Negative correlation between medial frontal activity during inhibitory control and impulsiveness in abstinent heroin dependents: an fMRI study

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Introduction: Impulsiveness is a hallmark of substance abusers [1] and believed to be a stable personality trait which can be measured by Barratt Impulsiveness Scale (BIS) and Go/NoGo task [2]. Although many studies have reported the neural dysfunction during Go/NoGo task or more impulsiveness in addicts, few studies focus on the association between the neural activation detected by fMRI with a Go/NoGo task and the impulsiveness measured by BIS. In this study, we combined the neurobiological method (fMRI) and laboratory performance (BIS) to explore the rapid-response impulsivity in abstinent heroin dependents (AHD).

Materials and Methods Subjects: Thirty male AHD (33.0± 5.9 years) participated in the study after written informed consents were obtained. The drug abstinence was determined by the negative presence of morphine in the urine-analysis. **fMRI acquisition**: All subjects received three scans: a SPGR high-resolution, a T_1-Flair anatomical scan and a 6:50 fMRI-BOLD scan. All images were acquired at a 3.0 T GE Excite HD scanner using a standard GE head coil. The imaging parameters for SPGR acquisition (TR=10.4 ms, TE=4.8 ms, Thickness=1.0 mm, Matrix=256×256, FOV=240 mm, 140 slices in axial plane, acquired resolution in plane=0.9×0.9 mm^2); T_1-FLAIR provided the same localization information as the fMRI images (TR=2300 ms, TE=23 ms, Thickness= 5.0 mm, Slice skip=1.0 mm, Matrix= 256×256, FOV=240 mm, Slices= 20). The whole-brain functional images were acquired using a single-shot echo-planar imaging sequence (TR =2000 ms, TE = 25 ms, Bandwidth = 125 kHz, Matrix = 64×64, FOV =240 cm, Thickness=5.0 mm, Spacing=1.0 mm, Slices=20 and 5 dummy scan). **Go/NoGo paradigm**: A block-design paradigm programmed by Presentation Software (0.53 version) was developed to probe inhibitory control, which was detailedly explained in our prior work [3].**BIS 11th version (BIS-11)**: The Chinese version questionnaire contains a total of 30 items and is divided into three subscales: attention, motor and non-planning, each of which is answered on a 4-point Likert scale and the level of impulsiveness is calculated by summing up the scores for each item. Subjects completed the BIS-11 after the task procedure.

Data analysis: A two-stage fMRI analysis was performed by AFNI software. Among the 30 participants, the data of 4 were eliminated due to excessive head motion (elimination criteria: translational motion > 1.0 mm and rotation > 1.0°). After temporally and spatially filtering data (FWHM= 6.0 mm), the first and last five time points were omitted and a general linear model was employed to process the individual data. The signal change percentage (SCP) maps were transformed into a common Talairach space for further regression analysis. After locating and analyzing the areas of brain that showed significant activation during inhibition control, a 3dRegAna program was used to perform a regression analysis to determine the association between the SCP in certain areas and the individual scores of BIS-11. Activation was reported if they exceeded $P_{(uncorrected)}$ <0.03, $P_{(corrected)}$ < 0.05 and a minimum cluster activation volume of 1500 mm^3.

Results: The activation induced by inhibitory control in AHD was detailedly reported and discussed [3]. Regression analysis revealed a significant negative correlation between the non-planning score of BIS-11 and the SCP of activated areas during inhibitory control in the bilateral cingulated cortex (CC) and medial frontal gyrus (mFG), the left postcentral gyrus and the cuneus. The statistic parametric map of left medial frontal gyrus (L-mFG) and the correlation between SCP within L-mFG were shown in Figure 1.

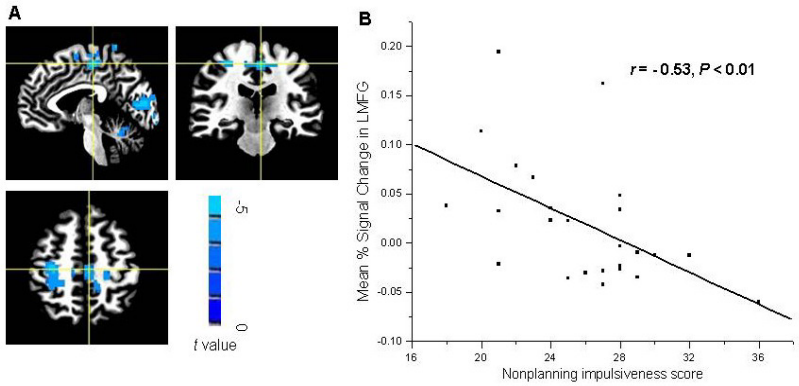

Fig.1 A Statistical parametric maps of brain region showing significant activation negatively associated with the non-planning score of BIS-11, within the areas activated during response inhibition. The region corresponds to the L-mFG: x, y, z = -4, -22, 49; *t*-value = -2.1; 32 voxels. B Correlation between mean percentage of signal change within the L-mFG shown in Fig. 1 A and the non-planning scores of BIS-11. The correlation coefficient is $r = -0.53$; $p < 0.01$

Discussion and Conclusion: The CC and mFG are the important neural substrates for inhibitory control and impulsiveness [4], which may be the most sensitive brain areas to the neurotoxicity of heroin. Although we cannot determine the causality from the present result, the personality-related association between the nonplanning-key scores and the activations in bilateral CC and mFG indicates that in AHD, even after abstinence from heroin for months, the lack of self-control and intolerance of cognitive complexity which is corresponding to the high BIS-scores contributes, at least partly, to the persistent dysfunction of the target brain areas.

Reference: 1. Allen T.J., et al. (1998). Drug Alcohol Depend 50:137–145; 2. Swann A.C., et al. (2002). Biol Psychiatry, 51: 988–994; 3. Fu L.P., et al. (2008). Neurosci Lett.438:322-326; 4, Braver T.S., et al. (2001). Cereb Cortex 11:825–836.