A connectivity-based parcellation of the left dorsal premotor cortex

Submission Number: 6485

Submission Type: Abstract Submission

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Introduction:
In a previous study, we performed connectivity-based parcellation (CBP) of the right dorsal premotor cortex (PMdr) [1] and characterized the functional profile of the derived clusters via meta-analytic functional decoding. This way PMdr was divided into five functional subregions (Fig. 1A) highlighting a cognitive-motor gradient along a rostro-caudal axis formed by a rostral cognitive cluster, a central "core" cluster, a caudal motor cluster, an "eye-field" ventral cluster, and a hand-related dorsal cluster. Here, we examined whether or not a similar organization emerged for the left PMd (PMdl) using the same approach.

Methods:
A PMdl volume of interest (VOI) was defined based on a series of meta-analytic findings [2,3,4,5,6]. Whole-brain coactivation patterns for each voxel within this VOI were identified by meta-analytic connectivity modeling (MACM, [7]) across all experiments in the BrainMap database activating this particular voxel. Based on those coactivation patterns, CBP [7] was performed using k-means [8] clustering. The most stable k clustering solution was determined by topological, cluster separation, and information-theoretic criteria. MACM performed on BrainMap and resting state functional connectivity were then combined to examine the derived clusters' brain-wide functional connectivity (FC). Finally, each cluster was functionally characterized by combining forward and reverse inferences on Behavioral Domain and Paradigm Class meta-data in BrainMap.

Results:
CBP identified three stable solutions: a four (4k), six (6k) or eight (8k) cluster solution. 4k revealed that the PMdl could be divided in three subregions along the rostro-caudal axis and that a central cluster furthermore emerged within this organization splitting the middle subregion in a ventral and dorsal part (Fig. 1B). 6k and 8k further subdivided the rostral and central clusters. As in our previous PMdr parcellation, we focused on the first stable and most parsimonious solution, i.e., 4k. Conjunctions of each cluster's unique RS and MACM results relative to all other clusters showed that the rostral cluster was specifically connected to dorsolateral prefrontal (DLPFC) and inferior parietal cortex, the caudal one to motor and sensorimotor areas, the middle one to language areas and the central cluster to superior DLPFC, superior parietal cortex and fusiform gyrus (Fig. 2). Functional decoding furthermore revealed that the rostral cluster was preferentially related to high-level cognition and the caudal one to motor-related functions. In turn, both, middle and central clusters showed a mixed functional profile. The central cluster was associated with a broader range of functions including visual and space-related cognition, while the middle one was associated with speech production (Fig. 3).
Combined unique resting state and meta-analytic functional connectivity of the four left PMd clusters: rostral cluster (red), caudal cluster (green), middle cluster (blue), central cluster (yellow)
Conclusions:

CBP of PMdl mirrored the cognitive-motor rostro-caudal gradient highlighted in PMdr [1] with a cognitive rostral cluster, a caudal primarily motor cluster and an intermediate zone that was further subdivided. In contrast to the three-partition of the latter in PMdr with clear functional preferences, we here found a two-partition on the left, comprising a middle cluster and a central cluster, with both showing mixed profiles. Whereas, the former was connected to speech regions and function, the latter was connected to the superior parietal cortex and fusiform gyrus and associated with visuo-spatial functions. Thus, while we found an integrative subregion centrally located and an "eye-field" subregion ventrally located in the PMdr, the visuo-spatial functions are associated to a more central integrative cluster in the PMdl. In sum, our PMdl findings replicate the rostro-caudal gradient observed for the right homotopic area but also demonstrate some striking differences in the functional organization of the left PMd, which might be due to this hemisphere's selective involvement in speech processing.

Modeling and Analysis Methods:

- Motor Behavior:
Visuo-Motor Functions

Neuroanatomy:
Cortical Anatomy and Brain Mapping

Keywords:
Meta- Analysis
Other

\[1\] Indicates the priority used for review

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**Figure 1.** A; right PMd parcellation (Genon et al., 2014), B; left PMd parcellation.

-CBP of the PMd. A. rostral(red), caudal(green), central(blue), ventral(yellow), dorsal(light blue). B. rostral(red), caudal(green), middle(blue), central(yellow)

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