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Inhibition during Early Adolescence Predicts Alcohol and Marijuana Use by Late Adolescence

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Abstract

Objective—Adolescent substance use has been associated with poorer neuropsychological functioning, but it is unclear if deficits predate or follow the onset of use. The goal of this prospective study was to understand how neuropsychological functioning during early adolescence could predict substance use by late adolescence.

Method—At baseline, participants were 175 substance use-naïve healthy 12–14 year-olds (41% female) recruited from local schools. Participants completed extensive interviews and neuropsychological tests. Each year, participants' substance use was assessed. By late adolescence (ages 17–18), 105 participants transitioned into substance use, while 75 remained substance-naïve. Hierarchical linear regressions examined how baseline cognitive performance predicted subsequent substance use, controlling for common substance use risk factors (i.e., family history, externalizing behaviors, gender, pubertal development, and age).

Results—Poorer baseline performance on tests of cognitive inhibition-interference predicted higher follow-up peak drinks on an occasion ($\beta = -.15$; $p < .001$), more days of drinking ($\beta = -.15$; $p < .001$), and more marijuana use days ($\beta = -.17$; $p < .001$) by ages 17–18, above and beyond covariates. Performances on short term memory, sustained attention, verbal learning and memory, visuospatial functioning, and spatial planning did not predict subsequent substance involvement ($ps > .05$).

Conclusions—Compromised inhibitory functioning during early adolescence prior to the onset of substance use was related to more frequent and intense alcohol and marijuana use by late adolescence. Inhibition performance could help identify teens at risk for initiating heavy substance use during adolescence, and potentially could be modified to improve outcome.

Keywords

adolescence; alcohol; cannabis; inhibition; longitudinal; marijuana; neuropsychological functioning

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INTRODUCTION

Adolescence is a period of dramatic physical, emotional, and social changes that contribute to substantial increases in alcohol and drug involvement (Brown et al., 2008). Nearly a third of US 8th graders report lifetime alcohol use and 15% report lifetime marijuana use. These rates increase to 65% for alcohol and 45% for marijuana by 12th grade (Johnston, O'Malley, Bachman, & Schulenberg, 2013). Because of the potentially deleterious neurocognitive impact of alcohol and drug use, factors involved in the initiation and escalation of substance use during adolescence require careful consideration and could provide crucial information for preventions and interventions.

Adolescent alcohol or other drug involvement has been linked to poorer neuropsychological functioning over time (Jacobus & Tapert, 2013a, 2013b; Squeglia, Spadoni, Infante, Myers, & Tapert, 2009). However, burgeoning research suggests that neuropsychological deficits on a range of cognitive tests predate substance use, leaving youth more vulnerable to initiation of substance use. For example, poorer baseline working memory in early-adolescent non-drinkers was related to increased alcohol use by mid-adolescence (Khurana et al., 2013), and worse scores on tests of attention at ages 14 to 16 have been associated with greater substance use frequency at ages 22 to 24 (Tapert, Granholm, Leedy, & Brown, 2002). Furthermore, adolescents with better language skills and greater positive alcohol expectancies during adolescence (ages 14–16) were classified as more frequent drinkers at an eight year follow-up and adolescents with lower alcohol expectancies and poorer verbal skills were classified as less frequent drinkers (Tapert, McCarthy, Aarons, Schweinsburg, & Brown, 2003). Interestingly, better visuospatial ability has been found in mid-adolescent drinkers who later engaged in more frequent alcohol and drug use (Hanson, Medina, Padula, Tapert, & Brown, 2011).

Deficits on tests of executive functioning have also been found to contribute to substance use initiation. Specifically, longitudinal studies suggest that executive functioning in adolescents may be predictive of future alcohol and drug use, above and beyond the effects of behavioral factors such as conduct and attentional deficiencies (Aytaclar, Tarter, Kirisci, & Lu, 1999; Tapert, Baratta, Abrantes, & Brown, 2002; Tapert, Granholm, et al., 2002). Preliminary evidence suggests that another component of executive functioning, decision-making, may also be associated with future substance use. Notably, male college-aged drinkers who displayed a disadvantageous pattern of decision making in the Iowa Gambling Task exhibited significantly increased heavy drinking episodes and frequency and quantity of alcohol consumption over a two year follow-up (Goudriaan, Grekin, & Sher, 2011). Similarly, adult females who initiated ecstasy use 18 months after intake showed different strategies and reaction times at baseline during tasks of decision-making than persistent ecstasy naïve females (Schilt, Goudriaan, Koeter, van den Brink, & Schmand, 2009).

