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Impulsivity in abstinent alcohol-dependent patients: relation to control subjects and type 1–/type 2–like traits

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Abstract

Extensive literature has linked behavior control problems in childhood to risk for alcoholism, but impulsivity in alcohol-dependent adults has not been well characterized. Using a variety of laboratory measures of impulsivity, we assessed whether detoxified alcohol-dependent patients [(ADP); $n = 130$] were more impulsive than control subjects [(CS); $n = 41$]. In comparison with CS, ADP demonstrated (1) increased rates of commission errors, but not omission errors, in a continuous performance test, (2) a more severe devaluation of delayed reward, (3) increased rates of risky responses in a new risk-taking paradigm, and (4) higher psychometric scores of impulsivity and aggression. Across all subjects, aggressiveness correlated significantly with severity of delay discounting. A post hoc analysis of data obtained for male ADP indicated that, in comparison with patients with late onset of problem drinking and no problem-drinking parent, those ADP with earlier age of problem drinking and who reported a problem-drinking father (type 2–like alcohol dependence) demonstrated faster response latencies and more responses to non-target stimuli (commission errors) in the continuous performance test, as well as higher psychometric aggression. In contrast, these subtypes of male ADP did not differ in delay discounting and risk taking. These findings collectively indicate that, in comparison with CS, ADP are more impulsive in several dimensions, with elevated impulsivity in a working memory task as well as aggressivity characteristic of alcohol-dependent men with type 2–like features.

Keywords: Alcoholism; Impulsivity; Aggression; Behavior; Continuous performance test; Typology; Risk taking

1. Analysis 1

1.1. Introduction

Understanding the individual neurobehavioral differences underlying vulnerability to alcohol dependence is a fundamental research question, as emphasized by Enoch Gordis (2000, p. 269): "Even in the face of a growing melding of disciplines, the importance of behavior in disease etiology cannot be overemphasized." Although attempts to pinpoint a specific alcoholic "personality" have not been very successful, results of psychosocial research on alcoholism have indicated that hyperactivity and antisocial behavior in childhood are predictive of alcohol dependence [reviewed in Mulder (2002)]. The link between generalized impaired behavior control and alcohol dependence is suggested by epidemiologic associations between alcohol dependence and other formal psychiatric syndromes characterized by poor behavior control, such as attention deficit hyperactivity disorder, conduct disorder, and antisocial personality disorder (Clark et al., 1997; Lewis & Bucholz, 1991; Rohde et al., 1996). Results of longitudinal assessments also link childhood behavior problems to increased incidence of problem drinking at follow-up [see, for example, Myers et al. (1995, 1998)]. Most notably, symptoms of conduct disorder manifested before alcohol abuse are predictive of (1) rates of drinking in later adolescence (Clark et al., 1998; Duncan et al., 1997), (2) incidence of alcohol dependence in adolescence and young adulthood (Yoshino et al., 2000), and (3) increased likelihood of relapse to drinking behavior after rehabilitation therapy (Brown et al., 1996). In addition, results of large-scale genetic epidemiologic research support the notion of a common neurobiologic factor underlying both behavior control problems and alcohol dependence (Slutske et al., 1998).

In several reports collectively, investigators (Ciesielski et al., 1995; Giancola & Moss, 1998) suggest that alcoholism-prone individuals are characterized by frontal lobe impairment—specifically deficits in executive cognitive functioning

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(ECF), which includes response inhibition, attention, working memory, strategy, and assessment of behavior consequences. Findings of electrophysiologic studies indicate that behaviors characteristic of impaired ECF may be evident in alcohol-dependent individuals. For example, blunted anterior brain P300 event-related potential responses to novel stimuli have been linked to alcohol dependence and other problem behavior (Bauer & Hesselbrock, 1999; Costa et al., 2000), and they potentially represent a heritable underpinning of alcoholism vulnerability (Begleiter et al., 1998). Moreover, in nondependent young male drinkers, both decreased resting left frontal lobe slow alpha electroencephalographic activity and poor frontal lobe–dependent neuropsychologic task performance accounted for significant variance in age at first alcohol experimentation and frequency of getting drunk (Deckel et al., 1995). Results of other investigations have revealed substandard performance in frontal lobe tasks in nondependent adolescent (Ozkaragoz & Noble, 1995) and adult (Giancola et al., 1993) subjects with a family history of alcoholism.

Because ECF decrements are related to alcoholism risk, it follows that impulsivity, as an aspect of ECF, would be elevated in individuals with a full-blown alcohol dependence outcome, owing to not only premorbid characteristics but also chronic alcohol neurotoxicity. Evaluation of imaging data indicates that frontal lobe atrophy (Pfefferbaum et al., 1998) and whole brain atrophy (Bjork et al., 2003) are related to alcohol dependence chronicity itself, and interpretation of functional magnetic resonance imaging data indicates that suppression of prepotent motor responses recruits several regions of frontal lobe neocortex (Garavan et al., 1999; Horn et al., 2003). It is not surprising that subjects with extensive histories of alcohol dependence show impairment on neuropsychologic tasks (Beatty et al., 2000; Nicolas et al., 1997). Further, among alcoholic patients performing a go/no-go task, spatial separation between centroids of p300 event-related potential maxima during go (posterior) versus no-go (anterior) trials correlated inversely with psychometric novelty-seeking and impulsivity scores (Fallgatter et al., 1998), supporting the suggestion of a blunted frontal lobe–generated event-related potential during response suppression in the more impulsive subjects.

In the primary analysis of the current study, we compared the behavior of alcohol-dependent patients (ADP) and control subjects (CS) on different types of impulsivity measures because impulsivity is a multifaceted trait (Evenden, 1999). First, one element of impulsivity is acting without thinking, which may be operationalized as poor behavior inhibition in rapid stimulus-discrimination tasks such as the continuous performance test (CPT). Commission errors in the CPT (responses to non-target stimuli) have been interpreted as a measure of impulsivity, and they have been elevated in children with disruptive behavior disorders (Dougherty et al., 2003a; Newcorn et al., 2001), as well as in men with histories of conduct disorder (Dougherty et al., 2000a). In comparison with findings for other adolescent patients, commission errors were increased in adolescent psychiatric patients with alcohol use disorder (Pogge et al., 1992). We tested subjects with the immediate memory task (IMT)/delayed memory task (DMT), a challenging version of the CPT designed for use with adults and adolescents. We hypothesized that ADP would show increased commission and omission errors on both IMT and DMT subtasks.

A second operational definition of impulsivity is preference for a small immediate reward over a larger delayed reward (Ainslie, 1975). We assessed the degree to which subjects would devalue a monetary reward the longer the delay to its presentation. Drug experimentation itself is motivated by immediate, salient reward, which is unchecked by consideration of long-term (less salient) aversive consequences. Laboratory paradigms have shown that, in comparison with CS, individuals with alcohol dependence (Vuchinich & Simpson, 1998) and subjects with other substance dependencies (Petry & Casarella, 1999) devalue delayed rewards more severely, supporting the idea of a generalizable preference for immediate gratification in individuals with histories of substance dependence. A hyperbolic function (Mazur, 1987) has been shown to fit the observed rate at which human beings and other mammals discount delayed reward, typically explaining more than 85% of the variance in choice behavior [reviewed in Bickel and Marsch (2001)]. In comparison with control groups, persons dependent on alcohol (Petry, 2001; Vuchinich & Simpson, 1998), nicotine (Mitchell, 1999), and other substances (Petry & Casarella, 1999) have demonstrated an elevated preference for small immediate rewards. We hypothesized that, in accordance with previous findings, ADP, in comparison with CS, would show higher delay discounting and would assign lower subjective worth of a standard reward ($10) at different delays to presentation.

Finally, we assessed risk-taking behavior. Laboratory paradigms of risk taking have also shown that, in comparison with CS, persons with substance dependencies show preference for risky response options (Lane & Cherek, 2000; Rogers et al., 1999). In comparison with CS, young adults with criminal conviction histories and other indices of risky behavior persisted in choosing (and being punished for) a risky response option after receipt of an infrequent reward (Lane & Cherek, 2000). In a similar manner, both children of alcoholics (Giancola et al., 1993) and adults with extensive histories of substance dependence (Lane et al., 1998) have shown increased perseveration when reward contingency was eliminated or changed to punishment. These findings indicate that, in comparison with aversive stimuli, appetitive stimuli exert greater control over behavior in persons with substance abuse or those at risk for its development. We used a new behavioral paradigm to assess the degree to which a subject would persist in reward-directed responding under conditions in which the likelihood of potential reward and potential punishment were concurrently increased over time. We hypothesized that, in comparison with CS, ADP

would emit more reward-directed responses under increasingly risky conditions.

1.2. Materials and methods

1.2.1. Subjects

The ADP (96 men; 34 women) were patients undergoing treatment at the National Institutes of Health Clinical Center (Bethesda, MD). The CS (27 men; 14 women) were community-recruited with the use of advertisements. All recruitment, screening, and testing procedures were reviewed and approved by the NIAAA Institutional Review Board in accordance with the Declaration of Helsinki 1978. All subjects provided written informed consent to participate.

