

## Movement-Specific Repetition Suppression in Ventral and Dorsal Premotor Cortex during Action Observation

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**There are several models of premotor cortex contributions to sensorimotor behavior. For instance, the ventral premotor cortex (PMv) appears to be involved in processing visuospatial object properties for grasping, whereas the dorsal premotor cortex (PMd) is involved in using arbitrary rules to guide advance motor planning. These models have focused on individual movements. Here, we examine the premotor responses evoked during the processing of individual movements functionally embedded in an action. We tested whether processing hand–object interactions and action end states would differentially engage PMv and PMd. We used a repetition suppression (RS)–functional magnetic resonance imaging paradigm in which we independently manipulated the observed grip, the end position of the object (independent of its spatial location), and the hand trajectory. By comparing novel and repeated trials for each of these action components, we could isolate RS effects specific to each of them. Repeating the grasp component attenuated activity in right PMv, whereas repeating the end state of the action reduced blood oxygen level-dependent activity in the left PMd. These results suggest that PMv is involved in controlling the kinematic means of an appropriate hand–object interaction, whereas PMd is focused on specifying the desired end state of an action.**

**Keywords:** action observation, PMd, PMv, premotor cortex, repetition suppression

### Introduction

Anatomical features indicate that the lateral premotor areas on the precentral gyrus of primate cortex can be subdivided into a ventral and a dorsal part—ventral premotor cortex (PMv or F4–F5) and dorsal premotor cortex (PMd or F2–F7), respectively (Barbas and Pandya 1987; Rizzolatti and Luppino 2001). This physiological distinction appears to have a functional counterpart in the form of differential contributions of PMv and PMd to sensorimotor processing and action selection (Rizzolatti et al. 1988; Matelli et al. 1991; Passingham et al. 1998; Passingham and Toni 2001; Toni et al. 2001; Raos et al. 2003; Grol et al. 2007). For instance, it has been suggested that PMd and PMv can be distinguished on the basis of the type of correspondence between sensory stimuli and motor responses. That is, sensorimotor transformations might follow different computational rules depending on whether they are based on spatial or arbitrary associations (Passingham 1993; Wise and Murray 2000; Shadmehr and Wise 2005). In this framework, it has been shown that PMv is involved in controlling movements guided by spatial information—for instance, the shape of an object to be grasped (Rizzolatti et al. 1988; Fogassi et al. 2001; Toni et al. 2001; Umiltà et al. 2007; Spinks et al. 2008), whereas

PMd is crucially involved in learning and performing arbitrarily instructed movements (Passingham 1985; Petrides 1985; Kurata and Hoffman 1994; Chen and Wise 1995; Cisek and Kalaska 2004). A related view suggests a distinction between direct and indirect sensorimotor mapping in PMv and PMd: whereas PMv is involved in processing sensory properties of a stimulus to guide movement planning, PMd extracts motor information from a sensory cue by way of rule learning (Hoshi and Tanji 2006, 2007). Other authors have pointed out a similar distinction between direct perception–action associations in PMv, and action selection based on arbitrary relations among physically distant events in PMd (Diamond 2006), extending into the auditory domain (Chen et al. 2008). Some models have put more emphasis on the surface structure of motor behaviors, stressing the differential involvement of ventral and dorsal premotor areas in planning distinct movement types (Jeannerod 1988). In this framework, the involvement of PMv in hand–object interactions like grasping has been taken to suggest that neurons in this area represent a “vocabulary” of potential actions associated with intrinsic object properties (Rizzolatti et al. 1988; Murata et al. 1997). In contrast, the activity of neurons in PMd could be interpreted as coding arm movements directed to specific locations in space (Georgopoulos et al. 1986; Gentilucci et al. 1988; Murata et al. 1997; Hoshi and Tanji 2000; Davare et al. 2006). More recently, it has also been suggested that premotor areas might jointly represent perceptual events and the body part or action category with which this stimulus property has been habitually associated, an idea known as the “habitual pragmatic event map account” (Schubotz et al. 2008). In this view, ventral premotor areas are involved in the visual representation of objects, the hand, and potential grasping acts, due to the “default” pragmatic significance of objects for grasping. In contrast, PMd would process spatial stimulus properties and desired action outcomes. These properties and outcomes would not be rigidly associated with a single body part but could be flexibly combined, for instance, by maximizing smoothness of neurally encoded features (Graziano et al. 2002).

These models of premotor function are mostly based on studies dealing with individual movements, that is, movements aimed at a given goal without consideration for serial dependencies between multiple motor events. Yet, our behavioral repertoire relies on actions in which individual movements are integrated into a functional unit—we do not just grasp objects, we use them. For instance, a cup might be grasped to drink from it or to put it in the dishwasher. The present study assesses the contribution of the human premotor cortex to processing specific elements of various motor events embedded in a functional unit. Elaborating on the hypothesis that PMd

might code dominant stimulus–response mappings across learned parameters (Toni et al. 2002; Schubotz and von Cramon 2004; Hoshi and Tanji 2006, 2007), we tested whether processing object-related movements defined by nonspatial object features would preferentially rely on PMd, over and above the known contributions of this region to specifying arm and hand movements in space (Kalaska et al. 1997; Grol et al. 2007; Verhagen et al. 2008). In contrast, we hypothesized that processing object-related movements guided by hand–object relationships would preferentially rely on PMv, over and above the contributions of this region to controlling arm and hand movements in space (Ehrsson et al. 2000; Grol et al. 2007; Verhagen et al. 2008). Crucially, we avoided to disrupt the temporal relationship between the individual movements constituting the action and hence its functional relevance. Accordingly, we distinguished cerebral responses evoked by each motor element not by imposing artificial experimental delays between events (Toni et al. 1999; Hoshi and Tanji 2000; Beurze et al. 2007) but rather by making use of repetition suppression (RS) effects: the phenomenon that repeated processing of a given feature leads to a reduction of neural activity in neurons tuned to that particular feature (Miller and Desimone 1994; Thompson-Schill et al. 1999; Henson et al. 2000; Grill-Spector and Malach 2001; Rice et al. 2007). RS paradigms have recently been used in combination with functional magnetic resonance imaging (fMRI) to study the motor system during observation of goal-directed movements (Hamilton and Grafton 2006, 2007, 2008; Kable and Chatterjee 2006). The use of action observation approaches to examine the motor system draws on the widely supported assumption that processes underlying action observation and execution show considerable overlap, both cognitively and neurally (Grezes and Decety 2001; Cisek and Kalaska 2004; Hamilton et al. 2004; Schubotz and von Cramon 2004; Calvo-Merino et al. 2005; Dinstein et al. 2007). Furthermore, RS paradigms have been successfully used to study movement execution, indicating that not only sensory systems but also parts of the motor system are capable of decreasing their activity in response to repetition (Pellijeff et al. 2006; Hamilton and Grafton, 2009). More generally, movement-related RS effects might be an instance of a broad organizing principle, namely, the notion that the brain might specify a motor plan in terms of differences from the preceding movement (Rosenbaum et al. 2007).

