Connectivity-Based Parcellation of the Human Posteromedial Cortex

Ya Qin Zhang1, Lingzhong Fan2, Yu Zhang2, Jiaojian Wang1, Maohu Zhu2, Yuanchao Zhang1, Chunshui Yu3 and Tianzi Jiang1,2,4

1Key Laboratory for NeuroInformation of the Ministry of Education, School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu 625014, China 2LIIAMA Center for Computational Medicine, National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China 3Department of Radiology, Tianjin Medical University General Hospital, Tianjin 300052, China and 4The Queensland Brain Institute, The University of Queensland, Brisbane, Queensland 4072, Australia

Address correspondence to Tianzi Jiang, LIIAMA Center for Computational Medicine, National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China. Email: jiangtz@nlpr.ia.ac.cn, tianzi.jiang@gmail.com.

Regional structural and functional variations in the posteromedial cortex (PMC) have been found in both animals and humans, strongly suggesting the presence of subdivisions. However, there is no consensus on how to subdivide the human PMC. Here, we investigated the anatomical parcellation scheme and the connectivity pattern of each subdivision of the human PMC using diffusion tensor imaging data from 2 independent groups of volunteers. The parcellation analyses of the 2 datasets consistently demonstrated that the human PMC can be parcellated into 5 subregions. The dorsal portion of the PMC was subdivided into anterior, central, and posterior subregions, which participate in sensorimotor, associative, and visual functions. The ventral PMC contained a transitional region in the dorsal portion and a ventral subregion that is the core of the default mode network. The parcellation results for the human PMC and its anatomical connectivity patterns were further supported by evidence from the macaque PMC. Furthermore, functional connectivity analysis revealed that each subregion exhibited a specific pattern similar to that of its anatomical connectivity. The proposed parcellation scheme may facilitate the study of the human PMC at a subtler level and improve our understanding of its functions.

Keywords: atlas, connectivity, cortex parcellation, diffusion tensor imaging, parietal cortex

Introduction

The posteromedial cortex (PMC) is an association area involved in a variety of functions, including visuo-spatial imagery, episodic memory retrieval, self-processing, and consciousness (Cavanna and Trimble 2006; Cavanna 2007). Clinically, studies indicate that the PMC is the first cerebral region to increase activity in conscious waking from a vegetative state (Andreassen et al. 1995; Maquet et al. 1997; Laureys et al. 1999). The PMC is the most active area during the resting state and plays a pivotal role in the default mode network (DMN; Fransson and Marrelec 2008). Given its complex and various functions, the PMC is a region with high heterogeneity, strongly suggesting the presence of subdivisions. However, the human PMC is not yet clearly mapped and is generally taken as a homogeneous structure because of its deep location, which makes it difficult to study noninvasively. With modern neuroimaging, it has become possible to explore the organization of the human PMC conveniently in vivo, and several recent studies have provided functional subdivisions (Margulies et al. 2009; Cauda et al. 2010; Zhang and Li 2012). However, a consensus scheme for subdividing the PMC has not yet developed, even though the segmentations are all based on functional connectivity. Consequently, other aspects of the human PMC need to be studied to clarify its parcellation scheme.

Previous studies have led to the hypothesis that functional heterogeneity is linked with structural diversity, and the function of a brain region might be determined by its neuronal circuits (Parvizi et al. 2006). Thus, functional segregation would be constrained by the patterns of anatomical connectivity (Passingham et al. 2002; Averbeck et al. 2009). Although many studies have identified subregions of the human PMC with particular functional characteristics, the corresponding anatomical organization remains unclear. Thus, it is necessary to explore the anatomical connectivity and organization of the PMC in order to gain a better understanding of its subdivisions. A proposed subdivision scheme for the PMC (Morecraft et al. 2004), primarily derived from anatomical connectivity studies in monkeys, identified 5 distinct regions in both hemispheres. However, several studies in humans have found asymmetry in the posterior parietal cortices, suggesting that the right posterior parietal cortex may play a more important role (Sack et al. 2002; Wilson et al. 2005; Sheremata et al. 2010; Koch et al. 2011). Considering the asymmetry of the posterior parietal region to which the PMC belongs, we were particularly interested in subdivisions of the right PMC in humans. The left PMC was also parcellated for completeness.

