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# Iowa Gambling Task scores predict future drug use in bipolar disorder outpatients with stimulant dependence



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## ABSTRACT

Poor decision-making is associated with poor recovery in persons with bipolar disorder and drug relapse in persons with stimulant dependence. Cognitive predictors of stimulant use in those with comorbid bipolar and stimulant dependence are surprisingly absent. Our goal was to determine if a single baseline assessment of decision-making (Iowa Gambling Task, IGT) would predict future drug use in bipolar disorder outpatients with comorbid stimulant dependence. Ninety-four men and women of multiple race/ethnic origins consented to participate in a 20-week study. Data analyses were performed on 63 comorbid bipolar outpatients completing at least four study weeks and 28 cocaine dependent volunteers without a mood disorder who participated as cocaine controls. There were no significant differences in IGT scores between comorbid patients and cocaine controls. In the comorbid group, IGT scores significantly predicted future drug use during the study. Age, sex, race, years of mental illness, or mood state did not significantly influence IGT scores. This is the first longitudinal study to show that IGT scores obtained at a single baseline assessment predicts future objective drug use in comorbid bipolar disorder outpatients with cocaine or methamphetamine dependence. Evaluating decision-making with the IGT may provide clinicians with valuable insight about the trajectory of their patients' risk for future drug use. These data suggest a need to augment existing treatment with cognitive restructuring to prevent slips and relapses in comorbid bipolar patients. The lack of a bipolar control group and a modest sample size may limit data interpretations.

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## 1. Introduction

Poor decision-making is a hallmark characteristic in persons with stimulant dependence (Bechara et al., 2001; Bechara, 2003; Aharonovich et al., 2003, 2006) and in those with bipolar disorder during manic, hypomanic, depression, and euthymic mood phases (Murphy et al., 2001; Clark et al., 2001; Martinez-Aran et al., 2004; Adida et al., 2011). The inability to make good decisions is associated with drug relapse and treatment attrition in those with substance use disorders (Bechara et al., 2001; Bechara, 2003; Aharonovich et al., 2003, 2006; Bowden-Jones et al., 2005), and poor functional recovery in those with bipolar disorder (Denicoff et al., 1999; Clark et al., 2002; Jaeger et al., 2007; Martino et al., 2009). However, decision-making in relation to drug use outcomes in those with comorbid bipolar and stimulant dependence is unknown.

The lifetime substance abuse rate in those with bipolar disorder is ~60% with ~30% of this subset consisting of stimulant use disorders (Regier et al., 1990; Goldberg et al., 1999; Strakowski and DelBello, 2000; Strakowski et al., 2000; Cassidy et al., 2001). Chronic substance use worsens bipolar illness, significantly interferes with recovery, and facilitates poorer prognostic outcomes than in those without comorbid substance abuse (Regier et al., 1990; Goldberg et al., 1999; Strakowski and DelBello, 2000; Strakowski et al., 2000; Cassidy et al., 2001). Thus, it is worthwhile to examine decision-making as a clinically relevant and therapeutic target in patients with comorbid bipolar disorder and stimulant dependence.

The most well-known and widely used decision-making assessment in addiction research is the Iowa Gambling Task (IGT). The consensus in the prevailing literature focuses on IGT comparison data, that is, in comparison to healthy controls those with addiction disorders make poorer, riskier decisions based on immediate rewards (Bolla et al., 2000; Bartzokis et al., 2000; Grant et al., 2000; Bechara et al., 2001, 2000; Bechara and Damasio, 2000; Bechara, 2003; Bolla et al., 2003; Bechara and Martin, 2004; Verdejo-Garcia et al., 2006, 2007; van der Plas et al., 2009; Buelow

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and Suhr, 2009; Toplak et al., 2010). Only four small studies have examined IGT scores as a 'predictor' of future drug use in substance abusing populations. However, these investigations quantified drug use as binary 'yes or no' self-reports of drug use in abstainers versus non-abstainers (Bowden-Jones et al., 2005; De Wilde et al., 2013) or utilized subjective reports of drug use frequency (Schilt et al., 2009; Goudriaan et al., 2011). The IGT has never been used to predict an objective measure of drug use in a prospective, longitudinal design.