We have used an fMRI–RS paradigm to test human subjects during observation of object manipulations arbitrarily instructed by color cues (Fig. 1). Subjects were shown action movies where an object, consisting of 2 parts of different color, was grasped and then inserted into one of 2 colored destination slots (end state). The object part to be grasped and the action end state were independently instructed and selectively repeated across subsequent videos. Thus, the GRASP condition was defined by the particular hand–object relationship of the action. The PLACE condition, in contrast, was defined by the end state of the action; this end state was made independent of a specific spatial location or arm movement because the location of the colored slots was varied over trials. The object part to be grasped and the destination slot were instructed by 2 color cues, the colors of which corresponded with the colors of the object and the slots, respectively. Hence, the visuovisual association between the color cues, the object parts, and the object destinations was nonspatial and comparable across

conditions; what differed was whether the instruction referred to a grasping movement or to a color-defined destination. By independently manipulating novel and repeated presentations of grasping movements and subsequent placing movements, as well as the hand TRAJECTORY between the initial and final position of the object, we could isolate cerebral responses sensitive to these different action components.

## Materials and Methods

### Subjects

Eighteen healthy right-handed male volunteers participated in the study ( $22 \pm 3$  years, mean  $\pm$  standard deviation). They all had normal or corrected-to-normal vision and gave written informed consent according to institutional guidelines of the local ethics committee (CMO region Arnhem-Nijmegen, The Netherlands).

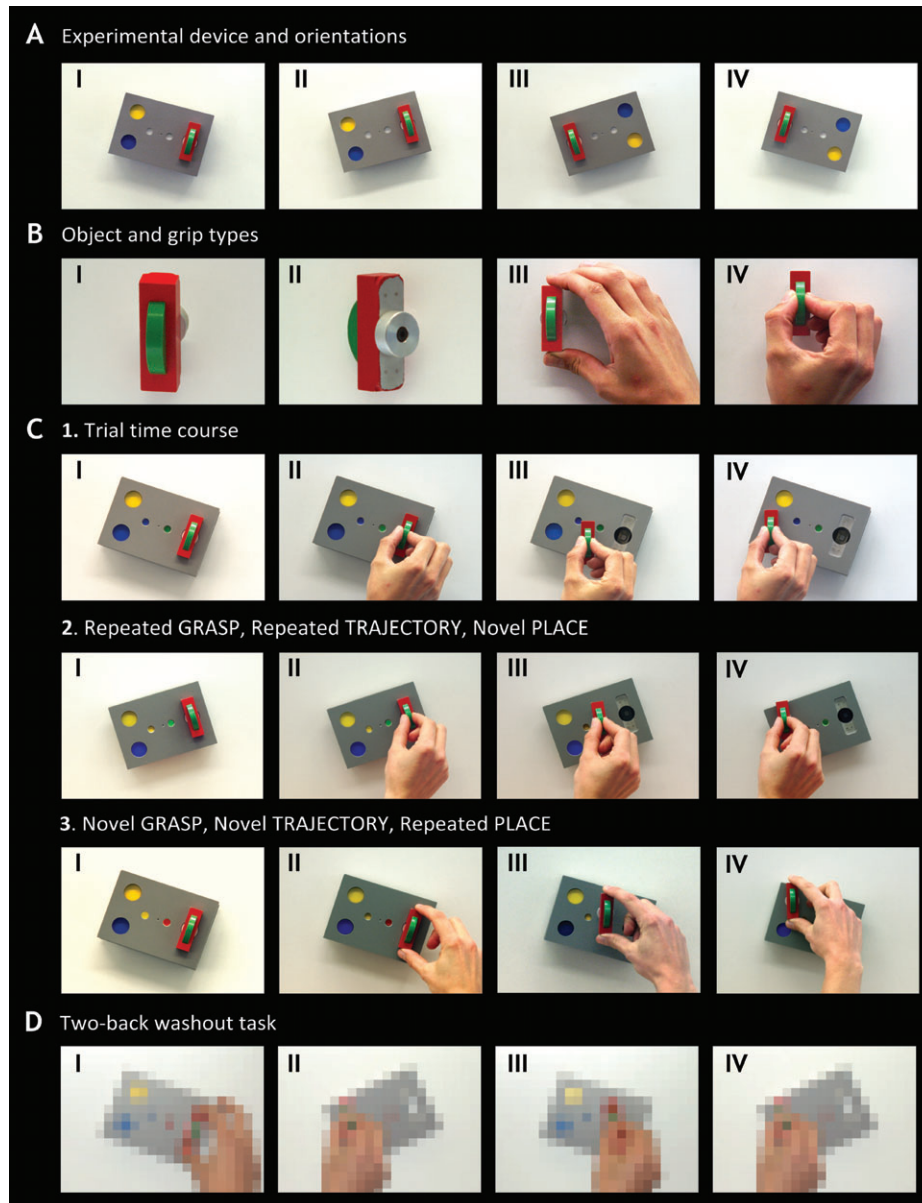
### Experimental Setup and Task Apparatus

Subjects were lying supine in the MR scanner. The visual stimuli were projected onto a screen that the subjects could see via a mirror that was attached to the head coil. An optical response button box (MRI Devices, Waukesha, WI), positioned on the upper leg, was used to record subjects' responses during the task. Presenting the video clips and recording the button responses were carried out using a PC running Presentation 10.1 (Neurobehavioral Systems, San Francisco, CA).