We first determined the anatomical connectivity profiles of each voxel within the PMC using diffusion tensor imaging (DTI) and then provided a voxelwise clustering of the human PMC based on the distinct anatomical connectivity patterns. After that, another dataset at higher resolution was used for replication. Finally, we examined specific patterns of anatomical connectivity and resting-state functional connectivity (rsFC) in each PMC subregion as well as the axonal connections validated by tracer studies in the macaque.

Materials and Methods

Subjects

We acquired diffusion-weighted images from a group of 21 healthy right-handed subjects (dataset 1; 11 males and 10 females; age (mean ± standard deviation [SD]), 23.3 ± 1.8; range 19–25 years) and a completely independent group of 10 healthy right-handed subjects for replication (dataset 2; 3 males and 7 females; age 25.2 ± 1.8; range 22–29 years). All subjects signed a written, informed consent form that was approved by the Medical Research Ethics Committee of Tianjin Medical University.

Data Acquisition

For dataset 1, all images were performed on a 3-T GE Signa HDxt scanner (Software Version 14). Echo-planar imaging blood oxygen...
level-dependent images of the whole brain were acquired in 40 axial slices (repetition time [TR] 2000 ms; echo time [TE] 30 ms; flip angle [FA] 90°; matrix 64 × 64; field of view (FOV) 240 × 240 mm²; 4 mm thickness, 0 mm gap, and 3.75 × 3.75 mm² in-plane resolution). The functional magnetic resonance imaging (fMRI) scanning was carried out in darkness, and the participants were explicitly instructed to keep their eyes closed and move as little as possible. In each participant, 180 volumes were obtained. Anatomical T₁-weighted images were collected using a high-resolution T₁-weighted brain volume (BRAVO) 3-dimensional MRI sequence, with 176 contiguous 1-mm sagittal slices (TE 3.12 ms; TR 7.79 ms; matrix 256 × 256; FOV 256 × 256 mm²; FA 90°; voxel size 1 × 1 × 1 mm³). Diffusion-weighted images were collected using echo-planar imaging with 45 contiguous 3-mm axial slices and 55 noncollinear diffusion gradients (TE 64.2 ms; TR 15000 ms; b-value 1000 s/mm²; matrix 128 × 128; FOV 256 × 256 mm²; FA 90°; voxel size 2 × 2 × 2 mm³).

For dataset 2, all images were captured on the same scanner as for dataset 1. Anatomical T₁-weighted images were collected using a high-resolution T₁-weighted BRAVO 3-D MRI sequence, with 188 contiguous 1-mm sagittal slices (TE 2.98 ms; TR 7.79 ms; matrix 256 × 256; FOV 256 × 256 mm²; FA 90°; voxel size 1 × 1 × 1 mm³). Diffusion-weighted images were collected using echo-planar imaging with 69 contiguous 2-mm axial slices and 50 noncollinear diffusion gradients (TE 73 ms; TR 15000 ms; b-value 1000 s/mm²; matrix 128 × 128; FOV 256 × 256 mm²; FA 90°; voxel size 2 × 2 × 2 mm³).

Data Analysis

DTI Analysis

Data were analyzed using the FMRIB Software Library (FSL; http://www.fmrib.ox.ac.uk/fsl). Diffusion data were first corrected for eddy currents and head motion by affine registration to a reference volume. Then, the probability distributions of fiber directions were calculated for each brain voxel using a multiple fiber extension (Behrens et al. 2007) of a previously published diffusion modeling approach. To compensate for the distance-dependent bias, probability counts were corrected by the length of the pathway in the connectivity-based parcellation. The connectivity distribution is the expected length of the pathways that cross each voxel times the number of samples that cross it (Tomassini et al. 2007). While in the section of anatomical connectivity fingerprints of the PMC subregions, we were interested in absolute measures of connection probability and did not correct for distance. We drew 5000 samples from the connectivity distribution from each voxel in the seed region in each subject.

mbscs

Figure 1. Definition of the PMC mask. The PMC is limited anteriorly by the mbscs, posteriorly by the pof, and inferiorly by the ccs. mbscs, marginal branch of the cingulate sulcus; pof, parieto-occipital fissure; ccs, corpus callosum sulcus.

