Neurocognitive Indicators Predict Results of an Informed-Consent Quiz Among Substance-Dependent Treatment Seekers Entering a Randomized Clinical Trial*

BRIAN D. KILUK, PH.D.,[†] CHARLA NICH, M.S., AND KATHLEEN M. CARROLL, PH.D.

Department of Psychiatry, Division of Substance Abuse, Yale University School of Medicine, 950 Campbell Avenue, 151D, West Haven, Connecticut 06516

ABSTRACT. Objective: This study sought to determine the extent to which key aspects of a clinical trial's protocol were recalled by participants entering a clinical trial for alcohol and illicit substance-use treatment after standard informed-consent procedures, as well as to explore the possible relationships between recall, neuropsychological functioning, and substance-use outcomes. **Method:** Before entering a randomized clinical trial testing the effectiveness of a computer-based training version of cognitive-behavioral therapy, 76 participants (55% male) meeting criteria for current substance dependence (according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) completed a 14-item true/false quiz that assessed their comprehension of

basic information provided in the consent form. **Results:** Only 15% of participants correctly answered all 14 consent quiz items. The percentage of correct recall was associated with measures of intelligence ($r = .29, p = .01$) and attention ($r = -.26, p = .04$). Quiz scores were also moderately associated with the amount of substance use during the treatment period ($r = -.26, p = .03$). **Conclusions:** These findings highlight the importance of formally evaluating research participants' understanding of the informed-consent process, and they call to attention the potential utility of a brief neuropsychological screening to identify individuals in need of enhanced consent procedures, particularly within vulnerable populations, such as substance users. (*J. Stud. Alcohol Drugs*, 71, 704-712, 2010)

RESEARCH PARTICIPANTS' UNDERSTANDING Of the varied information provided to them during the informed-consent process is of utmost importance to their exercise of autonomous decision making, so much so that it is a requirement of federal regulations (Basic HHS Policy for Protection of Human Research Subjects, 1991; Festinger et al., 2007). However, despite the centrality of informed consent in research, available evidence suggests that participants in clinical research often fail to understand or recall much of the information provided to them, including the study procedures, associated risks and benefits of participation, and their rights as a participant (Festinger et al., 2007). This lack of understanding during the informed-consent process is a particular concern for especially vulnerable populations, such as those with mental illness, developmental disability, or dementia; in those cases, additional steps are often needed to enhance the individual's comprehension and autonomy in decision making about research participation (Dresser, 1996).

Although not specifically included in the category of "especially vulnerable" populations, a number of crucial issues arise when obtaining informed consent from alcohol

and illicit substance users, both because of factors unique to the population and because of the various conditions that frequently co-occur with substance use (Gorelick et al., 1998; McCrady and Bux, 1999). Protocols involving treatment for alcohol and illicit substance use may involve multiple challenges to the informed-consent process, including current or recent intoxication of participants, as well as acute withdrawal symptoms, which can impair attention, cognition, or recall of important information (Munro et al., 2000; Saxton et al., 2000; Tapert and Brown, 2000). Comorbid psychopathology, cognitive impairment secondary to substance use, prior head trauma, poor nutrition, or limited educational attainment are just some of the comorbid conditions common among substance users that could affect their ability to comprehend the requirements of the research (McCrady and Bux, 1999). Additionally, impulsivity—considered to be both a contributor and consequence of substance use (Allen et al., 1998; De Wit, 2009; Moeller et al., 2002; Potenza, 2007)—may play a role in the thoroughness with which substance users review the research consent form and may affect the informed-consent process, particularly when financial incentives are involved.

There is substantial evidence that chronic use of alcohol and other psychoactive substances may be associated with significant cognitive impairment, and neuroimaging studies have revealed multiple cognitive changes and deficits (Bolla et al., 2003; Goldstein and Volkow, 2002; Volkow et al., 1994; Wang et al., 1992). Neuropsychological testing has

Received: October 6, 2009. Revision: February 3, 2010.

*This research was supported by National Institute on Drug Abuse grants R37-DA 015969, K05-DA00457, K05-DA00089, and P50-DA09241.

[†]Correspondence may be sent to: Brian D. Kiluk at the above address or via email at: brian.kiluk@yale.edu.

also demonstrated impairment among individuals with long-term histories of drug and alcohol dependence on measures of verbal problem solving, motor speed, information processing speed, and memory (Errico et al., 1991; Ersche and Sahakian, 2007; Ersche et al., 2006; Fals-Stewart et al., 1994; Grant, 1987). Overall, neuropsychological findings indicate that between one third and three fourths of individuals who chronically misuse alcohol or other psychoactive substances have some measurable cognitive impairment (Bates and Convit, 1999; Rourke and Loberg, 1996). These data raise questions regarding how well substance-misusing research participants can understand and recall information provided during the informed-consent process.

Although several studies have attempted to evaluate the informed-consent process within vulnerable populations in terms of assessing participants' understanding of information provided (Agre and Rapkin, 2003; Janofsky et al., 1992; Wirshing et al., 1998), very little research has focused on the comprehension of consent forms among alcohol and illicit substance users. Rounsaville and colleagues (2008) reported that only 55% of a sample of 130 young marijuana-dependent adults enrolling in a randomized treatment trial correctly answered four multiple-choice questions regarding basic elements of the trial, immediately following review of the consent form. Additionally, Festinger and colleagues (2007) reported that participants averaged 35% correct at 2 weeks following the informed-consent procedure, and no one responded correctly to 7 of the 17 questions, including items dealing with issues such as purpose of the study, benefits, risks, whom to contact with questions, and the circumstances in which participants could be removed from the study. Although scores from a neuropsychological test battery revealed the sample scored within the normal range, regression analyses indicated verbal intelligence, reading level, memory, and attention were significant predictors of consent recall (Festinger et al., 2007).

