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Decision-making Processes as Predictors of Relapse and Subsequent Use in Stimulant Dependent Patients

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Abstract

Background—Decision-making processes have been posited to affect treatment outcome in addicted patients.

Objective—The present multi-site study assessed whether two measures of decision-making predicted relapse and subsequent use in stimulant-dependent patients.

Methods—160 methamphetamine- or cocaine-dependent patients participating in a multi-site clinical trial evaluating a modified 12-step facilitation intervention for stimulant-dependent patients (STAGE-12) were assessed. Decision-making processes of risk and delay [Iowa Gambling Task (IGT)] and response reversal [Wisconsin Card Sorting Task (WCST)] were obtained shortly after treatment admission followed by assessment of stimulant use over the next six months. The relationships of the IGT and WCST (Perseverative Errors) with relapse (yes/no) and days of stimulant use during the 6-month period following post-randomization were evaluated.

Results—Performance on the IGT and WCST did not significantly predict relapse status or time to relapse. Unexpectedly, better performance on the IGT was associated with a fewer number of stimulant use days ($p = 0.001$). In contrast, worse performance on the WCST (more perseverative errors) was associated with a greater number of stimulant use days ($p = 0.0003$). The predictive

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effects of perseverative errors on subsequent use were confined to methamphetamine-dependent and Minority participants.

Conclusions—Decision-making processes, as measured in the current study, do not uniformly predict relapse or subsequent use. A decrease in the salience attribution of nondrug reinforcers may explain the positive relationship between IGT performance and post-relapse use. More comprehensive and global measures of impulsiveness may better assess relapse risk and use.

Keywords

impulsivity; decision-making; methamphetamine use disorder; cocaine use disorder; gambling task; relapse

Introduction

Relapse is experienced in up to 75% of stimulant-dependent patients within six months of an index treatment episode (1, 2). An increasingly viable literature has posited that deficits in cognitive functioning may contribute to poor treatment retention and heightened relapse risk. These deficits include processes that are automatic, rapid, and unconscious [variously referred to as System 1 (3), Impulse Drive (4), or Impulsive (5)] and those that are controlled, slow and conscious (e.g., System 2, Impulse Control, or Reflective). These latter decision-making processes are particularly relevant to relapse, as they refer to the capacity to select a choice with the optimal outcome for long-term gain. In an individual with a substance use disorder, the decision to use a drug following treatment would appear to reflect a deficit in the appropriate assessment of short-term gain (i.e., drug use) with long-term consequences.

A key component of the decision-making process is to consider a potential reward's (or punishment's) relative value, the probability of the reward occurring, and the temporal relation between reward receipt and reward value (6). Both methamphetamine (7) and cocaine- (8) dependent patients have been found to perform significantly worse on measures assessing the probability of reward vs. loss relative to the reward's value [e.g., Iowa Gambling Task (IGT)], as well as assigning a temporal value to both monetary and drug rewards [e.g. Delayed Discounting Procedure, (9)]. A second key component of the decision-making process is the ability to reverse strategy in the presence of changing circumstances. When a response that previously produced a positive outcome suddenly becomes aversive (e.g., the previously positive, rewarding effects of drug use begin to cause severe, negative consequences), a reversal in cognitive and behavioral strategies is required to suppress the course of action that is now no longer appropriate. Thus, response reversal considers the positive and negative attributes of a potential response, followed by a decision to either maintain or change the present direction of responding. Neurocognitive tasks assessing response reversal alter the directional salience of a stimulus (i.e., rewarded stimuli become aversive) but the quantity and probability of the rewards remain constant. Impaired performance on a commonly used measure of response reversal, the Wisconsin Card Sorting Task (WCST), has been reported in participants with both methamphetamine (10) and cocaine (11-15) dependence, although not all investigators have observed differences (16, 17).

The relevance of decision-making to treatment retention and relapse, however, remains tenuous. In a multi-site study of six Therapeutic Communities, five measures of executive functioning, including the IGT, accounted for a relatively small amount of the variance in treatment retention in cocaine-dependent participants (18). Performance on the IGT predicted relapse in 33 cocaine-dependent subjects (using cocaine concentration in hair as a marker of relapse) and drug use IGT predicted outcome in 33 cocaine-dependent patients (19) and future drug use in 63 subjects with co-morbid stimulant dependence and bipolar disorder. Poorer performance on the WCST predicted worse treatment retention, but not cocaine use, in 80 cocaine-dependent patients (20). In 37 opioid-dependent patients, poorer performance (decision-making) on the Cambridge Gamble Task and the IGT significantly predicted relapse at 3 months post-treatment (21). However, this difference was only evident in a subsample of patients from a community outpatient treatment program. Poorer performance on the IGT predicted relapse at three months post-treatment in a small group of alcohol-dependent (n=11) participants (22) and poorer performance on the IGT, but not the Delayed Discounting Task, predicted relapse in 37 polysubstance-dependent patients (23).