A growing body of research suggests that future substance users show premorbid deficiencies in response inhibition (Norman et al., 2011; Wetherill, Squeglia, Yang, & Tapert, in press), a key component of executive functioning that measures the ability to voluntarily suppress a learned, automatic response upon presentation of novel information or

stimuli. Impulsivity is often suggested as the behavioral correlate of a deficient response inhibition system (Bari & Robbins, 2013; Horn, Dolan, Elliott, Deakin, & Woodruff, 2003). Importantly, impaired inhibitory control and elevated impulsivity have been shown in persons with alcohol and other substance use disorders (Courtney et al., 2011; Kamarajan et al., 2005; Lawrence, Luty, Bogdan, Sahakian, & Clark, 2009; Uekermann, Daum, Schlebusch, Wiebel, & Trenckmann, 2003). Adolescent boys at risk for substance use with positive family history of alcoholism perform worse on response inhibition tasks than family history negative controls (Nigg et al., 2004). In addition, poor response inhibition during early adolescence is associated with greater substance use and related problems during mid-late adolescence (Nigg et al., 2006; Tarter, Kirisci, Habeych, Reynolds, & Vanyukov, 2004; Tarter, Kirisci, Reynolds, & Mezzich, 2004).

Together, these findings indicate the presence of detectable neurocognitive impairments prior to substance use initiation in later users. Understanding the neuropsychological functions that predate substance use initiation is crucial to specifying the consequences of substance use on brain development, as well as to identifying at-risk youth as potential targets of preventive efforts. In the current study, we examined the influence of neuropsychological functioning on future alcohol and marijuana involvement in a sample of adolescents who were characterized prior to initiating substance use. Based on previous findings, we hypothesized that premorbid differences in memory, attention, visuospatial functioning, and executive functioning (i.e., planning and problem solving and inhibition) in substance-naïve 12–14 year-olds would influence initiation and maintenance of substance use by age 17–18.

METHODS

Participants

At baseline, participants were 175 healthy 12–14 year-olds (41% female) recruited through flyers sent to households of students attending San Diego area public middle schools (Squeglia, Pulido, et al., 2012; Squeglia, et al., 2009). Extensive screening and background information were obtained from the youth, their biological parent, and one other parent or close relative. The study protocol was executed in accordance with the standards approved by the University of California, San Diego Human Research Protections Program.

Baseline exclusionary criteria included: any suggestion of prenatal alcohol (>2 drinks during a given week) or illicit drug exposure; experience with alcohol or drugs, defined as 10 total days in their life on which drinking had occurred, or > 2 drinks in a week; premature birth (i.e., born prior to 35th gestational week); history of any neurological or DSM-IV (American Psychiatric Association, 2000) Axis I disorder, determined by the NIMH Diagnostic Interview Schedule for Children –version 4.0 (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), any history of head trauma or loss of consciousness (>2 minutes), chronic medical illness, learning disability or mental retardation, or use of medications potentially affecting the brain; 3 lifetime experiences with marijuana and any use in the past three months; 5 lifetime cigarette uses; and any history of other intoxicant use (Squeglia, Pulido, et al., 2012; Squeglia, et al., 2009; Wetherill, et al., in press); contraindication to MRI (e.g., braces); inadequate comprehension of English; and non-correctable sensory problems. At

baseline, the final sample was 175 adolescents, typically from families of relatively high socioeconomic status with high average estimated IQ and school grades (see Table 1).

Measures

Substance use measures—At baseline, the Customary Drinking and Drug Use Record (Brown et al., 1998) was administered in person to obtain quantity and frequency of lifetime and recent (past year) alcohol, marijuana, and other drug use, withdrawal/hangover symptoms, and DSM-IV (American Psychiatric Association, 2000) abuse and dependence criteria. Breathalyzer and urine toxicology screens confirmed self-report data at baseline. Substance use information was updated annually via phone after the participant's baseline assessment. Parent's and/or informant's (sibling, friend, roommate) report of youth substance use was collected as collateral evidence.