To expand on previous findings and further examine the various areas of neuropsychological and cognitive function that may affect the ability to understand and recall information during the informed-consent process among substance users, we used data from a randomized clinical trial evaluating the efficacy of a computer-based training version of cognitive-behavioral therapy (CBT4CBT) for substance-use disorders (Carroll et al., 2008). Data from this trial included a 14-item true/false consent quiz assessing participants' understanding of basic elements of the study, as well as various measures assessing neuropsychological and cognitive functioning associated with substance use. Based on prior research, we hypothesized that deficits in intelligence, memory, and attention would be associated with lower scores on the informed-consent quiz. Although there is little documented evidence of a relationship between impulsivity and consent recall, we hypothesized that higher scores on measures of impulsivity would be associated with lower scores on the in-

formed-consent quiz. Also, as a result of the dearth of studies on informed consent with substance users, we explored the relationship between participant's understanding of the study and their baseline characteristics (including history of substance use). Finally, in an attempt to replicate previous findings from our group suggesting a modest positive relationship between recall and treatment outcome (Rounsaville et al., 2008), we examined the relationship between consent recall and treatment outcome.

Method

Participants

As described in more detail in the main study report (Carroll et al., 2008), participants were 77 individuals seeking treatment for alcohol and/or illicit substance use at a community-based outpatient treatment center. These participants were drawn from a larger pool of 155 individuals screened, and 77 were determined to be eligible for participation in the randomized clinical trial. Individuals were excluded if (a) they had not used alcohol or illegal drugs within the past 28 days or failed to meet criteria for a current substance-dependence disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994), (b) had an untreated psychotic disorder that precluded outpatient treatment, or (c) were unlikely to be able to complete 8 weeks of outpatient treatment because of a planned move or pending court case from which incarceration was likely to be imminent.

Informed-consent procedure

During the intake/screening session, a member of the research staff provided potential participants with a detailed explanation of the study, its risks and benefits, and their rights and responsibilities before asking them to provide written informed consent. Informed-consent procedures consisted of a detailed review of the consent form by a research assistant while the potential participant followed along with his or her own copy. The five-page consent form was worded in the second person, written at a sixth grade reading level, and used various headings/subheadings to organize the sections and enhance readability. It included explanation of the various protocol treatments offered, the randomization process, the schedule of assessments and follow-up interviews, risks and benefits, as well as the amount of compensation for participation (following the guidelines provided by the Yale School of Medicine Human Investigations Committee). Participants were also given time to read the entire consent form silently and were offered the opportunity to ask any questions for clarification; however, participant questions

were not documented. This process took approximately 20–30 minutes, but participants were afforded as much time as needed for review of the consent form. Next, the participant was asked to complete a 14-item true/false quiz to assess his or her knowledge of some of the most basic, but crucial, aspects of the trial. After the quiz was completed, the research staff reviewed the participant's responses and clarified any question that the participant had not answered correctly, reviewing the relevant sections of the consent form until it was clear the participant understood the issues raised.

Treatments

All participants were offered standard treatment at the outpatient clinic, which consisted of weekly individual and group sessions of general drug counseling during the 8-week study period. Also, all participants met twice weekly with an independent clinical evaluator who collected urine and breath specimens, assessed recent substance use, and monitored other clinical symptoms. Participants were randomized to either standard treatment (i.e., treatment as usual) or standard treatment plus access to an interactive, multimedia version of CBT4CBT (for description, see Carroll et al., 2008). The CBT4CBT program consisted of six lessons based closely on a National Institute on Drug Abuse–published cognitive-behavioral therapy manual (Carroll, 1998) used in several previous randomized clinical trials with a range of substance-misusing populations (Carroll et al., 1994, 2004, 2006).

Measures

Participants completed the consent quiz, as well as the cognitive and neuropsychological measures used for these analyses at the baseline assessment. Current and lifetime diagnoses of substance use and psychiatric disorders were assessed using the Structured Clinical Interview for the DSM-IV (SCID; First et al., 1995), and the Addiction Severity Index (ASI; McLellan et al., 1992) was used to assess substance use and related problems. The Substance Use Calendar, similar to the Timeline Followback (Fals-Stewart et al., 2000; Hersh et al., 1999), was administered weekly during treatment to collect self-reports of drug and alcohol use during the 28-day period before randomization and throughout the 56-day treatment period. Urine toxicology screens and breath samples were obtained at every assessment visit to verify participant self-report of illegal drug use.

Informed-consent quiz. This was a 14-item quiz that instructed participants to respond “true” or “false” to a series of statements regarding information provided in the consent form (items are listed in Table 1). The instructions included a statement allowing participants to refer to the accompanying consent form to assist with their responses. The quiz was scored based on the percentage of items answered correctly during the initial administration. Three of the items on the quiz (#7, #8, #13) were used to identify “careless responding” by participants (e.g., not reading each question, responding all true or all false), in that they referred to highly

TABLE 1. Informed-consent quiz: Correct item response frequencies

Item (correct response)	<i>n</i>	%
1. Participation in this research study is voluntary (TRUE)	76	100%
2. I can withdraw from this study at any time without loss of services at this clinic or other negative consequences (TRUE)	75	98.7%
3. Any information I provide to the study staff can be shared with anyone who asks for it (FALSE)	73	96.1%
4. If I choose to participate, I will be assigned to either regular standard treatment at this clinic, or standard treatment plus computer learning (TRUE)	72	94.7%
5. I will be randomized (that is, selected by the luck of the draw) to one of 2 groups (TRUE)	65	85.5%
6. No matter what group I am assigned to, I will receive medication (FALSE)	73	96.1%
7. I will be assigned to treatment depending on my favorite color (FALSE)	74	97.4%
8. I will be asked to provide urine samples 45 times each week (FALSE)	74	97.4%
9. Even if I do not complete treatment at the clinic, the study staff will contact me up to 6 months for follow-up interviews (TRUE)	42	55.3%
10. I will receive \$35 for completing each follow-up interview (TRUE)	56	73.7%
11. The treatment part of the study will last for 1 week (FALSE)	70	92.1%
12. I may have the option of participating in an additional study of brain functioning using neuroimaging (TRUE)	43	57.3%
13. All study publications will mention me by name (FALSE)	65	85.5%
14. I may contact Dr. Carroll (the study's principal investigator), the Yale Human Investigations Committee, or other members of the research team if I have any questions about the study or my rights as a participant (TRUE)	68	89.5%

Note: *N* = 76 randomized participants completed the quiz.

unlikely procedures (e.g., the study would require 45 urine screenings per week).