The video recordings of the object manipulations shown in the experiment were made with a Sony Handycam HDD DCR-SR90 Digital HDD video camera. The object manipulations were performed by a right-handed person, using a device that was designed for this purpose (see Fig. 1A). The device consisted of a wooden box that contained 2 circular slots in yellow and blue, respectively. Attached to the box was an aluminum object consisting of a large red bar and a smaller green bar. Fixed to the back of the object was a disk of similar size as the 2 circular slots; in between trials, this disk was positioned into a third slot on the side of the box contralateral to the other slots, serving as a starting position for the object. The object could be removed from the box by grasping it at either the 2 ends of the larger (red) block, which required a nearly full extension of the actor's thumb and index finger, or at the smaller (green) part, which required a precision grip with the thumb and index finger oriented in an angle of  $90^\circ$  with respect to the larger grip (Fig. 1B). By grasping the object using one of these grips, the object could be pulled out from the starting slot, transported toward one of the two colored slots, and inserted into this slot by fitting the disk into it (Fig. 1C). Two small circular slots on the middle of the box, which could take different colors by mechanical rotation of a multicolored disk within the box, served as instruction cues. The instruction cue closest to the object could take the colors red and green; the instruction cue closest to the colored slots could take the colors yellow and blue. By means of an electromotor, the box could be rotated into either an oblique ( $30^\circ$ ) orientation in which the side containing the slots was higher than the object in the starting position (orientation 1; see Fig. 1A I, III) or an oblique orientation ( $-30^\circ$ ) in which the side containing the slots was lower than the object in the starting position (orientation 2) (Fig. 1A II, IV). These 2 orientations were designed such that, in retinal space, the position of the lower slot in orientation 1 overlapped with the position of the higher slot in orientation 2; because the object was located on the rotating axis of the box, its position in retinal space did not change with orientation. Hence, by varying the orientation of the box, the actor's hand trajectory from the object's starting position to the slots could be upward (to upper slot in orientation 1), horizontal, (to lower slot in orientation 1 or upper slot in orientation 2), or downward (to lower slot in orientation 2).

### Experimental Design, Time Course, and Procedure

Subjects were shown video clips of object manipulations performed by an actor. The object manipulations consisted of grasping the object and removing it from the box, transporting it toward one of the two slots,



**Figure 1.** Experimental apparatus and video stimuli. (A) Experimental device, containing circular slots (yellow, blue) and a manipulable object (red–green), in 4 possible configurations (panels I–IV). (B) Details of the manipulable object: front view (panel I) showing the large red block and the small green bar, back view (panel II) showing the disk to be fitted into the circular slots, view of an actor grasping the object at the tips of the red block (panel III), and view of an actor grasping the object on either side of the green bar (panel IV). (C-1) Example of 4 still video frames from a single video (i.e., one trial of the experiment): the blue and green circles in the central portion of the device instruct the actor to grasp the green portion of the object and insert it into the blue slot (panel I); the actor grasps the object at the required part (panel II); the actor transports the object to the slot, following a horizontal trajectory (panel III); finally, the actor inserts the object into the required slot (panel IV). (C-2) (panels I–IV) Example of 4 still video frames from a single video trial that involves a repetition of the GRASP component with respect to the previous trial (C-1), that is, the object is again grasped at the green part; a repetition of TRAJECTORY component, that is, the path from initial position to end position is again horizontal; and a novel PLACE component, that is, the destination slot is now yellow. (C-3) (panels I–IV) Example of 4 still video frames from a trial that involves a novel GRASP component with respect to the previous trial (C-1), that is, the object is now grasped at the red part; a novel TRAJECTORY component, that is, the path from initial position to end position is now diagonal upward; and a repetition of the PLACE component, that is, the destination slot is again yellow. (D) Example of 4 scrambled images used in the 2-back washout task.

and inserting it into the slot (Fig. 1C II–IV). On each video clip, the movements were preceded by color cues on the box that indicated the required manipulation (Fig. 1C I). The instruction slot closest to the object indicated whether the object had to be grasped at the red (large) part or the green (small) part, by turning red or green, respectively, defining the GRASP condition. The instruction slot closest to the destination slots could turn either yellow or blue and, by means of corresponding colors, indicated the slot in which the object had to be inserted. This condition was labeled PLACE. The fact that the box could be rotated into 2 alternative orientations (Fig. 1A) resulted in 3

possible hand trajectories from the starting position toward the slots: a diagonal upward, horizontal, and diagonal downward path (condition TRAJECTORY). Varying the orientation of the box in this way was done to dissociate the characteristics of the PLACE condition from a fixed location in retinal space and from a specific movement path toward it.

Subjects were instructed to monitor whether the movements of the actor on the video were correct, that is, whether the actor grasped the object part and chose the destination slot as indicated by the 2 color cues. As soon as subjects noticed that an error was made by the actor, they had to press a button. When an error in grasping the object was

observed, subjects had to press a button with their right index finger; conversely, when the object was brought toward the incorrect slot, subjects had to press a button with their right middle finger.

The experiment was preceded by a 10-min training session outside the scanner and another 5-min training inside the scanner. The percentage of error trials in these training sessions was high (ca. 20%) to ensure that subjects were attentive and well trained in detecting error trials. The percentage of error trials during the fMRI scanning session was kept low (2.3% or 6 trials). This was done to maximize the amount of trials to be used in the contrasts of the main conditions. The number of GRASP error trials (in which the object was grasped at the wrong part) and PLACE error trials (in which the object was transported to the incorrect slot) was balanced.

Each video trial lasted 4 s. During the first 800 ms, subjects saw the box with the color cues that indicated the required object manipulation. After 800 ms, the actor's hand appeared and performed the object manipulation. The video clip ended once the object had been inserted into one of the slots (Fig. 1C).

In between trials, videos of the box without color cues were shown, lasting 3 s. During these intervals, the box was rotated from the previous orientation, via a horizontal position, to the orientation of the upcoming trial, which could be either the same or different with respect to the preceding trial. On the video clips before the first trials of each block, the initial orientation of the box was horizontal. These rotation intervals were shown to give the subjects a continuous view of the device, even if it was shown in different orientations in subsequent trials. The box was rotated back and forth between trials of repeated orientation to match the amount of motion perceived before trials of repeated and altered orientation.

In the second half of the experiment, the videos showed the device in a different configuration (Fig. 1A III, IV), in which the location of the object and the slots on the box, and hence the direction of the transport movement, was reversed, as were the colors of the upper and lower slots. This was done to avoid a systematic relationship between the characteristics of the GRASP and PLACE conditions and fixed parts of the visual field.