To more definitely assess the relationship between decision-making and relapse, we administered the IGT and WCST in a large sample of cocaine- and methamphetamine-dependent patients participating in a multi-site, ancillary study to a National Drug Abuse Treatment Clinical Trials Network (NIDA CTN) trial on a modified 12-step facilitation for stimulant-dependent individuals (STAGE-12). The STAGE-12 trial was designed to evaluate the efficacy of a modified 12-Step facilitation intervention integrated into intensive outpatient treatment, relative to substance abuse intensive outpatient treatment as usual without the integrated 12-step facilitation intervention, in improving outcomes in stimulant-dependent individuals (24). Following the 8-week Stage-12 or Treatment-as-Usual (TAU) intervention, participants were further assessed at three and six months post-randomization.

We hypothesized that poorer performance on the IGT and WCST would predict increased rates of relapse and, in those who relapsed, more days of stimulant use. Since the IGT assesses processes predicted to be more impaired in stimulant-dependent patients than response reversal (14, 25), we further hypothesized that IGT performance would be a stronger predictor of relapse and more days of stimulant use than the WCST.

Methods

Participants

Six participating substance abuse community treatment programs (CTPs) recruited stimulant dependent individuals participating in the STAGE-12 trial. Participants were adults seeking outpatient substance use disorder (SUD) treatment who had used stimulants in the prior 60 days, and had a current diagnosis of stimulant dependence based on the DSM-IV Checklist. Of participants randomized into the STAGE-12 trial, 183 were eligible for the present study because they endorsed methamphetamine or cocaine as their primary drug of choice and did not have a seizure disorder or a history of stroke. The study was approved by the Institutional Review Boards of the participating sites and all participants provided informed consent. Participants were compensated for their participation; the amount of compensation was not contingent upon performance on the neurocognitive tasks.

Procedures

See Donovan et al. (24, 26) for a description of the STAGE-12 study procedures. Briefly, methamphetamine- and/or cocaine dependent participants who met eligibility criteria were randomized to Stimulant Abuser Groups to Engage in 12-Step (STAGE-12) or treatment as usual (TAU). Participants randomized to TAU received treatment as ordinarily provided by the site. Participants assigned to STAGE-12 received eight treatment sessions that replaced eight sessions typically provided. STAGE-12 is a comprehensive and systematic introduction to 12 Step recovery and fellowship (e.g., literature, meeting attendance, etc.). Participants in the present study completed a single session (typically within a week following randomization into the STAGE-12 trial) in which baseline characteristics and behavioral measures were obtained, including the IGT and WCST. The average time between randomization and testing was 7.4 days (SD = 3.6). The current analyses included participants randomized to both the STAGE-12 and TAU conditions.

Measures

Baseline Characteristics—Baseline assessments included basic demographic information and measures of stimulant use at intake, including self-report using the Timeline Follow-Back (TLFB) procedure (27). Participants self-reported their race and ethnicity.

Decision-Making Tasks

Iowa Gambling Task (IGT) (28): In the IGT, subjects choose between decks of cards offering high payments with occasional high penalties or decks offering low payments but more frequent lower penalties; the optimal, long-term strategy is the low pay/low penalty deck. Participants click a mouse to pick a card and attempt to obtain the highest overall "winnings." Each card carries an immediate reward, but some cards also carry a penalty. Two decks pay higher amounts, but come with higher penalties, leading to an overall loss (disadvantageous decks). The other two decks pay less, but have lower penalties, leading to an overall gain (advantageous decks). The amount of reward and penalty, along with the net gain or loss, is displayed on the screen for the participant. Participants are allowed to select 100 cards. Performance was measured by the number of cards selected from the advantageous decks minus the cards selected from the disadvantageous decks (28); higher scores reflect a more optimal assessment of a card's value relative to the likelihood of its occurrence. For scoring purposes, post-hoc analyses considered 5 blocks of cards of 20 trials each. Block 2, when the optimal long-term strategy remains uncertain, has been posited to assess "decisions under ambiguity," whereas Blocks 3-5, when the outcome depends on known probabilities, are thought to primarily reflect "decisions under risk" (29).

Wisconsin Card Sorting Test (WCST): The WCST (30, 31) requires the examinee to shift his or her behavior in response to environmental feedback (i.e., set shifting). The WCST has strong evidence of predictive validity in non-substance use disorders (32, 33). In the electronic version of this test, participants were instructed to match 128 response cards, one at a time, to four stimulus cards by clicking a mouse. The cards were sorted along three dimensions (color, form, and number), and participants utilized feedback following each selection to modify their responses and successfully sort the cards. The sorting principle

changed after ten consecutive correct responses, allowing for assessment of perseverative responding and cognitive flexibility (i.e., the participant's ability to generate alternative strategies). Performance scores were converted to age and education corrected normative T scores. The primary predictor of interest was Perseverative Errors, as this variable best reflects set-shifting capabilities.

