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Adolescent Heavy Episodic Drinking: Neurocognitive Functioning during Early Abstinence

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Abstract

Introduction—The present study investigated the rate and pattern of neuropsychological recovery in heavy episodic drinking teens during the initial days to weeks of abstinence from alcohol.

Method—Adolescents (ages 16–18) with histories of heavy episodic drinking (HED; $N=39$) and socio-demographically similar control teens (CON; $N=26$) were recruited from San Diego area schools. HED and CON were comparable on 5th grade standardized math and language arts test performance to ensure similar functioning prior to onset of substance use. Participants were administered three neuropsychological test batteries with 2-week intervals during a 4-week monitored abstinence period.

Results—HED teens performed worse overall than CON on tests of prospective memory ($p=.005$), cognitive switching ($p=.039$), inhibition task accuracy ($p=.001$), verbal memory ($p's<.045$), visuospatial construction ($p's<.043$), and language and achievement ($p's<.008$). The statistically significant group $\times$ time interaction for block design demonstrated normalization within the four weeks of abstinence for the HED ($p=.009$).

Discussion—This study identified cognitive performance deficits associated with heavy episodic drinking in adolescence during early abstinence and with sustained 4-week abstention. These findings suggest alcohol-related influences on several underlying brain systems that may predate the onset of alcohol abuse or dependence or take longer than four weeks to recover.

Mesh/Key Words

Adolescence; Neuropsychological Tests; Alcohol Consumption; Memory Deficits; Achievement; Adolescent Development

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Alcohol is the most commonly used intoxicant during adolescence. By their senior year of high school, 71% of students have consumed alcohol and 54% have been drunk (Johnston, O'Malley, Bachman, & Schulenberg, 2012). According to national data, 41% of high school seniors drank alcohol in the past month, and 23% of seniors reported heavy episodic drinking (5 drinks in males, 4 drinks in females within a 2-hour period) in the prior two weeks (Johnston et al., 2012). Compared to adults, adolescents drink alcohol less frequently but in higher doses, and such heavy episodic drinking among adolescents may be more harmful than consuming alcohol in moderation (1 or 2 drinks) every day (Tapert & Schweinsburg, 2005). Consuming greater quantities of alcohol in one sitting is concerning because heavy alcohol consumption associates with high risk, life-threatening outcomes including motor vehicle accidents, alcohol poisoning, illegal activities, school failure, and risky sexual behavior (Hingson, Heeren, Winter, & Wechsler, 2005). A growing number of animal and human studies also suggests that heavy episodic drinking appears to alter developmental trajectories and to interfere with normal neuroanatomical and neurocognitive development (Brown et al., 2008; Brown & Tapert, 2004; Crews, Braun, Hoplight, Switzer, & Knapp, 2000; Hommer et al., 1996; Nixon, Tivis, Ceballos, Varner, & Rohrbach, 2002; Spear & Varlinskaya, 2005).

Animal research suggests that adolescents are more vulnerable than adults to ethanol-induced decrements in functioning, especially following chronic, intermittent exposure to high levels of ethanol, which is considered the analog of 'heavy episodic drinking' in humans (White et al., 2000). Adolescent rats show more susceptibility to hippocampal injury (Nixon et al., 2002; Slawecki, Betancourt, Cole, & Ehlers, 2001; Ward et al., 2009) and to frontal-anterior cortical damage (Crews et al., 2000), and adolescent rats exposed to ethanol continue to show structural and functional abnormalities into adulthood (Slawecki, 2002; Slawecki & Roth, 2004; White et al., 2000). In particular, adolescent rats seem to experience (1) lower initial brain sensitivity to ethanol (Roehrs, Beare, Zorick, & Roth, 1994; Silveri & Spear, 1998), (2) abnormal development of sensitivity to alcohol-induced motor impairments (White et al., 2002), and (3) slower onset and magnitude of sedation following alcohol exposure (Little, Kuhn, Wilson, & Swartzwelder, 1996; Silveri & Spear, 1998; Swartzwelder, Richardson, Markwiese-Foerch, Wilson, & Little, 1998). That adolescents have reduced sensitivity to ethanol-induced motor impairing and sedative effects may theoretically allow youth to drink greater quantities of alcohol and attain higher blood alcohol concentrations with less sedation than would be expected in adulthood. The concurrence of reduced susceptibility to the sedating and motor impairing effects of alcohol with an enhanced vulnerability to alcohol-induced neuroanatomical and neurocognitive deficits presents a concerning effect during adolescence.

The extant human literature is consistent with animal research and suggests that heavy and recent alcohol exposure in adolescence is associated with poorer neuropsychological outcomes relative to those of non-drinkers. Studies of adolescents with alcohol use disorders (AUD) and of nonclinical populations of heavy episodic drinkers (HED) have consistently found deficits on executive function measures of planning, decision-making, verbal working memory, and inhibition (Giancola & Mezzich, 2000; Giancola & Moss, 1998; Giancola, Shoal, & Mezzich, 2001; Goudriaan, Grekin, & Sher, 2007; Moss, Kirisci, Gordon, & Tarter, 1994). Adolescents with AUDs also demonstrate deficits in verbal learning and

recognition discriminability (Brown, Tapert, Granholm, & Delis, 2000; Hanson, Medina, Padula, Tapert, & Brown, 2011; Tapert et al., 2001), and they have shown mild decrements in visuospatial memory (Brown et al., 2000) such as delayed recall of a complex figure (Squeglia, Spadoni, Infante, Myers, & Tapert, 2009).