Family background—At baseline, the Family History Assessment Module (Rice et al., 1995) ascertained familial density of alcohol use disorders (AUD) in first- and second-degree relatives. Family history density scores were calculated by adding 0.5 for each biological parent and 0.25 per biological grandparent (Zucker, Ellis, & Fitzgerald, 1994) endorsed by either youth or parent as having AUD or SUD for a possible score of 0 to 4. FH density scores ranged from 0 to 2.25 in the current sample.

Socioeconomic status—Socioeconomic background information (i.e., educational attainment, occupation, and salary of each parent) was obtained from parents and converted to a Hollingshead Index of Social Position score (Hollingshead, 1965)

Pubertal development—The Pubertal Development Scale (Petersen, Crockett, Richards, & Boxer, 1988) is a reliable and valid 5-item self-report measure of pubertal maturation and was measured at baseline for boys and girls.

Psychopathology and mood—Adult Self Report (Achenbach & Rescorla, 2001) (for youth 18+ years) and the Child Behavior Checklist (CBCL; (Achenbach & Rescorla, 2001) (for youth < 18 years) provided age- and gender-normed continuous measures of internalizing and externalizing psychopathology. The Conduct Disorder Questionnaire (CDQ; (Brown, Gleghorn, Schuckit, Myers, & Mott, 1996) was used to determine if youth met DSM-IV (American Psychiatric Association, 2000) diagnostic criteria for conduct disorder. Beck Depression Inventory-II (BDI-II; (Beck, Steer, & Brown, 1996) and Spielberger State-Trait Anxiety Inventory (STAI; (Spielberger, Gorsuch, & Lushene, 1970) assessed recent depressive symptoms and anxiety.

Neurocognition—A comprehensive neuropsychological battery was completed at baseline to assess cognitive functioning on six cognitive domains that were hypothesized to affect initiation of alcohol and marijuana use during adolescence: (1) cognitive inhibition-interference, (2) short term memory, (3) sustained attention, (4) verbal learning and memory, (5) visuospatial functioning, and (6) spatial planning and problem solving. Domains were determined by a factor analysis of the z-scores of the 24 total neuropsychological test variables ascertained (Squeglia, Jacobus, Sorg, Jernigan, & Tapert,

2013). Cognitive inhibition-interference was comprised of D-KEFS Color-Word Interference Conditions 3 and 4 time to complete (seconds). Short term memory was comprised of: Wechsler Intelligence Scale for Children-3rd edition (WISC-III; (Wechsler, 1991) Digit Span digit forward and digit backward raw scores, and Wechsler Adult Intelligence Scale-4th edition (WAIS-IV; (Wechsler, 2008) Letter-Number sequencing raw scores. Sustained attention consisted of: Digit Vigilance Test (Lewis, 1995) total time (seconds), WISC-III Coding raw score, and Delis-Kaplan Executive Function System (D-KEFS; (Delis, Kaplan, & Kramer, 2001) Trails Conditions 1, 2, 3, and 4 (i.e., Visual Scanning, Number Sequencing, Letter Sequencing, Letter-Number Switching) time to complete (seconds). Verbal learning and memory consisted of California Verbal Learning Test-Children's version (CVLT-C; List A Total 1–5 raw, Short Delay Free and Cued Recall raw, and Long Delay Free and Cued Recall raw scores; (Delis, Kramer, Kaplan, & Ober, 1994). Visuospatial functioning was comprised of Rey-Osterrieth Complex Figure Copy and 30-minute Delay Accuracy scores (Rey & Osterrieth, 1993), Wechsler Abbreviated Scale of Intelligence (WASI; (Wechsler, 1999) Block Design raw scores, and Hooper Visual Organization Test (Hooper, 1958) raw total. Spatial planning and problem solving included the WISC-III Mazes total score, WASI Matrix Reasoning total score, and D-KEFS Towers total achievement score. All timed raw scores (i.e., Digit Vigilance, Trails, Color-Word Interference) were reversed-coded so that longer times corresponded to poorer performance. An overall Global Functioning score was calculated by averaging all of subtest z-scores together.