Sustained attention: Conners Continuous Performance Test-II (CPT-II; Conners, 2004). The CPT-II is a standardized, computer-administered continuous performance test in which participants are instructed to respond as quickly as possible to a target stimulus and refrain from responding to a more rarely occurring nontarget stimulus. The CPT-II is a general measure of sustained attention and provides measures of response time (amount of time elapsed between presentation and response), and two types of error scores (omission and commission). All of the measures of the CPT-II are converted to *T* scores and percentiles. Inattention is indicated by a pattern of high numbers of omissions and long reaction times, whereas impulsivity is indicated by high numbers of commissions and short reaction times. Data from the original standardization sample provided evidence of adequate consistency in terms of split-half reliability (α ranging from .83 to .95) and satisfactory test-retest reliability (r ranging from .55 to .84) (Conners, 1994, 2004).

General intelligence: Shipley Institute of Living Scale (Shipley, 1940; Zachary, 1986). This is a self-administered test that consists of two subtests: a 40-item vocabulary test and a 20-item test assessing abstract thinking. Scores from the vocabulary and abstraction subtests are summed and converted into an estimate of full-scale IQ from the Wechsler Adult Intelligence Scale (WAIS) by taking into account the age of the respondent and referencing conversion tables presented in the literature (Zachary et al., 1985). The composite scores from the Shipley correlate well with other measures of intelligence (Zachary et al., 1985). The test was used in this study as a brief test of intelligence.

Risk taking: The Balloon Analogue Risk Task (BART; Lejuez et al., 2002). The BART is a computer-simulated assessment of risk-taking behavior that instructs participants to use the computer mouse to inflate a balloon on the computer screen to a desired level before it explodes while the participant simultaneously earns money for each inflation. The BART consists of 30 trials, and participants were informed that their objective was to obtain the largest amount of money possible while avoiding balloon explosions. Adjusted values were calculated for the average number of balloon pumps and explosions, indicating an index of adaptive and maladaptive risk-taking behavior, respectively. Research has found the BART to be correlated with measures of sensation seeking, impulsivity, and deficiencies in behavioral restraint, as well as with self-reported occurrence of addictive, health, and safety risk behaviors (Lejuez et al., 2002, 2003).

Impulsivity: Barratt Impulsiveness Scale-Version 11 (Patton et al., 1995). The Barratt Impulsiveness Scale-Version 11 is a 30-item, self-report questionnaire designed to measure levels of impulsiveness. All items are answered on a 4-point scale ("rarely/never, occasionally, often, or almost always/always") and are summed to create an overall score.

Factor analytic work identified three separate domains/subtraits of impulsivity, which are labeled motor impulsiveness (i.e., acting on spur of the moment and perseverance), nonplanning impulsiveness (i.e., inability to plan and think carefully), and attentional impulsiveness (i.e., inability to focus on the task at hand and cognitive instability) (Patton et al., 1995). The Barratt Impulsiveness Scale-Version 11 has demonstrated strong psychometric properties in both psychiatric and nonclinical populations (Hollander and Berlin, 2008; Mobini et al., 2006; Spinella, 2007).

Motivation/impulsivity: Behavioral inhibition system/behavioral approach system (BIS/BAS; Carver and White, 1994). The BIS/BAS is a 20-item self-report questionnaire designed to measure individual differences in sensitivity of Gray's (1990, 1991) proposed neurobiologically based motivational systems: the BAS and the BIS. The items are scored on a 4-point Likert scale, ranging from "strongly disagree" to "strongly agree," and consist of one BIS subscale and three BAS subscales: reward responsiveness, drive, and fun seeking. The BIS subscale is considered a measure of a person's behavioral motivations based on avoidance (inhibition), whereas the three BAS subscales are thought to measure a person's behavioral motivations toward something desired. All subscales have demonstrated adequate internal consistencies (Alloy et al., 2006; Carver and White, 1994), good test-retest reliability, construct validity (Leone et al., 2001), and satisfactory levels of convergent and discriminant validity (Carver and White, 1994).

Processing speed/memory: WAIS-III digit symbol-coding (Wechsler, 1997). The digit symbol-coding subtest of the WAIS-III requires that the participant copy symbols that are paired with numbers and is usually viewed as the ability to make associations quickly and accurately. Much of the research to date strongly suggests that speed is the prime determinant of digit symbol performance, with memory playing a subsidiary role (Joy et al., 2004). Digit symbol-coding is considered a reliable subtest with reliability coefficients at or above .81 at all of the 13 age groups in the standardization sample (Wechsler, 1997).

Analytic strategy

To determine participants' recognition of the information (and, on some level, basic comprehension of the information) provided in the consent form, we examined the frequency of correct responses to the 14 items on the informed-consent quiz and used correlations to assess its relationship with baseline variables. Analyses of variance were used to compare scores on the quiz among categorical baseline variables (e.g., gender, race, educational level). Finally, we evaluated the relationship of cognitive functioning to the amount of information correctly recalled during the consent process by examining correlations between the various cognitive/neuropsychological scores and the percentage of correct re-

sponses on the quiz, as well as examining results of multiple regressions controlling for potential covariates.