Outcome Measures—The measures of stimulant use included self-report of use for each day of the study assessed using the TLFB (34). Since more than half of the sample did not use stimulants during follow-up, relapse (yes/no) and days of stimulant use among users were considered as outcome variables. Research visits were completed at screening/baseline, study weeks 2, 4, and 8 (during treatment), and at three and six months post-randomization (post-treatment). Urine drug screens (UDS) were obtained at baseline, 4 weeks, 8 weeks, and 3 months post-baseline. If a UDS was positive for stimulant use but no stimulant use was recorded on the TLFB during that month then 1 stimulant use day was imputed on the TLFB.

Data analysis

Of the 183 randomized participants, 173 (94.5%) reported substance use status at least one month post-randomization. Of these, 13 met criteria for both cocaine- and methamphetamine-abuse/dependence or both methamphetamine- and other stimulant abuse/dependence so were excluded from further analyses. The primary outcome of total days of stimulant use during the 6-month assessment period was converted to average days of use per month during the months for which data were available because not all participants completed the 6-month follow-up and the average per month was multiplied by 6 to obtain a count of the number of stimulant use days that would have occurred in the full 6-month period. Count data such as number of days of use typically follow a Poisson distribution. However, more participants had zero use during follow-up than would be expected based on the Poisson distribution (73/160 or 45.6%). As excess zeros commonly occur with count data (referred to as zero-inflated count data), one statistical approach [hurdle model; (35)] is to assume that all participants have the potential to use drugs but resistance to drug use (a hurdle) must be overcome before drugs are used. The existence of the hurdle results in an excess of participants with zero use. We chose to use a hurdle model because, in conformity with the assumptions of this model, we believed any participant could have a relapse during the study, but the fact that participants have chosen to enter treatment and treatment itself provided resistance to subsequent drug use. The hurdle model contained two parts: a model describing the probability of use versus non-use and a model describing the amount of use among users. Each hurdle model contained random site effects and fixed effects for the decision-making task score (IGT or WCST Perseverative Errors) and pre-specified covariates. The covariates were gender, education, minority status, stimulant diagnosis category (methamphetamine dependence presence versus absence), days of stimulant use 30 days prior to the study, and treatment group (Stage 12 versus TAU). The model also included interaction terms between each covariate and the decision-making task score. SAS Proc NLMIXED was used (SAS program based on (35)). The hurdle model described above was repeated where participants were excluded if drug use was confirmed by the UDS but no drug use was reported on the TLFB (n=4). The effect of decision making processes on time

to relapse was analyzed using a Cox Proportional Hazards model with the same covariates described above. In addition, mean IGT and WCST values were compared between participants who relapsed within 1 month, relapsed within 2 to 6 months, and who did not relapse within 6 months.

Results

Sample Characteristics

160 stimulant-dependent participants had post-randomization stimulant use data available for at least one month: 93.1% at Month 2; 89.4% at Month 3; 82.5% at Month 6 (which included self-reports at Months 4 and 5). These participants were diagnosed with methamphetamine-only dependence (n=42) and cocaine-only dependence (n=118). Participants averaged 39.2 (SD=9.4) years of age and had 12.0 (SD=1.6) years of education. Approximately 30.6% (n=49) were male; 40.6% (n=65) were non-Hispanic Caucasians, 49.4% (n=79) African Americans, and 9.4% (n=15) Hispanics (non-white and white). Due to the small number of Hispanics, these participants were considered jointly with African-American participants as Minorities. However, all findings below were similar if only non-Hispanic Caucasians and African-Americans were considered.

IGT and WCST Measures at Baseline

Total net scores for the IGT were similar to those reported by others (8, 36, 37) (Table 1). Mean scores for the WCST measure was well within clinical norms (T-score slightly less than 50). The IGT did not significantly correlate with Perseverative Errors (r=0.06, p=0.47), suggesting that the IGT was measuring a different cognitive construct than the WCST. IGT and WCST scores were higher in non-Hispanic Caucasians relative to the Minority participants (IGT: t=2.1, p=0.04, WCST Perseverative Errors: t=2.6, p=0.01) (Table 2). IGT and WCST scores did not significantly differ between men and women, Stage-12 vs. TAU treatment groups, or those who presented with UDS positive vs. negative urines.

