

## Data-driven Parcellation of Resting State Functional Connectivity Networks of the Frontal Lobe in New World and Old World Primates

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**TARGET AUDIENCE:** Functional neuro-imaging groups.

**PURPOSE:** Being off-limits to the invasive anatomical techniques, our knowledge of human brain connectivity lags far behind that about nonhuman primate neuroanatomy. The most conclusive way to bridge this gap is to directly compare functional connectivity measures across species. In recent years, resting state functional connectivity based MRI studies (rsfc-MRI) has been proven to be a robust and powerful measure to map the intrinsic functional architecture of the human brain. However, several of these findings are inconsistent with the well-known anatomical connections in the nonhuman primates, thus raising concerns about real homology and appropriate interpretation of methods. The proposed study is intended to investigate the homology of the primate frontal lobe using a novel imaging approach that bridges the evolutionary division between new world monkeys (Ceboidea) and old world primates (Cercopithecoidea). To reduce the subjective influence on the identification of functional connectivity maps, we implemented an unsupervised self-organization mapping<sup>1,2</sup> (SOM) technique to study the functional connectivity network of the frontal eye field (FEF) of macaques and squirrel monkeys. Comparison of these connectivity maps across monkey species is a promising initial step to establish the degree of homology of these cortical sub-regions in primates, and thus close the gap between rsfc-MRI and neuroanatomical data.

**METHODS:** We collected whole brain resting state fMRI data from isoflurane anesthetized squirrel (new world, n=2, *Simia sciureus*) and macaques (old world, n=7, *Macaca radiata*) monkeys to compare their functional connectivity maps of frontal lobe at rest. New world and old world monkeys were scanned at 9.4T Varian and 3T Philips human MRI scanners, respectively. 3D T1-weighted whole brain structural images and 300 (1x1x1 mm<sup>3</sup> voxel size) or 200 (1.5x1.5x1.5 mm<sup>3</sup>) GE EPI images (TR/TE 1500/19.6 ms at 9.4T and TR/TE 2000/15 ms at 3T) were collected for each run. Resting state EPI data were analyzed using identical procedures including slice time correction, global signal correction, temporal band pass filtration (0.01Hz-0.1Hz) and spatial smoothing. All analyses were performed with customized Matlab code. ROIs around FEF region were manually outlined on axial images in squirrel and macaque monkey brain based on respective anatomic atlas. A data-driven self-organized mapping (SOM) was implemented to cluster the voxels within the ROIs into pre-defined number of groups (2-3 clusters, Figure 1). The linearized one dimensional connectivity maps (vectors) representing each voxel's functional connectivity with rest of the brain were the inputs to the SOM algorithm.

**RESULTS:** The parcellation (clustering) results of the FEF regions are quite consistent across animals in both species (data not shown). Figure 2 shows the mean functional correlation maps of the parcellated sub-regions i.e., green (a) and red (b) while performing two cluster analyses. The inter-subregional connectivity difference is quite prominent in both species. There was a high degree of similarity of the connectivity maps of different parts of FEF region between new world (B) and old world (A) monkeys (comparing (a) and (b) in figure A and B). These observed differential connectivity maps of FEF region are consistent with the known differential anatomical connectivity networks in both species<sup>3</sup>.

**DISCUSSION AND CONCLUSION:** Our results demonstrate that data-driven SOM analysis is a robust parcellation method to perform functional segregation of resting state cortical networks. Particularly, this application can be promising to analyze brain regions whose anatomic organization is sparsely known. We strongly believe that application of efficient segmentation methods such as SOM across the species will be able to identify homologous as well as evolutionary important patterns of cortical organization.

**REFERENCES:** [1] Kohonen T, Somervuo P (2002): How to make large self-organizing maps for nonvectorial data. *Neural Networks* 15(8-9): 945-52.

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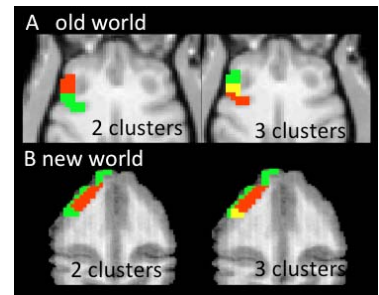


Figure 1. SOM parcellation of prefrontal regions of old world (A) and new world (B) monkeys with pre-defined 2 or 3 clusters.

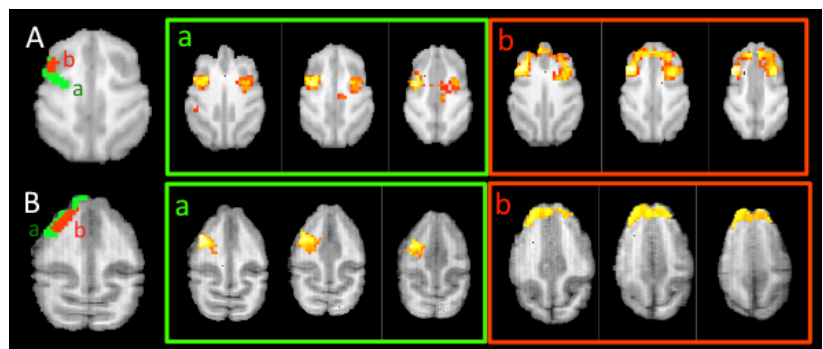


Figure 2. SOM parcellated red (b) and green (a) voxel clusters around FEF regions in old world (A) and new world (B) monkeys. Differential Resting state connectivity maps of red cluster (b with red outline) and green cluster (a with green outline).