

# Alcohol-induced performance impairment: a 5-year re-examination study in heavy and light drinkers

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## Abstract

**Background** The theory of behavioral tolerance to alcohol posits that greater experience with drinking to intoxication leads to less impaired cognitive and psychomotor performance. However, the degree to which behavioral tolerance develops or changes over time in adults due to repeated heavy alcohol drinking has not been clearly demonstrated.

**Method** We examined data from the first 6 years of the Chicago Social Drinking Project to test whether chronic heavy drinkers (HDs;  $n = 86$ ) and light drinkers (LDs;  $n = 69$ ) exhibit behavioral tolerance or changes in perceived impairment at two testing phases in early adulthood. Tasks were the Grooved Pegboard and Digit Symbol Substitution Test (DSST) given at initial testing and then repeated in a re-examination phase 5 years later. Alcohol (0.8 g/kg) and placebo were administered at separate sessions in each phase for a total of 620 individual laboratory sessions.

**Results** HDs exhibited less impairment over time on the Pegboard task but not on the DSST, while LDs did not exhibit behavioral tolerance on either task. HDs reported persistently lower perceived impairment compared to LDs.

**Conclusions** These findings demonstrate that behavioral tolerance in HDs is evident over time on rote fine motor skills

(Pegboard) but not more complex skills integrating motor speed, encoding, and short-term memory (DSST). The results have implications for our understanding of alcohol-induced impairments across neurobehavioral processes in heavy drinkers and their ongoing risks for alcohol-related consequences over time.

**Keywords** Alcohol · Tolerance · Human · Motor learning · Working memory

## Introduction

Drinking alcohol to intoxication decreases cognitive and psychomotor abilities and increases risk for accidents, injuries, and premature death (NHTSA 2014). Cognitive and behavioral effects of alcohol have been measured in controlled laboratory settings for over a century (Eckardt et al. 1998). Results have consistently shown that alcohol doses producing breath alcohol concentrations (BrACs) above 0.05 g/dl impair performance on cognitive and psychomotor tasks (Eckardt et al. 1998; Moskowitz and Robinson 1988). Individuals with heavier prolonged drinking histories tend to exhibit pharmacokinetic tolerance, as indexed by faster BrAC declining rates compared with lighter, less experienced drinkers (Whitfield and Martin 1994). Many studies over the past century have demonstrated that heavier and more experienced drinkers are less impaired by alcohol on objective/performance measures and report less subjective impairment from alcohol compared to lighter or infrequent drinkers (Ekman et al. 1964; Goldberg 1943; Hollingworth 1924). However, the degree to which behavioral tolerance, i.e., reduced alcohol-induced psychomotor or cognitive impairment (Kalant et al. 1971), develops or changes over time in adults due to repeated heavy alcohol drinking has not been clearly demonstrated. It is unclear, for

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example, what amount of alcohol or duration of drinking produces behavioral tolerance in adult drinkers, and whether behavioral tolerance reaches a stable maximum or continues to increase with persistent drinking.

Behavioral tolerance involves not only cellular adaptation to repeated dosing of alcohol (i.e., pharmacodynamic changes in receptor sensitivity to alcohol) but also contextual factors, practice, and learning under the influence of alcohol (Kalant 1998). In contrast to the improved performance associated with behavioral tolerance, chronic alcohol use is associated with impairment in executive functions, visuospatial abilities, and balance (Sullivan 2000), which are likely attributable to white matter deficits and alterations to the cerebro-cerebellar and basal forebrain circuitry which may counteract effects of tolerance on performance in heavier drinkers (Chanraud et al. 2010). Sustained heavy alcohol drinking results in compensatory recruitment of other brain regions to accomplish tasks (Crews et al. 2005; Sullivan and Pfefferbaum 2005), which is also evident in heavy drinkers with shorter drinking histories (Tapert et al. 2004). Thus, compensatory learning processes may contribute to behavioral tolerance by distributing and/or redirecting the workload across additional brain regions even at lower drinking levels and shorter chronicity than those of protracted alcohol dependence.