Adolescent and young adult heavy drinkers commonly show decrements in aspects of visuospatial function including block constructions, spatial working memory, and pattern recognition (e.g., Brown et al., 2000; Sher, Martin, Wood, & Rutledge, 1997; Tapert & Brown, 1999; Tapert et al., 2002; Tapert et al., 2004; Weissenborn & Duka, 2003). Studies also suggest higher error rates among AUD youth (Tarter, Mezzich, Hsieh, & Parks, 1995; Tapert et al., 2004) and deficits in processing speed, motor speed, and attention (Medina et al., 2007; Sher et al., 1997). Finally, alcohol abusing adolescents have been shown to have significantly lower verbal and full scale IQ scores (Brown et al., 2000; Giancola et al., 2001) and lower academic achievement in math, reading, and spelling (Moss et al., 1994; Tarter et al., 1995) than their nondrinking peers.

While many of these studies report deficits across several neurocognitive domains, to date no study has investigated the rate and pattern of neuropsychological recovery in heavy episodic drinking teens throughout the initial days to weeks of abstinence from alcohol (Brown et al., 2008). Further, to the best of our knowledge, no existing study has ensured groups' comparable academic functioning that predates initiation of substance use (e.g., standardized academic test scores), which limits the ability to make generalizations about the impact of alcohol as compared to preexisting differences. By ensuring comparable, premorbid academic functioning and by following adolescents over several weeks of abstinence, this study aimed to elucidate the pattern of neurocognitive recovery during early abstinence from heavy alcohol use. Such knowledge may have important implications for clinical intervention and for strategies to improve academic functioning and reduce relapse risk.

The present study examined cognitive performance of youth engaged in heavy episodic drinking during adolescence, a critical time of brain development. Drinking and nondrinking participants completed a neuropsychological battery three times at 2-week intervals over four weeks of monitored abstinence. We aimed to (1) identify neuropsychological deficits associated with recent heavy episodic drinking during adolescence, and (2) determine whether alcohol-induced neurocognitive deficits improve with abstinence. Based on prior research, we hypothesized that (1) recent heavy episodic drinking youth would display neuropsychological deficits during early abstinence relative to similar nondrinking peers in the domains of executive functioning, learning and memory, visuospatial construction, working memory, attention, processing speed, and learning and achievement, and (2) abstaining heavy episodic drinkers would demonstrate improvements in these cognitive domains over a four week abstinence period when compared to nondrinking teens studied at comparable timepoints. In other words, we expected that prolonged abstinence would be linked to normalization of functions previously shown to be affected by alcohol.

Method

Participants

In accordance with the University of California, San Diego (UCSD) Human Research Protections Program and high school district policies, written informed assent (adolescent participant) and consent (parent/legal guardian) were obtained prior to participation. The current study examined 65 adolescents (ages 16–18) who were classified into two groups: heavy episodic drinkers (HED) ($N=39$) and nondrinking controls (CON) ($N=26$). Classification criteria for the heavy episodic drinkers (HED) included 50 lifetime drinking episodes, 1 past month heavy episodic drinking episodes, 1 alcohol withdrawal symptom in the prior two weeks, and limited experience with marijuana and other drugs. Nondrinking controls (CON) had fewer than 10 lifetime experiences with alcohol; had no history of heavy episodic drinking, alcohol withdrawal symptoms, or drug use; and did not meet criteria for heavy drinking status. HED and CON were drawn from the same schools and similar on socio-demographics including age, gender (46% female), ethnic composition (75% Caucasian), grades completed, socioeconomic status (Hollingshead, 1965), and recent grade point average. 5th grade standardized tests (i.e., California Standards Test) of math and language arts were also comparable between HED and CON (Table 1).

Participants were recruited from high schools and colleges throughout the San Diego area via mailings and flier distribution (Tapert et al., 2004). The fliers advertised an “Adolescent Development Project,” and no information regarding substance use criteria was described in the flier or discussed prior to screening. Participants responding by phone were informed of the study protocol and assessment schedule (see below), potential risks and benefits, and the confidentiality of their participation. All interested teens and their guardians underwent an extensive screening process to determine eligibility, and those potentially eligible (i.e., recent heavy episodic drinkers or non-drinkers) were mailed consent packets. After completing the assents/consents, teens and their guardians participated separately in more detailed, structured clinical interviews performed by a different interviewer for each family member.

To minimize confounds, exclusionary criteria included history of a DSM-IV Axis I disorder other than alcohol abuse, extensive other drug use, head trauma, a learning disorder, neurological dysfunction, or serious medical illness; family history of bipolar I or psychotic disorder; significant prenatal alcohol or drug exposure; sensory problems; use of psychoactive medications; and substance use during the abstinence protocol. Overall, 3% of the 2,300 teens who responded to the recruitment fliers (approximately 15,000 were distributed) initiated the study. Others did not enroll because they were non-users who were not similar to heavy episodic drinkers (46%), had a history of a psychiatric disorder or psychotropic medication use (25%), used marijuana or other drugs extensively (22%), or were eligible but not interested in the abstinence protocol (7%).

