ACADEMIC
PRESS

When the same response has different meanings:
Recoding the response meaning in the lateral prefrontal cortex

Marcel Brass,[a],* Hannes Ruge,[a] Nachshon Meiran,[b] Orit Rubin,[b] Iring Koch,[c] Stefan Zysset,[a] Wolfgang Prinz,[c] and D. Yves von Cramon[a]

[a] *Max Planck Institute of Cognitive Neuroscience, Leipzig, Germany*
[b] *Ben-Gurion University of Negev, Beer-Sheva, Israel*
[c] *Max Planck Institute for Psychological Research, Munich, Germany*

Abstract

The ability to adapt our behavioral repertoire to different situations and tasks is crucial for our behavioral control. Since the same motor behavior can have different meanings in different task situations, we often have to change the meaning of our responses when we get into a different task context. In a functional MRI experiment we manipulated this response recoding process. Subjects were required to execute two simple spatial tasks in a task switching paradigm. In one condition both tasks required the same set of responses, hence each response had two different meanings depending on the relevant task (bivalent condition). In the other condition subjects used a separate set of responses for each task (univalent condition). While subjects were required to recode the meaning when switching from one task to the next in the bivalent condition, response recoding was not required in the univalent condition. We demonstrate that the lateral prefrontal cortex is involved in recoding of response meaning. These results extend previous assumptions on the role of the prefrontal cortex in behavioral control.
© 2003 Elsevier Inc. All rights reserved.

Introduction

One of the most fascinating properties of intelligent behavior is the human ability to apply a restricted behavioral repertoire to an infinite number of different task situations. Pressing a light switch, for example, can have different outcomes (switch the light on or off) depending on the context. To be able to use the same physical response (pressing the light switch) to achieve different goals (switching the light on or off) one has to recode the response meaning when switching from one task situation to the next (Meiran, 2000; Schuch and Koch, 2003). We will refer to this process as "response recoding." Recently it was found that neurons in the prefrontal cortex of monkeys represent the response meaning depending on a given task context (Asaad et al., 2000). In this study prefrontal cortex neurons were found to be activated in preparation of a specific response but only when the response occurred in a given task context. These results suggest that the prefrontal cortex might be involved in processing task-context specific response information (the response meaning).