fMRI Preprocessing

Most of the preprocessing steps were carried out by analysis of functional neuroimages (AFNI; http://afni.nimh.nih.gov/afni) and FSL. The first 10 images were discarded because of instability of the signal and adaptation of the subjects to the situation. The remaining fMRI images were first corrected for within-scan acquisition time differences between slices and then realigned to the first volume to correct for interscan head motion. Motion time courses were obtained by estimating the values for translation and rotation for each of the 170 consecutive volumes. The participants in this study had <1.5 mm maximum displacement in x, y, or z and <1.5° angular motion about each axis. After that, the functional images were spatially smoothed with a Gaussian kernel of 6 × 6 × 6 mm³ to decrease spatial noise. The FMRI waveform of each voxel was temporally band-pass filtered (0.01 < f < 0.08 Hz), and the linear drift of the signal was removed. The preprocessing steps described above were processed by AFNI. Subsequently, we spatially registered the realigned, smoothed, and temporally filtered images to the Montreal Neurological Institute (MNI) space and resampled them to 3 × 3 × 3 mm³ by FSL. Besides discarding the data from subjects with large amounts of head motion, several sources of spurious or regionally nonspecific variance were then removed by regression of nuisance variables: 6-parameter rigid-body head motion (obtained from motion correction), the signal averaged over the whole brain, the signal averaged over the lateral ventricles, and the signal averaged over a region centered in the deep cerebral white matter.

Definition of PMC Seed Masks

The seed mask was manually drawn on a template of standard (MNI 152) space (Fig. 1). Mask boundaries were defined as follows. In the dorsal portion of the PMC, the anterior boundary was the marginal branch of the cingulate sulcus. The ventral extension line of the marginal branch was taken as the anterior limit of the mask at more ventral levels where the marginal branch was absent. In addition, the PMC mask is limited posteriorly by the medial portion of the parieto-occipital fissure and inferiorly by the corpus callosum sulcus (Crichtley 1953). Subsequently, we warped the PMC mask into the individual diffusion space using SPM8 (https://www.fil.ion.ucl.ac.uk/spm/). For each subject, we first registered the skull-stripped T₁ image to the individual b0 image, where the registered T₁ image was normalized to the standard template to get the transform matrix. Then, the seed mask in the diffusion space was obtained by applying the inverse of the transform matrix to the PMC mask in standard space. After these steps, every resulting mask was visually inspected for possible errors or necessary modification.

Connectivity-Based Parcellation

All the probabilistic fiber tracking was performed in the native diffusion space, while data were stored in a down-sampled lower resolution (5 × 5 × 5 mm³) space for reasons of data storage and noise reduction. We set a threshold to these down-sampled data to remove the false connections with lower probability as follows. First, probabilistic tracking was performed in a seed voxel located on the posterior cingulate for 3 subjects. Then a threshold was chosen to remove apparent false connections while keeping the cingulum intact. As a result, a threshold of 10 met this purpose. Thus, the probabilities of connection from each voxel of the seed region (at 2 × 2 × 2 mm³ resolution) to each voxel in the low-resolution brain (5 × 5 × 5 mm³) used 10 as the threshold, and they were stored in a matrix. Information about the connectivity was stored in this M-by-N matrix, where M denotes the number of voxels in the seed mask and N the number of voxels in the low-resolution brain space. Then, for each pair of voxels in the seed mask, we calculated the correlation between their connectivity profiles, resulting in an M-by-M cross-correlation matrix.

The individual cross-correlation matrix was used as an input to a spectral clustering algorithm (Ng et al. 2002) to group voxels with similar connectivity profiles together. We did not add the weight of the spatial distance, so the grouping of voxels was entirely dependent on the diffusion information. The number of clusters was chosen by...
the experimenter, and set to the highest number that produced a consistent, comparable, and spatially similar pattern of clustering across subjects (Anwander et al. 2007; Beckmann et al. 2009; Mars, Jbabdi, et al. 2011; Mars, Sallet, et al. 2011). Here, we tried parcellation numbers from 2 to 8 clusters and used the Dice coefficient (Dice 1945) to help measure the similarity of parcellation results between subjects. Reasonable consistency was achieved at numbers of component clusters from 2 to 5, and the highest number (5 clusters) was chosen (Fig. 2).

For visualization purposes only, the probabilistic tractography results of all voxels in each cluster were summed for each subject and then transformed into standard MNI space and averaged across subjects.

