Default Mode Network Abnormality in ADHD Rat Model

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Purpose: Resting state functional MRI (rs-fMRI) is an emerging neuroimaging method, examining the connectivity of brain neural circuits. This technique has been used to study neurophysiological and neuropsychiatric disorders, including attention deficit and hyperactivity disorder (ADHD).[1] Several rs-fMRI literatures showed the abnormalities of connectivity within default mode network (DMN), or of the connectivity between DMNs and cognitive networks in human.[2] Since the existence of rs-networks in rodents have been proved[3-5], we then concern the feasibility of employing rs-fMRI on ADHD rat model. In this work a seed-based analysis was carried out to compare the rs-networks between normal and ADHD rats. **Material & Method:** Spontaneously hypertensive rats (SHR) were used to model ADHD according to Sagvolden's work[6], and Wistar Kyoto rats (WKY) were the control group. A total of 15 male rats (SHR=10, WKY=5, all 6 weeks) were scanned using 7T Bruker Clinscan with a surface coil for signal receiving. Aneasthesia was induced with around 1.5% isoflurane mixed with O_2. Respiratory rate were maintained 65-75 times/min throughout whole scan period and body temperature was maintained by 37℃ water circulation. 525 consecutive volumes with 11 coronal slices were acquired using gradient echo EPI with TE/TR=20ms/1000ms, FOV=30mm, matrix size=64x64 and 1mm slice thickness. All data were pre-processed by tools below: Image registration by Automated Image Registration (AIR), slice timing and smoothing (1mm Gaussian kernel) by SPM8, temporal detrend and frequency filtering (0.002 - 0.1Hz) by REST toolkit. Seed-based and other analysis was performed on self-designed Matlab scripts. 25 priori ROIs were defined as seeds according to Paxinos coordinates for network comparison. Correlation coefficient maps from all animals in each group were subject to one sample t test against 0 and $p<0.005$ was thresholded to generate final maps.

Results: Fig.1 displays the cross-correlation maps based on retrosplenial cortex (RSC) region at bregma -4.8mm. RSC corresponds to posterior cingulate cortex in humans and is one of the central hubs of DMN.[5] SHR presents clusters including cingulate cortex, posterior parietal cortex, auditory cortex, somatosensory cortex and caudate putamen. On the other hand, WKY shows a similar but condense pattern. The major difference between these two groups is in caudate putamen area (black hollow arrows). Fig. 2 shows the connectivity difference among 25 priori ROIs, which demonstrates the connective organizations are unequal in SHR and WKY. **Discussions:** Putamen is not a part of DMN network in literatures. However, we found a positive connection between caudate putamen and RSC in SHR group. In Cao's work[7], the decrease of inverse connectivity between putamen and DMN in ADHD children was found. Although it may be far to link rat and human together, the enhancement of positive connectivity in our results and the decrease of inverse connectivity in Cao's work appear to have same trend and be similar in a certain extent. Since putamen is mainly involved in the regulation of motor behavior and caudate nucleus is related to social behavior, the symptoms of ADHD may be tied to this network abnormality. In the connectivity difference shown in Fig. 2, we observe that SHR tends to have stronger connectivity in long-physical-distance connection over WKY. Quantification and qualitative analysis of this whole brain organization still remain advanced investigations. **Conclusion:** In this study we demonstrate the abnormality of DMN in ADHD rat. Therefore rs-fMRI approach can be utilized on further exploration of the functional networks in ADHD rat.

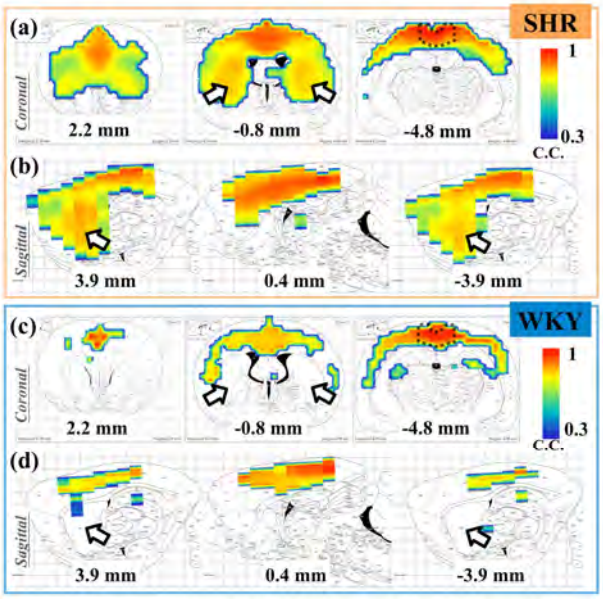

Fig. 1. DMN map based on RSC. (Dash line ROI at bregma -4.8mm) **(a,b)** SHR shows a wide spread activation area and **(c,d)** WKY presents a similar but condense one. Note that SHR exhibits a unique cluster in caudate putamen (black hollow arrows).

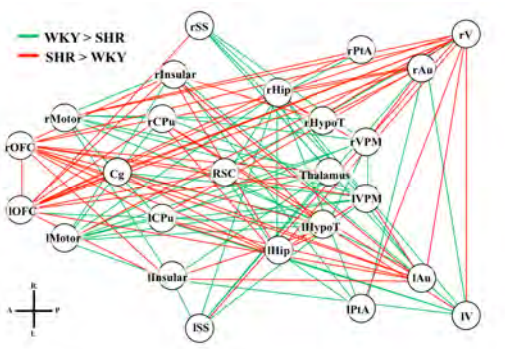

Fig. 2. Connectivity difference among 25 priori ROIs.

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