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# Real and imagined grasping movements differently activate the human dorsomedial parietal cortex

Valentina Sulpizio<sup>1\*,3</sup>, Anna Neri<sup>4</sup>, Patrizia Fattori<sup>1</sup>, Claudio Galletti<sup>1</sup>, Sabrina Pitzalis<sup>2,3</sup> and Gaspare Galati<sup>3,4</sup>

<sup>1</sup> Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

<sup>2</sup> Department of Movement, Human and Health Sciences, University of Rome "Foro Italico", Rome, Italy

<sup>3</sup> Cognitive and Motor Rehabilitation and Neuroimaging Unit, Santa Lucia Foundation (IRCCS Fondazione Santa Lucia), Rome, Italy

<sup>4</sup> Brain Imaging Laboratory, Department of Psychology, Sapienza University, Rome, Italy

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**\*Correspondence:**

Valentina Sulpizio, PhD

Biomedical and Neuromotor Sciences - DIBINEM

University of Bologna

Piazza di Porta San Donato 2

40126 - Bologna (Italy)

Phone: 00390512091748

email: [valentinasulpizio@gmail.com](mailto:valentinasulpizio@gmail.com)

## Abstract

Object prehension typically includes a transport phase (reaching) and a grip phase (grasping). Within the posterior parietal cortex (PPC), grasping movements have been traditionally associated to a lateral activation, although recent monkey evidence suggests also a medial involvement. Here, we wanted to determine whether grasping-related activities are present in the human dorsomedial parietal cortex, by focusing on two cortical regions specialized in the monkey in controlling limb movements, i.e., V6A (composed by its ventral and dorsal sectors, V6Av and V6Ad, respectively) and PEc, both recently defined also in humans. We acquired functional magnetic resonance images while participants performed both real (pantomimed) and imagined grasping of visually-presented objects. We found that the human areas V6Ad (hV6Ad) and PEc (hPEc) were both activated by real grasping, whereas hV6Ad only was activated by the imagery of grasping movements. hV6Av was not involved in either types of grasping. These results speak against the traditional notion of a medial-to-lateral segregation of reaching versus grasping information within the PPC and strengthen the idea that the human dorsomedial parietal cortex implements the whole complex pattern of visuomotor transformations required for object-oriented actions. Our findings suggest that hV6Ad is particularly involved in implementing all the visuomotor transformations needed to create an abstract representation of the object-directed action, while hPEc is involved in implementing the sensorimotor transformations needed to actually perform that action.

**Keywords:** precuneate cortex; human V6A; human PEc; hand orientation; motor imagery; functional magnetic resonance.

## Introduction

Prehension of an object requires both transporting the hand toward the object (reaching component) and shaping the hand according to it (grip component). The classic dominant view, derived from monkey studies (Jeannerod et al., 1995) and that remains deeply influential even to date (Rizzolatti and Kalaska, 2013), posits that these components are largely anatomically segregated within the posterior parietal cortex (PPC): the dorsomedial PPC, which primarily includes area V6A, P<sub>Ec</sub> and the medial intraparietal area (MIP), would be involved in reaching movements (Colby and Duhamel, 1991; Ferraina et al., 2001; Battaglia-Mayer et al., 2000; Fattori et al., 2001, 2005), while the dorsolateral PPC, especially the anterior intraparietal area (AIP), would be involved in grasping movements (Sakata et al., 1995; Murata et al., 2000; Baumann et al., 2009). However, several lines of evidence are not entirely consistent with the notion of independent neural coding for grasp and reach movements, particularly with respect to the macaque area V6A (Galletti et al., 2003; Fattori et al., 2004, 2017; Galletti and Fattori, 2018 for recent review). Monkey area V6A shows grasping-related responses, besides reaching-related ones, reflecting sensitivity to wrist orientation and grip formation (Fattori et al., 2009, 2010; Gamberini et al., 2011; Breveglieri et al., 2016, 2018). In addition, it has been demonstrated that different grasping-relevant information, such as grip types and hand configurations, can be decoded from V6A activity pattern (Filippini et al., 2017; Nelissen et al., 2018). Mainly based on this evidence, it has been recently proposed that V6A is involved in the fast control of visually-guided prehension, including object grasping (Fattori et al., 2017; Galletti and Fattori, 2018).

As shown in Figure 1, macaque area V6A is located in the anterior bank of the parieto-occipital sulcus (POs). The area has been divided in a ventral (V6Av) and a dorsal (V6Ad) sector based on cytoarchitectonic criteria (Luppino et al., 2005). Both sectors host visual and somatosensory cells, with area V6Av showing a majority of visual cells and area V6Ad a majority of cells sensitive to somatic stimulation (Gamberini et al., 2011). Both subdivisions of area V6A respond to reach-to-grasp actions (Gamberini et al., 2011; Breveglieri et al., 2016, 2018), and V6Ad is particularly involved in controlling the hand-to-object interaction, with cells selectively modulated by the type of grip used (Fattori et al., 2010). Moving anteriorly from V6Ad, the dorsomedial PPC hosts a distinct cytoarchitectonic area, called P<sub>Ec</sub> (Pandya and Seltzer, 1982). Area P<sub>Ec</sub> is specialized in the integration of hand- and eye-related information (Ferraina et al.,

2001), is well equipped to control arm-reaching actions (Hadjidimitrakis et al., 2015; Piserchia et al., 2017), and shares many somatosensory and visual properties with V6A (Gamberini et al., 2018). At present, however, PEc cells have not yet been specifically tested for grasping. Overall, macaque evidence supports the notion that at least one area (V6A) of the dorsomedial circuit is recruited by grasping movements (Fattori et al., 2017).

In humans, grasping-related activity has been mainly associated to the dorsolateral PPC, with many studies reporting activations in a region in the anterior IPS sulcus (aIPS), a likely human homologue of monkey AIP, during reaching-to-grasp (Culham et al., 2003; Hinkley et al., 2009; Frey et al., 2005; Grafton et al., 1996), haptic object manipulation (Hinkley et al., 2009; Binkofski et al., 1999), arm transport and grip formation (Cavina-Pratesi et al., 2010), and pantomimed grasping (Shikata et al., 2003; Simon et al., 2002; Johnson-Frey et al., 2005; Króliczak et al., 2007; Bozzacchi et al., 2012; Makuuchi et al., 2012). Recently, a growing number of studies have started to report grasping-related activity also on the most medial part of human PPC, as in macaque. These studies reported grasping-related foci of activation in the cortical territory extending from the dorsalmost part of the POs to the cingulate sulcus (Monaco et al., 2011; Gallivan et al., 2011; Gutteling et al., 2015; Vesia et al., 2017; Styrkowiec et al., 2019; see also Fattori et al., 2017 for a recent review). In particular, by using decoding techniques from activation patterns and adaptation, it has been observed that the cortical region likely corresponding to the human homolog of macaque area V6A (hV6A; Pitzalis et al., 2013; Tosoni et al., 2015) plays a role in processing wrist orientation and grip formation (Gallivan et al., 2011; Monaco et al., 2011), well in line with clinical observations that lesions to the same cortical region do not only lead to reaching errors, but also to difficulties in achieving an appropriate wrist posture (Jeannerod 1986; Perenin and Vighetto 1988; Jakobson et al., 1991). Although macaque area PEc has never been explicitly tested with grasping tasks, recent fMRI data on humans reveal the recruitment of the anterior precuneus, where PEc is located in the macaque (see Figure 1), during action tasks like reaching and grasping (Monaco et al., 2011), in haptically guided grasping of tools (Styrkowiec et al., 2019), and when a multivoxel pattern classifier was applied to discriminate between grasping and pointing movements (Gutteling et al., 2015). Notably, however, all these studies, described such dorsomedial activations in terms of whole-brain neural circuits, not ascribed to specific dorsomedial parietal areas.

The cortical territory extending in humans from the POs to the cingulate sulcus has been recently described by our group as hosting the human homologues of monkey V6 (Pitzalis et al., 2006; 2015), V6Av (Pitzalis et al., 2013; 2015), V6Ad (Tosoni et al., 2015; Pitzalis et al., 2019), and PEc (Pitzalis et al., 2019). These regions show a trend in the functional specialization following a posterior-to-anterior axis, with the most posterior hV6 and hV6Av involved in the visual analysis of motion (Pitzalis et al., 2010) and the anterior hV6Ad and hPEc specialized in the visuomotor control of arm (Tosoni et al., 2015) and arm/leg (Pitzalis et al., 2019) movements, respectively. However, the role of these regions during grasping is still largely unexplored.

Here, we wanted to determine whether grasping-related activity is present in the dorsomedial PPC areas hV6A, as it is the case in monkey (Fattori et al., 2017), and hPEc, as suggested by the above recalled recent reports in humans (Monaco et al., 2011; Styrkowiec et al., 2019; Gutteling et al., 2015). To this aim, we acquired functional magnetic resonance images while participants performed: 1) a pantomimed grasping action requiring to execute the complex pattern of hand movements (extension/flexion of fingers and wrist rotation) necessary to grasp a visually-presented object (real grasping), and 2) an imagined grasping action requiring to mental simulate the grasping of that particular object, and thus in the absence of real hand/fingers movements (imagined grasping). Since we were interested in grasping only (i.e., the shaping of the hand in relation to the shape and size of the object), without reaching, we explicitly asked participants to imagine the object very close to their hand so as to abolish the transport phase of the hand toward the object.