Potential CS first underwent a comprehensive physical evaluation and The Structured Clinical Interview for DSM–IV (SCID), conducted by a licensed social worker. The screening protocol excluded from behavior testing (as a control) any applicant demonstrating a serious physical illness or psychiatric disorder. In addition, potential CS were excluded from testing if they reported either parent as having a suspected drinking problem. Applicants who met criteria for past major depressive episode (more than 1 year before the interview), however, were not excluded because of the high prevalence of a lifetime history of a major depressive episode in nonpsychiatric community samples. The CS ranged in age from 19 to 63 years (mean age, 38.5 ± 11.6 years).

The ADP were recruited from the inpatient treatment program at NIAAA. The average length of hospitalization in this program is roughly 28 days. All patients met *DSM–IV* [*Diagnostic and Statistical Manual of Mental Disorders* (4th ed.); American Psychiatric Association (1994)] criteria for alcohol dependence. Patients were excluded from participation if they demonstrated a history of seizures, subnormal IQ (<80), craniofacial features suggestive of fetal alcohol syndrome, or evidence of other neurologic disorder. In addition, patients with psychotic symptoms were excluded. Other co-morbid psychopathologies were noted, but were not an exclusion criterium. Approximately 80% of patients met criteria for at least one co-morbid mood disorder, and 40% met criteria for at least one co-morbid anxiety disorder. Subject recollection during clinical interviews precluded confident delineation of primary (pre–alcohol dependence) versus secondary mood or anxiety disorder. The patients ranged in age from 20 to 64 years (mean age, 39.8 ± 8.0 years).

Behavioral testing of all subjects took place in a testing office adjacent to the inpatient unit. The ADP were tested no sooner than 1 week after admission, to allow for detoxification and stabilization. Nursing assessments confirmed that each participating patient had completed acute detoxification and was stable before testing commenced. Previous pilot testing (data not shown) indicated no significant behavior differences in any measure between patients who were allowed to smoke before testing and subjects who were retained on the unit for testing after overnight cessation. Therefore, to avoid confounds arising from acute nicotine withdrawal, smoking was not restricted before participation.

1.2.2. Behavioral tasks

1.2.2.1. Immediate memory task/delayed memory task. The IMT/DMT used in the study is a CPT designed for use with adolescent and adult subjects. Elevated rates of commission errors (failure to restrain responses to non-target stimuli) in variants of the CPT are characteristic of human subjects with extensive real-world histories of impulsive-aggressive behavior (Halperin et al., 1995), and they are commonly construed as a measure of impulsivity (Raggio et al., 1999). In comparison with observations for age-matched CS, IMT/DMT commission errors were elevated both in children (Dougherty et al., 2003a) and in men (Dougherty et al., 2000a) with histories of conduct disorder. In addition, low doses of alcohol have been shown to increase commission errors in the DMT (Dougherty et al., 1999), as well as to change stimulus discriminability and responding bias (Dougherty et al., 2000b).

With the IMT, for a 5-min period a five-digit number was displayed on the subject's monitor for 0.5 s, once per second. These numbers measured 2.0 × 3.3 cm and were presented in black on a white background. Each subject was instructed to click the left computer mouse button when presented with a five-digit number he or she thought was identical to the preceding number. Three different types of trials—"target," "catch," and "random"—were programmed to occur at random, and responses the subject made to the trial types were designated "correct detections," "commission errors," and "random errors," respectively. In a target trial, two identical (randomly generated) five-digit numbers appeared on the screen in succession. In a catch trial, the number presented differed from the preceding number by only one of the five digits (its position and value were determined randomly). A random trial consisted of the sequential presentation of two randomly generated five-digit numbers. A random number automatically followed a catch or target trial. The probability of target, catch, and random sequence trials was programmed to be 33%, 33%, and 34%, respectively.

The DMT subtask also required responding to an identical number presented twice in succession. However, this variant required retention of stimuli longer owing to the imposition of three identical distracter stimuli ("12345") between each numeric stimulus to be remembered and compared with its successor. The three presentations of the distracter stimulus occurred at the same rate (500 ms on-screen, alternating with 500 ms blank screen) as for all other stimuli. A sample series of stimuli in the DMT might be

….12345…32476… 12345… 12345… 12345 … 32976…,

where the 32976 is a catch stimulus. Responses to the 12345 distracter were termed "distracter errors." The 5-min IMT and DMT blocks were each preceded by a 30-s rest period, during which the words "Please rest" were displayed on

the screen. The IMT was always first and alternated with the DMT, with each subtask presented twice. Before the test began, subjects were read an instruction script and underwent a practice IMT/DMT session with 60-s blocks and stimuli presented at half speed (1,000 ms on, 1,000 ms off). To discourage indiscriminant responding, subjects were compensated (typically receiving between $4 and $6) on the basis of accuracy of their performance by using a formula that credited hits, but penalized commission errors. A sign summarizing these contingencies was placed beneath the computer monitor.

The IMT/DMT data were averaged across the two blocks, and the outcome variables included the following:

- rates of hits as a percentage of target trials presented
- rates of commission errors as a percentage of catch trials presented
- a nonparametric measure of stimulus discriminability [A' (Grier, 1971)], where A' values range from 0.5 (chance performance) to 1.0 (perfect discrimination)
- a nonparametric measure of response bias [B''D (Donaldson, 1992)], where B''D values range from −1 (liberal reporting criterion) to 1.0 (conservative reporting criterion)
- latency to respond to both target and catch stimuli.

Nonparametric measures of signal detection were analyzed because parametric measures of discriminability (d') and response bias (β) assume normally distributed intensities of signal and noise, which have not been established for this task.

1.2.2.2. Risk-taking task. The risk-taking task (RTT) was designed to observe reward-directed behavior under conflict conditions, in which subjects could risk losing all reward the longer they responded for reward. Unlike the Iowa Gambling Task (Bechara et al., 2002), a widely used paradigm, in which

1. subjects select responses from among several discrete options,
2. high reward response options are also laden with even higher probabilities of loss (rendering the high-rewarded option as disadvantageous), and
3. it is incumbent on the subject to learn an advantageous response strategy,

we designed an alternative task, in which

1. the relative reward/punishment contingency of a single response option changes over time (increasingly rewarded behavior also becomes increasingly risky),
2. risk-laden responding is advantageous, and
3. relative reward and loss probabilities are implied to the subject before testing (to ostensibly minimize intersubject behavior differences due to learning).

The task was also designed to reflect the contingencies of alcohol drinking, where successive beverage consumption responses can be intensely rewarding to the drinker, but the rewarding behavior becomes increasingly laden with risk.

The RTT was divided into 24 trials, in which subjects could (1) earn points worth money by repeatedly clicking a computer mouse cursor on a "GO" circle and (2) terminate the trial and keep winnings by clicking on a "STOP" icon. Atop the screen was the "Total Points Earned" counter, which tabulated total session earnings. Below it, in the middle of the screen, was a counter that read "Points Earned This Trial." Finally, below the two counters were the GO and STOP icons: the former, a 2.5-cm green circle on the left marked "GO" in black letters, and the latter, a 2.5-cm red octagon to the right marked "STOP" in white letters.

Each trial began with a green background on the screen for 30 s. During this phase, each left click of the mouse on the GO circle advanced the trial point counter by two points, and there was no possibility of loss of earnings. This phase was included for two reasons: (1) to allow the subject to accumulate assets that could be risked and (2) to provide a motor control for individual differences in mouse-responding rates (see below). A fixed-interval schedule of reinforcement of 0.333 s was also imposed throughout the task to help equalize rates of reinforcement across subjects with different motor skills, where each click on the GO circle also resulted in the circle disappearing for 0.333 s, during which time mouse clicks were recorded but had no consequence.

After 30 s, the screen changed to yellow for a randomly determined time, ranging from 2 to 15 s. Under the yellow-screen condition, each response on the GO circle earned the subject two more points than were earned on the previous response, such that the reward for successive responses on the GO circle increased arithmetically. The subject was instructed (see below) that for him or her to keep the trial earnings, he or she must click on the STOP icon at some point before the screen turned from yellow to red, but that he or she would never know how much yellow time was to be allotted for GO responses. If the subject stopped the trial within the allotted yellow time, the screen turned blue and read "You just earned XX points!". Conversely, if the subject did not click on STOP within the (randomly) allotted time, the screen turned red and read "BUST! No points this trial!" Therefore, the trial conditions created a conflict, in which continued responding on GO had the possibility of great reward as well as increased likelihood that the trial would be terminated before the subject could click on STOP to retain the trial point earnings. After either a red-screen BUST or a blue-screen win outcome, a right-pointing white arrow containing the words "Next Trial" appeared at the bottom of the screen. Subjects could click the mouse arrow as soon as desired to advance to the next trial.