Follow-up procedures—At baseline, all 175 substance-naïve 12 to 14 year old youth were administered a comprehensive interview and neuropsychological test battery by trained lab assistants. Participants were assessed annually (99% follow-up rate) using rigorous follow-up procedures (Kleschinsky, Bosworth, Nelson, Walsh, & Shaffer, 2009; Twitchell, Hertzog, Klein, & Schuckit, 1992). Each year, an over-the-phone or in-person interview assessed current substance use and psychiatric functioning. At follow-up, participants were classified as continuous controls (baseline control who maintained abstinence over the follow-up), moderate substance users (baseline control who transitioned into moderate alcohol and/or marijuana use), or heavy substance users (baseline control who transitioned into heavy alcohol and/or marijuana use) at each time point (see Figure 1). At follow-up, 70 participants were classified as continuous controls, while 105 were moderate or heavy substance use transitioners (see Table 1). Continuous non-users were at least 17 years of age at follow-up, to allow sufficient time to transition into heavy use. 16 year old substance users were included, as it was clear that by that age, substance use had onset. In this sample, all youth who endorsed marijuana use also endorsed heavy alcohol use.

Data analysis—Statistical analyses were carried out in SPSS (Rel. 18.0.0. 2009. IBM, Chicago, IL). Continuous control and substance use transitioner groups were compared using a two-tailed Student's t-test. Hierarchical linear regressions were run, using the entire sample ($N=175$), to examine if baseline cognitive performance (global and 6 domain scores) predicted future alcohol and marijuana use, above and beyond commonly observed predictors of youth substance use (i.e., family history density of substance use disorders, baseline alcohol and marijuana use, externalizing behaviors, gender, baseline pubertal

development, and age at follow-up). Baseline grade point average was also controlled for, as it differed between groups. Dependent variables were: (1) follow-up past year peak alcoholic drinks, (2) total lifetime drinking days, and (3) total marijuana use days. Other drug and tobacco use were not examined due to infrequency of endorsement in this sample (see Table 2). All substance involvement variables were positively skewed, so logarithmic transformations were applied (Tabachnick & Fidell, 2007). All neuropsychological measures were normally distributed and free from outliers.

Because males and females have different neurodevelopmental trajectories (Lenroot & Giedd, 2006), follow-up analyses examined if gender moderated the effect of neuropsychological functioning on substance use. Hierarchical linear regressions were run with covariates entered on Step 1 (i.e., family history density of substance use disorders, baseline alcohol and marijuana use, externalizing behaviors, age at follow-up, baseline pubertal development, and grade point average), gender and transformed substance use variables (centered) on Step 2, and the interaction between gender and substance use variables on Step 3.

RESULTS

At baseline, continuous control and substance use transitioner groups were well matched on age, race, socioeconomic status, years of education, pubertal development, depressive and anxiety symptoms, and internalizing symptoms (see Table 1). Substance use transitioners included more males and conduct disorder diagnoses (9% vs. 0%), higher family density of substance use disorders and externalizing symptoms (although well within the average range), and lower grade point average (although still in the high average range), compared to continuous controls. At follow-up, substance use transitioners and continuous controls were well matched on age, years of education, internalizing symptoms, and grade point average. Substance use transitioners continued to have more conduct disorder diagnoses, although a slight decrease from baseline (9% at baseline to 7% at follow-up), as well as more externalizing behaviors (still within normal range), and lower grade point average (although well above average). At baseline, substance use transitioners had tried alcohol (0–10 times) and marijuana (0–2 times) more often than continuous controls, and as expected, substance use transitioners had significantly more alcohol and marijuana lifetime use occasions at follow-up (see Table 2).

Hierarchical regressions

From the entire sample ($N=175$), poorer baseline performance on tests of inhibition predicted higher follow-up past year peak alcoholic drinks [$F(9,163)=6.726$, $p<.001$; $R^2=.02$, $p=.03$, $\beta=-.16$], total lifetime drinking days [$F(9,163)=6.77$, $p<.001$; $R^2=.02$, $p=.03$, $\beta=-.16$], and total marijuana use days [$F(9,163)=6.94$, $p<.001$; $R^2=.02$, $p=.03$, $\beta=-.16$] by age 17, above and beyond covariates (i.e., family history density of substance use disorders, baseline alcohol and marijuana use, externalizing behaviors, gender, baseline pubertal development, age at follow-up, and grade point average; see Figure 2). For all three models, 23% of the total variance in substance use was accounted for by predictors. Performance on baseline global cognitive functioning, as well as tests of short term memory, sustained

attention, verbal learning and memory, visuospatial functioning, and spatial planning and problem solving were not related to substance use involvement by late adolescence. Of note, analyses were rerun using zero-inflated Poisson regression due to the large number of zeros in the substance use variables, and results remained unchanged. Groups were not significantly different on global or domain-specific neurocognitive functioning ($ps > .11$; see Table 3).