The design resulted in 8 possible object manipulations per block (according to the  $2 \times 2 \times 2$  design of ORIENTATION, GRASP, and PLACE, each with 2 levels). For instance, one of these object manipulations was to grasp the object at its green part (GRASP) and bring it to the blue slot (PLACE), with the box rotated upward (ORIENTATION) (Fig. 1C). For each of the 8 object manipulations, 10 video clips were created. The same was done for the blocks in which the box was oriented upside down. Although the object manipulations were similar, creating multiple video clips for each one ensured that subjects did not see identical video clips during repeated trials but instead saw slight, natural variations between the movements.

Specific RS effects were elicited by systematically manipulating the characteristics of the required object manipulations (GRASP,

TRAJECTORY, and PLACE) over trials. A feature could be either novel or repeated with respect to the previous trial, yielding 2 levels (Novel, Repeated) for all conditions (GRASP, TRAJECTORY, and PLACE). For instance, the required PLACE movement in a trial could be a repetition of the PLACE movement in the previous trial, but the TRAJECTORY and GRASP could be novel (see Fig. 1D). GRASP, TRAJECTORY, and PLACE were never repeated more than once.

The experiment consisted of 28 blocks of 9 video trials, generating a total of 252 trials. Each block was composed of 9 trials of 4 s and 9 rotation intervals of 3 s, preceding the trials, resulting in a block duration of circa 63 s. After each block, a "washout task" was presented. This task was included to minimize carryover RS effects from the last trials of a block onto the first trials of the next block. In the washout task, a series of 10 scrambled images of video frames was shown in succession, with a duration of 2.5 s per image (Fig. 1D). Subjects had to perform a 2-back task, that is, press a button with their right index finger if the image they saw was identical to the second latest one. The video blocks and washout blocks were separated by delay intervals of variable length (3.3–12.1 s between washout and video blocks and 1.3–4.1 s between video and washout blocks) (Fig. 2).

In the experiment, the 8 movements occurred with equal frequency. The first trial of each block was not included in the main analysis. Trials 2–9 of each block were balanced with respect to the number of Novel and Repeated trials within the conditions GRASP, TRAJECTORY, and PLACE, although the amount of Novel trials exceeded the amount of Repeated trials in each condition (58% Novel trials, 42% Repeated trials).

### Behavioral Analysis

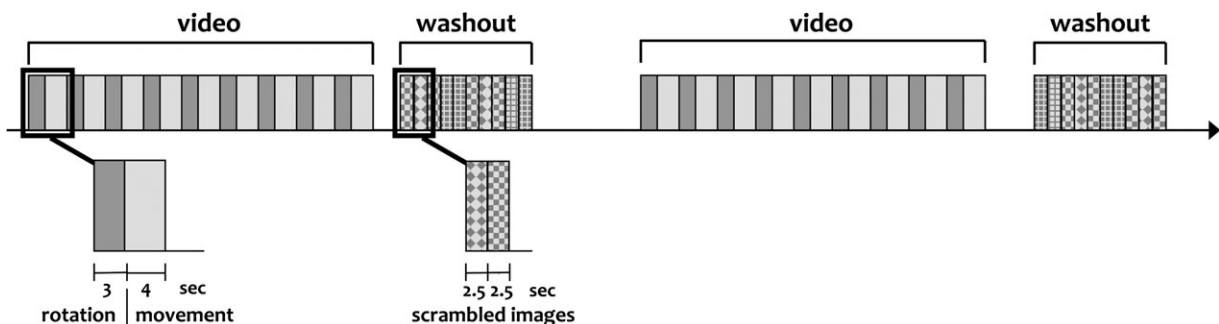
During the experiment, button responses to error trials and the 2-back task were recorded; the timing of these button presses was used to create a regressor modeling of the responses. In addition, correct responses to the error trials (hits) were separated from incorrect responses (false alarms) or missed error trials (misses).

### Image Acquisition

Images were acquired using a Siemens 3-T Trio MRI system (Siemens, Erlangen, Germany). Blood oxygen level-dependent (BOLD) sensitive functional images were acquired using a single-shot gradient echo-planar imaging (EPI) sequence (time repetition [TR]/time echo [TE] = 2.3 s/40 ms, 31 transversal slices, voxel size =  $3.5 \times 3.5 \times 3.5$  mm). At the end of the scanning session, anatomical images were acquired using a magnetization-prepared rapid gradient-echo sequence (TE/TR = 3.93/2300 ms, 192 sagittal slices, voxel size =  $1.0 \times 1.0 \times 1.0$  mm, field of view = 256 mm).

### Image Analysis

Functional data were preprocessed and analyzed with Statistical Parametric Mapping (SPM) 2 (preprocessing and first-level analysis)



**Figure 2.** Experimental time course. There were alternating blocks of action videos and washout trials. A block of action videos was composed of 9 successive trials (4 s each). Before each trial, first the device was shown (3 s, see Fig. 1A); at the start of each trial, the colored instruction appeared in the central portion of the device (see Fig. 1C I), and 800 ms later the actor started performing the instructed object manipulations (3.2 s, see Fig. 1C II–IV). The subject was asked to press a button when the actor performed a wrong movement (2.3% of trials). After 9 trials, and following a delay period of variable length (1.3–4.1 s), the subjects were asked to perform a 2-back memory task, in a washout block of 10 successive trials. In this washout block, 10 successive scrambled images were presented (see Fig. 1D), and the subjects were asked to press a button when the current image was the same as the one shown 2 trials before. The washout task was followed by a rest interval of variable length (3.3–12.1 s) until the next video block (Fig. 2).

and SPM5 (second-level analysis) (www.fil.ion.ucl.ac.uk/spm). The first 5 volumes of each participant's data set were discarded to allow for T1 equilibration. The image time series were spatially realigned using a sinc interpolation algorithm that estimates rigid-body transformations (translations, rotations) by minimizing head movements between each image and the reference image (Friston et al. 1995).

The time series for each voxel was realigned temporally to acquisition of the middle slice. Subsequently, images were normalized onto a custom Montreal Neurological Institute (MNI)-aligned EPI template (based on 26 male brains acquired on the Siemens 3-T Trio at the Donders Institute) using both linear and nonlinear transformations.

Finally, the normalized images were spatially smoothed using an isotropic 10-mm full-width-at-half-maximum Gaussian kernel. Each participant's structural image was spatially coregistered to the mean of the functional images (Ashburner and Friston 1997) and spatially normalized by using the same transformation matrix as applied to the functional images.