In cognitive psychology the influence of the task context on task performance is usually investigated in so-called task-switching paradigms. A number of neuroimaging studies have used this paradigm to investigate task-related control processes (Brass and von Cramon, 2002; Dove et al., 2000; Kimberg et al., 2000; Omori et al., 1999; Pollmann et al., 2000; Sohn et al., 2000). However, to our knowledge recoding the response meaning was never directly investigated with functional MRI. Some previous studies have manipulated the stimulus-response mapping (S-R mapping) between two tasks, which probably involves response recoding (Dove et al., 2000; Nagahama et al., 2001; Pollmann et al., 2000). Reversing the S-R mapping yielded activation in the prefrontal cortex. However, because these studies did
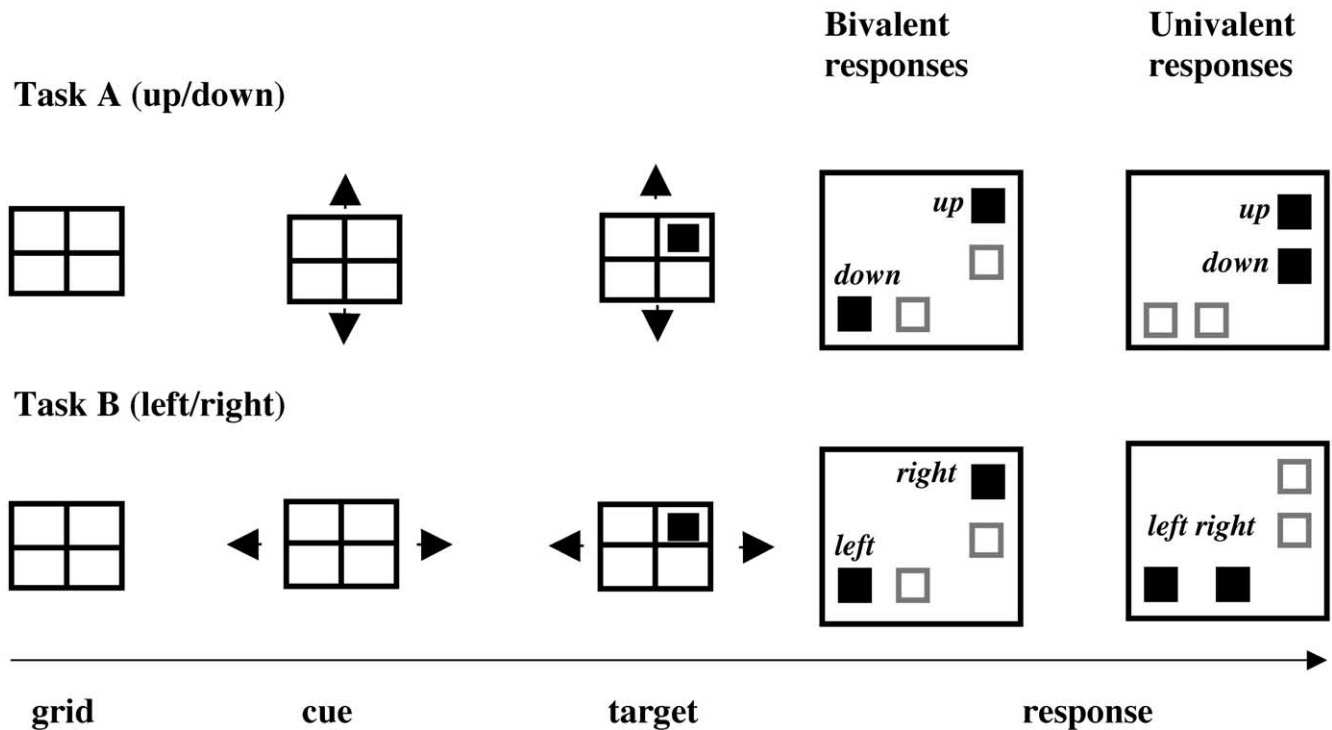
Fig. 1. Schematic drawing of the two tasks. In the up/down task, subjects were required to indicate whether the target was in the upper or lower half of the grid (task A). In the left/right task, subjects were required to indicate whether the target was on the left or the right side of the grid (task B). Two arrows pointing in the left/right or up/down direction indicated which task subjects had to execute. In the bivalent condition, subjects used the same buttons in both tasks. In the univalent condition, each task had a different set of responses.

not manipulate response recoding independently from task switching, it is not clear whether the prefrontal activation was due to general task-set reconfiguration or to response recoding.

The aim of the present study was to directly investigate the cortical basis of our ability to use the same physical response to achieve different goals. To do so, we compared a situation in which subjects were required to recode the meaning of their responses while switching from one task to the next with a situation in which they were not required to recode the response meaning.

Methods

Experimental design

In the study we used a paradigm in which subjects had to switch between two simple spatial tasks (Meiran, 1996). In one task (task A) they were required to decide whether a square, which was presented in a two-by-two grid, was in the upper or lower half of the grid, and in the other task (task B) subjects had to decide whether the square was on the left or on the right side of the grid (Fig 1). The task executed in a given trial was indicated by two arrows presented either above or below the grid (task A), or on the right or the left side of the grid (task B). In both tasks, subjects responded

with their index fingers of the left and right hand. This response mapping can be termed bivalent, because each response has two different valences (up/right, down/left), one for each task (note that for the top-right and bottom-left target positions the S-R mapping was identical in both tasks). Therefore, subjects had to recode the response meaning when they switched from one task to the other (switch trials). The top-right key for example might indicate "up" in one task and "right" in the other. To isolate this response recoding mechanism, we introduced a second condition in which subjects were not required to recode the response meaning, when they switched between tasks. In this condition, subjects responded with the index and middle finger of the right hand to the up/down task, and with the index and middle finger of the left hand to the left/right task. Since each task required a separate set of responses, each response was univalent, that is to say, it had only one meaning, and therefore, a task switch was not accompanied by the need to recode response meaning. Participants used the same keys pads for the univalent and bivalent condition (see Fig. 1).