Reproducibility
To explore the reproducibility of the connectivity-defined clusters, dataset 2 was preprocessed by the same method as dataset 1 to get the cross-correlation matrices. We used the spectral clustering algorithm with 5 as a constraint for identifying clusters, and these cross-correlation matrices as input. Additionally in both datasets, we transformed the clusters for each subject into MNI standard space and then calculated the cluster overlaps across subjects. We also calculated the maximum probabilistic map (MPM) of clusters. This map showed to which cluster a given voxel of the PMC most likely belonged and provided a continuous atlas of the PMC without overlap.

Anatomical Connectivity Fingerprints of PMC Subregions
In this part, 5 distinct clusters in the right PMC were used as seed masks for each subject. Target masks were defined by using the 50% probability map in the probabilistic Harvard-Oxford cortical and subcortical structural atlases (http://www.fmrib.ox.ac.uk/fsl/data/50% probability map in the probabilistic Harvard-Oxford cortical and subcortical structural atlases). All the extra PMC cerebral areas (both cortical and subcortical) were included as target areas and were defined separately for each hemisphere. These target areas were then transformed from MNI space into individual diffusion space. The probabilistic tractography was run from voxels within each cluster of the PMC to assess connectivity with every target region in each subject. After computing the mean probability of connection for each seed-target combination, the value was then normalized on an individual basis by dividing by the size of the target volume. These steps adjusted our data for the size of the seed and target regions. Finally, the mean probabilistic connectivity from the seed region to the target region was computed across all subjects.

Functional Connectivity of the PMC
For each subregion of the PMC, voxels with a probability >50% in the MPM were chosen as a seed region. The time signal of each seed region was computed by averaging the time signals of all voxels within this region. The strength of functional connectivity was measured by Pearson correlations between the averaged time series of each seed region and whole-brain voxels in each subject. Then, Fisher’s z transform (Zar 1999) was applied to normalize the original correlation maps. After that, a one-sample t-test of these normalized correlation maps was performed to identify voxels significantly correlated with a given PMC cluster.

Reference to Macaque Data
In the macaque, differences from the human lateral parietal cortex in subregions and their connectivities have been documented (Glover 2004; Mars, Jbabdi, et al. 2011). However, the subdivisions of the macaque PMC were very similar to those of humans in the present study, suggesting that the PMC is similarly organized in humans and monkeys. Thus, we were interested in whether consistent corresponding connectivity patterns could also be found in the 2 species and summarized the previous tract tracer studies according to the widely used parcellation in the macaque (Pandya and Seltzer 1982; Morecraft et al. 2004) using the CoCoMac database (http://cocomac.org, version uploaded on 29.02.2008; Stephan et al. 2001).

Results

Connectivity-Based Parcellation
In dataset 1, spectral clustering revealed a clear segregation of the PMC into 5 clusters in each hemisphere (Fig. 3). The anatomical connectivity pattern of each cluster is illustrated in Figure 4. In detail, the dorsal portion of the PMC was divided into 3 distinct anterior–posterior regions. The most anterior subregion (cluster 1), along the marginal branch of the cingulate sulcus, was richly connected to sensorimotor regions, such as the supplementary motor area (SMA), paracentral lobule, cingulate motor area, dorsal premotor cortex, and dorsal precentral and postcentral gyri. Connections were also observed with the supracalcarine cortex, dorsolateral prefrontal cortex, superior parietal lobule, angular gyrus, and rostral superior temporal gyrus. The most posterior portion (cluster 3), running along the parieto-occipital sulcus and extending as far as the area posterior to the retrosplenial cortex in some subjects, had strong connections with vision-related areas, including the cuneus, supracalcarine cortex, intracalcarine cortex, lingual gyrus, and lateral occipital lobule. The cingulate motor area, superior parietal lobule, supramarginal gyrus, rostral superior temporal gyrus, and inferior temporal gyrus also had connections with cluster 3. The central portion (cluster 2) between clusters 1 and 3 showed widespread connections with the superior parietal lobule, supramarginal gyrus, angular gyrus, and superior temporal gyrus. Additional connections were observed in the dorsal premotor cortex, but much fewer than in cluster 1. Both dorsal and ventral regions were found in the ventral portion of the PMC. The dorsal region (cluster 4) was situated at the level of the subparietal sulcus and the ventral region (cluster 5) mainly occupied the posterior cingulate and retrosplenial cortex. Areas connected with these 2 subregions were quite different between the hemispheres. In the ipsilateral brain, the 2 subregions shared close connectivity with the medial prefrontal cortex, cingulate areas, and cortex around the calcarine sulcus. In the contralateral brain, cluster 4 had connections with the cingulate motor cortex, paracentral lobule, and supracalcarine cortex, while cluster 5 had sparse connections with extra PMC areas.

