Overlap and Segregation in Predorsal Premotor Cortex Activations Related to Free Selection of Self-Referenced and Target-Based Finger Movements

In reaching movements, parietal contributions can be distinguished that are based on representations of external space and body scheme. By functional magnetic resonance imaging, we examined 16 healthy subjects to see whether such segregation similarly exists in the frontal lobes when visuomotor actions are not specified but when free choices are allowed. Free selection was button based (target based) or finger based (self-referenced), with invariant instructions as control. To avoid a visual attention bias, instructions were auditory presented. Statistical parametric mapping revealed that free button selection with the same finger was associated with increased activations in the anterior cingulate cortex (ACC), right posteroventral prefrontal cortex (PFC) including the rostral extension of the dorsal premotor cortex (pre-PMd), and the anterodorsal PFC. Prefrontal activation related to free finger selection (pressing the same button) was restricted to an anteromedial segment of the posteroventral PFC/pre-PMd. Bilateral inferior parietal activations were present in both free-choice conditions. Pre-PMd and parietal contributions to free selection support concepts on early-stage action selection in dorsal visuomotor pathways. The rostral–caudal segregation in pre-PMd activations reflected that in anterior direction, frontal processing is gradually less involved in selection of environmental information but increasingly committed to self-referenced selection. ACC particularly contributes to free selection between external goals.

Keywords: action selection, fMRI, parietal cortex, prefrontal cortex, visuomotor

Introduction

Object manipulation implies visuomotor transformations that require an adequate representation of the object’s shape and its position in space. Along segregated processing streams, these perceptual characteristics contribute to the motor aspects prehension and direction, respectively. The neural underpinning of such aspects in higher order motor control is anchored in circuitry distributed over parietal and premotor cortical regions (Binkofski et al. 1999; Matelli and Luppino 2001). Within these parietopremotor networks, the left anterior parietal cortex facilitates the integration of target shape and hand posture (Grafton et al. 1996; Binkofski et al. 1998; Busbaum et al. 2006), whereas the superior parietal cortex, with a right-hemisphere dominance in humans, is particularly involved in navigating the hand to the object (Mountcastle et al. 1975; Corbetta et al. 1993; Wise et al. 1997; Vallar 1998). In a previously conducted reaching paradigm for positron-emission tomography (PET), we have demonstrated such parietal segregation by comparing pointing with the same finger to different targets (I) with a condition in which subjects touched the same target with different fingers (II). This resulted in activation increases of respectively the (right) superior parietal and left anterior parietal cortex (de Jong et al. 2001). Due to the auditory given instruction, thus avoiding an attention bias induced by the visual cueing, the parietal segregation was inferred to reflect “target-based” and “self-referenced” components in the preparation of commands for purposeful movement.

The above-mentioned results have all been obtained with paradigms in which stimulus-response combinations were invariably defined. However, beyond the execution of these actual visuomotor interactions, evaluation takes place and decisions are made whether the external demand for a specific action is indeed compatible with a state of internally defined goals or whether the external challenge should be inhibited or changed. This evaluation is based on a selection between response options in which functions of the (medial) frontal cortex are considered to play a prominent role (Frith et al. 1991; Miller and Cohen 2001; Rushworth et al. 2004, Rushworth 2008). In functional imaging studies, a consistent increase of cerebral activations distributed over the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (PFC) has been found when comparing free-choice selection with unequivocally instructed selection (Frith et al. 1991; Hyder et al. 1997; Desmond et al. 1998; Cunnington et al. 2006). Considering possible methodological imbalance regarding the intrinsic involvement of working memory and attention demands in the applied paradigms, the role of the dorsolateral PFC in free selection has been an issue of debate (Hyder et al. 1997; Desmond et al. 1998; Hadland et al. 2001; Lau, Rogers, Ramnani, and Passingham 2004). In this respect, Mueller et al. (2007) have recently provided arguments that particularly the ACC is critically involved in free selection.