The experiment consisted of two blocks, one bivalent block (128 trials) in which subjects used only two response keys and a univalent block (128 trials) in which subjects used four response keys. In each block, 16 null events were randomly inserted. The blocks were counterbalanced across subjects. Before each block, a short practice phase was carried out to familiarize the subjects with the response
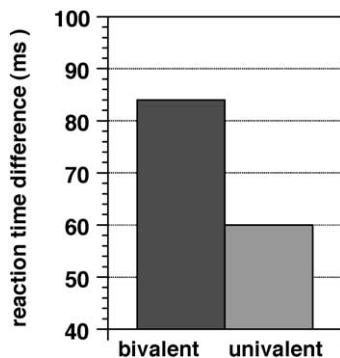
Fig. 2. Reaction time differences of switch and repetition trials in the bivalent and univalent condition for the short CTI.

mapping. The exact timing of the trials was as follows: The grid was presented for 300 ms. Then the cue was presented, and after 100-ms cue target interval (CTI), the target appeared. In half of the trials the CTI was 2000 ms. Error trials were excluded from the reaction time and fMRI analysis.

Subjects

A total of 22 subjects (11 females and 11 males) who gave informed consent participated in the present study. All participants (mean age: 25.4 years) were right handed as assessed by a German adaptation of the Edinburgh Handedness Inventory (Oldfield, 1971) and had no neurological abnormalities. Four subjects were excluded from fMRI analysis due to strong movement artifacts.

fMRI analysis

The experiment was carried out on a 3-T scanner (Medspec 30/100, Bruker, Ettlingen). Sixteen axial slices (19.2 cm FOV, 64 × 64 matrix, 5 mm thickness, 2 mm spacing), parallel to the AC-PC plane, and covering the whole brain were acquired, using a single shot, gradient recalled EPI sequence (TR 1500 ms, TE 30 ms, 90° flip angle). Prior to the functional runs, 16 corresponding anatomical MDEFT slices and 16 EPI-T1 slices were acquired. Stimuli were displayed by an LCD projector on a back-projection screen mounted in the bore of the magnet behind the participants' head. Participants viewed the screen, wearing mirror glasses.

Analysis of fMRI data was performed using the LIPSIA software package (Lohmann et al., 2001). First, functional data were corrected for movement artifacts. Then, the temporal offset between the slices acquired in one scan were corrected using a sinc interpolation algorithm. Data were filtered using a spatial Gaussian filter with sigma = 0.8. A temporal high-pass filter with a cutoff frequency of 1/160 Hz was used for baseline correction of the signal. In addition, a global scaling was carried out. All functional data sets were individually registered into 3D space using the

subjects' individual high-resolution anatomical images. This 3D reference data set was acquired for each subject during a previous scanning session. The 2D anatomical MDEFT slices, geometrically aligned with the functional slices, were used to compute a transformation matrix containing rotational and translational parameters that register the anatomical slices with the 3D reference T1 data set. These transformation matrices were normalized to the standard Talairach brain size (Talairach and Tournoux, 1988) by linear scaling, and finally applied to the individual functional data. The statistical evaluation was carried out using the general linear model for serially autocorrelated observations (Friston et al., 1995). The design matrix for event-related analysis was created using a model of the hemodynamic response with a variable delay. The model equation was convolved with a Gaussian kernel with a dispersion of 4 s FWHM. Contrast maps were generated for each subject. As the individual functional data sets were all aligned to the same stereotactic reference space, a group analysis was subsequently performed. A one-sample t test of contrast maps across subjects (random effects model) was computed to indicate whether observed differences between conditions were significantly different from zero. Subsequently, t values were transformed into z scores. To protect against false positive activations, only regions with a z score higher than 3.1 ($P < 0.001$, uncorrected), and with a volume larger than 270 mm^3 were reported.