The fMRI time series were analyzed using an event-related approach in the context of the general linear model (GLM). In this approach, each trial (corresponding to an action video clip) was modeled as one event. Thus, one event encompassed both the grasping and placing movement components. Due to their proximity in time, the 2 subsequent movements are not distinguishable in terms of BOLD response using a conventional fMRI design, and hence, they cannot be directly compared. Using an RS protocol allowed us to compare each movement phase with its novel or repeated presentation, which are similar in timing. A consequence of this procedure is that time courses describing the late and early movement phases of a trial cannot be statistically discerned within our model. Single-subject models consisted of 8 separate regressors describing observation of the object manipulation videos, according to a  $2 \times 2 \times 2$  design with levels (Novel, Repeated) on the factors GRASP, TRAJECTORY, and PLACE. The first trial of each observation block was modeled by a separate regressor. The duration of each observation trial was 4 s, corresponding to the length of the video clips. In addition, we modeled the washout blocks (duration 10 s). Error trials and button responses (both responses to the washout task and false alarm button presses during the action observation task) were combined into a separate regressor: onsets of button responses (during both video and washout blocks) were derived from the recordings, and responses were assigned a fixed duration of 1 s. The regressor included also error trials not detected by the subject (misses) in order to remove these from the main analysis; onset of these undetected errors was set to 2 s after onset of the video clip, with a duration of 1 s. The videos of the rotating box preceding the trials were considered baseline and not modeled separately.

Each effect was modeled on a trial-by-trial basis as a concatenation of square-wave functions. Each of these 11 square-wave functions were then convolved with a canonical hemodynamic response function and its temporal derivative and downsampled at each scan in order to generate 22 regressors modeling the main effects described above (Friston et al. 1995).

Head movement effects were accounted for as described in Friston et al. (1996) by including a Volterra expansion of the 6 rigid-body motion parameters as nuisance covariates (Worsley and Friston 1995), which consisted of linear and quadratic effects of the 6 realignment parameters belonging to each volume and also included spin-history effects as linear and quadratic effects of motion parameters in the previous volume, giving a total of 24 regressors (Lund et al. 2005).

### Statistical Inference

The statistical significance of the estimated evoked hemodynamic responses was assessed using *t* statistics in the context of a multiple regression analysis. For each subject, 6 contrasts of the parameter estimates for observation of the object manipulation videos were calculated (GRASP Novel [Gn], GRASP Repeated [Gr], TRAJECTORY Novel [Tn], TRAJECTORY Repeated [Tr], PLACE Novel [Pn], and PLACE Repeated [Pr]) and entered into a multiple regression analysis to assess effects at the group level, considering each subject as a random variable.

In our main analysis, we were specifically interested in assessing, for each factor, the *differential* effects of novel versus repeated processing of actions, as compared with other factors. That is, we aimed to isolate

brain areas that showed a decreased response during repeated presentations of one factor (as compared with novel presentations) but no decreased response to repetitions (as compared with novel presentations) of the other factors. Therefore, RS effects evoked by each factor were independently estimated [i.e., GRASP (Gn - Gr), TRAJECTORY (Tn - Tr), and PLACE (Pn - Pr)], and significance was assessed within those voxels showing between-conditions differential RS effects. For instance, search of RS effects to PLACE (Pn - Pr) was confined to voxels with significant ( $P < 0.05$ ) RS  $\times$  condition interactions [i.e., [(Pn - Pr) - (Gn - Gr)] and [(Pn - Pr) - (Tn - Tr)]. In this way, we isolated RS effects specific to a given factor by means of a formal and direct comparison with other conditions.

We report the results of a random-effects analysis, with inferences drawn at the voxel level, corrected for multiple comparisons using family-wise error (FWE) correction (FWE  $< 0.05$ ) and degrees of freedom corrected for nonsphericity at each voxel (Friston et al. 1996). Because we were specifically interested in the responses within dorsal and ventral precentral areas, we created a region of interest that included bilateral Brodmann area (BA) 6 (Geyer 2003) and BA 44 (Amunts et al. 1999), using the SPM Anatomy Toolbox (Eickhoff et al. 2005). Furthermore, to formally test whether the effects we report were lateralized to one hemisphere, we assessed the relevant task  $\times$  hemisphere interactions, using a repeated-measures GLM to compare beta values of condition-specific RS effects at a given local maximum and at the contralateral location.

We performed 2 further post hoc group-level analyses. First, to assess the global pattern of cerebral responses to the observation of the action movies, we contrasted (over the whole brain) the BOLD responses evoked by these movies to the responses evoked by the 2-back washout task. Second, to assess the presence of generic RS effects (i.e., RS effects that did not differentiate between conditions—see main analysis), we contrasted (over the whole brain) the BOLD responses evoked by novel and repeated trials across conditions (i.e., GRASP, PLACE, and TRAJECTORY). Because previous RS studies that distinguished action kinematics, object goals, and outcomes during action observation have yielded effects in posterior parietal areas (Hamilton and Grafton 2006, 2007, 2008), we also confined this post hoc analysis to volumes of interest (VOIs) centered around the coordinates reported in those studies, that is, spheres with a 10-mm radius around the following coordinates: left anterior intraparietal sulcus (IPS; -52, -32, 44 [Hamilton and Grafton 2006]; -52, -20, 38 [Hamilton and Grafton 2007]) and right inferior parietal lobule (58, -30, 32 [Hamilton and Grafton 2008]). Within each VOI, we tested for both generic RS effects and condition-specific RS effects (see main analysis).

### Anatomical Inference

Anatomical details of significant signal changes were obtained by superimposing the relevant SPMs on the structural images of the subjects. The atlas of Duvernoy (1999) was used to identify relevant anatomical landmarks. When applicable, BAs were assigned on the basis of the SPM Anatomy Toolbox (Eickhoff et al. 2005).

## Results

### Behavioral Performance

The subjects were attentive to the GRASP and PLACE movements performed by the actor, detecting on average 95% of the observed erroneous object manipulations (i.e., 5% misses), with 1.4% of false alarms.