In animal studies, rodents show diminished alcohol-induced behavioral impairment over repeated alcohol administrations on temporal maze learning (Chen 1972), balance and coordination (Leblanc et al. 1976), and operant conditioning paradigms (Chen 1979). In humans, longer drinking histories lead to improvements in compensatory learning processes over time (Fillmore and Vogel-Sprott 1996; Vogel-Sprott 1992), but collectively, alcohol impairment is relative to the complexity of the task (Hindmarch et al. 1991). Heavier drinkers do not show less alcohol-induced psychomotor performance impairment compared with lighter drinkers on some tasks, particularly when compared with regular light drinkers. In these cases, heavier drinkers appear to be more likely to show behavioral tolerance on basic motor response tasks such as a finger-to-finger apposition task as opposed to more cognitively demanding tasks such as divided attention, short-term memory, and go/no-go tasks (Brumbach et al. 2007; Miller et al. 2012; Mitchell 1985; Weissenborn and Duka 2003). The scope of research on behavioral tolerance in humans has been exclusively cross sectional, with no longitudinal data on alcohol-induced psychomotor impairment within the same individuals over time.

To examine the effects of drinking histories on behavioral and subjective responses to alcohol over time, we established the Chicago Social Drinking Project (CSDP), a prospective alcohol examination and re-examination study in heavy and light non-alcohol-dependent drinkers who were initially enrolled in young adulthood (mean age 25 years). Subjective effects of alcohol from the first cohort are published elsewhere

(Conrad et al. 2012; King et al. 2011, 2014, 2016). Psychomotor performance was measured in CSDP on two tasks ranging in neurocognitive complexity and shown to be sensitive to the effects of alcohol (Moskowitz and Robinson 1988), including a test of motor speed and fine motor coordination (Pegboard; Lafayette Instruments, Lafayette, IN; Bornstein 1985; Lezak et al. 2004) and a test of perceptual motor processing speed and executive functioning (Digit-Symbol Substitution Task; from WAIS-R; Wechsler 1997; Glosser et al. 1977). Alcohol produced similar impairment on these tasks in light and heavy drinkers, indicating that heavy social drinkers at an average age of 25 years did not show an advantage on psychomotor performance under the influence of an intoxicating dose of alcohol (Brumbach et al. 2007). Heavy drinkers were deemed at risk for alcohol harm because they showed similar alcohol impairment as their light-drinking counterparts, but they had lower self-perception of their impairment (Brumbach et al. 2007).

In the current study, we continued to examine heavy and light drinkers from the CSDP by comparing their performance on these same psychomotor tasks from the initial testing phase to a re-examination phase conducted 5 to 6 years later. The longitudinal design allowed us to assess whether drinking patterns through young-to-middle adulthood (transition from the 20s to early 30s) related to behavioral tolerance in either of these two well-characterized drinking groups. Thus, we were able to assess whether persistent light drinking or heavy drinking patterns over 5 to 6 years led to changes in behavioral tolerance or self-perceived impairment relative to the initial testing. We were also able to compare perceived and actual performance impairment between the drinking groups to determine if their relationship differed over time in heavy and light drinkers.

## Method

### Design

The CSDP is a longitudinal, repeated, within-subject, double-blinded, randomized laboratory study of alcohol and placebo beverage responses in humans. The study was conducted at the Clinical Addictions Research Laboratory at the University of Chicago and approved by the University of Chicago Institutional Review Board. Participants were 190 non-dependent young adult drinkers in the first cohort of the study (see King et al. 2011). They completed two sessions conducted from 2004 to 2006 and then annual follow-up interviews. Of the original sample, 156 participants returned to the laboratory for identical re-examination sessions 5 to 6 years later, from 2009 to 2011, depending on when they enrolled, with a mean interval between phases ( $63 \pm 1.5$  months SD). Details

of follow-up procedures and retention strategies are published elsewhere (King et al. 2014; Smith et al. 2017).

**Participants** At enrollment, the sample included heavy and light drinkers; heavy drinkers (HDs) were a priori defined as weekly binge drinkers (1–5 days weekly consumption of  $\geq 5$  drinks per occasion for men,  $\geq 4$  for women) who consumed between 10 and 40 drinks per week for at least the past 2 years. Light drinkers (LDs) were also weekly drinkers who averaged consuming  $< 6$  drinks per week for at least the past 2 years with no/rare binge episodes. Eligibility for the re-examination phase required current drinking (i.e., at least one drink in the past month), and having no major medical or psychiatric contraindications, and being agreeable to the possibility of receiving any of the substances described (i.e., alcohol, stimulant, or sedative) that might create physical states ranging from being jittery and restless to sluggish and tired. The majority of the initial testing sample was eligible and returned to the laboratory for the re-examination phase (86 of 104 HD—83%; 70 of 86 LD—81%; see King et al. 2016 for detailed exclusions). To facilitate re-examination, transportation and lodging arrangements were provided to 37% of participants who no longer resided in the area. Also, one female LD was unable to adequately execute the performance tasks due to excessively long fingernails at re-examination testing, thus the sample for analyses in the present study was  $n = 86$  HD and  $n = 69$  LD.

