FUNCTIONAL CONNECTIVITY HUBS IN THE CONSCIOUS MARMOSET MONKEY
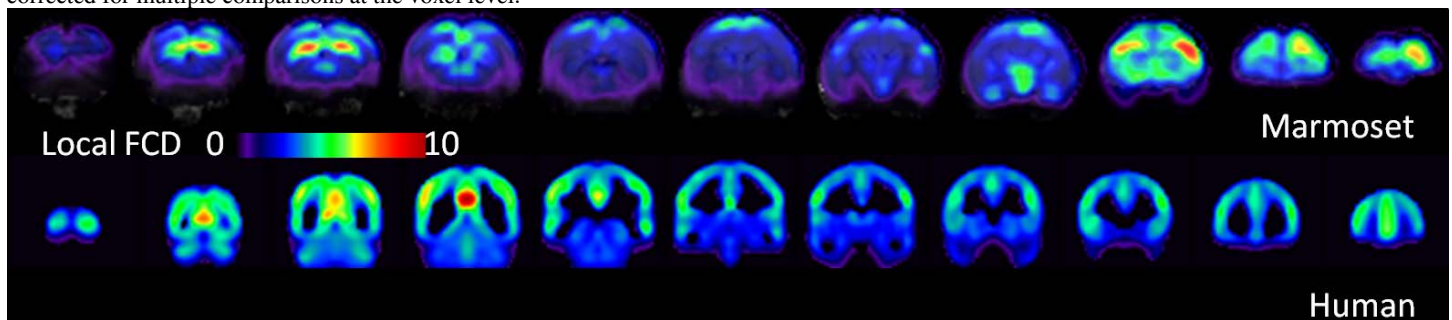
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Target audience: Researchers interested in understanding the organization of the primate brain and on the application of a new non-human primate model for studying resting state functional connectivity (RSFC).

Introduction: Due to ease of data collection and disposal of the requirement for task engagement, the study of RSFC in humans has witnessed fast growth in recent years. Use of this approach opens avenues toward exploring brain functional networks and their interactions, and findings suggest its potential as a biomarker for disease and abnormal brain function, and for characterizing functional diversity among individuals. Animal models provide a method for exploring mechanisms underlying RSFC but the need for anesthesia is a challenge to the analysis of resting state data. We have developed a protocol to train marmoset monkeys (*Callithrix jacchus)* to tolerate light restraint during fMRI protocols, and have recently reported its successful employment for acquisition of resting-state data[1,2]. Here we extend these findings to utilize a data-driven method to investigate whether the marmoset brain exhibits local Functional Connectivity Density (*l*FCD) patterns that recapitulate those observed in the human brain.

Methods: Six male marmoset monkeys were exposed to a three-week period of behavioral acclimation for restraint in an MRI, and scanned on a single day in a 7.0T Siemens scanner. A high-resolution anatomical RARE scan (FOV=4.5×4.5cm, mtx=160x160, slice thick=2mm, resol=0.281mm, 15 slices) as well as eight 10min-long single-shot gradient-echo EPI scans (TE/TR=24/1500msec, 400 time points, slice thick=2mm, 15 slices, mtx=80×80, resol=0.562mm) were collected in resting conditions for each monkey. Standard AFNI data pre-processing steps were applied to functional datasets, including skull-stripping and slice timing correction. In a single (concatenated) step, the EPI data were registered to a single base volume of the first EPI session, to the individual monkeys' RARE, and to a standard template of a male marmoset brain[3]. Ultrafast (each *l*FCD map required < 2 min computation time) data-driven FCD mapping[4] with a stringent correlation threshold R > 0.6 was used to map the main functional connectivity hubs (highly interconnected regions) in the marmoset brain with high spatial resolution (0.5-mm isotropic). Individual animals' EPI sessions were averaged, and voxelwise within-subjects ANOVA was used to assess the statistical significance of *l*FCD using a threshold $P_{FWE} < 0.05$, corrected for multiple comparisons at the voxel level.

Results: The *l*FCD in marmosets was highly significant in the whole brain (t-score > 5), and inter-subject variability was quite low. The strength of the *l*FCD hubs was maximal in the visual cortex and posterior cingulum (Fig. 1, top row), regions that also contain the strongest *l*FCD hubs in humans (Fig. 1, bottom row, average map across 979 healthy human subjects[4]). The parietal and frontal cortices also included prominent *l*FCD hubs in the marmosets, with local maxima centered on somatosensory cortex and frontal pole, respectively. Species-specific differences emerged, with cortical visual hubs stronger in the marmoset, and temporal and posterior parietal cortical hubs stronger in the human.

Discussion: Here we present for the first time an approach to studying resting state functional connectivity hubs in an awake nonhuman primate. Analysis of the *l*FCD graph-theory metric in the marmoset suggests that awake marmosets have strong patterns of connectivity that bear good correspondence to those observed in awake humans, with hubs centered on visual, posterior cingulate, somatosensory, and frontal cortices. These data provide a platform for mechanistic neurobiological examination for existing disease models established in the marmoset.

Conclusion: The marmoset holds great promise as a research model in neuroscience applications that can be addressed with RSFC.

References:
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