To carry out a region of interest (ROI) analysis, we determined the most activated voxel of the interaction contrast within a search radius of 10 mm around Talairach coordinates $x = 41$, $y = 26$, and $z = 21$ for each subject. From this voxel, we extracted the time course of the signal. Then, we subtracted the time course of the null event from the time course of the relevant conditions (Burock et al., 1998). We determined the percent signal change as the largest value in a time window between 4 and 6 s after cue presentation. The signal change difference for the bivalent condition was computed by subtracting the signal change of repetition trials from switch trials.

Results

Behavioral results

The behavioral data replicate previous studies; they show that subjects were significantly slower in switch trials (transition from task A to B or task B to A) than in repetition trials (repetition of task A or task B), $F(1,17) = 82.3$, $P < 0.001$. This switch effect (635 vs. 594 ms) reflects the costs of switching from one task to the next. This effect was larger in the bivalent (51 ms) than in the univalent condition (31 ms), $F(1,17) = 12.2$, $P < 0.01$, indicating, that the switch costs were reduced when subjects were not required to recode the response meaning when switching from one task to the next (see Fig. 2 for this reduction in the short CTI
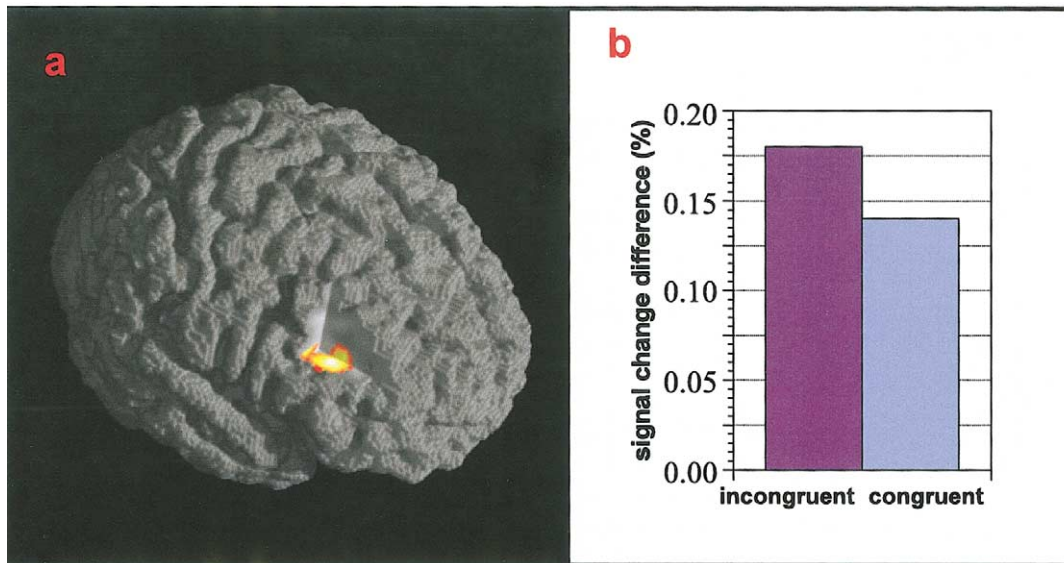
Fig. 3. (a) Lateral prefrontal activation in the right hemisphere (Talairach coordinates; $x = 41$, $y = 26$, $z = 21$; volume size $= 515$ mm^3), which was significantly activated ($z > 3.1$) in the interaction contrast of switch by valence for the short CTI. (b) The signal change diagram indicates that this cortical region showed an activation difference between switch and repetition trials in the bivalent condition for incongruent and congruent trials.

condition). Furthermore, there was a main effect for CTI, $F(1,17) = 128.9$, $P < 0.001$. Subjects were faster, when they were able to prepare the task (563 ms), compared to the condition were they were not able to do so (666 ms). Finally, a two-way interaction of switch by CTI was found, $F(1,17) = 50.3$, $P < 0.001$, showing that the switch costs were largely reduced in the long CTI condition (10 ms) compared to the short CTI (72 ms).

fMRI results

The comparison of the switch effect in the bivalent and the univalent condition revealed the cortical regions that were sensitive to the recoding of response meaning. Hence, the relevant contrast is the interaction of valence by switch [(switch bivalent − repetition bivalent) − (switch univalent − repetition univalent)]. In the short CTI condition, the right lateral prefrontal cortex (LPFC) was significantly stronger activated in this interaction contrast (Fig. 3a), demonstrating its prominent role in response recoding. For the long CTI condition, no cortical activation was found for this interaction. Further analysis with the short CTI trials indicated that there was a stronger activation in switch than in repetition trials in the bivalent condition ($z > 3.1$), in which subjects were required to recode the response meaning when they switched from one task to another. No significant activation difference was found in the univalent condition, in which subjects used different sets of responses for the two tasks.