This involvement of the ACC in free selection of specific movements is in line with earlier findings that have discriminated between a role of the lateral premotor system in converting behaviorally relevant stimuli into action and a specific role of the medial premotor system in the internal ordering of movements (Halsband and Passingham 1982; Goldberg 1985; Mushiake et al. 1991). This theory has been refined by the identification of functional subdivisions of the (human) medial premotor system, anatomically corresponding with caudal parts of the medial frontal cortex, that selectively contribute to the free selection of movements (Mueller et al. 2007). In this, the ACC is involved in the free selection of behavioral goals, whereas the presupplementary motor area (pre-SMA) plays a dominant role in the initiation of movements in the absence of a cue. This pre-SMA function has indeed elegantly been demonstrated by Lau, Rogers, Haggard, and

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comfortably press the buttons without making large movements that might cause artifacts in the MR signal. In between the button presses, subjects placed their right hand on their trunk. The left arm remained in rest beside the body. To further avoid artifacts induced by arm and shoulder movements, pillows supported the right elbow and shoulder and the right upper arm was fixated. Before scanning, subjects were asked whether they could comfortably press all the buttons and could see their hand and the button box via the mirror. Stimuli were presented using the ‘Presentation’ program (Neurobehavioral Systems, Inc., Albany, CA).

**Experimental Procedure**

The experimental paradigm consisted of 4 stimulus-response conditions and 1 control condition. The auditory stimuli consisted of numbers presented with 3-s intervals. After each such stimulus, a response was given by pressing a button of the response box. Instructions for each condition were also auditory presented. In condition 1 (fixed finger selection), the numbers 2-5 coded for the second to fifth finger of the right hand, ordered from index finger to pink. After subjects heard one of these numbers they had to press the third button with the corresponding finger. In condition 2 (free finger selection), the numbers 6-9 were similarly presented and only served as a cue to give a response. This response implied that subjects had to choose themselves which of the fingers 2-5 would be used to press the third button. In condition 3 (fixed button selection), the presented numbers 1-4 coded for the first to fifth button, ordered from left to right on the response box. In response to each of these stimuli, subjects had to press the corresponding button with their right index finger. In condition 4 (free button selection), the numbers 6-9 again served as a cue after which subjects had to make a choice themselves which of the buttons 1-4 would be selected to press with their index finger. In the control condition (listening), the presented numbers 6-9 were paced similar to the experimental conditions, whereas no response was given. In the free-choice conditions, subjects were explicitly instructed to make a new choice after each stimulus, which implied that they should not select series of either the same button or the same finger. As a consequence, repeats might indeed naturally occur.

The experiment consisted of a practice block (5 min) followed by two 18-min runs of task performance during functional imaging. In between these 2 runs, an anatomical $T_1$-weighted scan (7 min) was made. The 2 runs contained 8 blocks each. Each block contained the 4 stimulus-response conditions, whereas the control condition was placed in between blocks. The order of the conditions and stimuli was randomized and balanced. In each block segment, containing a single condition, the task was successively preceded by an auditory-presented task instruction followed by a silent interval (together 3000 ms). The subsequent task consisted of a stimulus, a number, followed by a silent interval in which a response had to be given (together 3000 ms). The stimulus-response trials were presented 8 times in each block segment. In this way, the number of stimuli (128 per condition) was balanced for the free-choice and fixed conditions.

**MRI Characteristics**

Data acquisition was performed using a 3-T Philips MR system (Philips Medical Systems, Best, the Netherlands) with a standard 6-channel SENSE head coil. A $T_1$-weighted 3-dimensional anatomical scan was acquired to obtain high-resolution anatomical information, matrix size $= 256 \times 256$ in axial orientation. Functional images were acquired with a gradient-echo $T_2^*$ blood oxygen level-dependent contrast technique using the following scanning parameters: time repetition $= 3000$ ms, time echo $= 35$ ms, 41 slices, isotropic voxels $3.5 \times 3.5 \times 3.5$ mm, axial orientation, 363 volumes per run.