Decision-making Measures as Predictors of Relapse (Hurdle Model)

Neither the IGT (t=-0.4, df=4, p=0.69) or WCST Perseverative Errors (t=0.6, df=4, p=0.61) significantly predicted relapse in stimulant-dependent participants. Relapse results were still non-significant after exclusion of participants with discrepancies between the UDS and TLFB.

Decision Making Measures as Predictors of Time to Relapse

Neither the IGT (hazard ratio=1.005, chi-square=1.3, p=.260) nor the WCST (hazard ratio=0.998, chi-square=0.07, p=.803) were significant predictors of time to relapse. Also, there were no significant differences in IGT between participants who relapsed within 1 month, 2-6 months, or who did not relapse (relapse within 1 month mean=-1.99, relapse within 2 to 6 months mean=-2.43, no relapse mean=-1.00, f=0.4, p=0.960) nor were significant differences found in the WCST (relapse within 1 month mean=48.9, relapse within 2 to 6 months mean=45.9, no relapse mean=46.6, f=0.6, p=0.537).

Decision-making Measures as Predictors of Days of Stimulant Use (Hurdle Model)

Among those who used stimulants, higher scores (signifying better performance) on the IGT significantly predicted more days of stimulant use (t=6.6, df=4, p=0.0028) (Fig. 1). This relationship was evident for four of the five blocks (Block 1: t=5.6, p=0.0051; Block 3: t=6.8, p=0.0025; Block 4: t=7.6, p=.00016; Block 5: t=6.9, p=0.0024). Both baseline days of stimulant use (t=-7.1, df=4, p=0.0021) and education (t=-9.8, df=4, p=0.0006) significantly interacted with IGT Total Score. Stimulant use 30 days prior to baseline had a larger effect on participants with lower IGT scores and a smaller effect on participants with higher levels on IGT (see Supplement), although the positive relationship between IGT and post-randomization days of stimulant use persisted for all levels of baseline days of stimulant use. The positive relationship between IGT Total Score and days of stimulant use post-randomization was primarily evident for those individuals with lower education (see Supplement). Other covariates did not significantly interact with IGT in predicting days of stimulant use post-randomization.

Lower scores (worse performance) on WCST Perseverative Errors significantly predicted more days of stimulant use post-randomization (t=-10.0, df=4, p=0.0005) (Fig 1). The covariates minority status (t=-11.0, df=4, p=0.0004) and drug of choice (t=-7.5, df=4, p=0.0017) significantly interacted with Perseverative Errors (each covariate was significant independent of the other covariates, although drug of choice and minority status were highly related). The relationship between WCST Perseverative Errors and days of stimulant use post-randomization was only apparent for those participants who were Minorities or methamphetamine-dependent (Fig. 2). The two graphs in Figure 2 may appear inconsistent as the inverse relationship between WCST Perseverative Errors and days of stimulant use post-randomization was observed for Minority participants (92% of whom were cocaine-dependent) (Fig 2, upper panel) but was not observed for cocaine-dependent participants (Fig 2, lower panel). Similarly, an inverse relationship was observed for methamphetamine-dependent participants (who were 83% Caucasian) (Fig 2, lower panel) but was not observed for Caucasians (Fig 2, upper panel). However, there was a positive association between WCST Perseverative Errors and days of stimulant use post-randomization in Caucasian cocaine-dependent participants; 25% of cocaine-dependent participants were Caucasian and 46% of Caucasians were cocaine-dependent. The covariates baseline days of stimulant use (t=9.5, df=4, p=0.0007) and education (t=-9.0, df=4, p=0.0009) also significantly interacted with WCST Perseverative Errors, although the main effect (inverse relationship between WCST Perseverative Errors and days of stimulant use post-randomization) was evident for all levels of baseline stimulant use and those with 10 or 12 or more years (but not 10 years) of education (see Supplement).

In order to examine the magnitude of effects of the IGT and Perseverative Errors on the probability of stimulant use during the study (relapse) and the amount of stimulant use during the study for those participants that relapsed, hurdle model estimates were determined. These estimates provided for a hypothetical participant with ‘high’, ‘medium’, and ‘low’ measures for IGT and WCST Perseverative Errors T-score (Table 3). A stimulant-dependent participant with an IGT of 14 (75th percentile) was projected to use stimulants during the six-month post-randomization period for an additional 4.4, or 29%, more days,

than a participant with an IGT score of -18 (25th percentile). In contrast, a participant with a Perseverative Errors score of 37 (25th percentile) would be projected to use stimulants for an additional 7.0, or 59%, more days than a participant with a score of 55 (75^{th} percentile). The same pattern of results for IGT and WCST were observed after exclusion of participants with discrepancies between the UDS and TLFB.