To put our argument one step further, we carried out an ROI analysis to test whether the right LPFC showed also a switch-specific difference in congruent trials (top-right and bottom-left target position) of the bivalent condition. In

these trials the response to a given stimulus does not depend on the task. Nevertheless, a significantly stronger activation, $t(17) = 3.47$, $P < 0.005$, was found in switch compared to repetition trials (Fig. 3b). Apparently, subjects changed the response meanings even in this condition where response meaning is not conditional on the task.

Discussion

By manipulating the overlap of response sets in the univalent and bivalent condition, we demonstrate that the LPFC mediates the change of response meaning when the person switched from one task to the next. An alternative explanation of this interpretation might be that participants, instead of recoding the response in switch trials, represent the response in a multidimensional response space. However, in incongruent trials this is not a reasonable strategy, since the same stimulus requires two different responses depending on the relevant task.

A puzzling aspect of the present results is the finding that the response recoding effect was modulated by the CTI manipulation. This indicates that response recoding is not independent from task preparation. There are different possible explanations why prolonging the cue-target interval affects response recoding. We assume that general task-set preparation has an influence on response recoding by reducing the ambiguity of the task context, which in turn makes response recoding less demanding (Ruge et al., unpublished data). The alternative explanation would suggest that participants are, at least to some degree, able to anticipatorily recode the response meaning before the stimulus is pre-

sented. However, in this case one would expect a difference between switch and repetition trials in the preparation phase, which was not found. Furthermore, such an assumption is at odds with most behavioral theories of task switching, which assume that response-related control mechanisms are independent of task preparation (Schuch and Koch, 2003; Meiran, 2000). A third possible explanation is not cognitive and simply assumes that participants used the preparation interval to disambiguate the response meaning by slightly changing the position of their hands (more horizontally for the left/right task and more vertically for the up/down task). In a previous study with a 4-s preparation interval, Dove (2000) found a primary motor hand activation in the preparation phase that might support this interpretation.

Importantly, the response recoding effect was also found in congruent trials of the bivalent condition, which indicates that even when the S-R relations are identical for both tasks, subjects nevertheless recode the response meaning. Furthermore, this finding indicates that the activation difference between switch and repetition trials does not depend on S-R mapping differences between the conditions.

The role of the LPFC in cognitive control

Our results extend previous assumptions on the role of the LPFC in cognitive control. Recent theories have emphasized the involvement of the LPFC in task-related control processes, such as "implementing control" (MacDonald et al., 2000), or "imposing an attentional set" (Banich et al., 2000). As an important finding, the present study shows that the LPFC is not only involved in implementing control on a general level of task rules, but also on the level of response codes. From a broader theoretical perspective such a functional diversity of LPFC seems to be very reasonable. Recent theories have pointed to its general role in processing context-related rules to guide behavior (Miller and Cohen, 2001; Duncan, 2001). Context-related rules can be implemented on different hierarchical levels. The highest level refers to the task set that defines the relevant S-R relations for a given task. On a lower level the stimulus and response meanings for a given task are defined. The question is open whether the same cortical regions are responsible for configuring information on these different hierarchical levels. There is some evidence that task set configuration and task preparation are located more posterior close to the precentral sulcus (Konishi et al., 2001; Brass and von Cramon, 2002; Dove et al., 2000). In contrast the present activation is located more anterior in a region that was found to be involved in manipulation of working memory content (D'Esposito et al., 1998; Fletcher and Henson, 2002) and in response selection (Frith, 2000).