Before the test began, subjects were presented with two practice trials with yellow durations fixed at 10 s. During the first trial, they were instructed to continuously click on GO across the entire green–yellow–red screen color series, allowing themselves to BUST. Subjects invariably witnessed

during this practice trial the rapid advancement of their counter from roughly 100 to 120 points accrued during the green condition to several hundred points in the arithmetically accelerating reward schedule before busting. In the second practice trial, subjects were instructed to continue clicking on GO only two or three times once the screen turned yellow to experience the alternative, non-loss outcome. The following was read to the subjects before the first practice trial:

> In this task, you will be able to earn points worth money by repeatedly clicking the left mouse button when the mouse arrow is on top of this green circle marked "GO" (POINT OUT CIRCLE). Each time you click on the GO circle, you will add points to a point counter. Your goal is to get as many points as you can, because the more points you get, the more money I will give you after the session.
>
> This task is divided up into "trials" in which you can earn points worth money. Each trial will begin with a green background on the screen, which will then change colors to yellow then red, like a stoplight. When the screen is green, each click on the GO circle will add points to a counter in the middle of the screen. After a while, the screen will turn from green to YELLOW, and you may continue clicking on the GO circle to earn more points if you wish. Not only that, but once the screen becomes yellow, each click you make will earn you more points than the last click, so you will be earning points at a faster and faster rate the longer you keep clicking on the GO circle. You can thus earn a LOT of points worth money by continuing to click on the GO circle after the screen turns yellow.
>
> When the screen changes from green to yellow in each trial, it will remain yellow for a random length of time before changing to red, ranging from a short period of time to a long period of time. For you to keep your points for a trial and add them to your grand total at the top of the screen, you must move the mouse arrow to the STOP sign and click the left mouse button while the screen is still yellow. If the screen changes to red before you click on STOP, you will BUST and you will lose all the points you had earned for that trial. Therefore, continuing to click on the GO circle after the screen turns yellow is like a gamble. The longer you click on GO after the screen turns yellow, the greater your chance both of earning a lot of extra points for money, or busting. This is because you'll never know how much yellow time the computer is going to give you for any given trial before changing to red. In each trial, it is up to you to decide when to stop earning points and click on the STOP sign once the screen turns yellow.
>
> Each trial will end when either the screen turns red or when you click on STOP. Whether you STOP in time to keep your points or whether you BUST, you are to start the next trial by clicking on an arrow labeled "next trial". After a certain number of trials, the screen will tell you the session is over. You will receive 10¢ for every 100 points you get, so earning thousands of points will earn you several dollars. You will now have two practice trials to see what the task is like. For this first practice trial, click on GO repeatedly until you bust, but watch your point counter…. In this 2nd practice trial, click on GO a handful of times once the screen turns yellow then click on STOP.

This task was structured so that the optimal strategy entailed taking some risk. With successive responses in the yellow-screen condition, the risk of busting rose linearly (because the randomly generated bust times are uniformly, but not normally, distributed); however, reward increased arithmetically. For example, a completely risk-averse strategy (clicking on STOP as soon as the screen turned yellow) would earn the subject about 2,400 points (100 or so points from the non-risk responses in all 24 trials) worth $2.40. A subject's consistently intending to respond roughly 20 times (taking slightly less than the mean duration of 8.5 s) during the yellow phase would result in 12 or so busts. However, in the remaining trials, the subject would earn 6,240 points [100 (green) + 420 (yellow) = 520 points × 12 trials] worth $6.24. Finally, a subject's consistent intent to respond 40 times (about 14 s) would result in a vast majority of bust trials. However, in the one trial or two trials in which the subject clicked on STOP in time, the reward would be greater than $15 per trial.

The primary datum of interest in the RTT was ratio of the number of yellow-screen rewarded responses divided by the number of green-screen rewarded responses across all trials, defined hereinafter as "trial average" risky responding. The yellow-screen/green-screen ratio score allowed us to assess risk-taking preference while controlling for individual differences in motor skill (tapping speed). In addition, the ratio of the maximum number of yellow-screen rewarded responses emitted in a trial (again divided by the number of green-screen rewarded responses) was defined as "trial maximum" risky responding and served as a secondary measure of extreme risk taking.

Finally, we assessed changes in risk taking/exposure across trials. We performed a repeated-measures analysis of variance (ANOVA) of yellow-screen responses each subject made before stopping in the first six non-bust trials (averaged) versus the final six non-bust trials (averaged). Time was the within-subject factor (two levels), and group was the between-subject factor.

1.2.2.3. Two-choice delay-discounting task. The two-choice delay-discounting task assesses the degree to which a subject devalues a reward as a function of how long the subject must wait to receive it. [See Mitchell (1999) for full description.] Briefly, the subject was presented with a series of choices between receiving (1) a standard $10 reward (either in cash or by mailed check as required) at time points ranging

from the conclusion of testing (i.e., now) to 7, 30, 90, 180, or 365 days after testing was completed or (2) one of several immediate alternative monetary rewards ($0.01, $0.25, $0.50, $1.00, $1.50, $2.00, $2.50, etc. … up to $10.50). The total number of possible choices presented was 137, representing all permutations of immediate reward amounts versus delay intervals for the larger reward (excluding the identical item question). To enhance the realism of the task, actual reward (selected from a random question) was delivered.

At each of the six delay intervals for the standard reward, we calculated a "switchpoint": the dollar value of an immediate reward above which the subject opted for the immediate alternative over the delayed standard reward. The switchpoint at each time interval could thus be interpreted as the effective "worth" of the $10 standard reward with that delay. The pattern of reward devaluation across increasing delays (switchpoint values plotted against delay intervals) has typically followed a hyperbolic function (Mazur, 1987):

$$V = \frac{M}{1 + k(X)}$$

where V is the effective value of standard reward M at delay interval X, and the constant term k describes the subject's severity of delay discounting. Using a least-squares, iterative procedure, we calculated for each subject the discounting constant k that best fit observed subject switchpoints to that predicted by the hyperbolic-discounting function. Because this version of the delay-discounting task involved an actual reward delivery, subjects whose responses indicated switchpoints less than $2 for all delay intervals were debriefed, and data obtained for subjects whose extreme preference for immediate reward was driven by uncertainty about his or her future whereabouts were excluded.

1.2.2.4. Questionnaire measures. Four psychometric instruments were used to gather additional information through subjects' responses to on-screen questions by mouse-click:

1. Barratt Impulsiveness Scale, Version 11 (BIS-11) (Patton et al., 1995), a multidimensional measure of impulsivity with Attentional, Motor, and Nonplanning subscales
2. Buss-Perry Aggression Questionnaire (BPAQ) (Buss & Perry, 1992), a revision of the Buss-Durkee Hostility Inventory (Buss & Durkee, 1957) with improved psychometric characteristics
3. Sensation Seeking Scale, Version 5 (SSS) (Zuckerman et al., 1978), a personality measure of sensation seeking and risk taking
4. Life History of Aggression (LHA) (Coccaro et al., 1997), for which the subject estimates number of aggressive incidents since adolescence.

Finally, as part of inpatient procedures, ADP were interviewed about their lifetime drinking histories, from which an estimated cumulative number of years of heavy drinking [(YHD), defined a priori as >90 drinks per month] was calculated and used in the study as a covariate.

1.2.3. Data analysis

Laboratory measures and questionnaire responses were directly compared between ADP and CS by using independent, two-tailed t tests. Where group differences were detected in a measure, the effect size of the group difference was also calculated (Cohen, 1988). Although explicit confounds of fetal alcohol syndrome were unlikely in this dataset, we repeated pairwise analyses after excluding patients ($n = 20$) who reported during their clinical interviews that their mother had a lifetime incidence of a drinking problem to explore the possibility that any apparent significant differences between ADP and CS resulted in part from subtler prenatal alcohol exposure effects.

Finally, across all subjects, we performed a limited number of correlations between laboratory impulsivity measures and analogous questionnaire measures of impulsivity to assess the internal validity of the laboratory measures. First, because CPT commission errors have been shown to correlate particularly with physical fight initiation (Dougherty et al., 2003b; Halperin et al., 1995) and general conduct disorder histories (Dougherty et al., 2000a), we hypothesized that IMT and DMT commission error rates would correlate with LHA scores. Second, we hypothesized that the risky/nonrisky response ratio in the RTT would correlate with sensation-seeking (total SSS) scores, because the SSS item content includes preference for risky activities. Finally, we hypothesized that total BIS-11 scores would correlate positively with IMT/DMT commission errors and with the delay-discounting constant k.

1.3. Results

As summarized in Table 1, chi-square and t test analyses indicated that ADP and CS did not differ in age, racial composition, or sex proportion. In comparison with ADP, CS had significantly more years of education.

1.3.1. Immediate memory task/delayed memory task

In comparison with CS, ADP made significantly more commission errors on IMT and DMT subtasks (Fig. 1A). The ADP also made more omission errors on the DMT.

Table 1
Group demographic data

	Alcohol-dependent patients ($n = 130$)	Control subjects ($n = 41$)	P value
Sex			n.s.
Male	96	27	
Female	34	14	
Age (years)	39.8 (8.0)	38.5 (11.6)	n.s.
Race			n.s.
Caucasian	105	27	
African American	22	10	
Hispanic	1	0	
Other	2	4	
Education (years)	13.6 (2.4)	16.9 (3.0)	<.0001

( ) Denotes standard deviation (S.D.). n.s. = Not significant.

