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RESEARCH ARTICLE

Holding your liquor: Comparison of alcohol-induced psychomotor impairment in drinkers with and without alcohol use disorder

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Abstract

Background: Behavioral tolerance to alcohol underscores the widely accepted notion that individuals who regularly drink alcohol become less sensitive to its impairing effects. However, previous research assessing alcohol-induced impairment in humans has primarily focused on social drinkers. This has limited our understanding of the nature and extent of behavioral tolerance among heavier drinkers, such as those with alcohol use disorder (AUD).

Methods: Data from three cohorts of the Chicago Social Drinking Project were evaluated to examine the acute effects of alcohol on psychomotor performance across the breath alcohol curve in light drinkers (LDs; $n = 86$), heavy drinkers (HDs; $n = 208$), and individuals with AUD (AUDs; $n = 103$). Before and at several intervals after ingesting either alcohol (0.8 g/kg, peak BrAC = 0.09 g/dL) or placebo in two random-order laboratory sessions, participants completed a test of fine motor coordination (Grooved Pegboard), a test of perceptual-motor processing (Digit Symbol Substitution Task), and a self-reported survey of perceived impairment. Sixty individuals with AUD completed a third session with a very high dose of alcohol (1.2 g/kg, peak BrAC = 0.13 g/dL).

Results: The AUD and HD groups, relative to the LD group, perceived less impairment and demonstrated greater behavioral tolerance to an intoxicating dose of alcohol, exhibited by reduced peak impairment and a quicker return to baseline performance on psychomotor measures. Among individuals with AUD who consumed the very high dose, impairment was more than double that following the usual high dose, and it exceeded the impairment among LDs following the usual high dose.

Conclusions: In this sample of young adult drinkers, relative to the LD group, those with heavier drinking patterns (AUD and HD groups) showed greater behavioral tolerance to 0.8 g/kg alcohol, a dose typically associated with a binge drinking episode. However, when challenged with a very high alcohol dose commensurate with high-intensity drinking, individuals with AUD showed substantial psychomotor impairment.

KEYWORDS
alcohol, impairment, psychomotor, tolerance, working memory

INTRODUCTION

Acute alcohol intoxication produces psychomotor and executive function deficits that often lead to significant harm and safety risks (i.e., accidents, impaired driving; Rehm, 2011). Controlled laboratory studies have demonstrated that moderate to high doses of alcohol (0.5–1.0 g/kg) slow a drinker's reaction time, impair motor coordination, and decrease performance on information processing and driving simulation tasks (Brumback et al., 2007, 2017; Day et al., 2015; Hiltunen, 1997; Marczinski et al., 2008; Miller & Fillmore, 2014; Mitchell, 1985). Alcohol also disrupts decision-making, judgment, and reasoning that may lead to impaired subjective perceptions of behavioral performance (Beirness, 1987; Brumback et al., 2007, 2017; Elliott et al., 2022; Marczinski, 2017; Marczinski et al., 2008). Despite 30% of U.S. traffic fatalities involving alcohol intoxication (BrAC ≥0.08 g/dL; National Highway Traffic Safety Administration, 2019) and the significant contribution that excessive drinking has towards the overall burden of disease and injury (Rehm, 2011), most research on alcohol's acute effects on performance has focused on social drinkers. This has limited our ability to understand the extent and nature of acute behavioral impairments during intoxication across the drinking continuum, particularly among drinkers with alcohol use disorder (AUD).

The widely accepted notion of behavioral (or functional) tolerance indicates that chronic heavy drinking is associated with reduced sensitivity to some of alcohol's impairing effects over time (NIAAA, 1995). Under this assumption, more experienced, heavy drinkers, such as those with AUD, would exhibit lower acute performance impairment after consumption of a given dose of alcohol relative to their less excessive drinking counterparts. Indeed, when compared with non-binge drinkers, binge drinkers (without alcohol dependence) showed alcohol-induced psychomotor tolerance to a driving simulation task (Marczinski et al., 2008; Marczinski & Fillmore, 2009). However, it is unknown whether behavioral tolerance to alcohol is evident in more extreme drinkers, particularly those with AUD relative to drinkers without AUD. There is a paucity of studies examining alcohol's effects on psychomotor performance in drinkers with AUD (Elvig et al., 2021), as this area of research is limited to a few preliminary studies from the 1940s–1970s in male-only samples described as having "alcohol addiction" (i.e., conducted prior to the DSM-5-based classification for AUD). Results of these older studies were equivocal: two studies showed intact short-term memory in "alcoholics" following consumption of 1.2 or 2.4 g/kg alcohol (Goodwin et al., 1970, 1973), but another study (Parker, 1974) showed similar alcohol-induced short-term memory and information processing impairments in alcohol-addicted and non-addicted participants. The few studies of motor coordination and gait in alcohol-addicted men demonstrated less alcohol-induced impairment relative to moderate drinkers and abstainers, particularly as blood alcohol concentrations rose (Goldberg, 1943), supporting observational reports (Mello & Mendelson, 1965; Mendelson & Mello, 1966). Collectively, it cannot be concluded from these studies that drinkers with AUD have tolerance to alcohol's ataxic or cognitive-impairing effects, and there are no contemporary studies comparing drinkers with AUD with other non-AUD drinking phenotypes. Further, the data in these aforementioned older studies utilized very small, primarily male samples (*N*'s = 2–17/group), tested only a single alcohol dose, and lacked appropriate controls and a consensus on diagnostic criteria for "alcohol addiction."