Following the above recalled fMRI evidence suggesting the involvement of dorsomedial regions (including areas hV6A and hPEc) in coding aspects of executed grasping movements (Monaco et al., 2011; Gallivan et al., 2011, Gutteling et al., 2015; Vesia et al., 2017; Styrkowiec et al., 2019), we hypothesized that both of these areas should respond to real grasping. Additionally, based on previous reports showing the anterior precuneus (including area hPEc) as predominantly proprioceptive-motor and the anterior POs (including area hV6Ad) as predominantly visuomotor (Filimon et al., 2009; Pitzalis et al., 2019), we expected to find a different sensitivity with respect to the 'pure visual' condition (imagined grasping). Finally, based on previous macaque reports demonstrating a higher visual sensitivity of V6Av and somatic sensitivity of V6Ad (Gamberini et al., 2011), we hypothesized a different functional

profile between the ventral and dorsal partitions of human area V6A. All these hypotheses have been verified in the present work, strongly supporting the view that, besides reaching, the dorsomedial parietal cortex is involved in selecting appropriate hand motor programs for grasping.

Overall, our results suggest a functional specialization within the dorsomedial PPC, with the dorsal (but not the ventral) sector of hV6A involved in creating a more abstract representation of the grasping action, being activated by both real and imagined grasping, and hPEc involved in more pragmatic aspects of that action, being activated by the real grasping only. The specific involvement of hV6Ad and hPEc in the control of hand action remains however largely unexplored being investigated here for the first time.

## Methods

### Participants

Twenty-five neurologically normal volunteers (22 females, mean age 26.5 s.d. 3.4) participated in the study. All participants were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971) and had normal or corrected-to-normal vision. All volunteers gave their written informed consent to participate in this study, which was approved by the local research ethics committee of the IRCCS Fondazione Santa Lucia in Rome, according to the Declaration of Helsinki.

### Stimuli and Task

Digitized black-and-white photographs of 34 different graspable objects commonly used in everyday life (Figure 2A) were presented in central vision. According to a written instruction, participants were required to perform a pantomime of an actual grasping by shaping the hand accordingly with the presented object (real condition, Figure 2B) or to imagine that movement without shaping the hand (imagined condition, Figure 2B). In our 'real' grasping condition, participants were instructed to move their fingers (extension and flexion) and to rotate their wrist in order to simulate the grasping of the visually-presented object, as if that particular object was located in the proximity of their hand. In the imagined condition, participants were



instructed to imagine the same pattern of movements without any actual hand movement. Although in the “real” condition participants did not actually interact with the object, we labelled this condition as “real” to account for the fact that, differently from the imagined condition, participants were required to actually move their hand. Although we are aware that there are important differences between pantomimed and actual grasping (Goodale et al., 1994; Króliczak et al., 2007), it has been proved that pantomimed grasping leads to parietal activations comparable to those elicited by actual grasping (Simon et al., 2002). Notice that in both real and imagined conditions, participants could not watch their hand, and their hand movements were performed with respect to a ‘remembered’ object not present anymore on the screen.

Both real and imagined blocks (16 s) were introduced by a 1-s written instruction presented at the center of the screen to inform the participants about the task to be performed, followed by eight consecutive trials. Each trial lasted 1875 ms and included the presentation of the graspable object photograph for 300 ms, followed by an inter-trial-interval of 1575 ms during which a pantomime of a real grasping or an imagined grasping were performed (Figure 2B). Before entering the scanner, participants completed a five-minutes training phase requiring them to familiarize with the real grasping movements. 34 practice trials (one for each object) were presented while participants were seated in front of the computer monitor located outside the MR room. Participants were instructed to extend and flex their fingers and to rotate the wrist in order to pantomime the grasping of each (visually presented) object as if that particular object was located just in front of their hand, very close to it. In particular they were required to adjust their fingers/wrist configuration as appropriate as possible for the objects presented and to make an aperture/closure of their hand as much as they needed to grasp the object. In no case participants had to imagine using the object. Additionally, they were required to refrain to move their shoulder/arm/forearm and to complete the movement before the next picture was presented. During this training phase, an experimenter checked whether participants moved their hand as requested in the instruction and provided feedback about the possible occurrence of no-required movements (shoulder and arm).

Then in the scanner, participants performed a short warm-up phase within the bore to familiarize again with the task. During the scanning session, an experimenter checked whether participants moved their hand only in the real grasping blocks and whether the movement

lasted as requested. All participants correctly followed the instructions and performed the task as requested. No appreciable differences of gesture amplitude across participants were observed.

The central fixation cross was always provided throughout all the experiment (also during the appearance of the photographs) to avoid exploratory eye movements. Each experimental run included eight blocks of real grasping (grasp), eight blocks of imagined grasping (imagine), and four blocks of fixation (fix).

#### Apparatus and procedure

Participants lay supine in the scanner, with both arms along the sides of their body and with their right hands positioned palm down. Any movement of head/shoulder/elbow was minimized by foam pads and a further circularly shaped foam cushion was positioned under the participants' wrist to support the hand. In order to minimize movements during the scans, subjects' heads were stabilized with foam padding and with a chin rest mounted inside the head coil.

Functional images were acquired using a 3T Siemens Allegra MR system (Siemens Medical systems, Erlangen, Germany) equipped for echo-planar imaging with a standard head coil and operating at the Neuroimaging Laboratory, Foundation Santa Lucia. Visual stimuli were presented by a control computer located outside the MR room, running in-house software ([Galati et al., 2008](#)) implemented in MATLAB (The MathWorks Inc., Natick, MA, USA). We used an LCD video projector with a customized lens to project visual stimuli to a projection screen positioned at the back of the MR tube. Visual stimuli were thus visible by participants through a mirror positioned inside the head coil. The timing of presentation of each stimulus was controlled and triggered by the acquisition of fMRI images.

We used blood-oxygenation level-dependent imaging ([Kwong et al., 1992](#)) to acquire echo-planar functional MR images (TR=2s, TE=30ms, flip angle=70°, 64×64 image matrix, 3 × 3 mm in-plane resolution, 30 slices, 2.5 mm slice thickness with no gap, ascending excitation order) in the AC–PC plane. Images were acquired starting from the superior convexity and extended ventrally so that to include the whole cerebral cortex, except for the ventral portion of inferior temporal and occipital gyri. For each participant we also acquired a three-dimensional high-

resolution anatomical image (Siemens MPRAGE sequence, TR=2s, TE=4.38ms, flip angle=8°, 512×512 image matrix, 0.5 × 0.5 mm in-plane resolution, 176 contiguous 1 mm thick sagittal slices). For each scan, we discarded the first four volumes in order to achieve steady-state, and the experimental task was initiated at the beginning of the fifth volume.

Each subject underwent a single acquisition session constituted by two functional scans and one anatomical scan. Each functional scan lasted 5'28" (160 functional MR volumes).

### Image Processing and Analysis

Images were preprocessed and analyzed using SPM12 (Wellcome Department of Cognitive Neurology, London, UK) and FreeSurfer 5.1 (<http://surfer.nmr.mgh.harvard.edu/>).

We first analyzed structural images following the “recon-all” fully automated processing pipeline implemented in FreeSurfer 5.1. This procedure allows us to obtain a surface representation of each individual cortical hemisphere in a standard space after performing intensity correction, transformation to Talairach space, normalization, skull-stripping, subcortical and white-matter segmentation, surface tessellation, surface refinement, surface inflation, sulcus-based nonlinear morphing to a cross-subject spherical coordinate system, and cortical parcellation (Dale et al., 1999; Fischl et al., 1999a,b; Desikan et al., 2006). The resulting surface reconstructions were transformed to the symmetrical FS-LR space (Van Essen et al., 2012) using tools in the Connectome Workbench software (<https://www.humanconnectome.org/software/get-connectome-workbench>), resulting in surface meshes with approximately 74K nodes per hemisphere.

Functional images were realigned within and across scans to correct for head movement and coregistered with structural MPRAGE scans using SPM12 (Wellcome Department of Cognitive Neurology, London, UK). Functional data were then resampled to the individual cortical surface using ribbon-constrained resampling as implemented in Connectome Workbench (Glasser et al., 2013), and finally smoothed along the surface with an iterative procedure emulating a Gaussian kernel with a 6 mm full width at half-maximum (FWHM).

Functional images were then analyzed for each participant separately on a vertex-by-vertex basis, according to the general linear model (GLM). Neural responses during “active” blocks

(real and imagined conditions) were modeled as box-car functions, convolved with a canonical hemodynamic response function and used as predictors in the GLM, with separate predictors for each condition. Passive blocks (fixation) were not explicitly modelled as GLM regressors and were thus treated as part of residual variance. Six head movement-related parameters (three for translations and three for rotations) were included as nuisance regressors.

Parameter estimated images from each participant and condition entered a group analysis where subjects were treated as a random effect. Group-level statistical parametric maps were obtained through a series of one sample t-tests comparing activity in each “active” block with the “passive” fixation block. We also performed direct contrasts between the two conditions. For all the above-described comparisons we created several statistical parametric maps, each of them thresholded at  $p < 0.05$  FDR-corrected at the cluster level, with a cluster-forming threshold of  $p < 0.001$  uncorrected.

Further analyses were conducted to account for the possibility that images could evoke different grip types or different amount of wrist rotation. To this aim we conducted two separate analyses in which each stimulus was modeled accordingly to whether it was associated, in a preliminary questionnaire (see supplementary materials), to 1) a ‘whole-hand’ prehension or to a ‘finger’ prehension, or to 2) a ‘small’ or ‘large’ amount of wrist rotation. We used separate regressors for each of combination of experimental condition (real and imagined) and grip type (whole hand and finger) (1), and for each of combination of experimental condition (real and imagined) and wrist rotation (small and large) (2).

The main corpus of analyses was conducted on three independently defined, theoretically motivated, regions of interest (ROIs) (see below). We analyzed ROIs only on the left hemisphere to account for the fact that participants used their right hand to perform the grasping task. For each participant and region, we computed a regional estimate of the amplitude of the hemodynamic response, obtained by entering a weighted spatial average (with weights provided by the probabilistic ROIs – see next paragraph for details) of the pre-processed time series into the individual GLMs. Regional hemodynamic responses were thus analyzed through a series of one sample t-tests, assessing for both real and imagined condition the presence of a reliable activation. We used a FDR procedure (Benjamini and Hochberg, 1995) in order to correct for multiple comparisons: the obtained distributions of  $p$  values were used to compute a  $p$  threshold that set the expected rate of falsely rejected null hypotheses to 5%. We further

analyzed the BOLD signal change as a function of region and condition by means of a repeated-measure ANOVA. For this analysis, we used a Bonferroni adjustment in order to create confidence intervals for all the pairwise differences between the factor levels.