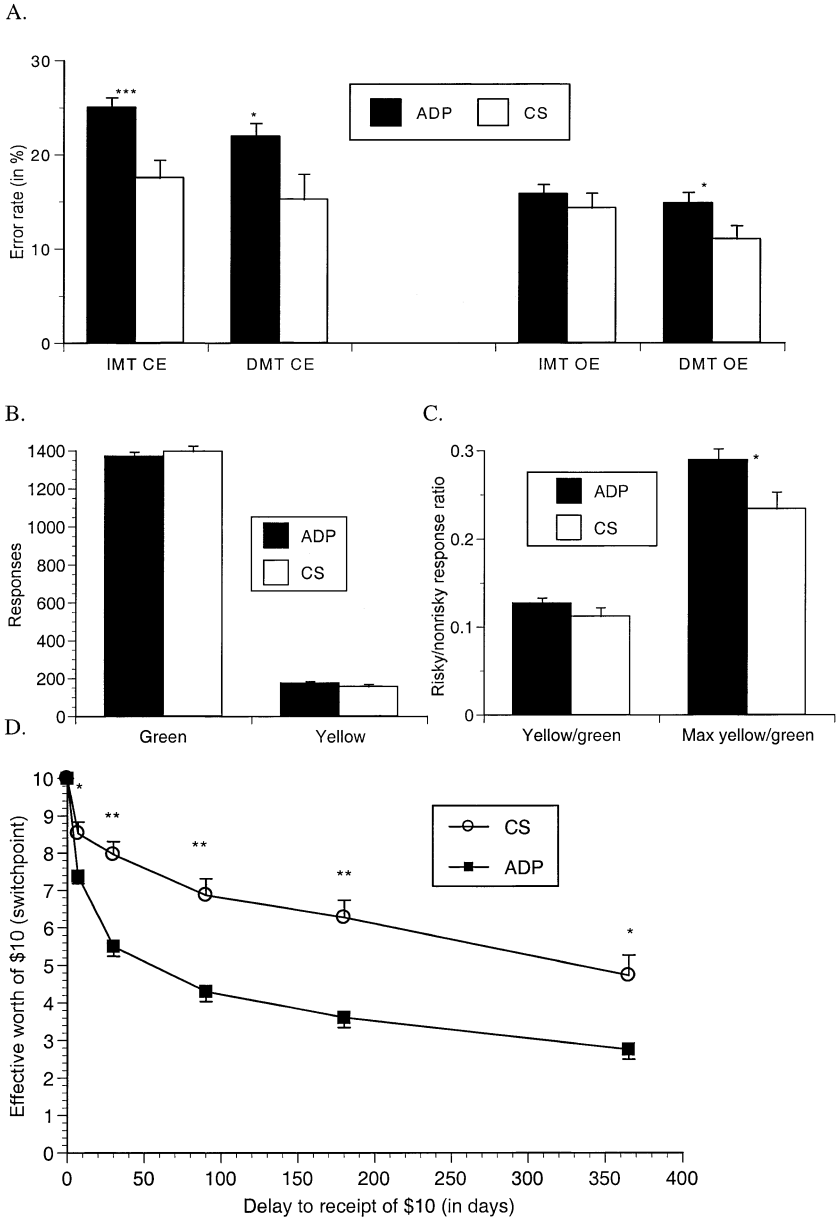

Fig. 1. Differences between detoxified alcohol-dependent patients [(ADP); $n = 130$] and control subjects [(CS); $n = 41$] in (A) omission error (OE) and commission error (CE) rates in the immediate memory task (IMT) and the delayed memory task (DMT), (B) raw nonrisky and risky response rates in a risk-taking task, (C) ratio of risky/nonrisky responses in a risk-taking task, and (D) discounting of a real $10 monetary reward with delay to presentation in a delay-discounting task. $^{*}P < .05$, $^{**}P < .01$, $^{***}P < .001$.

The difference in DMT omission error rates was no longer significant when the 20 ADP who reported having a problem-drinking mother were excluded. To assess whether this was due to reduced sample size and power, 20 ADP were randomly removed before a second analysis, and the group difference was significant. Results of this second analysis indicated that patients with a problem-drinking mother contributed substantially to the increased DMT omission error rates in ADP. In comparison with CS, the ADP demonstrated significantly lower A' (discriminability) scores on both subtasks. The ADP also demonstrated a significantly more liberal signal detection–responding criterion (B''D). Across all subjects, latency to respond to catch stimuli was inversely correlated with false alarm rates in both the IMT ($r = -.342$, $P < .0001$) and the DMT ($r = -.193$, $P < .05$).

1.3.2. Risk-taking task

Almost all subjects emitted many more GO responses than were actually reinforced (Fig. 1B), the result of a vigorous responding pace that did not appear to be restrained by the fixed-interval schedule of reinforcement. Despite the programmed incentive to emit risky responses, subjects

behaved suboptimally, the vast majority emitting few risky responses in the yellow-screen phase of the trial so as to protect modest gains. Roughly 25% of trials resulted in busts, typically because of 2- or 4-s (randomly assigned) yellow durations for those trials. Subjects occasionally verbalized displeasure when busting. There was no main effect of trial on risky responses in the non-bust trials, nor was there an interaction effect of group. Trial-average yellow-screen/green-screen (i.e., risky/nonrisky) response ratios did not differ significantly between ADP and CS (Fig. 1C). The ADP, however, demonstrated significantly more trial-maximum risky responses (as a ratio of nonrisky responses). The two groups had similar session earnings.

The practice trials of the RTT were intended to afford the subject the opportunity to discern that the benefits of extended risky responding in non-bust trials outweighed the penalties for several busts. Educated subjects may have been better able to discern the disproportionately advantageous impact of the arithmetic reward schedule during the yellow phase. To address this, group comparisons were performed again with education level as a covariate, and the adjusted means indicated more pronounced group differences in busts and in total trial and maximum trial risk taking in ADP. Conversely, education level (while we controlled simultaneously for group) independently correlated with trial average ($\beta = .316$, $P = .0004$) and trial maximum ($\beta = .295$, $P = .0008$) yellow-screen/green-screen response ratios.

1.3.3. Two-choice delay-discounting task

Data obtained for 11 ADP were excluded from analysis because the patient was unsure of his or her future whereabouts (such that delay discounting was effectively confounded with probability discounting). As shown in Fig. 1D, both ADP and CS discounted the standard reward with delays in a hyperbolic pattern, with more rapid discounting in ADP. In post hoc simple effect t tests of actual switchpoints, ADP demonstrated a significantly lower switchpoint value of the alternative immediate reward (all $P < .01$) at all delay time points (7–365 days). The calculated best-fit k values were accordingly significantly larger in ADP.

1.3.4. Questionnaire measures

In comparison with CS, ADP scored higher on almost every impulsivity/aggression questionnaire measure (Table 2).

1.3.5. Relation between age and impulsivity measures

In a post hoc analysis, we examined how age related to laboratory and questionnaire measures of impulsivity, and whether this relation would differ between ADP and CS. We suspected that age would correlate with impulsivity measures more strongly in ADP than in CS, for two reasons: (1) Chronic alcohol abuse accelerates brain shrinkage with age in ADP (Bjork et al., 2003), particularly in frontal lobe regions governing ECF and behavior control (Pfefferbaum et al., 1998), and (2) ADP as a group would have a greater range of impulsivity scores to strengthen correlations.

Spearman rank correlations indicated no significant correlations in CS between age and any impulsivity measure. In ADP, however, age correlated with both omission error rates and target response latency in the IMT ($r = .26$, $P = .003$ and $r = .29$, $P < .001$, respectively) and in the DMT ($r = .23$, $P = .009$ and $r = .28$, $P = .001$, respectively). In addition, among ADP, there was a negative correlation between age and the trial maximum yellow-screen/green-screen response ratio of the RTT ($r = -.19$, $P = .033$) and between age and the (log transformed) delay-discounting constant ($r = -.23$, $P = .013$). Finally, among ADP, age correlated negatively with total scores of the BPAQ ($r = -.223$, $P = .01$), the SSS ($r = -.34$, $P < .001$), the BIS-11 ($r = .23$, $P = .007$), and the LHA ($r = -.26$, $P = .003$). One-tailed Fisher z tests, however, indicated that no age × impulsivity measure correlation significantly differed between ADP and CS.

We further investigated how age and alcohol abuse chronicity related independently to ECF in ADP, as assessed with the IMT/DMT. We performed post hoc multiple regression analyses of IMT/DMT error rates from ADP, with age and cumulative YHD as simultaneous independent variables. Omission errors in both the IMT and the DMT partially correlated with age (IMT: $\beta = .235$, $P = .015$; DMT: $\beta = .212$, $P = .033$), but they did not partially correlate with YHD. Conversely, commission errors in the IMT partially correlated with YHD ($\beta = .200$, $P = .044$), but not with age. Commission errors on the DMT did not partially correlate with either age or YHD.

1.3.6. Correlations between questionnaire and laboratory impulsivity measures

To demonstrate the internal validity of the laboratory measures, Pearson correlations were performed between laboratory impulsivity measures and psychometric measures across all subjects. This matrix is presented in Table 3. Laboratory measures of impulsivity, with the exception of the delay-discounting constant k, did not appreciably correlate with questionnaire measures. Furthermore, none of the outcome measures from any of the three behavioral tasks correlated with outcome measures of any other behavioral task (all $r < .1$), supporting the idea that the three tasks assessed distinct elements of impulsivity.