![Figure 2](image-url)
Consistency Analysis

In dataset 2, where the number of clusters was set to 5, the results of parcellation also consistently identified 3 anterior–posterior clusters in the dorsal PMC and 2 dorsal–ventral clusters in the ventral PMC (Fig. 3a). The population probabilistic maps for individual PMC clusters after transformed into MNI space are shown in Figure 3b.

Anatomical Connectivity Fingerprints of PMC Subregions

Target regions with connection probability $P > 0.01$ (50 of 5000 samples) are summarized in Figure 5. Targets with the highest probability of connection with cluster 1 were thalamus, anterior division of the supramarginal gyrus, and postcentral gyrus. Thalamus, putamen, pallidum, and superior parietal lobule appeared to be predominantly connected with cluster 2. Cluster 3 had a high probability of connection with visual areas, including cuneus and superior lateral occipital cortex. Strong connections were also made with the anterior superior temporal gyrus, anterior middle temporal gyrus, and some subcortical structures, such as planum polare, thalamus, putamen, and amygdala. Clusters 4 and 5 shared a high probability of connection with the supracalcarine and intracalcarine cortices. In addition, cluster 4 strongly connected to the cuneus cortex, while the paracingulate and anterior cingulate gyri had a high probability of connection with cluster 5. In addition, the 3 clusters in the dorsal PMC had more connections with the contralateral brain, while the 2 clusters in the ventral PMC were closely connected with regions from the ipsilateral brain.

Functional Connectivity of PMC Subregions

The functional connectivity map derived from each PMC cluster is illustrated in Figure 6. Cluster 1 had rich positive correlations with the lateral superior frontal gyrus, middle frontal gyrus, insular cortex, precentral gyrus, postcentral gyrus, superior parietal lobule, supramarginal gyrus, posterior superior temporal gyrus, lateral occipital cortex, SMA, paracentral lobule, and middle cingulate gyrus. Negative correlations with cluster 1 were observed in the superior frontal gyrus, middle frontal gyrus, lateral occipital cortex, angular gyrus, middle temporal gyrus, and paracingulate gyrus. For cluster 2, positive correlations were found with the lateral superior frontal gyrus, middle frontal gyrus, superior parietal lobule, supramarginal gyrus, angular gyrus, lateral occipital cortex, temporo-occipital part of middle and inferior temporal gyri, and middle cingulate gyrus. Areas having negative correlations with cluster 2 were superior frontal gyrus, middle frontal gyrus, triangularis part of the inferior frontal gyrus, precentral gyrus, angular gyrus, middle temporal gyrus, lateral occipital pole, and parahippocampal gyrus. Cluster 3 showed positive correlations with the superior frontal gyrus, middle frontal gyrus, lateral frontal pole, superior parietal lobule, angular gyrus, lateral superior occipital cortex, cuneal cortex, supracalcarine cortex, and intracalcarine cortex. Superior frontal gyrus and central opercular cortex had negative correlations with cluster 3. For cluster 4, positive correlations were found with the middle frontal gyrus, angular gyrus, lateral superior occipital cortex, intracalcarine cortex, and posterior temporal fusiform cortex. Negative correlations with cluster 4 were observed in the lateral frontal pole and lateral occipital pole. Cluster 5 had widespread positive correlations with the superior frontal gyrus, middle frontal gyrus, frontal pole, angular gyrus, middle temporal gyrus, frontal medial cortex, anterior cingulate gyrus, supracalcarine cortex, intracalcarine cortex, parahippocampal gyrus, lingual gyrus, posterior temporal fusiform cortex and temporal occipital fusiform cortex, and negative correlations with the superior
frontal gyrus, middle frontal gyrus, insular cortex, inferior frontal gyrus, superior parietal lobule, supramarginal gyrus, angular gyrus, superior temporal gyrus, temporo-occipital part of the inferior temporal gyrus, SMA, and middle cingulate gyrus.

