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Learning and Memory in Adolescent Moderate, Binge, and Extreme-binge Drinkers

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Abstract

Background—Binge drinking has been linked to neurocognitive disadvantages in youth, but it is unclear if drinking at particularly heavy levels uniquely affects neurocognitive performance. This study prospectively examined (1) whether initiating moderate, binge, or extreme-binge drinking in adolescence differentially influences subsequent learning and memory performances, and (2) if dosage of alcohol consumption is linearly associated with changes in learning and memory over 6 years of adolescence.

Methods—Participants, who later transitioned into drinking, were administered verbal learning and memory assessments at project intake prior to the onset of substance use (age 12–16 years), and at follow-up approximately six years later (N=112). Participants were grouped based on alcohol involvement at follow-up as: moderate (≤4 drinks per occasion), binge (5+ drinks per occasion), or extreme-binge (10+ drinks per occasion) drinkers.

Results—Despite equivalent performances prior to onset of drinking, extreme-binge drinkers performed worse than moderate drinkers on verbal learning, and cued and free short delayed recall (ps< .05); binge drinkers did not differ from the other groups. No distinct thresholds in alcohol quantity to differentiate the three groups were detected, but estimated peak blood alcohol concentrations were linearly associated with verbal learning ($\hat{\beta}$ =−.24), and immediate ($\hat{\beta}$=−.27), short delay free ($\hat{\beta}$=−.28) and cued ($\hat{\beta}$=−.30) and long delay free ($\hat{\beta}$=−.24), and cued ($\hat{\beta}$=−.27) recall (ps< .05).

Conclusions—Drinking quantity during adolescence appears to adversely affect verbal learning and memory in a dose-dependent manner. The acquisition of new verbal information may be particularly affected, notably for those who initiated drinking 10+ drinks in an occasion. Although

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classification of drinkers into categories remains critical in the study of alcohol, it is important to consider that subtle differences may exist within drinking categories.

Keywords

binge drinking; extreme-binge drinking; learning and memory; adolescence

Introduction

Adolescence is a time of rapid neurological development often occurring in parallel with increasing alcohol use, which continues to be the most commonly used substance among 8–12th grade students. Of particular concern is the high prevalence of heavy episodic or binge drinking reaching 0.08g/dL blood alcohol concentration (BAC; NIH, 2004). Nationwide, 23% of high school students have consumed ≥5 drinks in a row at least once in the past 30 days (Kann et al., 2014), with a trend of increasing prevalence of binge drinking for students between 9th (14%) to 12th grade (29%). Compared to their moderate drinker counterparts, high school binge drinkers are almost 11 times more likely to exhibit poorer academic performance and engage in health risk behaviors (Miller et al., 2007). In college students, binge drinking is associated with poorer academic and occupational performances, risky behaviors, and eventual alcohol use disorder (Jennison, 2004).

While there has been an overall decline nationwide in the prevalence of consuming ≥5 drinks per occasion among adolescents (Johnston et al., 2014), a significant portion of youth still engage in risky alcohol use. Among college freshman, 41% of men (34% of women) were identified as binge drinkers and 28% (10% for women) of them endorsed drinking at least 10 drinks per occasion in the past two weeks, a pattern of alcohol consumption that has been termed “extreme-binge drinking” (Patrick et al., 2013;White et al., 2006). Between 2005–2011, more than 20% of 12th graders reported consuming 5+ drinks at least once in the past two weeks, 11% consumed 10+ drinks, and 6% consumed 15+ drinks per occasion (Patrick et al., 2013).

To date, investigations of alcohol use commonly utilize the threshold of 5+ drinks to characterize binge drinking; however, this definition includes a wide range of alcohol consumption quantities, from 5 (sometimes 4 for women) drinks up to 15+ drinks. Although the use of 4–5 drinks as the cut-off for binge drinking is widely accepted in the literature, and serves as an important standard for examining the effects of acute alcohol use, some have questioned the validity of a single cutoff to characterize this diverse group of drinkers (Jackson, 2008;Wechsler and Nelson, 2001). A recent prospective study found that in adults, the optimal threshold that best predicted likelihood of experiencing short-term consequences (i.e., hangover symptoms) was approximately 1–2 drinks per occasion, while the optimal threshold for long-term consequences (i.e., problematic alcohol and drug use 10 months later) was 13 drinks in men and 9 in women (Jackson, 2008). Thus, the 4–5 drinks threshold did not serve as a useful predictor of either short- or long-term consequences of alcohol use in this case.

It is unclear whether the effects of alcohol intoxication on neurocognitive functioning are ubiquitous among all levels of heavy episodic drinking (HED), or if extreme-binge drinkers

are at greater risk compared to other drinkers at lower levels of consumption. Using a longitudinal design and controlling for cognitive performances prior to alcohol use initiation, the aims of the current study were twofold. First, this study sought to determine the thresholds in alcohol quantity and corresponding estimated BAC (eBAC), based on the peak number of drinks consumed in the past three months, that optimally stratified adolescent drinkers on verbal learning and memory (VLM) performance. Estimated BAC level was used in lieu of number of drinks to minimize possible confounding effects of biological (i.e., gender, height, and weight) and environmental (i.e., duration of drinking) variations among drinkers. There are no currently accepted BAC threshold levels to demarcate risk for long-term effects on learning and memory in youth. Drinking to a higher eBAC was hypothesized to predict worsened VLM performances. The second aim was to examine whether current *a priori* categorizations of alcohol use (i.e., moderate, binge, and extreme-binge drinkers) and its corresponding eBAC predicts significant differences in verbal learning and memory among adolescents. It was hypothesized that performance would decline across drinking groups, with extreme-binge drinkers showing the greatest decrease in cognitive functioning, followed by binge drinkers, compared to moderate drinkers.