Results

Participant characteristics

Of the 158 potential participants consented and screened for eligibility, 77 were determined to be eligible and randomized to a treatment group. The mean age of the sample of 77 randomized participants was 41 ($SD = 10.3$). Fifty-five percent of the participants were male, and 45% identified themselves as African American, 12% as Hispanic, and 36% as White. Approximately 25% had not completed high school, 39% were high school graduates, 27% reported some college-level education, and 8% reported having a college degree. More than half (52%) of the participants had never been married, relatively few held a full-time job (16%), and most (62%) reported being currently unemployed for greater than 1 month.

Regarding substance use and comorbid psychopathology, on average, the participants reported they first used alcohol at age 14 ($SD = 4.2$) and first used an illicit drug at age 15 ($SD = 3.3$). The majority (58%) reported their primary drug of choice to be cocaine, whereas 18% reported alcohol, 16% reported opiates, and 8% reported marijuana to be their primary drug of choice. Participants reported using their primary drug a mean of 9 days ($SD = 8.6$) of the 28 days before the baseline assessment. Twenty-five percent met the criteria for a DSM-IV lifetime diagnosis of major depressive disorder (3% current), and 25% met the criteria for a lifetime anxiety disorder (6% current).

Quiz responses

Of the 77 participants who provided informed consent and were randomized, 76 completed the informed-consent quiz (1 missing because of unknown reasons). Of these, only 11 (14.7%) answered all 14 questions correctly, with a mean of 87.1% ($SD = 9.2$) correct. As shown in Table 1, all of the participants were able to correctly acknowledge that their participation in the study was voluntary, and almost all (98.7%) realized that they could withdraw at any time without negative consequences. The most frequent incorrect responses were to the statements regarding contact for follow-up interviews (55.3% correct) and information about additional neuroimaging study participation (57.3% correct).

Relationship with baseline variables

Performance on the informed-consent quiz was not significantly associated with any of the baseline substance-use variables assessed (which included quantity/frequency of alcohol and drug use during the 28 days before baseline

assessment) or the total number of years used alcohol and drugs during their lifetime. Quiz scores were significantly negatively correlated with the pretreatment ASI employment composite score ($r = -.26, p = .02$). Also, quiz scores did not significantly differ by gender, $F(1, 74) = 0.33, p = .56$; race, $F(2, 68) = 2.31, p = .11$; marital status, $F(5, 70) = 0.89, p = .49$; or employment status, $F(1, 74) = 0.41, p = .52$. There was a statistically significant difference in quiz scores according to education level, $F(2, 73) = 4.72, p = .01$, with the participants reporting they had done some post-high school, college-level work ($n = 27$) obtaining a mean score of 90.7% ($SD = 6.8$), whereas high school graduates ($n = 30$) scored 86.7% correct ($SD = 9.1$), and those with less than a high school degree ($n = 19$) obtained lower scores of 82.7% ($SD = 10.4$). To account for co-linearity of the baseline variables, we ran a regression with both educational level and ASI employment composite scores as predictors of the consent quiz scores. Results demonstrated that educational level remained a significant predictor of the consent quiz scores ($\beta = -.26, p = .02$), although the ASI composite did not ($\beta = -.17, p = .13$).

Quiz scores and neuropsychological functioning

Overall, this sample scored similar to other substance-misusing samples for the majority of neuropsychological measures (Grant et al., 2000; Krishnan-Sinha et al., 2007; Spinella, 2007). As shown in Table 2, quiz scores were significantly negatively correlated with the omissions T score from the CPT-II ($r = -.26, p = .04$) and were positively correlated with the estimated full-scale WAIS IQ score converted from the Shipley Institute of Living Scale ($r = .29, p = .01$). No other scores from the cognitive or neuropsychological assessments were associated with consent form quiz performance; however, two of the subscales from the BIS/BAS (the BAS reward responsiveness and the BAS fun-seeking scales) had correlation values that approached significance levels ($r = -.21, p = .07$, for both scales). Greater amounts of missing data were present for some of the relationships because several neuropsychological tests were added to the baseline battery after the start of the randomized clinical trial. To account for co-linearity of the neuropsychological functioning variables, we ran a regression with both CPT-II omissions T score and the estimated full-scale WAIS IQ score as predictors of consent quiz scores. Although the two scores were not significantly correlated ($r = -.19, p = .08$), the estimated full-scale WAIS IQ was a stronger predictor of consent quiz scores ($\beta = .24, p = .06$) than the CPT-II omissions T scores ($\beta = -.22, p = .09$).

Results of the correlation between the various neuropsychological/cognitive indicators and the percentage of the "careless responding" items answered incorrectly are presented in Table 3. The percentage of incorrect responses were significantly correlated with CPT-II commissions T

TABLE 2. Relationship between informed-consent quiz and cognitive functioning

Cognitive/neuropsychological test	Total quiz score (% correct)	
	<i>r</i>	<i>n</i>
Conners Continuous Performance Test–II		
Omissions <i>T</i> score	-.26*	61
Commissions <i>T</i> score	-.01	61
Reaction Time <i>T</i> score	-.18	61
Shipley Institute of Living Scale		
Estimated WAIS full-scale IQ	.29*	75
Balloon Analogue Risk Task		
Adjusted number of pumps	.01	60
Adjusted number of explosions	.05	60
Barratt Impulsiveness Scale–Version 11		
Attentional impulsiveness	.02	68
Motor impulsiveness	-.02	68
Nonplanning impulsiveness	.16	68
BIS/BAS		
BIS subscale	.05	75
BAS reward responsiveness	-.21	75
BAS drive	-.08	75
BAS fun seeking	-.21	75
WAIS-III digit symbol-coding		
Scaled score	.14	59

Notes: WAIS = Wechsler Adult Intelligence Scale; BIS/BAS = Behavioral Inhibition System/Behavioral Approach System.

