DWI tractography based parcellation of human lateral premotor cortex identifies reproducible subregions with distinct fronto-parietal connectivity

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Introduction. Cytoarchitectonic and functional studies in macaques have led to the view of the pre-motor cortex (PMC) as a complex mosaic of different areas made of many structural and functional fields, each of which processes different aspects of motor behaviour [1, 2]. In the human lateral PMC most macro-anatomical landmarks do not always match micro-structurally defined borders and are topographically variable across different individuals. Experimental evidence suggests that there are two major divisions of lateral PMC which are part of distinct functional circuits: the ventral PMC (PMv), involved in the execution and the observation of object-related movements, and the dorsal PMC (PMd), responsible for directing movements based on spatial information and influencing the generation of movements. Tracer studies in non-human primates show that PMd and PMv have distinct patterns of anatomical connectivity. In macaque monkeys a differential involvement of PMd and PMv in segregated parieto-frontal circuits for action and space perception has been demonstrated [2]. Comparative studies in human and macaque brains showed that similar patterns of anatomical interactions between brain areas in both species can be found using diffusion tractography [3, 4]. Diffusion tractography can also be used to define cortical borders based on anatomical connectivity patterns in the human brains [5,6]. A previous preliminary study suggests that it is possible to differentiate human PMd and PMv in this way [7]. The purpose of this study is to test whether the PMd/PMv border can be reliably identified using tractography, to compare the location of the border to local sulcal landmarks, to test the reproducibility of this border, and to characterize the connectivity fingerprints of the two sub-regions to parieto-frontal circuits.

Methods. Seventeen healthy controls were included in the study, 8 of whom participated in a reproducibility study, undergoing 3 diffusion/structural scans on separate days. Diffusion-weighted (b=1000, 60isotropic diffusion directions, 2x2x2mm voxels) and T1-weighted images were acquired on a 1.5T Siemens Sonata MR scanner. A hand-drawn mask of the lateral PMC was defined on individual T1-weighted images registered to MNI standard space; the final lateral PMC mask was defined as the overlap of the individual masks. Intersection of that mask with cortical grey matter of each subject served as a seed mask for probabilistic tractography. Local diffusivity directions were estimated using a model that accounts for the existence of two fibre directions per voxel, allowing for recovery of crossing fibre information [8]. Cross-correlation between connectivity patterns [5] of each voxel within the seed mask was stored into a matrix and segmented using k-means clustering [6], giving two clusters representing PMd and PMv, with a sharp border between the two sub-regions. In order to assess the reproducibility of PMC parcellation across subjects and sessions, a plane dividing PMd and PMv was automatically computed using a linear support vector machine.

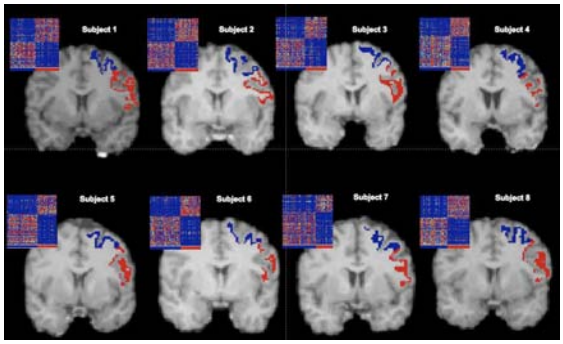


Fig. 1

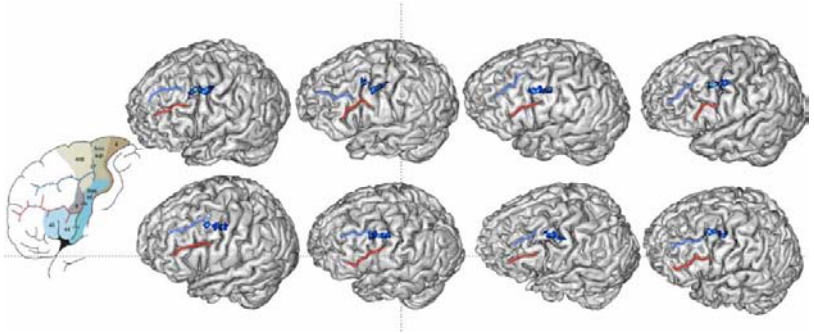
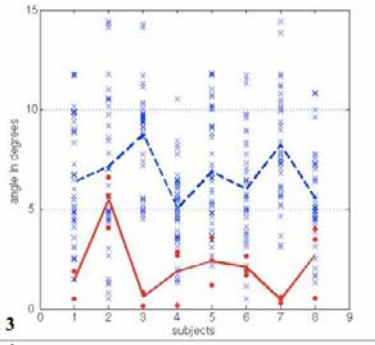