Materials and Methods

Participants

This study used data from a larger longitudinal substance use project (R01 AA13419) (Nguyen-Louie et al., 2015), and was approved by the University of California, San Diego Human Research Protections Program. Potential participants were recruited from San Diego area middle schools and were excluded for more than minimal substance use (e.g., at baseline, participants had <10 lifetime drinking days, <5 lifetime marijuana use, and no history of other intoxicant use), psychiatric diagnoses, and neurodevelopmental disorders. There were 295 adolescents between 12–16 years old at project entry who had limited experience with substances. As the current study focused on understanding the effects of alcohol use quantity on VLM, participants in the parent project were excluded from analysis if they: 1) had not initiated alcohol use, 2) did not have valid past 30-days alcohol use and neuropsychological testing data (e.g., could not complete an in-person follow-up interview), and 3) did not consume any alcohol in the past 30 days at follow-up. Further, five teens were no longer followed in the parent study due to death or severe medical illness. In total, 112 participants met criteria for analysis in this study. At baseline (Table 1), participants were healthy 12–16 year olds (36% female); 96% had never tried cigarettes; 93% had never tried marijuana; and 98% had never tried other drugs. The maximum number of tobacco, marijuana, and other drug use instances at baseline were two, three, and one times, respectively.

After 4–9 years (M=6.4; SD=1.2) post-baseline, youth were administered a follow-up interview and assessment (follow-up rates exceeded 95%). Groups were classified based on drinking patterns at follow-up. Moderate drinkers (n=32) consumed no more than 4 drinks, binge drinkers (n=45) consumed 5–9 drinks (Johnston et al., 2015), and extreme-binge drinkers (n=35) consumed ≥10 drinks (Patrick et al., 2013) in the past 3-month peak-drinking occasion. Groups were similar at baseline and follow-up on demographic

characteristics (age, pubertal development, socioeconomic status, family history of substance use disorder, level of psychopathological syndromes, and mood state at the time of testing). Youth who would transition into extreme-binge drinkers were more likely to be male and White, and had higher baseline externalizing scores than moderate drinkers. Fourteen-percent of the sample met DSM-5 (American Psychiatric Association, 2013) criteria for mild alcohol use disorder (AUD) at follow-up (Table 2).

Measures

Substance use—The Customary Drinking and Drug Use Record (Brown et al., 1998) and Timeline Follow-back (Sobell and Sobell, 1992) were administered at baseline and follow-up to assess quantity and frequency of substance use. The alcohol use variables of interest were number of drinks consumed during the peak drinking episode in the past three months, and corresponding eBAC level on this occasion, based on gender, body weight and height, number of drinks, and duration of drinking episode (Fitzgerald, 1995). Most recent intoxicant use prior to the testing session was three days.

Background—The Family History Assessment Module (Rice et al., 1995) was administered to youth and parents to assess familial history of substance use disorders (SUD). Family history negative (FHn) youth had no first- or second-degree relative with history of SUD, family history mild (FHm) had one second-degree relative with history of SUD, and family history positive (FHp) had at least one parent or at least two second-degree relatives with history of SUD. To obtain a continuous measure of SUD family history density, items were calculated as the weighted sum of biological parents and grandparents who endorsed two or more SUD symptoms (Zucker et al., 1994). A Hollingshead Index of Social Position score (Hollingshead, 1965), an index of socioeconomic status (SES), was calculated at baseline for each participant's parents; higher values indicated lower SES. The Pubertal Development Scale (Petersen et al., 1988), a valid and reliable self-assessment measure of pubertal maturation, was administered at baseline and follow-up.

Psychopathology—Psychopathological symptomology was assessed with the parent report Child Behavior Checklist (Achenbach, 1991a) at baseline, and the parallel Youth Self Report (YSR, <18 years old; Achenbach, 1991b) or Adult Self Report (ASR, age 18 or older; Achenbach and Rescorla, 2003) to obtain normed indices of Internalizing and Externalizing problem symptoms. Beck Depression Inventory–II (Beck et al., 1996) assessed depressed mood symptoms for the past two weeks prior to the neuropsychological assessment. Higher scores indicate more symptomology. Presence of DSM-IV psychiatric disorders (American Psychiatric Association, 2000) was assessed using the Mini International Neuropsychiatric Interview (Sheehan et al., 1998) at follow-up.

Neuropsychological test measures—VLM was measured using the California Verbal Learning Test-Children's Version (Delis et al., 1994) at baseline and CVLT-II (Delis et al., 2000) at follow-up. Measures of VLM were assessed using 12 standard scores, corrected for age and gender: (1) list A trial 1 (auditory attention skill); (2) list A trial 5 (immediate recall); (3) list A trials 1–5 total (global verbal learning ability); (4) list B – list A trial 5 (proactive interference); (5) short delay free recall (SDFR; immediate recall of target words

after a distractor list); (6) short delay cued recall (SDCR; recall after semantic cues); (7) long delay free (LDFR); and (8) cued recall (LDCR), measures of delayed memory 20 minutes after learning trials; (9) learning slope, average number of new words learned per trial; and (10) retention, number of words retained from list A trial 5 to short delay recall, calculated as immediate recall – SDFR (Delis et al., 2000); higher scores suggested poorer retention.

Participants were also administered the Wide Range Achievement Test (WRAT) Reading subtest at follow-up to assess general vocabulary knowledge. Version 3 (WRAT-3; Wilkinson, 1993) was administered to twenty-one participants (19% of the sample), and the remainder of the sample was administered version 4 (WRAT-4; Wilkinson and Robertson, 2006) when it became available.

