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Cognitive, Emotion Control, and Motor Performance of Adolescents in the NCANDA Study: Contributions From Alcohol Consumption, Age, Sex, Ethnicity, and Family History of Addiction

Edith V. Sullivan,
Stanford University School of Medicine

Susan F. Tapert,
Veterans Affairs San Diego Healthcare System, La Jolla, CA and University of California, San Diego

Devin Prouty,
SRI International, Menlo Park, CA

Ian M. Colrain,
SRI International, Menlo Park, CA

Fiona C. Baker,
SRI International, Menlo Park, CA

Stephen R. Hooper,
University of North Carolina School of Medicine

Bonnie J. Nagel,
Oregon Health and Sciences University

Torsten Rohlfing,
SRI International, Menlo Park, CA

Weiwei Chu,
SRI International, Menlo Park, CA

Correspondence concerning this article should be addressed to Edith V. Sullivan, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine (MC5723), 401 Quarry Road, Stanford, CA 94305-5723. edie@stanford.edu.
Edith V. Sullivan, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine; Ty Brumback, Department of Psychiatry, University of California, San Diego; Susan F. Tapert, Psychology Service, Veterans Affairs San Diego Healthcare System, La Jolla, CA and Department of Psychiatry, University of California, San Diego; Rosemary Fama, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, and Center for Health Sciences, SRI International, Menlo Park, CA; Devin Prouty, Center for Health Sciences, SRI International; Sandra A. Brown, Kevin Cummins, and Wesley K. Thompson, Department of Psychiatry, University of California, San Diego; Ian M. Colrain and Fiona C. Baker, Center for Health Sciences, SRI International; Michael D. De Bellis, Healthy Childhood Brain Development Research Program, Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine; Stephen R. Hooper, Department of Allied Health Sciences, University of North Carolina School of Medicine; Duncan B. Clark and Tammy Chung, Department of Psychiatry, University of Pittsburgh; Bonnie J. Nagel, Departments of Psychiatry and Behavioral Neuroscience, Oregon Health and Sciences University; B. Nolan Nichols, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, and Center for Health Sciences, SRI International; Torsten Rohlfing and Weiwei Chu, Center for Health Sciences, SRI International; Kilian M. Pohl and Adolf Pfefferbaum, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, and Center for Health Sciences, SRI International.

†Torsten Rohlfing is now affiliated with Google, Inc. None of the authors have conflicts of interest with the reported data or their interpretation.

Ty Brumback,
University of California, San Diego

Rosemary Fama,
Stanford University School of Medicine, and SRI International, Menlo Park, CA

Sandra A. Brown,
University of California, San Diego

Kevin Cummins,
University of California, San Diego

Wesley K. Thompson,
University of California, San Diego

Michael D. De Bellis,
Duke University School of Medicine

Duncan B. Clark,
University of Pittsburgh

Tammy Chung,
University of Pittsburgh

B. Nolan Nichols,
Stanford University School of Medicine, and SRI International, Menlo Park, CA

Kilian M. Pohl,
Stanford University School of Medicine, and SRI International, Menlo Park, CA

Adolf Pfefferbaum
Stanford University School of Medicine, and SRI International, Menlo Park, CA

Abstract

Objective—To investigate development of cognitive and motor functions in healthy adolescents and to explore whether hazardous drinking affects the normal developmental course of those functions.

Method—Participants were 831 adolescents recruited across 5 United States sites of the National Consortium on Alcohol and NeuroDevelopment in Adolescence; 692 met criteria for no/low alcohol exposure, and 139 exceeded drinking thresholds. Cross-sectional, baseline data were collected with computerized and traditional neuropsychological tests assessing 8 functional domains expressed as composite scores. General additive modeling evaluated factors potentially modulating performance (age, sex, ethnicity, socioeconomic status, and pubertal developmental stage).

Results—Older no/low-drinking participants achieved better scores than younger ones on 5 accuracy composites (general ability, abstraction, attention, emotion, and balance). Speeded responses for attention, motor speed, and general ability were sensitive to age and pubertal development. The exceeds-threshold group (accounting for age, sex, and other demographic factors) performed significantly below the no/low-drinking group on balance accuracy. Delay

Discounting performance was consistent with poor impulse control in the younger no/low drinkers and in exceeds-threshold drinkers regardless of age.

Conclusions—Higher achievement with older age and pubertal stage in general ability, abstraction, attention, emotion, and balance suggests continued functional development through adolescence, possibly supported by concurrently maturing frontal, limbic, and cerebellar brain systems. Determination of whether low scores for balance accuracy and performance indicative of poor impulse control on Delay Discounting by the exceeds-threshold group resulted from drinking or from other preexisting factors requires longitudinal study

Keywords

adolescent; development; alcohol; cognition; motor speed

Adolescence is a time of significant growth with respect to somatic size, brain structure, sexual maturity, and cognitive, motor, and emotional development (Giedd et al., 2014; Stiles & Jernigan, 2010; Witt, 2010). During their second decade, adolescents are presented with a plethora of options, including increased independence from parents and initiation of high-risk activities. The options of healthy to risky to dangerous activities is vast and poses serious challenges in decision making for teens, whose individual cognitive abilities and emotional maturity may well be at different stages of development. Among the high-risk behaviors adolescents are likely to initiate is drinking alcohol, commonly in binges. One recent study noted that 19% of high school seniors report having consumed five or more drinks in a row (binge episode) at least once in the previous 2 weeks (Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2015). To investigate how hazardous drinking might affect the normal course of brain structural and functional development, the National Consortium on Alcohol and NeuroDevelopment in Adolescence (NCANDA) has begun a longitudinal study of youth before engaging in heavy drinking compared with adolescents who have already initiated drinking at moderate to heavy levels. Presented herein are results from baseline, cross-sectional testing (Brown et al., 2015).

Cross-sectional studies suggest adolescents with a diagnostically determined drinking disorder show poorer neuropsychological performance than light and nondrinkers in various cognitive domains, including learning and memory (Brown, Tapert, Granholm, & Delis, 2000; Green et al., 2010; Sneider, Cohen-Gilbert, Crowley, Paul, & Silveri, 2013), executive function (Giancola, Mezzich, & Tarter, 1998; Parada et al., 2012), information processing (Tarter, Mezzich, Hsieh, & Parks, 1995), and language skills (Moss, Kirisci, Gordon, & Tarter, 1994). Longitudinal studies have extended these findings, suggesting that verbal memory (Hanson, Cummins, Tapert, & Brown, 2011; Nguyen-Louie et al., 2015), psychomotor speed (Nguyen-Louie et al., 2015), visuospatial abilities (Hanson et al., 2011; Nguyen-Louie et al., 2015; Squeglia, Spadoni, Infante, Myers, & Tapert, 2009; Tapert & Brown, 1999; Tapert, Granholm, Leedy, & Brown, 2002), and attentional functioning (Squeglia et al., 2009; Tapert et al., 2002) appear to worsen following the initiation (Squeglia et al., 2009) or continuation (Hanson et al., 2011; Tapert et al., 2002) of heavy drinking during adolescence and early adulthood. Untoward effects were also detected in youth who drank alcohol but did not meet diagnostic criteria for alcohol use disorder (Nguyen-Louie et al., 2015; Squeglia et al., 2009). Because many functions continue to mature during

adolescence and with pubertal development (e.g., Blakemore, Burnett, & Dahl, 2010; Hedman, van Haren, Schnack, Kahn, & Hulshoff Pol, 2012; Shaw et al., 2008; Sowell, Thompson, & Toga, 2004; Sullivan et al., 2011; for review, Stiles & Jernigan, 2010), initiation of hazardous drinking in these years of change may have a detrimental effect on the maturing brain.

Sex, socioeconomic status (SES), and ethnicity are factors in addition to age and puberty known to be associated with neuropsychological test performance during normal development and requiring consideration when assessing status of cognitive and motor functions (e.g., Akshoomoff et al., 2014; Noble et al., 2015; Noble, Houston, Kan, & Sowell, 2012). Typically, girls undergo sexual maturity earlier than boys (e.g., Cole, Pan, & Butler, 2014; Tanner, Whitehouse, & Takaishi, 1966) and advance earlier than boys in language skills (Neligan & Prudham, 1969), use of semantic knowledge (Hurks et al., 2010), facial emotion recognition and discrimination (Gur et al., 2012; Lawrence, Campbell, & Skuse, 2015), and components of episodic memory (Gur et al., 2012; Piper et al., 2011). By contrast, boys develop earlier than girls in mental rotation appreciation (Masters & Sanders, 1993; Voyer, Voyer, & Bryden, 1995), fine motor control (but see Denckla, 1973; Denckla, 1974; Piper, 2011), and physical strength (e.g., Dodds et al., 2014; McQuiddy, Scheerer, Lavalley, McGrath, & Lin, 2015). SES also plays a role in development (e.g., Lange, Froimowitz, Bigler, & Lainhart, 2010; Noble et al., 2015)—less for motor tasks (Largo et al., 2001) but more so for skills related to language, such as fluency, vocabulary, and reading (e.g., Noble et al., 2012), and executive functioning (Boelema et al., 2014). The contribution of parental education as an index of SES can be distinct from financial status in its relation to focal brain maturation and its effect on specific components of cognitive development, including language, memory, emotional control, and executive functioning (Lawson, Duda, Avants, Wu, & Farah, 2013; Noble et al., 2015; Noble et al., 2012). Compounding these SES-related disparities are known differences in education, nutrition, health care, and safety available to low income, often minority, youth (Coley, Leventhal, Lynch, & Kull, 2013; McLoyd, 1998).

To assemble a sample that is adequately large and nationally representative (cf., Brown et al., 2015) to test the influence of these relevant factors on developmental differences, multisite studies are essential. Further, to assess the constellation of functions potentially affected by alcohol and that are still developing, computerized test batteries provide a means to accomplish this efficiently. Indeed, the utility of computerized test batteries has been demonstrated in a wide variety of settings, including sport head injury (Rahman-Filipiak & Woodard, 2013; Taylor, 2012), active-duty military (Cole et al., 2013), diseases of aging (Canini et al., 2014; Dwolatzky, Dimant, Simon, & Doniger, 2010; Mielke et al., 2014), epilepsy (Martinelli, Cecato, Bartholomeu, & Montiel, 2014), and infectious diseases potentially affecting the brain (Koski et al., 2011). Batteries, such as the CANTAB (Robbins et al., 1994), PhenX Toolkit (McCarty, Berg et al., 2014; McCarty, Huggins et al., 2014), NIH Toolbox (Carlozzi et al., 2014; Heaton et al., 2014; Weintraub et al., 2014), and the University of Pennsylvania Web-Based Computerized Neurocognitive Battery (WebCNP; webcnp.med.upenn.edu/; Gur et al., 2012; Gur et al., 2010), each use multiple measures to assess principal cognitive domains of executive functions, several component processes of declarative memory, visuospatial abilities, emotion discrimination, and emotional control

valid for preadolescence through senescence and commonly affected in adolescents with alcohol use disorder (AUD) (for review, Squeglia, Jacobus, & Tapert, 2014). Benefits of most computerized batteries include acquisition of response time for individual trials for every test, thereby enabling assessment of speed of responding and efficiency scores based on speed–accuracy trade-off (Gur et al., 2010). As these batteries have evolved, the test length relative to the amount of information obtained has become briefer. Another advantage of computer-based testing is automated scoring and data uploading without labor-intensive and error-prone hand scoring, checking, and double entry into a computer database, especially useful in large-scale, multisite studies.

The primary aims of this study were to identify selective cognitive and motor functions showing evidence of continued maturation during adolescence and to distinguish functions spared and those vulnerable to hazardous drinking during this period of functional change (Brown et al., 2015; Winward, Bekman, Hanson, Lejuez, & Brown, 2014). The functions targeted were executive functions of planning, monitoring, mental flexibility, verbal fluency, attention, and inhibition; achievement based on reading, comprehension, math ability; episodic memory for verbal, visual, face, and spatial material; working memory for verbal and nonverbal material; emotion processing and regulation; reward seeking and learning; visual discrimination; and general intelligence. We tested the hypotheses that functions subserved by frontal, superior parietal, and medial temporal cortical regions, which continue to develop into late adolescence (Hedman et al., 2012; Raznahan, Greenstein, Lee, Clasen, & Giedd, 2012; Sowell, Thompson, Leonard et al., 2004) would exhibit age-related effects, where older adolescents would score higher on accuracy and speed measures of executive functions, emotion processing, episodic memory, and general ability. In exploratory analyses, we tested the hypotheses that adolescents who exceeded a threshold for no/low alcohol or drug exposure would perform more poorly than those who met these criteria on tests of functions commonly compromised in youth with alcohol use disorder, namely, executive functions, spatial working memory, emotion processing, and balance (e.g., Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014).