Thus, in an extension to the Chicago Social Drinking Project (King et al., 2006, 2011, 2021; King & Byars, 2004; Vena et al., 2020), we conducted a comprehensive examination of the acute effects of alcohol on psychomotor performance across the breath alcohol curve in a large sample of drinkers with and without AUD. Participants completed the Grooved Pegboard and Digit Symbol Substitution Test before and after ingesting a high alcohol dose (0.8 g/kg) or placebo in each of two random-order laboratory sessions (Brumback et al., 2007, 2017). In addition, a subset of drinkers with AUD completed the same laboratory session with a very high alcohol dose (1.2 g/kg) shown to be safe in this subpopulation (King, Vena, Howe, et al., 2022; Vena et al., 2020). This dose was undertaken to examine responses to alcohol consumption that more closely align with high-intensity drinking often reported in persons with AUD. We hypothesized that compared with light and heavy social drinkers, those with AUD would demonstrate greater psychomotor tolerance, exhibited by lower peak impairment after consuming the usual high alcohol dose (0.8 g/kg) and a quicker return, that is, "recovery" to their pre-consumption baseline. Further, we hypothesized that participants with AUD would self-report that they were less impaired after drinking alcohol than light or heavy social drinkers, but that they would exhibit significant impairment and perception of impairment after consuming the very high alcohol dose (1.2 g/kg).

METHODS

Design

Data were examined from the 397 participants enrolled in the first three cohorts of the Chicago Social Drinking Project (CSDP), a placebo-controlled, within-subject laboratory study examining acute responses to oral alcohol administration. Participants in the first two cohorts were enrolled between 2004 and 2011 (young adult light and heavy drinkers) and participants in the third cohort were enrolled between 2016 and 2019 (young adult drinkers with AUD). All participants attended two random-order, double-blinded

experimental sessions during which they consumed either a beverage with 0.8 g/kg alcohol (referred to as the "usual high dose") or a placebo beverage. A subset of drinkers with AUD also completed an additional third session in which they consumed a beverage with 1.2 g/kg alcohol (referred to as the "very high dose"; for details, see *Very high alcohol dose session* and King, Vena, Howe, et al., 2022; Vena et al., 2020). During each session, participants completed behavioral and subjective measures at baseline and several timepoints after consuming their blinded beverage. Study sessions were separated by at least 48 h and conducted in a comfortable living room-like environment at the Clinical Addictions Research Laboratory at the University of Chicago. The University of Chicago Institutional Review Board (IRB) approved the CSDP and all study procedures.

Participants

Study candidates were recruited via flyers, newspaper and online advertisements, and word-of-mouth referrals. Initial inclusion criteria across all cohorts were age between 21 and 35 years, weight between 110 and 210 pounds, good general health, no current major medical conditions, and for females, not currently pregnant, lactating, or desiring to be pregnant in the next 3 months. Applicants were also evaluated for predominant alcohol drinking patterns and needed to meet criteria (below) for one of three groups: (a) light drinkers (LD; $n = 86$) who consumed ≤6 drinks per week with rare binge drinking episodes; (b) heavy drinkers (HD; $n = 208$) who consumed at least 10 drinks weekly with 1–5 heavy drinking episodes per week; and (c) drinkers with AUD (AUD; $n = 103$) who consumed 28 or more drinks per week (21 or more for women) with at least 11 heavy drinking occasions per month.

Interested candidates were screened by phone for initial inclusion criteria and those deemed eligible were invited to attend an in-person screening. During this visit, candidates provided informed consent, verified age by photo ID, and completed a brief physical history. To assess patterns of recent alcohol use, including heavy/binge (>5 drinks per occasion for men, >4 for women; NIAAA, 2022) and high-intensity (>10 drinks per occasion for men, >8 for women; NIAAA, 2022; Patrick, 2016) drinking episodes, candidates completed interviews with trained staff, which included a past-month alcohol and cigarette Timeline Follow-Back (Sobell & Sobell, 1992) and the Alcohol Quantity-Frequency Interview (Cahalan et al., 1969).

Candidates with current major psychiatric and/or substance use disorders (except for nicotine) were excluded based on the non-patient version of the Structured Clinical Interview for DSM-IV (for screens conducted from 2005 to 2011; First et al., 1995) or DSM-5 (screens from 2016 to 2019; First, 2015). Light and heavy drinkers were excluded if they met lifetime criteria for DSM-IV alcohol dependence. In contrast, for drinkers with AUD, candidates must have met two or more DSM-5 criteria in the past year. For ethical reasons, participants with AUD also had to score <10 on the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar) at screening and prior to each session.

Other exclusionary criteria were having positive results on an alcohol breathalyzer, urine toxicology screen (except for THC), a pregnancy test (for females), or an abnormal hepatic panel result (AST, ALT, GGT greater than 2 standard deviations of normal range). Candidates were also excluded for significant substance use patterns that could affect participation (i.e., cannabis use >3 times/week, other illicit drug use >2 times past month). Additional surveys included the Alcohol Use Disorder Identification Test (AUDIT; Babor et al., 2001), and a two-generational biological family history tree for AUD (Mann et al., 1985). Family history was defined as positive by having at least one biological first-degree relative or two or more second-degree relatives with AUD, and negative if no AUD for two generations, else deemed undetermined (i.e., in cases of adoption, lack of knowledge of AUD among first-degree family relatives, or knowledge of only one secondary family member with AUD).

Procedure

The methodology was standard across all laboratory sessions. Study sessions began between 10:00 AM and 3:00 PM. Participants were instructed to abstain from alcohol and recreational drugs for at least 48 h prior to each session, and to abstain from cigarettes, caffeine, and food for 3 h prior. Upon arrival, each participant reported any past 24-h alcohol/drug use and underwent an alcohol breathalyzer test (Alco-Sensor IV, Intoximeter, St. Louis, MO). They also provided a urine sample for a pregnancy test (for women), and told that they could be randomly tested for drugs at either session. For standardization purposes, the drug test was always conducted prior to the second session. Sessions were canceled and rescheduled if there was a positive alcohol or drug test result (except for THC) and participants were excluded from the study if they had a positive pregnancy test.