At both testing phases, participants were screened for major Axis I psychiatric and substance dependence disorders (excluding nicotine dependence) with the non-patient version and alcohol use disorder (AUD) module of the structured clinical interview for DSM-IV (SCID; First et al. 1995), and drinking was assessed by a past-month time-line follow-back calendar (TLFB; Sobell and Sobell 1992), and typical alcohol use and alcohol-related consequences were assessed with the Alcohol Use Disorders Identification Test (AUDIT; Saunders et al. 1993) and the Drinker Inventory of Consequences (DrInC-2R; Miller et al. 1995). As outlined in our prior report (King et al. 2014), HDs largely remained with excessive drinking patterns over the interim period between testing phases, albeit with some variability, while LDs largely continued with low-risk drinking.

**Laboratory procedures: initial phase and re-examination phase (5 years later)** Both study phases included two 4½ h individual laboratory sessions separated by at least 24 h that commenced between 12 p.m and 5 p.m. Most participants completed the two laboratory sessions between 2 and 7 days apart (initial testing phase, 81% of participants; re-examination phase, 74% of participants). The time between sessions did not differ by drinking group and were similar between testing phases [initial testing phase:  $m(sd) = 6.0$  days (0.4); re-examination phase:  $m(sd) = 6.6$  days (0.6)].

Upon arrival, the participant completed pre-session self-report measures to confirm compliance with 3-h abstinence from food, caffeine, and cigarette smoking and underwent objective breath and urine tests to confirm compliance with recent recreational drug (i.e., cocaine, amphetamine, methamphetamine, opiates, and MDMA) and alcohol abstinence (requested to be abstinent 48 h prior to testing) and confirm non-pregnancy in women as required by our IRB for all studies that may administer alcohol. Each participant then consumed a standard snack at 20% daily calories based on sex and body weight.

Following baseline subjective and objective measures, participants consumed the study beverage in the presence of the researcher over a 15-min period. Beverages were presented in lidded, clear plastic cups in two equal portions with each portion consumed over 5 min separated by a 5-min rest. Beverages contained either a high dose alcohol (0.8 g/kg, 16% volume; mixture of 95% ethanol with flavoring, sucralose, and water) or placebo (0.0 g/kg; 1% ethanol as taste mask with same flavoring and sucralose mixture). Beverages were prepared based on participants' body weight, and sex with doses for females were reduced to 85% to account for differences in body water and metabolism.

The study employed the alternative substance paradigm, wherein the participant was informed that the allocated beverage might contain a stimulant, sedative, alcohol, placebo, or a combination of these substances (Conrad et al. 2012). Performance tasks took place after the blinded BrAC reading and subjective measures at pre-beverage baseline and several post-beverage time points to assess dynamic changes over the BrAC curve. At the end of the session, participants completed a validity check item on which they indicated what they believed to be the contents of the beverage. Groups did not differ in number of correct identifiers of alcohol as the only active ingredient in the beverage (initial testing phase, LD 42%, HD 37%; re-examination phase, LD 39%, HD 48%;  $\chi^2_s \leq 1.1$ ,  $ps \geq .33$ ), and there were no differences between correct and incorrect identifiers on peak performance impairment ( $ps \geq .14$ ). At the end of each session, approximately 180–210 min after beverage consumption when BrAC was  $\leq 0.04$  g/dl, a car service transported the participant home. The participant agreed not to drive or operate machinery for at least 12 h following testing.

## Dependent measures

**Performance tasks** At each testing phase, participants completed two psychomotor tasks, the Digit-Symbol Substitution Test (DSST) and the Grooved Pegboard, at pre-drink baseline and then repeated over the BrAC curve at 30, 60, 120, and 180 min after ingestion. The DSST is a 90-s paper-and-pencil task that measures perceptual motor processing speed. The task requires the participant to write symbols in boxes beneath

integers based on a key provided at the top of the page. The task instructions emphasized the participant work toward both speed and accuracy, with the number of correct items recorded as the main dependent variable. Five different but equivalent forms were used within each session (i.e., a different form at each time point). The Grooved Pegboard is a measure of motor speed and fine motor coordination and requires participants to quickly retrieve, rotate, and insert small metal pegs into 25 slotted holes on a board. Each participant completed the task using his/her non-dominant hand, and the main dependent measure was the time (in seconds) for the participant to position all 25 pegs correctly. To reduce a potential confound of early learning effects on pegboard performance, participants practiced the task during the screening session at both phases.

