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Behavioral approach and orbitofrontal cortical activity during decision-making in substance dependence

Dorothy J. Yamamoto[a], Marie T. Banich[b,d], Michael F. Regner[a,c], Joseph T. Sakai[b], Jody Tanabe[a,b,*]

[a] Departments of Radiology, University of Colorado Anschutz Medical Campus, Aurora, CO, 80045, USA
[b] Department of Psychiatry, University of Colorado Anschutz Medical Campus, Aurora, CO, 80045, USA
[c] Department of Bioengineering, University of Colorado Anschutz Medical Campus, Aurora, CO, 80045, USA
[d] Institute of Cognitive Science, University of Colorado Boulder, Boulder, CO, 80309, USA

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ABSTRACT

Behavioral approach, defined as behavior directed toward a reward or novel stimulus, when elevated, may increase one's vulnerability to substance use disorder. Behavioral approach has been associated with relatively greater left compared to right frontal activity; behavioral inhibition may be associated with relatively greater right compared to left frontal brain activity. We hypothesized that substance dependent individuals (SDI) would have higher behavioral approach than controls and greater prefrontal cortical activity during decision-making involving reward. We hypothesized that behavioral approach would correlate with left frontal activity during decision-making and that the correlation would be stronger in SDI than controls. 31 SDI and 21 controls completed the Behavioral Inhibition System/Behavioral Approach System (BIS/BAS) scales and performed a decision-making task during fMRI. Orbitofrontal (OFC) and dorsolateral prefrontal activity were correlated with BIS and BAS scores. Compared to controls, SDI had higher BAS Fun Seeking scores ($p < 0.001$) and worse decision-making performance ($p = 0.004$). BAS Fun Seeking correlated with left OFC activity during decision-making across group ($r = 0.444$, $p < 0.003$). The correlation did not differ by group. There was no correlation between BIS and right frontal activity. Left OFC may play a role in reward-related decision-making in substance use disorder especially in individuals with high behavioral approach.

1. Introduction

Drug use is associated with novelty seeking and impulsivity, both of which play a role in Gray's Reinforcement Sensitivity Theory (Gray, 1970, 1981, 1987; McNaughton and Corr, 2004). Gray proposed systems controlling behavior and emotion: a behavioral activation (approach) system that directs behavior toward a reward and is associated with novelty seeking, impulsivity, and positive emotions and a behavioral inhibition system that analyzes risk, resolves conflicting goals, and is associated with negative affect. Behavioral approach has been linked to the dopaminergic system (Depue and Collins, 1999) and genetic polymorphisms associated with high dopamine activity (Reuter et al., 2006). Individuals with high behavioral approach sensitivity are more likely to abuse alcohol and drugs which have rewarding properties involving dopamine function (Franken et al., 2006). In contrast, a highly active behavioral inhibition system has been associated with anxiety and anxiety-related disorders (Johnson et al., 2003; Maack et al., 2012) that are often treated with drugs that modulate serotonin (Ravindran and Stein, 2010).

To quantify individual differences in behavioral approach and inhibition, Carver and White developed the behavioral inhibition/behavioral approach (BIS/BAS) scale (Carver and White, 1994) which has shown validity in healthy and clinical populations (Jorm et al., 1998; Kasch et al., 2002; Leone et al., 2001). Alcohol, tobacco, and drug use are associated with high BAS scores (Balconi et al., 2014a; Franken et al., 2006; Johnson et al., 2003; Knyazev, 2004; Yen et al., 2009). The BAS Drive and Fun Seeking subscale scores, in particular, have been shown to be higher in heroin, cocaine, and amphetamine dependent subjects than controls (Franken et al., 2006; Perry et al., 2013). In contrast, high BIS scores have been weakly, if at all, associated with substance use (Franken and Muris, 2006; Knyazev, 2004).

EEG studies suggest that approach behaviors in controls are associated with greater left relative to right hemisphere activity (Coan and Allen, 2003; Harmon-Jones and Allen, 1998; Sutton and Davidson, 1997; Wacker et al., 2013), a finding supported by fMRI studies (Beaver et al., 2006; Krmpotich et al., 2013). Beaver et al. (2006) found an

* Corresponding author at: Department of Radiology, 12700 E 19th Avenue Mail Stop L954, Aurora, CO 80045, USA.
E-mail address: jody.tanabe@ucdenver.edu (J. Tanabe).

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association between BAS scores and left orbitofrontal cortex (OFC) activity in response to rewarding food cues in controls. Krmpotich et al. (2013) reported a correlation between BAS scores and resting state left dorsolateral prefrontal cortex (DLPFC) activity in controls and stimulant dependent individuals. However, these prior fMRI studies did not investigate decision-making. Filling this gap in the literature is important because reward related decision-making is an important feature of substance use disorder (SUD) and may elucidate mechanisms by which behavioral approach increases the risk for substance use.

Dorsolateral prefrontal and orbitofrontal cortex have been implicated in impaired decision-making in SUD (Li et al., 2010; Olsen et al., 2015). The OFC is important for salience attribution of a stimulus, and may be overly active in drug users especially in response to drug cues (Chase et al., 2011; Schoenbaum and Shaham, 2008). The DLPFC is important for cognitive control and response inhibition. Ersche et al. (2005) found that during risky decision-making right DLPFC activity was higher in healthy controls while left OFC activity was increased in drug users, possibly reflecting lowered cognitive control (associated with DLPFC) and increased salience attribution (associated with OFC) of reward in drug users. The relationship between these nodes of the decision-making network and behavioral approach has not been well studied in SUD.