1.3.7. Discriminant function analysis

To determine how well laboratory impulsivity measures discriminated between ADP and CS, we performed discriminant function analyses with group membership as the categorical variable. For each of the three behavioral tasks, the measure showing the most significant group difference was entered as the predictor variable. These analyses indicated that the (log transformed) delay-discounting constant k singly predicted group membership with 68.75% accuracy,

Table 2
Differences between alcohol-dependent patients and control subjects in impulsivity measures

Measure	Alcohol-dependent patients (n = 130)	Control subjects (n = 41)	P value	d value
Immediate memory task				
Omission errors	15.8% (11.4)	14.3% (10.2)	n.s.	
Commission errors	25.0% (12.1)	17.5% (12.4)	<.01	0.60
Discriminability (A')	0.872 (0.061)	0.901 (0.052)	<.001	
Response bias (B''D)	−0.269 (0.439)	−0.048 (0.498)	<.05	
Response latency-targets (ms)	538.1 (75.1)	572.6 (101.2)	<.05[a]	
Response latency-catch (ms)	537.4 (82.1)	581.5 (124.8)	<.01	
Delayed memory task				
Omission errors	14.8% (13.2)	11.0% (10.2)	<.05[a]	0.31
Commission errors	21.9% (15.8)	15.2% (17.0)	<.05[a]	0.41
Discriminability (A')	0.882 (0.081)	0.921 (0.067)	<.01	
Response bias (B''D)	−0.224 (0.595)	−0.021 (0.594)	.06	
Response latency-targets (ms)	599.0 (102.1)	629.5 (104.9)	.10[a]	
Response latency-catch (ms)	584.3 (118.4)	601.7 (132.3)	n.s.	
Risk-taking task				
Winnings	$3.39 (1.07)	$3.44 (0.99)	n.s.	
Risky/nonrisky responses (trial average)	0.127 (0.072)	0.112 (0.062)	n.s.	
Controlling for education (adjusted mean)	0.134	0.094	<.01	
Risky/nonrisky responses (trial maximum)	0.289 (0.152)	0.235 (0.125)	<.05[a]	0.15
Controlling for education (adjusted mean)	0.301	0.198	<.01	
Busts	7.1 (4.3)	5.8 (3.6)	.08[a]	0.31
Controlling for education (adjusted mean)	7.5	4.7	<.001	
Delay-discounting constant k	0.062 (0.107)[b]	0.013 (0.025)	<.01	0.66
Buss-Perry Aggression Questionnaire	64.8 (16.8)	45.3 (6.0)	<.0001	1.14
Physical subscale	19.0 (7.2)	13.0 (3.5)	<.0001	
Hostility subscale	17.8 (6.0)	11.0 (2.1)	<.0001	
Anger subscale	15.2 (5.0)	10.5 (2.5)	<.0001	
Verbal subscale	12.9 (3.6)	10.8 (2.9)	<.01	
Sensation Seeking Scale, Version 5	20.5 (5.8)	15.6 (7.2)	<.0001	0.75
Thrill/adventure-seeking subscale	6.8 (2.5)	5.3 (3.2)	<.05	
Experience-seeking subscale	5.9 (1.8)	4.9 (2.3)	<.01	
Disinhibition subscale	4.9 (2.2)	2.7 (2.1)	<.0001	
Boredom susceptibility subscale	2.9 (1.9)	2.7 (1.8)	n.s.	
Barratt Impulsiveness Scale Version 11	70.6 (11.7)	57.4 (8.7)	<.0001	1.07
Nonplanning subscale	27.2 (5.0)	22.1 (4.0)	<.0001	
Motor subscale	25.7 (4.5)	21.2 (3.6)	<.0001	
Attentional subscale	17.7 (3.7)	14.0 (2.6)	<.0001	
Life History of Aggression	19.6 (8.6)	5.8 (4.2)	<.0001	1.42
Aggression subscale	11.5 (5.6)	4.8 (3.4)	<.0001	
Consequences/antisocial subscale	7.6 (3.8)	0.9 (1.5)	<.0001	
Self-directed aggression subscale	0.46 (1.0)	0.03 (0.2)	<.0001	

( ) Denotes standard deviation (S.D.).
[a]Group difference not significant ($P > .10$) when alcohol-dependent patients with problem-drinking mothers (n = 20) were excluded.
[b]Data obtained for 11 alcohol-dependent patients were excluded (see Methods). Data were log transformed.

and IMT commission errors and trial maximum yellow/green responses in the RTT (singly) predicted group membership with 59.4% and 56.4% accuracy, respectively. Finally, we performed an exploratory forward-stepwise analysis using each of the laboratory impulsivity task parameters listed in Table 2 as candidate predictor variables. This analysis also revealed that the behavioral variable that best predicted group membership was the (log transformed) delay-discounting constant k. The next two forward steps revealed that the discriminability statistic A' for the IMT added statistically significant predictive power, followed by the trial maximum yellow-screen/green-screen response ratio in the RTT. No other variable accounted for significant remaining predictive power. These three behavior variables collectively identified subjects with 73.5% accuracy, of which 64.5% of ADP and 78.0% of CS were correctly classified.

1.4. Discussion

To our knowledge, this is the first study of impulsivity in alcoholism in which differences from CS in several behavioral measures of impulsivity were assessed concurrently. As hypothesized, ADP were more impulsive than CS in almost all impulsivity measures. Most notably, in comparison with CS, ADP discounted the value of a monetary reward with delay to presentation more severely. Second, the ADP made more commission errors in the IMT and the DMT,

Table 3
Correlations between questionnaire and behavioral measures of impulsivity

	IMT commission errors	DMT commission errors	Risk-taking task: risky/nonrisky response ratio	Delay-discounting task: discounting constant *k*
BPAQ total score	.14	.07	.05	**.31**
BIS-11 total score	.10	.15	.09	.18*
SSS total score	.06	−.04	.20*	.08
LHA total score	.14	.06	.01	**.35**

Significant correlations ($P < .0001$) expressed in boldface type.
*$P < .05$ uncorrected for multiple comparisons.
BPAQ = Buss-Perry Aggression Questionnaire; BIS-11 = Barratt Impulsiveness Scale Version 11; DMT = delayed memory task; IMT = immediate memory task; SSS = Sensation Seeking Scale, Version 5; LHA = Life History of Aggression.

as well as more omission errors in the DMT. Third, ADP emitted a greater maximum number of progressively risky (but advantageous) responses in a new risk-taking task, and this group difference became magnified when the lower education level of ADP was controlled for. Finally, ADP scored markedly higher on questionnaire measures of impulsivity and aggression.

In agreement with several previous descriptions of severe delay discounting of small rewards in substance-dependent (Mitchell, 1999; Petry, 2001; Petry & Casarella, 1999) or heavy-drinking (Vuchinich & Simpson, 1998) individuals, ADP, in comparison with CS, devalued a small reward ($10) with delay to presentation more severely. This was evident not only in a significant group difference in the a priori least-squares, best-fit delay-discounting constant *k*, but also in the subjective value (switchpoint) of $10 at each of the delay intervals. It is interesting that the effect size of the group difference in this task was much larger than with the other laboratory impulsivity measures. In accordance, among all behavioral measures, the severity of delay discounting demonstrated the best predictive discrimination between ADP and CS, correctly identifying more than two thirds of subjects.

The more severe delay discounting in ADP may have been magnified by use of real reward. Despite debriefing ADP with extreme devaluation (and exclusion of some data), ADP may still have guided their choices by practical concern over their future whereabouts. However, we note that there was a significant group difference in the subjective value of the standard reward at the 7-day delay, at which time the most patients would still be on the patient care unit to be handed the delayed $10 reward in cash (which frequently occurred). Several debriefed patients insisted that their pronounced preference for immediate reward was not influenced by concern that they would ever receive the delayed reward payment. Typical comments were "I guess I just like getting stuff now" or "I hate waiting for anything."

On the basis of reports that the frontal lobes are involved in behavior control (ECF) [see, for example, Horn et al. (2003)], coupled with findings that dysfunctional ECF is both a potential risk factor for (Deckel et al., 1995; Harden & Pihl, 1995) and potential consequence of (Pfefferbaum et al., 1998) alcohol dependence, we hypothesized that ADP would show performance deficits in the IMT/DMT. The ADP not only made more commission errors in both the IMT and the DMT, they also made more omission errors in the distracter-laden DMT. The DMT omission error difference was not significant when the ADP who reported having a problem-drinking mother were excluded. We note, however, that the DMT omission error difference from that of the CS was still significant when 20 patients were randomly excluded, supporting the suggestion that these ADP with a problem-drinking mother in particular may feature attentional deficits.

Age correlated with IMT and DMT omission errors in ADP, but not in CS, supporting the idea of a detrimental effect of chronic alcohol intoxication on vigilance. These age correlations remained significant after we controlled for alcohol use chronicity as YHD. We note, however, that our measure of YHD only tabulated epochs that patients recalled consuming 90 or more drinks per month. Omission errors may have related to the totality of chronic heavy alcohol use across adolescence and adulthood irrespective of reporting on a retrospective drinking history measure. Conversely, commission errors on the IMT related to YHD (while we controlled for age). This offers some evidence that chronic alcohol abuse also affects executive cognitive governance of behavior control.