* $p < .05$.

scores ($r = .26$, $p = .04$) and were negatively correlated with BIS subscale scores ($r = -.26$, $p = .02$). No other significant relationships were observed between scores on the neuropsychological/cognitive tests and the amount of “careless responding” items answered incorrectly. To account for collinearity of the neuropsychological functioning variables, we ran a regression with both commissions’ *T* scores and BIS subscale scores as predictors of “careless responding” scores. The two neuropsychological functioning variables were not significantly correlated ($r = -.09$, $p = .24$). CPT-II commissions’ *T* scores remained a stronger predictor of the “careless responding” section of the consent quiz scores ($\beta = .24$, $p = .06$) than the BIS subscale score ($\beta = -.15$, $p = .25$).

Quiz scores and substance-use outcomes/treatment retention

Simple correlations revealed that performance on the informed-consent quiz was not significantly associated with any of the primary substance-use outcome variables, including duration of longest continuous period of abstinence (urine confirmed) and the proportion of urines submitted during treatment that were positive for any drug. However, after removing the three “careless responding items,” correct scores on the 11 remaining quiz items were negatively correlated with the proportion of urines submitted during treatment that were positive for any drug ($r = -.26$, $p = .03$, $n = 71$). Also, variables representing the participants’ retention in treatment (e.g., number of individual and group sessions,

TABLE 3. Relationship between cognitive functioning and “careless responding”

Cognitive/neuropsychological test	Careless responding item score (% incorrect)	
	<i>r</i>	<i>n</i>
Conners Continuous Performance Test–II (CPT-II)		
Omissions <i>T</i> score	.01	61
Commissions <i>T</i> score	.26*	61
Reaction Time <i>T</i> score	-.14	61
Shipley Institute of Living Scale		
Estimated WAIS full-scale IQ	-.16	75
Balloon Analogue Risk Task		
Adjusted number of pumps	-.07	60
Adjusted number of explosions	-.10	60
Barratt Impulsiveness Scale–Version 11		
Attentional impulsiveness	-.09	68
Motor impulsiveness	-.07	68
Nonplanning impulsiveness	.19	68
BIS/BAS		
BIS subscale	-.26*	75
BAS reward responsiveness	-.10	75
BAS drive	-.02	75
BAS fun seeking	-.21	75
WAIS-III digit symbol-coding		
Scaled score	-.15	59

Notes: WAIS = Wechsler Adult Intelligence Scale; BIS/BAS = Behavioral Inhibition System/Behavioral Approach System.

* $p < .05$.

number of cognitive-behavioral therapy modules completed, number of homeworks completed) were not significantly associated with the performance on the consent form quiz.

Discussion

This investigation sought to examine substance users’ ability to comprehend and recognize information provided during the informed-consent process when entering a randomized clinical trial, and to identify specific cognitive and neuropsychological factors that predicted their ability to recall such information. Results indicated that, although participants recalled 87% of the information correctly on average, less than 15% of participants correctly responded to all 14 items testing their ability to recall basic consent form information, despite extensive review of information from research staff and opportunity to refer to the consent form when responding to items. In terms of cognitive and neuropsychological indicators, we found (a) those with higher scores on a brief measure of intelligence performed better on the quiz than those with lower scores, (b) those with higher scores on a measure of inattention performed worse on the quiz than those with lower scores, and (c) those with scores indicating higher impulsivity and low inhibition were more likely to respond incorrectly to odd/unusual quiz items. Also, we found that, after omitting items intended to detect careless responding, performance on the informed-consent quiz was associated with the proportion of urines submitted posi-

tive for any drug during the treatment period. This intriguing result was consistent with a prior study by Rounsaville and colleagues (2008), who found quiz scores moderately associated with substance-use outcomes.

This study thus adds to the small, but important, literature on the use of systematic assessment to evaluate participant comprehension of consent forms and, hence, to provide truly informed consent (McCrary and Bux, 1999). The average percentage of information correctly recognized here is consistent with Fureman et al. (1997), who reported a relatively high level of understanding (81%) among injection drug users. However, it was striking that such few participants (<15%) responded correctly to all quiz items immediately following a detailed review of the protocol and consent form. Although the items on which participants did most poorly (items 9 and 12) could be considered less directly related to the clinical trial procedures, participants were afforded the opportunity to refer back to the consent form for assistance with their answers. Others have reported poor rates of recall of consent information among research participants (Daugherty et al., 2000; Miller et al., 1994), as well as among substance users (Festinger et al., 2007; Rounsaville et al., 2008), highlighting the need for greater attention paid to the evaluation of participants' understanding of study procedures and their rights, particularly with vulnerable populations.

Our findings on the association between intelligence, attention, and amount of consent information correctly recalled among substance users are consistent with previous research (Festinger et al., 2007), and combined with the extensive literature regarding cognitive and neuropsychological impairments among those with a history of chronic substance use, certainly have implications for the development of enhanced informed-consent procedures for such populations. Although a comprehensive neuropsychological screening battery during the preconsent process would be impractical (Fals-Stewart et al., 1994), the use of a thorough quiz may help to identify individuals who need additional or enhanced consent procedures. Examples for enhancing the consent process might include improving the readability of a consent form by simplifying the writing style, modifying the format, reducing length, or even using computer or video technology. Although extensive research has demonstrated benefits of improving consent form readability (Agre and Rapkin, 2003; Coyne et al., 2003; Dresden and Levitt, 2001), a systematic review (Flory and Emanuel, 2004) reported limited success through the use of multimedia and enhanced consent forms, but found an extended discussion between a study team member and research participant to be most promising as a way to improve understanding. Results of the current study, including a consent quiz, may provide useful information for identifying those who do not fully understand the many aspects of the research study and may facilitate an extended discussion of the procedures.