Data Analysis

Model predictors—Dependent variables were CVLT-II standard scale scores at follow-up as indicated above. Measures were free from outliers, right-skewed and censored at the maximum correct responses; no transformations were performed. Estimated BAC levels yielded a normal distribution (range: 0.01–0.49 g/dL; M=0.20; SD=0.12).

Covariates and moderators—The following covariates were considered due to their association with HED or cognitive performance: body weight and height, YSR/ASR attention problems and externalizing T-scores (Seguin et al., 2009), SES (Raizada and Kishiyama, 2010), SUD familial density (Tapert and Brown, 2000), lifetime alcohol and marijuana use, past 30-days marijuana and tobacco use at follow-up, days since last alcohol and marijuana use, baseline and follow-up ages and baseline CVLT performances. To better capture the unique effects of alcohol use on verbal learning and memory, and address possible confounds in VLM performance with general verbal achievement and vocabulary knowledge, models controlled for standardized scores on the WRAT Reading subtest at follow-up. Possible moderation effects of race/ethnicity and gender were examined. Participants who engaged in more HED exhibited heavier marijuana use and more lifetime alcohol use (Table 2), so these indices were considered for covariates in initial analyses. To better understand the effects of substance use independent of innate differences in cognitive functioning, performance on the CVLT at baseline was included as covariates in all analyses (Tapert et al., 2003).

Among the potential covariates assessed, only YSR/ASR attention T-score, baseline CVLT performance, and WRAT Reading performance significantly accounted for variance in the dependent variables (i.e., CVLT performance; ps<.05), and were included in analyses as covariates. Covariates were not significantly associated with the predictor variable of interest, eBAC. YSR/ASR externalizing T-scores at follow-up were significantly associated with eBAC (r = .22, no group differences were detected) and VLM performances (r = −.24 to −.36, ps <.05). However, externalizing symptomology was not a significant predictor of VLM performance in the multivariate model that included attention T-score and baseline CVLT performances, suggesting that the effects of externalizing symptomology on VLM was, in part, due to its association with other predictor variables (i.e., attention

symptomology, $r = .64$, $p = <.0001$) and was no longer a statistically significant predictor of VLM when other predictors were accounted for. No collinearity between attention and externalizing symptomology was detected (variance inflation factor = 1.00). Thus, YSR/ASR externalizing T-score and other predictors that were not significant predictors in the final model were removed as potential covariates to increase degrees of freedom and decrease the probability of Type II error. Follow-up neuropsychological performance did not significantly differ by gender and race/ethnicity ($p>.05$). To clarify whether findings would be affected by gender and externalizing symptomology, post-hoc exploratory models were examined covarying only for gender, externalizing, WRAT reading, and baseline CVLT scores.

Quantitative relationship between drinking and learning and memory—To test hypothesis one, locally weighted scatterplot smoothing regressions (LOWESS; Trexler and Travis, 1993) were used to determine the thresholds in alcohol quantity and eBAC that optimally stratified adolescent drinkers. Unlike traditional models, LOWESS regressions do not fit data to an *a priori* function. This exploratory method allows for a data-driven approach in examining the association between alcohol use quantity and VLM, reducing the number of functions examined before the best fit of the data is determined, decreasing Type I error and increasing power. LOWESS regressions were plotted for each CVLT measure of interest (Figure 1). As an exploratory tool, LOWESS regressions do not provide statistical indices to determine whether the observed locally weighted plots significantly differ from a zero slope. Thus, follow-up ordinary least-squares (OLS) regressions were applied to the data based on the curvature and shape of LOWESS regressions ($\alpha=.05$) to determine statistical significance. Results of LOWESS regressions showing a linear fit would indicate a continuous linear relationship between VLM and alcohol use; a step-function fit indicates discrete, categorical differences in performance at certain thresholds of alcohol quantity. If the LOWESS regressions resembled a straight line, data were fitted by OLS linear regressions; step functions were followed up with ANCOVA models. Reported regression coefficients are in standardized betas ($\hat{\beta}$). Analyses using censored regression (Tobit) models to account for ceiling effects of the response variable yielded equivalent results to OLS regression in tests of significance, and coefficients and standard error estimates. Statistical analyses were conducted in SPSS 23 using the univariate general linear and linear regression models (IBM Corp., Version 23.0. Armonk, NY: IBM Corp.) and STATA 13.1 “lowess” function (StataCorp, College Station, TX).

Categorical comparison of drinking groups—To test hypothesis two, moderate, binge, and extreme-binge drinker groups were compared on follow-up verbal learning and memory performance, in ten separate analyses of covariance (ANCOVA) models, one for each VLM outcome performance measure, controlling for YSR/ASR attention problems T-score, follow-up WRAT Reading performance, and baseline performance on the same VLM measure.

Exploratory follow-up analyses—To understand the facets of VLM affected by alcohol use in adolescent drinkers, follow-up partial Pearson’s correlation analyses were performed with the remaining CVLT indices and past 3-month peak eBAC level, controlling for

attention problems T-score and baseline CVLT and follow-up WRAT Reading performances. These were standard scores for: Trial B, semantic, serial, and subjective clustering; percent recall from primacy, middle, and recency of word list; total learning slope for trials 1–5; across-trial recall consistency; total repetitions; total intrusions; and recognition trial total hits, false positives, recognition discriminability, and response bias. To explore whether drinkers exhibited difficulties with retrieval of learned material, the difference between immediate and SDFR (SDFR – list A trial 5) and LDFR (LDFR – list A trial 5) were also examined. Bonferroni correction (Miller, 1981) for multiple comparisons was applied ($\alpha_{B=}$.003). LOWESS graphs and linear regression analyses were performed, as described above, with VLM indices that were significantly correlated with peak eBAC level.