Discussion

This study explored the relationship between decision-making and relapse and subsequent post-relapse use in a large, multi-site sample of methamphetamine- and cocaine-dependent participants. The IGT and WCST did not predict whether or when use would or would not occur, but did predict days of use once an individual relapsed. Unexpectedly, IGT score positively predicted days of stimulant use post-randomization; the better the performance, the more days of drug use. In contrast (and consistent with our hypotheses), worse performance on the WCST, as measured by Perseverative Errors, significantly predicted increased days of drug use. This relationship was limited to Minority and methamphetamine-dependent individuals.

The positive association between IGT scores and days of stimulant use was not in the direction hypothesized. The recent use of stimulants may have improved the IGT performance of those who later went on to more frequent stimulant use post-randomization. Healthy adults administered stimulants, for example, show improvement on performance of cognitive function tasks, including on probabilistic learning tasks [see review in (38)]. However, urine drug screens positive for methamphetamine or cocaine did not significantly predict IGT performance (data not shown), suggesting that recent stimulant use did not explain this relationship. Alternatively, better performance on the IGT may, paradoxically, be consistent with a more severe use history and treatment outcome within a given population of stimulant-dependent individuals. Goldstein and Volkow (39) have posited that substance-dependent individuals attribute heightened salience to substance- and substance-related cues and a muted sensitivity to non-substance reinforcers. According to this model, drug and drug cues develop exaggerated importance to the addicted individual while non-drug stimuli (e.g., money, food, and other stimuli necessary for survival) lose importance. Consistent with this formulation, stimulant-dependent individuals in our study with a more significant disorder (e.g., more days use pre-baseline, more days use post-randomization) may attribute attenuated salience to non-drug reinforcers (e.g., money won during IGT) relative to those with less severe stimulant dependence. The more severely dependent group would, therefore, be less swayed by the high reward cards than the less severely dependent group. This interpretation is also congruent with the absent relationship between IGT and days of stimulant use during the 2^{nd} block of cards (cards 21-40). This latter finding reveals that the association between IGT and days of use post-randomization did not reflect differences during the block associated with “decisions under ambiguity” (Block 2), but primarily reflected “decisions under risk” (Blocks 3-5) (29). During this latter period of decision-making - when risk assessment is relatively stable - the salience attributed to the monetary reinforcers may be more relevant to participant responses. Thus, less biased responding to high reward/high loss IGT decks in those with more severe dependence may be most easily detectable during these blocks.

Although the WCST requires persistent set-shifting (as the rules change repeatedly throughout the task), it does not require the assessment of risk. Previous studies support the dissociation between IGT and WCST performance (14, 29). Toplak et al. (40) has suggested that, whereas WCST captures cognitive functions encapsulated by executive functions and intelligence, the IGT assesses the distinctly different process of decision-making. These findings are consistent with conceptualizations that differentiate between intelligence (e.g., response reversal) and rationality (e.g., meta-cognitive strategies or “reflective mind”) (40, 41) and between crystallized (e.g., learning and acquired skills) vs. fluid (e.g., cognitive flexibility) intelligence (42). Our finding that worse WCST Perseverative Errors scores positively predicted post-randomization days of stimulant use in the hypothesized direction, in contrast to the opposite relationship between IGT and post-randomization days of stimulant use, adds additional support to the dissociable nature of these two measures. The differential findings observed between the IGT and WCST may reflect specific alterations in regions identified as relevant to both decision-making and addictive processes; the IGT assessment of salience and risk may reflect striatal and anterior cingulate cortex activity (43) whereas behavioral inhibition (WCST) may reflect activity in the lateral orbitofrontal cortex (44). Finally, our observation that the relationship between WCST Perseverative Errors and days of stimulant use was significant only for minority and methamphetamine dependent subjects was unexpected and deserving of further study.

In general, our hypotheses were not confirmed. The neurocognitive measures employed did not predict whether or when relapse would occur and associations with days of use were in opposing directions. In retrospect, the extant literature is not at odds with our findings. Although a number of studies have found a powerful predictive effect of impulsivity upon future drug use, the strongest effects are observed for a combined complex of cognitive, behavioral, observational, and genetic variables. The construct of “neurobehavioral disinhibition” in children, for instance, is predictive of later substance use (45). This construct consists of externalizing behavioral symptoms, a temperament survey, and six neurocognitive measures. Another model of “self-control” in children predicting later substance use incorporates measures of impulsive aggression, hyperactivity, lack of persistence, inattention and impulsivity as well as observational measures from parents and teachers (46). Several genotypes associated with impulsive behaviors also influence the predisposition to substance use (47). Similar complex influences would be expected to play a role in relapse risk. The literature supporting impulsivity, as assessed by neurocognitive measures, and relapse risk and post-relapse days of use of stimulant-dependent patients is, in fact, relatively scant. Verdejo-Garcia et al. reported IGT performance predicted cocaine relapse in 33 participants (19), although six tasks of decision-making accounted for only 14% of the variance in relapse in opioid-dependent participants (23) and performance on the WCST did not predict cocaine use during an outpatient medication trial (20). Nejtek et al. (48) also found IGT performance significantly predicted drug use in co-morbid cocaine and bipolar disordered subjects. Using the same population as reported in the present study, however, Winhusen et al. (49) used a more global self-report measure of frontal system functioning to predict stimulant use during the eight weeks of treatment. In that analyses, participants with elevated scores on the Disinhibition domain of the self-report Frontal Systems Behavior Scale (FrSBe) reported greater stimulant use during treatment (40.5% vs.