#### Probabilistic regions of interest (ROIs)

We investigated three regions of interest (hV6Av, hV6Ad, and hPEc) that were defined by our group in previous studies (Pitzalis et al., 2013; Tosoni et al., 2015; Pitzalis et al., 2019). All these regions were created on previously collected data on samples of participants distinct from the participants of the current study (see below).

*Retinotopically defined hV6Av.* It was created in our previous retinotopic study (Pitzalis et al., 2013) by combining retinotopic ROIs from an independent sample of 12 participants. Each retinotopic region was defined on the individual's brain flattened cortical surface based on reversal of the direction of phase change across the cortical surface as obtained by the Fourier analysis of polar angle data (see Pitzalis et al., 2006, 2013 for further details about the dataset and the analysis procedure). In the absence of a functional localizer for hV6Av, the retinotopic criterion is the only way to isolate the ventral sector of area V6A.

*Functionally defined hV6Ad.* It was probabilistically defined on an independent sample of 17 participants and created by combining the individual ROIs, each of them identified on each individual's brain surface by analyzing data of a delayed visuomotor task previously used by our group to maximally activate arm-movement-related neurons in the human V6Ad (see Tosoni et al., 2015; Pitzalis et al., 2019 for similar procedures). This task included pointing (hand- and foot-based) and saccade blocks, each of them modeled as box-car functions, convolved with a canonical hemodynamic response function. We defined hV6Ad as the cortical region responding stronger during any eye/hand/foot pointing movement toward a visual target, as compared to the fixation period. Each ROI was created on each individual hemisphere, applying the GLM to the surface-transformed smoothed fMRI images. The contrast map was corrected for multiple comparisons at the cluster level ( $p < 0.05$ ), after defining clusters of adjacent vertices surviving at least an uncorrected voxel-level threshold of  $p < 0.001$ . Each individual ROI was then selected by isolating single activation peaks and their neighbourhood through a watershed segmentation algorithm as applied to surface meshes (Mangan and Whitaker, 1999).

*Functionally defined hPEc.* It was probabilistically defined by averaging individual functional ROIs from an independent sample of 44 participants who underwent a pure motor task (not contaminated by the presence of visual stimulations) consisting in long-range active leg/arm movements (described in [Pitzalis et al., 2019](#)). The hPEc was defined on each individual's brain surface as the region responding stronger to active leg movements as compared to the fixation period. Although hPEc was defined as a leg-related region, it also showed a reliable arm-related response ([Pitzalis et al., 2019](#)). The procedure and the statistical threshold are the same as for hV6Ad.

Figure 3A shows the anatomical location of the probabilistic hV6Av, hV6Ad and hPEc overlaid onto the inflated Conte69 atlas surface ([Van Essen et al., 2012](#)). hV6Av (yellow) is located in or near the anterior bank of the dorsal end of POs. hV6Ad (blue) is located anteriorly to hV6Av and occupies the posterior portion of the dorsal surface of the superior parietal lobule, extending from the anterior bank of the dorsalmost part of the anterior wall of POs to the caudal portion of the precuneate cortex (behind the subparietal sulcus). hPEc (green) is the most anterior region and occupies the dorsal surface of the superior parietal lobule in correspondence of the dorsalmost portion of the anterior precuneus, just behind the dorsal tip of the cingulate sulcus. All these ROIs were defined on the surface cortical reconstruction as automatically obtained by FreeSurfer software package. In each ROI each node was assigned a weight equal to the proportion of subjects in the ROI-defining sample who showed activation in that node: these values were used to weight the contribution of each node during the extraction of regional signals (see previous paragraph). Note that this approach is only modestly affected by across subjects variation in ROI position. A more detailed description of the amount of overlap across participants of each ROI is provided in Supplementary Figure 1. Present data will be made available on request in compliance with the requirements of the funding institutes, and with the institutional ethics approval.

## Results

### Real and imagined grasping activity in hV6A and hPEc

The histogram in Figure 3B shows the BOLD percent signal change for real and imagined conditions in the three ROIs (hV6Av, hV6Ad, and hPEc). To test the hypothesis about the

presence of grasping-related positive responses, the percent signal change of these regions was compared to zero using a series of one-tailed t-tests. All the reported results are corrected for multiple comparisons using an FDR procedure (see the Method section). In the real condition, both hV6Ad and hPEc showed significant positive responses (hV6Ad:  $t_{24} = 2.83$ ;  $p < 0.01$ ; hPEc:  $t_{24} = 3.23$ ;  $p < 0.005$ ). In the imagined condition, only hV6Ad showed a significant positive response ( $t_{24} = 2.27$ ;  $p < 0.05$ ). hV6Av did not show any significant response neither to real nor to imagined condition while PEc exhibited a significant negative response ( $t_{24} = -3.8$ ;  $p < 0.001$ ).

Further, to reveal any significant grasping-related difference, we compared the two regions showing significant response in at least one grasping condition (hV6Ad and hPEc) as a function of the experimental condition (real vs. imagined) by means of a 2 by 2 repeated-measure ANOVA. We found a main effect of region ( $F_{1, 24} = 8.56$ ;  $p < 0.01$ ;  $\eta_p^2 = 0.26$ ) indicating that hV6Ad responded stronger than hPEc, a main effect of condition ( $F_{1, 24} = 27.32$ ;  $p < 0.001$ ;  $\eta_p^2 = 0.53$ ) indicating a stronger activation for real than imagined grasping, and a significant interaction ( $F_{1, 24} = 8.66$ ;  $p < 0.01$ ;  $\eta_p^2 = 0.26$ ) indicating that the two regions differed only in the imagined condition (hV6Ad > hPEc;  $p = 0.0001$ ).

Further regional analyses were conducted to explore the sensitivity of both hV6A and hPEc to different grip types and to the amount of wrist rotation. In a first analysis we compared the two grip types (whole hand vs. finger) as a function of condition (real vs. imagined) in a 2 by 2 repeated-measure ANOVA. In both hV6Ad and hPEc we found no significant effect of grip type (hV6Ad:  $F_{1,24} = 2.77$ ;  $p = 0.11$ ;  $\eta_p^2 = 0.10$ ; hPEc:  $F_{1,24} = 0.97$ ;  $p = 0.33$ ;  $\eta_p^2 = 0.04$ ) neither a significant grip type by condition interaction ( $F_{1,24} = 1.60$ ;  $p = 0.22$ ;  $\eta_p^2 = 0.06$ ), indicating a less stringent separation between the two types of grip. In a second analysis, to reveal any significant difference as a function of the amount of wrist rotation evoked by each graspable object, we compared the two levels of wrist rotation (small vs. large) as a function of condition (real vs. imagined) by means of a 2 by 2 repeated-measure ANOVA. We found a significant wrist rotation by condition interaction ( $F_{1,24} = 6.44$ ;  $p = 0.02$ ;  $\eta_p^2 = 0.21$ ) in the hV6Ad, indicating a stronger activation during large wrist rotation as compared to small wrist rotation, but only in the real condition ( $p = 0.02$ ). No significant effect of wrist rotation ( $F_{1,24} = 1,18$ ;  $p = 0.29$ ;  $\eta_p^2 = 0.05$ ) neither a significant wrist rotation by condition interaction ( $F_{1,24} = 2,59$ ;  $p = 0.12$ ;  $\eta_p^2 = 0.09$ ) were instead observed in the area hPEc.

As expected, we found that area hV6Av was not modulated neither by grip type (main effect of grip type:  $F_{1,24} = 2.75$ ;  $p = 0.11$ ;  $\eta_p^2 = 0.10$ ; grip type by condition interaction:  $F_{1,24} = 1.20$ ;  $p = 0.28$ ;  $\eta_p^2 = 0.05$ ) nor by the amount of wrist rotation (main effect of wrist rotation:  $F_{1,24} = 1.05$ ;  $p = 0.32$ ;  $\eta_p^2 = 0.04$ ; wrist rotation by condition interaction:  $F_{1,24} = 3.94$ ;  $p = 0.06$ ;  $\eta_p^2 = 0.41$ ).

#### Whole-brain activations

Beyond the regional approach, we further conducted a whole-brain analysis in order to have a general picture of the brain regions involved in both real and imagined grasping. Figure 4 shows group activation maps as resulting from different contrasts overlaid onto atlas Conte69 and rendered in two different inflated views (dorsomedial and lateral).

Figure 4A shows brain regions more activated during real grasping as compared to the fixation baseline. These included a wide network of cortical areas in the fronto-parietal cortex. The frontal activation encompassed the hand territory of the left (contralateral to the moving hand) primary motor and somatosensory areas (M1 and S1), the bilateral dorsal premotor area (PMd) and supplementary and cingulate motor areas (SMA and CMA). The frontal activation also extended ventrally along the bilateral precentral gyrus (pCg) so that to include the pars opercularis of the bilateral inferior frontal gyrus, well corresponding to the ventral premotor area (PMv), and the pars triangularis of the left iFg (iFg-PT). The parietal activation included the bilateral posterior intraparietal sulcus (pIPs), with the adjoining superior (SPL) and inferior (IPL) parietal lobules, and the bilateral supramarginal gyri (sMg). A strong focus of activation was found in the bilateral (but stronger in the left hemisphere) anterior intraparietal sulcus (aIPs), probably corresponding to the homologue of the monkey area AIP. The parietal activation also included the dorsal exposed surface of SPL, extending from the caudalmost hV6Ad to the rostralmost hPEc, just behind the cingulate sulcus. A small spot of activation was also found in the superior temporal gyrus (sTg) of the right hemisphere. The average anatomical positions of hV6Ad and hPEc (indicated by a black outline) were overlaid onto the left hemisphere of the activation group map shown in the close-up (black box) of Figure 4A. Notably, as expected from regional analyses, this activation partially encompassed the two independent ROIs.