Results

Changes in VLM Performances Over Time

Among the CVLT variables examined, participants showed significantly improved performances in standardized scores between baseline and follow-up in list A trial 1, short delay cued recall, learning slope, and recognition hits, ps<.05. Within each group, moderate drinkers showed significantly improved performances between baseline and follow-upon list A trial 5, short delay free recall, short delay cued recall, and learning slope, yet decreased performance on list A trial 1. Binge drinkers showed significantly improved performance in learning slope only. Importantly, extreme binge drinkers showed no significant changes in their VLM performances between baseline and follow-up. These changes were above and beyond effects due to getting older, as age is already corrected for in standardized scores.

Quantitative Relationship Between Drinking and Learning and Memory

LOWESS regressions—Among the verbal and learning indices, LOWESS regressions showed linear associations between alcohol use and list A trial 5, list A trials 1–5, SDFR, SDCR, LDFR, and LDCR (Figure 1). No step- or other non-linear functions were observed.

Follow-up OLS regressions—Based on the shape of LOWESS graphs, OLS regressions were conducted for each VLM index. Controlling for baseline CVLT and follow-up WRAT Reading performance and attention problems T-score in all models, higher eBAC level during the peak alcohol use occasion in the past three months significantly predicted linearly poorer performances on list A trial 5 ($t(98)=-2.65$, $p=.009$, $\hat{\beta}=-.24$, $R^2\Delta=6\%$), list A trials 1–5 total ($t(98)=-3.22$, $p=.002$, $\hat{\beta}=-.27$, $R^2\Delta=7\%$), SDFR ($t(98)=-3.19$, $p=.002$, $\hat{\beta}=-.28$, $R^2\Delta=8\%$), SDCR ($t(98)=-3.43$, $p=.001$, $\hat{\beta}=-.30$, $R^2\Delta=9\%$), LDFR ($t(96)=-2.72$, $p=.008$, $\hat{\beta}=-.24$, $R^2\Delta=6\%$), and LDCR ($t(96)=-2.96$, $p=.004$, $\hat{\beta}=-.27$, $R^2\Delta=7\%$). No significant associations between eBAC level and list A trial 1, proactive interference, learning slope, and retention were found. Results were unchanged in models covarying for gender, externalizing, WRAT reading, and baseline CVLT scores.

Drinking Group Effects

Controlling for baseline CVLT and follow-up WRAT Reading performance and attention problems T-score, three of ten VLM measures differed between moderate, binge, and extreme-binge drinkers (Figure 2): list A trials 1–5 ($F(2, 97)=4.68$, $p=.011$, $\eta^2=.09$), SDFR

(F(2, 97)=4.07, p=.020, η^2=.08), and SDCR (F(2, 96)=4.80, p=.010, η^2=.09); Figure 2. Bonferroni post-hoc tests revealed that extreme-binge drinkers performed worse than moderate drinkers on all three measures. No pair-wise differences were detected between moderate and binge drinkers or binge and extreme-binge drinkers. No significant group differences were detected for list A trial 5, long delay free and cued recall, proactive interference, learning slope, and retention (p>.05). In follow-up models covarying for gender, externalizing, WRAT reading, and baseline CVLT scores, results remained unchanged for dependent variable short delay cued recall; however, short delay free recall (p=.082) and list A trials 1–5 (p=.057) failed to reach significance.

Exploratory Follow-up Analyses

Among the 17 additional VLM indices tested, three were significantly correlated with past 3-month peak eBAC level: percent recall from recency of word list (r=0.23), recognition trial total hits (r=−0.21), and total recognition discriminability (r=−0.21). Results were not significant after Bonferroni correction.

Higher peak eBAC levels significantly predicted greater percent recall from recency of word list, (t(106)=2.35, p=.020, $\hat{\beta}$=.22, $R^2\Delta$=6%), and lower discriminability, (t(97)= −2.43, p=.012, $\hat{\beta}$=−.24, $R^2\Delta$=6%), controlling for baseline CVLT performance, follow-up WRAT reading performance, and attention problems T-score. Based on the curvature of LOWESS graphs for recognition trial total hits (Figure 1), follow-up OLS regression examined linear, quadratic, and cubic effects of eBAC level on this measure. There was a significant linear (t(93)=2.59, p=.011) and quadratic (t(1093)= −2.34, p=.018) effect; the cubic term did not reach statistical significance (t(93)=1.94, p=.055). No interaction effects with gender and race were found. In follow-up models covarying for gender, externalizing, WRAT reading, and baseline CVLT scores, results remained unchanged for dependent variable total recognition discriminability; however, recognition trial total hits (p=.080) and percent recency recall (p=.126) were no longer statistically significant.