**Discussion**

In the present study, we characterized the anatomical organization of the human PMC based on the anatomical connection profile. First, 5 subregions were assessed using DTI and probabilistic fiber tracking in 2 datasets. Specifically, the dorsal PMC comprised 3 anterior–posterior regions, and the ventral PMC included 2 dorsal–ventral regions. Then the anatomical and functional connectivity patterns of these subregions were examined to assess their potential roles.

DTI and probabilistic fiber tracking are feasible and powerful tools to investigate connectivity profiles and to identify subregions of brain areas in vivo (Johansen-Berg et al. 2004; Rushworth et al. 2006; Anwander et al. 2007; Klein et al. 2007; Tomassini et al. 2007; Beckmann et al. 2009; Menke et al. 2010; Schubotz et al. 2010; Solano-Castiella et al. 2010; Bach et al. 2011; Mars, Jbabdi, et al. 2011). However, it has been claimed that signal-to-noise ratio and artifacts influence parcellation results (Bach et al. 2011). Consequently, 2 independent datasets at different resolutions were used in the current study to avoid bias from image acquisition, and the consistency of the 2 parcellation results further confirmed the 5 clusters in the human PMC.

In the dorsal PMC, the 2 datasets consistently demonstrated striking anterior–posterior differentiation and identified 3 clusters. Supporting evidence was provided by previous

**Figure 4.** Fiber tract patterns as obtained from probabilistic tractography for 5 right PMC subregions. Probabilistic fiber tracts generated from individual diffusion spaces were projected back into MNI space and averaged across subjects.
cytoarchitectonic studies in which gradual rostrocaudal architectural changes are reported within the dorsal PMC (Brodmann 1909; Vogt 1911; Economo and Koskinas 1925; Schepersjans, Eickhoff, et al. 2008). Recent cytoarchitectonic studies further subdivide the dorsal PMC into 5 areas, in which 5L and 5M may correspond to cluster 1, 7A to cluster 2, and 7P and 7M to clusters 3 of the present work (Schepersjans, Eickhoff, et al. 2008; Schepersjans, Hermann, et al. 2008). In addition, recent functional research also suggests heterogeneous characteristics from anterior to posterior of the dorsal PMC (Zhang and Li 2012). It has been claimed that the anterior portion of the dorsal PMC is related to the sensorimotor network, while the posterior portion is interlinked with visual areas. Interestingly, our clusters identified by DTI-based parcellation were also related to areas identified in these functional investigations of the PMC (Margulies et al. 2009; Cauda et al. 2010). Transmitter receptor distribution studies also revealed that the dorsal–rostral and dorsal–caudal PMC are similar to the somatosensory cortex and visual areas, respectively (Schepersjans et al. 2005). Besides, activation of the dorsal-anterior PMC has the strongest correlation with self-centered mental imagery strategies, whereas the dorsal-posterior portion is associated with successful episodic memory retrieval (Cavanna and Trimble 2006). Moreover, the dorsal-anterior portions of the PMC are also reported to be involved in the preparation or execution of spatially guided behaviors (Wenderoth et al. 2006), while the dorsal-posterior portions are implicated in mental imagery (Hanakawa et al. 2003; Knauff et al. 2003), and processing of self-relevant information and emotions (Cavanna et al. 2010). For the dorsal-central PMC, we found strong connections with its anterior and posterior regions in the medial wall, and also with the superior parietal lobule and temporoparietal areas in the lateral surface. These connections suggested that the dorsal-central region may be a bridge for the anterior sensorimotor and posterior visual regions, as well as the integration of related cognition. This region was also described as a part of the frontoparietal control system in an earlier report (Vincent et al. 2008).