Given the evidence that behavioral approach is associated with substance use and greater left relative to right hemisphere activity, the present study sought to investigate relationships between BIS/BAS and right and left prefrontal brain activity during risky decision-making in substance dependent individuals (SDI). We hypothesized that i.) compared to controls, SDI would have higher behavioral approach, ii.) SDI would have greater OFC activity during risky decision-making, iii.) left OFC and DLPFC activity during decision-making would correlate with BAS scores, and iv.) right OFC and DLPFC activity would correlate with BIS scores. Finally, we hypothesized that the association between left frontal activity and BAS would be stronger in SDI than in healthy controls.

2. Materials and methods

2.1. Subjects

Fifty-two subjects were recruited: 31 substance dependent individuals (SDI) and 21 controls. This sample has not been previously reported. All 52 subjects underwent diagnostic and drug dependence interviews and provided behavioral measures consisting of BIS/BAS and decision-making. One control did not have BIS/BAS data due to technical reasons; remaining subjects completed the entire BIS/BAS questionnaire. Seven subjects were excluded for excessive head motion (6 SDI) or claustrophobia (1 control). Hence, imaging data are reported on 45 subjects: 25 SDI (14M/11F) and 20 controls (11M/9F). Inclusion criteria: SDI met DSM-IV criteria for stimulant dependence. SDI were recruited from a residential treatment program at the University of Colorado Denver Addiction Research and Treatment Service (ARTS).

Average abstinence from drugs and alcohol was 13 months (range = 2–31, standard deviation = 7.9). Abstinence from drugs, nicotine, and alcohol was monitored by direct supervision and random drug screening at ARTS. Controls were recruited from the community and excluded if they met DSM-IV criteria for lifetime abuse or dependence on drugs or alcohol. Exclusion criteria for all subjects: neurological illness, schizophrenia, bipolar disorder, major depression within the last 2 months, head trauma with loss of consciousness > 15 min, HIV, or IQ ≤80. All subjects provided written informed consent approved by the Colorado Multiple Institutional Review Board. All subjects but two were confirmed right-handed: One subject was left-handed and for one subject handedness data was not obtained.

2.2. Screening and drug dependence assessments

All subjects received structured interviews administered by trained personnel. Lifetime drug dependence was assessed for stimulants, nicotine, alcohol, cannabis, opioids, club drugs, sedatives, and hallucinogens using the computerized Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM) (Cottler et al., 1989). The Computerized Diagnostic Interview Schedule–Version IV (C-DIS-IV) was administered to exclude subjects with schizophrenia, bipolar disorder, and current major depression. Subjects were not excluded for antisocial personality disorder (ASPD) as comorbidity of ASPD with stimulant use is common in the U.S. (Compton et al., 2005) particularly in residential treatment programs. Thirty of 31 SDI and 5 of 21 controls met DSM-IV criteria for ASPD. IQ was estimated with matrix and verbal reasoning Wechsler Abbreviated Scale of Intelligence subtests (Psychological Corporation, 1999).

2.3. Behavioral measures

2.3.1. Behavioral inhibition system/behavioral activation system (BIS/BAS)

Behavioral inhibition and approach were measured using the Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales (Carver and White, 1994). The BIS scale assesses the tendency to respond with negative affect and behaviors that respond to goal conflict and generate anxiety (e.g., “I worry about making mistakes.”). The BAS scale assesses the tendency to respond with positive affect and behaviors that approach appetitive stimuli. BAS is divided into three subscales that focus on different aspects of approach behavior: (1) Drive, relating to persistent pursuit of desired goals (e.g., “I go out of my way to get things I want.”); (2) Fun-Seeking, the tendency to seek out novel rewards and act impulsively (e.g., “I often act on the spur of the moment.”), and (3) Reward Responsiveness, the tendency to experience a positive response to the occurrence or anticipation of reward (e.g., “It would excite me to win a contest.”). These scales have shown validity in assessing differences among individuals on emotional response to aversive or appetitive stimuli (Carver and White, 1994; Leone et al., 2001). Each subscale measures a different aspect of approach and were analyzed separately (Carver and White, 1994).

2.3.2. Decision-making task

Subjects played a modified version of the Iowa Gambling Task during fMRI scanning, as described previously (Cauffman et al., 2010; Thompson et al., 2012). Briefly, subjects began with a hypothetical $2000, were presented four decks of cards, and instructed to earn as much money as possible. For each trial, the computer selected a deck and subject was asked to “Play” or “Pass” by pressing the appropriate button. “Play” resulted in a single positive or negative monetary value, along with the running total. “Pass” resulted in no change. Two decks resulted in a net gain (good) and two in a net loss (bad) when played over time. To perform well, subjects must learn to “Pass” on bad decks and “Play” on good decks. For each trial, the subject was given 2 s to make a decision followed immediately by feedback of 4 s duration. There were 50 trials of each deck (200 trials total). Decision-making trials were interspersed with 43 motor control trials and 59 fixation crosses in pseudorandom order to effectively jitter trial onsets. Motor control trials were identical to task trials except the subject was told which button to press. Task time was 26 min (two 13 min runs). The current task differed from prior studies (Yamamoto et al., 2014, 2015) in that we included an explicit control for motor activity. Decision-making variables of interest were the number of passes on bad decks, plays on good decks, and motor control (instructed presses).

2.4. MRI acquisition

Functional MR images were acquired on a 3T scanner with an 8-