Method

Participants

This report presents the initial, cross-sectional analysis of neuropsychological data collected on 831 adolescents recruited across five sites in the United States (University of California at San Diego, SRI International, Duke University Medical Center, University of Pittsburgh Medical Center, and Oregon Health & Science University) and enrolled in the NCANDA study. Assessment was the same across all sites and used a combination of computerized and traditional neuropsychological tests. The NCANDA study is designed to follow adolescents (age 12 to 21 at entry) annually for 4 years. Of the total group, 692 met criteria for no-to-low alcohol or drug exposure, and as an initial exploration of the effects of alcohol and drug exposure, an additional 139 adolescents with a history of drinking beyond the age-specific, no/low thresholds were also tested (see Brown et al., 2015).

Informed consent—All participants underwent an informed consent process with a research associate trained in human subject research protocols. Adult participants or the parents of minor participants provided written informed consent before participation in the study. Minor participants provided assent before participation. The Internal Review Boards of each site approved this study, and each site followed this procedure to obtain voluntary informed consent or assent, depending on the age of the participant.

Recruitment strategy—Participants were recruited through local schools and colleges, public notices, and targeted catchmentarea calling. Over 7,500 individuals contacted NCANDA sites for screening, and 2,548 target participants (as well as one biological parent per participant) completed a screening interview, ultimately yielding a sample of 831 participants.

A demographic interview inquiring about health and academic functioning, including those associated with initiation of drinking relevant to the adolescents, was completed by each youth and one parent to confirm participant eligibility (Anderson, Tomlinson, Robinson, & Brown, 2011; Brown et al., 2008; Zucker, Donovan, Masten, Mattson, & Moss, 2008). Additional inclusion and exclusion criteria were confirmed using a combination of the Semi-Structured Assessment of the Genetics of Alcoholism (SSAGA; Bucholz et al., 1994; Hesselbrock, Easton, Bucholz, Schuckit, & Hesselbrock, 1999) and the Family History Assessment Module (Rice et al., 1995). For full ascertainment procedures see Brown et al. (2015).

The majority of participants (83%) had limited exposure to alcohol or other drugs (Supplemental Table 1), which was required, because a primary aim of NCANDA is to determine neurocognitive precursors to, and changes following, the onset of heavy alcohol use. A small portion of the sample (17%) that exceeded criteria for alcohol use was recruited using the same methods and was included to represent a range of drinking for future trajectory analyses. These individuals who exceeded drinking thresholds were also allowed to exceed nicotine and marijuana exposure criteria, but were required to meet all other inclusion criteria (including other drug use; Supplemental Table 1). The exceeds-threshold group included largely the older age ranges, although some younger drinkers were also enrolled (Supplemental Table 2). The exceeds-threshold group did not differ from the larger sample on parental education, sex distribution, or ethnic background (see Brown et al., 2015 for full description of the two samples). The value of recruiting this subsample with more extensive drinking history will be realized in subsequent longitudinal analyses; however, at baseline this group serves as a *de facto* comparison group to the no/low-drinking group.

Each site contributed 15%–26% of the sample. The sample was distributed across age groups and matched for sex with the largest proportion (44%) from the 12- to 14-year-old age group. There were no significant age group or sex differences across sites. The sample is roughly equivalent to reported census numbers (U.S. Census Bureau, 2011 https://www.census.gov/library/publications/2011/compendia/statab/131ed/population.html) and is reflective of the counties surrounding NCANDA collection sites (see Brown et al., 2015 for comparison with census data). By design, compared with the no/low drinking group, the

sample that exceeded drinking thresholds was biased toward the oldest age group with more than 60% over age 18.

Screening was conducted to facilitate oversampling for risk for future alcohol use (e.g., family history of alcohol problems, externalizing disorder symptoms), matching sex within age groups, and meeting enrollment targets for age and racial/ethnic groups. An additional 607 participants met eligibility criteria after screening but were not enrolled in the study as enrollment targets for age, sex, and racial/ethnic categories had already been fulfilled.

Participants were excluded based on age, MRI contraindications, physical limitations, parental availability/consent, substance use history, serious medical conditions, history of traumatic brain injury, ongoing psychotropic medication use, prenatal alcohol/drug exposure, and presence or history of learning disabilities or neurodevelopmental disorders; all of which were confirmed by in-person interviews following initial screening. Specifically, participants were screened for medical conditions that could affect MRI, brain development, or study participation, including diabetes, recurrent migraine, and traumatic brain injury with loss of consciousness >30 min. Additionally, participants were screened for neurodevelopmental conditions that could affect brain development or study participation evidenced by history of and persistence in severe learning disorder, pervasive developmental disorder, or other condition requiring repeated or persistent specialized education (e.g., estimated IQ >2 *SD* below mean). Individuals with a history of mood and anxiety disorders that were not likely to interfere with study participation were not excluded (e.g., major depressive disorder, anxiety/panic [with the exception of claustrophobia], and posttraumatic stress disorder [PTSD]). Such disorders were endorsed in the sample commensurate with recent epidemiological reports of these age ranges: 7% ($n = 50$) of the no/low drinking group and 13% ($n = 18$) of the exceeds drinking group endorsing lifetime major depressive disorder, and all other anxiety disorders endorsed by <1% of either sample (Substance Abuse and Mental Health Services Administration (SAMHSA) Center for Behavioral Health Statistics and Quality, 2015). Inclusion and exclusion criteria were minimized to increase our ability to recruit a more representative sample.

No/low versus exceeds-threshold drinking groups—Participants completed the Customary Drinking and Drug Use Record (CDDR, Brown et al., 1998) to characterize their past and current alcohol and substance use. By definition, the no/low-drinking group reported no lifetime heavy drinking occasions (i.e., no episodes in which they drank four or more drinks for female and five or more for male youth); however, 18% of the no/low-drinking group reported some history of drinking. A preponderance of endorsement of drinking history in the no/low-drinking group came from participants over 18 years of age (i.e., 43% of 18 and over participants reported at least one lifetime drink, whereas only 3% of those under age 15 reported the same). In addition, the conservative thresholds for lifetime cigarette, marijuana, and other drug use (Supplemental Table 1) yielded a relatively clean sample with 5% endorsing any nicotine exposure, 9% endorsing marijuana exposure, and 2% endorsing other drug exposure. By contrast, the drinking group that exceeded thresholds endorsed drinking at levels above age-matched national norms (Substance Abuse and Mental Health Services Administration (SAMHSA), 2015; see Brown et al., 2015) with 85% reporting a heavy drinking occasion in the last year and 33% in the past month. In

addition, 32% endorsed a history of cigarette use, although only 5% (n = 7) reported smoking at least once per week and ranged from one to six cigarettes smoked per day. Marijuana use was more prevalent in the exceeds group with 68% endorsing lifetime exposure and 12% (n = 17) reporting use at least once/week.

Alcohol and drug testing—All participants submitted samples to a 12-panel urine toxicology screen for amphetamine, methamphetamine, cocaine, phencyclidine, benzodiazepines, barbiturates, opiate, oxycodone, propoxyphene, methadone, tricyclic antidepressants, marijuana, and a breathalyzer for alcohol to confirm absence of evidence for recent use of drugs of abuse. Positive screens other than marijuana were sent for GC/MS confirmation, and if confirmed, participants were excluded from testing that day. Participants with positive alcohol or drug results were then asked to abstain from alcohol for at least 24 hr and other drugs for 72 hr prior to assessment sessions and were tested again for alcohol and drugs on the return visit. Self-report of recent nicotine, caffeine, and medication use was also obtained at each assessment.

Analysis groups—The first set of analyses focused on neuropsychological data acquired across the five NCANDA recruitment sites in 344 male and 348 female adolescents, ages 12.0- to 21.9-years-old (see Table 1), who met basic alcohol and drug use criteria for no-to-low exposure (Supplementary Table 1) in the NCANDA study. The second set of analyses compared performance of the no/low-drinking group with an independent group of 139 adolescents (64 male, 75 female) whose alcohol consumption exceeded the thresholds (Supplemental Tables 1–2) and were deemed a moderate/high-drinking group; nine met lifetime criteria for *DSM–IV* alcohol abuse, and none met criteria for alcohol dependence.

Participants were characterized by age, sex, pubertal stage using the self-assessment Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988; Shirtcliff, Dahl, & Pollak, 2009), self-identified ethnicity, and SES determined as the highest level of education achieved by either parent (Akshoomoff et al., 2014; see Table 1). In light of the substantial differences in salaries and incomes across the five geographically distributed data collection sites, we expressed SES with reference to parental education level, which is less subject than family income to geographical differences in the United States. Most subjects reported a single self-identified ethnicity (Caucasian, African American, Asian, Pacific Islander, and Native American) with some reporting mixed heritage. There were adequate numbers of the first three types to assign categorical ethnicity, with dual-heritage identifications assigned to the minority ethnicity group (e.g., Asian-Caucasian was categorized as Asian; see Table 1).

Neuropsychological Tests

Test selection conformed to the requirements of the NIH funding announcement (RFA-AA-12–006), which noted that data collection sites use a common neuropsychological battery, tapping eight functional domains: (a) executive function (planning/monitoring, mental flexibility, verbal fluency, attention, inhibition); (b) memory (verbal, visual, face, spatial, and working); (c) emotion processing and regulation; (d) reward seeking and learning; (e) handedness and dexterity; (f) visual discrimination; (g) intelligence; and (h)

achievement (reading, comprehension, math ability). Other considerations for test selection included recognized validity of domain assessment, validation for age range, reliability, score range, and practice effects. Accordingly, the final test battery comprised selected tests and measures from the WebCNP and traditional neuropsychological tests. Table 2 lists the functional domains, test names, specific cognitive and motor processes assessed, and brain regions reported to support each process. Supplemental Table 2 lists the composite domains, test measures, and variable names entered into each composite domain, and scoring procedure for each measure. Delay Discounting (Bickel et al., 2007; Stanger, Budney, & Bickel, 2013; Stanger et al., 2012) was included to examine reward seeking and decision-making and can be considered to provide a measure of impulsive behavior.

Test Procedures

Testing was conducted in quiet rooms by laboratory assistants trained with annual reliability evaluations to criterion and calibrated annually by a centrally trained psychometrician using procedures established by the NCANDA Data Analysis Component. The battery of tests was administered in the same order across all sites. Scheduled breaks were offered to participants to minimize fatigue. Scoring was completed without intervention for the computer tests via WebCNP, LimeSurvey (www.limesurvey.org/), or Blaise (www.blaise.com); all other tests were double scored and entered into NCANDA-specific forms through the Research Electronic Data Capture (REDCap) system. The total test battery was generally completed in about 3 hr.

WebCNP—We selected 15 WebCNP tests, which took approximately 60 min and were installed on Apple laptop computers (13-inch MacBook Air, OS × 10.8). The battery consisted of computer-administered and computer-scored tests representing seven of the eight functional domains, yielding accuracy and speed measures (uncorrected for age, sex, ethnicity, or socioeconomic factors) for all tests used in the current analysis (Table 2 and Supplemental Table 3). Test results were uploaded to the software platform, Scalable Informatics for Biomedical Imaging Studies (SIBIS; Rohlfing, Cummins, Henthorn, Chu, & Nichols, 2014; Nichols & Pohl, 2015) at SRI International. The WebCNP has established construct validity and reliability and was standardized on upward of 10,000 participants (depending on the measure) with a broad, age range (8- to 90-years-old; Gur et al., 2010). Descriptions of the 15 WebCNP tests are arranged by functional domains; most tests have both accuracy and speed (response time) measures (Supplemental Table 3). The descriptions are modified from the WebCNP support manual.

Abstraction—*Conditional exclusion* measures abstraction and mental flexibility. There are three principles for choosing an object: line thickness, shape, and size. These change as the participant achieves 10 consecutive correct answers for each principle. The participant has 48 trials to make 10 consecutive correct answers for each principle. There is only one principle in effect for any trial, but a response may match more than one principle. The participant is not told what the ruling principle is and must derive the correct principle through feedback. If the participant does not achieve a principle within 48 trials, the test ends.

Matrix analysis test, a measure of abstraction and mental flexibility, is a multiple choice task in which the participant must conceptualize spatial, design, and numerical relations that range in difficulty from very easy to increasingly complex. The participant chooses a square that best fits in the missing space of a pattern. Patterns are made up of 2 × 2, 3 × 3, and 1 × 5 arrangements of squares. Each item has five response options.

Logical reasoning, a measure of verbal intellectual ability, is a multiple-choice task in which the participant must complete verbal analogy problems.

Attention—The *continuous performance* task has two parts: one in which the participant must press the spacebar whenever lines form a complete number, and one whenever lines form a complete letter. Each part lasts 1.5 min. Each stimulus flashes for 300 ms followed by a blank page displayed for 700 ms, giving the participant 1 sec to respond to each trial.

Emotion—For *emotion recognition*, participants view a series of 40 faces and indicate what emotion the face is showing: happy, sad, angry, scared, or no feeling. There are four female faces for each emotion (4 × 5 = 20) and four male faces for each emotion (4 × 5 = 20).