Figure 4B shows brain regions more activated during imagined grasping as compared to the fixation baseline. These were a subset of regions activated also by the real grasping, including a left-lateralized network of regions encompassing both the frontal (PMd, SMA/CMA, pCg, iFg-



PO, iFg-PT) and the parietal (aIPs, pIPs, sMg) cortex. The dorsomedial view, where the center of hV6Ad and hPEc are marked by a black spot, shows that the parietal activation extended up to the dorsal margin of the POs so as to partially include the hV6Ad in correspondence of its lateral portion, while the territory around hPEc did not respond to the imagined grasping, in line with the regional results (Figure 3B). In the right hemisphere, small foci of activation were found in correspondence of CMA, pCg and dorsalmost pIPS.

Figure 4C shows brain regions more activated during real as compared to imagined grasping. This network included all the fronto-parietal regions activated by the real > fixation contrast, but the left pIPs and the bilateral posterior precuneus. The rostralmost precuneus was instead particularly activated and completely included the hPEc cortical territory.

The imagined > real contrast did not reveal any significant positive activation.

## Discussion

We have described a bilateral fronto-parietal network of areas commonly activated by both real and imagined grasping movements of the right hand in humans. Among these areas (more extended in the left hemisphere), our results demonstrate the involvement in the control of grasping movements of two specific cortical regions in the dorsomedial portion of the superior parietal lobule, hV6Ad and hPEc. hV6Ad was activated by both real and imagined grasping while hPEc by real but not by imagined grasping.

Although previous studies have demonstrated that the dorsolateral portion of PPC is the most common parietal portion activated by grasping movements, visually-guided grasping, object manipulation without vision, and visual inspection without grasping (see [Culham et al., 2006](#) for a review), the hV6Ad grasping-related activity found here is well in line with recent evidence of a dorsomedial parietal activation observed during grasping in both monkeys and humans. In monkeys, the involvement of V6A in grasping-related movements was originally proposed by a lesional study ([Battaglini et al., 2002](#)) showing that V6A lesions disrupt not only reaching but also grasping and, specifically, wrist orientation. Several electrophysiology studies in monkeys also revealed that the macaque area V6A exhibited grasping-related activity, with many neurons sensitive to different distal components of the act of prehension, such as wrist orientation and grip formation ([Fattori et al., 2004, 2009, 2010, 2012](#); see also [Fattori et al.,](#)

2017 for a recent review). It was reported, in particular, that V6A cells were modulated by hand orientation both during preparation and movement periods (Fattori et al., 2009). Additionally, their cells are able to discriminate among the different hand grips needed to grasp objects of widely different shapes (Fattori et al., 2010). Further, the majority of V6A cells responded to the presentation of tridimensional objects in the peripersonal space, and approximately half of these neurons are selective for the object shape (Fattori et al., 2012) and affordance (Breviglieri et al., 2015). Recently, it has been demonstrated that V6A neural signals can be reliably used to decode grasping information during different scenarios (presence and absence of visual information regarding object and hand-object interaction) and during action preparation and execution (Filippini et al., 2017). A recent neuroimaging study in monkeys (Nelissen et al., 2018) has used multivariate pattern analysis to determine whether hand configurations could be decoded from functional magnetic resonance imaging responses obtained from different nodes of the reaching and grasping circuits. According to the above-mentioned electrophysiology studies, the authors observed that, beyond the lateral grasping circuit, also the medial reaching circuit, and V6A in particular, conveyed robust grasp-specific information.

In humans, a growing number of studies implicates the anterior bank of the dorsalmost part of POs and the SPL cortical region anterior to it (the putative human homologue of the monkey V6A; Pitzalis et al., 2013; Tosoni et al., 2015; see Pitzalis et al., 2015 for a review) in the preparation and execution of hand reaching and pointing movements (Astafiev et al., 2003; Connolly et al., 2003; Prado et al., 2005; Filimon et al., 2009; Gallivan et al., 2009; Cavina-Pratesi et al., 2010; Tosoni et al., 2015). A recent fMRI study in humans (Gallivan et al., 2011) has used pattern recognition techniques to decode object-directed grasp and reach actions from intention-related activity before movement execution. The authors found that preparatory activity in dorsomedial regions that included the possible human homologue of the monkey V6A, decoded planned grasp versus touch movements. Additionally, Monaco et al. (2011) observed that a region in the parieto-occipital cortex likely corresponding to macaque area V6A exhibited fMRI adaptation when the object was repeatedly grasped with the same orientation, but not when it was reached out without grasping (or simply looked at) with the same orientation, suggesting that hand orientation, rather than object orientation, was the critical factor. Finally, human patients with cortical lesions to the presumed homologue region of

monkey V6A showed not only misreaching but also distal deficits concerning grasping-related movements (optic ataxia syndrome: [Karnath and Perenin, 2005](#)), such as hand orientation ([Perenin and Vighetto 1988](#)), grip aperture, and inability to scale the grip aperture to the object size ([Jeannerod 1986; Jakobson et al., 1991](#)). Notably, these distal impairments were the same observed by [Battaglini et al. \(2002\)](#) after V6A lesion in monkey. Compatibly with this view, we observed that hV6Ad is particularly activated by large amounts of expected wrist rotation during the real grasping condition. This is also in line with the observation that the macaque area V6A contains neurons sensitive to wrist orientation ([Fattori et al., 2009, 2010, 2017](#)). Additionally, [although we did not observe any grip-related modulation in this area, we cannot conclude that hV6Ad is insensitive to grip formation but rather that](#) grip-related information might be contained in a more fine-scaled spatial patterns of activations, as observed by previous studies using more advanced fMRI analyses, such as multivoxel analysis techniques ([Gallivan et al., 2011; Nelissen et al., 2018](#)).

An important result of the present work is the selective involvement of the dorsal sector of the human homologue of the monkey area V6A in the grasping action (both real and imagined) and the lack of any significant response to grasping conditions in the nearby ventral sector of V6A (hV6Av). Monkey evidence supports this view, by showing a visual-to-motor trend in the two V6A subdivisions, with V6Av mainly dominated by visual neurons and V6Ad by somatomotor neurons ([Gamberini et al., 2011, 2018](#)). This trend is also supported by connectivity data, since V6Av receives inputs mainly from visual areas while V6Ad from parietal associative areas as well as frontal premotor cortex ([Gamberini et al., 2009; Passarelli et al., 2011](#)). A similar gradient of functional specialization was also found in humans ([Tosoni et al., 2015](#)), where hV6Av and hV6Ad have been distinguished based on both functional properties and their patterns of cortico-cortical connections. Indeed, [Tosoni and co-workers \(2015\)](#) revealed that hV6Ad was strongly selective for the execution of spatially directed pointing movements involving wrist rotation while hV6Av was more activated by visual stimulation (optic flow), and equally by saccade and pointing movements. In addition, the authors found that hV6Ad, but not hV6Av, showed resting-state functional connections with the lateral parietal lobe, in correspondence of the putative human homologue of monkey area AIP, and with dorsal premotor cortex previously associated with grasping-related movements (see [Culham et al., 2006](#) and [Turella and Lingnau, 2014](#) for reviews). These human data perfectly agree with the known cortical

connections of macaque V6Ad with AIP and dorsal premotor cortex (Gamberini et al., 2009). Overall, these data suggest that, in the human, only the part of V6A more involved in the somatic control of arm movements (hV6Ad) is active during grasping, whereas the part of V6A more involved in the visual domain (hV6Av) is not.

Besides area hV6Ad, we also found evidence of a pantomimed grasping-related activity in the putative human homologue of monkey area PEc, a region located anteriorly to hV6Ad, in the dorsomedial PPC, which has been recently described by our group (Pitzalis, et al., 2019). Similarly to the monkey counterpart, we found that the hPEc responded to both upper and lower limbs movements (although legs movements elicited stronger activations) during a pure motor task in absence of a visual feedback (Pitzalis, et al., 2019), but to date the effect of grasping activity on this area has never been studied in humans, and neither in monkeys. A recent human fMRI study exploring haptically guided grasping movements (Styrkowiec et al., 2019) has found signal modulations in the precuneus, bilaterally, in a region likely corresponding to the human PEc (Pitzalis, et al., 2019). In monkeys, several studies reported a clear PEc involvement in arm reaching movements (Ferraina et al., 2001; Hadjidimitrakis et al., 2015; Piserchia et al., 2017), but no study so far has specifically investigated the effect of grasping. Future studies are needed to assess whether PEc can be defined in humans during to not visually guided hand and foot grasping movements; this should shed new light on the role of the area in the controlling the hand/foot interaction with the objects in the environment, as previously hypothesized in the macaque (Gamberini et al., 2018).

Beyond similarity in response profile between hV6Ad and hPEc during the real (pantomimed) grasping condition, we found that only hV6Ad was activated by the imagined grasping condition, in line with previous reports showing a similar activation of the SPL for both real and imagined grasping (Decety et al., 1994; Grafton et al., 1996; Binkofski et al., 1999; Grezes and Decety, 2001). On the other side, the hPEc negative response during imagined grasping could be explained if considering the deactivation as a consequence of filtering out irrelevant information (Amedi et al., 2005). One speculative hypothesis is that real movements should not require much filtering because the area is particularly sensitive to the somatosensory aspects inherent the control of the object prehension. On the other side, imagined movements could require more filtering to stop the planned (preferred) movement and to create a mental image of such an action, thus leading to the observed deactivation. Overall, the hPEc functional profile

is in line with a recent MVPA study on hand action representations revealing that a region likely corresponding to the human homologue of macaque P<sub>Ec</sub> was able to discriminate between different executed actions, but not between different imagined or observed actions (Filimon et al., 2014). Overall, it appears that hV6Ad and hP<sub>Ec</sub> are more involved in cognitive and pragmatic aspects of the control of grasping (and in general of prehension; see Fattori et al., 2017), respectively. Consistently with this view, we successfully revealed the human homologue of macaque P<sub>Ec</sub> using a pure motor task where we asked the subjects to perform in the scanner unseen real and long-range leg and arm movements (Pitzalis et al., 2019).