**Data Analysis**

Image processing and statistical analysis were conducted with statistical parameter mapping (SPM) version 5 (2005, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm). All volumes obtained were used for data analysis. Preprocessing with SPM included realignment, coregistration, and spatial normalization (template of Montreal Neurological Institute.
Images were smoothed using a Gaussian filter of 8-mm full-width half-maximum. Cortical activations were rendered onto the surface of a standard MNI brain. For the projection on brain slices, we used the mean $T_1$-weighted anatomy scan of all the subjects. For the statistical analysis of regional differences in cerebral activations, all conditions were modeled in a blocked design at subject level. To identify the distributions of increased activations related to cerebral processing beyond audiovisual stimulation in the conditions 1–4, each of these 4 conditions was contrasted to the control condition (5) at subject level, after which each contrast was separately analyzed at group level using 1-sample $t$-tests. Differences between conditions 1–4 were analyzed by making comparisons at second level using a 2-way repeated-measures analysis of variance (ANOVA; random effect analysis), in which free and instructed selections were in the first factor and finger and button selections in the second. The resulting set of voxel values for the indicated contrasts constituted the associated SPM of the $t$ statistics ($\text{SPM}_t$) and were thresholded at initial voxel response height $P < 0.001$ with extent threshold $k = 20$ voxels. Resulting clusters of increased activation were considered statistically significant at cluster-level $P < 0.05$, corrected for the entire brain volume. In addition, all clusters at $P < 0.001; k = 20$ (uncorrected) are presented. Conditions were assumed to be dependent and equally variant, whereas subjects were assumed to be independent and equally variant.

Differences in response times between the 4 stimulus–response conditions were analyzed by a 2-way ANOVA for repeated measures using the means of single subjects for each condition in each run. The reaction times concerned the interval between beginning of the stimulus and the recorded response. To evaluate habituation effects, differences in reaction times between the first and second run between conditions were also analyzed by means of a 2-way ANOVA for repeated measures. By measuring response diversity in the free button selection condition, an indicator was obtained to assess whether subjects indeed randomly selected a button without a bias for either specific buttons or for a specific sequence. To that end, the fraction of responses on each of the 4 buttons was measured as well as the variation of consecutive button presses. This variation was quantified by the sum of the deviations of the 16 combinations (4 possible outcomes per button) from equal distribution. These differences from equal distribution in the choice of responses as well as in consecutive responses were expressed in a continuum in which 0% was a total equal response distribution and 100% was a total unequal response distribution. Habituation effects were also evaluated by comparing these values between the first and second run by means of paired $t$-tests. In addition, subjects rated the perceived difficulty of conditions after performance in the scanner. The scale of this rating was from 1 to 10 in which 10 was most difficult. Differences in perceived difficulty between conditions were analyzed using a 2-way ANOVA for repeated measurements.

## Results

### Behavioral Results

Analysis of the behavioral parameters revealed that the reaction times in the 2 free selection tasks (2 and 4) were highly similar, but significantly shorter than in the fixed selection tasks 1 and 3. 

#### Figure 1

**Figure 1.** Behavioral data (16 subjects). (A) Reaction times obtained for the 4 stimulus–response conditions during both runs of scanning. For each condition the mean (±standard deviation [SD]) of 16 subjects is presented, whereas each subject value is based on the mean of all measurements in a given condition and run. (B) The subjective difficulty rating (score 1–10), presented by the mean (±SD) of 16 subjects. (C) Decreases of reaction times in the second compared with the first run for each condition. (D) Diversity in selected responses (sel) and the difference between 2 consecutively selected responses (seq) in run 1 (sel1, seq1) and run 2 (sel2, seq2), respectively. These parameters were available for Free-BS and expressed in a scale varying from 0% (total equal) to 100% (total unequal). FS, finger selection; BS, button selection; Fix, fixed; **$P < 0.01$, ***$P < 0.001$.**
Contrasting fixed finger selection to fixed button selection (condition 1 > 3) showed a similar pattern of increased activations, distributed over the left primary sensorimotor cortex and right cerebellum, with bilateral increases that included the lateral and medial premotor cortex (SMA) as well as the anterior parietal cortex (Table 1 and Fig. 3A). This distribution strongly resembled the patterns of the visuomotor tasks compared with baseline. No prefrontal increase of activation was seen. In the right hemisphere, the increase of anterior parietal activation extended further in posterior direction than in the left hemisphere. In addition to these motor-related cortical regions, bilateral increases of activation were seen around the lateral occipitotemporal junction, putative visual area V5, and subcortically in the pulvinar and pallidum. The opposite contrast, that is, the comparison of fixed button selection with fixed finger selection (condition 3 > 1), revealed an increase of activation restricted to the left fusiform gyrus (Fig. 3B). This fusiform increase, however, did not appear in the comparison of fixed button selection with the passive baseline condition, whereas even an increase of baseline-related activation was found at this location when compared with fixed finger selection. These effects thus suggest a decrease of activation in fixed finger selection.