The participant was then provided a snack equal to 20% of their daily kilocalorie needs based on sex and weight (55% carbohydrates, 10% protein, and 35% fat; Schofield, 1985) to reduce any hunger effects and minimize potential alcohol-induced nausea. Once the snack was consumed, the participant completed baseline subjective, objective, and performance measures.

Beverage administration

To reduce expectancy effects, the study employed the alternative substance paradigm such that participants were told that the beverage might contain a stimulant, a sedative, alcohol, a placebo, or a combination of these substances (Conrad et al., 2012). Beverages were served in clear-lidded cups with a straw for ingestion and consisted of water, a flavored drink mix, a sucralose-based sugar substitute, and 190-proof EtOH (1% volume for placebo as a taste mask, 16% volume based on body weight for the alcohol beverages). To adjust for sex differences in metabolism and body water content, females received a modified dose that was 85% of that for males.

Approximately 45 min after arrival at experimental time 0, the participant received their assigned beverage divided into two or three portions and consumed evenly over a 15-min period. The research assistant remained in the room for the duration of beverage consumption to monitor the time and to engage in light conversation with the participant.

At baseline and 30, 60, 120, and 180 min after beverage consumption, the participant underwent blinded breathalyzer readings and completed performance measures administered by the research assistant. Upon completion of each study session, the research assistant confirmed the participant's BrAC level of ≤0.04 g/dL and arranged for their transportation through a ride-share service. After the final study session, the participant was informed of the contents of their beverages for each session and then compensated $150 or $200 (cohort 1 and 2, respectively) for participation in two sessions.

Very high alcohol dose session

In addition to the usual high dose and placebo sessions, a subset ($n = 60$) of drinkers with AUD underwent an additional randomized session with a very high dose of alcohol (1.2 g/kg; King, Vena, Howe, et al., 2022; Vena et al., 2020). This session was single-blinded for the participant and required a longer duration of 7–8 h to allow the BrAC to descend to ≤0.04 g/dL before session release. Participants who completed this additional session were compensated $325 for three sessions.

Measures

Performance measures included the Grooved Pegboard (Lafayette Instruments, Lafayette, IN), a test of fine motor coordination, and the Digit Symbol Substitution Test (DSST; Wechsler, 1997), a test of short-term memory and perceptual-motor processing speed. The Pegboard task consisted of a 4" ×4″ metal board with 25 holes (5 x 5 arrangement) with randomly oriented notches. Participants were instructed to use their non-dominant hand to retrieve, rotate, and insert a grooved metal peg into each hole as quickly as possible. The dependent measure was the amount of time it took to fill all 25 slotted holes. The DSST was a paper and pencil task with a reference key consisting of number-symbol pairings at the top of the page and rows of numbers on the rest of the page. For 90 s, the participant used the key to consecutively and correctly input the corresponding symbol for each number. Each session used five different versions of the test to reduce learning effects. The dependent measure was the total number of correct symbols completed within the time frame.

At 30 and 180 min post-beverage consumption, participants also completed a self-rating scale measuring their perceived impairment. This consisted of four items, each rated on a 10-point scale anchored at 1 for "not at all" and 10 for "extremely." Items assessed how impaired the participant felt, how unsafe they felt it would be to drive an automobile, how much they felt that others would know they were behaving unusually, and if they would be more likely than usual to do something they might later regret. At each timepoint and dose, factor analysis revealed that all four items loaded onto a single factor [λ range: 1.35–2.82], so a mean composite score was used as the main dependent measure of perceived impairment.

Statistical analyses

Participant characteristics were compared across groups using one-way ANOVAs for continuous variables or χ^2 tests for categorical variables. These analyses were conducted in Statistica 14. For the main performance outcomes (Pegboard completion time and DSST scores) and perceived impairment, Generalized Estimating Equations (GEE) examined group, dose, time, and their interactions. Because drinkers with AUD had poorer baseline DSST scores relative to HDs and LDs, F (4.2, 2df), $p = 0.02$; AUD < HD = LD, $ps = [0.01, 0.64]$, GEE models for both Pegboard and DSST data included baseline performance as a covariate. To explore the effects of background variables on performance, we repeated GEEs with family history of AUD, age, educational attainment, and sex as covariates. Further, the AUD and HD groups endorsed more frequent cigarette and cannabis use than the LD group, so GEE analyses were repeated including them as covariates. GEE analyses were run in R (3.6.1) using the geepack module (Højsgaard et al., 2006). The criterion of $p < 0.05$ was used to determine significance for all statistical tests.

To examine the magnitude of alcohol-induced impairment, a separate GEE model compared the groups on peak impairment change scores. Peak impairment was calculated by subtracting each participants' baseline score from the worst alcohol post-consumption score, and then subtracting the concomitant change score from the placebo session. This was chosen to maintain standard temporal sequence between alcohol and placebo sessions and to reduce artifacts from fatigue and slowness observed in the placebo session toward the latter timepoints. Linear regressions and correlation tests were conducted to examine the association of actual performance impairment with perceived impairment.

For dose–response analyses in the subset of drinkers with AUD who completed the very high alcohol dose, GEE was used to examine the effects of dose (placebo, usual high dose, very high dose), time, and their interaction (controlling for baseline performance) on the main performance measures. As in the main analyses, the GEE tests were repeated with the inclusion of age, sex, education, and family history of AUD as covariates.

RESULTS

Demographic and drinking characteristics for the three drinking groups (LD, HD, and AUD) are summarized in Table 1. Groups were well-matched on demographic variables, with no significant differences in mean age, sex, or racial composition. As expected, compared with LDs and HDs, the AUD group engaged in more frequent

TABLE 1 Demographic and drinking characteristics across groups.