Further, only a few studies have examined IGT decision-making in bipolar disorder. Most are comparison studies, exclude comorbidities, and show little, if any, IGT performance differences between healthy controls and those experiencing acute or remitted manic states, depressed or euthymic mood states (Clark et al., 2001, 2002; Frangou et al., 2008; Yechiam et al., 2008; Adida et al., 2011; Martino et al., 2011). Together, the literature suggests a clear and present gap in our understanding about decision-making in relation to drug use in the comorbid bipolar population.

The high rate of stimulant abuse in bipolar disorder and the harmful effects that drug use has on illness recovery suggest a critical need to identify those who are prone to continue drug use, slip or relapse. Predicting the drug use potential in comorbid bipolar patients is an important prevention tool to avert poor prognoses. Using a single cognitive test to predict future drug use prior to treatment onset should provide some real-world therapeutic and economic benefits. The current study was designed to test the hypothesis that baseline IGT scores would significantly predict future drug use in comorbid bipolar disorder with cocaine or methamphetamine dependence.

## 2. Methods

### 2.1. Study design and protocol

A longitudinal study was designed to determine if a single baseline assessment of decision-making using IGT scores could predict future drug use in those with comorbid bipolar disorder with cocaine or methamphetamine dependence (comorbid group) up to 20-weeks after task administration. Comparison studies among bipolar types (I versus II) and various mood states are well-documented as cited earlier. However, there are no investigations comparing decision-making between patients with comorbid bipolar and stimulant dependence to those with stimulant dependence without bipolar illness. To help test our hypothesis we thought it was important to obtain empirical data to better understand the potential range of IGT performance in the comorbid group as a function of their addiction. Thus, we recruited subjects meeting DSM-IV criteria for cocaine dependence without a mood disorder (cocaine control group) and compared their IGT scores to the comorbid group.

In accordance with the Declaration of Helsinki, university Institutional Review Board approval of this research protocol was obtained. A Confidentiality Certificate was issued by the National Institute of Mental Health. Prior to study enrollment, eligible volunteers provided written, informed consent to participate.

Those enrolled in the comorbid group attended weekly study visits for 20-weeks as part of a clinical pharmacotherapy trial reported in detail elsewhere (Nejtek et al., 2008). Every four weeks after study assessments were completed, comorbid subjects received a \$40 gift card to a local discount retail store. As drug use in cocaine abusers is well-studied, the cocaine control group was not followed longitudinally as our focus was not to predict their drug use risk. Thus, subjects in the cocaine control group attended one study visit where demographic information was collected, the IGT was administered, and afterward controls received their gift card.

### 2.2. Inclusion/exclusion criteria

Volunteers for the comorbid bipolar and cocaine control groups of all race/ethnic origins were invited to participate and were recruited from clinician referrals at local mental health clinics and/or drug treatment centers. Eligibility for the comorbid group included meeting DSM-IV criteria for current bipolar I or II disorder plus current cocaine or methamphetamine dependence, 20–50 years old; English-speaking with a high school diploma or equivalent or a Shipley IQ test score of >85, and participated in weekly outpatient behavioral addiction treatment (i.e. Intensive Outpatient Classes, Alcoholic Anonymous, Narcotics

Anonymous, Dual Recovery Anonymous, etc.). Demographic eligibility for the cocaine control group was the same as for the comorbid group, but excluded any current DSM-IV mood disorder, any substance dependence other than cocaine, and psychotropic medications.

Both comorbid and cocaine control group volunteers were excluded if they were hospital inpatients, persons undergoing detoxification, suffering acute withdrawal symptoms, or incarcerated inmates. In addition, those with a substance-induced mood disorder, those who had attempted suicide in the past 6 months, a history of special education, mental retardation, dementia, brain injury, a central nervous system disorder, HIV/AIDS, cataracts, glaucoma; currently using benzodiazepines, sedatives/narcotics, prescription stimulants, use of any antipsychotic medications, and those receiving polypharmacy (i.e. more than two psychotropic medications) were ineligible. As we were interested in examining an ecologically valid sample, subjects with positive urine drug tests at study entry were allowed to participate.