The evidence provided here to suggest that the amount

of information recalled during the consent process may be associated with substance-use outcomes adds to the importance of identifying participants who cannot correctly recall basic study information. This preliminary finding, consistent with prior evidence reported by Rounsaville and colleagues (2008), may suggest an important relationship between the cognitive processes needed for recognition memory and the effectiveness of alcohol and/or illicit substance-use treatments. However, this finding should be interpreted with caution because the current study required the exclusion of certain "careless responding" items to achieve a relationship between the two variables.

Despite the relationships found in this study between attention, general intelligence, and the amount of recall on a consent quiz, there were also several null findings between quiz scores and neuropsychological indicators. The lack of relationship between quiz scores and impulsivity measures may indicate that impulsivity does not affect participants' ability to recall information during the informed-consent process, or it may be the result of the limitations of the true/false format as a valid measure of recall and/or comprehension. However, a relationship was suggested between subscales measuring impulsivity and the quiz items designed to indicate "careless responding" on the part of the participant. Those whose scores indicated impulsiveness were more likely to respond incorrectly to the obvious quiz items, suggesting either they may not have fully read/understood the consent form or they impulsively responded to the quiz items testing their recognition of information. Although there is ample evidence to suggest impulsivity affects basic cognitive processes (Dickman, 1993), especially in addiction (Potenza, 2007), this is—to our knowledge—the first study to test a relationship between impulsivity and recall of information provided during the informed-consent process.

The principal limitation of this study is the correlational nature of the findings, opening the possibility that other factors may have accounted for the apparent relationships between quiz score, neuropsychological measures, and substance-use outcomes, such as motivation, interest, or even reading level, which were not measured in this study. Additionally, because of the numerous correlations calculated, a more conservative α level of .01 may have been warranted. Nevertheless, very few research studies with substance users have examined participants' ability to understand informed consent, and our results are consistent with evidence of a relationship between informed consent and neuropsychological functioning (Festinger et al., 2007), as well as with substance-use outcomes (Rounsaville et al., 2008). Another limitation of the findings is that the consent-form quiz was specific to this particular study and, thus, has no demonstrated psychometric properties. Although the quiz items were taken directly from the consent form used in this study, lending it reasonable face validity, development of the quiz did not undergo any rigorous tests of reliability or validity

typically conducted on an assessment instrument. Similarly, the use of a true/false format may have overestimated the extent to which participants fully understood the study information and was more likely a measure reflecting recognition rather than true recall of information because of the forced choice structure. The quiz did, however, include items covering the most basic aspects of the study; also, the opportunity for participants to ask questions and for the research staff to review participants' incorrect responses suggests that it could be considered a reasonable assessment of participants' comprehension of the informed-consent process.

This study is one of the first to examine and demonstrate a relationship between neuropsychological measures and the amount of information recalled during the consent process, as well as a relationship between a consent form quiz and substance-use outcomes. Despite the limitations, these findings call attention to the need for increased vigilance during the informed-consent procedures with substance users and emphasize the potential utility of including an assessment of understanding, much like the quiz presented here. Also, future research might examine the utility of a brief neuropsychological prescreening, as compared with a simple consent form quiz, to identify individuals in need of additional resources during the informed-consent process, particularly within vulnerable populations such as substance users.