	LD ($N=86$)	HD ($N=208$)	AUD ($N=103$)	p-value
General				
Age, years	26.1 (3.4)[b]	25.1 (2.7)[a]	27.0 (4.0)[c]	<0.001
Education, years	16.7 (2.0)[c]	15.6 (1.5)[b]	14.4 (1.9)[a]	<0.001
Sex, % male	51%	61%	50%	0.15
Race, % White	69%[a]	80%[b]	64%[a]	0.005
Ethnicity, % Latinx	6%[a]	10%[a]	23%[b]	<0.001
Drinking characteristics				
AUD Symptom counts[1]	0.1 (0.2)[a]	2.1 (1.7)[b]	6.1 (2.5)[c]	<0.001
AUDIT	3.3 (1.2)[a]	11.9 (3.9)[b]	19.8 (6.6)[c]	<0.001
DrInC-2R score	2.6 (3.4)[a]	14.2 (9.8)[b]	33.4 (22.6)[c]	<0.001
Age of first drink, years	17.5 (2.4)[a]	15.4 (2.2)[b]	15.4 (2.6)[c]	<0.001
Family History of AUD[2]	37%[a]	43%[a]	73%[b]	<0.001
Past month (28 days) drinking patterns				
Drinks per Week	2.6 (1.3)[a]	19.4 (7.6)[b]	38.7 (17.3)[c]	<0.001
Drinks per Drinking Day	1.7 (0.5)[a]	5.8 (3.0)[b]	7.2 (2.6)[c]	<0.001
Drinking days (any past month alcohol consumption)	22.9%[a]	51.9%[b]	77.1%[c]	<0.001
Light drinking days [1–4 drinks (3 for women)]	22.6%	21.9%	18.5%	0.24
Heavy drinking days [>5 drinks (4 for women)]	0.3%[a]	30.0%[b]	58.6%[c]	<0.001
Medium intensity days [5–9 drinks (4–7 for women)]	0.3%[a]	21.8%[b]	32.9%[c]	<0.001
High-intensity days [> 10 drinks (8 for women)]	0%[a]	8.2%[b]	25.7%[c]	<0.001
Past year substance use patterns				
Weekly cigarettes use, % yes	6%[a]	49%[b]	51%[b]	<0.001
Weekly cannabis use, % yes	0%[a]	11%[b]	39%[c]	<0.001
Weekly other drug use[3], % yes	0%[a]	0%[a]	16%[b]	<0.001

Note: Data are means (SD) or %, except where indicated. Superscripts (a, b, c) are used to denote group differences.

[1]DSM-IV was used for light drinkers (LD) and heavy drinkers (HD), and DSM-5 was used for drinkers with alcohol use disorder (AUD) as this cohort was enrolled when DSM-5 was available.

[2]Family history of AUD = one biological first degree relative or two or more secondary relatives with AUD

[3]Other drug use includes cocaine, barbiturates, hallucinogens, and inhalants.

heavy drinking occasions (58.6% of past month days vs. 0.4% and 30%, respectively) and high-intensity drinking (25.7% of past month days vs. 0% and 8.2%, respectively). Likewise, the AUD group (vs. LD and HD groups) endorsed problems and consequences consistent with hazardous alcohol use, as indicated by elevated scores on the AUDIT and DrINC-2R as well as the number of AUD symptoms (see Table 1). Notably, the majority of drinkers with AUD (61.2%) met the criteria for severe AUD, with 19.4% moderate AUD and 19.4% mild AUD (See Table S1 for endorsement rates of each AUD symptom).

Breath alcohol concentrations (BrAC)

The usual high dose of alcohol produced the expected biphasic BrAC curve with a steep rising ascent to peak BrAC at 60-min followed by a gradual declining limb of alcohol elimination for the next few hours (Figure 1). Mean peak BrAC was slightly higher in HDs [mean (SEM), g/dL: 0.092 (0.001)] relative to LDs and drinkers with AUD [0.085 (0.002) and 0.087 (0.001), respectively; $p=0.001$].

Performance measures

For Pegboard, as expected, the usual high dose of alcohol acutely impaired performance relative to placebo as indicated by slower task completion times, particularly during the rising limb to peak BrAC interval, that is, 30–60 min after drinking, with performance gradually recovering as BrAC declined (Figure 2A; dose × time, $p<0.001$; alcohol > placebo at all timepoints, $ps<0.001$). Comparisons across groups showed differences in alcohol-induced Pegboard impairment (group × dose × time, $p=0.003$) such that impairment was similar across groups during the rising BrAC limb, but the AUD and HD groups showed quicker recovery of performance than the LD group during subsequent timepoints (see Table 2 for post-estimation comparisons).

These outcomes did not change after the inclusion of covariates in the analyses. Based on coefficient estimates, faster Pegboard completion times were associated with younger age ($p=0.04$) and female sex ($p=0.002$), but not any other covariates. In terms of peak impairment, the magnitude of alcohol's effects was lowest in the AUD group and greatest in the LD group, with the HD group intermediate (Figure 2B; group × dose, $p=0.017$; alcohol dose, AUD < HD < LD, $ps \leq 0.026$). As shown in Figure 2A, Pegboard performance during the placebo session was relatively stable with no group differences.

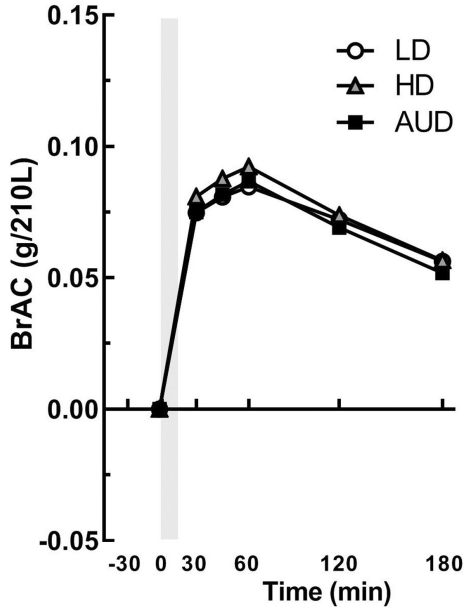

FIGURE 1 Mean breath alcohol concentrations (BrAC) for light drinkers (LD), heavy drinkers (HD), and drinkers with AUD (AUD) group during the (0.8 g/kg) alcohol dose sessions. Light gray vertical bar indicates drinking period.