Measures

Structured clinical interview—After providing their assent/consent, adolescent participants and their parents were separately administered confidential structured clinical

interviews assessing demographics, social and academic functioning (Brown, Vik, & Creamer, 1989), family history of psychiatric disorders using the structured clinical interview of Family History Assessment Module Screener (Rice et al., 1995), and personal history of Axis I psychiatric disorders using the Computerized Diagnostic Interview Schedule for Children (DISC; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Parents completed the Child Behavior Checklist (CBCL; Achenbach & Ruffle, 2000) and teens completed the Youth Self Report (YSR; Achenbach & Ruffle, 2000) to assess levels of internalizing and externalizing psychopathology. Teen substance use history was documented using the Customary Drinking and Drug Use Record (CDDR; Brown et al., 1998), which assessed lifetime and recent tobacco, alcohol, and drug use (12 classes), withdrawal symptoms, DSM-IV abuse and dependence criteria, and other negative consequences associated with heavy drinking. Good inter-rater reliability, internal consistency, and test-retest ability have been demonstrated with the CDDR among adolescent participants (Brown et al., 1998; Stewart & Brown, 1995). The Timeline Followback (TLFB; Sobell & Sobell, 1992) modified to include other drugs was used to collect frequency and quantity of alcohol, marijuana, and other drug use for the six weeks prior to initiating the protocol and for the four week duration in the study.

Neuropsychological test battery—The thrice-repeated neuropsychological (NP) battery assessed five key domains: (1) *executive functioning*, (2) *learning and memory*, (3) *visuospatial construction*, (4) *working memory, attention, processing efficiency, and psychomotor speed*, and (5) *language and achievement*. Standardized neuropsychological tests included the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) Vocabulary and Block Design; Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997): Arithmetic, Digit Span, and Digit Symbol; California Verbal Learning Test - Second Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000); Rey-Osterrieth and Taylor Complex Figures copy and 30-minute delayed recall (Osterrieth, 1944; Strauss & Spreen, 1990; Taylor, 1989); Delis-Kaplan Executive Functioning System (D-KEFS; Delis, Kaplan, & Kramer, 2001) Trail Making and Color-Word Interference; a modified version of the Memory for Intentions Test (MIST; Raskin & Buckheit, 1999) to examine prospective memory; and the Wide Range Achievement Test-4 (WRAT-4; Wilkinson & Robertson, 2006) Reading subtest. Alternate forms were used when possible to reduce practice effects (i.e., Rey-O figure at times 1 and 3, and Taylor figure at time 2; alternation of CVLT-II lists also).

State measures—At each testing session, teens completed the Hamilton Depression and Anxiety Rating Scales (Hamilton, 1996) and the state scale of the Spielberger State Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970). These measures have well-established psychometric properties (Hamilton, 1996; Spielberger et al., 1970). The Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988) assessed baseline mood prior to testing.

Procedures

All eligible CON and HED participants who initiated study protocol were monitored for abstinence (see below) and assessed using neuropsychological tests at three timepoints over

their four-week participation. At each timepoint, a 150-minute NP battery was administered by a trained neuropsychometrist. Prior to each session, all participants provided a urine sample, submitted a breathalyzer reading (Intoximeter, St. Louis, MO), and completed affective state and personality questionnaires. Upon completion of the NP battery, the participants rated their level of focus, how hard they tried, how seriously they took the session, and level of effort on a scale of 1 (low) to 10 (high). Participants were compensated for their participation and abstinence throughout the protocol with the largest payment at the third assessment wave to encourage study completion.

At all appointments, adolescents participated in a toxicology screening protocol to minimize the possibility of their substance use. HED were first studied within 14 days of heavy episodic drinking and subsequently at two 2-week intervals over four subsequent weeks of monitored abstinence (1st testing session: $M = 5.56$ days since last HED episode, $SE = 0.60$; 2nd testing session: $M = 19.52$ days since last HED episode, $SE = 0.70$; 3rd testing session: $M = 32.81$ days since last HED episode, $SE = 0.70$). CON teens followed the same abstinence monitoring and neuropsychological testing protocol at the same time intervals. Abstinence was monitored and facilitated through behavioral and biochemical procedures including 10-panel drug urine testing and breathalyzer. Supervised urine and breath samples were collected three times per week to assess for recent use of alcohol with ethyl glucuronide (EtG) and ethyl sulfate (EtS) metabolites and use of methamphetamines, cocaine, THC (cannabis), benzodiazepines, methadone, barbiturates, ecstasy, opiates, PCP, and oxycodone. We utilized an observed sample collection procedure to minimize the likelihood of participant tampering. Samples were analyzed by Redwood Toxicology (Santa Rosa, CA) using cloned enzyme donor immunoassay (CEDIA) kits. If abstinence maintenance was confirmed via subject self-report, breathalyzer, and quantitative toxicology results, participants continued to be scheduled for neuropsychological assessments. Abstinence was also facilitated using a standardized Motivational Interviewing protocol (Miller & Rollnick, 1991) demonstrated to encourage the maintenance of abstinence for adolescents in prior research (Brown, Anderson, Schulte, Sintov, & Frissel, 2005; Schweinsburg et al., 2005). Eleven HED teens drank alcohol during the abstinence period (detected via positive ETG toxicology screen and then confirmed with self-report) and data collected after their alcohol use were excluded from the analyses.