Discussion

This study aimed to examine whether VLM significantly differed among adolescent moderate, binge, and extreme-binge drinkers and to determine threshold values in the number of drinks that optimally stratified adolescent drinkers into groups differing in VLM performances. This is the first study to examine VLM among moderate, binge, and extreme-binge drinkers and to do so with a longitudinal design. LOWESS regressions allowed for the examination of the association between alcohol use and VLM without fitting the data to a particular function, thereby minimizing the number of analyses necessary to determine these threshold values. Results showed no clearly defined categorical groups. Rather, the effect of alcohol quantity on VLM followed a linear dose-dependent relationship, highlighting the importance of potential variations in alcohol's effects on cognition between and within drinking groups. The strict use of categorical comparisons may overlook important differences in neurocognition that may be detected using a linear quantitative approach. For example, examining eBAC level as a continuous measure (i.e., linear regression models) indicated that increased drinking negatively influenced performances on long term cued and

recall memory, but no significant differences were found when statistical analyses were performed by drinker group (i.e., ANCOVA models). We found that for every additional drink consumed, and corresponding eBAC increase, there was a linearly increasing deleterious effect on immediate recall, global verbal learning ability, short and long verbal recall, overall word recognition discriminability and greater reliance on recency of stimulus presentation, above and beyond attention problems, general word knowledge (i.e., WRAT Reading), and VLM performance before alcohol use initiation. When VLM performances were examined in moderate, binge, and extreme-binge drinkers using *a priori* cut-offs in drinking quantity, similar, but not identical, results were found. On average, extreme-binge drinkers recalled 8–12% less words than moderate drinkers and 4–5% less than binge drinkers while binge drinkers recalled 4–5% less words than moderate drinkers in short and delay recall VLM conditions. It should be noted that participants in this study are healthy adolescents primarily from middle-class households. While 14% of the sample met criteria for DSM-5 mild AUD at follow-up, only one participant had received prior treatment. Thus, it was of little surprise that overall, participants performed close to age-appropriate levels on the CVLT. The effects of alcohol use on VLM may exhibit a different pattern in treatment seekers or individuals with more severe drinking patterns. However, results of the current study highlight the importance of subtle differences in VLM performances, even among healthy adolescent drinkers.

The ten CVLT measures initially examined in this study assessed key aspects of VLM hypothesized to be affected in adolescent drinkers based on the extant literature (Mahmood et al., 2010). Results suggest that subtle deficits in VLM performance among heavier (i.e., extreme-binge) adolescent drinkers may be related to disadvantages during the acquisition part of learning and not an issue of retrieval, as evidenced in the significant relationship between increasing peak drinks and worsening performances in list A trial 5 and list A Trials 1–5. Heavier drinkers did not exhibit greater interference by a second word list and results did not indicate poorer attention allocation to the task (i.e., no significant differences in list A trial 1). After accounting for learning, short- and long-term memory among drinkers were not significantly different and once the word list had been acquired, the information appeared to be retained in memory equally by all drinkers, as indicated by no differences in retention and short- and long-term memory minus list A trial 5. A possible reason for heavier drinkers performing poorer on recall trials is that extreme-binge drinkers were able to acquire and encode the word list successfully but experienced difficulty during retrieval. In this case, it was expected that heavy drinkers would perform similar to moderate drinkers on recognition trials despite poorer performances on cued and recall memory trials. Follow-up exploratory analyses showed that participants who drank heavily performed linearly worse on recognition trial total hits and discriminability compared to lighter drinkers. These results suggest that recognition did not aid retrieval of information by decreasing demand on recall memory. This further supports the observation that heavier drinkers did not successfully acquire and encode the word list during learning, thereby affecting their recall in delayed trials. No significant differences in learning slope were found, suggesting that while heavier drinkers acquired fewer words overall, the rate at which these words were acquired across trial was not significantly different from more moderate drinkers. However, heavier drinkers appeared to rely more heavily on words presented later in the list during

recall (i.e., recency). Although preliminary, results also indicate a quadratic trend in the relationship between eBAC level and recognition memory, suggesting that the association between alcohol consumption and VLM changes as eBAC level increases and that binge drinkers may have a “yes bias” in recognition trials. However, results for recency and recognition memory should be interpreted with caution, as *p*-values exceeded that required by Bonferroni correction.

In this study, the distribution of FH status was not statistically different among drinker groups (Table 1). VLM performance, peak eBAC, and past three-month maximum drinks consumed did not differ based on FH status ($p>.05$). Although no effect was found on single-occasion HED, FHm youth tended to have 10–14% more lifetime drinking days than FHn and FHp youth. Boys tended to have less lifetime drinking days than girls in the FHn, but not FHp, group. These results suggest that the biological and environmental effects of FH are most prominently observed in macro-level alcohol use behaviors, such as lifetime patterns, but are weaker in short-term episodic drinking behaviors.

No gender differences in VLM or interactions were found, but the extreme-binge group had 40–53% more boys than did the moderate and binge groups, consistent with epidemiological data showing that high school boys are up to 3 times more likely to be extreme-binge drinkers (Patrick et al., 2013;Maki et al., 2001). Reasons for this phenomenon include differences in body lipid and water content, pharmacokinetics of alcohol, and subjective expectancies of alcohol’s effects (Holmila and Raitasalo, 2005). College students who engage in more prepartying (i.e., drinking before going out) and drinking games are more likely to engage in extreme-binge drinking (Fairlie et al., 2015). One possible mechanism for an effect of gender on VLM include fluctuating levels of estrogen (e.g., during the menstrual cycle or estrogen replacement therapy), for which high levels are associated with better performance in VLM in women (Islam et al., 2008;Maki et al., 2001). Future studies can ascertain the role of gender and hormonal level on VLM, as this information is not currently available for this sample.