The group-based analyses of the present work allowed us to have a general picture of the brain regions activated by grasping movements. These maps clearly showed that the activation for real grasping mainly covers the lateral portion of the cortical territory hosting the probabilistically defined hV6Ad and hP<sub>Ec</sub> (see the close-up view in Figure 4A), thus suggesting that the most medial portions of these areas are less responsive (or not at all) to real grasping movements. A similar observation can be also made for the imagined condition (Figure 4B), where the activation primarily includes the most dorsolateral portion of the hV6Ad ROI. Future investigations using multivariate pattern analysis could verify whether spatially segregated neural populations do really exist within areas hV6Ad and hP<sub>Ec</sub>, and which could be the reason(s) of this segregation.

Beyond the involvement of the SPL and the anterior intraparietal sulcus, where the possible human homologue of monkey AIP is located, we showed a distributed network of fronto-parietal regions, more extended in the left hemisphere, commonly activated by real and imagined grasping, well in line with previous studies. For example, pIPS, pMd and pMv and bilateral SMA/CMA are involved in the transport and grip component of grasping movements (Monaco et al., 2011; Cavina-Pratesi et al., 2010); iFg and sMg have been recently demonstrated as being commonly activated during motor observation, execution, and even motor imagery (Filimon et al., 2007; Filimon et al., 2014; Keyser and Gazzola 2009; for reviews, see Grèzes and Decety, 2001; Molenberghs et al., 2009, 2012; Caspers et al., 2010).

Overall, we found that the cortical circuit involved in grasping-related movements partially overlaps with the brain regions previously associated with reaching movements (Culham et al. 2003, Castiello 2005; Filimon et al., 2007), although some degrees of specialization for grasping

is observed in the most ventral portion of premotor and motor cortices which have been found to activate more strongly during grasping than reaching (Culham et al., 2003; Frey et al., 2005; Cavina-Pratesi et al., 2010). Although many previous studies have attempted to locate separate/distinct neural representations for reaching and grasping movements, it appears that the areas involved in different hand movements are not modularly organized but rather organized in highly distributed and overlapping networks with gradients of preference for one movement compared to the other (see Filimon, 2010 for a review). This notion is further supported by recent imaging data from humans indicating that the dorsomedial visual stream (Grol et al. 2007; Verhagen et al. 2012, 2013) is involved in the control of the entire act of prehension.

One possible limitation of the current study is the use of pantomimed instead of actual grasping. Other researchers have also previously used pantomimed because of the difficulty of studying real grasping in the MR environment (Shikata et al., 2003; Simon et al., 2002; Johnson-Frey et al., 2005; Bozzacchi et al., 2012; Makuuchi et al., 2012). Although the use of pantomimed actions should have eliminated activation foci evoked by the tactile stimulations produced by hand-object interaction during an actual grasping, we observed a widespread (tactile) sensorimotor activation, probably due to a mutual stimulation among fingers during grasping. It has been proposed that brain areas typically involved in real actions may not necessarily be activated by pantomimed actions (Kròliczak et al., 2007). However, these authors showed that the activation differences between pantomimed and actual grasping were not found in the parietal cortex, but in the insula and superior temporal cortex. In any case, we are aware that future studies using actual grasping paradigms are needed to check whether hV6Ad and hPEc are actually activated (as we hypothesize) by (real) hand-to-object interaction.

In conclusion, our results show that two important parietal nodes specialized in controlling limb movements, hV6Ad and hPEc, strongly interconnected to each other at rest (Pitzalis et al., 2019), are involved in the control of grasping movements. This argues against the classic view of a functional segregation within the human parietal cortex between lateral and medial circuits controlling grasping and pointing/reaching movements, respectively (Jeannerod et al., 1995; Luppino et al., 1999). Rather, recent electrophysiological studies on both human and macaque found significant decoding of grip type in areas that are not usually or only partially related to

grasping (Klaes et al., 2015; Schaffelhofer and at., 2015; Nelissen et al., 2018), thus suggesting the existence of a more distributed network of regions implicated in prehension movements. The present study supports the view, first advanced in macaque monkey (Fattori et al., 2004, 2009, 2010; see Fattori et al., 2017, Galletti and Fattori 2018 for reviews), that the dorsomedial parietal circuit also controls grasping, that is the more distal aspect of reach-to-grasp action. The present results also suggest that, despite similarities, hV6Ad and hPEc have distinct roles, with the hV6Ad involved in implementing all the visuomotor transformations needed to create an abstract representation of the object-directed action, and hPEc more specifically engaged in implementing the sensorimotor transformations needed to actually perform that action.

## Captions

**Figure 1.** Brain location of macaque areas V6Av, V6Ad and PEc. Dorsal (left) and posteromedial (right) views of the surface-based 3D reconstructions of the ATLAS brain of the macaque (left hemisphere) showing the extent of areas V6Av (yellow) V6Ad (blue) and PEc (green). The fundus of main sulci is indicated by dashed lines and labelled as follow: Cs: central sulcus; Cgs: cingulate sulcus; SPs: sub-parietal sulcus; POs: parieto-occipital sulcus; IPs: intraparietal sulcus; a, anterior; p, posterior; m, medial.

**Figure 2.** Stimuli and experimental paradigm. **A.** Examples of visual stimuli used in the experiment. **B.** Example of trial sequence. Participants were presented pictures describing common-use graspable objects and were instructed either to pantomime the grasping gesture by shaping the hand configuration accordingly to the object shape and orientation (“grasp” instruction) or to imagine such an action (“imagine” instruction). Participants alternated these “active” blocks with “passive” fixation blocks.

**Figure 3.** Brain location of hV6Av, hV6Ad and hPEc and their functional response to the grasping (real and imagined) conditions. **A.** Individual ROIs coming from independent samples of participants are overlapped onto an inflated Conte69 brain atlas (left hemisphere) in different views (superior, dorsomedial and medial). The color saturation represents the proportion of participants whose region included that node: the higher the color saturation, the higher the probability that the node belongs to the corresponding region. hV6Av is indicated in yellow, hV6Ad in blue and hPEc in green. More details about the proportion of across-subjects overlap

within each ROI are provided in Supplementary Figure 1. The fundus of main sulci is indicated by dashed lines and labelled as follow: Cgs: cingulate sulcus; PCs: post-central sulcus; POs: parieto-occipital sulcus; Cs: central sulcus; pIPs: posterior intraparietal sulcus; SPs: sub-parietal sulcus; sTPs: secondary transverse parietal sulcus. **B.** The plot shows the average of BOLD signal change as a function of condition (real and imagined grasping) estimated in each ROI. \*  $p < 0.05$  FDR-corrected.

**Figure 4.** Whole-brain results. Group-activation map associated to different contrasts, showing **(A)** Brain regions more activated in the real (grasping) condition than fixation (Fix), **(B)** Brain regions more activated in the imagined (grasping) condition than fixation, **(C)** Brain regions more activated in the real as compared to the imagined condition. Each activation map is displayed on the lateral and dorsomedial views of the inflated Conste69 atlas (Van Essen et al., 2012) of both left (LH) and right (RH) hemispheres. Activations are labelled as followed: M1/S1, primary motor and somatosensory areas; aIPs: anterior intraparietal area; pIPs: posterior intraparietal sulcus; sMg: supramarginal gyrus; pCg: precentral gyrus; iFg-PT: pars triangularis of the inferior frontal gyrus; pMd: dorsal premotor area; pMv: ventral premotor area; SMA/CMA: supplementary and cingulate motor areas; sTg: superior temporal gyrus. The centers of mass of hV6Ad and hPEc are marked by black spots. Other labels as in Figure 3.

**Supplementary Figure 1.** Across-subjects overlap within the probabilistic defined ROIs. Plots show the frequency distribution of cortical nodes according to the amount of across-subjects overlap (i.e., the proportion of subjects, in the ROI-defining sample, who showed activation in each cortical node), for hV6Av **(A)**, hV6Ad **(B)** and hPEc **(C)**, respectively. **D.** Extent and anatomical location of each probabilistic region (V6Av in yellow, hV6Ad in blue and hPEc in green) after applying a threshold of 0.2, thus retaining nodes belonging to the ROI in at least 20% of participants.

## Bibliography

Amedi, A., Malach, R., et al., 2005. Negative BOLD differentiates visual imagery and perception. *Neuron* 48 (5), 859–872.



- Astafiev, S.V., Shulman, G.L., Stanley, C.M., Snyder, A.Z., Van Essen, D.C., Corbetta M., 2003. Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. *J. Neurosci.* 23:4689–4699.
- Battaglia-Mayer, A., Ferraina, S., Mitsuda, T., Marconi, B., Genovesio, A., Onorati, P., Lacquaniti, F., Caminiti, R., 2000. Early coding of reaching in the parietooccipital cortex. *J. Neurophysiol.* 83(4):2374-91
- Battaglini, P.P., Muzur, A., Galletti, C., Skrap, M., Brovelli, A., Fattori, P., 2002. Effects of lesions to area V6A in monkeys. *Exp. Brain. Res.* 144:419–422.
- Baumann, M.A., Fluet, M.C., Scherberger, H., 2009. Context-specific grasp movement representation in the macaque anterior intraparietal area. *J. Neurosci.* 29:6436–6448.
- Benjamini, Y., and Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Stat. Soc. Series B* 57, 289–300.
- Binkofski, F., Buccino, G., Posse, S., Seitz, R.J., Rizzolatti, G., and Freund, H.J., 1999. A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur. J. Neurosci.* 11, 3276–3286. doi: 10.1046/j.1460- 9568.1999.00753.x
- Breveglieri, R., Galletti, C., Bosco, A., Gamberini, M., Fattori, P., 2015. Object affordance modulates visual responses in the macaque medial posterior parietal cortex. *J. Cogn. Neurosci.* 27:1447–1455.
- Breveglieri, R., Bosco, A., Galletti, C., Passarelli, L., Fattori, P., 2016. Neural activity in the medial parietal area V6A while grasping with or without visual feedback. *Sci. Rep.* 6:28893. doi: 10.1038/srep28893.
- Breveglieri, R., De Vitis, M., Bosco, A., Galletti, C., Fattori, P., 2018. Interplay Between Grip and Vision in the Monkey Medial Parietal Lobe. *Cereb. Cortex.* 28(6):2028-2042. doi: 10.1093/cercor/bhx109.