Emotion differentiation measures the ability to detect emotion intensity. The participant views pairs of faces and chooses the face showing greater intensity of emotion (anger, fear, happiness, sadness), or chooses a central button labeled “Equal.” The stimuli are created using software to morph faces into differing intensities of emotion. There are 36 trials, divided into happy, sad, angry, and fearful faces. Of the 36 trials, four show no emotional difference. The remaining 32 trials have emotion differentials in increments of 10% ranging from 10%–60%, distributed more heavily toward 30% and 40% items. Trials are presented in random order, and the test is a forced-choice task with no time limit per trial.

Episodic memory—In the *face memory* test, participants are first shown 20 faces that they will be asked to identify later during *immediate* and *delayed* recognition trials. During immediate recall, participants view a series of 40 faces; 20 faces are targets for memory and 20 are distractors. Participants decide whether they had been shown the face by choosing one of four buttons, presented in a 4-point scale: *definitely yes*, *probably yes*, *probably no*, and *definitely no* via the mouse. Delayed memory is tested approximately 25 min after immediate memory.

The *word memory* test is a verbal analogue to face memory and follows the same procedure for *immediate* and *delayed* recognition.

Visual object learning requires participants to view 10 three-dimensional euclidean shapes that they will be asked to identify for both *immediate* and *delayed* recognition in the same manner as face memory and word memory.

Working memory—*Short fractal N-back* measures attention and working memory. Participants view fractal designs displayed on the computer screen and indicate the “target design.” There are three trial types. During the 0-back, the target design is designated before the trial and the participant responds each time they see it. For the 1-back and 2-back the target design is indicated by the repetition of a design, with the participants responding when

they see a design for the first time for 1-back or the second time for 2-back. In all trials, the participant has 2,500 ms to respond.

Motor speed—*Motor praxis* is the first WebCNP test in the battery and measures sensorimotor ability by having the participant use the mouse to click on a shrinking box when it moves to a new position on the screen. This test screens a participant's dexterity, an essential ability to perform the WebCNP tests.

General ability—*Vocabulary* comprises five subtests, each containing 10 multiple-choice items with four response choices. The questions in each section are presented in order of increasing difficulty. A section is discontinued if the participant answers five questions incorrectly. Each subtest uses a different measure of verbal knowledge. In Part 1, the participant chooses a word "closest in meaning" to the target word. In Part 2, the participant chooses the word that has a similar meaning to a bolded phrase within a sentence. In Part 3, the participant selects the one word that is not a valid English word. In Part 4, the participant selects the word that is opposite in meaning to the target word. In Part 5, the participant must choose the correct sentence based on contextual use of a target word.

Traditional tests—Administration and scoring of these "pencil-and-paper tests" follows published instructions. The Wide Range Achievement Test-4 (WRAT4) assesses general ability in *word reading* (blue form) and *math calculation* (Wilkinson & Robertson, 2010); these scores were included in the General Ability composite. *Grooved pegboard* (Lezak, Howieson, & Loring, 2004; Matthews & Kløve, 1964) measures manual dexterity; the score is the number of seconds a participant took to complete insertion of pegs into holes for each hand separately and entered into the motor speed composite. The *Digit Symbol* subtest of the Wechsler Adult Intelligence Scale-IV was administered as prescribed (Wechsler, 2008); only the raw scores were used in analysis in the motor speed composite. Postural stability, measured with the modified *Fregly-Graybiel Walk-a-Line* ataxia test (Fregly, Graybiel, & Smith, 1972; Sullivan, Deshmukh, Desmond, Lim, & Pfefferbaum, 2000), uses four conditions and was conducted twice if the first trial was not completed perfectly (arms folded, eyes closed, feet straight on a line of the floor): stand heel-to-toe for 60 s; stand on one and then the other foot for 30 s each; walk heel-to-toe for 10 steps; these scores comprised the balance composite. Handedness was determined with the *Edinburgh Handedness Questionnaire* (Oldfield, 1971), visual acuity with the *Landolt C* test (Bach, 2007), and color vision with the *Ishihara Test* (Ishihara, 1983).

Cognitive test of reward-seeking and impulsivity—The *Delay Discounting* task assessed preference for smaller immediate versus larger delayed reward (Stanger et al., 2012). The task was administered and scored by computer (13-inch Dell Inspiron 5323 running Windows 7). Participants are asked to choose between accepting a smaller amount of money today compared with a larger amount of money at varying delays (e.g., 1 day, 1 week, 1 month, or 6 months). The primary outcome variable from the delay discounting is k, which represents the rate of discounting. Because k is positively skewed, the natural log is used ($\ln k$; Mazur, 1987). $\ln k$ was determined by fitting the data with a nonlinear search function "nls" in R. A steeper rate of discounting is related to greater preference for short-

term gains over larger longer-term gains and indicates greater impulsive choice or "impulsivity." The task was completed for two values ($100 and $1,000) at varying delays. The delay rate, ln*k*, was calculated for each of the two values and each of the four delays, yielding eight total variables. Subjects who had an indifference point 20% or larger than the previous point were excluded (Lee, Stanger, & Budney, 2015). Data for the two monetary conditions ($100 and $1,000) were first analyzed separately and then those subjects who had valid data for both values were analyzed together to determine the effect of the monetary value.

The computerized Delayed Discounting task implemented here was published by Stanger et al. (2012) and has been validated in an adolescent sample. Use of two reward amounts reduces economic context effects across the age and SES range of our sample. Delayed discounting tasks like this one have shown discriminant validity across a range of substance use disorders, where those who use drugs are more likely to favor immediate rewards than non-users (MacKillop et al., 2011).

Scalable Informatics for Biomedical Imaging Studies (SIBIS)

The informatics infrastructure for collecting data consisted of the Research Electronic Data Capture (REDCap) system (Harris et al., 2009), University of Pennsylvania Web-Based Computerized Neurocognitive Battery (WebCNP; https://webcnp.med.upenn.edu/), LimeSurvey (http://www.limesurvey.org/), and Blaise (http://www.blaise.com). All data collected were automatically merged onto a REDCap server hosted by the NCANDA Data Analysis Component at SRI International. Specifically, test scores not collected directly through entry forms in REDCap were automatically uploaded from the laptop of the collection sites via secure encrypted connections to a Subversion (https://subversion.apache.org/) server, then automatically imported into REDCap. The data used in this manuscript were then organized via a formal, locked data release (VERSION: NCANDA_DATA_00010_V4). Additional information about the NCANDA Data Management System has been published elsewhere (Nichols & Pohl, 2015; Rohlfing et al., 2014).

Data Analysis

The primary independent variable in this cross-sectional analysis was age; the dependent variables were neuropsychological test scores, submitted to empirically driven data reduction to derive composite scores, reflecting the targeted neuropsychological functions. Covariates of interest were sex, self-described ethnicity, highest parental education achieved as a surrogate for SES, study site, and pubertal development stage.

The primary analysis tools were the General Additive Model (GAM; Hastie & Tibshirani, 1986, 1990; Wood, 2006, 2011) and analysis of variance (ANOVA) from the "mgcv" package in R Version 3.1.0 (http://www.r-project.org/), testing for the predictive value of the main effect of age with selective covariates. Additional analyses used a General Linear Model (GLM). The initial GAM (Model 1) tested the predictive value of age and 4 covariates—site, ethnicity, SES, and sex—on each performance score.

$$domain_i \sim \beta_0 + S_1(\text{age}_i) + \beta_2 \text{site}_i + \beta_3 \text{ethnicity}_i + \beta_4 \text{SES}_i + \beta_5 \text{sex}_i + \varepsilon_i$$ Model 1:

Age was allowed to be a nonlinear smooth effect, implemented via thin plate splines with three knots (Wood, 2003). Roughness penalties for the smooth effects were estimated using generalized cross-validation (Wood, 2004). Subsequent GAMs replaced age with PDS as the principal variable.

Many scores were modulated by several or all covariates. Therefore, the contributions of the covariates were examined in a stepwise manner with submodels excluding various covariates and categorical predictions. The first set of analyses focused on the no/low-drinking group, and the second set compared performance by the no/low and exceeds-threshold groups. The sample sizes vary slightly across models tested (noted in the results tables) because not all participants had data for all covariates.

Results

The results are presented in two main parts. The first part focuses on the seven accuracy and seven speed, theoretically driven, composite scores that represent the functional domains targeted in the NCANDA study, the Delay Discounting task to assess reward seeking and decision making, and pubertal development as a predictor of performance. The second part examines potential performance differences between the no/low-drinking and the exceeds-threshold groups.

Part 1: Performance by the No/Low-Drinking Group (*N* = 692)

Construction of composite scores and performance on individual measures— Composite score construction followed three steps (Gur et al., 2012; Sullivan, Shear, Zipursky, Sagar, & Pfefferbaum, 1994). First, each measure was standardized on scores achieved by all male and female adolescents who met NCANDA entry criteria (maximum N = 692) and expressed as a Z-score ($M = 0 \pm 1$SD). Not all participants had scores for all measures, typically due to computer failure, participant's refusal to perform a test, or lack of testing time; Table 3 presents the sample sizes for each composite score. Next, all scores for which a low score signified good performance were transformed by multiplying scores by −1 so that high scores for all measures (i.e., accuracy and speed) were in the direction of good performance (Figures 1 and 2). Finally, the mean Z-score of all individual measures that comprised a composite was calculated. Accuracy and speed composite scores were calculated separately, are presented in box plots in Figures 1–2, and were used as the dependent measures in testing factors using the GAM.

Factors contributing to variance of composite scores: Age, SES, site, ethnicity, and sex—The initial GAM tested the predictive value of age on each composite score covarying for site, SES, ethnicity, and sex.

Accuracy components: When the full model tested for the contribution of site, SES, ethnicity, and sex, the amount of variance accounted for ranged from a high of 39.9% for

general ability to a low of 5.5% for working memory (see Table 3). Removing covariates from the full model produced a significant decrease in variance accounted for per composite: SES for all seven composites (higher parental SES predicted higher scores), site for four composites, ethnicity for four composites, and sex for one composite. When age alone was entered into the model, age was a significant factor (older participants had higher scores) for five of the seven composites, with the exceptions of episodic and working memory (see Figure 3). Age varied in its contribution to performance, where the greatest was for general ability, accounting for 14.8% of the variance, and the least was for episodic memory and working memory at 0.3% (see Table 3). Age-by-sex interactions were identified in the balance and general abilities composites; in both cases, older boys performed better than older girls despite lack of differences in the younger ages.

Speed components: The full model accounted for a high of 30.2% (motor speed) to a low of 0.8% (working memory). Removing covariates from the full model produced a significant but modest decrease in variance accounted for per composite: SES for three composites, site for two composites, ethnicity for four composites, and sex for three composites (see Table 3). When age alone was entered into the model, age was a significant factor in five of the seven composites: abstraction, attention, episodic memory, general ability, and motor speed (Table 3; Figure 4). An age-by-sex interaction was identified for episodic memory, such that older girls performed better than older boys despite lack of differences in the younger ages.

Total accuracy, total speed, and accuracy-speed difference: These analyses were based on two composite scores, which were means of all accuracy composites and of all speed composites. The full model accounted for 30.5% of the variance for accuracy but only 8.5% of the variance for speed. SES, site, and ethnicity were significant contributors to the overall accuracy variance, but only ethnicity was significant in the model testing speed. Age alone accounted for 12.1% for accuracy and 6.6% for speed variance; older male and female participants achieved higher scores than their younger counterparts. The difference of accuracy Z-score minus speed Z-score showed an age-by-sex interaction, where older boys had higher accuracy-speed scores than the girls (see Figure 5).

Pubertal development and composite score variance—As would be expected, higher PDS scores were highly correlated with older age in both sexes (see Figure 6). As with age, these relations were best described by nonlinear functions, where the boys started with lower PDS scores than girls at the younger ages, the girls achieved maximum pubertal status, on average, at age 16 years, and the boys did so in their early 20s. PDS score was then used in place of age as the predictor, keeping sex, SES, site, and ethnicity as covariates. The proportion of variance of the full GAM accounted for ranged from a high of 37.5% (general ability) to a low of 5.3% (working memory) for the accuracy composites and from 24.4% (motor speed) to 0.7% (working memory) for the speed composites (see Table 4). When PDS alone was entered into the model, PDS accounted for significant variance in five accuracy and three speed composites (see Table 4). Applying the GAM with PDS to the total composite scores revealed that all factors combined accounted for 27.2% of the accuracy variance but only 5.6% of the speed variance. Accuracy scores were higher with greater pubertal development in both sexes, although boys achieved higher scores than girls for

abstraction and general ability accuracy (see Figure 6). Independent contributions of age versus PDS to performance were not forthcoming, probably because age and PDS were so highly correlated.