Group differences in IMT/DMT error rates were also reflected in markedly poorer target–catch discrimination statistics (A') as well as a more liberal responding criterion (B''D) for both subtasks in ADP. The ADP also had faster response times to target and catch stimuli. As with a previous report with this paradigm (Dougherty et al., 2000a), reaction times were inversely correlated with error rates across all subjects, which seemed to point to a "fast-guess" mechanism of impulsive response, in which motor behavior is initiated before adequate processing of stimuli (Sergeant & Scholten, 1985).

Trial-maximum risk taking in the RTT was higher in ADP, and trial-average risky responses were higher in ADP when their lower education level was controlled for. However, group differences were modest, possibly owing to a general tendency toward risk aversion (and suboptimal earnings). Because a risk-aversive decision to preserve modest,

but certain, gains is a well-established violation of rational choice in decision making (Kahneman & Tversky, 1979), the task was programmed such that progressively risky responses were overtly paired with disproportionately rewarding contingencies to elicit risk-taking behavior by the subjects. Despite this structure, subjects typically responded so as to conserve modest gains, rather than to take risks for large gains, with a median number of roughly six responses (<3 s) emitted during the yellow phase in non-bust trials. This resulted in typical winnings of a little more than $3.

Second, comparison of risky responding between the first and last non-bust trials of the task revealed no evidence of learning the financially advantageous response strategy across trials. We surmise that even the modest losses (usually less than 20¢ worth of points) in bust trials likely elicited a risk-aversive, gain-preservation strategy even in the ADP, and subjects were reluctant to risk further losses by subsequent experimentation with more risky responses in later trials. Ignorance of the ample number of trials may have contributed to this cautious strategy.

Finally, the relative risk/reward contingencies programmed into the task elicited both risk taking arising from impulsivity and risk taking arising from strategic acumen. Incorporation of individual differences in education level across subjects accounted for significant variance in risk taking. Our controlling for the lower education level in ADP magnified the group difference in risk taking to where adjusted mean trial-average and trial-maximum risky response rates were approximately 50% higher in the ADP. In accordance, the multiple regression analysis indicated a direct partial correlation between years of education and risky responses. This raises a possibility that well-educated subjects were best able to discern the optimal strategy and emit more risk-taking responses by rational choice. Conversely, lesser-educated ADP may have behaved more in accordance with facile, intuitive cognitive strategies (Kahneman, 2003) and less in accord with rational choice.

The largest group differences, however, were found in questionnaire measures of impulsivity, most notably in the LHA and BPAQ aggression questionnaires. This was to be expected because the co-incidence of aggression and alcohol intoxication has been documented extensively in epidemiologic research [see, for example, Pihl and Peterson (1995) and Wells et al. (2000)]. Elevated BIS-11 (Ketzenberger & Forrest, 2000) and SSS (Kilpatrick et al., 1982; Marra et al., 1998) scores in alcohol-dependent individuals, in comparison with scores in CS, have also been reported previously, and high psychometric sensation seeking in particular has been shown to relate both to drinking behavior and to subjective stimulation during the ascending limb of the blood-alcohol curve in nondependent drinkers (Erblich & Earleywine, 2003).

Few of our hypothesized correlations between questionnaire and objective laboratory impulsivity measures were significant. First, IMT/DMT commission error rates did not correlate with any psychometric measure. In a previous report (Dougherty et al., 2000a), IMT commission errors correlated directly with BIS-11 scores. However, that study population featured a subject group selected for childhood conduct disorder, with a mean education level of roughly 11 years. It is possible that the ADP in the current study population were better functioning, with a reduced range of impulsivity. Risky responding in the RTT mildly correlated with SSS scores, but this was not significant when multiple correlations were controlled for. The general suppression of risky responses likely blunted correlations with psychometric measures. In contrast, the delay-discounting constant *k*, which had the highest effect size of group difference, correlated with BIS-11, LHA, and BPAQ scores. However, only the correlations with the LHA and BPAQ scores were significant after correction for multiple comparisons.

A poor correlation between questionnaire and behavioral measures of impulsivity has been noted (Barratt et al., 1997). It may be that the lack of correlation between behavioral and questionnaire measures arose because the questionnaire measures used in the current study assess trait characteristics, whereas behavioral measures are more vulnerable to state characteristics, such as mood, fatigue, or other transient factors. For example, the questionnaire measures correlated better with age of onset of heavy drinking (AOHD) than did the laboratory behavior. Finally, the absence of correlations among the three behavioral measures themselves supported the suggestion that each task assessed a different element of impulsivity, such that, in the post hoc stepwise discriminant function analysis, a measure from each task accounted for a significant amount of distinct variance in predictive power.

The current study featured several methodologic advantages:

1. a large sample size
2. concurrent use of several different behavioral and psychometric measures
3. monitoring of all ADP to ensure a similar functional (detoxified) state
4. education level of patients similar to that of respondents meeting lifetime criteria for alcohol dependence in a large epidemiologic study (Hasin & Grant, 2002), suggesting generalizability of data
5. introduction of a new risk-taking task designed to assess progressively risky responses.

However, there are some limitations of this report. First, the incentive structure of the RTT design did not successfully elicit many risky responses in most subjects, diminishing the sensitivity of the task. Second, the majority of subjects met criteria for a mood disorder, and the presence of psychiatric symptoms itself is related to laboratory impulsivity (Swann et al., 2002). However, there were no significant or systematic differences in laboratory behavior between ADP with and without psychiatric co-morbidity (data not shown). Finally, the sample size precluded meaningful investigation

of sex differences in impulsivity as well as sex by group interactions.

These findings collectively support the suggestion that, on the whole, CS and detoxified ADP differ in response inhibition, risk taking, delay discounting, and self-reported impulsivity and aggression, but behavioral and questionnaire impulsivity did not appreciably correlate. The group differences nevertheless provide some evidence for construct validity of the laboratory impulsivity tasks, in which the group difference in delay discounting was the most striking. Among questionnaire measures, those with item content encompassing aggressive temperament (BPAQ) and actual history of aggressive acts (LHA) had the highest effect sizes, and they also correlated with delay discounting severity.

2. Analysis 2

2.1. Introduction

Analysis 1 indicated that, as a group, ADP are generally more impulsive than CS in several dimensions. How might impulsivity relate to individual differences in personal and familial drinking histories among ADP? Alcohol dependence is heterogeneous with regard to several behavioral, psychiatric, and pathophysiologic variables, including age of onset of alcohol dependence and family history of alcohol dependence, as well as co-morbid affective symptoms, behavior problems, and substance abuse. Classification schemes to distinguish subtypes of alcohol dependence have been proposed. For example, Babor's type A/type B dichotomy (Babor et al., 1992) describes a subtype of alcoholism (type A) characterized by later onset and less collateral psychiatric dysfunction, as well as a severe subtype (type B) characterized by early onset of alcohol-related problems, family history of alcoholism, and greater severity of dependence and psychopathology. In a similar manner, Cloninger presented a classification scheme (Cloninger, 1987, 1995), which features an early-onset and more severe subtype, characterized by increased impulsivity and aggression (type 2), as well as a later-onset subtype, with less impulsivity and aggression (type 1). Elevated heritability of alcoholism is also a defining component of the type 2 subgroup (Cloninger, 1987), and type 2 alcohol dependence showed the greatest heritability among alcoholism subtypes in subsequent study of twins (van den Bree et al., 1998) and adoptees (Sigvardsson et al., 1996).

These typologies thus share a demarcation of (primarily male) alcohol-dependent individuals with young age of onset of alcohol dependence, a positive family history of alcohol dependence, and more severe psychiatric and behavioral disturbance. However, little is known about the relation between impulsivity measured as a continuous variable and individual characteristic features of the type 1/2, A/B–like dichotomies. Finn et al. (2002) reported increased impulsivity in a community sample of young, early-onset alcoholics, in which increased commission errors were specific to early-onset alcoholics with childhood conduct disorder. To assess whether the type 1/type 2 traits are reflected in objective laboratory impulsivity measures, in the second analysis of the current study, we examined whether AOHD and parental history of alcohol dependence among ADP correlated with measures of impulsivity, either singly or in combination.

Because increased antisocial behavior and incarceration for violence (Buydens-Branchey et al., 1989) as well as increased pathologic gambling (Lejoyeux et al., 1999) have been reported in subjects with early-onset alcohol dependence, and because impulsivity correlates with alcohol use in adolescence (Barnes et al., 1999), we hypothesized that age of onset of problem drinking would correlate negatively with laboratory impulsivity scores. In addition, because presence of an alcoholic parent is selectively correlated with impaired performance in tests of ECF (Ozkaragoz & Noble, 1995) and because the type 2/B aggressive subtype of alcoholism has shown the greatest heritability (van den Bree et al., 1998), we hypothesized ADP with a problem-drinking parent would show greater impulsivity than ADP with no alcoholic parent. Finally, because the type 2 or type B alcoholic is jointly characterized by young age of onset of alcoholism, family history of alcoholism, and behavioral problems, we hypothesized that male ADP with both an early onset of heavy drinking and a problem-drinking biologic father would be particularly more impulsive than male ADP selected for absence of both factors.