The comparison of free with fixed finger selection (condition 2 > 1) showed bilateral increases of activation both on the lateral surface of the superior frontal gyrus, referred to as the posterodorsal PFC (with focus of maximum in Brodmann’s area [BA] 8), and in the inferior parietal cortex (Table 1 and Fig. 4A). The latter had the highest T value in the left hemisphere. The posterodorsal PFC partly included the rostral extension of the pre-PMD (BA 6). For button selection, the comparison of the free with the fixed condition (4 > 3) was also dominated by prefrontal activation increases. This pattern included a cluster of activation on the lateral convexity of the superior frontal

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**Visuomotor Selection Tasks vs. Baseline Control**

| Left, x = -4 mm | Right, x = 4 mm |
|-----------------|-----------------|
| **Fixed Button** | **Fixed Finger** |
| **Free Button** | **Free Finger** |

**Figure 2.** Task-related cerebral activations (SPM[t], surface projected). (A) Group results (16 subjects) of contrasting each of the 4 visuomotor tasks to the baseline condition of passive viewing while listening to the numbers. Regional increases of activation are rendered onto the surface of a standard anatomical brain volume (MNI, SPM 2005). This shows a general similarity in primary motor cortex activation in the left hemisphere as well as activations in parietal and premotor regions. Further description is given in the text. (B) In addition, midline activations are projected on sagittal slices (left hemisphere, x = −4 mm) derived from a mean of the normalized anatomical images of all subjects. All regional activations with initial voxel-height threshold P < 0.001 (uncorrected) and extent k = 20 are depicted. The hair-cross in the sagittal sections indicates traversing the anterior and posterior commissures (AC-PC) plane (z = 0 mm) and the VCA (y = 0 mm). R, right hemisphere; ant., anterior side of the brain; M.1, primary motor cortex; PMd, dorsal premotor cortex; Par, parietal cortex.
Positive x 0.05, whole-brain corrected at cluster level). In addition, clusters are reported that reached coordinates refer to the voxels of maximum increase within clusters of significant activation (P < 0.05, whole-brain corrected at cluster level). In addition, clusters are reported that reached fixed selection conditions, compared with fixed selection, were further demonstrated by conjunction analysis of these 2 comparisons with inclusive masking (Fig. 5BC). In the pre-PMD, the activation related to free finger selection was anterior to that of free selection. In the inferior parietal cortex, this spatial relationship was reversed, in such a way that the activation related to free finger selection was located posterior. This parietal segregation was particularly evident in the right hemisphere.

The opposite contrasts, that is, fixed versus free selection (1 > 2 and 3 = 4, respectively), showed increases of activation in the auditory cortices for both comparisons (Table 1). In the 2 fixed selection conditions, the increase of activation was stronger in the secondary than the primary auditory cortex, whereas it was more pronounced on the left side. When comparing fixed with free finger selection (condition 1 > 2), additional increases of activation were seen in premotor areas on the left precentral gyrus, the dorsal parietooccipital junction, cerebellar vermis, thalamus, and mesencephalon. After contrasting fixed to free button selection (condition 3 > 4), such increases of activation beyond the auditory cortices were present in the left middle temporal gyrus, posterior cingulate gyrus, and fusiform gyrus. The auditory cortex effects were also seen when the passive baseline task was contrasted to the 4 stimulus–response tasks, in such a way that the baseline-related increases were stronger in the comparison with the free than compared with the fixed selection task. This may thus imply a differential decrease of activations in the stimulus–response tasks, complemented by a relative increase of auditory attention focused on passive number listening.

Discussion

The aim of the present study was to assess whether the parietal segregation in motor functions of the hand, that distinguished
target-based and self-referenced cerebral processing, is maintained in the PFC when responses are not unequivocally instructed but freely selected. When the free selection modes of respectively finger and target selection were contrasted to their fixed selection equivalents, prefrontal activations were indeed prominently present with differential effects in both dorsal PFC and ACC. A particular novel finding was the role of the posterodorsal PFC and adjacent pre-PMd. The association between pre-PMd and parietal activation increases suggested that neuronal processing underlying free selection takes place already within visuomotor circuitry. The rostral part of the PMd (BA 6) was referred to as “pre-PMd” in accordance with the annotation of Picard and Strick (2001). In monkey, it has also been referred to as area F7 (Luppino and Rizzolatti 2000).

