

Altered interoception and resting-state functional connectivity in the insular system of cocaine dependents

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Introduction Drug addiction is a chronic and relapsing brain disorder characterized by compulsive drug seeking and use despite negative consequences. Accumulative evidence has indicated the involvement of the insular system in drug addiction. For example, abnormal structure (1) and functional activity (2) in the insula were found in cocaine dependents; damage to the insula was found to disrupt addiction to smoking (3). These studies highlight the important role of the insula in drug addiction. Meanwhile, studies on healthy subjects demonstrated that the insula, especially the anterior insula, plays a fundamental role in interoception (4). Based upon these findings, addiction models were proposed from the interoception view (5, 6), linking the insula system and its interoceptive function to drug addiction. However, there is remarkable paucity of research addressing the relationships between the interoception, neurobiological measures of insula and addiction behaviors. The current study aimed to examine the interoceptive function, intrinsic functional connectivity (FC) of the insula and their relationship in cocaine dependents and healthy controls.

Methods Forty-seven cocaine dependents and 47 healthy controls matched on age, gender, IQ and education participated in the study. Toronto Alethymia Scale (TAS-20) was used to assess the interoceptive function. Resting-state fMRI data of 6 min was collected on each participant and processed with the following steps including slice-timing and head motion corrections, normalization, smoothing, detrending, low-pass filtering (0.1Hz), and removing of potential confounding factors by regression. Anterior insular seeds were adopted from previous study (7) (Fig. 1a). A mixed 2x2 ANOVA (hemisphere x group) was employed to examine potential differences in insular FC. Relationships between TAS and addiction behaviors as well as FC were examined.

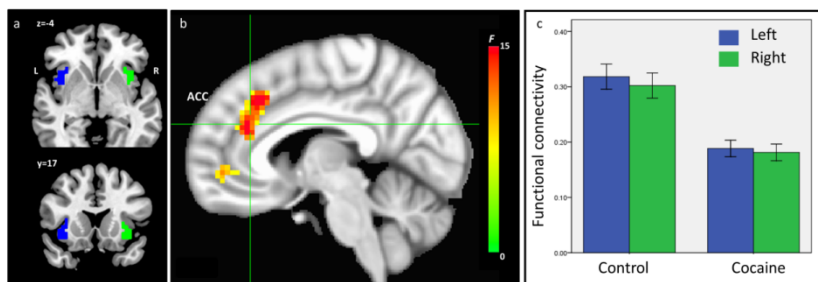


Fig. 1 Decreased resting-state functional connectivity between the insula and ACC in cocaine dependents. a) Bilateral insular seeds. b) Regions of group effects. c) Mean functional connectivity strengths between the insula and ACC.

Results Decreased functional connectivity between the anterior insula and ACC was found in cocaine group (Fig. 1b,c). The TAS total score was significantly higher in the cocaine dependents than the controls (Fig. 2). Positive correlation between the total score of TAS and cocaine dependence (numbers of DSM-IV criteria met) was found (Fig. 3a). In addition, score on the TAS subscale, externally oriented thinking, was found positively correlated with the cocaine current use (money spent for cocaine) (Fig. 3b). A negative correlation between TAS score and functional connectivity of insula-ACC was found in the controls but not in the cocaine dependents (Fig 3c).

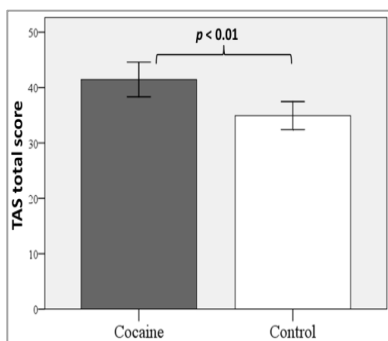


Fig. 2. Difference in TAS total score.

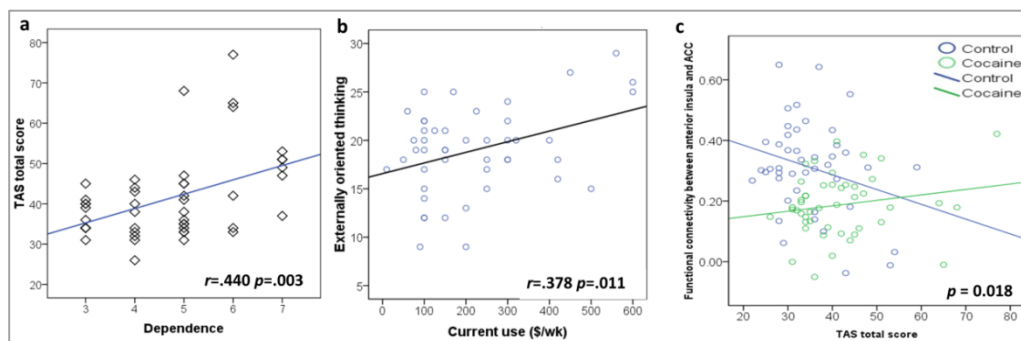


Fig. 3 Relationships between TAS, addiction behaviors and functional connectivity.

Discussion Elevated TAS score and decreased insular functional connectivity were observed in the cocaine dependents, and the relationship between the TAS measure and insular functional connectivity was different between cocaine individuals and controls. Consistent with previous studies which reported elevated TAS measures in substance-addicted individuals such as alcoholics (8), difference in TAS may imply alterations of interoceptive function in cocaine dependents, which has been suggested to relate to cue-induced craving, poor perception of emotion in drug dependents (5, 6). Decreased functional connectivity between the insula and ACC may reflect cognitive deficit depicted by hypoactivity in both insula and ACC in an fMRI study using a GO/NoGo task (2). Altered relationship between the insula-ACC connectivity and TAS score indicates a disturbance of interoception suggested in the addiction models (6), which is also supported by the correlation between TAS and addiction behavior found in the current study. In conclusion, the present study revealed alterations in interoception and insular functional connectivity in cocaine dependents, suggesting disturbance of interoceptive function and underlying neurobiological bases in drug addiction.

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