. However, it is unlikely that the reduced amount of task rule activation observed for the task-cue condition compared to the rule-cue condition in the preparation period of the present study was exclusively caused by the persisting cue presentation. The reason is that a strategic delay in task preparation (as a result of the prolonged cue availability) should have led to a reduced level of task rule activation in the rule-cue condition as well as the task-cue condition, especially since participants had to specify the task goal first before they could activate the task rules. Given this, it remains plausible that active task rule retrieval and rule activation were indeed facilitated by the rule-cue (even if it involves a volitional-strategic component to make use of the rule information) and the observed activation changes in rule-related regions are associated with these processes in the present paradigm.

Our interpretation receives support from a recent study by Ruge et al. (2009), which separated task-cue-related preparatory activity from rule-related activity in a way that differed from that in our study. In their study, participants were presented with either task-cue-first or target-stimulus-first trials when performing a task-switching paradigm with an ambiguous stimulus consisting of a digit (odd/even decision) and a letter (vowel/consonant decision). On task-cue-first trials, a cue informed participants about the task to be performed upon the presentation of the target stimulus; this was similar to the task-cue in the present study. On target-stimulus first trials, the presentation of the target stimulus preceded the presentation of the task-cue. When comparing the preparation-related activity in both kinds of trials, Ruge et al. found regions in the lateral PFC, near the IFJ, in medial frontal areas, in pre-motor and in posterior parietal brain areas to be activated more strongly under the target-stimulus-first condition than under the task-cue-first condition. This suggests that the preparation of task set parameters was induced more strongly when the target stimulus information was presented first compared to when the task-cue information was provided first.

The findings of Ruge et al. (2009) and those of our study may be considered as being complementary, in that they reveal different ways of how the cognitive system may flexibly adapt the task preparation to the specific task demands under different conditions of information provided prior to task execution. The findings of Ruge et al.'s may be interpreted by assuming that the presentation of umbiguous target information, rather than of task-cue information, evokes stronger recruitment of preparation-related brain regions because of a relatively unselective preparation of task rule parameters. On the other hand, our findings show that the presentation of task rule information prior to the target stimulus encourages stronger preparation-related activity which, however, leads to a selective and more complete preparation of the specific task parameters of the upcoming task.

The present findings indicate that a major region associated with online task rule activation is the LPFC, which showed significant rule-related activity in anterior, middle, and posterior portions. Earlier studies with single-cell recordings in monkeys (Wallis and Miller, 2003; White and Wise, 1999) or fMRI in humans (Bunge et al., 2003; see also Crone et al., 2006a,b) had already shown an association of the LPFC with the retrieval of task rules from long-term memory. For example, in Bunge et al. (2003), participants learned different rules of how to respond to probe stimuli in a separate learning phase prior to the fMRI scanning session. Similar rules (e.g., press left key if two stimuli match each other) were associated with different types of rule-cue (verbal or symbolic cues). In the fMRI scanning session, participants had to activate the acquired rule knowledge upon presentation of the rule-cues and then, after a delay, process two sequentially presented probe stimuli (same, different). Bunge et al. found ventral regions in the left LPFC to be active during the delay after rule-cue presentation, to be sensitive to the difficulty of the rule, and to be insensitive to the type of rule-cue. Because of the insensitivity of these regions to the type of rule-cue, ventral LPFC regions were assumed to be related to abstract rule knowledge; this was in contrast to regions in the left and right DLPFC which proved to be sensitive to the different types of rule-cue and were, therefore, assumed to be related to the specific rule knowledge.

about the degree of online rule activation in the LPFC because the cues used did not permit distinguishing between general task information and specific rule information.

A recent study of MacDonald et al. (2000) used the Stroop paradigm (color naming of a written (color) word or reading the color word) in combination with a task-cueing manipulation to investigate brain regions associated with task rule processing. In that paradigm, a task-cue specified whether the next upcoming trial required color naming or word reading. Interestingly, the magnitude of cue-related activity increased with the expected difficulty of the next upcoming task: the left LPFC was more strongly activated when the cue indicated to participants that they would have to process the more difficult color naming task, as compared to the word reading task. The present findings extend the results of MacDonald et al., because they show that the degree of activity in a particular LPFC region varies with the amount of the task information provided by the cue about the upcoming task. The more information about the specific task rule is provided by the cue (rule-cue versus task-cue), the stronger the activity during task preparation (i.e. during cue processing). This does not contradict accounts assuming that different types of information provided by external cues may be related to activation in different regions of the LPFC (Koechlin et al., 2003; Koechlin and Summerfield, 2007).