Data analyses

Chi-square tests (for categorical variables) and t-tests (for continuous variables) compared socio-demographic characteristics between groups. To test for HED-CON *differences and changes over time*, we utilized linear mixed effects models to look for group effects at time 1 and time 3, time effects, and group by time interactions. In the mixed model analyses, the fixed variables were timepoint and group, the random variable was the individual subject, and the dependent variable was the standard, age-scaled, or raw score of the NP domain in question. These analyses modeled error structures among repeated dependent variables by using fixed effects, specifying a covariance structure for both between and within subjects, and fitting the means model accounting for specific covariates (Singer & Willett, 2003; Rabe-Hesketh & Skrondal, 2005; Gelman & Hill, 2007). Because groups differed in their

CBCL externalizing behavior ($p=.002$), family history of alcohol dependence ($p=.004$), and lifetime marijuana use ($p<.001$), the mixed model analyses controlled for these variables.

Results

Demographics, substance use, and mood

As mentioned previously, the groups were similar on socio-demographic characteristics (Table 1). To ensure CON and HED were comparable on pre-drinking academic performance, 5th grade California Standards Test (CST) scores in language arts and mathematics were examined, and the groups did not differ statistically ($p's>.05$). While standardized test scores of CON were slightly higher than those of HED (Language Arts: 370.27 ± 11.06 and 354.80 ± 11.48 , respectively, $p=.141$; Math: 394.73 ± 21.59 and 352.30 ± 14.60 , respectively, $p=.064$), both groups ranged from the "basic" to "proficient" level. Participants were typically from lower-middle to upper-middle class families and of average to above-average intelligence. Heavy episodic drinkers self-reported slightly higher CBCL externalizing behavior ($p=.002$), although still within normal range on average.

Lifetime and recent (i.e., days/month in the 3 months prior to initiating study) heavy episodic drinking episodes were, as designed, greater in the HED sample ($p's<.001$). The lifetime marijuana episodes in HED youth were modest for a population with such high levels of drinking experience (average alcohol exposure of 230.50 ± 27.50 vs. average marijuana exposure of 57.62 ± 11.46). HED youth had limited lifetime episodes with other drugs (Table 1).

STAI anxiety and Hamilton depression ratings were similar and within the normal range at all assessments, and both groups had similar PANAS pre-testing mood states ($p's>.05$). Additionally, groups did not differ in their effort ratings following each NP session with both groups indicating moderately high levels of focus, effort, and seriousness.

Neuropsychological performance

Neuropsychological test scores at each of the three test sessions are presented in Table 2. The following analyses investigated neurocognitive differences and changes in adolescent heavy episodic drinkers compared to nondrinking teens. A False Discovery Rate (FDR) correction for multiple comparisons was used to recalculate p -values from the mixed models (Benjamini & Hochberg, 1995). All reported p -values were generated from the FDR correction.

Executive functioning—The MIST examined prospective memory: abilities to monitor time, maintain a planned activity in mind, and initiate appropriate action. HED youth performed significantly worse on the MIST at the first timepoint (b (SE) = -1.09 (0.30), $z = -3.58$, $p=.005$) and did not improve to levels of CON over repeated testing ($p's>.106$; Figure 1). CON performed consistently across time ($p's>.483$) with an overall 2% increase in performance, on average, from Time 1 to Time 3. HED showed most improvements from the first to second timepoint (i.e., between weeks 1 and 3 of abstinence, on average). HED showed a 6% increase in performance from Time 1 to Time 3, but this improvement still left their performance 11% lower than that of CON. HED youth performed worse on the D-

KEFS Trail Making Number-Letter Switching at the first timepoint (b (SE) = -1.15 (0.46), $z = -2.49$, $p = .039$) and did not improve to levels of CON ($p > .238$; Figure 1). Both CON and HED showed a 17% score increase from Times 1 to 3, with HED consistently performing 8–10% lower. On D-KEFS Color-Word Interference, HED made 50–100% more errors than CON at Time 1 (b (SE) = 2.56 (0.79), $z = 3.24$, $p = .001$) and across time ($p > .382$; Figure 1). While HED accuracy improved with time, they still made nearly double the errors as CON by the third timepoint. No initial differences or group $\times$ time interactions were identified on D-KEFS Color-Word Interference Inhibition Switching trial ($p > .090$).

Learning and memory—On tests of verbal memory, HED youth showed poorer performance at Time 1 on short delay cued recall (b (SE) = -0.60 (0.27), $z = -2.26$, $p = .044$), long delay cued recall (b (SE) = -0.76 (0.24), $z = -3.19$, $p = .005$), and long delay free recall (b (SE) = -0.70 (0.23), $z = -2.98$, $p = .010$). HED verbal memory did not improve to levels of CON, performing 0.36–0.48 standard deviations below CON across time ($p > .292$; Figure 2). Although HED scores were consistently lower, they did not differ statistically at the first timepoint or across time on verbal learning (CVLT-II total words recalled trials 1–5; $p > .288$) or visuospatial memory (Rey-Osterrieth and Taylor Complex Figures 30-minute delayed recall; $p > .280$).