- Bozzacchi, C., Giusti, M.A., Pitzalis, S., Spinelli, D., Di Russo, F., 2012. Similar cerebral motor plans for real and virtual actions. *PLoS One* 7(10):e47783. doi: 10.1371/journal.pone.0047783.
- Caspers, S., Zilles, K., Laird, A.R., Eickhoff, S.B., 2010. ALE meta-analysis of action observation and imitation in the human brain. *NeuroImage* 50(3):1148–1167.
- Cavina-Pratesi, C., Monaco, S., Fattori, P., Galletti, C., McAdam, T.D., Quinlan, D. J., Goodale, M.A., Culham, J.C., 2010. Functional magnetic resonance imaging reveals the neural substrates of arm transport and grip formation in reach-to-grasp actions in humans. *J. Neurosci.* 30:10306–10323.
- Colby, C.L., Duhamel, J.R., 1991. Heterogeneity of extrastriate visual areas and multiple parietal areas in the macaque monkey. *Neuropsychologia* 29:517–537.
- Connolly, J.D., Andersen, R.A., Goodale, M.A., 2003. fMRI evidence for a ‘parietal reach region’ in the human brain. *Exp. Brain. Res.* 153(2):140–145. doi:10.1007/s00221-003-1587-1
- Culham, J.C., Danckert, S.L., DeSouza, J.F., Gati, J.S., Menon, R.S., Goodale, M.A., 2003. Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Exp. Brain Res.* 153(2):180–189. doi:10.1007/s00221-003-1591-5.
- Culham, J.C., Cavina-Pratesi, C., Singhal, A., 2006. The role of parietal cortex in visuomotor control: What have we learned from neuroimaging? *Neuropsychologia* 44, 2668-2684.
- Dale, A.M., Fischl, B., Sereno, M.I., 1999. Cortical surface-based analysis: I. Segmentation and surface reconstruction. *Neuroimage* 9, 179–194.
- Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazziotta, J.C., Fazio, F., 1994. Mapping motor representations with positron emission tomography. *Nature* 371: 600–602.
- Desikan, R.S., Ségonne, F., Fischl, B., Quinn, B.T., Dickerson, B.C., Blacker, D., Buckner, R.L., Dale, A.M., Maguire, R.P., Hyman, B.T., 2006. An automated labeling system for subdividing

the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage* 31, 968–980. <https://doi.org/10.1016/j.neuroimage.2006.01.021>

Fattori, P., Gamberini, M., Kutz, D. F., Galletti, C., 2001. “Arm-reaching” neurons in the parietal area V6A of the macaque monkey. *Eur. J. Neurosci.* 13:2309–2313.

Fattori, P., Breveglieri, R., Amoroso, K., Galletti, C., 2004. Evidence for both reaching and grasping activity in the medial parieto-occipital cortex of the macaque. *Eur. J. Neurosci.* 20:2457–2466.

Fattori, P., Kutz, D. F., Breveglieri, R., Marzocchi, N., Galletti, C., 2005. Spatial tuning of reaching activity in the medial parieto-occipital cortex (area V6A) of macaque monkey. *Eur. J. Neurosci.* 22:956–972.

Fattori, P., Breveglieri, R., Marzocchi, N., Filippini, D., Bosco, A., Galletti, C., 2009. Hand orientation during reach-to-grasp movements modulates neuronal activity in the medial posterior parietal area V6A. *J. Neurosci.* 29:1928–1936.

Fattori, P., Raos, V., Breveglieri, R., Bosco, A., Marzocchi, N., Galletti, C., 2010. The dorsomedial pathway is not just for reaching: grasping neurons in the medial parieto-occipital cortex of the macaque monkey. *J. Neurosci.* 30:342–349.

Fattori, P., Breveglieri, R., Raos, V., Bosco, A., Galletti, C., 2012. Vision for action in the macaque medial posterior parietal cortex. *J. Neurosci.* 32:3221–3234.

Fattori, P., Breveglieri, R., Bosco, A., Gamberini, M., Galletti, C., 2017. Vision for prehension in the medial parietal cortex. *Cereb. Cortex* 27:1149–1163.

Ferraina, S., Battaglia-Mayer, A., Genovesio, A., Marconi, B., Onorati, P., Caminiti, R., 2001. Early coding of visuomanual coordination during reaching in parietal area PEc. *J. Neurophysiol.* 85: 462–467.

Filippini, M., Breveglieri, R., Akhras, M. A., Bosco, A., Chinellato, E., Fattori, P., 2017. Decoding Information for Grasping from the Macaque Dorsomedial Visual Stream. *J. Neurosci.* 37(16):4311-4322. doi: 10.1523/JNEUROSCI.3077-16.2017

Filimon, F., Nelson, J.D., Hagler, D.J., and Sereno, M.I., 2007. Human cortical representations for reaching: mirror neurons for execution, observation, and imagery. *Neuroimage* 37, 1315–1328. doi: 10.1016/j.neuroimage.2007. 06.008

Filimon, F., Nelson, J.D., Huang, R.S., Sereno, M.I., 2009. Multiple parietal reach regions in humans: cortical representations for visual and proprioceptive feedback during on-line reaching. *J Neurosci.* 29:2961–2971.

Filimon, F., Rieth, C.A., Sereno, M.I., Cottrell, G.W., 2014. Observed, executed, and imagined action representations can be decoded from ventral and dorsal areas. *Cereb. Cortex* 25:3144–3158.

Frey, S. H., Vinton, D., Norlund, R., Grafton, S.T., 2005. Cortical topography of human anterior intraparietal cortex active during visually guided grasping. *Brain Res. Cogn. Brain Res.* 23(2–3):397–405.

Fischl, B., Sereno, M.I., Dale, A. M., 1999a. Cortical surface-based analysis: II. Inflation, flattening, and a surface-based coordinate system. *NeuroImage* 9, 195–207.  
<http://doi.org/10.1006/nimg.1998.0396>

Fischl, B., Sereno, M.I., Tootell, R.B.H., Dale, A.M., 1999b. High- resolution intersubject averaging and a coordinate system for the cortical surface. *Human Brain Mapping* 8, 272–284. [https://doi.org/10.1002/\(SICI\)1097-0193\(1999\)8:4<272::AID-HBM10>3.0.CO;2-4](https://doi.org/10.1002/(SICI)1097-0193(1999)8:4<272::AID-HBM10>3.0.CO;2-4)

Galati, G., Committeri, G., Spitoni, G., Aprile, T., Di Russo, F., Pitzalis, S., Pizzamiglio, L., 2008. A selective representation of the meaning of actions in the auditory mirror system. *Neuroimage* 40, 1274–1286.

Galletti, C., Fattori, P., 2018. The dorsal visual stream revisited: Stable circuits or dynamic pathways? *Cortex* 203-217. doi: 10.1016/j.cortex.2017.01.00

Galletti, C., Kutz, D. F., Gamberini, M., Breviglieri, R., Fattori, P., 2003. Role of the medial parieto-occipital cortex in the control of reaching and grasping movements. *Exp. Brain Res.* 153: 158–170.

- Gallivan, J. P., Cavina-Pratesi, C., Culham, J. C., 2009. Is that within reach? fMRI reveals that the human superior parieto-occipital cortex encodes objects reachable by the hand. *J. Neurosci* 29, 4381–4391.
- Gallivan, J. P., McLean, D. A., Valyear, K. F., Pettypiece, C. E., Culham, J. C., 2011. Decoding action intentions from preparatory brain activity in human parieto-frontal networks. *J. Neurosci.* 31: 9599–9610.
- Gamberini, M., Passarelli, L., Fattori, P., Zucchelli, M., Bakola, S., Luppino, G., Galletti, C., 2009. Cortical connections of the visuomotor parietooccipital area V6Ad of the macaque monkey. *J. Comp. Neurol.* 513:622–642. <https://doi.org/10.1002/cne.21980>
- Gamberini, M., Galletti, C., Bosco, A., Breveglieri, R., Fattori, P., 2011. Is the medial posterior parietal area V6A a single functional area? *J. Neurosci.* 31:5145–5157.
- Gamberini, M., Dal Bò, G., Breveglieri, R., Briganti, S., Passarelli, L., Fattori, P., Galletti, C., 2018. Sensory properties of the caudal aspect of the macaque's superior parietal lobule. *Brain Struct. Funct.* <https://doi.org/10.1007/s00429-017-1593-x>.
- Glasser, M. F., Sotiropoulos, S. N., Wilson, J. A., Coalson, T. S., Fischl, B., Andersson, J.L. et al., 2013. The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* 80, 105–124. <http://doi.org/10.1016/j.neuroimage.2013.04.127>.
- Goodale, M.A., Jakobson, L.S., and Keillor, J.M., 1994. Differences in the visual control of pantomimed and natural grasping movements. *Neuropsychologia* 32, 1159–1178.
- Grafton, S.T., Fagg, A.H., Woods, R.P., Arbib, M.A., 1996. Functional anatomy of pointing and grasping in humans. *Cereb. Cortex* 6(2):226–37.
- Grèzes, J., Decety, J., 2001. Functional anatomy of execution, mental simulation, observation, and verb generation of actions: a meta-analysis. *Hum. Brain Mapp.* 12, 1–19.
- Grol, M.J., Majdandžić, J., Stephan, K.E., Verhagen, L., Dijkerman, H.C., Bekkering, H., Verstraten, F.A., Toni, I., 2007. Parieto-frontal connectivity during visually guided grasping. *J. Neurosci.* 27: 11877–11887.