**Perceived impairment** At 30- and 180-min time points prior to completing performance tasks, participants completed three subjective items assessing perceived impairment used previously in our lab (Brumback et al. 2007): (1) “how impaired do you think you are at present?”, (2) “how unsafe do you think it would be to drive an automobile at present?” and (3) “if I were at work now, others might think I was intoxicated or behaving unusually.” Each item was rated on a 10-point scale anchored at 1 for “not at all” and 10 for “extremely.” Ratings on these three items were highly intercorrelated (initial testing:  $r_s \geq .73$ ,  $p_s < .001$ ; re-examination:  $r_s \geq .60$ ,  $p_s < .001$ ). To simplify analyses, the mean of the three items was used as the measure of overall perceived impairment for each participant.

## Analyses

Demographic variables were compared from initial testing phase to 5-year re-examination phase via t-tests (for continuous variables) and  $\chi^2$  tests (for categorical variables). Initial analyses were conducted separately in each drinking group as the primary purpose was to examine performance impairment across the BrAC curve within each group over time. Mixed linear models were utilized for repeated-measure analyses on BrAC and performance data. For BrACs, the models included phase (initial, re-examination) and time (30, 60, 120, and 180 min after alcohol), since baseline time points and placebo session measures were all zero and therefore not included in the analysis. For performance measures models, phase, dose, and time (5 levels) were included. Covariates in the models included BrAC (time-varying), sex, average drinks per month, and smoking days in prior month. Significant effects were further examined by Tukey’s HSD post-hoc tests. Outlier data ( $\pm 2.5$  SD from the mean) observed in 2.4% of the performance data were excluded from analyses, with no difference in number of data points censored between HD and LD:  $t(153) = .46$ , ns. Significance for all analyses was set at  $p < .05$ . Effect sizes ( $\eta^2_p$ ) reflecting the variance accounted

for by specific effects are provided for all significant effects from mixed models (Lakens 2013).

To directly compare behavioral tolerance between groups, mixed model analyses were conducted on change scores (i.e., alcohol-placebo) at each time point for both initial and re-examination testing, with BrAC and sex as covariates (group  $\times$  phase  $\times$  time). In these models, a group  $\times$  phase  $\times$  time interaction would indicate differential behavioral tolerance between the groups.

Additional analyses using linear regression models examined the effects of drinking behavior during the interim 5 to 6 years on changes in alcohol-induced peak performance impairment. For these models, change scores were calculated to characterize the change in peak impairment (i.e., peak impairment minus the baseline measure) for the re-examination phase relative to the initial phase to yield a single outcome for each task. Average drinks per month over the 5-year interim period, peak BrAC change (re-examination phase minus initial phase), and sex were included as covariates.

Mixed models were constructed to test differences in perceived impairment (alcohol-placebo) at the two time points at which it was assessed (30 and 180 min after alcohol) in both testing phases (i.e., group  $\times$  phase  $\times$  time). The relationship between perceived impairment ratings and actual performance impairment was then examined by entering the perceived impairment rating as a predictor into mixed models of performance at the two corresponding time points (30 and 180 min).

## Results

### Participants

Demographic variables from initial testing to re-examination were compared within each group (see Table 1). The HDs continued with heavy drinking patterns, remaining 2–3-fold higher than in LDs who largely continued with low-risk drinking but with less frequent binge drinking and fewer alcoholic drinks per month (Fig. 1). HDs exhibited increases in alcohol consequences over time while LDs maintained minimal sub-threshold alcohol consequences (Forcehimes et al. 2007).

### BrAC

As expected, BrACs followed the usual biphasic pattern after alcohol consumption with a steep ascending limb peaking 60 min after consumption followed by a slow alcohol elimination phase and declining limb through the final time points at 180–195 min after ingestion (Fig. 2). HDs had higher BrACs at the initial versus re-examination phase (phase  $F(1, 83) = 10.4$ ,  $p < .01$ ,  $\eta^2_p = 0.11$ ), but this was not the case for LDs (phase:  $F(1, 66) = 0.4$ , ns) who exhibited similar BrACs at both phases.