Performance on delay discounting—The $100 and the $1,000 conditions showed the same pattern of results with respect to influential covariates. For both monetary conditions, age, SES, and ethnicity (but not sex) contributed significantly to performance. For the $100 condition, there was a significant effect of age (t=−5.434, p=.0000), with the full model accounting for 9.1% of the variance. For the $1,000 condition, there was a significant effect of age (t=−6.387, p=.0000), with the full model accounting for 9.8% of the variance. In both cases, older adolescents waited a longer time for a larger monetary reward than did younger adolescents. A significant difference between the conditions indicated that adolescents waited longer for greater monetary reward in the $1,000 condition relative to the $100 condition (mean difference = 0.966 ln$k$, paired t(df = 559) = 14.462, p = .0000; see Figure 7).

Part 2. Performance Differences: No/Low-Drinking Group Versus Exceeds-Threshold Group

To examine the effects of exceeding exposure criteria, we expanded the GAM to include a dichotomous group covariate. The results indicated that the exceeds group performed more poorly than the no/low-exposure group on one accuracy composite (Figure 8B and Table 5). On the Delay Discounting task, the exceeds-threshold group did not wait as long for greater monetary award as did the no/low-drinking group on the $1,000 condition ($t$ = 2.004, p = .0455).

As a confirmatory analysis, we constructed a sample matching the exceeds group on sex, age, and ethnicity and compared the two groups with Welch two-sample t tests. These results (see Table 5) showed essentially the same pattern of deficit in the exceeds groups as with the full Group GAM. Although the balance score was lower in the exceeds than no/low-drinking group, the group difference showed only a trend (p = 0.0614) toward significance. Reasons for this discrepancy include differences in the distributions of the two domain scores over the age ranges examined and, alternatively, chance.

Secondary analyses explored the effects of family history of drug or alcohol use disorders in two ways. First, chi-square analysis of performance by family history positive (FHP) versus negative (FHN) in no/low versus exceeds groups revealed a trend for higher incidence of FHP in the exceeds group (27.6%) versus the no/low group (18.4%; χ^2 = 3.0165, p = .082). Second, the influence of FHP on performance was added to Model 1 of the GAM, first within the no/low group alone and then in the entire sample (no/low + exceeds). For the no/low group, FHP individuals had lower mean scores on general ability accuracy (t= −2.195, p = .0285, N = 663) and total accuracy (t=−1.940, p = .0528, N = 639). When the exceeds group was added to the no/low group, the pattern held, with FHP having lower mean scores on general ability accuracy (t = −3.258, p = .0012, N = 774) and total accuracy (t = −2.632, p = .0087, N = 748). Thus, there was a small effect of FHP on two accuracy measures irrespective of group.

Exploratory analyses examined potential relations between drinking history variables and performance and indicated that poorer scores on two accuracy measures (abstraction: $p = .0506$; general ability: $p = .0530$) were marginally related to more binge episodes reported in the past year. In addition, the number of days of alcohol use in a lifetime was included as a factor in the GAM, along with age, sex, site, and ethnicity. These analyses revealed that poorer performance was related to more lifetime days of drinking alcohol on two accuracy measures (attention: $t = -2.507$, $p = .0135$; episodic memory: $t = -3.132$, $p = .0022$). Although one could interpret these relations to support a dose effect, whereby greater amount of alcohol was associated with lower scores on certain functions, an equally compelling argument could be made that the youth with greater alcohol use had preexisting differences putting them at risk for low performance. Correlations between amount drunk in a lifetime and performance on these two measures in the exceed group yielded contradictory findings, each supporting one of the two different arguments: For attention accuracy, the number of days using alcohol showed little direct correlation with poorer performance ($r = +.058$, $p = .5004$); for episodic memory accuracy, the alcohol-performance correlation was only modest ($r = -.164$, $p = .0565$).

We also considered drug consumption as a factor in performance, with the most used drugs being marijuana and nicotine (i.e., cigarettes). The few participants who engaged in either drug, however, precluded formal analysis of potential relations between these drugs and performance: Only nine in the exceeds-threshold group had more than 100 total days of marijuana use in lifetime; 19 had more than 30 total days of marijuana use in lifetime; five had smoked more than 100 cigarettes in lifetime; and 10 had smoked more than 30 cigarettes in lifetime.

Discussion

The analysis of these cross-sectional, neuropsychological data on youth, age 12 to 21 years, examined at their baseline visit, used general additive modeling to evaluate factors commonly modulating performance, notably, age, sex, ethnicity, SES, and PDS, and to test potential performance differences between the larger group of 692 no/low drinkers and the smaller group of 139 adolescents who exceeded age-specific, drinking thresholds. The performance metrics were hypothesis-driven composite scores of accuracy and speed derived from multiple measures of selected cognitive and motor component functions.

Accuracy composite scores, which involved general ability, abstraction, attention, emotion, and balance, were more sensitive to age differences than were speed scores. Nonetheless, composite scores that reflected speeded responses for attention, motor speed, and general ability were also sensitive to age and pubertal development. In support of the study hypotheses, older and more pubertally advanced adolescents in general achieved higher scores than younger ones on overall accuracy and speed measures. The accuracy domains showing an age effect involved executive functions, emotion processing, and general ability as predicted but not episodic memory, which was also predicted but not forthcoming. Regarding performance of the exceeds-threshold group, balance accuracy and Delay Discounting distinguished them from the no/low group. The Delay Discounting test was successful in detecting age and alcohol history differences, such that younger adolescents in

the no/low-drinking group and adolescents in the exceeds-threshold group, regardless of age, exhibited performance consistent with impulsive behavior.

Age and Demographic Factors Contributing to Cognitive and Motor Performance

Overall, the hypothesis-driven functional composites derived from a combination of computerized and traditional neuropsychological tests were adequately sensitive to detect age- and sex-related differences in certain functional domains. Use of composite scores for data reduction has provided useful functional summaries in developmental studies, affording measurement redundancy and robustness for assessment of selective functions (Carlozzi et al., 2014; Gur et al., 2012; Heaton et al., 2014; Nitzburg et al., 2014; Weintraub et al., 2014). In particular, relative to younger ages, the older adolescents in the NCANDA cohort exhibited greater accuracy in tests assessing abstraction, mental flexibility, logical reasoning, and vocabulary. In addition, older adolescents showed greater postural stability and responded faster than younger ones on tests assessing abstraction, attention, episodic memory, mental flexibility, psychomotor speed, and eye-hand coordinated movement. These age-related differences are consistent with performance improvement and efficiency, notable in these processes considered components of executive functions, including delayed gratification, observed over this decade of adolescence. Stage of pubertal development was found to be another factor to consider in neuropsychological studies of adolescents and provided further evidence, albeit cross-sectional, on the relevance of pubertal development on cognitive and motor functioning (cf., Stiles & Jernigan, 2010).

The distributions of several accuracy and speed composite scores had adequate variance to detect small differences with age, up to a maximum of 14.8% for general ability accuracy and 17.0% for motor speed. Despite the tight distribution of scores for attention accuracy relative to the rectangular distribution of scores for episodic memory accuracy, the former but not the latter composite exhibited a significant age effect (cf., Gur et al., 2012). Further, the composite scores were differentially modulated by demographic variables, consistent with the assumption that the composites assembled reflected different functions (also see Boelema et al., 2014). Specifically, SES (defined as highest parental education achieved) and self-identified ethnicity exerted the most consistent effects, although accounting for only 1.0% to 4.5% of the variance for a particular accuracy or speed composite score. Of note were four instances showing age-by-sex interactions. Older male adolescents had a performance advantage over older female adolescents on two accuracy measures—balance and general ability—but the opposite effect, in favor of the older female adolescents, emerged for speeded responses on the episodic memory composite. The interaction involving the accuracy-speed difference score indicated that older boys were faster and more accurate in their responses than older girls, despite minimal sex difference in the younger adolescents. The male performance advantage, notable in accuracy measures, was echoed in the comparisons based on pubertal development, such that boys at more advanced pubertal stages performed more accurately and responded more quickly than girls at a comparable pubertal stage, determined with the self-report PDS. A salient sex difference, in favor of the female youth, involved the emotion composite, which assessed abilities to identify and discriminate facially expressed emotions, a sex difference that comports with other studies of emotion detection differences between the sexes (Gur et al., 2012; Williams et al., 2009).

Alcohol Consumption and Performance in Adolescents

Even after accounting for age, sex, and other demographic factors, the group with greater drinking experience performed below the no/low-drinking group on balance accuracy. Exploratory quantitative analysis of the number of heavy drinking episodes over the past year, however, did not identify it as a significant covariate of performance on the composite measures in the exceeds-threshold group.

Impulsive behavior, high-risk taking, and questionable decision-making are all considered externalizing behaviors that have the potential of providing a basis for experimenting with alcohol and drugs, providing gateways to addiction (Fein, Di Sclafani, & Finn, 2010; Kendler, Prescott, Myers, & Neale, 2003). Impulsive behavior assessed by the Delay Discounting task showed significant age effects in the no/low-drinking group, where younger adolescents chose the lesser reward ($100) earlier (i.e., showed greater discounting) than the older ones, who opted for a larger reward ($1,000) at a longer delay. As observed in the younger, no/low-drinking youth, the exceeds-threshold drinking youth, who were generally in the older age range, exhibited a preference for a smaller, more immediate award at the expense of a larger delayed reward. The pattern of discounting behavior exhibited by the exceededthreshold youth is typical of heavy drinking adolescents and may convey some ongoing risk for real-world temporal discounting (Isen, Sparks, & Iacono, 2014; Stanger et al., 2013).

A function presenting a challenge for the exceeds-threshold group was postural stability, which in the current study was measured when participants had not drunk within 48 hr prior to testing. Prior studies examining the effects of acute alcohol on balance reported that nondependent adolescents who showed little sway in response to acute alcohol were more likely to develop alcohol dependence than youth who exhibited excessive sway (Schuckit, 1994), yet without alcohol challenge adolescents who carry familial risk of alcohol use disorder show greater postural sway than noncarriers (Hill, Steinhauer, Locke-Wellman, & Ulrich, 2009). Further, chronic alcohol dependence in adults can result in significant postural instability that remains detectable even in abstinent alcoholics, although sustained sobriety can result in at least partial resolution of imbalance (Smith & Fein, 2011; Sullivan, Rosenbloom, Lim, & Pfefferbaum, 2000). The predictive value of stability testing performance absent acute alcohol challenge awaits longitudinal study.

The small effect of positive family history on general ability and total accuracy present in both the no/low-drinking and the exceeds-threshold groups suggests that low performance can precede initiation of hazardous drinking and that family history carries a liability for compromised neuropsychological performance potentially exacerbated by initiation of substantial drinking or drug consumption. This possibility has been borne out in large cohort studies (e.g., Lovallo et al., 2013; Porjesz & Rangaswamy, 2007) and smaller-scale studies (e.g., Cservenka, Fair, & Nagel, 2014; De Bellis et al., 2008; Herting, Fair, & Nagel, 2011; Hill et al., 2001; Hill et al., 2000; Hill et al., 2009; Jacobus et al., 2009) typically revealing poorer performance or compromised brain structure or function in positive family history than negative family history adolescents, even in adolescents and young adults with similar histories of alcohol drinking.

Limitations

Caution must be taken before drawing conclusions about the direct or indirect role of drinking on performance in the exceeds-threshold group, because the observed group differences could be antecedent to the current assessment and reflect characteristic and familial features of youth at-risk for hazardous drinking (e.g., Begleiter, Porjesz, Bihari, & Kissin, 1984; Nigg et al., 2004; Nixon & Tivis, 1997; Pulido, Anderson, Armstead, Brown, & Tapert, 2009; for review, Sher, Grekin, & Williams, 2005), thus highlighting the need for longitudinal study (cf., Squeglia et al., 2009; Tapert et al., 2002). Most (94%) of the adolescents in the higher alcohol consumption group did not meet *DSM–IV* criteria for alcohol abuse or alcohol dependence, raising further suspicion that the poorer performance in this group relative to the no/low-drinking group may be preexisting, given that detection of alcohol-related impairment is typically associated with more chronic alcohol abuse (for review, Squeglia, Jacobus, & Tapert, 2014). It is also critical to recognize that youth exceeding drinking criteria did not show performance impairment in a clinical sense, but rather exhibited statistically lower performance levels than observed in the no/low-drinking group (also see Winward, Hanson, Tapert, & Brown, 2014) and likely not so compromised as occurs in youth in treatment (Brown et al., 2000; Tapert & Brown, 1999; Tapert et al., 2002).

Despite the large sample sizes reported herein, this study has limitations. First, this initial report of NCANDA neuropsychological data presents a cross-sectional view of cognitive and motor development, thus precluding inferences about change, which await longitudinal assessment of this cohort. Second, the composites comprised different numbers of tests, likely with differential ability to detect developmental change. Given previous analyses based on the tests that entered the composites, however, we are encouraged that the derived summary scores comprising multiple measures will have the power to detect developmental changes and modulation by different sources of demographic variance. Further, longitudinal analysis will be poised to reveal which tests are most sensitive to change and detection of alcohol and drug use and other mental health and social factors that might change the normal trajectory of development of selective functional processes. Finally, the potential of “ceiling effects” looms in studies of healthy participants. Nonetheless, even tests with ceiling effects can be sensitive to decline in longitudinal testing because of the potential of detecting fall from the ceiling with pathology or other untoward life events.