Visuospatial construction—On WASI Block Design, HED performed approximately 9% worse than CON at the initial testing (b (SE) = -5.22 (2.15), $z = -2.43$, $p = .039$). A group $\times$ time interaction was a trend at the second testing (b (SE) = 2.33 (1.24), $z = 1.88$, $p = .059$) and statistically significant at the third testing (b (SE) = 3.63 (1.38), $z = 2.63$, $p = .009$) with HED improving their performance to that of CON (Figure 3). From Time 1 to Time 3, CON showed a 7% improvement in Block Design performance, while HED scores improved 9% by Time 2 and another 6% from Time 2 to Time 3, showing the bigger percent change from weeks 1–3 of abstinence, on average, and continued improvement from weeks 3–5 of abstinence, on average. On direct copy of the Rey-Osterrieth and Taylor Complex Figures, HED performed more poorly than CON at the initial testing (b (SE) = -2.18 (.99), $z = -2.21$, $p = .043$) and did not improve with time ($p > .585$), with HED 6–8% worse than CON across assessments (Figure 3).

Working memory, attention, processing efficiency, and psychomotor speed

Groups performed similarly and did not differ statistically in their performance at the first testing or across time on all measures of verbal working memory [WAIS-III Digit Span backwards ($p > .288$) or Arithmetic ($p > .290$)], attention and processing efficiency [D-KEFS Trail Making Visual Scanning task ($p > .288$); WAIS-III Digit Span forward ($p > .634$); D-KEFS Color-Word Interference Color Naming ($p > .291$) and Word Reading ($p > .796$)], and psychomotor speed [WAIS-III Digit Symbol ($p > .232$); D-KEFS Trail Making Number Sequencing ($p > .474$) and Letter Sequencing ($p > .568$)].

Language and achievement—HED performed, on average, 12% worse than CON on WASI Vocabulary (average versus high average range; $p = .005$) and, on average, 7% worse than CON on WRAT-4 Reading (both groups in average range; $p = .008$). Given the statistically (though not clinically) significant difference in WASI Vocabulary scores

between groups, we also conducted the NP analyses covarying for Vocabulary T-score. All results remained consistent, except the finding for the initial difference on the MIST was reduced to a trend ($p=.058$). Of note, covarying for 5th grade math and language arts standardized test scores did not alter findings.

Discussion

This study examined neurocognitive differences and patterns of recovery in abstinent, adolescent heavy episodic drinkers compared to nondrinking peers. Importantly, groups had comparable California Standards Test (CST) math and language performance on standardized tests that pre-date initiation of drinking in the heavy episodic drinking group, suggesting similar functioning prior to alcohol use. We found that adolescents with histories of an average of over 200 lifetime drinking episodes who initiated heavy episodic drinking at an average age of 15.33 differed from socio-demographically similar nondrinkers across several neuropsychological domains both during the early stages of abstinence and with continued abstinence. The findings are consistent with prior results in youth with much greater alcohol use histories (e.g., Brown et al., 2000; Giancola & Moss, 1998). Heavy episodic drinking adolescents performed worse on prospective memory, cognitive switching, inhibition task accuracy, verbal memory, visuospatial abilities, and language and achievement.

Studies on adolescents with alcohol use disorders have consistently found deficits in executive functioning, and the current study, which focused on a nonclinical population of heavy episodic drinkers, also identified deficiencies in prospective memory, cognitive switching, and inhibition task accuracy. Prospective memory requires multiple skills: monitoring time, remembering the task to be performed, and self-initiating the task at the appropriate time. Poorer performance in prospective memory, cognitive switching, and response inhibition may apply to academic and professional settings, as goal-oriented behavior and cognitive flexibility are essential to stay on task, quickly shift mental modes, and respond accurately.

Longer lasting and heavier drinking patterns among adolescents have been linked to disruptions in the hippocampus, a brain structure critical for learning and memory, with adolescent drinkers showing smaller hippocampal volumes and disturbed hippocampal white matter integrity (De Bellis et al., 2000; Medina, Schweinsburg, Cohen-Zion, Nagel, & Tapert, 2007; Nagel, Schweinsburg, Phan, & Tapert, 2005). Our study involved youth earlier in their drinking careers and identified poorer performance in both short delay and long delay verbal memory that did not resolve within five weeks of abstinence, on average. Poorer verbal memory is likely to have a significant influence on daily functioning as recall of verbal information occurs when following instructions, remembering lists, taking exams, and other daily activities.

Our finding of poorer visuospatial abilities among heavy episodic drinking adolescents is consistent with many adolescent studies reporting an association between visuospatial impairments and frequency of alcohol use (Brown et al., 2000; Hanson et al., 2011; Squeglia et al., 2009) and withdrawal symptoms (Brown et al., 2000; Tapert et al., 2001; Tapert et al.,

2002; Tapert and Brown, 1999). We found initial differences on two- and three-dimensional constructions (i.e., complex figure drawing, block design); however, only performance on the block constructions showed improvements to levels of nondrinking peers, while complex figure reproduction remained poorer across time. This finding could suggest more recovery of mental rotation and spatial navigation functions, whereas spatial organization and fine motor skills may take longer to recover.