The reaction times in the free selection mode of the 2 tasks were shorter than in the fixed selection conditions. This effect was opposite to the findings in previous studies that have addressed the issue of free versus fixed selection (e.g., Lau, Rogers, Ramnani, Passingham 2004, Lau et al. 2006; Mueller et al. 2007). Moreover, our reaction times were generally longer (ca., 1200–1400 ms) compared with the literature (often around 600 ms). The prolonged reaction times may (partially) be caused by the fact that 1 of 4 options had to be selected, whereas in many studies the choice is only between 2 options. Such relation with the number of selection possibilities has been demonstrated by Lau, Rogers, Ramnani, and Passingham in their 2004 study (free selection from 5 targets took ~1400 ms).

Moreover, manual performance was more elaborate in our paradigm because the fingers were not positioned near the buttons. The essential difference with previous studies, however, was that we found longer reaction times in fixed selection compared with free selection. This may be due to the fact that we used auditory instruction cues, whereas all previous studies used visual stimuli in their stimulus–response paradigms. Indeed, in our study, visual information was only used to achieve adequate visuomotor performance. If we had
The identified patterns of frontal activations related to the 2 free selection conditions showed both overlap and differences in the representations of self-referenced and target-based visuomotor actions. In free target selection, using the same (index) finger, increased activation was prominently present not only in the pre-PMd and adjoined posterodorsal PFC of the right hemisphere but also in the anterodorsal PFC and ACC.

Significant prefrontal activation related to free finger selection was restricted to a posterodorsal PFC location (bilateral) that anteromedially bordered the posterodorsal PFC/pre-PMd activation in free target selection. The ACC and dorsal PFC activations related to free selection of targets were generally in line with our hypothesis. In the dorsal PFC, however, we employed visual instruction cues, for example, by enlightening 1 of 4 buttons, motor responses to such a marked target would have been enhanced in fixed and not in free button selection. With respect to stimulus-driven attention in our paradigm (with auditory cues), the free and fixed modes of selection were balanced (Kincade et al. 2005). A consequence of auditory stimuli was the transition of auditory information to the visuomotor domain. The extra constraints of such transition in fixed selection, due to the precisely coded target that had to be selected, apparently outweighed free selection without such constraint.

Reaction times were recorded for both the button and finger selection tasks. For button selection, such recordings also enabled the assessment of diversity in button selection. In finger selection, however, only the third button was pressed. This inevitably implied that the distribution of fingers that were actually used could not be quantified in the same way. However, the random response distribution shown for button selection supports the assumption that finger selection was similarly unbiased. The fact that the finger as well as the button selection task showed faster responses in free than in fixed selection also indicated that the instructions were followed with similar accuracy.

**Differences between the Fixed Selection Tasks**

With regard to the imaging data, the comparison between the 2 fixed selection tasks revealed particularly strong increases of activation in relation with finger selection. This pattern of increases included the contralateral primary motor cortex, whereas no specific activation increases could be attributed to fixed button selection. We therefore assumed a misbalance at the level of actually executed movements (finger manipulation) between the 2 tasks (Gerloff et al. 1998). The increase of response times in fixed finger compared with fixed button selection supported such misbalance. The latter may have been a reason why we did not replicate the parietal segregation between self-referenced and target-based movements in fixed selection mode (de Jong et al. 2001). In our previous PET study on reaching, the performed movements were virtually identical with regard to such movement complexity. Only minimal variation existed in distal hand movements. Moreover, the targets in the previous reaching paradigm were at larger distance and more spatially dispersed, thus requiring a stronger demand on spatial navigation than in the current paradigm with targets in peripersonal space (Makin et al. 2007). Variation in the direction of such reaching was nevertheless accomplished by only minimal differences in proximal arm movements. Such real reaching, however, cannot be performed in an MR scanner as it would induce too much movement artifacts in signal recording.