Conclusion

This cross-sectional analysis provides a baseline report of normal adolescents who have been rigorously screened for psychiatric, substance use, and medical conditions. Even though these neuropsychological tests were typically designed to detect pathology and thus may be less sensitive to variation in nonpathological individuals, the composite scores had adequate power to identify age, pubertal, sex, ethnicity, and SES differences depending on the function examined. We speculate that higher achievement with older age and pubertal stage in general ability, abstraction, attention, emotion, and balance suggests continued functional development through adolescence, possibly supported by concurrently maturing frontal, limbic, and cerebellar brain systems (cf., Gogtay et al., 2004; Pfefferbaum et al.,

2015; Sowell, Thompson, Leonard et al., 2004). Determination of whether the performance differences noted between no/low-drinking adolescents and adolescents with greater drinking experience could be attributable to drinking or to other modulating factors requires longitudinal study focused on both groups. Some of the no/low-drinking youth may initiate heavy to hazardous alcohol consumption along with use of other substances during their developmental years in the course of the NCANDA study and may align with family history of alcohol or drug problems. On the other hand, the youth with greater drinking experience may either continue drinking or abstain, affording the opportunity to observe a return to the norm.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Correction to Sullivan et al. (2016)

In the article “Cognitive, Emotion Control, and Motor Performance of Adolescents in the NCANDA Study: Contributions From Alcohol Consumption, Age, Sex, Ethnicity, and Family History of Addiction,” by Edith V. Sullivan, Ty Brumback, Susan F. Tapert, Rosemary Fama, Devin Prouty, Sandra A. Brown, Kevin Cummins, Wesley K. Thompson, Ian M. Colrain, Fiona C. Baker, Michael D. De Bellis, Stephen R. Hooper, Duncan B. Clark, Tammy Chung, Bonnie J. Nagel, B. Nolan Nichols, Torsten Rohlfing, Weiwei Chu, Kilian M. Pohl, and Adolf Pfefferbaum (*Neuropsychology*, Vol. 30, No. 3, pp. 449–473. http://dx.doi.org/10.1037/neu0000259), a computation to invert speed scores so that higher scores reflected better performance was originally applied only to scores of the no/low group and are now applied to the alcohol-drinking group. Correction to the manuscript is limited to speed scores differences between no/low and alcohol-drinking groups. Re-analysis of the corrected data found no group differences in any of the speed composites. All statements indicating group differences in speed scores, as well as Table 5 and Figure 8A, have been corrected in the online version of this article.

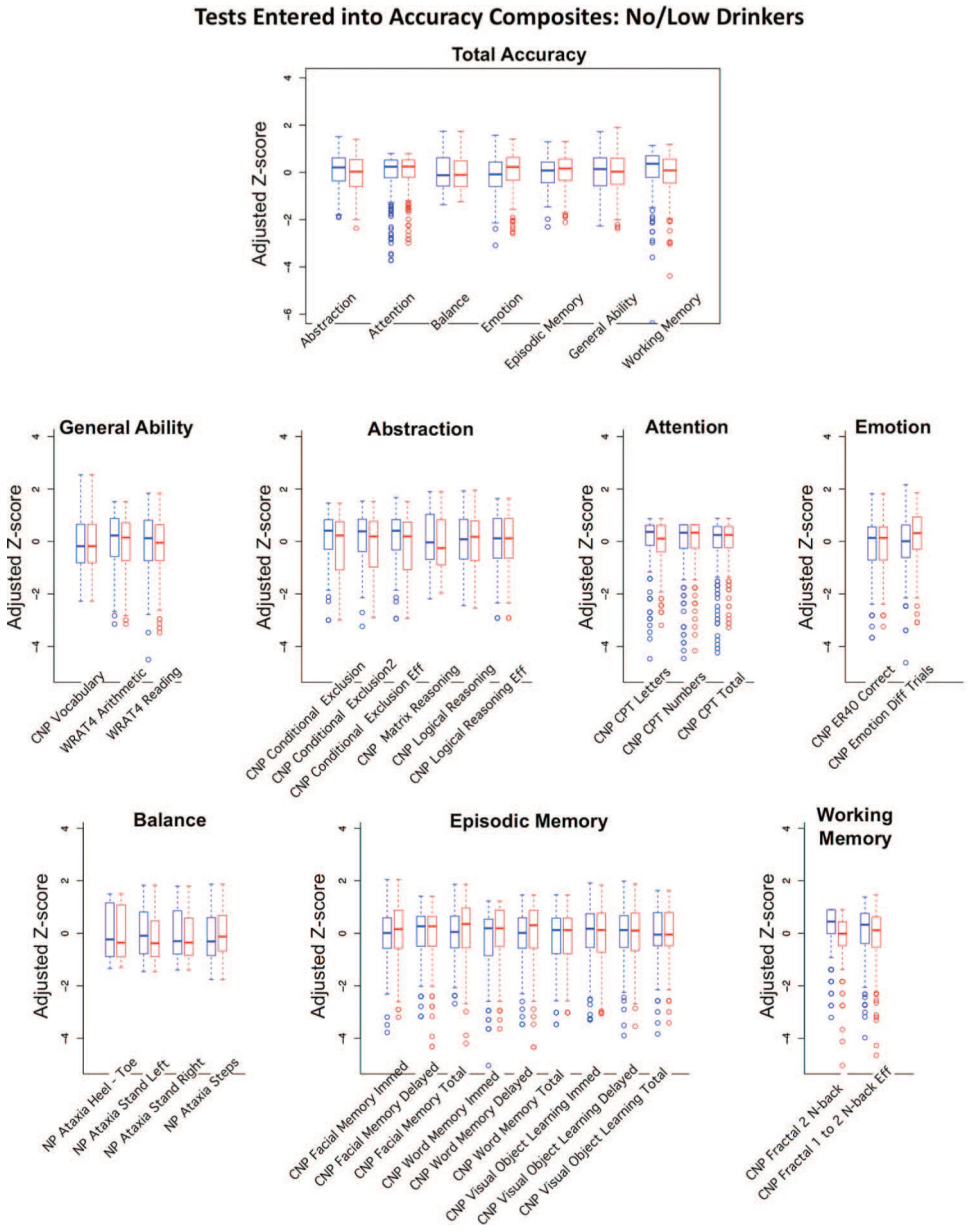


Figure 1.

Accuracy composite scores. Box plots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants. The top figure presents the summary scores for each of the seven composite scores determining the total accuracy composite score. The remaining seven sets of box plots show the individual measures that were entered into each accuracy composite score.

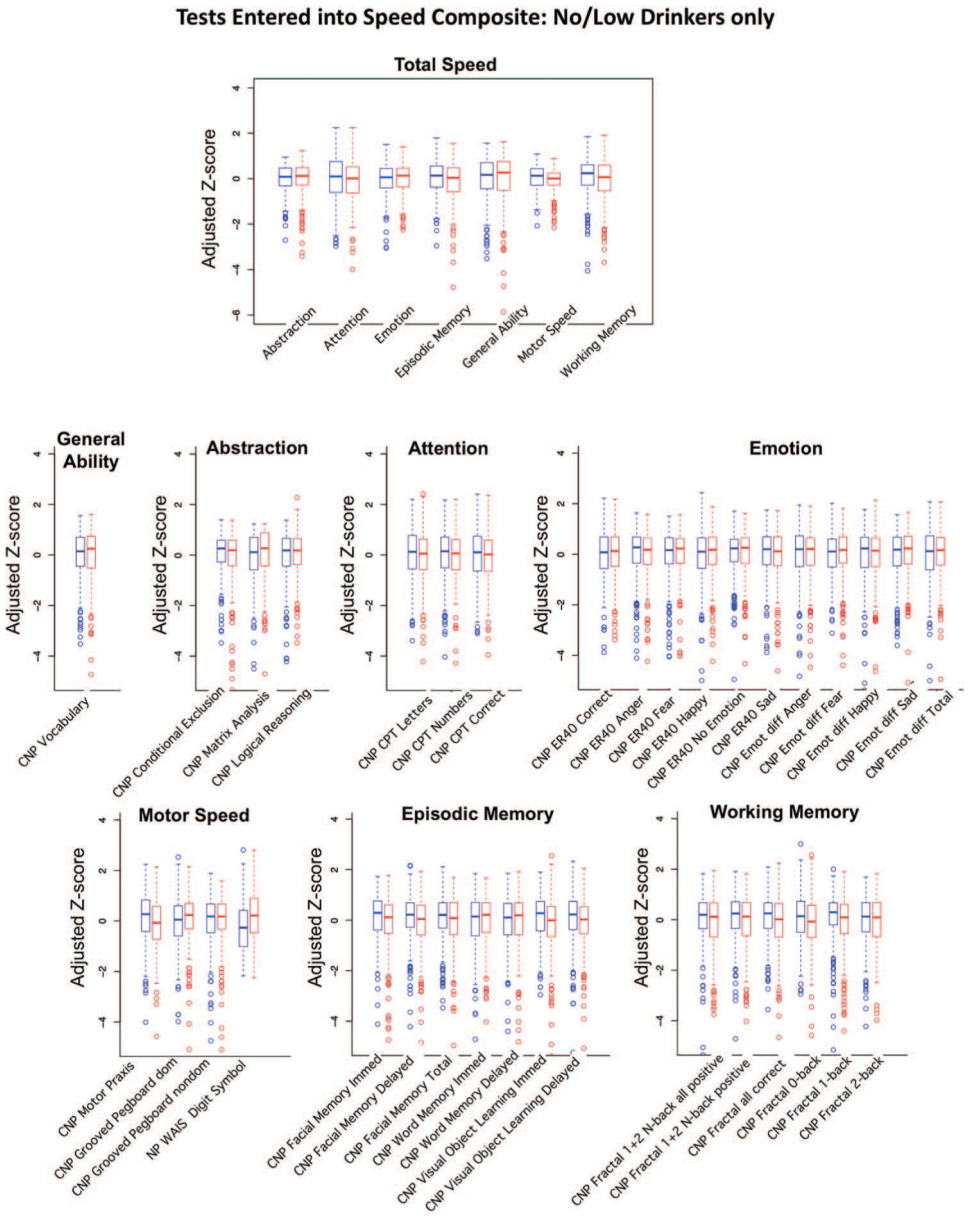


Figure 2.

Speed composite scores. Box plots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants. The top figure presents the summary scores for each of the seven composite scores determining the total speed composite score. The remaining seven sets of box plots show the individual measures that were entered into each speed composite score.

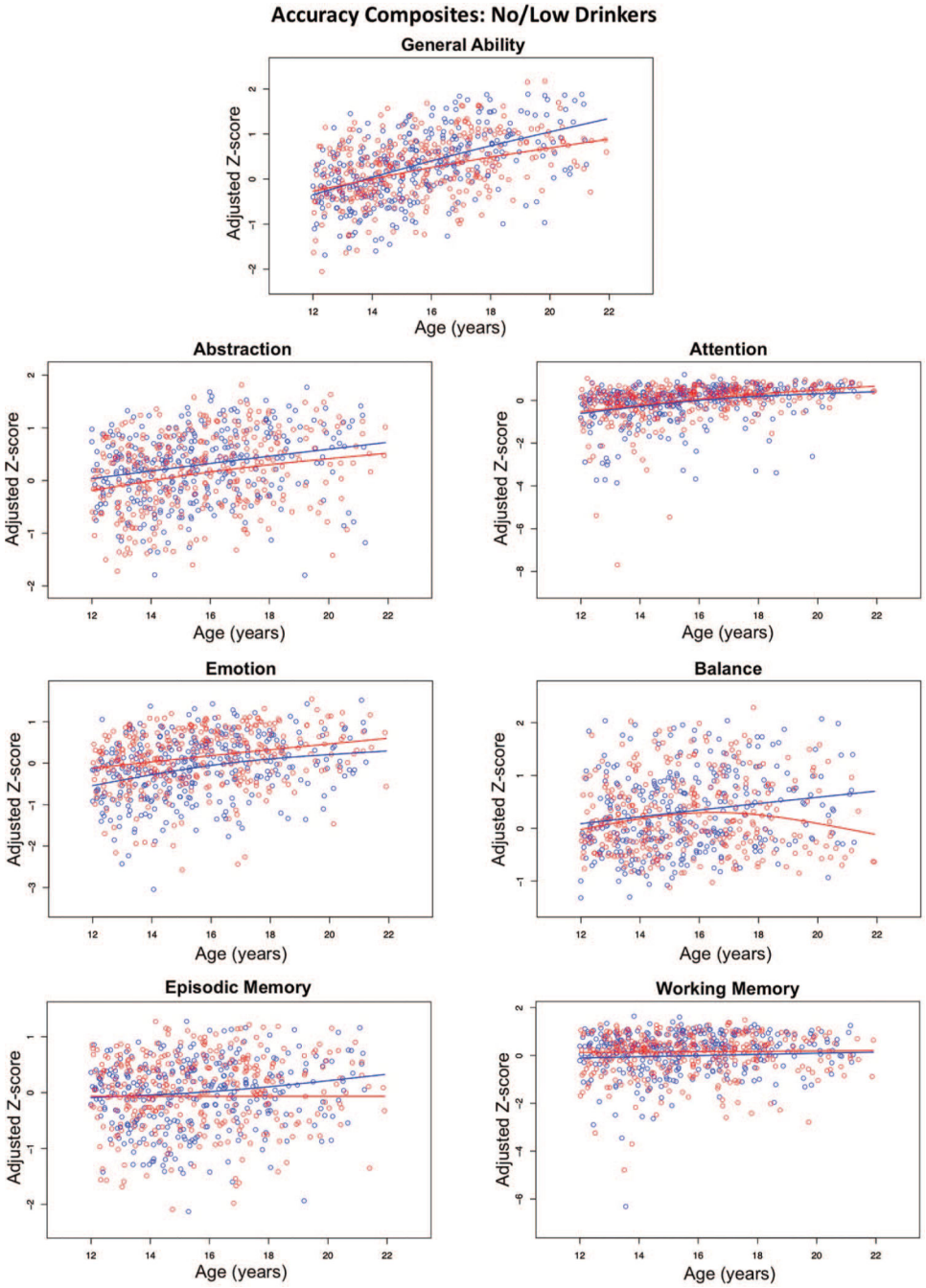


Figure 3.

