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## **Introduction**

Substance dependent individuals (SDI) show behaviors in real-life in that they prefer choices that bring immediate benefits, even if these choices were coupled with negative future consequences. The "gambling task", which simulates real-life decisions in the way it factors reward, punishment, and uncertainty of outcomes, has been shown to be sensitive to the decision-making impairment of SDI. In this study, we investigate the hypothesis that impaired decision-making in SDI is closely related to emotion process<sup>1</sup> using Iowa gambling task (IGT) and fMRI.

### Material and Methods

**Subjects:** Thirteen normal subjects (10 men and 3 women) participated in this study. Age range was from 23 to 42 years (mean 28.15 yrs). All subjects were right-handed. They had no history of any psychiatric or neurological disorders, or serious physical illnesses and had no within second-degree relatives with a history of major psychiatric disorders. Seventeen right-handed, SDI (methamphetamine abusers) was included in this study. The mean age of SDI was 35.8 years (range = 33-39).

Task: Participants performed the control task and risk taking task (active task). This Iowa Gambling Test (IGT) is a computerized gambling card game that tests the ability to choose between high gains with a risk for even higher losses, and low gain with a risk for smaller losses. Compared with the active task, the four decks used for the control task were equal in gains and losses. Participants were commanded to picked cards from the decks sequentially in the fixed order of A-B-C-D-A-B-C-D-etc. For Iowa gambling risk task, the subjects were instructed to try to gain as much money as possible by drawing 100 selections from a choice of four decks. Two of decks are more risky and disadvantageous, producing immediate large rewards but these are accompanied by significant money loss due to extreme punishments. The other two decks are advantageous; reward is modest but more consistent and punishment is low. this tasks was repeated We developed a computerized version of the IGT according to the original version ; play money was converted form dollars to Korea won.

**fMRI:** fMRI experiment were achieved on a 3T whole body scanner equipped with a 8ch head coil (Signa Exite HD,GE,USA). fMRI parameters were as follows; echo plannar image, repetition time(TR) = 5s, echo time(TE) = 40ms, field of view (FOV) = 240mm, matrix =  $64\times64$ , 31 slice with 4mm slice thickness and no slice gap. Anatomic T1weigted image were as follows; 3D SPGR, TE = 3.9ms, FOV = 240 mm, matrix =  $256\times256$ , 120 slice with 1.3 slice thickness. The raw fMRI data over the IGT were analyzed. The data were divided into two phases (50 trials each) and the activations were analyzed for each phase by testing the BOLD signal differences between the active and the control Task. fMRI data analysis was performed using statistical parametric mapping (SPM2, http://fil.ion.ucl.ac.uk/spm).

### **Results and Discussion**

Normal subjects showed the typical pattern with decreases in high risk cards (deck A and B) and increases in low risk cards (deck C and D) over time. SDI subjects chose the disadvantageous decks more frequently than the advantageous decks during the IGT (Fig.1). SDIs were impaired in their performance on the IGT. The results of normal subject showed the activity in right dorsolateral prefrontal cortex (DLPFC) and the right medial superior frontal cortex during ambiguous decision-making (the first half of 100 trials in the IGT). Risky decision making (the second half of 100 trials in the IGT) on the other hand was more associated with activity in right orbitofrontal cortex (OFC), ventromedial anterior cingulated cortex (ACC), and cerebellum (Fig.2). Normal subject data showed the differences in the neural structures of decision-making such as the IGT depending in the nature of the decision being made. These finding are consistent with recent evidence of neuroimagings studies by supporting that the cognitive division of mPFC including dorsal portion of ACC palys mojor role in ambiguous decision making and the risky decisionmaking was associated with significant activities within ventral aspect of ACC, a network implicated in emotion and reinforcement.<sup>2</sup> The results of SDI subjects showed superior medial frontal cortex, parietal cortex, and cerebellum during ambiguous decision-making and risky decisionmaking (Fig.3). Previous study reported on dysfunctions in decision-making and associated decreased cortical activation among methamphetamine users. Relative to control participants and the control task, methamphetamine users failed to activate, or activated less, regions within the DLPFC, OFC, while performing the prediction task. SDI subject failed to activate ventromedial cortex and DLPFC. These differences of frontal activation area were accompanied by an increased susceptibility to the influence of immediately preceding trial outcome. Thus functional changes in dorsolateral, orbitofrontal and venrotomedial cortices may impact the executive system, as evidenced by the atypical patterns of expectancy, compulsion and decision-making observed in users of cocaine.

#### **References**

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Fig.1. Decision-making over time.



Fig.2. fMRI map were shown (a) ambiguous decision-making (first 50 trials) and (b) risky decision-making (latter 50 trials) in normal subject. P-value is 0.01.



Fig.3. fMRI map were shown (a) ambiguous decision-making (first 50 trials) and (b) risky decision-making (latter 50 trials) in SDI subject. P-value is 0.01.