Rat Brain Possesses a Default Mode Network

H. Lu[1], Q. Zou[1], W. Rea[1], E. A. Stein[1], and Y. Yang[1]
[1]National Institute on Drug Abuse, NIH, Baltimore, MD, United States

Introduction PET and fMRI studies have identified a set of human brain regions that exhibit high baseline blood flow and become less active during attention-demanding cognitive tasks (*1, 2*). This so-called "default mode network (DMN)" has been shown to be present in nonhuman primates under anesthesia (*3*).

The evolutionary clade of rodents is about 35 million years earlier than that of old world monkeys and human (*4*). Although many of the structures and functions of subcortical nuclei are conserved across these three species, the neocortex, in particular, "association" cortex has extensively expanded in the primate as a result of evolutionary pressure, which is considered to be crucial in the development of higher cognitive and behavioral functions (*4, 5*). On the other hand, the so-called "limbic system" (cingulate cortex, prefrontal cortex etc) which represents critical elements of the DMN is also seen in rodents. Thus, a DMN in rodents, once demonstrated, would not only suggest that an operational DMN is a common feature in the mammalian brain, perhaps induced via parallel evolution as a result of natural selection, it would also introduce a novel approach for comparing brain development across species.

Methods Adult SD rats (n=16, dexmedetomidine + isoflurane) underwent longitudinal resting-state fMRI scans (Bruker 9.4T) separated by one week. A total of 119 scan sessions of data were acquired using signal-shot gradient echo EPI sequence (TR/TE:1000/15ms, FOV=3.5×3.5cm^2, matrix size=64×64). Each session lasted 4.5 min. Geometric distortions in EPI images were corrected using the PLACE method (*6*). Data pre-processing included slice-timing correction, linear and quadratic trend removal and spatial smoothing with a Gaussian kernel (FWHM = 0.6 mm). Images from individual animals were then co-registered onto a common 3D space aligned with rat stereotaxic atlas. Group ICA (Melodic) was applied to identify brain networks.

Results Consistent with previous reports (*7-9*), we have identified several networks, including bilateral insular, whisker barrel and the forelimb cortices. A particular interesting network is shown in Fig. 1. It includes bilateral orbital (OC), prelimbic, cingulate (Cg1/Cg2), retrosplenial granular and dysgranular cortex (RSG/RSD), rostral and dorsal posterior parietal cortex (PtPR, PtPD), perirhinal, entorhinal and temporal association cortical regions (TeA) and hippocampus. RSG/RSD is the homologous structure of human posterior cingulate cortex (PCC), while OC and prelimbic cortex are thought to be rat representations of the prefrontal cortex (*5*). Despite the small volume of parietal and temporal association cortices in the rat brain, these connectivity patterns remarkably mirror the DMN of the human brain, which includes PCC, orbitofrontal and ventral anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC), rhinal cortex, hippocampus, inferior temporal cortex (ITC) and inferior parietal cortex (IPC) (*2, 10*). Notably, the connectivity between anterior and posterior cingulate cortices includes the entire medial dorsal cortical ridge in the rat, as shown in the axial and sagittal planes (Fig. 1), but it is more focal in humans (*1, 2*).

Network analysis reveals two clusters of network within the network as shown in Fig. 2. One is the parietal subsystem clustered at RSC, and the other is the temporal-prefrontal subsystem. The organization of DMN in rats bears remarkable similarity to that in humans (*11*).

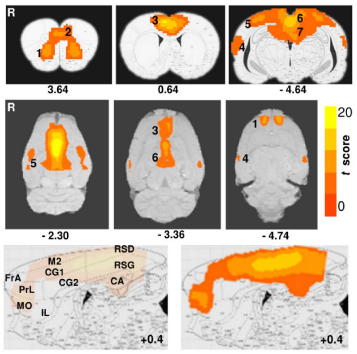

Fig. 1. Rat DMN. Significant clusters in the coronal plane (top) include: 1, orbital cortex; 2, prelimbic cortex (PrL); 3, cingulate cortex (CG1/CG2); 4, temporal association cortex (TeA); 5, posterior parietal cortex (PPC); 6, Retrosplenial cortex; 7, hippocampus (CA). Middle panel shows the same connectivity map in the axial plane. Note the strong connectivity between prefrontal and posterior cingulate cortices, as shown in the sagittal plane (bottom, medial-lateral: +0.4 mm).

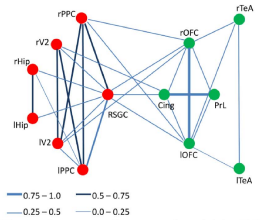

Fig. 2. Two clusters of network within DMN: parietal subsystem clustered at RSC, and the temporal-prefrontal subsystem. Numbers are correlation strength between regions. Abbreviation: rHip/lHip, right/left hippocampus; Cing, cingulate cortex; rOFC/lOFC, right/left orbital frontal cortex.

Discussion The anatomy of the connectivity maps shown in Fig. 1 bears remarkable similarity to the DMN reported in human and nonhuman primates, suggesting the existence of DMN in rodents. Our data raise interesting questions about the functions of DMN across species, and open novel opportunity to investigate the physiological basis of DMN using rodent model.

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