Accuracy composite scores. Scatterplots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants plotted over age.

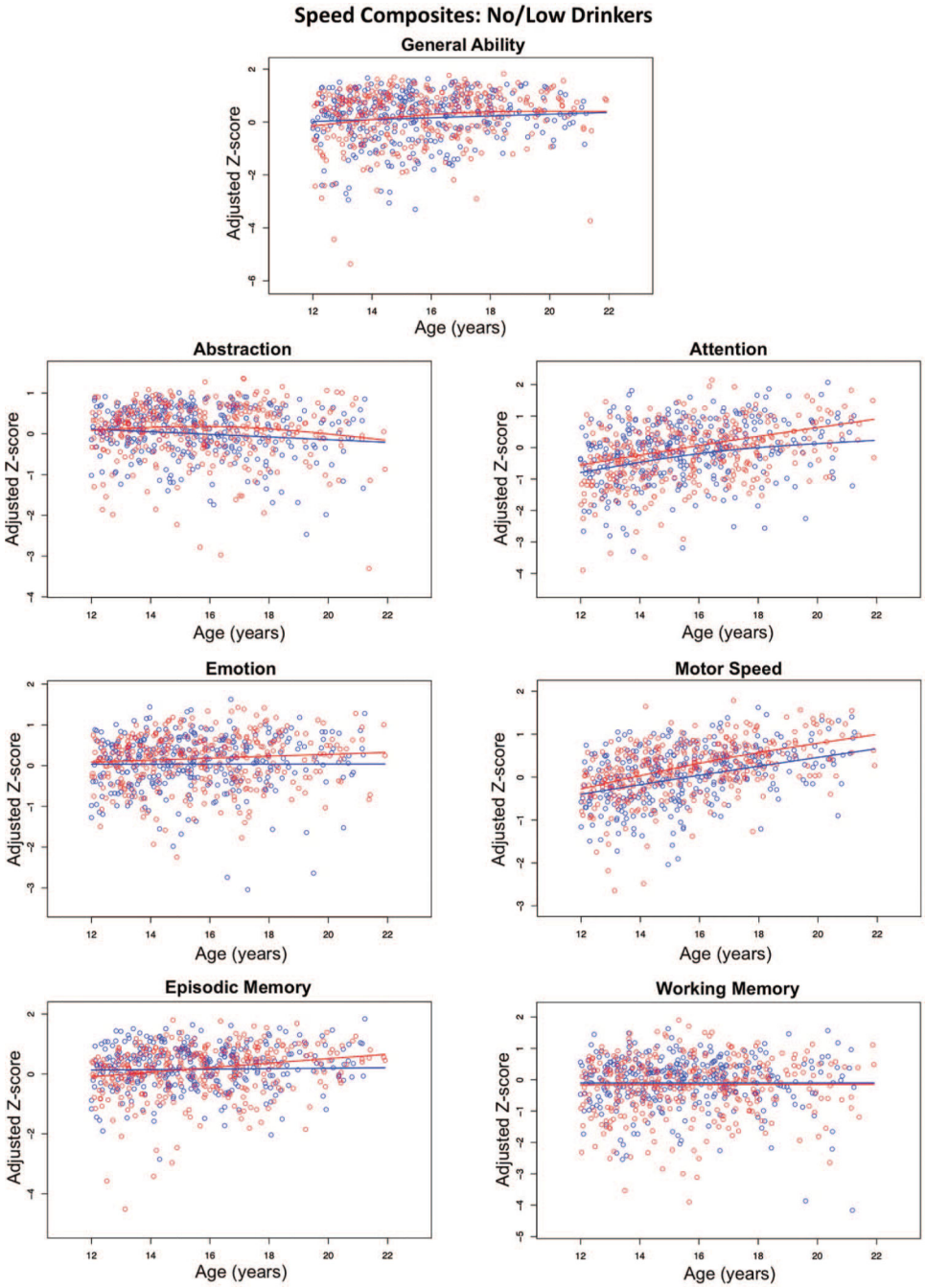


Figure 4.

Speed composite scores. Scatterplots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants plotted over age.

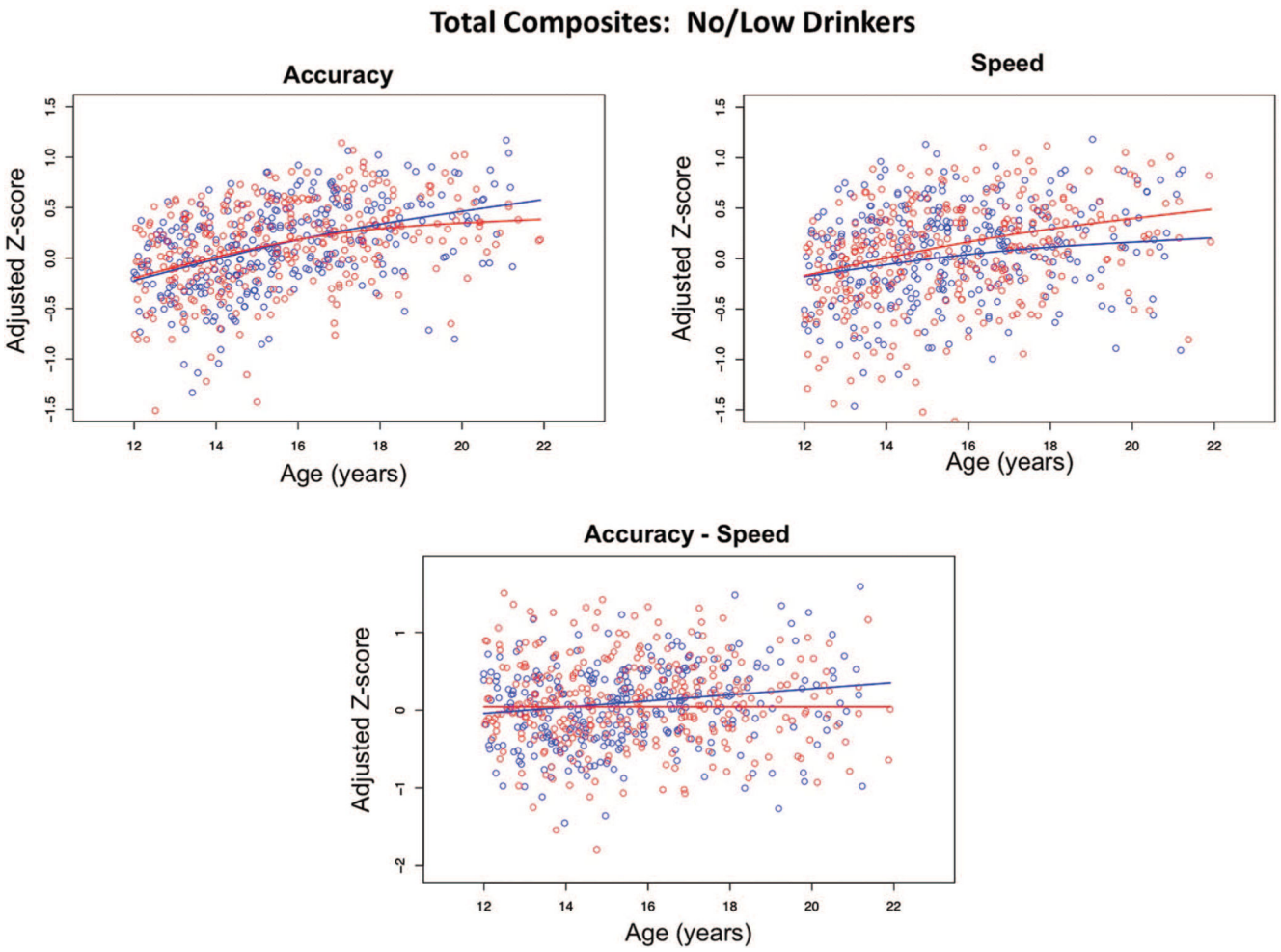


Figure 5.

Total composite scores. Scatterplots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants plotted over age.

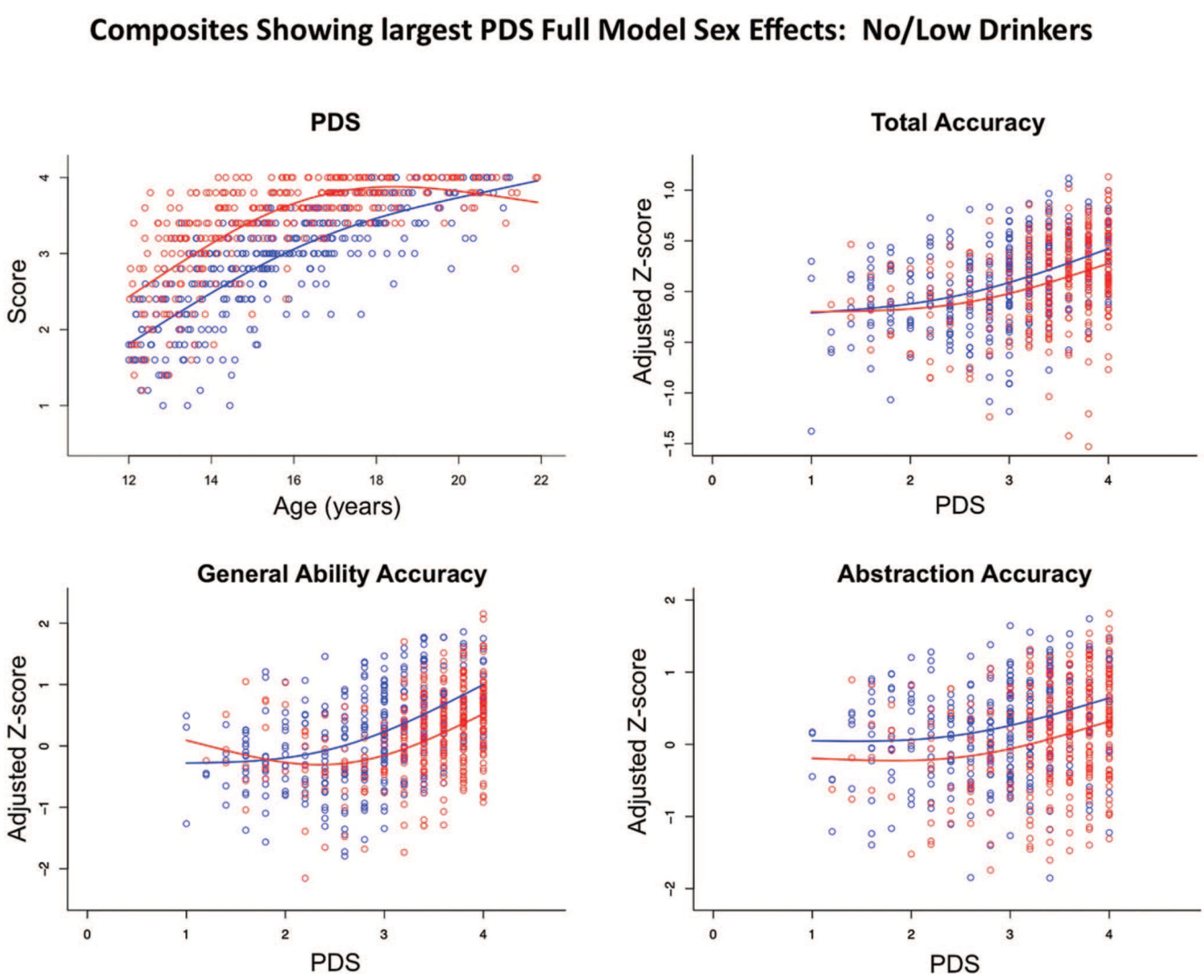


Figure 6.

