Within Hemisphere Connectivity differentiates Humans from Nonhuman Primates: a Resting-State fMRI Study

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Introduction Functional connectivity could be inferred from spontaneous BOLD signal fluctuations arising from low frequency (<0.1Hz) brain activity. Spatially distinct regions with synchronized brain activity comprise intrinsic connectivity networks (ICNs, or some times called resting-state networks) [1-3]. Recently, functional connectivity studies have demonstrated the ability to identify ICNs in anesthetized macaques [4]. As such, rsfMRI paves the ground for comprehensive studies on the similarity/discrepancies between NHPs and humans.

Herein, we exam the hypothesis of altered ICNs across species, potentially due to evolutionary processes. We investigated the ICNs in four primate species (humans, chimpanzees, baboons, and capuchin monkeys), which spanning four levels in the evolutionary tree, using resting state fMRI to evaluate the intra- and inter- hemispheric coherences of spontaneous BOLD fluctuation. The information gained might shed light on understanding the origin of ICNs as well as the functional evolution of the brain. This study provides the most compelling evidence to date for across-species comparisons.

Methods One hundred, five, twenty-four and twenty-five resting-state fMRI scans were acquired from one hundred human subjects (45 males, 55 females, age=42.1±11.2), five chimpanzees (Pan troglodytes, 44–57kg), fourteen baboons (Papio hamadryas spp., 14-19 kg) and eight capuchin monkeys (Cebus apella, 1-5 kg), respectively. Animals were anesthetized with 1-2% isoflurane and mechanically ventilated. End-tidal CO_2, O_2 saturation, heart rate, respiration rate, and rectal temperature were monitored continuously and maintained within normal ranges.

All MRI studies were performed on a 3T Siemens TIM-Trio. Gradient echo EPI was used for BOLD images with TR/TE=3000/30ms. For humans, images were acquired with 1.7x1.7x3 mm resolution for 8.5 min; in chimpanzees, images were acquired with 1.5x1.5x1.9 mm resolution for 30 min; in baboons and capuchins, images were acquired with 1x1x1.9 mm resolution for 30 min. Allometrically-scaled high-resolution 3D T1-weighted images were collected for every subject.

Data were processed using FSL and AFNI. Image pre-processing includes motion correction, brain extraction, temporal band-pass filtering at 0.01-0.08 Hz and spatial smoothing with 4 mm (NHPs) or 6 mm (human) FWHM Gaussian kernel. All images were registered to high-resolution brain templates. Temporal-concatenated independent component analysis was performed at low dimensionality (20). The extracted ICNs were identified and compared with known human ICNs based on their spatial similarity. Lateralization indexes (LI) defined as LI = (Left – Right) / (Left + Right) where Left and Right represents the number of activated voxels in the corresponding hemisphere (Z>2.3) were also calculated for each ICs. The strength of homotopic connectivity, which has been proposed as an index referring tendencies of hemispherical asymmetry, was also calculated.

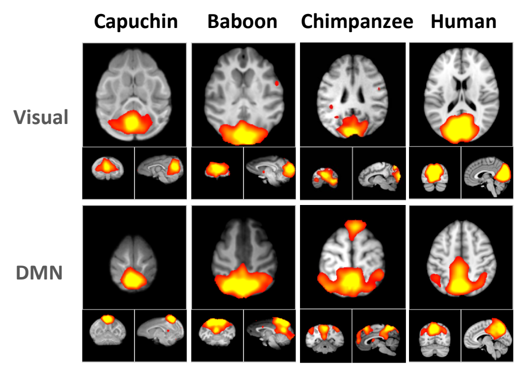

Figure 1. "Symmetrical" Intrinsic Connectivity Networks across Primate Species.

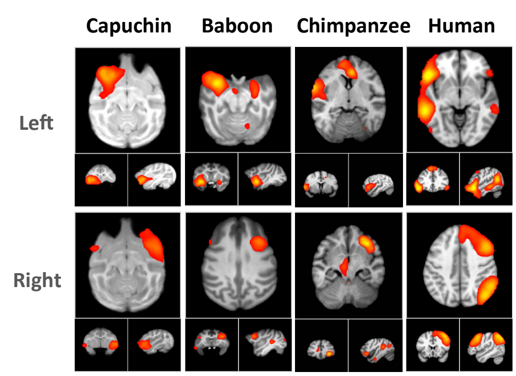

Figure 2. "Asymmetrical" Intrinsic Connectivity Networks across Primate Species.
* color bar: Z-scores from 3 to 8.

Results and Discussion

Figure 1 shows the symmetrical ICNs across primate species. Those include the visual network and the posterior default mode network (DMN), which pertain to basic brain function, such as the sensory-motor function. Interestingly, the strongly left- and right-lateralized ICNs encompassing the frontoparietal cortex are shown for all primate species (**Figure 2**). The right-lateralized ICNs in nonhuman primates show a frontal-parietal connectivity in baboons and chimpanzees, but not in capuchins. The left-lateralized ICNs in nonhuman primates only exhibit a frontal component. Contrary to expectation, these ICNs were strikingly similar in all species, suggesting that functional laterality emerges early in the primate lineage. Laterality indices indicated significant lateralization of these ICNs in all species (data not shown). This strongly argues against hemispheric specialization as a unique feature of humans.

Conclusions In summary, our results provide the most compelling evidence to date that functional laterality is phylogenetically conserved in primates. As in humans, functional laterality is far more profound than anatomical asymmetry. Furthermore, the notable difference in functional laterality between humans and NHP is the left-lateralized ICN, where within-hemisphere (inter-lobar) connectivity existed only in humans.

References: [1] Biswal et al., MRM (1995). [2] Fox and Raichle. Nat Rev Neurosci (2007). [3] Smith et al., PNAS (2009). [4] Vincent et al. Nature (2007).