Alcohol dependent adolescents have frequently demonstrated significantly lower verbal IQ and reading achievement scores (Brown et al., 2000; Giancola et al., 2001; Moss et al., 1994; Tarter et al., 1995). The present study's finding of poorer vocabulary and reading scores in nonclinical, heavy episodic drinking youth is consistent with such prior research. Given that the drinkers and nondrinkers had comparable math and language scores in 5th grade, it is possible that the poorer vocabulary and reading skills observed in adolescence may be at least partially due to related environment, brain, or behavior changes occurring after the onset of heavy drinking.

Unlike prior research, our study did not identify statistically significant deficits in verbal learning, visuospatial memory, working memory, attention, or psychomotor speed when comparing heavy episodic drinking youth, who have not yet experienced substantial alcohol related problems, to nondrinking youth. Intensity of alcohol use may not yet be severe enough to manifest in differences. Alternatively, methodological differences (e.g., variations in abstinence protocol or drug use eligibility criteria; sample size) may also have contributed to incongruent findings.

The present design allowed us to identify significant improvements across time, suggesting that both groups improved with repeated testing and that the two-week interval between neuropsychological assessments is short enough to evidence practice effects. The improvement seen across time supports the importance of including controls to compare to heavy episodic drinkers. As expected, tasks on which both groups improved with repeated testing showed greater performance increases in the heavy drinkers. Despite greater improvement (i.e., steeper slope) from their Time 1 to Time 3 assessment, heavy drinkers did not perform to levels of nondrinkers on prospective memory, cognitive switching, inhibition task accuracy, verbal memory, or two-dimensional visuospatial construction, performing approximately 5–10% lower and committing 50–100% more errors across time. Assuming adolescents respond to initial abstinence in a similar pattern as adults, they would show an initial improvement in attention, memory, and visuospatial skills within the first two weeks of abstinence, with gradual recovery thereafter (Bates, Voelbel, & Buckman, 2005; Fein, Bachman, Fisher, & Davenport, 1990; Reed, Grant, & Rourke, 1992; Sullivan, Rosenbloom, & Pfefferbaum, 2000). Our study detected significant improvements in prospective memory, cognitive switching, inhibition task accuracy, and visuospatial abilities from weeks 1 to 3 of abstinence, on average. However, we only identified an improvement significant enough to bring drinkers' performance to that of nondrinkers on the three-dimensional visuospatial construction task. It may be that a longer period of recovery is needed before the expected improvements seen in adult populations become evident among adolescent drinkers.

We demonstrated that we can repeatedly and intensively assess functioning of 16- to 18-year-olds with and without histories of heavy episodic drinking. Our efforts to measure sustained abstinence were sufficient for this length of time. We went to great lengths to measure continuous abstinence, including the collection of urine samples from all participants on Sunday mornings. These procedures were necessary to detect alcohol exposure in 11 heavy episodic drinking participants (who were discontinued from the study) and to report confidently abstinence in the other drinkers. The study also provides preliminary evidence to support the success of the motivational interviewing protocol to sustain abstinence in a population of heavy episodic drinking adolescents (Brown et al., 2005; Miller & Rollnick, 1991; Schweinsburg, et al., 2005).

This study featured many design strengths but has several limitations. First, the sample was carefully selected yet modest in size, which limited our statistical power and prevented further exploration of associations between neuropsychological performance and gender, family history, or alcohol use characteristics. Second, as expected, heavy episodic drinkers had some exposure to marijuana or other drugs. While we did covary for marijuana exposure in the mixed models, it is possible that other substance use, although limited, may have contributed to group differences. Of note, the heavy episodic drinkers consumed alcohol four times more than marijuana in their lifetimes, and had an average of approximately ten lifetime experiences with other drugs. Third, while the study established a relationship between heavy episodic drinking and neurocognitive impairments among adolescents, the directionality and causality can only be determined by longitudinal studies that examine adolescents prior to any substance involvement.

In summary, consistent with our hypotheses and with previous studies, 16- to 18-year-old heavy episodic drinking adolescents with recent, frequent drinking and limited other drug exposure exhibit modest but significant neurocognitive functioning differences during early abstinence and, in many cases, with sustained abstinence. Though requiring replication, we found decrements in prospective memory, cognitive switching, inhibition task accuracy, verbal memory, visuospatial abilities, and language at the first testing that improve but not to levels of nondrinking peers even after four weeks of sustained abstinence (with the exception of 3-dimensional block construction). In the present sample, scores on tasks of verbal learning, working memory, attention, and psychomotor speed did not differ as a function of youth drinking experience. Our findings, coupled with extant literature in this field, suggest that deficient neuropsychological functioning is present among adolescents with recent histories of heavy episodic drinking relative to their nondrinking peers. These cognitive differences persist across four to six weeks of abstinence, suggesting a possible alcohol-induced impact to underlying brain systems, particularly given that groups were comparable on pre-drinking academic test performance. This possibility coincides with the animal literature's finding that adolescence is a time of enhanced sensitivity to the neurotoxic effects of alcohol.