Gender did not moderate the effect of neuropsychological functioning on substance use by late adolescence on any of the cognitive domains ($ps > .43$). Overall ($N=175$), females ($n=72$) outperformed males ($n=103$) on global neuropsychological functioning, which was driven by better performance on tests of sustained attention and verbal learning and memory ($p<.05$; see Table 4). Females performed better than males at a trend level ($ps<.06$) on tests of cognitive inhibition-interference and visuospatial functioning. Among substance use transitioners ($n=105$), females ($n=32$) performed better than males ($n=73$) globally, as well as on tasks of sustained attention, verbal learning and memory, and visuospatial functioning ($ps<.05$). Among continuous controls ($n=70$), females ($n=40$) also outperformed males ($n=30$) globally, and on tests of sustained attention and verbal learning and memory ($p<.05$; see Table 4). Female substance use transitioners ($n=32$) did not differ from female continuous control ($n=40$), male substance use transitioners ($n=73$), or male continuous controls ($n=30$; $p<.05$).

DISCUSSION

These findings suggest that compromised inhibitory functioning in early adolescence predates substance use, and is related to greater subsequent alcohol and marijuana use by late adolescence. Inhibitory functioning predicted subsequent substance use above and beyond variability attributable to other common predictors of youth substance use, including family history of substance use disorders, externalizing behaviors, gender, pubertal development, academic achievement, and age. Performance on other cognitive domains, including short term memory, sustained attention, verbal learning and memory, visuospatial functioning, and spatial planning and problem solving, did not relate to substance use involvement by late adolescence, and gender did not moderate the effects.

Inhibition, or impulse control, is a hallmark of executive functioning and refers to the ability to withhold a prepotent response in order to select a more appropriate, goal-directed response (Luna, Padmanabhan, & O'Hearn, 2010; Stevens, Kiehl, Pearson, & Calhoun, 2007). Previous prospective neuropsychological research suggests that inhibition plays a crucial role in adolescent substance use initiation. Specifically, poorer performance on a task of response inhibition was related to the onset of alcohol use-related problems and illicit drug use in adolescents, independent of familial risk, ADHD, and conduct disorder symptoms (Nigg, et al., 2006). Aberrant brain activation patterns may underlie observed premorbid neuropsychological differences. Neural circuitry underlying inhibitory control undergoes significant neurodevelopment during adolescence (e.g., (Durstun et al., 2006; Velanova, Wheeler, & Luna, 2008), with brain activation transitioning from diffuse prefrontal and parietal activation to localized prefrontal activation (Luna, et al., 2010; Luna & Sweeney, 2004). Longitudinal studies using functional neuroimaging have shown that

even in the presence of comparable performance, atypical brain activation during response inhibition tasks predicted later alcohol use (Norman, et al., 2011), substance use and dependence symptoms (Mahmood et al., 2013), and alcohol-related consequences, like blackouts (Wetherill, Castro, Squeglia, & Tapert, 2013). Furthermore, baseline brain activation in substance naïve youth during early adolescence has been found to be predictive of greater substance involvement by late adolescence, above and beyond common predictors of early substance use initiation, such as familial substance use disorder, male gender, externalizing behaviors, and age (Squeglia, Pulido, et al., 2012). Together, these findings suggest that neural vulnerabilities, both in behavior and neural response patterns during response inhibition, could be useful markers of vulnerability to initiating substance use during adolescence.

Interestingly, none of the other cognitive domains predicted future substance use, despite previous research showing that working memory (Khurana, et al., 2013), attention (Tapert, Baratta, et al., 2002), and visuospatial functioning (Hanson, et al., 2011) related to future substance use. This study was interested in cognitive predictors of substance *use* and not *problem use*, in particular. Other cognitive domains may be more predictive of *problem use* levels, as opposed to simple initiation of use. The current sample included high functioning adolescents from upper middle class neighborhoods, with no co-occurring psychopathology (e.g., ADHD) who were performing in the high average range in school. Findings could be more pronounced if youth were sampled from a more cognitively disadvantaged or less educated group. Furthermore, deficits on cognitive domains like attention and working memory might play a more prominent role in less advantaged youth or teens with higher rates of behavioral problems than those described in this study. However, as most teens do not have behavioral or psychological problems, the current findings are very important to the emergent literature on alcohol risk factors.