In the present study, a considerable amount of activation was found in posterior regions of the LPFC near the right IFJ. This region had been shown to be associated with mechanisms involved in the 'actualization' of a current task representation (e.g., uploading new task parameters or a new task representation by the bilateral posterior regions of the LPFC) in situations with changing tasks (Brass and von Cramon, 2002, 2004; Derrfuss et al., 2005; Gruber et al., 2006). The present findings are consistent with this, while additionally showing that the degree to which a new task representation is uploaded in advance depends on the specificity of the information provided by the cue. A larger amount of presented task information permits a more complete uploading of the task parameters required on the upcoming trial, and this is accompanied by an increased amount of neural activity in brain areas near the IFJ.

The observed rule-related activation in the right aPFC is consistent with studies suggesting that this region is critical for difficult retrieval processes on both episodic-memory (Della-Maggiore et al., 2002; Nyberg et al., 2000) and working-memory contents (Christoff and Gabrieli, 2000; Leung et al., 2005; MacLeod et al., 1998; Soto et al., 2007). For example, the meta-analysis of MacLeod et al. showed that the right aPFC is activated especially in WM tasks in which a high, rather than a low, number of items has to be maintained in memory. In the present paradigm, the richer rule information provided by the rule-cues may have induced the participants to more strongly activate and retrieve the task-relevant S–R associations from memory, compared to the task-cue condition. This additional effort during task preparation provides a likely explanation for the observation of rule-related activation in the right aPFC in the present study (see also Stern et al., 2007).

Further rule-related activation was found in medial frontal regions and here specifically within the pre-SMA. Single-cell and tracer studies suggest that regions of the pre-SMA receive direct input from the LPFC, while the neural regions in the SMA proper are connected to the motor areas (Picard and Strick, 2001; Tanji, 1994). The specific connections to the LPFC make the pre-SMA most appropriate for the preparation of the specific task rule during sensori-motor performance (Hikosaka et al., 1996). In line with this, several authors have shown the pre-SMA to be involved in the acquisition and control of arbitrary S–R associations in humans (Gordon et al., 1995; Halsband and Freund 1990; Hikosaka

et al., 1996; Picard and Strick, 1996; Sakai et al., 1998, 1999) and monkeys (Halsband and Passingham, 1985; Halsband et al., 1994). In the present study, we found the pre-SMA to be activated in conditions promoting task rule activation as well as conditions of general task preparation. However, the fact that there was additional activation in the pre-SMA in rule-cue compared to task-cue conditions suggests that providing participants with explicit rule information leads to an enhanced preparation of (specific) S–R associations.

The observation of rule-related activation in the parietal cortex is consistent with the assumption that regions along the intraparietal sulcus are involved in the activation of motor representations which are spatially mapped to different sensory stimuli (Andersen, 1987; Caminiti et al., 1996; Schubert et al., 1998; Stein, 1989). A number of neuroimaging studies have revealed parietal activation when participants have to produce motor responses upon the presentation of sensory stimuli in various kinds of behavioral paradigms (Brass and Von Cramon, 2002, 2004; Bunge et al., 2002, 2003; Snyder et al., 1997; Stelzel et al., 2008; Zysset et al., 2006). The present findings additionally suggest that the parietal involvement is modulated by the amount of prior information provided about the motor response that has to be performed upon stimulus presentation: the more information is provided about the S–R rule, the larger the amount of neural computations in parietal areas involved in processing the required S–R association.

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A larger activation was found during the preparation period (cue-only trials) for task switch compared to task repetition conditions in the medial SFG. This extends findings of other studies, pointing to an association of this region with switching between tasks (e.g., Dove et al., 2000; Yeung et al., 2006). It is also consistent with the view that the pre-SMA has an anticipatory role during the intentional reconfiguration of a response set (Rushworth et al., 2002).

A related ROI analysis revealed the observed increase of switch-related (compared to repetitions) activation in the medial SFG region to be similar in the rule-cue and task-cue conditions. Additionally, the ROI analysis showed that the general amount of activity in switch-related regions was larger with rule-cues than with task-cues. In our view, this latter finding suggests that, given sufficient task rule information, the need to prepare for a task switch evokes efficient processes of re-loading the task rule information already during the preparation period of the task processing.

