Complex organization of primate frontal-parietal cortex

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RATIONALE

Traditional techniques such as invasive tract-tracing or cytoarchitecture are labor intensive, time consuming, and more importantly, cannot be used to study the brain of living animals, including humans. Recently, resting-state functional connectivity has been shown to reflect anatomical organization (Goulas et al., 2017, *J Neurophys*), thus allowing for the comparison of such organization across species (Mars et al., 2011, *J Neurosci*).

Various models have been independently proposed for frontal (rostral-caudal, dorsal-ventral premotor dissociation), parietal (rostro-caudal, medial-lateral) and fronto-parietal ("onion model") organization.

Here we attempt to retrieve those organization schemas using resting-state functional connectivity and data-driven clustering algorithms.

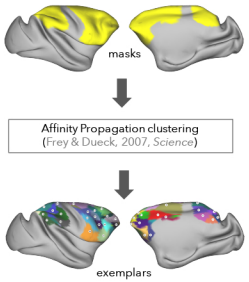
APPROACH

Data

Resting-state fMRI scans were acquired for 7 healthy macaques (*Macaca mulatta*) under light anesthesia with isoflurane (7 males, median age = 4.39 years; median weight 8.3 kg).

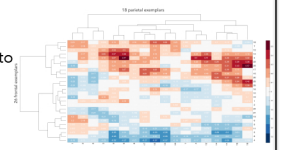
Analyses

To obtain the fronto-parietal connectivity networks, we first parcellated the frontal and the parietal masks (shown in yellow) based on their connectivity with the ipsilateral hemisphere.



Affinity Propagation clustering provided a solution with 26 frontal parcels and 18 parietal parcels, along with one representative vertex (called **exemplar**) for each parcel that best described the inherent connectivity profile of the rest of the vertices in the parcel.

We then focused specifically on the connectivity profile of these exemplars, frontal to parietal and vice versa, (right) to understand the organization of frontal cortex, parietal cortex, and the fronto-parietal networks.

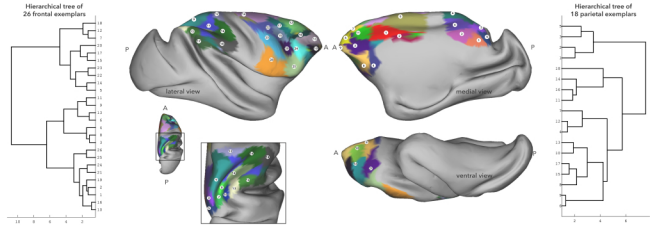


We further analyzed the evolution of these hierarchical branches and then created an '**affinity matrix**' that summarized the connectivity of the frontal and parietal branches with one another. These affinities demonstrated the major organizational pathways connecting the two cortices.

RESULTS

Parcellation

Data-driven clustering based on each frontal and parietal vertex's connectivity with the whole brain revealed independent clusters that formed the basis for subsequent analyses



Frontal cortex

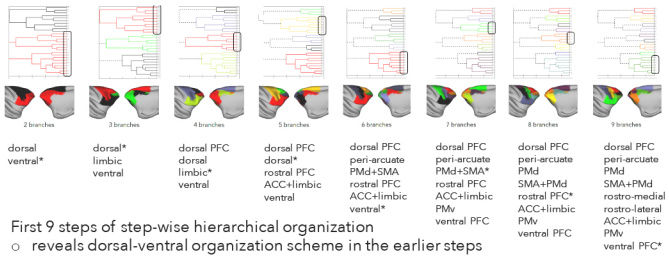
Exemplar	Anatomical region	Exemplar	Anatomical region
1,2	mid-cingulate cortex (area 24)	18,12,7,11	dorsal PFC (area 9)
3,4,8	peri-genual ACC (areas 32,25)	13	dorsolateral PFC (area 46)
14,22	dorsal premotor (F2)	17,15,20	ventral PFC (area 12)
5	supplementary motor area (F3)	6,9	fronto-polar cortex (area 10)
23,26,25	ventral premotor (F4, F5)	10,16,19,21	orbito-frontal cortex (areas 11,13)
24	peri-arcuate cortex (area 8)		

Parietal cortex

Exempla	Anatomical region
1,2,3,4,5,7	medial SPL (V6A, PEci, PGm)
6,9,12	dorsal SPL (PEc)
16,11,14	ventral SPL (PE)
18	anterior IPL (PF)
17	middle IPL (PFG)
15,8,10,13	posterior IPL (PG, Opt)

Frontal hierarchy

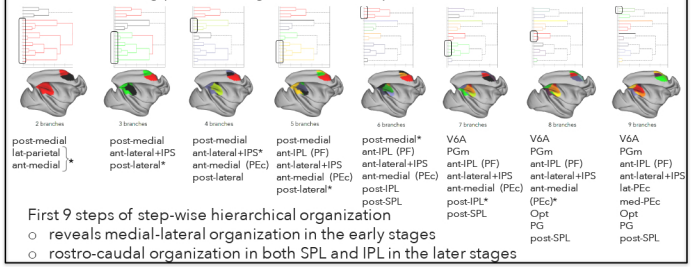
Hierarchical clustering of the 26 frontal exemplars based on their parietal connections show the following pattern of organization of the frontal cortex



First 9 steps of step-wise hierarchical organization
- reveals dorsal-ventral organization scheme in the earlier steps
- rostral-caudal organization scheme is revealed step-5 onwards

Parietal hierarchy

Hierarchical clustering of the 18 parietal exemplars based on their frontal connections show the following pattern of organization of the parietal cortex

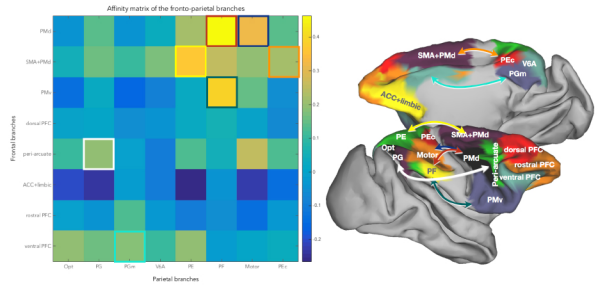


First 9 steps of step-wise hierarchical organization
- reveals medial-lateral organization in the early stages
- rostro-caudal organization in both SPL and IPL in the later stages

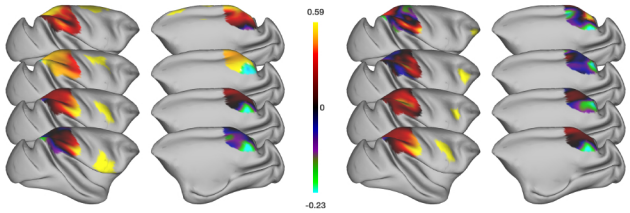
RESULTS

Affinity matrix

Connectivity matrix of the 8 frontal and the 8 parietal branches, along with a schematic representation of the preferred connections indicated by arrows.
- The main anatomical connections can be inferred.
- Provides evidence for multiple organizational models, thereby revealing the complexity of the fronto-parietal network.



Connectivity strength of certain selected frontal seed regions (shown in yellow), with that of the parietal cortex provides evidence for the -
- dorsal-ventral organization of the premotor cortex (left)
- rostral-caudal connections being organized in an "onion model" (right)



SUMMARY

Clusters based on whole-brain resting-state functional connectivity mimic anatomical areas established using traditional histological methods.

While the theories describing the organization of frontal, parietal and the fronto-parietal networks are often proposed mutually exclusive of each other, our results based on **resting-state fMRI provide evidence for a complex organization**, supporting multiple theories.

More information

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