### Imaging Data

#### Main Analysis-Specific RS Effects

RS effects evoked by GRASP but not by TRAJECTORY and PLACE were found in the right inferior frontal cortex (64, 10, 4; Table 1 and Fig. 3). This response was assigned with 50% probability to BA 44 (Amunts et al. 1999; Eickhoff et al. 2005)

being anterior to the inferior part of BA 6 and was classified as PMv (Rizzolatti et al. 2002). Formal testing of the RS effect  $\times$  hemisphere interaction revealed that this cluster showed a strong tendency for being lateralized to the right hemisphere ( $F_{1,17} = 4.13, P = 0.06$ ).

RS effects evoked by PLACE but not by the other conditions were found over the left dorsal precentral cortex ( $-24, -14, 62$ ) (Table 1 and Fig. 4). This cluster fell within the 50% probability border of BA 6 (precentral gyrus) and was classified as PMd (Geyer 2003). Its maximum was located circa 15 mm anterior

to the center of cytoarchitecturally defined BA 4a and 4p within M1 (Geyer et al. 1996), suggesting that the cluster may correspond to the rostral portion of PMd, known as pre-PMd (Picard and Strick 2001). Formal testing of the RS effect  $\times$  hemisphere interaction revealed that this cluster was lateralized to the left hemisphere ( $F_{1,17} = 4.35, P = 0.05$ ). There was also a second, smaller cluster of activity in dorsal precentral cortex ( $-32, -13, 52$ ), along the left precentral sulcus.

There were no significant RS effects specifically evoked by TRAJECTORY, over and above those evoked by GRASP or PLACE.

**Table 1**

MNI coordinates of the clusters of activation showing differential RS to GRASP and PLACE, obtained by comparison of novel versus repeated trials

Movement component	Anatomical region	Laterality	MNI coordinates			T value	P value
			x	y	z		
GRASP	Inferior frontal cortex (PMv)	R	64	10	4	4.2	0.038
PLACE	Precentral cortex	L	-32	-12	44	4.3	0.029
PLACE	Precentral cortex (PMd)	L	-24	-14	62	5.0	0.003

Note: All results are corrected for multiple comparisons across the search volume using an FWE correction method with a threshold of  $P < 0.05$ . R, right; L, left.

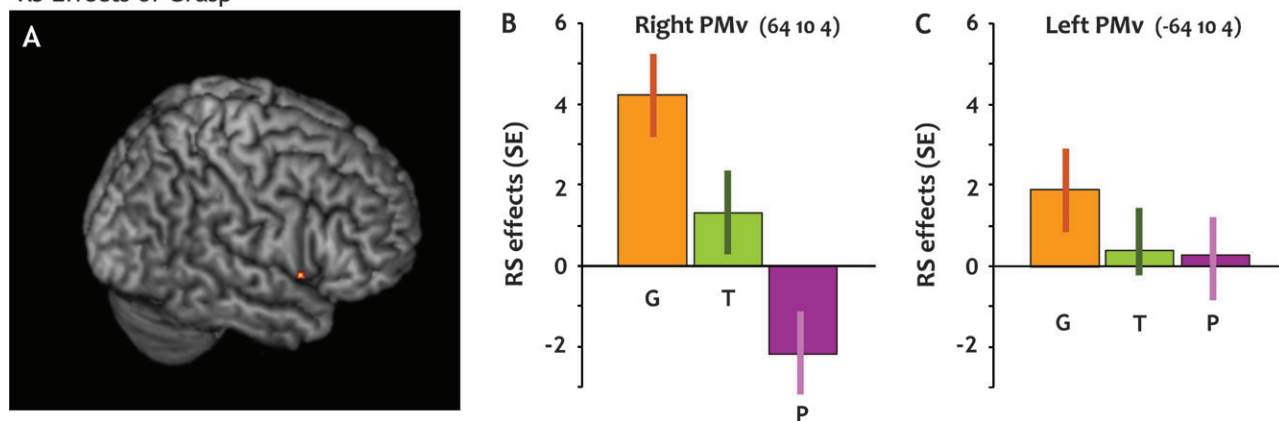
### Activity Related to Action Observation

Figure 5 shows the overall activity related to observing the action movies, over and above performing the 2-back task. Observation of the color cues and subsequent movements in the action videos evoked activation within a distributed parietofrontal network.

### Generic RS Effects

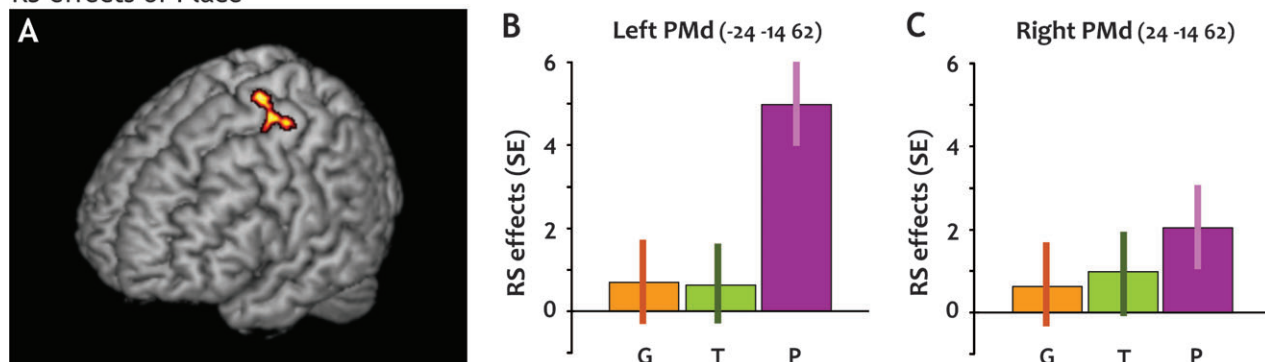
We also assessed whether the action observation task induced any generic RS effects in our subjects, by contrasting novel with repeated GRASP, PLACE, and TRAJECTORY trials. Whole-brain

### RS Effects of Grasp



**Figure 3.** Differential RS effects following repeated processing of GRASP. SPM (A) and effect size of differential RS effects in left (B) and right (C) hemispheres. There were larger RS effects during repeated processing of GRASP than TRAJECTORY or PLACE in the PMv in the right hemisphere. Panel A illustrates the results of a random-effects analysis, superimposed on a rendered representative brain of the MNI series. Panel B illustrates the effect size (in standard error [SE] units) estimated for the RS effect (i.e., novel vs. repeated trials) estimated for each movement component (i.e., GRASP, G; TRAJECTORY, T; and PLACE, P) in the right PMv. Panel C illustrates the effect size (in SE) of the RS effects in the contralateral coordinate in left PMv. As can be seen, the RS effects to GRASP are lateralized to the right hemisphere.

