Resting State Network in ADHD Rat Model Using Group ICA

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Introduction: Attention deficit and hyperactivity disorder (ADHD) has been commonly studied and related to genetic expression abnormality of chromosome.[1] The failure of inhibitory process in brain neural signal transmission may consequently result in hyperactive behavior of ADHD with irregular activations in the brain disorder locations. To discover the brain functional networks, resting state (RS) functional MRI (fMRI) has been utilized for comparing ADHD and normal group in human studies. However, the results of functional networks in ADHD are somehow inconsistent [2], underscoring the need for further investigations using animal models. Recently RS functional networks were proved to exist in rats[3-5], suggesting the feasibility of using rodents to model neurophysiological disorders. Here we proposed to compare the RS functional networks of normal rats and ADHD rats. Once ADHD syndrome is detectable in rat RS fMRI, it opens the way for examining ADHD drugs on rat model. **Material & Method:** Spontaneously hypertensive rats (SHR) were used to model ADHD according to Sagvolden's work[1], and Wistar Kyoto rats (WKY) were the control group in our study. A total of 12 male rats (SHR=6, WKY=6, all 13 weeks) were scanned using 7T Bruker Clinscan with a surface coil for signal receiving. Anaesthesia was induced with 1.5% isoflurane mixed with air. The heart rate and respiratory rate were monitored throughout whole scan period and the body temperature was maintained by 37℃ water circulation. Resting state functional images were acquired using gradient echo echo-planar-imaging (EPI) with TE/TR=25ms/1000ms. Field of view, matrix size, slice number and slice thickness were 30mm, 64x64, 5 and 1mm, respectively. All data were pre-processed by various tools: Image registration by Automated Image Registration (AIR), slice timing and smoothing (0.8mm Gaussian kernel) by SPM8, temporal detrend and frequency filtering (0.08 - 0.2Hz) by REST toolkit. Group ICA analysis was carried out by GIFT software package. Functional activation locations were labelled based on Paxinos coordinates. **Results:** As shown in Figure 1, resting state networks including primary somatosensory cortex (S1), secondary somatosensory cortex (S2), hippocampus, caudate putamen (CPu) and cingulate cortex (Cg) were found both in WKY rat and SHR, which were similar to previous reports. Interestingly, SHR rat model has more networks than that in normal WKY rat in our experiment. Bilateral primary somatosensory cortex and insular cortex presented resting state networks in SHR rats. Moreover, the activation intensity was different between these two rat models. Compare with normal WKY rats, the z-score intensities of somatosensory cortex region and cingulate cortex were higher in SHR model, while SHR gave weaker network at hippocampus area contrarily. Comparison of RS activation regions of all 5 slices in SHR and WKY rats were listed in Table 1. **Discussion:** In this study, RS network differences between normal rats and ADHD rats were discovered in primary somatosensory, entorhinal cortex and insular cortex. The functional activity of the somatosensory cortex is stronger in ADHD than that in normal rats. This may be speculated to be the possible reason of the attention deficit, since rats are sensitive to external environmental influences. The insular cortex is an emotion-related functional area that implies the particular RS network exhibited in SHR is associated with the impulsive behavior in ADHD. However, the underlying connections between RS networks and neuropsychological function should be examined carefully. Our result demonstrates the feasibility to evaluate RS functional network differences of ADHD via rat model, suggesting the possibility of numerous case studies on ADHD RS networks. Further study can be conducted comprehensively using rat model in the future.

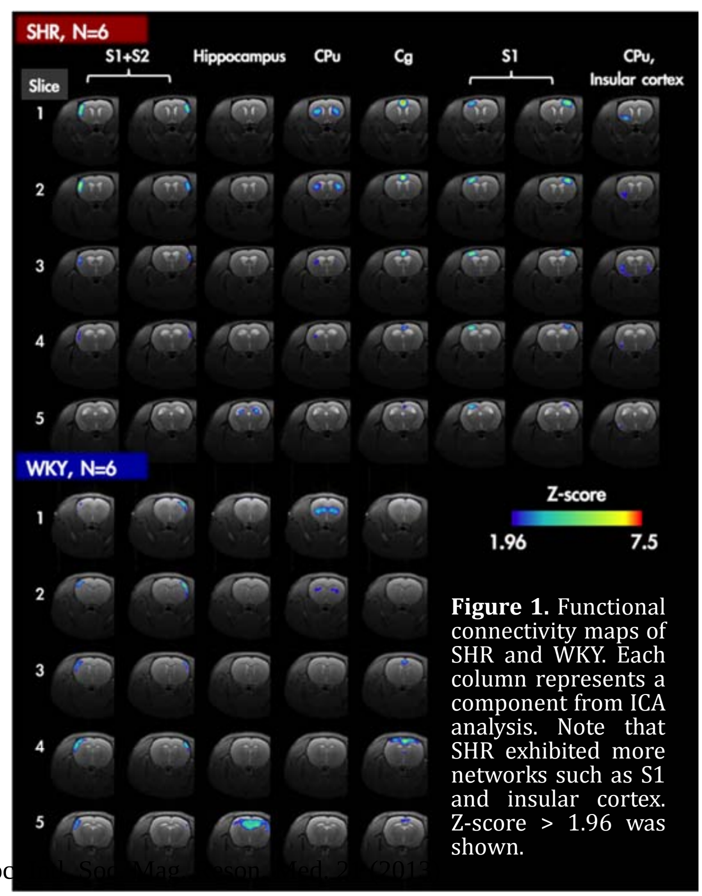

Figure 1. Functional connectivity maps of SHR and WKY. Each column represents a component from ICA analysis. Note that SHR exhibited more networks such as S1 and insular cortex. Z-score > 1.96 was shown.

References:

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Table 1. Comparison of RS activation regions in SHR and WKY.

Slice	S1	S1+S2	Hippocampus	CPu	Insular cortex	Motor cortex	Cingular cortex
1	S	S,W		S,W		S,W	S
2	S	S,W		S,W	S	S,W	S
3	S	S,W		S	S	S,W	S,W
4	S	S,W			S	S,W	S,W
5	S	W	S,W				S,W

S: SHR, W: WKY.