Response selection, working memory, and learning of visuomotor associations

It is important to note that the present findings go beyond the general assumption that the LPFC is involved in response selection since we did not manipulate response selection in the narrow sense. Regarding response selection requirements switch and repetition trials did not differ in the univalent and the bivalent condition. We would rather argue that the LPFC is responsible for manipulating the response meaning in relation to the relevant task demands. In this sense our findings are in accordance with recent results from the working memory field, which showed the involvement of the LPFC in response-related working memory processes (D'Esposito et al., 2000; Rowe et al., 2000; Pochon et al., 2001). From this perspective, it is reasonable to assume that response recoding is based on the online manipulation of response representations in working memory. Such an interpretation would integrate the working memory perspective and the response selection perspective on LPFC function. Another possible explanation was put forward by Passingham, Toni, and Rushworth (2000) who argued that the lateral prefrontal cortex is involved in learning of visuomotor associations. Since participants could not built up a permanent stimulus-response association in the bivalent condition of the present experiment, they had to rearrange the stimulus-response associations during the whole experiment. Therefore, it is reasonable to assume that response recoding and learning of stimulus-response associations might involve similar cortical and functional mechanisms.

Response recoding and the format of response representations

Finally, our data clearly show that response representations are not restricted to the "motor" or "physical" properties of the responses, since in both tasks of the bivalent condition, subjects were required to execute exactly the same responses. Rather our data suggest that responses are represented on a more abstract level. This assumption is in accordance with recent theories of action control and response coding (Hommel et al., 2002; Prinz, 1997). These theories assume that response representations contain intended outcomes or action goals. Motor control is achieved by manipulating these response representations. It is this abstract representation of our actions that allows us to use identical motor behavior for different purposes, depending on our intentions and on contextual constraints. The prefrontal cortex is involved in manipulating response representation when no standard stimulus response mapping can be applied (Toni et al., 2001), and therefore the task context has to be taken into account. In this sense, response recoding is required whenever the same motor acts are used in different tasks, which is the case in a number of cognitive paradigms. In daily life, this response recoding process is highly relevant, because it enables primates to use their

restricted behavioral repertoire to achieve an infinite number of action goals.

Acknowledgments

References

Asaad, W.F., Rainer, G., Miller, E.K., 2000. Task specific neural activity in the primate prefrontal cortex. J. Physiol. 84, 451–559.

Banich, M.T., et al., 2000. Prefontal regions play a predominant role in imposing an attentional "set:" evidence from fMRI. Cogn. Brain Res. 10, 1–9.

Brass, M., von Cramon, D.Y., 2002. The role of the frontal cortex in task preparation. Cereb. Cortex 12, 908–914.

Burock, M.A., Buckner, R.L., Woldorff, M.G., Rosen, B.R., Dale, A.M., 1998. Randomized event-related experimental designs allow for extremely rapid presentation rates using functional MRI. Neuroreport 9, 3735–3739.

D'Esposito, M., Aguirre, G.K., Zarahn, E., Ballard, D., Shin, R.K., Lease, J., 1998. Functional MRI studies of spatial and nonspatial working memory. Cogn. Brain Res. 7, 1–13.

D'Esposito, M., Ballard, D., Zarahn, E., Aguirre, G.K., 2000. The role of prefrontal cortex in sensory memory and motor preparation: an event-related fMRI study. Neuroimage 11, 400–408.

Dove, A., 2000 Lokalisierung an internen Kontrollprozessen beteiligter Hirngebiete mit Hilfe des Aufgabenwechselparadigmas und der ereigniskorrelierten funktionellen Magnetresonanztomographie [Lacalization of internal control processes using the task-switching paradigm and event-related functional MRI]. Doktorarbeit [Phd thesis], Universität Leipzig.

Dove, A., Pollmann, S., Schubert, T., Wiggins, C.J., von Cramon, D.Y., 2000. Prefrontal cortex activation in task switching: an event-related fMRI study. Cogn. Brain Res. 9, 103–109.

Duncan, J., 2001. An adaptive coding model of neural function in prefrontal cortex. Nat. Rev. Neurosci. 2, 820–828.