The ventral PMC parcellation yielded 2 clusters, and in most cases, it was possible to identify their relationships with the cytoarchitectonically defined areas 21 and 23 (Brodmann 1909). The dorsal part of the ventral PMC, cluster 4, shared some functional connections with other PMC clusters, such as connectivity with the dorsal prefrontal area, supramarginal gyrus, angular gyrus, and lateral occipital cortex, but the strength was much less than that of the other 4 PMC clusters. On the other hand, cluster 4 had anatomical connections with all other surrounding regions, as well as the cingulate gyrus, which belongs to the limbic system. The variety of connections might indicate cluster 4 to be a transition zone. This hypothesis is supported by a functional study in which almost all PMC areas showed both positive and negative correlations with this cluster (Cauda et al. 2010). Strong evidence was also provided by an apparent shift from parietal isocortex to limbic cortex in terms of cytoarchitecture (Pandya and Selzer 1982) and, thus, this region is often proposed as belonging to both the precuneus and posterior cingulate cortices (Cavanna 2007). In addition, this region is known to be implicated in the task-positive network (Cauda et al. 2010), spatial orientation, and memory tasks (Spiers and Maguire 2007; Beckmann et al. 2009). For the most ventral region of the PMC, connections with medial prefrontal, anterior cingulate, posterior cingulate, and intracalcarine cortices were found by both anatomical and functional analysies to be part of the DMN. Specifically, in this study, experimental results showed that only the ventral portion of the PMC is a core node of the DMN, which has a dorsal terminus near the subparietal sulcus. Although previous studies included the whole PMC in the DMN (Fransson and Marrelec 2008; Hagmann et al. 2008), recent work has provided strong evidence of functional heterogeneity in the human PMC and supports our view. A functional study demonstrated that connectivity with the parahippocampal area, which is characteristic of the DMN, is
Figure 6. rsFC maps from 5 distinct subregions of the right PMC. Statistical parametric maps using a voxel-level statistical threshold of $P < 0.05$ corrected for false discovery rate. Caret software (Van Essen et al. 2001) was used to visualize these maps.

Figure 7. Schematic drawings of areas connected with each subregion of the macaque PMC. Colored dots beneath each area indicate the presence of a connection to the respective subregion of the macaque PMC. Connections depicted here were obtained from and named according to the CoCoMac database (http://cocomac.org, version uploaded on 29.02.2008; Stephan et al. 2001).
selective within the PMC (Cauda et al. 2010). Others highlighted that, in fact, the precuneus is not a component of the DMN (Buckner et al. 2008; Margulies et al. 2009). Another study suggested that the posterior cingulate cortex is a midline core of the DMN (Andrews-Hanna et al. 2010). Furthermore, intracranial electrophysiological recording from a human revealed that the most ventral portion of the PMC responds to autobiographical self-referential stimuli (Dastjerdi et al. 2011). Electroencephalography also pointed out that the spatial domain of its core is close to the retrosplenial cortex, including the depth of the callosal sulcus and the posterior cingulate area 23a, and is almost the same as cluster 5 in the current study.

In the macaque, the connectivity patterns of the PMC closely resemble those of humans (Fig. 7). The caudal and medial part of the superior parietal lobule (area PEc) in the macaque mainly connected to the premotor cortex, primary motor area, superior parietal lobule, caudal inferior parietal lobule, caudal parietal operculum, rostral SMA, paracentral lobule, and caudal cingulate cortex. This pattern is quite consistent with that of cluster 1 in the human PMC. The medial part of parietal area PG (area PGM) in the macaque has widespread connections with the lateral prefrontal cortex and cingulate areas. Connections to these areas were also found in cluster 2 in the human PMC. In macaques, rich connections with visual areas and superior temporal sulcus are typical of the parieto-occipital area (area PO), and in humans, a similar pattern was found for cluster 3 in the PMC. Besides, connections from area 31 to the dorsolateral prefrontal cortex and caudal cingulate areas in macaques are consistent with the functional connectivity of cluster 4 in the human PMC. In addition, area 23 of the macaque has many connections with the lateral and medial prefrontal cortex, inferior parietal lobule, cingulate cortex, and paracingulate gyrus. This pattern strongly resembles anatomical and functional connections of cluster 5 in humans. These connections demonstrated that areas PEc, PGM, PO, 31 and 23 of the macaque are comparable with clusters 1–5 in humans, respectively, which support the concept of homology of the PMC in macaques and humans.

In summary, 5 distinct subregions in the human PMC were assessed by means of probabilistic tractography in this study. Analyses of anatomical and functional connectivities showed that the dorsal-anterior PMC mainly interacts with the sensorimotor system, while the dorsal-posterior PMC connects strongly with vision-related areas. The dorsal-central PMC seemed to be an association region and the dorsal portion of the ventral PMC might be a transition zone. The most ventral PMC is richly connected to the limbic system, suggesting involvement in the DMN. The human PMC has an anatomical organization and connections resembling those of the macaque PMC.

Notes
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