Fig. 2

Results. Connectivity-based segmentation of the PMC shows a very sharp edge between PMv and PMd in all subjects, as reported in Fig. 1 for 8 subjects. The projection of this boundary onto the cortical surface lies between the levels of the inferior and superior frontal gyrus in the majority of subjects (Fig. 2).). Fig. 3 (left) shows the angle between the separating planes (computed by the SVM) within subject (different sessions – in red) and across subjects (blue). These planes are shown for subject 1 in Fig.3 (right). They are very reproducible across subjects, and vary much less within subject than across subjects. Analyzing the anatomical connections of PMC sub-regions in the context of a prefrontal/parietal circuit, we demonstrate that PMv is mainly connected to the anterior intraparietal sulcus (AIPL) and angular gyrus (ANG), as well as ventral and dorsal parts of the lateral prefrontal cortex (PFvl, PFdl); by contrast strong PMd connections are observed with the superior parietal lobule (SPL) and intra-parietal sulcus (IPS) as well as the dorso-medial parts of the frontal lobe and cingulate cortex (PFdl+dm, Cing_gyrus and Cing_sulcus). Fig. 4 shows the mean relative contribution of the PMd (blue) and PMv (red) connections to the PM connectivity to each parietal and prefrontal target in 17 subjects.



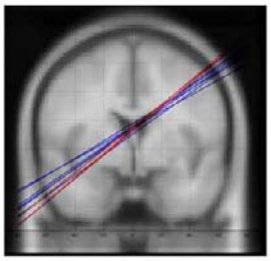
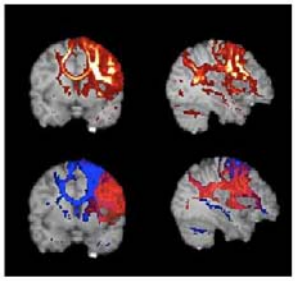
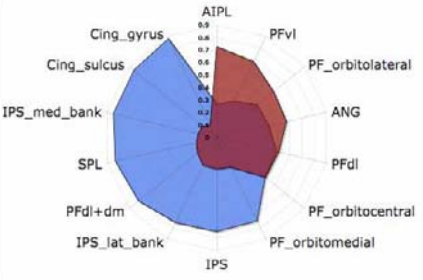


Fig. 3

Fig. 4





Conclusions. Anatomical connectivity defined a sharp border between PMd and PMv in the human brain. The border lies between the inferior and superior frontal gyri, confirming suggested homologies with the macaque brain [1]. The separation between the two regions is reproducible within subjects, and shows a small amount of variability across subjects. Connectional fingerprints to the ipsilateral parieto-frontal areas suggest the possibility to identify anatomically distinct networks for specific sensori-motor transformations, which resemble those described in animal model studies as circuits for object manipulation and visuo-spatial integration.

References. [1] Geyer et al (2000) Anat Embryol 202:443–474; [2] Rizzolatti G, et al. (1998) Electroencephalogr Clin Neurophysiol 106(4):283-96; [3] Rushworth et al (2006) Cereb Cortex 16(10):1418-30; [4] Croxson et al (2005) J Neurosci 25(39):8854-66; [5] Johansen-Berg et al (2004) PNAS 101:13335–13340; [6] Anwander et al (2006) Cereb Cortex May 17 Epub ahead of print; [7] Anwander et al (2005) ISMRM; [8] Behrens et al (2006) Neuroimage Oct 26 Epub ahead of print.