16.7%, OR = 3.40). Thus, more global constructs of impulsivity – rather than discrete neurocognitive measures – may prove more useful in predicting relapse risk (50). This is consistent with recent work revealing that personality and self-report measures of impulsivity (e.g., personality inventories, self-rating scales) differed substantially (more than 1.5 standard deviations) between cocaine-dependent and control participants, whereas group differences in neurocognitive measures of disinhibition and decision-making (e.g., IGT, WCST) were far more subtle (50).

Strengths of our study include a relatively large, diverse sample of both methamphetamine and cocaine dependent individuals and include individuals seeking treatment at several community treatment programs around the United States. Thus, our findings are relevant and likely generalizable to individuals in treatment for stimulant use disorders. Excellent follow-up rates minimized the likelihood that our findings were unduly influenced by participants who dropped out of the study after randomization. Although self-report was used to determine days of stimulant use, this approach has been found to accurately reflect substance use (51). Days of use was viewed as a proxy for relapse severity, but other potentially relevant measures of relapse severity were not included. Nevertheless, days of substance use (or days of abstinence) is a commonly used barometer of substance use severity (52-54). Finally, the WCST and IGT only assess a narrow range of cognitive processes. As the parent study was designed to assess the efficacy of a specific treatment approach, it was necessary for the cognitive battery to be limited in scope. Given our interest in assessing the predictive validity of decision making upon relapse, we utilized two of the most commonly used and well-accepted measures of this process. Finally, days of stimulant use over six months were relatively low (6.5 days in a hypothesized participant with an IGT score at the 75th percentile), suggesting that these findings may have limited clinical import.

Our findings suggest that neurocognitive measures of decision-making are differentially associated with substance use in treatment-seeking stimulant-dependent patients. Future studies assessing impulsivity in substance-dependent participants should consider more global measures of self-control and decision-making processes, including self-report measures (e.g. FrSBe, personality measures, Barratt Impulsivity Scale) and diagnostic criteria associated with behavioral dyscontrol (e.g. antisocial personality disorder, attention deficit disorder). These findings should also provide caution to treatment approaches targeting specific neurocognitive processes, as task performance may not necessarily be relevant to treatment outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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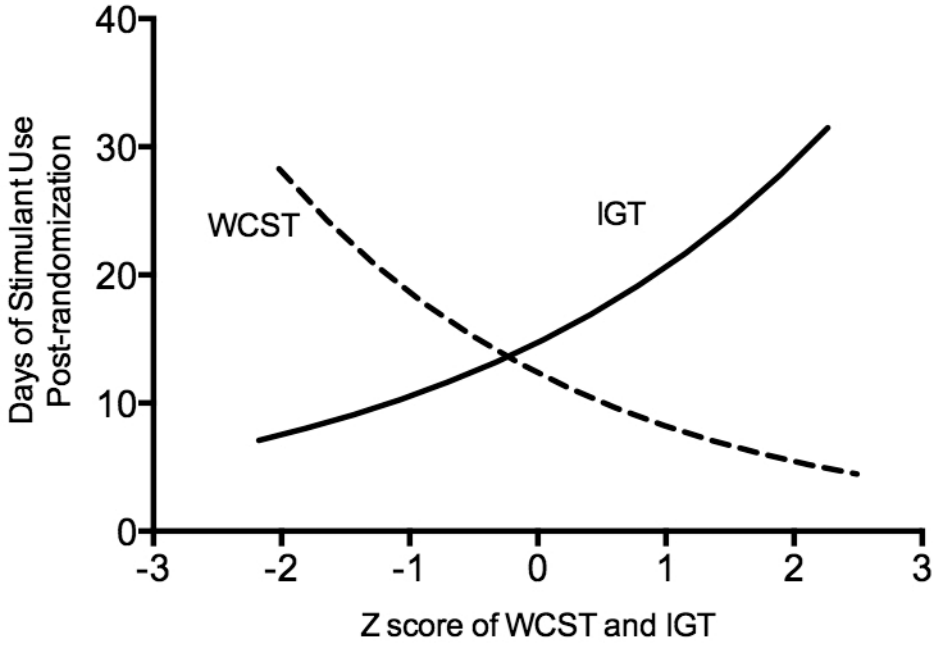

Fig 1.