References

- Agre, P., & Rapkin, B. (2003). Improving informed consent: A comparison of four consent tools. *IRB: Ethics and Human Research*, 25, 1-7.
- Allen, T., Moeller, F. G., Rhoades, H. M., & Cherek, D. R. (1998). Impulsivity and history of drug dependence. *Drug and Alcohol Dependence*, 50, 137-145.
- Alloy, L. B., Abramson, L. Y., Walshaw, P. D., Cogswell, A., Smith, J. M., Neeren, A. M., . . . Nusslock, R. (2006). Behavioral approach system (BAS) sensitivity and bipolar spectrum disorders: A retrospective and concurrent behavioral high-risk design. *Motivation and Emotion*, 30, 143-155.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.
- Basic HHS Policy for Protection of Human Research Subjects, 45 C.F.R. Subtitle A § 46.101-46.124 (1991).
- Bates, M. E., & Convit, A. (1999). Neuropsychology and neuroimaging of alcohol and drug abuse. In A. Calev (Ed.), *Neuropsychological functions in psychiatric disorders* (pp. 342-375). Washington, DC: American Psychiatric Press.
- Bolla, K. L., Eldreth, D. A., London, E. D., Kiehl, K. A., Mouratidis, M., Contoreggi, C., . . . Ernst, M. (2003). Orbitofrontal cortex dysfunction in abstinent cocaine users performing a decision-making task. *Neuroimage*, 19, 1085-1094.
- Carroll, K. M. (1998). *A cognitive-behavioral approach: Treating cocaine addiction*. National Institute on Drug Abuse Therapy Manuals for Drug Abusers: Manual 1, NIH Publication No. 98-4308. Rockville, MD: National Institute on Drug Abuse.
- Carroll, K. M., Ball, S., Martino, S., Nich, C., Babuscio, T., Nuro, K., . . . Rounsaville, B. J. (2008). Computer-assisted delivery of cognitive-behavioral therapy for addiction: A randomized clinical trial of CBT4CBT. *American Journal of Psychiatry*, 165, 881-888.
- Carroll, K. M., Easton, C. J., Nich, C., Hunkele, K. A., Neavins, T. M., Sinha, R., . . . Rounsaville, B. J. (2006). The use of contingency management and motivational/skills-building therapy to treat young adults with marijuana dependence. *Journal of Consulting and Clinical Psychology*, 74, 955-966.
- Carroll, K. M., Fenton, L. R., Ball, S. A., Nich, C., Frankforter, T. L., Shi, J., & Rounsaville, B. J. (2004). Efficacy of disulfiram and cognitive-behavioral therapy in cocaine-dependent outpatients: A randomized placebo controlled trial. *Archives of General Psychiatry*, 64, 264-272.
- Carroll, K. M., Rounsaville, B. J., Gordon, L. T., Nich, C., Jatlow, P. M., Bisighini, R. M., & Gawin, F. H. (1994). Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. *Archives of General Psychiatry*, 51, 177-187.
- Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology*, 67, 319-333.
- Conners, C. K. (1994). *Conners continuous performance test computer program 3.0: User's Manual*. Toronto, Canada: Multi-Health Systems.
- Conners, C. K. (2004). *The Conners continuous performance test II*. North Tonawanda, NY: Multi-Health Systems.
- Coyne, C. A., Xu, R., Raich, P., Plomer, K., Dignan, M., Wenzel, L. B., . . . Cella, D. (2003). Randomized, controlled trial of an easy-to-read informed consent statement for clinical trial participation: A study of the Eastern Cooperative Oncology Group. *Journal of Clinical Oncology*, 21, 836-842.
- Daugherty, C. K., Banik, D. M., Janish, L., & Ratain, M. J. (2000). Quantitative analysis of ethical issues in phase I trials: A survey interview of 144 advanced cancer patients. *IRB: Ethics and Human Research*, 22, 6-14.
- De Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: A review of underlying processes. *Addiction Biology*, 14, 22-31.
- Dickman, S. J. (1993). Impulsivity and information processing. In W. G. McCown, J. L. Johnson, & M. B. Shure (Eds.), *The impulsive client: Theory, research, and treatment* (pp. 151-184). Washington, DC: American Psychological Association.
- Dresden, G. M., & Levitt, M. A. (2001). Modifying a standard industry clinical trial consent form improves patient information retention as part of the informed consent process. *Academic Emergency Medicine*, 8, 246-252.
- Dresser, R. (1996). Mentally disabled research subjects: The enduring policy issues. *Journal of the American Medical Association*, 276, 67-72.
- Errico, A. L., Parsons, O. A., & King, A. C. (1991). Assessment of verbosequential and visuospatial cognitive abilities in chronic alcoholics. *Psychological Assessment*, 3, 693-696.
- Ersche, K. D., Clark, L., London, M., Robbins, T., & Sahakian, B. J. (2006). Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology*, 31, 1036-1047.
- Ersche, K. D., & Sahakian, B. J. (2007). The neuropsychology of amphetamine and opiate dependence: Implications for treatment. *Neuropsychology Review*, 17, 317-336.
- Fals-Stewart, W., O'Farrell, T. J., Freitas, T. T., McFarlin, S. K., & Rutigliano, P. (2000). The timeline followback reports of psychoactive substance use by drug-abusing patients: Psychometric properties. *Journal of Consulting and Clinical Psychology*, 68, 134-144.
- Fals-Stewart, W., Schafer, J., Lucente, S., Rustine, T., & Brown, L. (1994). Neurobehavioral consequences of prolonged alcohol and substance abuse: A review of findings and treatment implications. *Clinical Psychology Review*, 14, 755-778.
- Festinger, D. S., Ratanadilok, K., Marlowe, D. B., Dugosh, K. L., Patapis, N. S., & DeMatteo, D. S. (2007). Neuropsychological functioning and recall of research consent information among drug court clients. *Ethics and Behavior*, 17, 163-186.
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1995). *Structured clinical interview for DSM-IV axis I disorders - patient edition*