2.2. Materials and methods

2.2.1. Subjects

Subjects were subsets of male ADP from the previous analysis. Because there were not enough female ADP for meaningful analysis, and because the type 2 or type B impulsive-aggressive alcoholic subtype has been predominantly male, Analysis 2 was restricted to male patients.

2.2.2. Impulsivity measures

Behavioral and questionnaire measures described in Analysis 1 were used in this follow-up analysis. To reduce the number of correlations and comparisons, we analyzed only a subset of impulsivity measures.

2.2.3. Alcoholism severity measures

Near the conclusion of inpatient treatment, a semistructured, internally developed lifetime drinking history interview was administered by a social worker who was blind to the design and behavioral data of the study. Alcohol use history was first characterized as epochs of use patterns across the life span. From these epochs, we calculated three drinking history parameters:

1. age of onset of heavy drinking, defined a priori as the age at which the subject reported first consuming the equivalent of 90 drinks in 1 month,
2. years of heavy drinking (YHD), defined as the cumulative total (contiguous or noncontiguous) months

(summed into years) during which the subject drank 90 drinks per month, and
3. estimated total lifetime alcohol consumption (in kilograms), which is a summation of all alcohol ingestion, including epochs in which consumption did not reach 90 drinks per month.

In addition to the patient's self-reported drinking history, the patient was asked about the lifetime drinking history of first- and second-degree relatives. Responses were subjectively interpreted as "problem drinker" or "alcoholic" in addition to nonproblematic categories of lighter consumption or lifetime abstinence. Finally, each patient was administered the Michigan Alcoholism Screening Test (MAST) (Selzer, 1971) in the form of a semistructured interview. The MAST features yes/no endorsement of 25 symptoms or negative consequences specifically attributed to alcohol use (e.g., "Have you ever lost a job because of your drinking?"). Questions that best discriminate between clinical alcoholic and control populations are weighted more heavily in the scoring.

2.2.4. Data analysis

First, we determined whether AOHD (singly) inversely correlated with behavioral and questionnaire impulsivity. To assess the relation between AOHD and parameters of IMT/DMT performance, we controlled for individual differences in alcohol exposure by entering cumulative YHD as a simultaneous independent variable along with AOHD in multiple regression. For the RTT, we report partial correlations with AOHD while controlling for education level as a covariate. For the remaining tasks as well as for questionnaire measures, AOHD was directly correlated with each impulsivity measure by using Spearman rank-order correlation.

Second, we compared whether ADP who reported a problem-drinking parent (lifetime) were more impulsive than ADP who reported neither biologic parent with a history of a drinking problem. The former group of ADP (hereinafter referred to as "PDP+"; $n = 45$) endorsed either a "problem drinker" or "alcoholic" lifetime drinking history for either mother or father in the interview. In the PDP+ group, 31 subjects reported a problem-drinking father only, 8 reported a problem-drinking mother only, and 6 reported both parents as problem drinkers. The latter group of ADP ("PDP–"; $n = 51$) was defined by patient report of neither parent being a problem drinker or alcoholic. Patient recollection of drinking history of additional relatives was deemed too unreliable to incorporate additional relatives into any calculated familial alcoholism "loading" score or scheme. In addition, 9 patients were not able to definitively characterize the drinking history of both biologic parents and were excluded from this analysis.

Third, we isolated male ADP into conceptual approximations of the type 1/2 and type A/B classification schemes. "Type 1/A–like" ADP ($n = 22$) were patients whose AOHD scored at or above the median among all male patients in the dataset (age >22 years) and who reported having no problem-drinking parents. Conversely, "type 2/B–like" ADP ($n = 21$) were patients whose AOHD scored below the median (age <22 years) and who reported a problem-drinking father. This focus on paternal problem-drinking was intended to capture the male-specific pattern of inheritance (Cloninger et al., 1981) characteristic of type 2 alcoholism. We used analysis of covariance (ANCOVA) to compare IMT/DMT performance while controlling for age and YHD, and we used independent t tests to compare the remaining impulsivity measures between the type 1/A–like and type 2/B–like alcoholic patient groups.

2.3. Results

2.3.1. Age of onset of heavy drinking and impulsivity

The AOHD ranged from age 13 to 53 years (mean, 23.3 ± 7.9 years) and predictably correlated negatively with both YHD and estimated lifetime consumption. Correlations (full and partial) between impulsivity scores and AOHD are shown in Table 4, left. The AOHD did not correlate significantly with IMT/DMT error rates, either in direct correlation or when controlling for YHD. Among other measures, AOHD showed significant negative correlations only with BIS-11 and LHA scores (both significant to $P < .05$ after correction for multiple correlations).

2.3.2. Presence versus absence of heavy-drinking parent and impulsivity

In comparison with PHP– ADP, the PHP+ ADP made more omission errors in the IMT and DMT, which remained significant when we controlled for YHD (Table 4, middle). There were no significant differences in demographic variables, nor in drinking history measures, between the PDP+ ADP and the PDP– ADP. In addition, the PHP+ ADP and the PHP– ADP did not differ in questionnaire measures, risk-taking, or delay discounting.

2.3.3. Type 1/A–like versus type 2/B–like designation

2.3.3.1. Subtype differences in impulsivity. The type 1/A–like and type 2/B–like patient groups did not differ significantly in age, nor in number of co-morbid *DSM–IV* mood or anxiety diagnoses. However, in comparison with the type 2/B–like ADP, the type 1/A–like ADP had significantly more years of education [mean, 13.1 ± 2.3 and 14.7 ± 3.0 years, respectively; $t(41) = 2.009$, $P = .05$]. Commission error rates in the IMT (but not in the DMT) were significantly higher in type 2/B–like ADP, with no group difference in omission error rates (Table 4, right). In accordance, type 2/B–like ADP showed significantly lower RT to non-target stimuli in the IMT. The group difference in error rates (but not the RT difference) was no longer significant once the greater number of YHD in the type 2/B–like ADP was controlled for. There were no significant differences between the two groups in risk taking (with or without our controlling for education), nor in delay discounting. Finally, there was

Table 4
Relation between impulsivity and personal/parental drinking histories in male alcohol-dependent patients (ADP)

Measure	Correlation with age of onset of heavy drinking (n = 96)	Problem-drinking parent (PDP+) (n = 45)	No problem-drinking parent (PDP−) (n = 51)	Type 1–like male ADP (n = 22)	Type 2–like male ADP (n = 21)
Immediate memory task					
Omission errors	.18[a]	18.9% (13.0)	13.9% (10.7)**	15.7 (12.8)	20.4 (11.3)
Commission errors	−.15[a]	27.9% (12.0)	23.9% (13.2)	21.9 (11.0)	28.8 (11.1)**
Non-target response latency	.21[a,]**	513 (76)	548 (89)**	572 (18)	508 (18)**
Delayed memory task					
Omission errors	.15[a]	18.2% (15.4)	11.7% (10.9)**	10.0 (10.9)	14.1 (9.5)
Commission errors	−.08[a]	22.9% (16.5)	20.6% (15.7)	17.1 (14.6)	22.4 (15.8)
Non-target response latency	.06[a]	571 (120)	581 (115)	572 (24)	570 (28)
Risk-taking task					
Risky/nonrisky response ratio (all trials)	−.02[b]	0.122 (.073)	0.128 (.070)	0.153 (.077)	0.124 (.064)
Risky/nonrisky response ratio (trial maximum)	−.06[b]	0.275 (.145)	0.289 (.163)	0.332 (.174)	0.282 (.148)
Delay-discounting constant k (log transformed)	−.08	0.061 (.083)	0.072 (.140)	0.050 (.100)	0.040 (.046)
Buss-Perry Aggression Questionnaire	−.17	66.7 (14.0)	63.8 (14.7)	60.8 (12.3)	68.4 (15.6)*
Sensation Seeking Scale, Version 5	−.12	21.2 (5.9)	19.9 (5.9)	19.6 (5.1)	21.7 (6.0)
Barratt Impulsiveness Scale Version 11	−.30***	70.8 (10.3)	69.3 (12.7)	64.1 (13.6)	71.6 (12.8)*
Life History of Aggression	−.42****	21.4 (7.4)	18.8 (8.2)	14.7 (6.6)	22.8 (7.3)****
Age of onset of heavy drinking (>90 drinks/month)		22.7 (7.2)	23.8 (8.6)	31.0 (8.7)	17.7 (2.0)****
Estimated lifetime alcohol consumption (kg)	−.441****	555 (382)	627 (516)	428 (409)	641 (382)*
Controlling for age (adjusted mean)	−.582****	618	566	384	688***
Cumulative years of heavy drinking	−.329***	11.9 (7.1)	12.8 (8.0)	9.4 (9.1)	13.8 (6.4)*
MAST	−.428****	47.4 (19.9)	42.4 (16.3)	35.5 (11.5)	51.0 (16.0)****

Data are presented as Spearman rank-order correlations (column 2) and means and standard deviations (S.D.) (columns 3–6).
[a]Controlling for cumulative years of heavy drinking.
[b]Controlling for education level.
*$P < .10$, **$P < .05$, ***$P < .01$, ****$P < .001$ for significance level of either a correlation or a group difference.
MAST = Michigan Alcoholism Screening Test.

a trend toward higher BIS-11 and BPAQ scores and significantly higher LHA scores in type 2/B–like ADP.