In fixed finger selection, the increased activation around the lateral occipitotemporal junction (including putative visual area V5) might reflect higher level perceptual analysis of the observation of complex movements over simple movements (Peigneux et al. 2000). On the ventral surface of the occipitotemporal junction, that is, in the left fusiform gyrus, increased activation was related to passive observation, particularly when contrasted to fixed finger selection. When the fixed selection of the colored buttons was contrasted to fixed finger selection, a similar increase was seen. This fusiform gyrus activation might reflect a contribution to feature analysis and categorical organization of external objects (Ishai et al. 1999) and color (Chao and Martin 1999), including the retrieval of color information associated with visual identification of a number-coded button (Simmons et al. 2007). In general, the involvement of these extrastriate visual regions thus subtly reflected segregation between dorsal and ventral visual processing streams (Goodale and Milner 1992) associated with, respectively, increasingly demanding movement skill in visuomotor performance and relative perceptual dominance in the opposite tasks.
distinguished 2 separate clusters of activation of which the caudal one included the pre-PMd. The selective contribution of the ACC to only free target selection might reflect that it was specifically related to the engagement with environmental facilities. This would imply that the proposed intrinsic association of response conflict with free selection only concerns responses and actions that refer to external goals (Botvinick et al. 2004). In this respect, our finding is not at odds with previous experiments on free selection as those paradigms particularly concerned response selection linked to the differences between external signals (see Introduction). The increase of ACC activation in only free selection of external goals may further fit with its more general role in mediating responses to deal with environmental challenges (Devinsky et al. 1995), including action-outcome considerations (Rushworth et al. 2004). In this respect, one might argue that the overlap between the increased activations in the 2 free selection tasks, as revealed by conjunction analysis (Fig. 5A), represented the most specific aspects of cerebral processing underlying free selection.

The increase of dorsal PFC activations we found in free selection, when contrasted to fixed selection, were distributed over 2 main locations. The anterodorsal location (BA 46, 10) was consistent with coordinates that have been reported for the (antero) dorsal PFC activation related with free selection in previous paradigms (Frith et al. 1991; Lau, Rogers, Ramnani, and Passingham 2004; Mueller et al. 2007). It was the involvement of this PFC region that has previously raised the question concerning a working memory and attention bias in free compared with fixed selection (Hadland et al. 2001; Lau, Rogers, Ramnani, and Passingham 2004). Its anterior extension (BA 10) has been proposed to be particularly efficient in keeping an established action plan on track, whereas exploring the gain of new task sets within ongoing behavioral routines, a cognitive process referred to as branching (Koechlin and Hyafil 2007). Such mechanism indicates an intrinsic interdependence between memory functions and choice making. In this experiment, our might imply that while subjects divided their responses over the 4 buttons, they randomized such responses and thus kept in mind which buttons were pressed before. An argument against such an explicit memory explanation is the fact that subjects were instructed not to care too much about previous selections. The incidental selection of a button twice in a row was regarded as a natural consequence of free selection. Moreover, although this issue of sequence order existed also in free finger selection, the anterodorsal PFC did only show a weak subthreshold increase of activation in this condition when compared with fixed finger selection. Moreover, with regard to working memory, one may alternatively assume that it played a role in fixed selection because after hearing the number, it took up to 1500 ms to accomplish the response. Indeed, contrasts of each of the 4 stimulus-response conditions with baseline showed involvement the anterodorsal PFC, although with varying magnitudes.

**Posterodorsal PFC and Right Pre-PMd**

The increased activation of the posterodorsal PFC/right pre-PMd in free selection was a major new finding of the present study. This prefrontal region (BA 6, 8) has not been identified as a key region with previous functional imaging paradigms that addressed free selection, although Lau, Rogers, Ramnani, and Passingham (2004) have reported its coordinates. Our explanation for this discrepancy is that in the present visuomotor study, the visual target participated in the preparation of movement without playing a role as a cue. Previous designs dealt with visual selection (Lau, Rogers, Ramnani, and Passingham 2004; Lau et al. 2006; Mueller et al. 2007), simple selection between fingers (Frith et al. 1991), or choosing the onset of movement (Lau, Rogers, Haggard, and Passingham 2004). We focused on differences between self-referenced and target-based aspects of visuomotor control, which was the reason for both using auditory cues and allowing small differences in basic movements between the applied conditions. The fact that the resulting activation on the superior frontal gyrus extended from the “classical” right PMd (posterior to the VCA; Mayka et al. 2006) into rostral BA 6 and beyond further supports its involvement in higher order aspects of motor control (Luppino and Rizzolattii 2000; Picard and Strick 2001). This is consistent with the observations that dorsal BA 8 on the superior frontal gyrus, often referred to as part of the Frontal Eye Field, has no effector preference for saccades and may even be stronger implicated in reaching movements (Connolly et al. 2000; Grosbras et al. 2005; Levy et al. 2007).