Upper left: Pubertal Development Scale (PDS) scores of the no/low-drinking male (blue) and female (red) participants plotted over age. Upper right and lower left and right: Scatterplots of Z-scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants plotted as a function of PDS at time of testing.

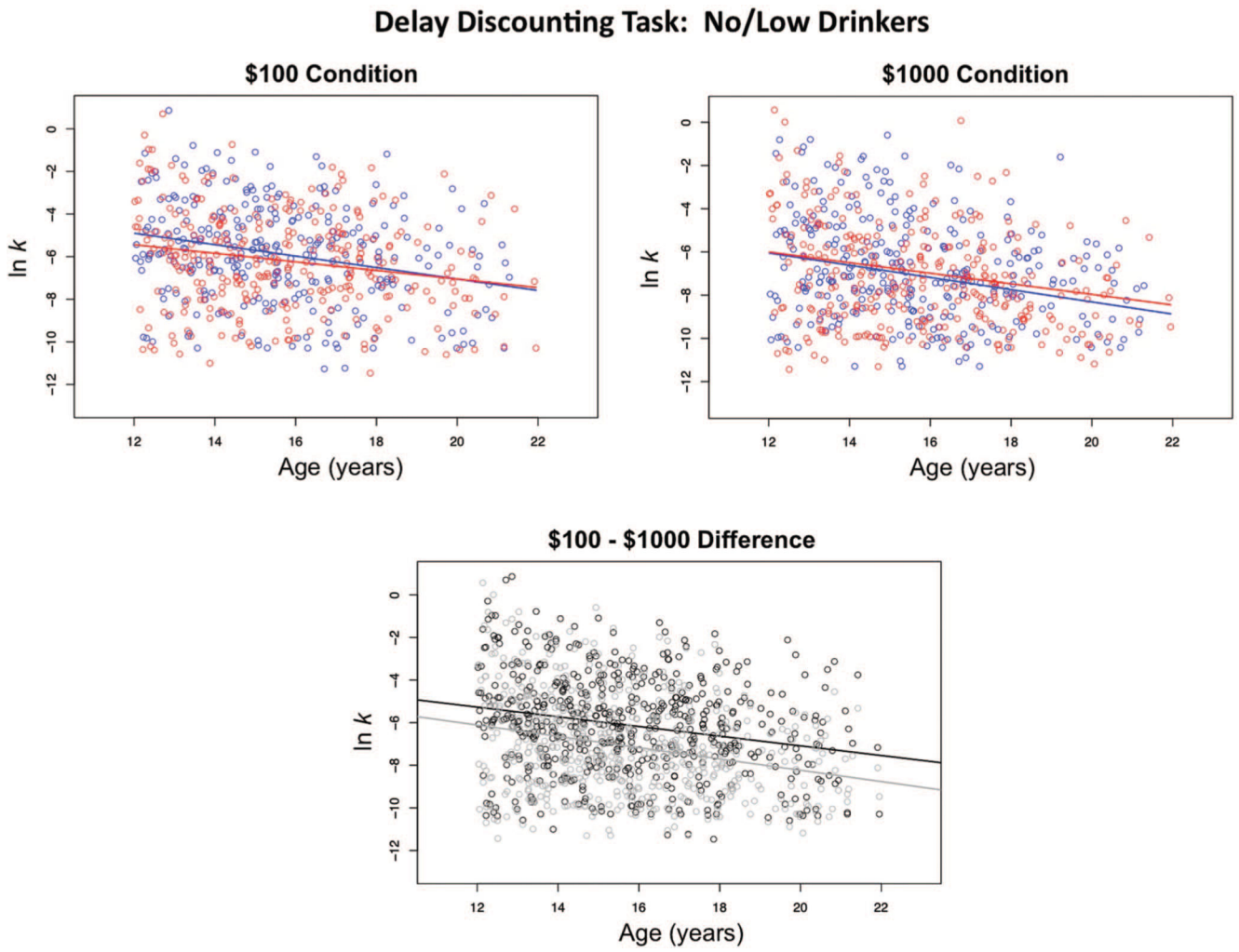
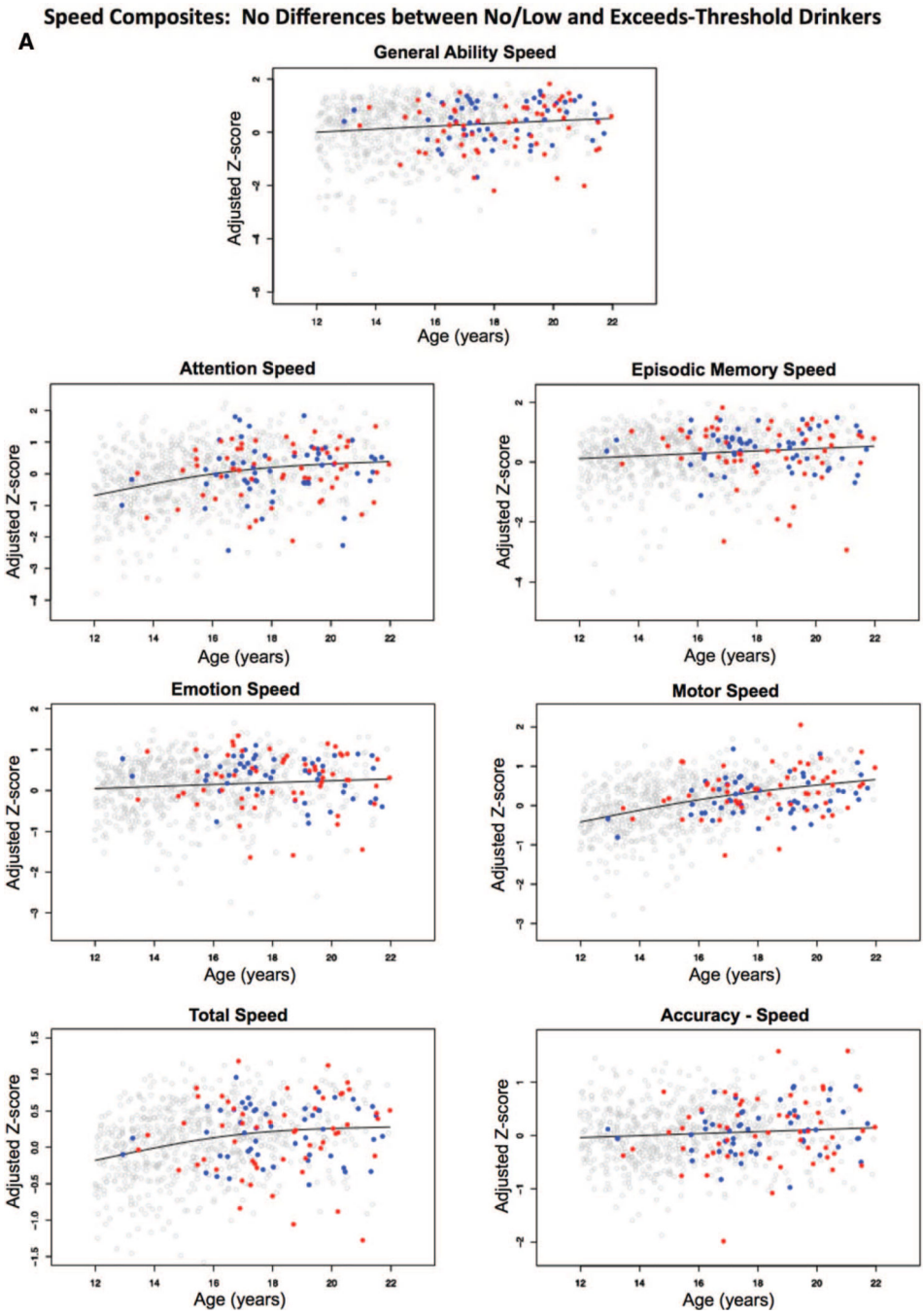


Figure 7.

Delay Discounting task scores. Top and middle: Scatterplots of ln*k* scores adjusted for site, ethnicity, and SES of the no/low-drinking male (blue) and female (red) participants plotted over age. Bottom: Scatterplots of ln*k* scores adjusted for site, ethnicity, and SES of the no/low-drinking participants plotted as a function of age (black = $100 condition; gray = $1,000 condition).



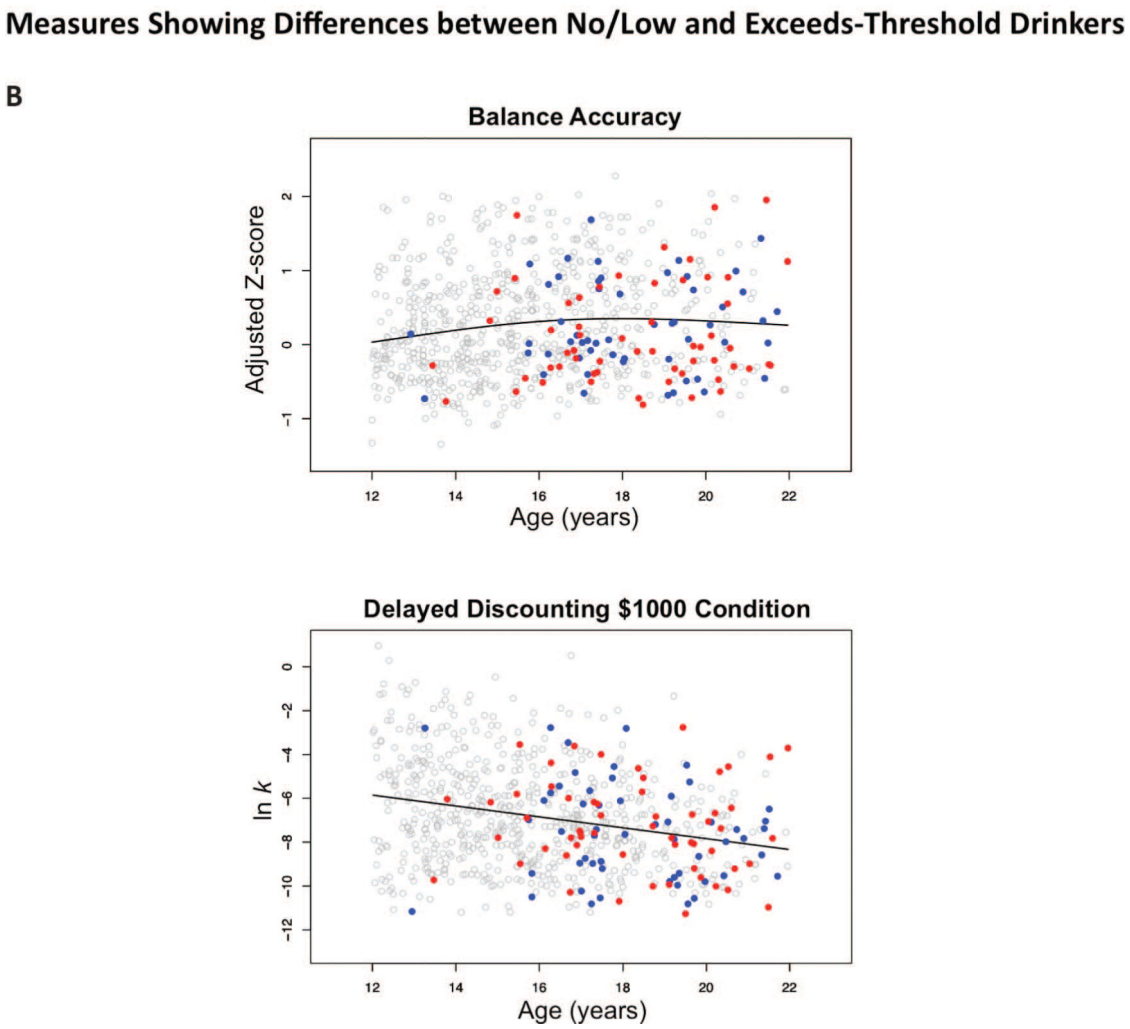


Figure 8.

A and B. Scatterplots (adjusted for site, ethnicity, SES, and sex) showing scores of the 692 no/low-drinking adolescents (open gray circles) and the 139 adolescents who exceeded age-specific thresholds for drinking (filled circles). blue = male; red = female.