### RS effects of Place

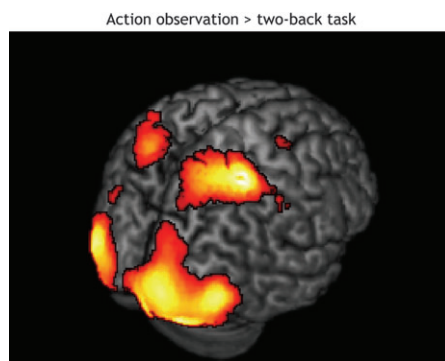


**Figure 4.** Differential RS effects following repeated processing of PLACE. SPM (A) and effect size of differential RS effects in left (B) and right (C) hemispheres. There were larger RS effects during repeated processing of PLACE than GRASP or TRAJECTORY in the PMd in the left hemisphere. Panel A illustrates the results of a random-effects analysis, superimposed on a rendered representative brain of the MNI series. Panel B illustrates the effect size (in standard error [SE] units) of the RS effect (i.e., novel vs. repeated trials) estimated for each movement component (i.e., GRASP, G; TRAJECTORY, T; and PLACE, P) in the left PMd. Panel C illustrates the effect size (in SE) of the RS effects in the contralateral coordinate in right PMd. As can be seen, the RS effects to PLACE are lateralized to the left hemisphere.

analysis revealed significant voxels (FWE corrected for search volume,  $P = 0.048$ ) within the right occipital cortex (local maximum at 28, -86, -12). VOI-based analysis centered on previously reported action-related RS effects within the parietal cortex (Hamilton and Grafton 2006, 2007, 2008) revealed significant voxels (FWE corrected for search volume,  $P < 0.05$ ) in the left anterior IPS (local maxima at -44, -28, 40; -44, -24, 36; and -44, -26, 44). Figure 6 illustrates the spatial distribution and the RS effects estimated in these regions. It can be seen that these RS effects do not differentiate between GRASP, PLACE, and TRAJECTORY. There were no suprathreshold condition-specific RS effects within the inferior parietal VOIs based on previous reports (Hamilton and Grafton 2006, 2007, 2008).

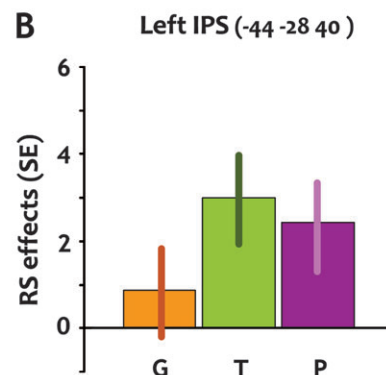
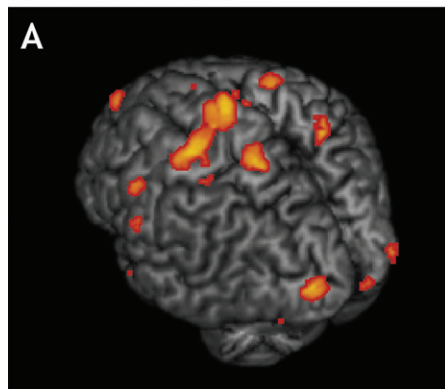
## Discussion

In the present study, we examined the premotor responses evoked during the observation of distinct motor elements combined into goal-directed object manipulations. We have used an RS protocol (Grill-Spector and Malach 2001) to isolate reductions in neuronal activity evoked by repeated processing of movement components related to either a grasping movement (GRASP) or to positioning the grasped object on a color-



**Figure 5.** Cerebral effects of observing the action videos, as compared with performing the 2-back memory task during the washout trials. SPMs of significant ( $P < 0.05$ , corrected for multiple comparisons) differential effects of observing action videos versus viewing scrambled images. There were effects, bilaterally, in occipital, parietal, and frontal areas.

## Generic RS effects



**Figure 6.** Generic RS effects following repeated processing of the action videos, irrespectively of movement component. SPM (A) and effect size (B) of RS effects that did not differentiate between movement components. Significant effects could be found across the cerebral cortex. Panel A illustrates the results of a random-effects analysis ( $P < 0.05$ , corrected for multiple comparisons) superimposed on a rendered representative brain of the MNI series. Panel B illustrates the effect size (in standard error [SE] units) of the RS effect (i.e., novel vs. repeated trials) estimated for each goal level (i.e., GRASP, G; TRAJECTORY, T; and PLACE, P) within VOIs (10-mm radius) centered around the left anterior IPS (-52, -32, 44 and -52, -20, 38), that is, at coordinates previously reported to be involved in processing action goals (Hamilton and Grafton 2006, 2007).

defined destination (PLACE). These movement components could be independently varied and were combined into meaningful actions. Repetition of the type of hand-object interaction (GRASP) reduced the response of a ventral precentral region of the right hemisphere. Repetition of the end state of the action (PLACE) reduced the response of the left dorsal precentral cortex. These findings support the notion that the ventral and dorsal portions of the human precentral gyrus process different action features. Namely, PMv appears to be involved in processing sensory properties of a stimulus to guide movement (Hoshi and Tanji 2006; Grol et al. 2007), whereas PMd extracts learned stimulus-response mappings, irrespectively of the spatial characteristics of the movements (Toni et al. 2001; Hoshi and Tanji 2006).

## Grasping

The repeated processing of trials with the same GRASP revealed RS effects in the ventral portion of the precentral gyrus (Fig. 3), that is, in the same region known to be involved in preparing reaching-grasping movements (Toni et al. 2001). These effects were differential in nature, suggesting that this region is specifically involved in processing an instructed goal (the part of the object to be grasped) that is spatially and temporally contiguous to the movement (the grip to use). In other words, the common features processed across repeated presentations of GRASP trials are related to the visuospatial properties of the grasped object part. This interpretation is consistent with the general notion that this portion of the motor system is involved in specifying spatial parameters of hand movements (Gentilucci et al. 1988; Kakei et al. 2001; Shadmehr and Wise 2005). The PMv involvement in processing GRASPs might also be seen as an instance of the ability of the ventral frontal cortex to identify stimuli and responses that are behaviorally relevant in the immediate future (Corbetta and Shulman 2002).