In analogy with the differences between the SMA and pre-SMA in monkeys, the caudal subdivision of the PMd (also coined F2) is involved in fine motor control and sensorimotor transformations, whereas the rostral part of the PMd (area F7 or the pre-PMd) is heavily interconnected with other prefrontal regions and functionally implicated in cognitive aspect of motor control (Picard and Strick 2001). Anatomical markers have also shown this rostral-caudal parcellation of the PMd (Geyer et al. 2000), whereas Simon et al. (2002) have demonstrated a similar functional segregation in the human PMd by using fMRI. They dissociated spatial attention-memory functions and motor preparation, represented by respectively rostral and caudal PMd activations. With regard to the involvement of this distinct prefrontal/pre-PMd region in action selection, which we inferred from the present study, the observed region-specific effects of PFC lesions in monkey are of particular interest (Petrides 2005). Petrides emphasized that lesions in the caudal dorsal PFC (including BA 8 and rostral BA 6) resulted in an impaired selection between competing responses based on conditional operations, whereas middorsolateral PFC lesions (BA 46, 9/46) led to impaired monitoring of information in working memory. Given the auditory coding of targets and fingers in our visuomotor paradigm, the posterodorsal PFC activations in free selection are consistent with the interpretation of Petrides. Beyond the role of the PMd in spatial sensorimotor transformations (Wise et al. 1997), Cisek and Kalaska (2005) have recently pointed at neuronal discharge characteristics in the PMd that reflected decision making concerning the direction of reaching. In our paradigm, the directional aspects were most prominently present in selecting 1 of 4 targets. The association between the pre-PMd activation and particularly free button selection thus fits with the described spatial decision function of the PMd in monkey.

In free finger selection, the caudal extension of posterodorsal PFC activation did not reach the VCA, whereas rostrally, it extended more anteromedial than the activation in free target selection. Another difference with regard to the posterodorsal PFC/pre-PMd was its bilateral distribution in free finger selection, opposed to the right-hemisphere lateralization in free target selection. This right-sided dominance in free
target selection also existed in the parietal cortex. These differences in the patterns of activation between the 2 tasks point at essential differences in free selection concerning self-referenced and target-based movements. In target selection, external visual information plays a dominant role to ensure adequate visuomotor control. Dorsal parietal premotor circuitry is crucially involved in processing such spatial sensorimotor transformations (Wise et al. 1997; Matelli and Luppiino 2001), with right-hemisphere dominance in humans (de Jong, Frackowiak, et al. 1999; Gitelman et al. 1999; Vallar 2007). In visuomotor control with free finger selection and only one target, external visual features are less demanding. The contribution of the anteromedial segment of the posterodorsal PFC may thus reflect a gradient in anterior direction along which prefrontal processing becomes less involved in the selection of environmental information but increasingly committed to self-referenced selection (Koechlin et al. 2003; Badre 2008).

In the present study, we did not find significant increases of either pre-SMA or medial prefrontal activation in free selection, whereas the equivalent regions on the lateral aspect of the superior frontal gyrus were prominently involved. This may suggest that also in conditions with increased visuomotor complexity, a distinction is maintained between lateral and medial premotor regions associated with respectively spatial and temporal motor preparation. It would be interesting, in this respect, to explore in balanced conditions whether the pre-SMA is indeed stronger implicated in free selection of temporal order (Mushiake et al. 1991; Lau, Rogers, Haggard, and Passingham 2004). On the other hand, increased working memory load has been suggested as an alternative explanation for pre-SMA activation related to free selection in previous functional imaging studies (Petit et al. 1998; Lau, Rogers, Ramnani, and Passingham 2004). As explained above, reaction times in the free selection conditions of our paradigm were not longer than in fixed selection, they were even shorter. The absence of free selection–related pre-SMA activation in our study might thus provide an argument for the suggested working memory explanation.