Another important consideration in interpreting the current results is the higher rate of cannabis use among extreme-binge drinkers. The literature is mixed regarding the effects of cannabis use on VLM in cannabis-using youth. For example, Solowij and colleagues (2011) found poorer performances in heavy cannabis users on learning, retention, and retrieval than nonusers, but another study from our group found no effect of cannabis use in concomitant drinkers (Mahmood et al., 2010). Neuroimaging evidence suggests possible deleterious effects of cannabis on structures important for learning and memory. Thus, it is possible that marijuana use was a contributing factor to VLM in this study. To account for this, analyses included lifetime and past 30-day marijuana use as covariates. Neither was significantly associated with VLM, and results were not changed after adding these covariates. Although extreme-binge drinkers used cannabis on average 7.4 days in the past month (compared to 1.5 and 3.7 days in binge and extreme being drinkers, respectively), this pattern of use is lower than in studies that reported associations between cannabis and VLM. Solowij et al. (2011) reported average use of 14 days per month over 2.4 years, and Bolla and colleagues (2002) reported at least 2 years of use, 3 times per week. To better understand whether cannabis use contributed to the lower cognitive performance in extreme-binge drinkers, we

conducted a linear regression examining the relationship between marijuana lifetime use days and VLM only in extreme-binge drinkers; no significant associations were found. Overall, due to the relatively low prevalence of marijuana use in the total sample and extreme-binge drinkers (57% reported less than 100 lifetime uses, 29% have not used in the past 30 days, and that only 12 extreme-binge drinkers used more than once a week in the past 30 days), it appears unlikely that cannabis use was a significant contributor to verbal learning memory performance in this sample. However, these findings do not preclude the possibility that marijuana has a deleterious effect on VLM among heavier users.

Interpretation of results is limited by the range of drinks tested in the analysis; it is unclear if, and how, the relationship between VLM and alcohol use may change with higher quantities and eBAC levels than those reported in this study. Although not a primary aim of the current study, we also examined the effects of heavy episodic drinking on spatial memory using the Rey Osterrieth Complex Figure task (not reported) and found no significant differences in performance among drinker groups, and no linear association with eBAC. A limitation, however, is that only one neuropsychological task of spatial memory was administered at follow-up, and, unlike the CVLT, the Complex Figure task only provides one measure of delayed memory. Further investigations are needed to better understand this with more comprehensive measures of spatial memory.

The twofold aims of this study were successfully examined and, in part, confirmed. Higher recent peak eBAC levels linearly predicted poorer performances on VLM in adolescent drinkers. In the same individual (i.e., with the same height and weight) and under the same drinking circumstances (i.e., duration of drinking), the effect of three vs. four drinks is equally as deleterious as four vs. five drinks (i.e., the cut-off for moderate vs. binge drinker category). Thus, even within the same drinker category, decrements in VLM performances for every additional drink still follow the same linear slope as between categories. Results confirm prior cross-sectional findings (Mahmood et al., 2010;Sneider et al., 2013). Another important implication of our findings was that no safe or harmless level of drinking was detected in the effect of alcohol consumption on VLM. Overall, findings suggest that in examining the effects of alcohol use on cognition, behavioral, or social outcomes, classification of drinkers into distinct categories based on quantity and frequency continues to serve an important role; at the same time, subtle differences within the same drinker categories should be considered to avoid a possible erroneous assumption that drinkers within such categories are homogenous in their alcohol use pattern or outcome.

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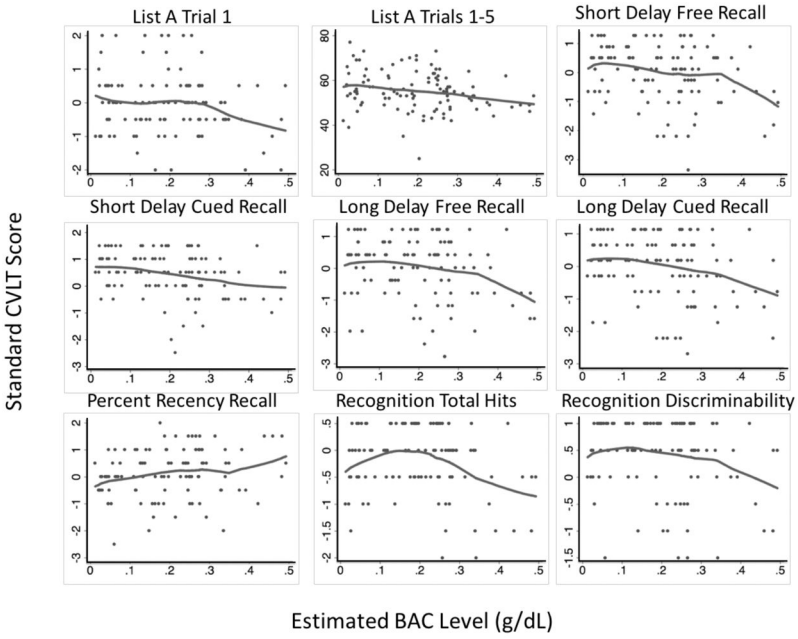

Figure 1.

Locally weighted scatterplot smoothing (LOWESS) regressions depict relationships between alcohol use and verbal learning and memory standard scores above and beyond baseline verbal learning and memory performance and attention problems and follow-up WRAT Reading performance. Based on the curvature and shape of LOWESS regressions, follow-up analyses utilized ordinary least squares regressions to examine the association between estimated peak blood alcohol level in the past 3-months and verbal learning and memory performance. All nine indices of verbal learning and memory showed significant linear relationships; there was also a significant quadratic relationship between recognition total hits and blood alcohol level (*p*s < .05).