Iowa Gambling Task (IGT) Total Score and Wisconsin Card Sorting Task (WCST) Perseverative Errors prediction of days of stimulant use in stimulant-dependent participants for six-months following post-randomization. Observed values of IGT and WCST were converted to a common scale by use of Z scores for both IGT (solid line) and WCST (dashed line) scores. Both lines show the estimated curves from the data. Main effects - IGT and Days of Stimulant Use: t=3.3, df=159, p=0.0013 [the higher (better) the IGT score, the more days of stimulant use]. Perseverative Errors and Days of Stimulant Use: t=-4.5, df=158, p<0.0001 [the more perseverative errors (or lower the t-score), the more days of stimulant use]. WCST T-scores of 30 and 60 are represented by z-scores of -1.2 and 1.0, respectively. IGT scores of -40 and 40 are represented by z-scores of -1.4 and 1.5, respectively.

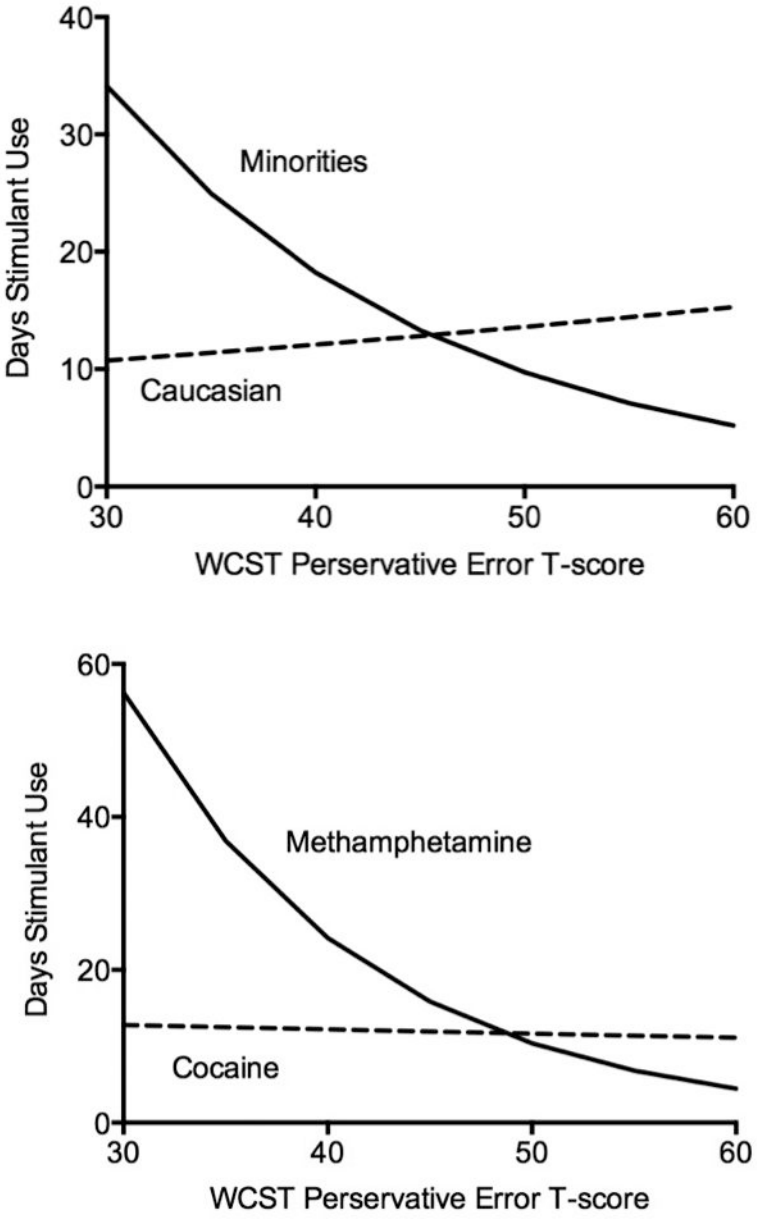

Fig 2.

WCST Perseverative Error Scores prediction of days of stimulant use for six months post-randomization with covariates race and drug of choice. Top panel: Race [Minority (n=93) and non-Hispanic Caucasian (n=66)]. Only Minority participants showed a relationship between WCST Perseverative Score and days of stimulant use post-randomization. Bottom panel: Primary drug dependence [methamphetamine (n=43) vs. cocaine (n=116)]. Only methamphetamine-dependent participants showed a relationship between WCST Perseverative Score and days of stimulant use post-randomization.