For the DSST, the usual high dose also impaired performance as indicated by lower scores relative to placebo, particularly during the rising to peak BrAC interval (Figure 3A; dose × time, $p<0.001$; alcohol < placebo at all timepoints, $ps \leq 0.025$). Alcohol-induced impairment differed across group and time (group × dose × time interaction, $p=0.014$) such that the AUD and HD groups were less impaired than LDs throughout the BrAC curve (see Table 2 for post-estimation comparisons). These main outcomes remained after the inclusion of covariates in the analyses. Based on coefficient estimates, better DSST scores were associated with younger age ($p=0.01$), female sex ($p<0.001$), and more years of education ($p=0.005$), but not any other covariates. In terms of peak impairment, as with the Pegboard task, the magnitude of alcohol's effects on DSST performance was lowest in the AUD group and greatest in the LD group, with the HD group intermediate (Figure 3B; group × dose, $p<0.001$; alcohol dose, impairment magnitude: AUD < HD < LD, $ps \leq 0.009$). As shown in Figure 3A, DSST performance in the placebo session was relatively stable but drinkers with AUD consistently performed worse than LDs or HDs. However, this difference did not persist after including education in the model as a covariate.

To assess the time course of recovery across groups, post-hoc χ^2 tests were conducted to identify the first alcohol session timepoint where scores were not significantly different from baseline scores. For the Pegboard, drinkers with AUD returned to baseline completion times at T3 (120 min; $p=0.726$), HDs returned to baseline completion times at T4 (180 min; $p=0.94$), but LDs' completion time remained worse throughout the study period (T4: $p=0.03$). For the DSST, returning to baseline scores took drinkers with AUD until T2 (60 min; $p=0.081$), HDs until T3 (120 min; $p=0.726$), and LDs until T4 (180 min; $p=0.081$).

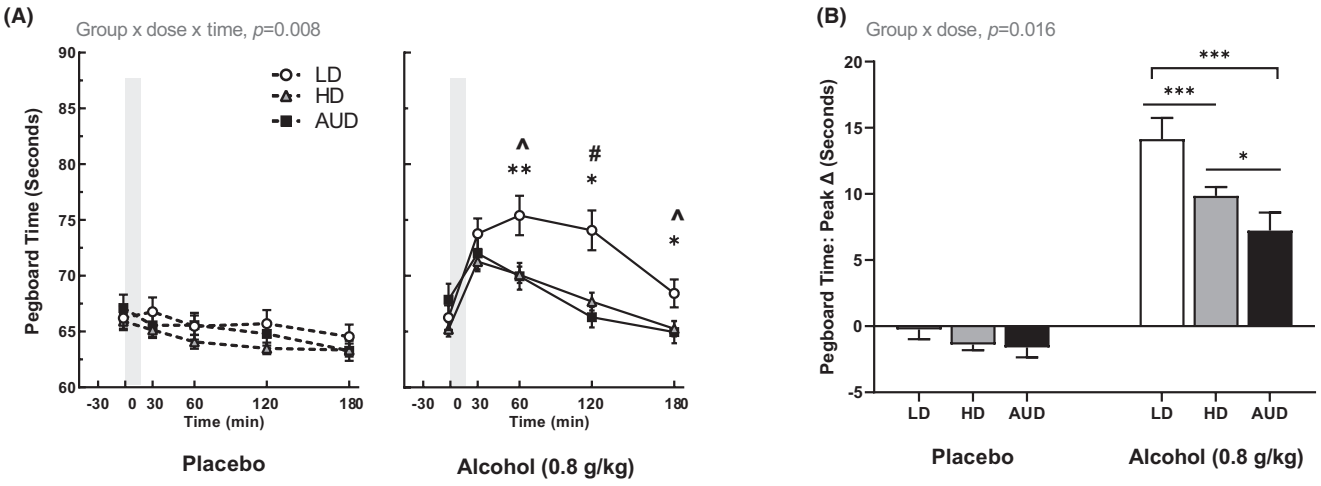

FIGURE 2 Pegboard performance. (A) Pegboard times are the number of seconds to complete task during the placebo (0.0 g/kg, left panel) and alcohol (0.8 g/kg, right panel) sessions. Raw data (means ± SEM) shown for illustrative purposes. Baseline group comparisons conducted with one-way ANOVA and post-beverage consumption (30, 60, 120, 180 min) comparisons based on GEE (group, dose, time) covarying for baseline performance. Light gray vertical bar indicates drinking period. (B) Baseline-corrected peak impairment change scores for placebo and alcohol sessions. ^LD > HD = AUD, #LD > HD > AUD; *$ps \leq 0.05$, **$ps \leq 0.01$, ***$ps \leq 0.001$. LD for light drinkers, HD for heavy drinkers, and AUD for drinkers with AUD.

TABLE 2 GEE summary of usual high-dose alcohol (0.8 g/kg) effects on psychomotor performance.

	Group × dose × time			Post-estimation comparisons examining group effect			
Alcohol responses	χ^2	*df*	*p*	+30 min	+60 min	+120 min	+180 min
Pegboard	17.3	6	**0.008**	LD = HD = AUD	LD > HD = AUD	LD > HD > AUD	LD > HD = AUD
DSST	16.0	6	**0.014**	LD < HD = AUD	LD < HD = AUD	LD < HD = AUD	LD < HD = AUD

Note: GEE results examine group, dose, and time effects and their interaction while controlling baseline scores. Post-estimation comparisons examine each timepoint for the group effect (LD for light drinkers, HD for heavy drinkers, and AUD for drinkers with AUD) for the 0.8 g/kg usual high dose. Bold indicates statistically significant value ($p < 0.05$).

