

Altered Frontostriatal Cortical Functional Connectivity in Heroin-dependent Individuals: A Resting-state fMRI Study

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Background:

Heroin addiction has been a serious social and healthy problem in China and always aroused scientific interest. Magnetic resonance imaging studies have associated heroin use with a large scale structural and functional brain abnormalities. It has been verified that normal brain functions is primarily depend on a dynamic balance between local neuronal assemblies activities and global integrative processes. The unbalance of this relationship is considered as the reflection of a brain disease. Resting-state functional connectivity analysis has revealed the heroin-induced brain high-ordered processing. Task-related PET and fMRI have explored the heroin-induced change of local neuronal assemblies activities. Noteworthy, measurement of amplitude of low frequency fluctuation (ALFF), a new research method of fMRI, has successfully characterized the nature and extent of signal change underlying spontaneous neuronal activities in heroin-dependent individuals (HD). However, few studies focused on the alteration of such metastable balance in resting state in HD.

Purpose:

This study applied ALFF measurement and functional connectivity analysis to investigate (a) the brain regions with heroin-use-induced ALFF alteration; (b) the resting-state functional connectivity properties of these brain regions.

Methods and materials

The present study was approved by Institutional Board of The Fourth Military Medical University, China. Seventeen male HD and 15 male non-drug using healthy controls (HC) matched on age, duration of education and cigarette smoking participated in this study. MRI scans, including T1 anatomy, resting-state fMRI and 3D T1 image covering whole brain sessions, were performed using a 3.0T GE scanner. The imaging data were mainly processed with SPM 8 and ALFF was calculated with REST software. Two-sample t-test was performed to see the ALFF differences between HD and HC groups, and $p < 0.01$ (AlphaSim corrected) was considered to be statistical significant. Partial correlations were performed between ALFF values in those regions with higher or lower ALFF relative to HC and heroin dependence by controlling for the possible effects of age and duration of education. The brain region which ALFF value correlated with heroin dependence, (Right caudate 9, 12, 3, diameter= 6 mm), was chosen as the "seeding" region for assessing functional connectivity properties in HD and HC. For between-group comparison, two-sample t-test was used to compare Z value maps between HD and HC ($p < 0.01$, AlphaSim corrected).

Results:

There were no significant on age ($p = 0.875$), duration of education ($p = 0.699$), cigarette smoking ($p = 0.308$) between the two groups. Relative to HC, the HD group showed a significantly decreased ALFF in the right caudate, right anterior cingulate cortex, right superior medial frontal cortex and a significantly increased ALFF was found in the bilateral cerebellum, left superior temporal gyrus and left superior occipital gyrus (Fig.1). The significant negative correlations were observed between ALFF value in the right caudate in HD individuals and duration of the heroin use ($r = -0.642$, $p = 0.0054$) or heroin daily dosage ($r = -0.817$, $p = 0.0021$) (Fig.2). Relative to HC, the HD individuals showed reduced functional connectivity between the right temporal gyrus, bilateral middle frontal gyrus (BA 46), right superior frontal gyrus (BA 6), left angular gyrus and right caudate ($p < 0.01$, corrected). Meanwhile, an enhanced functional connectivity was found between the right cerebellum and the right caudate ($p < 0.01$, corrected) (Fig. 3).

Discussion:

The present study showed the heroin-use-induced alteration of ALFF and functional connectivity. We demonstrated chronic heroin consumption can cause impaired low-frequency oscillations of neuronal activity of caudate and dysfunction of frontostriatal cortical network. The caudate, as a component of dorsal striatum, has been proven to play a key role in substance dependence. The dorsal lateral prefrontal cortex (DLPFC) (BA 46) functions in an executive manner, collecting and integrating information regarding potential outcomes and transforming this input into the selection of suitable cognitive and goal-motivated behavior. Furthermore, it has been thought DLPFC is involved in processing reward and guiding behavior. The reduced functional connectivity of caudate and DLPFC reflect an impaired frontostriatal cortical network in heroin users, which could logically be the neuronal substrate of inappropriate behavioral choice, such as drug seeking regardless of the potential negative outcome. We hope these findings might reveal the mechanisms underlying heroin addiction.

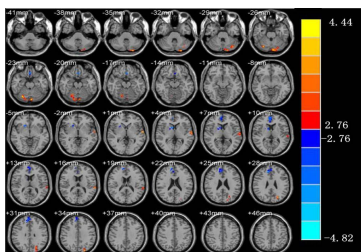


Fig.1 ALFF differences between HD and HC groups. The differences map from the bottom to the top, (every 3 mm), ($p < 0.01$, corrected, $T > 2.7633$ or < 2.7633 , cluster > 16). Blue indicates HD individuals had decreased ALFF compared with HC and the red indicates the opposite.

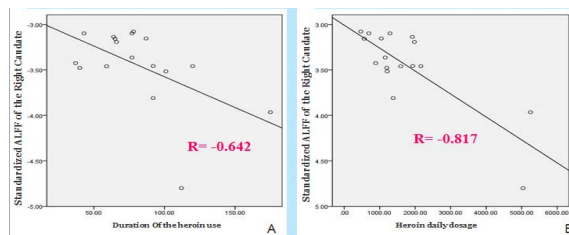


Fig.2 A, B. Bivariate scatter plots show the negative correlation between the duration of the heroin use and the standardized ALFF of the right caudate (Fig.2A), between the heroin daily dosage and the standardized ALFF of the right caudate (Fig.2B).

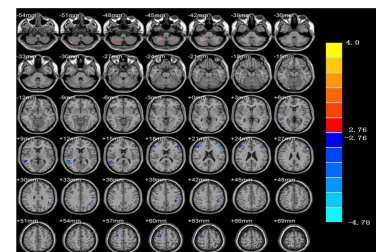


Fig.3 Functional connectivity of the right caudate between HD and HC. The differences map from the bottom to the top, (every 3 mm), ($p < 0.01$, corrected, $T > 2.7633$ or < 2.7633 , cluster > 16). Blue indicates HD individuals had decreased functional connectivity strength compared with HC and the red indicates the opposite.