- Gutteling, T.P., Petridou, N., Dumoulin, S.O., Harvey, Aarnoutse E.J., Kenemans, J.L., Neggers, S.F., 2015. Action preparation shapes processing in early visual cortex. *J. Neurosci.* 35, 6472–6480
- Hadjidimitrakis, K., Dal Bo, G., Breveglieri, R., Galletti, C., Fattori, P., 2015. Overlapping representations for reach depth and direction in caudal superior parietal lobule of macaques. *J. Neurophysiol.* 114, 2340e2352. doi: 10.1152/jn.00486.2015.
- Hinkley, L.B.N., Krubitzer, L.A., Padberg, J., Disbrow, E.A., 2009. Visual-manual exploration and posterior parietal cortex in humans. *J. Neurophysiol.* 102, 3433–46.
- Jakobson, L.S., Archibald, Y.M., Carey, D.P., Goodale, M.A., 1991. A kinematic analysis of reaching and grasping movements in a patient recovering from optic ataxia. *Neuropsychologia* 29, 803–809.
- Jeannerod, M., 1986. Mechanisms of visuomotor coordination: a study in normal and brain-damaged subjects. *Neuropsychologia* 24, 41–78.
- Jeannerod, M., Arbib, M.A., Rizzolatti, G., Sakata, H., 1995. Grasping objects: the cortical mechanisms of visuomotor transformation. *Trends Neurosci.* 18, 314–320.
- Johnson-Frey, S.H., Newman-Norlund, R., and Grafton, S.T., 2005. A distributed left hemisphere network active during planning of everyday tool use skills. *Cereb. Cortex* 15, 681–695. doi: 10.1093/cercor/bhh169.
- Karnath, H.O., Perenin, M.T., 2005. Cortical control of visually guided reaching: evidence from patients with optic ataxia. *Cereb. Cortex.* 15, 1561-9.
- Keysers, C., Gazzola, V., 2009. Expanding the mirror: vicarious activity for actions, emotions, and sensations. *Curr. Opin. Neurobiol.* 19, 666–671.
- Klaes, C., Kellis, S., Aflalo, T., Lee, B., Pejisa, K., Shanfield, K., Hayes-Jackson, S., Aisen, M., Heck, C., Liu, C., Andersen, R.A., 2015. Hand shape representations in the human posterior parietal cortex. *J Neurosci* 35:15466–15476.

Króliczak, G., Cavina-Pratesi, C., Goodman, D.A., Culham, J.C., 2007. What does the brain do when you fake it? An fMRI study of pantomimed and real grasping. *J. Neurophysiol.* 97, 2410-22.

Kwong, K.K., Belliveau, J.W., Chesler, D.A., Goldberg, I.E., Weisskoff, R.M., Poncelet, B.P., Kennedy, D.N., Hoppel, B.E., Cohen, M.S., Turner, R., 1992. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc. Natl. Acad. Sci. U.S.A.* 89, 5675–5679.

Luppino, G., Murata, A., Govoni, P., Matelli, M., 1999. Largely segregated parieto-frontal connections linking rostral intraparietal cortex (areas AIP and VIP) and the ventral premotor cortex (areas F5 and F4). *Exp. Brain Res.* 128, 181–187.

Luppino, G., Ben Hamed, S., Gamberini, M. et al., 2005. Occipital (V6) and parietal (V6A) areas in the anterior wall of the parieto-occipital sulcus of the macaque: a cytoarchitectonic study. *Eur. J. Neurosci* 21, 3056–3076. <https://doi.org/10.1111/j.1460-9568.2005.04149.x>

Mangan, A.P., Whitaker, R.T., 1999. Partitioning 3D surface meshes using watershed segmentation. *IEEE Trans. Vis. Comput. Graph.* 5 (4), 308–321.

Makuuchi, M., Someya, Y., Ogawa, S., Takayama, Y., 2012. Hand shape selection in pantomimed grasping: interaction between the dorsal and the ventral visual streams and convergence on the ventral premotor area. *Hum. Brain Mapp.* 33, 1821-33. doi: 10.1002/hbm.21323.

Molenberghs, P., Cunnington, R., Mattingley, J.B., 2012. Brain regions with mirror properties: a meta-analysis of 125 human fMRI studies. *Neurosci. Biobehav. Rev.* 36, 341–349.

Molenberghs, P., Cunnington, R., Mattingley, J.B., 2009. Is the mirror neuron system involved in imitation? A short review and meta-analysis. *Neurosci. Biobehav. Rev.* 33, 975–980.

Monaco, S., Cavina-Pratesi, C., Sedda, A., Fattori, P., Galletti, C., Culham, J.C., 2011. Functional magnetic resonance adaptation reveals the involvement of the dorsomedial stream in hand orientation for grasping. *J. Neurophysiol.* 106, 2248–2263.

Murata, A., Gallese, V., Luppino, G., Kaseda, M., Sakata, H., 2000. Selectivity for the shape, size, and orientation of objects for grasping in neurons of monkey parietal area AIP. *J. Neurophysiol.* 83, 2580–2601.

Nelissen, K., Fiave, P.A., Vanduffel, W., 2018. Decoding Grasping Movements from the Parieto-Frontal Reaching Circuit in the Nonhuman Primate. *Cereb. Cortex.* 28, 1245-1259. doi: 10.1093/cercor/bhx037.

Oldfield, R. C., 1971. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 9, 97–113. [https://doi.org/10.1016/0028-3932\(71\)90067-4](https://doi.org/10.1016/0028-3932(71)90067-4).

Pandya, D.N., Seltzer, B., 1982. Intrinsic connections and architectonics of posterior parietal cortex in the rhesus monkey. *J. Comp. Neurol.* 204, 196–210.

Passarelli, L., Rosa, M.G., Gamberini, M., Bakola, S., Burman, K.J., Fattori, P., Galletti, C., 2011. Cortical connections of area V6Av in the macaque: a visual- input node to the eye/hand coordination system. *J. Neurosci.* 31, 1790 –1801.

Perenin, M.T., Vighetto, A., 1988. Optic ataxia: a specific disruption in visuomotor mechanisms. I. Different aspects of the deficit in reaching for objects. *Brain* 111, 643–674.

Pisarchia, V., Breveglieri, R., Hadjidimitrakis, K., Bertozzi, F., Galletti, C., Fattori, P., 2017. Mixed body/hand reference frame for reaching in 3D space in macaque parietal area PEc. *Cereb. Cortex.* <http://dx.doi.org/10.1093/cercor/bhw039>.

Pitzalis, S., Galletti, C., Huang, R.S., Patria, F., Committeri, G., Galati, G., Fattori, P., Sereno, M.I., 2006. Wide-Field Retinotopy Defines Human Cortical Visual Area V6. *J. Neurosci.* 26, 7962–7973. <https://doi.org/10.1523/JNEUROSCI.0178-06.2006>.

Pitzalis, S., Sereno, M.I., Committeri, G., Fattori, P., Galati, G., Patria, F., Galletti, C., 2010. Human v6: the medial motion area. *Cereb Cortex* 20(2):411–424. doi:10.1093/cercor/bhp112

Pitzalis, S., Sereno, M.I., Committeri, G., Fattori, P., Galati, G., Tosoni, A., Galletti, C., 2013. The human homologue of macaque area V6A. *Neuroimage* 82, 517–530. <https://doi.org/10.1016/j.neuroimage.2013.06.026>.



Pitzalis, S., Fattori, P., Galletti, C., 2015. The human cortical areas V6 and V6A. *Vis. Neurosci.* 32, E007. <https://doi.org/10.1017/S0952523815000048>.

Pitzalis, S., Serra, C., Sulpizio, V., Di Marco, S., Fattori, P., Galati, G., Galletti, C., 2019. A putative human homologue of the macaque area PEc. *Neuroimage*. In press. doi: 10.1016/j.neuroimage.2019.116092.

Prado, J., Clavagnier, S., Otzenberger, H., Scheiber, C., Kennedy, H., Perenin, M.T., 2005. Two cortical systems for reaching in central and peripheral vision. *Neuron* 48, 849–858,.

Rizzolatti, G., Kalaska, J.F., 2013. Voluntary movement: the parietal and premotor cortex. In: *Principles of neural science*. Columbus, OH, USA: McGraw-Hill

Sakata, H., Taira, M., Murata, A., Mine, S., 1995. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb. Cortex.* 5, 429–438.

Schaffelhofer, S., Agudelo-Toro, A., Scherberger, H., 2015. Decoding a wide range of hand configurations from macaque motor, premotor, and parietal cortices. *J Neurosci* 35:1068–1081.

Shikata, E., Hamzei, F., Glauche, V., Koch, M., Weiller, C., Binkofski, F., Buchel, C., 2003. Functional properties and interaction of the anterior and posterior intraparietal areas in humans. *Eur. J. Neurosci.* 17, 1105–1110,.

Simon, O., Mangin, J.F., Cohen, L., Le Bihan, D., Dehaene, S., 2002. Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron* 33, 475–487.

Styrkowiec, P.P., Nowik, A.M., Króliczak, G., 2019. The neural underpinnings of haptically guided functional grasping of tools: An fMRI study. *Neuroimage* 194, 149-162. doi: 10.1016/j.neuroimage.2019.03.043.

Sulpizio, V., Boccia, M., Guariglia, C., Galati, G., 2018. Neural codes for one's own position and direction in a real-world "vista" environment. *Front. Hum. Neurosci.* 30 (12), 167. doi: 10.3389/fnhum.2018.00167.