- (SCID-I/P, version 2.0). New York: Biometrics Research Department, New York State Psychiatric Institute.
- Flory, J., & Emanuel, E. (2004). Interventions to improve research participants' understanding in informed consent for research. *Journal of the American Medical Association*, 292, 1593-1601.
- Fureman, I., Meyers, K., McLellan, A. T., Metzger, D., & Woody, G. (1997). Evaluation of a video-supplement to informed consent: Injection drug users and preventative HIV vaccine efficacy trials. *AIDS Education and Prevention*, 9, 330-341.
- Goldstein, R., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry*, 159, 1642-1652.
- Gorelick, D. A., Pickens, R., & Bonkovsky, F. (1998). Clinical research in substance abuse: Human subjects issues. In H. A. Pincus, J. A. Lieberman, & S. Ferris (Eds.), *Informed consent: A resource manual for investigators* (pp. 177-218). Washington, DC: American Psychiatric Press.
- Grant, I. (1987). Alcohol and the brain: Neuropsychological correlates. *Journal of Consulting and Clinical Psychology*, 55, 310-324.
- Grant, S., Contoreggi, C., & London, E. D. (2000). Drug abusers show impaired performance in a laboratory test of decision making. *Neuropsychologia*, 38, 1180-1187.
- Gray, J. A. (1990). Brain systems that mediate both emotion and cognition. *Cognition and Emotion*, 4, 269-288.
- Gray, J. A. (1991). Neural systems, emotion and personality. In J. Madden (Ed.), *Neurobiology of learning, emotion and affect* (pp. 273-306). New York: Raven Press.
- Hersh, D., Mulgrew, C. L., Van Kirk, J., & Kranzler, H. R. (1999). The validity of self-reported cocaine use in two groups of cocaine abusers. *Journal of Consulting and Clinical Psychology*, 67, 37-42.
- Hollander, E., & Berlin, H. A. (2008). Impulse-control disorder measures. In A. J. Rush, M. B. First, & D. Blacker (Eds.), *Handbook of psychiatric measures* (2nd ed., pp. 667-686). Arlington, VA: American Psychiatric Publishing.
- Janofsky, J. S., McCarthy, R. J., & Folstein, M. F. (1992). The Hopkins Competency Assessment Test: A brief method for evaluating patient's capacity to give informed consent. *Hospital and Community Psychiatry*, 43, 132-136.
- Joy, S., Kaplan, E., & Fein, D. (2004). Speed and memory in the WAIS-III Digit Symbol—Coding subtest across the adult lifespan. *Archives of Clinical Neuropsychology*, 19, 759-767.
- Krishnan-Sarin, S., Reynolds, B., Duhig, A. M., Smith, A., Liss, T., McFetridge, A., . . . Potenza, M. (2007). Behavioral impulsivity predicts treatment outcome in a smoking cessation program for adolescent smokers. *Drug and Alcohol Dependence*, 88, 79-82.
- Lejuez, C. W., Aklin, W. M., Zvolensky, M. J., & Pedulla, C. M. (2003). Evaluation of the Balloon Analogue Risk Task (BART) as a predictor of adolescent real-world risk-taking behaviors. *Journal of Adolescence*, 26, 475-479.
- Lejuez, C. W., Read, J. P., Kahler, C. W., Richards, J. B., Ramsey, S. E., Stuart, G. L., . . . Brown, R. A. (2002). Evaluation of a behavioral measure of risk taking: The Balloon Analogue Risk Task (BART). *Journal of Experimental Psychology: Applied*, 8, 75-84.
- Leone, L., Perugini, M., Bagozzi, R. P., Pierro, A., & Mannetti, L. (2001). Construct validity and generalizability of the Carver-White Behavioral Inhibition System/Behavioral Activation System Scales. *European Journal of Personality*, 15, 373-390.
- McCrary, B. S., & Bux, D. A. (1999). Ethical issues in informed consent with substance abusers. *Journal of Consulting and Clinical Psychology*, 67, 186-193.
- McLellan, A. T., Kushner, H., Metzger, D., Peters, R., Smith, I., Grissom, G., . . . Argeriou, M. (1992). The fifth edition of the Addiction Severity Index. *Journal of Substance Abuse Treatment*, 9, 199-213.
- Miller, C., Searight, H. R., Grable, D., Schwartz, R., Sowell, C., & Barbarash, R. A. (1994). Comprehension and recall of the informational content of the informed consent document: An evaluation of 168 patients in a controlled clinical trial. *Journal of Clinical Research on Drug Development*, 8, 237-248.
- Mobini, S., Pearce, M., & Grant, A. (2006). The relationship between cognitive distortion, impulsivity, and sensation-seeking in a non-clinical population sample. *Personality and Individual Differences*, 40, 1153-1163.
- Moeller, F. G., Dougherty, D. M., Barratt, E. S., Oderinde, V., Mathias, C. W., Harper, R. A., & Swann, A. C. (2002). Increased impulsivity in cocaine dependent subjects independent of antisocial personality disorder and aggression. *Drug and Alcohol Dependence*, 68, 105-111.
- Munro, C. A., Saxton, J., & Butters, M. A. (2000). The neuropsychological consequences of abstinence among older alcoholics: A cross-sectional study. *Alcoholism: Clinical and Experimental Research*, 24, 1510-1516.
- Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt Impulsiveness Scale. *Journal of Clinical Psychology*, 51, 768-774.
- Potenza, M. N. (2007). To do or not to do: The complexities of addiction, motivation, self-control and impulsivity. *American Journal of Psychiatry*, 164, 4-6.
- Rounsaville, D. B., Hunkele, K., Easton, E. J., Nich, C., & Carroll, K. M. (2008). Making consent more informed: Preliminary results from a multiple-choice test among probation-referred marijuana users entering a randomized clinical trial. *Journal of the American Academy of Psychiatry and the Law*, 36, 1-6.
- Rourke, S. B., & Loberg, T. (1996). The neurobehavioral correlates of alcoholism. In I. Grant & K. M. Adams (Eds.), *Neuropsychological assessment of neuropsychiatric disorders* (pp. 423-485). New York: Oxford University Press.
- Saxton, J., Munro, C. A., Butters, M. A., Schramke, C., & McNeil, M. A. (2000). Alcohol, dementia, and Alzheimer's disease: Comparison of neuropsychological profiles. *Journal of Geriatric Psychiatry and Neurology*, 13, 141-149.
- Shipley, W. C. (1940). A self-administering scale for measuring impairment and deterioration. *Journal of Psychology: Interdisciplinary and Applied*, 9, 371-377.
- Spinella, M. (2007). Normative data and short form of the Barratt Impulsiveness Scale. *International Journal of Neuroscience*, 117, 359-368.
- Tapert, S. F., & Brown, S. A. (2000). Substance dependence, family history of alcohol dependence and neuropsychological functioning in adolescence. *Addiction*, 95, 1043-1053.
- Volkow, N. D., Wang, G. J., Hitzemann, R., Fowler, J., Wolf, A., & Overall, J. (1994). Recovery of brain glucose metabolism in detoxified alcoholics. *American Journal of Psychiatry*, 151, 178-183.
- Wang, G., Volkow, N., Hitzman, R., Oster, Z., Roque, C., & Cestaro, V. (1992). Brain imaging of an alcoholic with MRI, SPECT, and PET. *American Journal of Physiologic Imaging*, 7, 194-198.
- Wechsler, D. (1997). *Wechsler Adult Intelligence Scale—Third Edition (WAIS-III)*. San Antonio, TX: Psychological Corporation.
- Wirshing, D. A., Wirshing, W. C., Marder, S. R., Liberman, R. P., & Mintz, J. (1998). Informed consent: Assessment of comprehension. *American Journal of Psychiatry*, 155, 1508-1511.
- Zachary, R. A. (1986). *Shipley Institute of Living Scale: Revised Manual*. Los Angeles, CA: Western Psychological Services.
- Zachary, R. A., Paulson, M. J., & Gorsuch, R. L. (1985). Estimating WAIS IQ from the Shipley Institute of Living Scale using continuously adjusted age norms. *Journal of Clinical Psychology*, 41, 820-831.