**Parietal Involvement in Free Selection**

As referred to before, in adequate visuomotor coordination, premotor–parietal interactions play a pivotal role (Wise et al. 1997; Binkofski et al. 1999). The introduction of free selection highlighted the role of the posterodorsal PFC and pre-PMd in the visuomotor paradigm we applied. The associated increases of parietal activations indicated that frontoparietal interconnections also play an important role in functions beyond strict sensorimotor tuning itself. The additional involvement of the inferior parietal cortex in free selection has been reported before (Ball et al. 1999; Mueller et al. 2007). This might reflect a top-down effect from prefrontal to parietal regions that have been implicated in movement intention (Snyder et al. 1997; de Jong, Willemsen, and Paans 1999; Andersen and Buneo 2002; Sirigu et al. 2004), thus guiding the selection of a distinct action plan. On the other hand, Couthard et al. (2008) have recently provided arguments from human lesion studies that the right posterior parietal cortex plays an independent role by activating competing motor plans in circumstances of response conflict, whereas interactions with the PFC are used to limit subsequent interference on performance. From monkey electrophysiological studies, a similar parietal decision function has been inferred (Scherberger and Andersen 2007). These recent observations thus support the idea that a contribution to action selection is already given in relative early stages of visuomotor processing.

The strong increase of right-hemisphere activation in free selection of target-based movements underscored the functional coherence between the posterodorsal PFC/pre-PMd and the parietal cortex at this level of spatial motor planning. Although we did not replicate the parietal segregation associated with the 2 fixed selection tasks in our previous paradigm (de Jong et al. 2001; explained above), the distinction between the strong right parietal activation in free target selection and the bilateral parietal activations in free finger selection, slightly more caudal and with minor left-sided preference, indicated consistency with the previously found segregation (see also Rusconi et al. 2005; Vallar 2007). The inferred frontoparietal networks in the present study did not completely match with circuitry comprising the dorsal premotor and superior parietal cortex consistently implicated in spatial visuomotor functions for the upper limb (Johnson et al. 1996; Galletti et al. 2003). The pre-PMd and associated posterodorsal PFC activations were located more rostral, whereas the parietal maximum of activation was lateral to the intraparietal sulcus, that is, in the inferior parietal cortex. From the present study, we cannot definitively conclude whether the free selection–related activations reflected a distribution of directly connected cortical regions or whether they pointed at satellites that interact via the caudal PMd and superior parietal regions. On the other hand, previously described patterns of parietal–prefrontal connections provide general support for the presence of functional interactions between the distributed activations in the present study (Pandya and Yeterian 1990; Johnson et al. 1996; Rozzi et al. 2006). These anatomical data also support the segregation we found between the representations of free finger and free target selection in the pre-PMd and parietal cortex, in such a way that it fits with the observations that rostral premotor and caudal parietal regions are functionally associated as well as preferentially connected, which similarly holds for caudal premotor and rostral parietal loci (Johnson et al. 1996). Particularly, the second division of the superior longitudinal fascicle and the occipitofrontal fascicle may establish direct connections between the posterodorsal PFC/pre-PMd and inferior parietal cortex in human (Makris et al. 2005, 2007).

**Conclusions**

Free selection in visuomotor control is largely accomplished by circuitry comprising the posterodorsal PFC/pre-PMd and inferior parietal cortex, regions that contribute to a dorsal visuomotor pathway. This relation between free selection and parietal premotor circuitry is consistent with the affordance competition hypothesis, which describes that relative early stages of visuomotor integration may already participate in action selection (Cisek 2007). The efficiency implicated by such early cortical contributions indeed increases effective decision making in the rostral PFC (Koechlin and Hyafil 2007). With regard to the hypothesized differences in the representations of free selection of self-referenced and target-based movements, relative to fixed selections, both overlap and segregation was found within putative pre-PMd-inferior
parietal networks, whereas the ACC only contributed to the free selection of environmental targets.

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