## Placing

The RS effects evoked by processing of trials with a repeated PLACE movement were localized in the dorsal portion of the precentral gyrus (pre-PMd [Picard and Strick 2001]). These RS effects were differential in nature, that is, stronger following

repeated presentation of actions with the same final destination than following repeated presentation of actions with the same type of grasping movement or hand trajectory. Accordingly, we infer that these differential RS effects isolate those premotor areas involved in specifying the features of the end position of the action, irrespectively of the initial grasping movement and of the movement between the initial and end position of the object.

Due to the fact that the orientation of the box was varied over trials (Fig. 1), the common features processed across repeated presentations of PLACE trials are related to the color and the object-centered position of the target slot. Accordingly, the RS effect in pre-PMd was largely abstracted from visuomotor properties. This confirms the notion that the role of PMd in action selection goes beyond its ability to code the spatial parameters of reaching movements. Rather, our findings are in line with the idea that the PMd might represent the “pragmatic meaning” of an action, that is, a movement- and effector-independent representation of its desired end state (Schubotz et al. 2008). More generally, the results are consistent with the known ability of the dorsal frontal cortex to manipulate abstract representations of stimuli and responses to select actions on the basis of future expectations (Petrides 2005; Koehlin and Summerfield 2007; Mars et al. 2008).

### **Interpretational Issues**

Differently from previous studies using RS paradigms (Hamilton and Grafton 2006, 2007, 2008; Lehky et al. 2006; Mahon et al. 2007), the present experiment was explicitly designed to induce planning of the required movements in subjects. First, the color cues indicating the required manipulations were presented in advance of the action movie; second, subjects were asked to judge the correctness of the observed actions on each trial. The high detection rate of violations of the arbitrary sensorimotor mappings and the activation of a distributed parietofrontal network during observation of the instruction cues and subsequent movements (Fig. 5) suggest that the observed actions induced first-person sensorimotor processes.

The present findings might appear at odds with recent results using a similar RS-fMRI approach (Hamilton and Grafton 2006, 2007, 2008). In those studies, action outcomes were differentiated according to their outcome level (from immediate to final). It was shown that repeated processing of the target object of a grasping act (“object goal”) evoked RS effects in the left anterior IPS (Hamilton and Grafton 2006, 2007), whereas repeated processing of the physical outcome of the action (for instance, an opened box) produced RS in right inferior parietal lobule (Hamilton and Grafton 2008). This discrepancy is likely related to differences in the analytical procedures: the parietal effects reported by Hamilton and Grafton were observed by assessing general RS effects evoked by a given outcome level, irrespectively of RS effects evoked by other outcome levels. In contrast, here we have isolated specific (i.e., differential) RS effects between different movement components. Accordingly, we could replicate the presence of general RS effects in VOIs centered around the coordinates reported by Hamilton and Grafton, but we did not find any GRASP- or PLACE-specific RS effects in those VOIs (Fig. 6). These results suggest that RS effects previously reported in inferior parietal cortex might reflect overlapping responses to different outcome levels rather than outcome-specific

responses. This is not to deny that other portions of posterior parietal cortex might process action plans at specific outcome levels. For instance, we recently reported that the posterior part of the left supramarginal gyrus showed stronger preparatory activity when actions were cued with their final goal than with their immediate goal (Majdandžić et al. 2007). Furthermore, in the present study, a whole-brain analysis of the RS effects specific to the PLACE condition revealed a small cluster in the left superior parietal lobule (24, -52, 68). The issue of whether posterior and inferior portions of parietal cortex might have different roles in processing action targets and outcomes remains a subject for future research.

It might be argued that the present RS effects might be due to different oculomotor or attentional demands between PLACE and GRASP. For instance, although the spatial location of the PLACE target (across repeated trials) was dissociated from a specific location in the visual field, it remained invariant with respect to the experimental device (Fig. 1D), raising the possibility that the RS effects observed in PLACE are driven by object-centered attentional phenomena (Olson 2003). In addition, in macaques, the pre-PMd, or F7 (Matelli et al. 1991), includes the supplementary eye field (SEF) (Schall 1991; Picard and Strick 2001), a region crucially involved in object-centered attention (Olson 2003). However, this interpretation is not compatible with the left-lateralized characteristics of the RS effects (Fig. 3) and with the spatial mismatch (>20 mm) between the putative location of human SEF and the present pre-PMd cluster (Luna et al. 1998; Grosbras et al. 1999; Merriam et al. 2001).

The lateralization to the left hemisphere of the PLACE effects in PMd might be driven by the fact that we scanned right-handed subjects observing right-hand movements. Yet, this explanation is not compatible with the right hemispheric lateralization of the RS GRASP effect in PMv. In fact, the pattern of lateralized effects we observed fits with previous reports indicating that the left premotor cortex is distinctively involved in selecting and preparing instructed motor responses involving either hand (Schluter et al. 1998; Verstynen et al. 2005; de Lange et al. 2006). The right-lateralized effect in PMv is congruent with previous reports indicating that the right premotor cortex seems privileged in integrating visuomotor information for spatially guided movements of either hand (Toni et al. 2001; Wenderoth et al. 2006).

### **Conclusions**

In the present study, we have tested whether distinct, successively performed movement components of an observed action evoke differential responses in ventral and dorsal premotor areas. Rather than studying individual movements in isolation, our experiment examined motor events embedded in a functional context, using an RS protocol. Having controlled for the effects of repeated processing of arm movements, we show that processing hand-object interactions was associated with increased involvement of PMv, whereas processing the movement end position was associated with activity in PMd.

Our findings suggest that PMd and PMv can be distinguished on the basis of their ability to specify a desired end state of an action and to control the kinematic means of an appropriate hand-object interaction. This categorization appears to reconcile some of the existing models of premotor function, that is, the notions of direct versus indirect sensorimotor mapping



(Hoshi and Tanji 2006, 2007), spatially guided versus arbitrarily instructed movements (Passingham 1993), and grasping versus reaching selection (Jeannerod 1988). We suggest that these dichotomies can be seen as instances of a general distinction between processing actions according to immediate or remote outcomes (Majdandžić et al. 2007). It remains to be seen whether this distinction generalizes across movements different from prehension and across different effectors.

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## Notes

*Conflict of Interest:* The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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