Altered Hippocampal Connectivity Network Associated with Impulsivity in Abstinent Heroin Addicts

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Introduction: Neurobiological and neuroimaging studies have demonstrated that the hippocampus, as a major node of memory processing, is involved in drug addiction. [1,2] However, little is known about the role of the hippocampal network and its relation to drug-seeking behaviors, such as impulsivity in addiction. In this study, we utilized resting-state functional connectivity fMRI (R-fMRI) to investigate the alteration of the hippocampus functional connectivity (HFC) network and its relation to impulsivity in abstinent heroin dependent subjects (HD) and control nondrug users (CN).

Methods: fMRI measurement: Twenty-two HD subjects and 15 age-matched CN subjects participated in this study. Written informed consent was obtained from each subject and the study was approved by the Research Ethics Committee of Beijing Ankang Hospital and Beijing Institute of Basic Medical Science and conducted in accordance with the Declaration of Helsinki. Impulsivity was measured by the Barratt Impulsive Scale (BIS, version 11). MRI scans were conducted at a GE 3.0T Signa LX scanner. 3D high-resolution anatomical images were acquired with an SPGR sequence prior to functional scans. The fMRI data were obtained by using single-shot EPI sequence (TE=25ms, TR=2000ms, FOV=24×24 cm, matrix=64×64, flip angle=90°, slice thickness=5 mm, space=1.0 mm). One hundred and eighty imaging volumes were acquired in each functional scan run. All subjects were instructed to keep their eyes closed, relax, and keep their head from motion. **Data preprocessing:** The fMRI datasets were analyzed with AFNI software and Matlab 7.5. The first five data points of each dataset were discarded to obtain the stable state. Physiological motion correction, volume registration, head motion correction, white matter, CSF and global signal removal were performed, and a band-pass filter was used to keep low-frequency fluctuation between 0.015 Hz and 0.1 Hz. **Functional connectivity analysis:** The seed ROIs located in both sides of hippocampus were manually selected based on anatomical distribution. The cross-correlation coefficient (CC) maps of individual subjects were generated by cross-correlating each voxel time course with the averaged time course of seed voxels. The Fisher's Z-transformation was then applied to the resulting datasets, which were normalized to a standard MNI image space, and resampled to the resolution of 2×2×2 mm^3. **Statistical analysis**: A one-sample *t*-test was used to identify the significant patterns of the HFC network in control and heroin groups of subjects. Analysis of covariance (ANCOVA) was used to detect any significant HFC network connectivity difference between groups. The gray matter volume served as the covariance of no interest to control grey matter atrophy. Further, to investigate the neural correlates of impulsivity, a whole-brain voxelwise linear regression analysis was implemented by correlating the HFC network connectivity and the BIS scores in CN and HD group subject, respectively. *AlphaSim* program was performed for correcting multiple comparisons.

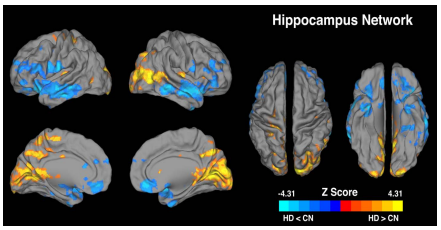

Fig. 1 Brain regions of the altered HFC network in the HD group compared to the CN group. Bright color indicates increased connectivity, while blue color indicates decreased connectivity (p< 0.05, cluster size > 8606 mm^3, corrected).

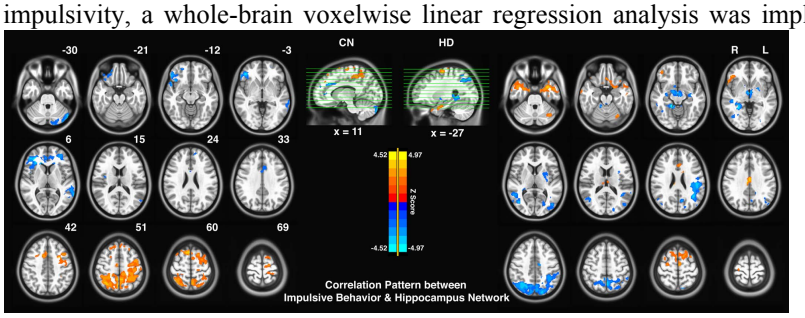

Fig. 2 Distinct neural correlates of impulsivity in healthy control group and heroin group (p < 0.01, cluster size > 1603 mm^3, corrected).Left: Control group, Right: Heroin group.

Results: Compared to the CN group, the HFC network activity in HD group was significantly increased in the brain regions, such as the bilateral precuneus and cuneus, right ventral striatum, posterior cingulate, and left motor cortex. It was significantly decreased in the bilateral temporal pole, ventromedial prefrontal cortex, anterior cingulate cortex (ACC), dorsolateral prefrontal cortex, amygdala and right nucleus accumbens (Fig. 1). In the HD group, a positive correlation pattern between the HFC network strength and the BIS scores was found in the bilateral middle temporal gyrus (MTG), superior and inferior frontal gyrus, and ACC; a negative correlation pattern was found in the bilateral thalamus, precuneus, cuneus, right ventral striatum and left inferior parietal cortex (IPC). In the CN group, a positive correlation pattern was found in the bilateral IPC, superior parietal cortex, precuneus and left somato-motor cortex, and a negative correlation pattern existed in the bilateral ACC, right middle frontal gyrus and insula, and left MTG.

Discussion and Conclusion: High-order cognitive behavior was determined by the neurocognitive network with a high-degree connectivity pattern among discrete brain regions. [3] The observed altered HFC network in heroin-dependent subjects may represent neuropathological damage, which might be a consequence of long-time exposure to heroin. Our study found a different impulsive correlation pattern between the two groups. This further extends our understanding of the neural underpinnings of the dysfunction of impulse control in heroin addiction.

References:

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Acknowledgements:

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