Because males and females have different neurodevelopmental trajectories (Lenroot & Giedd, 2006), follow-up analyses examined gender differences in neuropsychological functioning and substance use. We found that females outperformed males globally on tests of neuropsychological functioning, particularly on the domains of sustained attention and verbal learning and memory. However, when examining males and females separately, no differences were found between female transitioners and continuous controls and male transitioners and continuous controls. Previous research has shown that in substance-using teens, gender moderates the relationship between adolescent substance use and brain morphometry (Squeglia, Sorg, et al., 2012), neural activation (Squeglia, Schweinsburg, Pulido, & Tapert, 2011), and cognitive functioning (Squeglia, et al., 2009). In this study, gender did not moderate the relationship between premorbid cognitive functioning and subsequent initiation of alcohol and marijuana use. This suggests previous observed gender effects may be attributed to the substance use itself, as opposed to pre-existing neurocognitive features, with females often showing more vulnerability than males to deleterious consequences of heavy drinking. Of note, males were more likely to initiate heavy drinking over the follow-up than females. Therefore, the mechanism underlying males' higher rates of transition into heavy substance use could be attributable to factors other than cognitive functioning, such as environmental factors.

To limit fatigue in 12 to 14 year old participants, the neuropsychological test battery administered did not capture all facets of cognition, but was kept to ~3.5 hours. As such, tasks composing the “short term memory” domain tap only one component of the working memory system, and should not be interpreted as capturing executive working memory capacity in general (Cowan, Fristoe, Elliott, Brunner, & Sauls, 2006; Engle, Tuholski, Laughlin, & Conway, 1999). Executive working memory capacity may be more centrally involved in decision-making and behavioral regulation (Barrett, Tugade, & Engle, 2004; M. Endres, Donkin, & Finn, 2013; M. J. Endres, Rickert, Bogg, Lucas, & Finn, 2011), and should be examined in future studies.

These findings support the utility of neuropsychological testing in identifying cognitive vulnerabilities to initiating substance use during adolescence. Cognitive performance data could be used in preventative interventions to identify teens at risk for initiating heavy substance use during adolescence. Targeting teens with poorer inhibitory control could be a cost effective way of tailoring preventative interventions with teens at risk for substance use. Teens at the greatest neurobiological risk could benefit more from primary prevention programs implemented in schools and clinics. Future studies should examine if training to bolster inhibition and executive abilities could improve substance use outcomes.

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Figure 1.
Outcome substance use classification chart.

Figure 2.

Worse inhibition at ages 12 to 14 was related to more lifetime alcohol use (blue triangle) and marijuana use (green square) days, as well as higher peak number of drinks by ages 17 to 18. The figure shows raw data. Analyses were rerun using zero-inflated Poisson regression due to the large number of zeros in substance use variables, and results remained unchanged

Table 1

Demographic variables at baseline and follow-up for adolescents who remained nonusers or who transitioned into moderate to heavy substance use patterns by age 17 ($N = 175$).

	Continuous Non-Users ($N=70$) M (SD) or %	Substance Use Transitioners ($N=105$) M (SD) or %
BASELINE		
Age (range: 12–14)	13.45 (0.75)	13.63 (0.78)
Gender (% female)*	57%	30%
Race (% Caucasian)	56%	80%
Family history of alcoholism density (range 0–4)*	0.16 (0.29)	0.36 (0.50)
Conduct disorder in past year (%)*	0%	9%
ADHD in past year (%)	0%	0%
Hollingshead Index of Social Position score	21.81 (14.50)	21.14 (10.65)
Parent annual salary (\$)	\$133K (62)	\$150K (77)
Years of education completed	6.86 (0.64)	7.16 (0.91)
Females' Pubertal Development Scale total ^a	13.90 (3.25)	14.56 (4.02)
Males' Pubertal Development Scale total ^b	11.03 (2.70)	11.66 (3.04)
Beck Depression Inventory total	1.52 (2.87)	1.93 (2.77)
Spielberger State Anxiety total	27.59 (6.82)	28.17 (7.05)
CBCL Internalizing <i>T</i> -score	45.25 (8.32)	43.35 (8.26)
CBCL Externalizing <i>T</i> -score*	40.85 (7.28)	43.45 (8.12)
Grade point average*	3.62 (0.44)	3.40 (0.52)
FOLLOW-UP		
Age (range: 16–18) ^c	17.65 (0.53)	17.77 (0.72)
Conduct disorder in past year (%)*	0%	7%
ADHD in past year (%)	0%	0%
Years of education completed	10.93 (0.74)	11.23 (0.90)
CBCL/ASR Internalizing <i>T</i> -score	44.24 (7.59)	45.88 (10.08)
CBCL/ASR Externalizing <i>T</i> -score*	43.18 (7.54)	49.71 (10.50)
Grade point average*	3.79 (0.50)	3.58 (0.60)