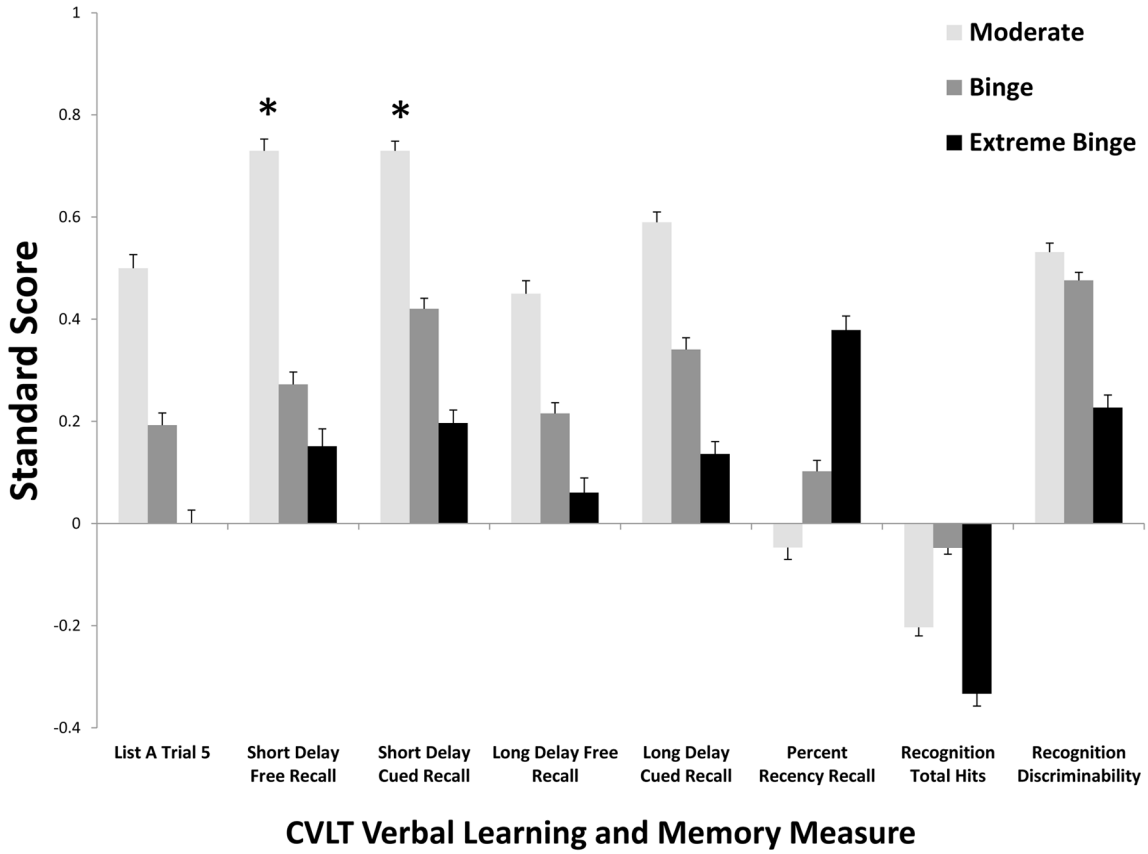

Figure 2.

Verbal learning and memory performances among moderate drinkers, binge, and extreme-binge drinkers at follow-up (*N*=112), were examined in ANCOVA models, controlling for attention problems, baseline performance on the same CVLT measures, and follow-up WRAT Reading performance. Differences were detected between moderate drinkers vs. extreme-binge drinkers, but not between moderate vs. binge drinkers or binge vs. extreme-binge drinkers. * Indicates significant group difference in performance at follow-up. Error bars indicate standard error. List A trials 1–5 also significantly differed between moderate and extreme-binge drinkers; performance in T-score metric and not indicated here. At baseline: moderate drinkers: 52.8 (*SE*=.32), binge drinkers: 53.9 (*SE*=.18), extreme-binge drinkers: 53.2 (*SE*=.22); at follow-up: moderate drinkers: 57.8 (*SE*=.27), binge drinkers: 55.0 (*SE*=.22), extreme-binge drinkers: 53.0 (*SE*=.20). CVLT scores were not significantly different among groups at baseline.

Table 1

Participant characteristics (*N=112)* at baseline.

	Moderate drinkers *n*=32	Binge drinkers *n*=45	Extreme binge drinkers *n*=35
	***M* (*SD*) or %**	***M* (*SD*) or %**	***M* (*SD*) or %**
Age	13.5 (0.8)	13.6 (0.7)	13.8 (0.8)
Gender (male) **	59%	53%	83%
Race (% white) **	56%	58%	94%
Hollingshead SES	26.3 (15.7)	24.2 (16.7)	20.0 (7.2)
FH density [a]	0.3 (0.4)	0.3 (0.6)	0.4 (0.5)
CBCL Internalizing T-score	45.1 (8.6)	45.7 (8.8)	43.0 (9.3)
CBCL Externalizing T-score *	43.1 (8.0)	41.6 (6.9)	47.1 (8.8)
CBCL Attention Problems T-score	51.5 (2.8)	51.2 (2.4)	52.1 (3.0)
BDI-II Total	2.6 (3.9)	1.8 (3.5)	2.1 (2.6)
List A Trial 1	0.3 (1.0)	0.3 (0.9)	0.3 (0.9)
List A Trial 5	0.2 (1.0)	0.2 (0.9)	0.4 (0.8)
List A Trials 1–5 Total (T-score)	52.8 (10.3)	53.9 (7.8)	53.2 (7.7)
Proactive Interference	−0.3 (1.2)	−0.2 (1.1)	−0.2 (1.2)
Short Delay Free Recall	0.2 (0.8)	0.2 (0.8)	0.2 (0.6)
Short Delay Cued Recall	0.4 (0.8)	0.2 (1.1)	0.2 (0.7)
Long Delay Free Recall	0.2 (0.9)	0.4 (0.7)	0.3 (0.7)
Long Delay Cued Recall	0.4 (0.7)	0.4 (0.7)	0.1 (0.8)
Learning Slope	1.2 (0.6)	1.2 (0.5)	1.3 (0.6)
Retention	0.1 (1.0)	0.1 (1.1)	0.1 (1.0)
Percent Recall from Word List Recency	0.2 (0.9)	0.2 (0.7)	0.4 (0.9)
Recognition Trial Total Hits	0.1 (0.4)	0.1 (0.5)	0.3 (0.3)
Total Recognition Discriminability	0.3 (0.5)	0.3 (0.5)	0.4 (0.4)

CBCL=Child Behavior Checklist parental report; BDI-II=Beck Depression Inventory II Total score

*Significant group (moderate drinkers vs. extreme-binge drinkers) difference, $p < .05$

**Significant group (moderate drinkers vs. extreme-binge drinkers and binge vs. extreme-binge drinkers) difference, $p < .05$

[a]First and second degree relatives, family history of alcohol and other substance use disorders; range 0–2.