Tosoni, A., Pitzalis, S., Committeri, G., Fattori, P., Galletti, C., Galati, G., 2015. Resting-state connectivity and functional specialization in human medial parieto-occipital cortex. *Brain Struct. Funct.* 220, 3307–3321

Turella, L., Lingnau, A., 2014. Neural correlates of grasping. *Front. Hum. Neurosci.* 8: 686.

Van Essen, D.C., Glasser, M.F., Dierker, D.L., Harwell, J., Coalson, T., 2012. Parcellations and hemispheric asymmetries of human cerebral cortex analyzed on surface-based atlases. *Cereb. Cortex* 22, 2241–2262. doi:10.1093/cercor/bhr291.

Verhagen, L., Dijkerman, H.C., Medendorp, W.P., Toni, I., 2012. Cortical dynamics of sensorimotor integration during grasp planning. *J Neurosci.* 32:4508–4519.

Verhagen, L., Dijkerman, H.C., Medendorp, W.P., Toni, I., 2013. Hierarchical organization of parietofrontal circuits during goal-directed action. *J Neurosci.* 33:6492–6503.

Vesia, M., Barnett-Cowan, M., Elahi, B., Jegatheeswaran, G., Isayama, R., Neva, J.L., Davare, M., Staines, W.R., Culham, J.C., Chen, R., 2017. Human dorsomedial parieto-motor circuit specifies grasp during the planning of goal-directed hand actions. *Cortex.* 92, 175-186. doi: 10.1016/j.cortex.2017.04.007.

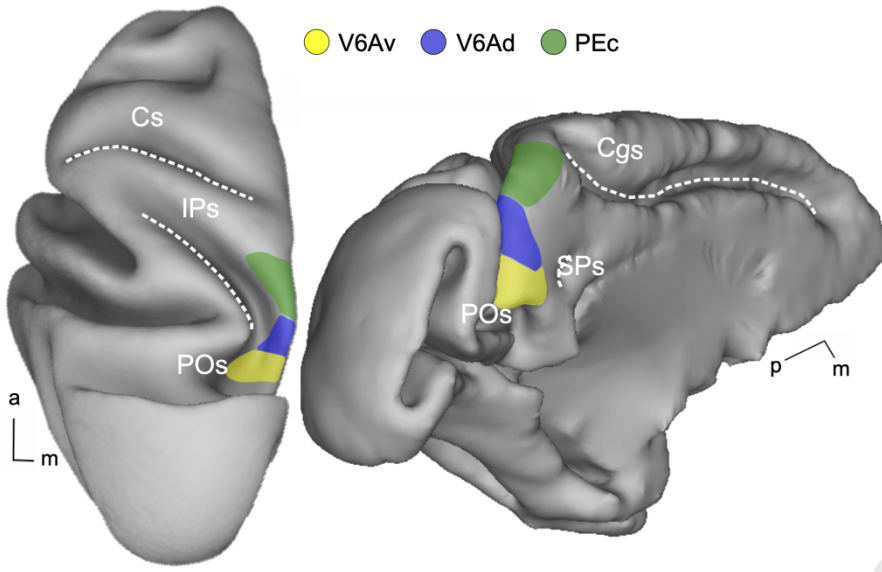
**Conflicts of interest**

We have no conflict of interest to declare.

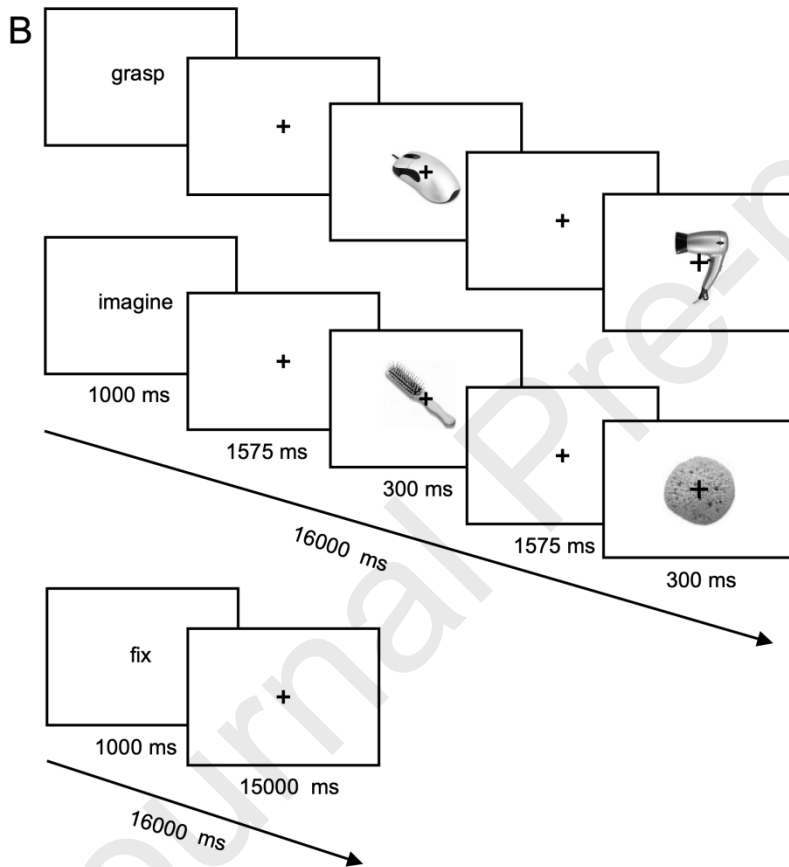
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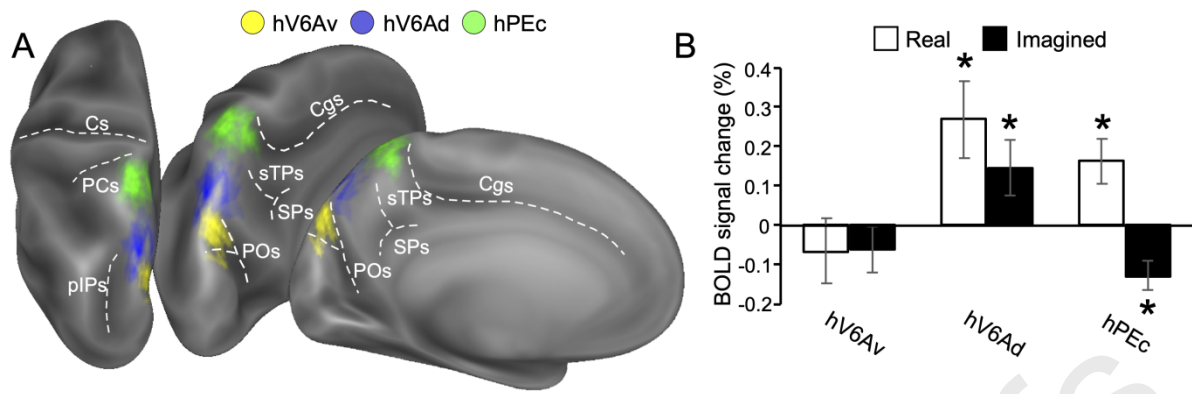
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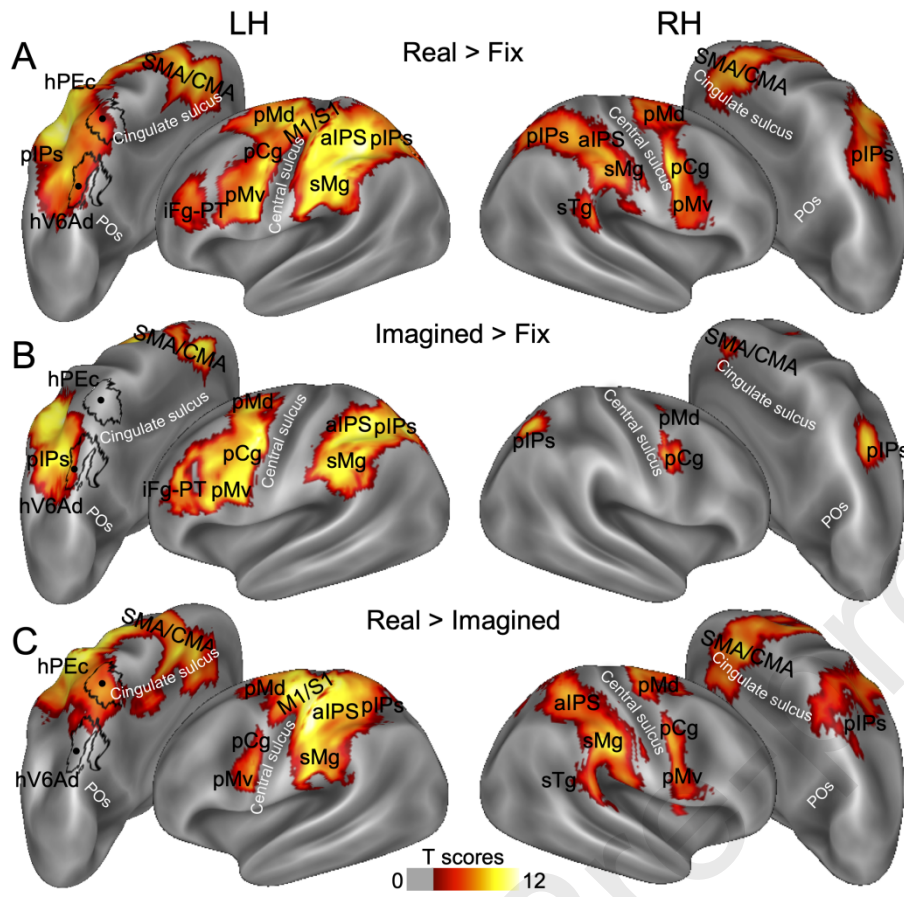


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The human dorsomedial parietal cortex responds to pantomimed grasping movements  
Areas hV6A and hPEc are differently activated by real and imagined grasping movements  
Areas hV6Ad and hPEc are respectively involved in cognitive and pragmatic aspects of the control of grasping

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