Table 1

Clinical Characteristics and Decision-making Performance (n=160)[a]

	All Subjects		Cocaine Dependent		Meth Dependent			
	n	Mean±SD	n	Mean±SD	n	Mean±SD	F Stat[b]	p-value
Age (years)	160	39.18±9.4	118	40.43±9.3	42	35.68±8.8	8.4	0.004
Education (years)	159	12.01±1.6	118	12.12±1.7	41	11.71±1.5	1.9	0.166
Age Onset Stim Use (years)	160	21.11±6.2	118	22.23±6.3	42	17.95±4.4	16.3	0.000
Years Stim Use	160	18.08±9.0	118	18.20±9.0	42	17.73±9.2	0.1	0.770
Stim Use 30 Days Prior to Baseline	160	4.86±6.4	118	4.56±5.7	42	5.71±8.1	1.0	0.318
Stim Use Days During Study (All)	160	11.51±25.2	118	10.86±24.8	42	13.31±26.4	0.3	0.590
Stim Use Days During Study (Users only)	87	21.16±31.1	59	21.73±31.7	28	19.96±30.3	0.1	0.806
IGT Total Net Score	158	-1.48±26.6	116	-1.60±26.7	42	-1.14±26.5	0.0	0.924
Block 1	158	-1.87±7.2	116	-1.45±7.6	42	-3.05±6.2	1.5	0.220
Block 2	158	0.72±7.2	116	1.03±7.6	42	-0.14±6.2	0.8	0.367
Block 3	158	0.24±8.5	116	0.0±8.6	42	0.81±8.4	0.3	0.615
Block 4	158	-0.20±8.8	116	-0.52±9.0	42	0.67±8.3	0.6	0.458
Block 5	158	-0.27±9.2	116	-0.57±9.3	42	0.57±9.1	0.5	0.494
WCST T-score	157	46.9±13.3	115	49.97±13.0	42	49.64±14.0	2.4	0.126

[a] Due to missing data, numbers in left column may not add up to 160 (total n).

[b] Comparison between cocaine and methamphetamine dependent subjects

Stim = stimulant; Meth – methamphetamine; IGT – Iowa Gambling Task; WCST – Wisconsin Card Sorting Tast (Perserverative Errors)

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Table 2

Decision-making Performance in Demographic and Clinical Groups[a]

	IGT[b]	T	P	WCST-Pers[c]	T	P
Gender		0.3	0.76		-0.5	0.59
Female (n=109)	-1.9 ±26.6			47.3±14.3		
Male (n=49;48)	-0.5±26.8			46.2±10.9		
Race		2.1	0.04		2.6	0.01
Non-Hispanic Caucasian (n=64)	4.1±29.6			50.5±14.2		
Minority[d], (n=93;92)	-5.2±23.9			44.7±12.1		
UDS Positive		0.4	0.69		0.5	0.62
UDS Positive (n=124;123)	-1.0±26.6			47.2±13.0		
UDS Negative (n=34)	-3.1±26.8			45.9±14.6		
Drug of Choice		-0.1	0.92		-1.4	0.15
Methamphetamine (n=42)	-1.1 ±26.5			49.6±14.0		
Cocaine (n=115;114)	-1.7±26.8			46.1±13.0		
Treatment Group		-0.3′	0.79		0.6	0.53
Modified 12-step (n=73;72)	-0.9±27.5			46.2±14.1		
TAU (n=85)	-2.0±25.9			47.6±12.7		
Relapsed (yes/no)		0.7	0.46		-0.5	0.64
Relapsed (n=85;84)	-2.9±24.3			47.4±13.9		
No relapse (n=73)	-0.2±29.1			46.4±12.7		

[a] Due to missing data, numbers in left column may not add up to 160 (total n).

[b] IGT – Iowa Gambling Task

[c] Wisconsin Card Sorting Task – Perseverative Errors (T-score)

[d] numbers in () refer to n for IGT and WCST, respectively

Table 3

Model Estimates for hypothetical subjects by level of IGT and WCST Perseverative Errors[a]

	Relapse (yes/no)[b]	Days of Stimulant Use [c]
IGT Net Total Score		
Low: IGT = -18 (25th percentile)	61.4%	15.1 days
Medium: IGT = -2 (50th percentile)	60.3%	17.1 days
High: IGT = 14 (75th percentile)	59.2%	19.5 days
WCST Perseverative Errors T-score		
Low: WCST = 37 (25th percentile)	57.8%	18.9 days
Medium: WCST = 47 (50th percentile)	59.7%	14.6 days
High: WCST = 55 (75th percentile)	61.1%	11.9 days

[a] All covariates were set at their mean values.

[b] No significant difference

[c] Days of use over six months