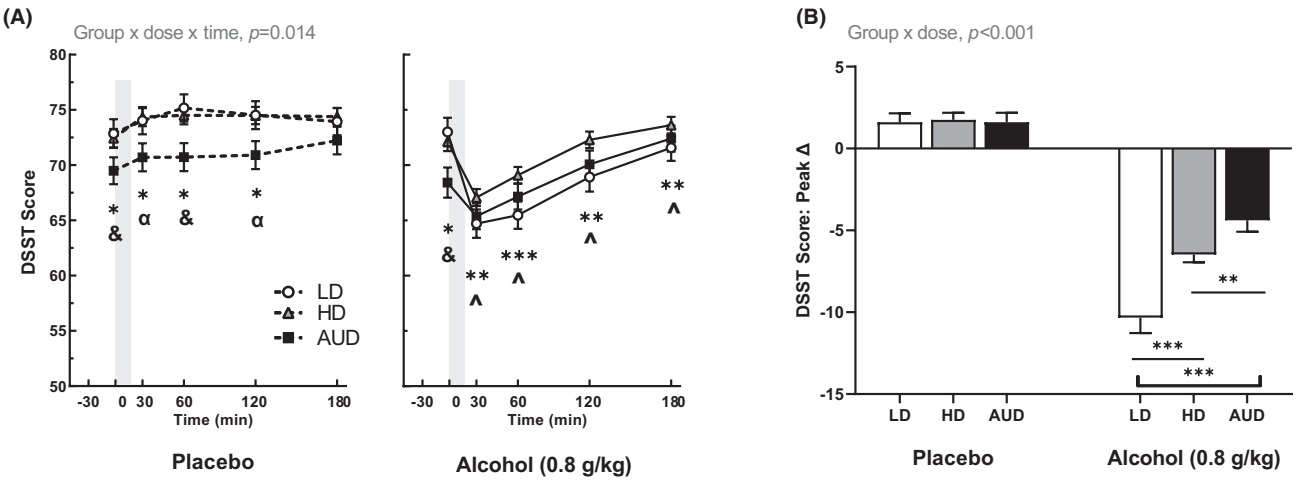

FIGURE 3 DSST Performance. (A) DSST scores are the number of symbol–number matches during the placebo (0.0 g/kg, left panel) and alcohol (0.8 g/kg, right panel) sessions. Raw data (means ± SEM) shown for illustrative purposes. Baseline group comparisons conducted with one-way ANOVA and post-beverage consumption (30, 60, 120, 180 min) comparisons based on GEE (group, dose, time) covarying for baseline performance. Light gray vertical bar indicates drinking period. (B) Baseline-corrected peak impairment change scores for placebo and alcohol sessions. $^{\alpha}$HD > AUD, $^{\&}$LD = HD > AUD, ^LD < HD = AUD; *ps ≤0.05, **ps ≤0.01, ***ps ≤0.001. LD for light drinkers, HD for heavy drinkers, and AUD for drinkers with AUD.

TABLE 3 Perceived impairment ratings by group.

	Time	LD	HD	AUD
Placebo Session	30 min	0.67 (0.13)	0.59 (0.07)	0.79 (0.12)
	180 min	0.30 (0.08)	0.26 (0.05)	0.27 (0.06)
Alcohol Session (0.8 g/kg)	30 min	5.58 (0.27)^{a}	3.92 (0.16)^{b}	3.44 (0.24)^{b}
	180 min	2.97 (0.25)^{a}	1.75 (0.13)^{b}	1.62 (0.19)^{b}

Note: Data are means ± SEM. Time indicates minutes post-beverage consumption. LD for light drinkers, HD for heavy drinkers, and AUD for drinkers with AUD. Superscripts (a, b, c) are used to denote significant group differences, $p < 0.05$.

Perceived impairment

As expected, the usual high dose produced greater ratings of perceived impairment relative to the placebo, and these ratings were higher on the ascending versus descending limb (Table 3; dose × time, $p < 0.001$). Ratings of alcohol-induced impairment differed across group and time (group × dose × time interaction, $p = 0.015$) such that the AUD and HD groups perceived less impairment than LDs at both the ascending and descending limbs (AUD = HD < LD, ps <0.001). Outcomes remained the same after including age, sex, education, cigarette use, cannabis use, and family history as model covariates. Based on coefficient estimates, higher ratings of perceived impairment were associated with younger age ($p = 0.02$) and more years of education ($p = 0.005$), but not any other covariates. During the rising limb, perceived impairment significantly correlated with impairment on both DSST ($r = 0.175$; $p < 0.001$) and Pegboard ($r = 0.12$; $p < 0.02$), and these relationships did not differ by group (group × perceived impairment; DSST: $p = 0.64$; Pegboard: $p = 0.07$).

Very high alcohol dose session

As stated previously, a subsample of $n = 60$ from the AUD group completed a very high alcohol dose (1.2 g/kg) challenge that produced a mean peak BrAC of 0.132 (0.003) g/dL at 60 min post-beverage

consumption. On both the Pegboard and DSST tasks, alcohol's effects for this subsample were dose-dependent, such that the very high dose (1.2 g/kg) produced significantly greater impairments than the usual high dose (0.8 g/kg) throughout the BrAC curve (Figure 4; dose × time, $p < 0.001$; see Table 4 for post-estimation comparisons). Further, for both Pegboard and DSST, the magnitude of peak impairment from the very high dose was significantly greater than that produced by the usual high dose (dose $ps \leq 0.001$; very high > high > placebo, $ps \leq 0.001$). Notably, the impairment that the AUD group showed after consuming the very high dose was greater than the impairment that LD showed to the usual high dose throughout the BrAC curve for the Pegboard task (T1: $p < 0.001$, T2: $p = 0.001$, T3: $p = 0.02$, T4: $p = 0.01$) and during the early declining limb (T3) for the DSST ($p = 0.004$).

