The Altered Value-based Intrinsic Network and its Association with Impulsive Behavior in Abstinent Heroin Dependent Subjects

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Introduction: Neurobiological and neuroimaging studies have demonstrated that the ventral medial prefrontal cortex (vmPFC), a major node for decision making, is crucial in drug addiction.[1,2] However, little is known about the role of the vmPFC 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 vmPFC network and its relationship 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). Total 180 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 on both sides of vmPFC were selected in accordance to literature. The cross-correlation coefficient (CC) maps of individual subjects were generated by cross-correlating the time course of each voxel with the averaged time course of seed voxels. The Fisher's Z-transformation was then applied to the resulting data sets, which were then normalized to a standard TLRC 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 vmPFC-FC network in control and heroin groups. Analysis of covariance (ANCOVA) was used to detect any significant difference in vmPFC-FC network connectivity strength between groups. The gray matter volume served as the covariance of no interest to control gray matter atrophy. The group level difference was then quantified with the beta- and delta-network index.[3] Further, to investigate the neural correlates of impulsivity, a whole-brain voxelwise linear regression analysis was implemented by correlating the vmPFC-FC network connectivity and the BIS scores in CN and HD group subject, respectively. *AlphaSim* program was performed to correct multiple comparisons.

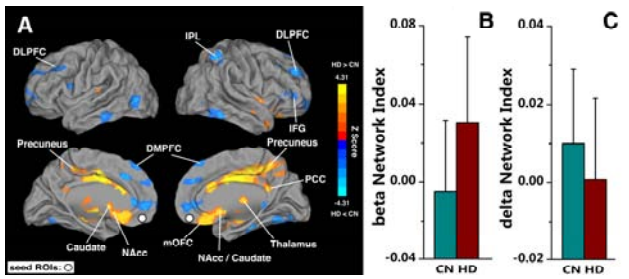

Fig. 1 Brain regions of the altered vmPFC network in the HD group compared to the CN group. Bright color indicates increased connectivity, while blue color indicates decreased connectivity (p< 0.05, cluster size > 4040 mm^3, corrected). A: group difference; B: beta-network index; C: delta-network index.

Results: Compared to the CN group, the beta-network index calculated from the brain regions of the bilateral precuneus, nucleus accumbens (NAcc), caudate, right medial orbital frontal cortex (mOFC), thalamus, posterior cingulate cortex (PCC) in the HD group was significantly increased. The delta-network index calculated from the regions of the bilateral dorsal lateral prefrontal cortex (DLPFC), dorsal medial prefrontal cortex (DMPFC), right inferior frontal gyrus (IFG) was significantly decreased (Fig. 1). In the HD group, the positive correlation between the vmPFC network and the BIS scores was found in those beta-network regions; the negative correlation was found in the delta-network regions. On the other hand, in the CN group, the positive correlation patterns were found in the delta-network regions and the negative correlation patterns were found in the beta-network regions.

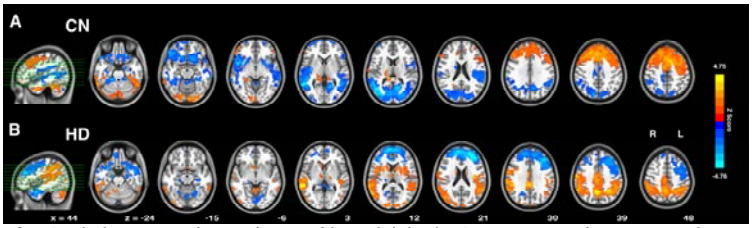

Fig. 2 Distinct neural correlates of impulsivity in CN group and HD group (p < 0.05, cluster size > 4040 mm^3, corrected).A: Control group; B: Heroin group.

Discussion and Conclusion: We demonstrated that the impulsive behaviors have neural correlates in the vmPFC network. The observed altered vmPFC network in heroin-dependent subjects may represent neuropathological damage, which might be a consequence of long-time exposure to heroin. Our study found distinct impulsive correlation patterns between CN and HD groups. This finding further extends our understanding of the neural underpinnings of the dysfunction of impulse control in heroin addiction.

References:

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