This study has the potential to contribute to improved methods for (1) measuring changes on important neurocognitive, affective, and behavioral domains associated with heavy episodic drinking in adolescents, and (2) monitoring and facilitating real life behavioral improvements associated with abstinence from alcohol. Poorer performance in prospective

memory, cognitive switching, inhibition accuracy, verbal memory, visuospatial ability, and language may affect adolescents' daily experiences in academic or occupational settings. With this knowledge, educators may be able to improve outcomes for these teens by considering their cognitive abilities during instruction and employing strategies of repetition and active learning to more effectively engage and instruct a population of heavy episodic drinking youth (Myers, Brown, & Mott, 1993; Roehrich & Goldman, 1993).

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Figure 1.

Executive functioning tasks of Memory for Intentions Test (MIST), D-KEFS Trail Making Number-Letter Switching, and D-KEFS Color Word Interference by heavy episodic drinking youth (HED) and controls (CON). ^a, ^b

^aFrom linear mixed effects models with standard error bars, controlling for externalizing behavior, family history of alcohol or drug related dependence, and lifetime marijuana use at three assessments over four weeks of abstinence. Average number of days since last heavy episodic drinking episode in HED youth was 5.56 days at Timepoint 1, 19.52 days at Timepoint 2, and 32.81 days at Timepoint 3.

Figure 2.
CVLT-II short and long delay verbal memory z-scores by heavy episodic drinking youth (HED) and controls (CON). ^{a, c}

^bAt the first timepoint, HED youth performed worse on MIST ($p=.005$) and Trail Making Switching standard score (SS; $p=.039$) and committed more errors than CON on Color Word Interference Inhibition ($p=.001$). Performance did not improve with time on all three tasks ($p's>.238$).

^cHED evidenced poorer short delay cued recall ($p=.044$), long delay cued recall ($p=.005$), and long delay free recall ($p=.010$) than CON at the initial testing. Poorer verbal memory continued across time ($p's>.292$).

Figure 3. Visuospatial construction tasks of Rey-Osterrieth and Taylor Complex Figures (CF) and Wechsler Abbreviated Scale of Intelligence (WASI) Block Design by heavy episodic drinking youth (HED) and controls (CON). ^{a, d}

^dHED performed more poorly than CON at the initial testing ($p=.043$) and across time ($p's>.585$) on 2-dimensional CF copying. On 3-dimensional block construction, HED performed worse than CON at the initial testing ($p=.039$) but improved their performance to that of CON by the third testing ($p=.009$), showing the biggest improvement between, on average, weeks 1–3 of abstinence.

Table 1

Demographic and Substance Use Characteristics for Control (CON) and Heavy Episodic Drinking (HED) Adolescents (ages 16–18)

	CON (N=26) M (SE)	HED (N=39) M (SE)	<i>p</i> - value
Age	17.61 (0.12)	17.71 (0.13)	.596
Gender	12F, 14M	18F, 21M	.601
% Caucasian	73%	77%	.687
% Family history positive ^a	31%	69%	.004
Grades completed	11.00 (0.12)	11.05 (0.15)	.805
Hollingshead SES score ^b	23.73 (2.41)	27.42 (2.30)	.285
Grade point average	3.64 (0.11)	3.32 (0.11)	.058
CBCL Externalizing T-score ^c	41.46 (1.60)	49.03 (1.49)	.002
CBCL Internalizing T-score ^c	43.54 (1.80)	45.58 (1.71)	.424
5 th grade standardized language arts score ^d	370.27 (11.06)	354.80 (11.48)	.141
5 th grade standardized mathematics score ^d	394.73 (21.59)	352.30 (14.60)	.064
Lifetime episodes using alcohol	0.73 (0.41)	230.50 (27.50)	.000
HED episodes in the 3 months prior to study	0.00	16.62 (1.81)	.000
Age at first HED episode	n/a	15.33 (0.18)	
Lifetime episodes using marijuana	0.00	57.62 (11.46)	.000
Marijuana days/month, 3 months prior to study	n/a	2.44 (0.70)	
Lifetime episodes using other drugs	0.00	9.90 (2.90)	.008
Time 1: days since heavy episodic drinking	n/a	5.56 (0.60)	
Time 2: days since heavy episodic drinking	n/a	19.52 (0.70)	
Time 3: days since heavy episodic drinking	n/a	32.81 (0.70)	

^a A first-degree biological relative with alcohol or drug related dependence

^b Hollingshead (1965) SES (socioeconomic status): Higher scores = lower SES

^c CBCL: Child Behavior Checklist

^d Scaled score on California Standards Test (CST)

Table 2

Marginal Means (SE) of Control (CON) and Heavy Episodic Drinking (HED) Adolescents (age 16–18) Demonstrate Differences and Changes in Neuropsychological Performance with Extended Abstinence