A dose-dependent pattern for the AUD group was also apparent with ratings of perceived impairment. The very high dose produced the greatest perceived impairment, followed by the usual high dose and then the placebo dose and this pattern was observed at both the ascending and descending limbs (dose × time, $p = 0.0023$; $ps < 0.001$ at 30 and 180 min for very high > high > placebo). Notably, during the ascending but not descending limb, the very high dose produced greater perceived impairment in the AUD group than that produced by the usual high dose in the LD group ($p < 0.001$).

DISCUSSION

The present study provides the first examination of alcohol-induced psychomotor performance impairment in young adult drinkers with AUD. The key findings can be summarized in three notable areas: First, relative to both HDs and LDs, drinkers with AUD demonstrated poorer baseline performance on the DSST task, which appeared to be related to their lower educational attainment but also could be due to underlying cognitive deficits (Grønkjær et al., 2019). Second, AUD and HD groups, relative to LD, exhibited comparatively greater behavioral tolerance to an intoxicating dose of alcohol on measures of fine motor ability (Pegboard) and working memory (DSST), and they perceived that they were less impaired. Third, and importantly, behavioral tolerance observed in drinkers with AUD may be dose-dependent, as when they were challenged with a very high alcohol dose, they showed substantial performance impairment on both Pegboard and DSST tasks.

In terms of public safety, while LDs showed the greatest impairment to the usual high dose of alcohol, their lack of behavioral tolerance may not be a significant concern as they rarely engage in binge drinking (<1% of days) and they also demonstrate awareness of impairment based on the self-report perception scale. On the other hand, participants with AUD engage in high-intensity drinking (8+/10+ drinks for women/men) about once every 4 days (Table 1). For them, the very high dose that produced a mean peak BrAC of 0.132 g/dL may provide an ecologically relevant dose commensurate with high-intensity drinking (King, Vena, Lee, et al., 2022). The magnitude of impairment produced by this very high dose was more than double of that produced by the usual high dose, indicating greater alcohol consumption exacerbates working memory and fine motor impairment at an exponential rate in drinkers with AUD. Further, the AUD group exhibited greater impairment after consuming the very high dose than the LD group did after consuming the usual high dose. Contextualized this way, the safeguarding effect of acute behavioral tolerance on society may be mitigated by the fact that a very high dose of alcohol, similar to the high-intensity drinking characteristic of AUD drinking, produces significant working memory and fine motor deficits in drinkers with AUD.

As the Chicago Social Drinking Project is an ongoing study that originated in 2004, the present findings provide an important extension to our prior reports. By examining drinkers with AUD, we could compare alcohol-induced performance effects across drinking phenotypes. In our first publication comparing psychomotor impairment in LDs and HDs at the usual high dose (Brumback et al., 2007), we observed minimal evidence of tolerance, as both groups showed similar impairment throughout the BrAC curve. Our 5-year re-examination of those participants (Brumback et al., 2017) showed that HDs (vs. LDs) developed functional tolerance, but only on the Pegboard task and only during the rising BrAC limb. Now,

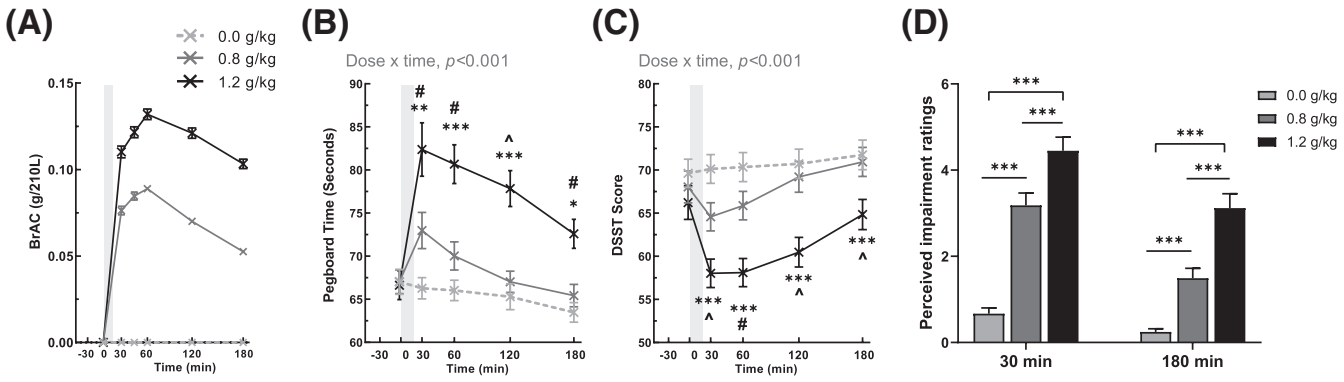

FIGURE 4 Dose–response data in drinkers with AUD. (A-C) Light gray vertical bar indicates drinking period. (A) BrAC for the very high alcohol dose (1.2 g/kg), usual high alcohol dose (0.08 g/kg), and placebo sessions. (B) Pegboard performance is shown as the time to complete a task in seconds. #P < H < V, ^P < V, H < V. (C) DSST performance is shown as the number of symbol–number matches. #P > H > V, ^P > V, H > V. (D) Perceived impairment ratings. Data are means ± SEM in AUD drinkers ($n = 60$). *$ps \leq 0.05$, **$ps \leq 0.01$, ***$ps \leq 0.001$.

TABLE 4 GEE analysis summary in drinkers with AUD for dose–response effects on psychomotor performance.