Fletcher, P.C., Henson, R.N.A., 2002. Frontal lobes and human memory: insights from functional neuroimaging. Brain 124, 849–881.

Friston, K.J., et al., 1995. Statistical parametric maps in functional imaging: a general linear approach. Hum. Brain Mapp. 2, 189–210.

Frith, C., 2000. The role of the dorsolateral prefrontal cortex in the selection of action as revealed by functional imaging, in: Monsell, S., Driver, J. (Eds.), Control of Cognitive Processes: Attention and Performance XVII. MIT Press, Cambridge, MA, pp.549–565.

Hommel, B., Müsseler, J., Aschersleben, G., Prinz, W., 2002. The theory of event coding (TEC). Behav. Brain Sci. 24, 849–937.

Kimberg, D.Y., Aguirre, G.K., D'Esposito, M., 2000. Modulation of task-related neural activity in task-switching: an fMRI study. Cogn. Brain. Res. 10, 189–196.

Konishi, S., Donaldson, D.I., Buckner, R.L., 2001. Transient activation during block transition. Neuroimage 13, 364–374.

Lohmann, G., Mueller, K., Bosch, V., Mentzel, H., Hessler, S., Chen, L., Zysset, S., von Cramon, D.Y., 2001. Lipsia—a new software system for the evaluation of functional magnetic resonance images of the human brain. Comput. Med. Imaging Graph 25, 449–457.

MacDonald III, A.W., Cohen, J.D., Stenger, V.A., Carter, C.S., 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288, 1835–1838.

Meiran, N., 1996. Reconfiguration of processing mode prior to task performance. J. Exp. Psychol. Learn. Mem. Cogn. 22, 1423–1442.

Meiran, N., 2000. Reconfiguration of stimulus task-sets and response task-sets during task-switching, in: Monsell, S., Driver, J. (Eds.), Control of Cognitive Processes: Attention and Performance XVII. MIT Press, Cambridge, MA, pp. 377–400.

Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. Annu. Rev. Neurosci. 24, 167–202.

Nagahama, Y., et al., 2001. Dissociable mechanisms of attentional control within the human prefrontal cortex. Cereb. Cortex 11, 85–92.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh Inventory. Neuropsychologia 9, 97–113.

Omori, M., et al., 1999. Neuronal substrates participating in attentional set-shifting of rules for visually guided motor selection: a functional magnetic resonance imaging investigation. Neurosci. Res. 33, 317–323.

Passingham, R.E., Toni, I., Rushworth, M.F., 2000. Specialisation within the prefrontal cortex: the ventral prefrontal cortex and associative learning. Exp. Brain Res. 133, 103–113.

Pochon, J.B., et al., 2001. The role of dorsolateral prefrontal cortex in the preparation of forthcoming actions: an fMRI study. Cereb. Cortex 11, 260–266.

Pollmann, S., Dove, A., von Cramon, D.Y., Wiggins, C.J., 2000. Event-related fMRI: comparison of conditions with varying BOLD overlap. Hum. Brain. Mapp. 9, 26–37.

Prinz, W., 1997. Perception and action planing. Eur. J. Cogn. Psychol. 9, 129–154.

Rowe, J.B., et al., 2000. The prefrontal cortex: response selection or maintenance within working memory? Science 288, 1656–1660.

Schuch, S., Koch, I., 2003. The role of response selection for inhibition of task sets in task shifting J. Exp. Psychol. Hum. Perc. Perf. 29, 92–105.

Sohn, M.-H., Ursu, S., Anderson, J.R., Stenger, V.A., Carter, C.S., 2000. The role of prefrontal cortex and posterior parietal cortex in task switching. Proc. Natl. Acad. Sci. USA 97, 13448–13453.

Talairach, P., Tournoux, J., 1988. A Stereotactic Coplanar Atlas of the Human Brain. Thieme, Stuttgart.

Toni, I., Rushworth, M.F.S., Passingham, R.E., 2001. Neural correlates of visuo-motor associations: spatial rules compared with arbitrary rules. Exp. Brain. Res. 141, 359–369.