Note: Proactive interference = list B – list A trial 5; Retention = number of words retained from list A trial 5 to short delay recall; Learning slope = average number of new words learned per trial. All verbal learning and memory indices are in standard (z) scores; List A Trials 1–5 Total is in T-score.

Table 2

Participant characteristics (*N=112)* at follow-up.

	Moderate drinkers *n*=32	Binge drinkers *n*=45	Extreme binge drinkers *n*=35
	***M* (*SD*) or %**	***M* (*SD*) or %**	***M* (*SD*) or %**
Age	19.7 (1.4)	19.3 (1.3)	19.7 (1.3)
Years between baseline and follow-up	6.7 (1.2)	6.2 (1.1)	6.3 (1.3)
Years of education completed	12.8 (1.2)	12.5 (1.3)	12.9 (1.2)
WRAT Reading Standard Score	104.2 (13.8)	104.4 (12.4)	106.7 (11.2)
YSR/ASR Internalizing T-score	43.7 (8.6)	42.9 (8.7)	40.6 (9.7)
YSR/ASR Externalizing T-score	44.2 (9.8)	46.6 (7.2)	50.0 (9.5)
YSR/ASR Attention Problems T-score	52.1 (3.5)	51.2 (2.7)	52.6 (3.9)
BDI-II Total	2.4 (2.8)	4.0 (6.4)	2.8 (5.2)
Lifetime drinking days **	58.5 (115.0)	127.6 (148.7)	241.9 (208.8)
Past month total drinks **	2.5 (4.2)	13.9 (12.2)	35.2 (31.0)
Average monthly alcohol use days ***	1.7 (3.0)	5.0 (4.8)	8.3 (6.2)
Past year average drinks in 24 hours ***	2.1 (1.2)	4.7 (2.2)	7.0 (3.2)
Past year peak drinks in 24 hours ***	4.1 (3.1)	8.6 (3.1)	13.0 (3.8)
Past 3-month maximum drinks	2.0 (1.0)	6.7 (1.2)	12.1 (3.2)
Estimated past 3-month peak BAC (eBAC) ***	.06 (.03)	.22 (.07)	.31 (.08)
Lifetime marijuana use days **	40.7 (188.7)	48.9 (89.8)	181.5 (272.9)
Average monthly marijuana use days *	1.5 (5.6)	3.7 (8.0)	7.4 (9.8)
Average monthly other drug use days	0.0 (0.0)	0.0 (0.0)	0.0 (0.2)
Past month tobacco use days **	0.0 (0.2)	2.0 (5.5)	6.2 (10.4)
DSM-5 Alcohol Use Disorder			
Mild *	0.0%	17.8%	22.9%
Moderate or Severe	0.0%	0.0%	0.0%
List A Trial 1	0.0 (0.9)	0.1 (1.0)	−0.2 (0.8)
List A Trial 5	0.5 (0.9)	0.2 (1.0)	0.0 (0.9)
List A Trials 1–5 Total (T-score) *	57.8 (8.8)	55.0 (9.7)	53.0 (6.5)
Proactive Interference	−0.1 (1.0)	−0.4 (1.0)	−0.3 (1.2)
Short Delay Free Recall *	0.7 (0.7)	0.3 (1.0)	0.2 (1.1)
Short Delay Cued Recall *	0.7 (0.6)	0.4 (0.9)	0.2 (0.8)
Long Delay Free Recall	0.5 (0.8)	0.2 (1.0)	0.1 (1.1)
Long Delay Cued Recall	0.6 (0.6)	0.3 (1.0)	0.1 (1.0)
Learning Slope	1.6 (0.5)	1.5 (0.5)	1.5 (0.5)
Retention	−0.2 (0.7)	−0.1 (0.9)	−0.2 (0.8)
Percent Recall from Word List Recency	0.0 (0.7)	0.1 (0.9)	0.4 (0.9)
Recognition Trial Total Hits	−0.2 (0.5)	0.0 (0.5)	−0.3 (0.8)
Total Recognition Discriminability	0.5 (0.6)	0.5 (0.7	0.2 (0.8)

*Significant group (moderate vs. extreme-binge) difference, $p < .05$

**Significant group (moderate vs. extreme-binge, and binge vs. extreme-binge drinkers) difference, $p < .05$

***Significant group (moderate vs. binge, moderate vs. extreme-binge, and binge vs. extreme-binge drinkers) difference, $p < .05$

YSR=Youth Self Report, ASR=Adult Self Report; BAC= blood alcohol concentration; DSM-5= Diagnostic and Statistical Manual of Mental Disorders, 5th ed.

Note: Proactive interference = list B – list A trial 5; Retention = number of words retained from list A trial 5 to short delay recall; Learning slope = average number of new words learned per trial. All verbal learning and memory indices are in standard (z) scores; List A Trials 1–5 Total is in T-score.