^aFemale participants: $N = 72$ (40 continuous controls; 32 substance use transitioners)

^bMale participants: $N = 103$ (30 continuous controls; 73 substance use transitioners)

^cAge range: All controls in this sample were at least 17 years of age, to all sufficient time to transition into heavy use. 16-year-old substance users were included, as it was clear that by age 16 they were already using.

* $p < .05$

Table 2

Substance use variables at baseline and follow-up for continuous controls and moderate to heavy substance use transitioners ($N = 175$).

	Continuous Non-Users (N=70) M (SD) or %	Substance Use Transitioners (N=105) M (SD) or %
BASELINE		
Lifetime alcohol use occasions (range: 0–10) *	0.00 (0.00)	0.47 (1.50)
Peak drinks on an occasion (range: 0–2) *	0.00 (0.00)	0.08 (0.30)
Lifetime marijuana use occasions (range: 0–3) *	0.00 (0.00)	0.28 (1.18)
FOLLOW-UP		
Lifetime alcohol use occasions (range: 0–501) **	0.71 (1.73)	62.45 (87.64)
Peak drinks on an occasion (range: 0–20) **	0.41 (0.96)	8.53 (4.06)
Lifetime marijuana use occasions (range: 0–1064) **	0.27 (1.37)	91.03 (196.52)

* $p < .05$;

** $p < .001$

Table 3

Baseline neuropsychological functioning z-scores on global and domain-specific cognitive domains between continuous non-users and substance use transitioners (ages 12–14; $N = 175$).

	Continuous Non-Users (N=70) M (SD)	Substance Use Transitioners (N=105) M (SD)
Global Neuropsychological Functioning	0.01 (0.56)	−0.03 (0.51)
Cognitive inhibition-interference domain	0.12 (0.91)	−0.10 (0.88)
Short term memory domain	−0.08 (0.81)	−0.21 (0.84)
Sustained attention domain	0.00 (0.67)	−0.02 (0.66)
Verbal learning and memory domain	0.04 (0.99)	−0.03 (0.78)
Visuospatial functioning domain	−0.08 (0.81)	0.02 (0.66)
Spatial planning and problem solving domain	0.06 (0.77)	−0.06 (0.67)

Table 4

Baseline neuropsychological functioning z-scores on global and domain-specific cognitive domains between continuous non-users and substance use transitioners, divided by gender (ages 12–14; $N = 175$).

	Continuous Non-Users (N=70) M (SD)		Substance Use Transitioners (N=105) M (SD)	
	<i>Female</i> (n=40)	<i>Male</i> (n=30)	<i>Female</i> (n=32)	<i>Male</i> (n=73)
Global Neuropsychological Functioning ^{a b c}	0.16 (0.52)	−0.19 (0.55)	0.18 (0.45)	−0.12 (0.48)
Cognitive inhibition-interference	0.29 (0.85)	−0.10 (0.95)	−0.03 (0.73)	−0.13 (0.94)
Short term memory	0.02 (0.70)	−0.21 (0.94)	0.03 (0.74)	−0.04 (0.89)
Sustained attention ^{a b c}	0.18 (0.61)	−0.25 (0.68)	0.34 (0.50)	−0.18 (0.66)
Verbal learning and memory ^{a b c}	0.26 (0.86)	−0.24 (1.08)	0.20 (0.76)	−0.13 (0.76)
Visuospatial functioning ^a	0.01 (0.81)	−0.21 (0.79)	0.22 (0.54)	−0.07 (0.70)
Spatial planning and problem solving	0.09 (0.74)	0.01 (0.82)	−0.04 (0.67)	−0.07 (0.67)

^aFemale substance use transitioners – Male substance use transitioners, $p < .05$

^bFemale continuous non-users – Male continuous non-users, $p < .05$

^cFemale – male, $p < .05$

Note: There were no cognitive differences between female substance use transitioners and continuous non-users ($p < .05$), or between male substance use transitioners and continuous nonusers ($p < .05$).