### 2.3. Study assessments

All subjects were evaluated with the Structured Clinical Interview for DSM-IV Clinician Version (SCID-IV-CV) to verify current and lifetime Axis I diagnoses for mood and substance use disorders (First et al., 1997) and the IGT. At the baseline visit both groups provided sociodemographic information, a urine drug sample was collected, and the IGT was administered. At baseline and at every weekly visit, the comorbid group was also evaluated with the Young Mania Rating Scale (YMRS<sub>11</sub>; Young et al., 1978), Inventory of Depressive Symptomatology – Clinician-rated (IDS-C<sub>30</sub>; Rush et al., 2000; Trivedi et al., 2004), and the 10-item Stimulant Craving Questionnaire (SCQ<sub>10</sub>; Tiffany et al., 1993) to measure manic, depressive symptoms and stimulant (cocaine or methamphetamine) craving.

The YMRS<sub>11</sub> and the IDS-C<sub>30</sub> are widely used instruments used to measure current manic and depression mood states (Young et al., 1978; Rush et al., 2000; Trivedi et al., 2004). In this study, the YMRS<sub>11</sub> symptom severity cutoff scores used were ≤12=normal, 13–19=minimal, 20–25=mild, 26–37=moderate, ≥38=severe. The IDS-C<sub>30</sub> symptom severity cutoff scores range from ≤11=normal, 12–23=mild, 24–36=moderate, ≥37=severe. The SCQ<sub>10</sub> is a simple modification of the Cocaine Craving Questionnaire (CCQ) used in our previous studies (Brown et al., 2002; Nejtek et al., 2002, 2004, 2008) to assess methamphetamine cravings in the same manner as cocaine. Factor analytic reliabilities of internal consistencies of this questionnaire range from 0.92 to 0.72 with raw scores ranging from 10 to 70 (Tiffany et al., 1993).

### 2.4. The Iowa Gambling Task, instructions, scoring

The IGT is a computerized assessment that features four card decks (e.g. A, B, C, D) shown on a color computer monitor (Bechara et al., 1994, 1999). Two decks (A+B) are considered 'high-risk' and contain some high dollar winning cards (e.g. \$100–1000), a few cards with small dollar losses (e.g. \$20–50), and several cards with substantial monetary losses (e.g. \$500–1250). Two other decks (C+D) are considered 'low-risk' as they have many more low dollar winning cards (e.g. \$75–50) but have lower monetary losses (e.g. \$25) thereby yielding small, but consistent monetary gains. In the present study, each deck was programmed to contain 60 cards with a maximum of 100 selections set with an inter-trial interval of 3 s. During the task, subjects who may run out of cards from a given deck must continue choosing from the remaining decks. The task automatically shuts off after the 100 selections are made.

Thus, subjects have 100 chances to learn the strategy to lose less and win more money during five learning blocks that contain 20 cards each. Block 1 consists of cards 1–20, Block 2 cards 21–40, Block 3 cards 41–60, Block 4 cards 61–80 and Block 5 cards 81–100. Net total scores for the entire IGT assessment (all blocks included) are calculated as the accumulated low risk minus high risk card choices [(C+D)–(A+B)]. Scores of ≤0 infer cognitive deficits associated with prefrontal brain injury or atrophy, while healthy controls score >10 (Bechara et al. 1994, 1999, 2001). In addition to the net total score [(C+D)–(A+B)], we analyzed total A+B scores and total C+D scores separately, and also the net total scores [(C+D)–(A+B)], for each Block 1 through 5 (for detail see Bechara et al. (1994, 1999, 2001, 2002) and Bechara and Damasio (2000)).

Task instructions given to the subjects were that they would receive a fictional \$2000 credit to start the game, that they should win as much money as they can, and that the card color does not determine how much they can win. In addition, subjects were told that some decks were worse than others and that no matter how much they lost they could still win if they stayed away from the worst decks. Subjects were instructed to treat the play money as if they were using their own real money, and that if they ran out of cards from any given deck, they were told to continue choosing from the remaining decks. To perform well, subjects need to learn to inhibit risky, reward-based decision-making and avoid choosing from the 'high-risk' card decks.

### 2.5. Drug use

In addition to the SCID-IV-CV life chart, self-report and case manager reports for each subject were used to determine the years of drug dependence and the

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