	Dose × time			Post-estimation comparisons examining dose effect			
Alcohol responses	χ^2	*df*	*p*	+30 min	+60 min	+120 min	+180 min
Pegboard	23.1	6	**<0.001**	P < H < V	P < H < V	P < V, H < V	P < H < V
DSST	95.9	6	**<0.001**	P > V, H > V	P > H > V	P > V, H > V	P > V, H > V

Note: GEE results examine dose and time effects and their interaction among AUD subsample while controlling baseline scores. Post-estimation comparisons examine each timepoint for the dose–effect (P for placebo, H for 0.8 g/kg usual high dose, V for 1.2 g/kg very high dose).
Bold indicates statistically significant value ($p < 0.05$).

with a larger HD sample reported herein (by including our second replication cohort; Roche et al., 2014) and the addition of our AUD cohort, the results of this study indicate a positive relationship between drinking levels and behavioral tolerance. The HD and AUD groups were generally quicker to recover to their baseline abilities after intoxication, that is, exhibit acute within-session tolerance, and showed lesser peak impairment than the LD group.

Though group differences in alcohol-induced impairment provide evidence for tolerance to a weight-standardized alcohol dose, the effect of tolerance depends both on time (since alcohol consumption) and the functional domain being evaluated (Elliott et al., 2022; Oscar-Berman & Marinković, 2007; Peterson et al., 1990; Van Skike et al., 2019). First, the recovery of function across all drinking groups was quicker for the DSST than for the Pegboard, indicating that alcohol may produce more sustained impairments in fine motor skills relative to working memory. Second, while all participants exhibited alcohol-induced impairments on the Pegboard task, group differences were not evident 30-min post-beverage consumption, indicating an absence of fine motor behavioral tolerance early in a drinking bout in the HD and AUD groups. Notably, this was an interval in which these groups perceived less alcohol impairment than their LD counterparts. This incongruence between actual and perceived impairment during the rising limb is important, as it is an interval when extreme binge drinking and front-loading (Ardinger et al., 2022) may be fueled by excessive drinkers' sensitivity to alcohol's stimulating and rewarding effects (Hendershot et al., 2015; King et al., 2011, 2021). Heavier drinkers with and without AUD may overestimate their ability to execute psychomotor tasks, leading to riskier decision-making and continued drinking. The present study results may help raise awareness that there are limits to alcohol tolerance in experienced drinkers, such that they can be significantly impaired at particular doses, despite not perceiving considerable impairment.

There are likely important neuropsychological underpinnings (Squeglia et al., 2014) to the psychomotor tolerance shown in drinkers in the HD and AUD groups. In human and rodent models, repeated alcohol exposures have been shown to produce functional changes in neural receptors and neurocircuitry (Bettinger & Davies, 2014), particularly with GABAergic and glutamatergic neurotransmission (Krystal et al., 2006), and these may play a role in psychomotor effects. Alcohol's impact on the motor and prefrontal cortex may diminish as the brain is exposed to more frequent and heavy doses of alcohol, as shown in the more experienced drinkers. From a cognitive perspective, individuals who regularly engage in excessive drinking become familiar with the sensations of being intoxicated and learn how to overcome impairing effects (Tiffany & Baker, 1986; Zack & Vogel-Sprott, 1995). Yet, as was shown by the very high dose, tolerance resulting from regular excessive drinking can be overcome by consuming alcohol at higher intensities.

The study results should be considered in light of the study's strengths and limitations. In comparison to older alcohol challenge studies (Goldberg, 1943; Goodwin et al., 1970, 1973; Parker, 1974), our current methodology has a larger sample size that ranged across the drinking continuum, more precise inclusion and exclusion criteria, and a rigorous study design that controlled for baseline performance and a placebo control. Nevertheless, there are several limitations worth noting. First, psychomotor assessments consisted of only two tasks and the findings may not be generalizable to other neuropsychological functions. However, the DSST and Pegboard are time-efficient and minimally disruptive measures of working memory and fine motor ability which are components inherent in many real-life behavioral and cognitive functions. A second limitation relates to the time-course of the fixed-dose administration and the very high dose not being tested in all drinker subgroups. In laboratory research, the fixed alcohol dose consumed in a short time frame allows examination of effects during rising, peak, and declining BrAC. There were ethical considerations in administering the very high dose to individuals who do not consume such a high intoxicating dose (7–8 drink equivalent; Vena et al., 2020), but this dose closely aligns with typical drinking in the AUD group (Table 1). Further, the peak BrAC (0.132 g/dL) produced by this very high dose matches the estimated BrAC of drinkers with AUD over a 3-h drinking interval in their natural environment (0.14 g/dL; D. J. Fridberg, Z. Lee, A.M. Fischer, J.F. Cursio, A.C King; unpublished data; King, Vena, Lee, et al., 2022). A third limitation is that while this study effectively characterized behavioral tolerance in psychomotor function across different drinking phenotypes, it cannot be concluded that habitual drinking caused the development of tolerance. The current study used a cross-sectional design yet testing this causal relationship in humans would have required a very challenging longitudinal design starting when participants were alcohol naïve.

In sum, this study showed that consuming an intoxicating dose of alcohol (BrAC = 0.09 g/dL) greatly hinders psychomotor functioning across drinker phenotypes. By comparing group psychomotor performance at several timepoints at this usual high dose, we discovered that heavier drinking groups experience quicker recoveries in performance and lesser peak impairment than lighter drinkers.

Despite this evidence for tolerance, when drinkers with AUD were given a very high alcohol dose (BrAC = 0.13 g/dL), their impairment more than doubled relative to their performance at the usual high dose. These results indicate that individuals with AUD are likely to retain more psychomotor function than lighter drinking groups at a moderate dose of alcohol, but when intoxicated by a very large dose that more closely approximates their typical drinking levels, their working memory and fine motor abilities are significantly impaired. Future studies examining other psychomotor functions at a range of alcohol doses may help to further elucidate the extent of behavioral tolerance across drinking phenotypes and their associations to alcohol-related injury and harm.

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CONFLICT OF INTEREST STATEMENT

Authors have no declarations of competing interests to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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