2.3.3.2. Subtype differences and alcoholism severity. As expected from a median split of AOHD, the type 2/B–like ADP, in comparison with type 1/A–like ADP, had a significantly younger AOHD, in which 75% reported heavy drinking by age 19 years. Type 2/B–like ADP, in comparison with type 1A–like ADP, also reported heavier alcohol use chronicity on the basis of estimated lifetime drinks and cumulative YHD. In accordance, mean MAST scores were higher in the type 2/B–like group.

2.4. Discussion

The above-described findings collectively indicate minimal differences in laboratory impulsivity among male ADP as a function of either AOHD or presence of a biologic parent with a lifetime drinking problem (PDP+) when each variable was considered singly. When AOHD was singly related to the continuous impulsivity variables, only BIS-11 and LHA scores (questionnaire measures of impulsivity and aggressive behavior history) showed the predicted negative correlation with AOHD. When male ADP were divided into groups with (PDP+) versus without (PDP–) a parent with a lifetime incidence of problem drinking, only omission errors in the IMT were increased in the PDP+ group. When male ADP with primarily adolescent AOHD and a problem-drinking father (type 2/B–like ADP) were compared with male ADP with adult AOHD and no problem drinking parent (type 1/A–like ADP), however, the type 2/B–like ADP demonstrated more impulsivity in the CPT, greater alcoholism severity, and higher psychometric aggression.

The negative correlations between AOHD and scores on well-established questionnaire measures of impulsivity (BIS-11) and aggression history (LHA) were in accord with our hypothesis. These results raise a possibility that impulsive/aggressive individuals are more prone to begin heavy drinking as adolescents (Barnes et al., 1999; Tarter et al., 2003), leading, in turn, to elevated lifetime incidence of aggressive acts and consequences for those acts (Brown et al., 1996; Duncan et al., 1997; Wells et al., 2000). Unfortunately, however, these questionnaires did not delineate historical epochs of personality tendencies or behavior.

It is surprising that there were no significant correlations between behavioral impulsivity measures and the age at which male ADP first started drinking the equivalent of 90

drinks per month. One possibility for this may be a restriction in range of behavior impulsivity (scores) once analysis was confined to inpatients almost universally characterized by extremely disrupted lives and poor decision making. A related possibility is that the behavioral impulsivity measures were not sufficiently calibrated to detect individual differences, or they simply had lower construct validity than that of the psychometric measures.

Comparison of behavior in alcohol-dependent sons of one problem-drinking parent (or of two problem-drinking parents) with that of alcohol-dependent sons of non-problem drinkers indicated only elevated IMT/DMT omission error ("miss") rates in the PDP+ patients. We suspect the more rigorous ECF demands of the IMT/DMT made it a uniquely sensitive behavioral measure for detecting differences between ADP. Indeed, performance deficits on tasks of ECF in particular have characterized genetically "at risk" youth (Giancola et al., 1996), with electrocortical data [such as those measured during ECF challenge tasks (Fallgatter et al., 1998)] fostering theories of general CNS disinhibition in individuals prone to alcohol dependence (Begleiter & Porjesz, 1999; Carlson et al., 1999).

These findings collectively lend some support to theories that a positive family history of substance dependence is a risk factor for alcoholism only as an indirect correlate of greater behavior problems in subjects with a positive family history of substance dependence. This is reflected in the current study in the consistent negative relation between actual tally of aggressive behavior/consequences (LHA scores) and AOHD—considered singly or jointly with PDP+ status (as an analog of the type 2/B alcoholic) coupled with the limited group differences in behavioral and questionnaire measures on the basis of the PDP dichotomy. For example, in a multifactorial group design, Bauer and Hesselbrock (1999) reported that P300 (event-related potential) decrements were more specific to actual conduct disorder symptoms than to a positive family history of substance dependence per se. In a similar manner, among nondependent subjects, neuropsychologic test performance did not differ between subjects with and without a positive family history of substance dependence (Hesselbrock et al., 1985). Finally, in young adults, commission errors were more closely related to conduct disorder history than to alcoholism per se (Finn et al., 2002).

We had expected that isolation of male ADP on the basis of both AOHD and paternal problem drinking (to create type 1/A–like and type 2/B–like groups) would collectively amplify group differences in impulsivity measures, but this was not the case for several behavioral data. Were we able to incorporate presence versus absence of co-morbid psychiatric disorder as a third axis/dimension of a type 1/2 or A/B dichotomy, group differences might have been magnified. For example, among parents of children with disruptive behavior disorders, IMT/DMT commission errors correlated directly with general *DSM–IV* symptoms (Swann et al., 2002). Unfortunately, our sample size precluded incorporation of additional group-defining variables. Moreover, the lifetime incidence of co-morbid psychopathology was very high in the ADP in general, reducing potential individual differences among patients in these measures.

The post hoc analysis was added as an attempt to assess whether differences in impulsivity measures among male ADP would reflect traditional typologies. In part because of the post hoc nature, this analysis suffered from some limitations. First, the drinking history interview measures as well as the interview questionnaire items concerning parental drinking were not validated psychometric instruments, as is the Semi-Structured Assessment for the Genetics of Alcoholism (Hesselbrock et al., 1999), which is designed to rigorously characterize familial alcoholism. Rather, our measures were designed "in-house" to provide a general clinical picture of each patient and his background. Therefore, we were not able to make best-guess estimates of actual parental alcohol dependence. Moreover, we did not collect collateral informant reports on family drinking history, and we relied solely on the patient's report. We believe, however, that patient reports on parental drinking levels were informed by enhanced perspective on what constitutes problematic levels of drinking owing to each patient having undergone weeks of cognitive and group therapy sessions about alcoholism before the interview.

Second, we used a dimensional approach to drinking history that focused on the drinking behavior/quantity, but did not attempt to pinpoint a specific age when the subject first exceeded the symptom threshold to meet *DSM*–IV criteria for alcohol dependence. It is possible that AOHD as historically defined in our laboratory may not coincide with precise age of onset of alcohol dependence, although we suspect the two would be highly correlated. Third, our patient accrual did not feature a large enough dataset of female ADP for meaningful analysis of how AOHD and PDP+/– would relate to impulsivity in female ADP.

Finally, we acknowledge that our sample size, coupled with generally high co-morbidity in the patients, precluded classifying patients as type 1/A and type 2/B subgroups on the basis of traditional multidimensional criteria (Epstein et al., 2002). Instead, we were limited to isolating patients by only two key criteria to create type 1/A–"like" and type 2/B–"like" groups. We note, however, that MAST scores were much higher in the type 2/B group, supporting the suggestion that our approximation of the traditional typologies captured, to some degree, the markedly severe pathophysiology of alcohol dependence in the type 2/B alcoholic.

3. General discussion

Analysis 1 and Analysis 2 revealed two key findings. First, in comparison with CS, ADP in general showed increased impulsivity in several dimensions, including poorer

behavior control in a rapid stimulus-evaluation task (IMT/DMT), more severe devaluation of reward with delay to presentation (delay discounting), increased risky responding (RTT), and markedly higher scores on impulsivity and aggression questionnaire measures. Analysis of behavioral data alone successfully identified the majority of subjects in discriminant function analysis. Second, differences in laboratory impulsivity among male ADP, on the basis of either parental problem drinking or AOHD singly, were inconsistent and minimal. Age of onset of heavy drinking alone correlated only with questionnaire measures of impulsivity and aggression, and presence of at least one problem-drinking parent correlated solely with increased omission errors (“misses”) on the IMT/DMT. Third, behavior differences among male ADP, based approximately on the type 1/A versus type 2/B typology, offered some objective behavioral support for theses dichotomies (Babor et al., 1992; Cloninger, 1987), in which the type 2/B ADP indicated more behavioral impulsivity in the IMT/DMT, in addition to more severe alcohol use histories and consequences, as well as greater questionnaire impulsivity and aggression.

In conclusion, the comparison between ADP and CS supports the idea that even detoxified ADP undergoing daily cognitive therapy show increased impulsivity. Among male ADP, the earlier onset, paternal-history positive subjects are characterized not by increased impulsivity in strategic choice contexts compared with other ADP but, rather, by greater ECF impairment in cognitively demanding contexts, in which they showed a relative inability to restrain a prepotent motor response. As such, these findings reflect Cloninger’s initial characterization of persons with type 2 alcohol dependence at rest as “hypovigilant, distractible, impulsive, and easily bored” (Cloninger, 1987, p. 411). Finally, the type 2–like ADP were characterized by more severe alcohol dependence pathophysiology and by more extensive histories of aggressive acts and related consequences. Future research is needed to characterize impulsivity in women with alcohol dependence on the basis of these variables.

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