	Time 1		Time 2		Time 3	
	CON (N=26) M (SE)	HED (N=39) M (SE)	CON (N=26) M (SE)	HED (N=31) M (SE)	CON (N=26) M (SE)	HED (N=28) M (SE)
Executive Functioning						
MIST Intention Total raw ^a	7.67 (0.23)	6.58 (0.19)	7.71 (0.22)	7.14 (0.20)	7.83 (0.22)	7.01 (0.20)
D-KEFS Trail Making Number-Letter Switching SS ^a	10.71 (0.34)	9.56 (0.28)	11.86 (0.34)	11.15 (0.30)	12.56 (0.34)	11.61 (0.30)
D-KEFS Color-Word Inhibition Switching SS	11.75 (0.43)	10.55 (0.36)	12.71 (0.43)	12.05 (0.38)	13.48 (0.42)	12.45 (0.38)
D-KEFS Color-Word Total Errors ^a	4.40 (0.58)	6.95 (0.49)	2.94 (0.58)	4.71 (0.53)	2.47 (0.58)	4.68 (0.54)
Learning and Memory						
Complex Figure Accuracy raw (30-min delay)	16.40 (0.92)	15.82 (0.77)	20.98 (0.92)	19.97 (0.84)	21.63 (0.93)	19.41 (0.85)
CVLT-II Trial 1–5 Total Recall T-score	52.02 (1.95)	52.86 (1.89)	50.04 (2.48)	50.97 (2.46)	59.97 (2.96)	55.41 (2.55)
CVLT-II Short Delay Cued Recall z-score ^a	0.36 (0.19)	−0.24 (0.16)	0.44 (0.19)	−0.40 (0.17)	0.84 (0.19)	0.38 (0.17)
CVLT-II Short Delay Free Recall z-score	0.16 (0.19)	−0.18 (0.16)	−0.05 (0.19)	−0.38 (0.17)	0.68 (0.19)	0.54 (0.17)
CVLT-II Long Delay Cued Recall z-score ^a	0.37 (0.18)	−0.40 (0.15)	0.37 (0.18)	−0.47 (0.16)	0.71 (0.18)	0.35 (0.16)
CVLT-II Long Delay Free Recall z-score ^a	0.42 (0.17)	−0.28 (0.14)	0.00 (0.17)	−0.66 (0.15)	0.88 (0.17)	0.40 (0.16)
Visuospatial Construction						
WASI Block Design T-score ^b	59.40 (1.43)	54.19 (1.39)	61.77 (1.53)	58.89 (1.49)	63.75 (1.62)	62.16 (1.51)
Complex Figure Accuracy raw (Direct Copy) ^a	27.89 (0.73)	25.70 (0.61)	29.31 (0.73)	26.93 (0.65)	28.74 (0.73)	27.05 (0.66)
Working Memory						
WAIS-III Digit Span Backward SS	7.17 (0.55)	7.94 (0.54)	8.854 (0.61)	8.37 (0.55)	7.86 (0.68)	8.97 (0.61)
WAIS-III Arithmetic SS	11.96 (0.61)	11.95 (0.60)	12.65 (0.67)	12.30 (0.65)	13.88 (0.71)	13.19 (0.66)
Attention						
D-KEFS Trail Making Visual Scanning SS	11.09 (0.28)	11.57 (0.23)	12.10 (0.28)	12.37 (0.24)	12.68 (0.28)	12.69 (0.25)
WAIS-III Digit Span Forward SS	11.01 (0.39)	11.01 (0.33)	11.28 (0.39)	11.47 (0.35)	11.66 (0.39)	11.52 (0.35)
Processing Efficiency						
D-KEFS Color-Word Int.: Color Naming SS	10.17 (0.52)	9.59 (0.44)	10.40 (0.51)	10.54 (0.46)	10.71 (0.52)	10.00 (0.46)

	Time 1		Time 2		Time 3	
	CON (N=26) M (SE)	HED (N=39) M (SE)	CON (N=26) M (SE)	HED (N=31) M (SE)	CON (N=26) M (SE)	HED (N=28) M (SE)
D-KEFS Color-Word Int.: Word Reading SS	11.35 (0.45)	10.99 (0.38)	11.62 (0.45)	11.00 (0.39)	11.66 (0.45)	11.15 (0.40)
Psychomotor Speed						
WAIS-III Digit Symbol SS	10.17 (0.50)	9.14 (0.42)	12.48 (0.50)	10.56 (0.43)	12.94 (0.50)	11.13 (0.43)
D-KEFS Trail Making Number Sequencing SS	10.96 (0.34)	11.03 (0.28)	12.80 (0.34)	12.77 (0.31)	13.30 (0.34)	13.03 (0.31)
D-KEFS Trail Making Letter Sequencing SS	11.39 (0.40)	11.09 (0.34)	12.46 (0.40)	12.46 (0.36)	13.42 (0.40)	13.29 (0.36)
Language and Achievement						
WASI Vocabulary T-Score ^c	62.69 (1.25)	54.90 (1.33)				
WRAT-4 Reading Standard Score ^c			105.85 (1.57)	98.81 (1.42)		

Note: SS = scaled score; Complex Figure = Rey-Osterrieth and Taylor Complex Figures copy and 30-minute delayed recall (Osterrieth, 1944; Strauss & Spreen, 1990; Taylor, 1989); D-KEFS = Delis-Kaplan Executive Functioning System (Delis, Kaplan, & Kramer, 2001); CVLT-II = California Verbal Learning Test - Second Edition (Delis et al., 2000); MIST = Memory for Intentions Test (Raskin & Buckheit, 1999); WASI = Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999); WAIS-III = Wechsler Adult Intelligence Scale-III (Wechsler, 1997); WRAT-4 = Wide Range Achievement Test-4 (Wilkinson & Robertson, 2006)

^a Initial group difference (at Time 1) but no group $\times$ time interaction

^b Initial group difference (at Time 1) and group $\times$ time interaction at 3

^c Group difference