Rule retrieval, or activation of the currently required task set, is presumed to be an important component of task-switching (Mayr and / INS; Kliegl, 2000; Rogers and Monsell, 1995; Monsell, 2003; Rubinstein et al., 2001). In the present study, the task rule information provided by rule-cues may have evoked preparatory processes that included even the rule representation, thus permitting a more complete task set reconfiguration (on switch trials) compared to the presentation of mere task-cues. This would explain why the task switch costs (i.e., error rates) were reduced in the rule-cue relative to the task-cue condition, and why the amount of neural activation was increased in preparation-related regions with rule-cues compared to the task-cues.

Previous findings point to the possibility that activity involved in switching task sets may be confounded by processes involved in the perception of the different cues presented on successive trials (Logan and Bundesen, 2003). However, in the present study, we can rule out such confounds on the observed fMRI activity. A post-hoc analysis, in which we compared the RTs in conditions with changing cues (rule-cue followed by task-cue, and vice versa) to the RTs in conditions with repeated cues, showed no additional influence of a cue change on the size of the task switch costs; the difference between the RTs in both conditions (i.e., ___ : task repeat and cue repeat; ___ : task repeat but cue switch) amounted to a negligible 1 ms.

Some previous fMRI studies had failed to find any additional region, or even activation, to be involved in preparing for task switches (as compared to repetitions), which was taken to cast doubt on the assumption that switch-specific control processes are operating during the preparation period (e.g., Brass and von Cramon, 2002, 2004; Gruber et al., 2006; Ruge et al., 2005; but see Chiu and Yantis, 2009, Slagter et al., 2006, and ERP studies, e.g., Lavric et al., 2008, for positive evidence). We agree that the kinds of preparatory processes occurring after cues that indicate a task repeat and cues that indicate a task switch are similar, but they are more intense in task switch situations. In other words, more control is required when preparing for switch trials, and the corresponding additional activation can be found in either the task preparation or the execution period, depending on the type of cue.

A possible reason for the discrepant findings concerning switch-related activations in the preparation period may lie in the different types of cues, or cue information, which were used in studies that failed to and that did find such activations. Studies that failed to find additional switch-related activation (see below) used arbitrary cues (e.g., in Brass et al., 2002, a square or diamond indicating an odd/even and or a number size task), whereas we used semantically unequivocal cues to indicate the upcoming task (see also Wylie et al., 2006). It would appear plausible that, if the cue is an arbitrary shape, a considerable amount of time needs to be spent to decode the cue and to represent the general task goal — that is, task rule activation may be delayed and moved to the target period. This might be the reason why studies that used such arbitrary cues failed to find any larger activation in the preparation for task switches compared to repetitions (Brass and von Cramon, 2002, 2004; Gruber et al., 2006; Ruge et al., 2005).

In our study, the word symbol 'gender' indicated the gender task and the symbol 'color' the color task. This use of semantic cues is similar to the conditions in other studies which also reported additional switch-related activity during the preparation period (e.g., Wylie et al., 2006). In the case of semantic cues, the cue specifies the task relatively directly, making it much easier for participants to establish the task representation (Miyake et al., 2004; Wylie et al., 2006) — and permitting them to activate the task rule already within the preparation period. As a consequence, the neural effort associated with the uploading of the task rule information would be increased on task switch compared to repetition trials, and this effort may be strong enough to evoke significant fMRI activation in the comparison of switch versus repetition trials during the task preparation period (Wylie et al., 2006).

Thus, these findings conform well with recent evidence from ERP studies indicating that switch-related neural activity can indeed be observed for processes associated with the task preparation (Lavric et al., 2008). Perhaps the use of more elaborate paradigms permitting further differentiation of the various components in switching activity (in particular, cue-related and task-related activity) may add to these findings in future studies (Monsell and Mizon, 2006).

Conclusions

The present study identified neural correlates of task rule activation and revealed these to be subcomponents of a general task preparation network. The processes of task rule activation are operating in task-cuing paradigms given that the cues provide explicit information about the task rule. In this case, part of the rule activation may be brought forward from after to before the onset of the target stimulus. This leads to increased neural 'effort' in rule activation-related regions that are a subset of the general task preparation-related regions, and to improved task performance. In addition, a stronger activation was observed in a rule-related region if participants prepared for a task switch, compared to a repetition, trial and if this preparation process included a change of the relevant task rule information. We conclude that the extent to which participants prepare in advance the parameters of an upcoming task depends strongly on the specificity and the amount of information provided prior to task processing; this in turn determines the degree of activation in brain regions associated with task preparation.

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