Table 1

National Consortium on Alcohol and NeuroDevelopment in Adolescence (NCANDA) Demographics for Neuropsychological Test Analysis (N = 831)

	No/low drinker (*N* = 692)		Male vs. Female		Exceeded-threshold (*N* = 139)		Male vs. Female		No/low vs. exceeds	
	Male	Female	t or χ^2	*p*	Male	Female	t or χ^2	*p*	t or χ^2	*p*
Age (years)										
N	344	348			64	75				
Mean	15.6	15.8	−.850	.3954	18.4	18.5	−.305	.7609	−14.841	.0000
Standard deviation	2.3	2.4			2.0	2.0				
Education (years)										
N	342	346			64	74				
Mean	8.9	9.2	−1.155	.2486	11.7	11.9	−.440	.6607	−14.524	.0000
Standard deviation	2.3	2.5			1.9	2.0				
Pubertal Development Scale										
N	339	345			62	73				
Mean	2.9	3.4	−10.917	.0000	3.5	3.8	−5.635	.0000	−11.553	.0000
Median	3.0	3.6			3.6	4.0				
Standard deviation	.7	.6			.5	.2				
Socioeconomic status										
N	326	326			54	58				
Mean	17.0	16.6	2.057	.0401	17.1	17.3	−.400	.6902	−1.743	.0832
Standard deviation	2.4	2.5			2.1	2.3				
Handedness										
N	343	348			64	75				
L/R/A	33/261/49	23/290/35	5.936	.0514	2/53/9	7/61/7	2.736	.2546	.527	.7685
Family history of alcoholism										
Negative/positive	318/26	316/32	.410	.5222	50/14	63/12	.445	.5047	12.464	.0004
Self-declared Ethnicity										
N	344	348	8.997	.1092	64	75	3.279	.3505	5.215	.3902
Caucasian	251	235			52	57				
African American	34	53			3	9				
Asian	27	25			6	4				

	No/low drinker (*N* = 692)		Male vs. Female		Exceeded-threshold (*N* = 139)		Male vs. Female		No/low vs. exceeds	
	Male	Female	t or χ^2	*p*	Male	Female	t or χ^2	*p*	t or χ^2	*p*
Pacific Islander	1	3			0	0				
American Indian	3	0			0	0				
Mixed	28	32			3	5				

Note. N = number; L/R/A = left/right/ambidextrous.

Table 2

Composite Domains: Tests, Functions, Processes, and Neural Substrates

Functional domain	Name of test	Cognitive or motor process	Brain regions associated with process	References
Abstraction	Conditional Exclusion Task†	Abstraction and concept formation	Frontal	Kurtz et al., 2004; Gunning-Dixon and Raz, 2003
	Matrix Analysis Test†	Abstraction and mental flexibility	Frontal and posterior parietal	Lee et al., 2006
	Logical Reasoning†	Verbal intellectual ability	Left Temporoparietal	Gur et al., 1982, 2000
Attention	Continuous Performance Test - Number Letter Version†	Visual attention and vigilance	Frontoparietal	Kurtz et al., 2001; Ogg et al., 2008
Balance	Walk-a-Line	Postural stability	Frontocerebellar	Fregly et al., 1972; Sullivan et al., 2000, 2006
Emotion	Emotion Recognition Test†	Emotion recognition	Temporo-limbic	Gur et al., 2002a, 2002b
	Measured Emotion Differentiation†	Emotion discrimination	Fronto-amygdala	Fossati, 2012
Episodic memory	Facial Memory Test†	Facial memory (immediate and delayed)	Frontal and bilateral anterior medial temporal	Gur et al., 1997; Jackson and Schacter, 2004
	Word Memory Test†	Word memory (immediate and delayed)	Frontal and bilateral anterior medial temporal	Gur et al., 1997; Jackson and Schacter, 2004
	Short Visual Object Learning Test†	Visual object learning and memory (immediate and delayed)	Frontal and bilateral anterior medial temporal	Glahn et al., 1997; Jackson and Schacter, 2004
General ability	Vocabulary Test†	General knowledge	Frontotemporoparietal	Lee et al., 2014
	WRAT-4 Math Calculations	Arithmetic	Frontoparietal	Wilkinson and Robertson, 2010; Gruber et al., 2001
	WRAT-4 Word Reading	Phonological expression	Temporoparietal	Wilkinson and Robertson, 2010; Christodoulou et al., 2014
Working memory	Short Fractal N-Back Test - 2 Back Version†	Attention and working memory	Dorsolateral prefrontal	Ragland et al., 2002; Rodriguez-Jimenez et al., 2009
Motor speed	Grooved Pegboard	Digit dexterity and psychomotor speed	Frontal	Matthews and Kløve, 1964; Kochunov et al., 2010
	Digit Symbol	Psychomotor speed	Frontal	Wechsler, 2008; Gautam et al., 2011

†Subtests of the WebCNP (Computerized Neuropsychological Testing System, University of Pennsylvania School of Medicine), Gur et al., 2010.

Table 3

Composite Scores: Proportion of Variance Accounted for by the Age Full Model (GAM†) and the Full Model Without SES, Site, Ethnicity, or Sex as Covariates

	N	FM	FM w/o SES	SES effect	FM w/o site	Site effect	FM w/o ethnicity	Ethnicity effect	FM w/o sex	Sex effect	Linear Age × Sex interaction	Age w/o covariates			
												R^2	*F*	*p*	*N*
Accuracy			††		††		††		††						
Abstraction	**657**	$\mathbf{R^2}$ = .167****	**.148**	.019	**.138**	.029	**.127**	.040	.164	.004	n.s.	**.039**	14.410	**.0000**	683
Attention	**664**	$\mathbf{R^2}$ = .125****	**.111**	.014	**.117**	.008	.120	.005	.124	.001	n.s.	**.096**	36.990	**.0000**	690
Balance	**652**	$\mathbf{R^2}$ = .096****	**.083**	.013	**.068**	.028	.096	.000	.097	.000	***t* = −2.498, *p* = .0127**	**.017**	6.209	**.0013**	676
Emotion	**664**	$\mathbf{R^2}$ = .104****	**.094**	.010	.104	.000	.102	.002	.085	.019	n.s.	**.072**	27.020	**.0000**	690
Episodic memory	**663**	$\mathbf{R^2}$ = .060****	**.039**	.022	.059	.001	**.048**	.012	.059	.001	n.s.	.003	1.151	.0670	689
General ability	**663**	$\mathbf{R^2}$ = .399****	**.310**	.089	**.371**	.028	**.352**	.047	.397	.002	***t* = −2.425, *p* = .0156**	**.148**	60.170	**.0000**	689
Working memory	**661**	$\mathbf{R^2}$ = .055****	**.048**	.007	.052	.003	**.030**	.025	.053	.002	n.s.	.006	2.483	.0516	687
Speed															
Abstraction	**657**	$\mathbf{R^2}$ = .025**	.024	.001	.030	.000	**.015**	.010	.026	.000	n.s.	**.011**	4.330	**.0060**	683
Attention	**660**	$\mathbf{R^2}$ = .123****	**.118**	.004	.117	.005	.125	.000	.121	.002	n.s.	**.103**	39.850	**.0000**	686
Emotion	**663**	$\mathbf{R^2}$ = .029***	.030	.000	.030	.000	**.009**	.020	.028	.001	n.s.	.004	1.192	.0646	689
Episodic memory	**663**	$\mathbf{R^2}$ = .048****	.048	.000	**.028**	.020	.049	.000	**.040**	.008	***t* = 1.981, *p* = .0480**	**.020**	6.733	**.0001**	689
General ability	**664**	$\mathbf{R^2}$ = .047***	**.040**	.007	.043	.004	**.039**	.008	.047	.000	n.s.	**.017**	6.087	**.0005**	690
Motor speed	**653**	$\mathbf{R^2}$ = .302****	**.290**	.012	**.293**	.009	**.255**	.047	**.295**	.007	n.s.	**.170**	67.790	**.0000**	677
Working memory	**661**	$\mathbf{R^2}$ = .008	.010	.000	.002	.006	.011	.000	**.002**	.006	n.s.	.000	.000	.6600	687
Total accuracy and speed															

	N	FM	FM w/o SES	SES effect	FM w/o site	Site effect	FM w/o ethnicity	Ethnicity effect	FM w/o sex	Sex effect	Linear Age × Sex interaction	Age w/o covariates			
												R^2	*F*	*p*	*N*
Accuracy	**639**	$\mathbf{R^2}$ = .305****	**.245**	.060	**.287**	.018	**.262**	.043	.305	.000	n.s.	**.121**	46.170	**.0000**	663
Speed	**639**	$\mathbf{R^2}$ = .085****	.085	.000	.089	.000	**.076**	.008	.086	.000	n.s.	**.066**	23.890	**.0000**	663
Accuracy-Speed	**632**	$\mathbf{R^2}$ = .057***	**.029**	.028	.051	.006	.051	.006	.055	.002	***t* = −2.698, *p* = .0072**	.002	.677	.1270	656

Note. GAM = general additive model; SES = socioeconomic status; FM = full model; w/o = without; n.s. = not significant.

†FM = GAM(domain~age + site + SES + ethnicity + sex).

††Bold font indicates significant χ^2 test of the effect of removing a covariate from the model ($p < .05$).

*$p \leq .05$.

**$p \leq .01$.

***$p \leq .001$.

****$p \leq .0001$.

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Table 4

Composite Scores: Proportion of Variance Accounted for by the Pubertal Development Scale (PDS) Full Model (GAM[†]) With Site, SES, Ethnicity, and Sex as Covariates

		PDS full model	Sex effect from the PDS	Full model[††]	PDS w/o covariates			
	N	R^2	*t*	*p*	*N*	R^2	*F*	*p*
Accuracy								
Abstraction	651	.165****	−4.360	**.0000**	675	**.018**	6.485	**.0005**
Attention	658	.097****	−1.910	.0566	682	**.059**	21.640	**.0000**
Balance	646	.099****	−1.946	.0528	668	**.011**	3.839	**.0036**
Emotion	658	.073****	1.441	.5010	682	**.051**	18.680	**.0000**
Episodic memory	657	.059****	1.308	.1914	681	.004	1.041	.0805
General ability	657	.375****	−4.905	**.0000**	681	**.079**	29.790	**.0000**
Working memory	656	.053****	−5.146	.1439	680	.000	.000	.7130
Speed								
Abstraction	651	.019*	.755	.4503	675	.003	.907	.0924
Attention	654	.064****	−3.343	**.0006**	678	**.036**	12.880	**.0000**
Emotion	657	.024**	.685	.4935	681	.003	.707	.1240
Episodic memory	657	.038****	−3.588	**.0004**	681	.002	.680	.1270
General ability	658	.053****	−.843	.3998	682	**.018**	6.676	**.0006**
Motor speed	647	.244****	−1.538	.1246	669	**.108**	40.740	**.0000**
Working memory	656	.007	−2.173	**.0302**	680	.000	.000	.4110
Total Accuracy and Speed								
Accuracy	634	.272****	−3.123	**.0019**	656	**.069**	24.750	**.0000**
Speed	634	.056****	−2.604	**.0094**	656	**.032**	11.170	**.0000**
Accuracy-speed	627	.059****	.469	.6391	649	**.005**	1.592	**.0398**

Note. GAM = general additive model; SES = socioeconomic status; w/o = without.

† Full model = GAM(domain PDS~site + SES + ethnicity + sex).

†† Bold font indicates significant χ^2 test of the effect of removing a covariate from the model ($p < .05$).

* $p \leq .05$.

** $p \leq .01$.

*** $p = .001$.

**** $p \leq .0001$.

Table 5

Composite Scores: No/Low vs. Exceeds-Threshold Drinking Groups

	Alcohol exposure effect from the age full model†				Alcohol exposure effect from matched samples††††			
	N No/low	*N* Exceeded threshold	*t*	*p*	*N* No/low	*N* Exceeded threshold	*t*	*p*
Accuracy			††	†††			††	
Abstraction	657	110	1.119	0.2637	127	110	1.266	0.2067
Attention	664	111	0.058	0.9539	127	111	0.251	0.8019
Balance	652	111	−2.322	**0.0205**	122	111	−1.880	0.0614
Emotion	664	111	−0.118	0.9062	127	111	−1.545	0.1237
Episodic memory	663	111	0.135	0.8927	127	111	1.044	0.2975
General ability	663	111	−0.655	0.5126	127	111	−0.947	0.3445
Working memory	661	111	1.195	0.2323	127	111	1.778	0.0768
Speed								
Abstraction	657	110	−0.695	0.4870	127	110	0.135	0.8930
Attention	660	111	−1.114	0.2657	127	111	−1.703	0.0899
Emotion	663	110	−1.918	0.0555	127	110	0.746	0.4560
Episodic memory	663	111	0.287	0.7741	127	111	−0.197	0.8436
General ability	664	111	−0.317	0.7512	127	111	−1.258	0.2096
Motor speed	653	110	−1.307	0.1917	124	110	−1.753	0.0809
Working memory	661	111	0.759	0.4481	127	111	0.022	0.9825
Total Accuracy and Speed								
Accuracy	639	109	−0.168	0.8666	122	109	0.014	0.9892
Speed	639	108	−4.082	0.6837	124	108	−1.279	0.2023
Accuracy-Speed	632	108	0.316	0.7520	122	108	1.044	0.6228

†Full model = gam(domain age~site + SES + ethnicity + sex + exposure).

††Negative *t*-values indicate No/low group > Exceeds-threshold group.

†††Bold font indicates significant χ^2 test of the effect of removing a covariate from the model ($p < .05$).

††††Welch two sample *t*-tests.