**Table 1** Background and alcohol drinking characteristics in heavy and light drinkers

Demographics	Heavy drinkers ( <i>n</i> = 86)		Light drinkers ( <i>n</i> = 69)	
	Initial testing	5 years later	Initial testing	5 years later
Age (years)	25.2 (0.3)	30.2 (0.3)***	26.0 (0.4)	31.0 (0.4)***
Education (years)	15.7 (0.2)	16.2 (0.2)**	16.5 (0.3)	18.0 (0.4)***
Employed (full-time) <sup>a</sup>	57%	71%	44%	64%*
Sex (female)	43%	–	51%	–
Race (Caucasian) <sup>b</sup>	83%	–	68%	–
Ethnicity (Hispanic or Latino) <sup>b</sup>	12%	–	6%	–
Body mass index	25.0 (0.3)	24.9 (0.4)	24.7 (0.4)	25.3 (0.4)
Age at first drink (years)	15.0 (0.3)	–	17.7 (0.3)	–
Cigarette Use (% weekly or more)	57%	33%***	6%	3%
Past month smoking days <sup>c</sup>	15.9 (9.2)	8.6 (11.2)***	5.2 (2.1)	3.7 (2.7)
Drinking variables at initial testing and average over 5-year follow-up <sup>d</sup>				
Alcohol drinks per month <sup>e</sup>	71.4 (3.0)	59.0 (3.4)**	10.4 (0.6)	12.2 (0.9)*
Binge occasions per month <sup>f</sup>	7.8 (0.4)	6.1 (0.3)***	0.1 (0.0)	0.4 (0.1)**
AUD symptom count	1.8 (0.2)	1.6 (0.1)	0.06 (0.03)	0.1 (0.04)*
AUDIT total score	11.4 (0.4)	11.1 (0.7)	3.3 (0.1)	3.6 (0.2)
DrInC-2R total	13.2 (0.9)	15.9 (0.9)**	2.1 (0.3)	3.6 (0.4)***

Note. Data are mean (SEM) or *N* (%)

Within-group comparisons with initial testing values \**p* < .05; \*\**p* < .01; \*\*\* *p* < .001

AUD alcohol use disorder; AUDIT Alcohol Use Disorders Identification Test; DrInC Drinker Inventory of Consequences, Recent Consequences (past 3 months)

<sup>a</sup> Comparison of full-time employment to part-time, unemployed or student

<sup>b</sup> Race and ethnicity were provided by participants among a list of options consistent with NIH classifications

<sup>c</sup> Average for those who reported past month smoking

<sup>d</sup> Follow-up values represent the mean of values reported on annual follow-up interviews at 1, 2, 4, and 5 years

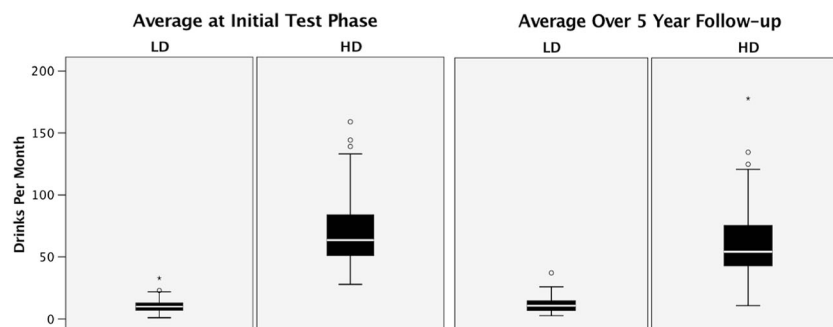
<sup>e</sup> Based on standard definition of one drink = 12 oz. beer, 5 oz. wine, or 1.5 oz. liquor, assessed timeline follow-back interview

<sup>f</sup> Binge defined as ≥5 drinks per occasion for males (≥4 for females)

**Performance measures**

**DSST** Overall, regardless of beverage type, for both HDs and LDs, performance on the DSST improved over time [HD, phase  $F(1, 83) = 25.0, p < .001, \eta^2_p = 0.25$ ; LD, phase  $F(1, 66) = 45.0, p < .001, \eta^2_p = 0.40$ ; Fig. 3]. At both phases, alcohol impaired DSST performance with fewer correctly

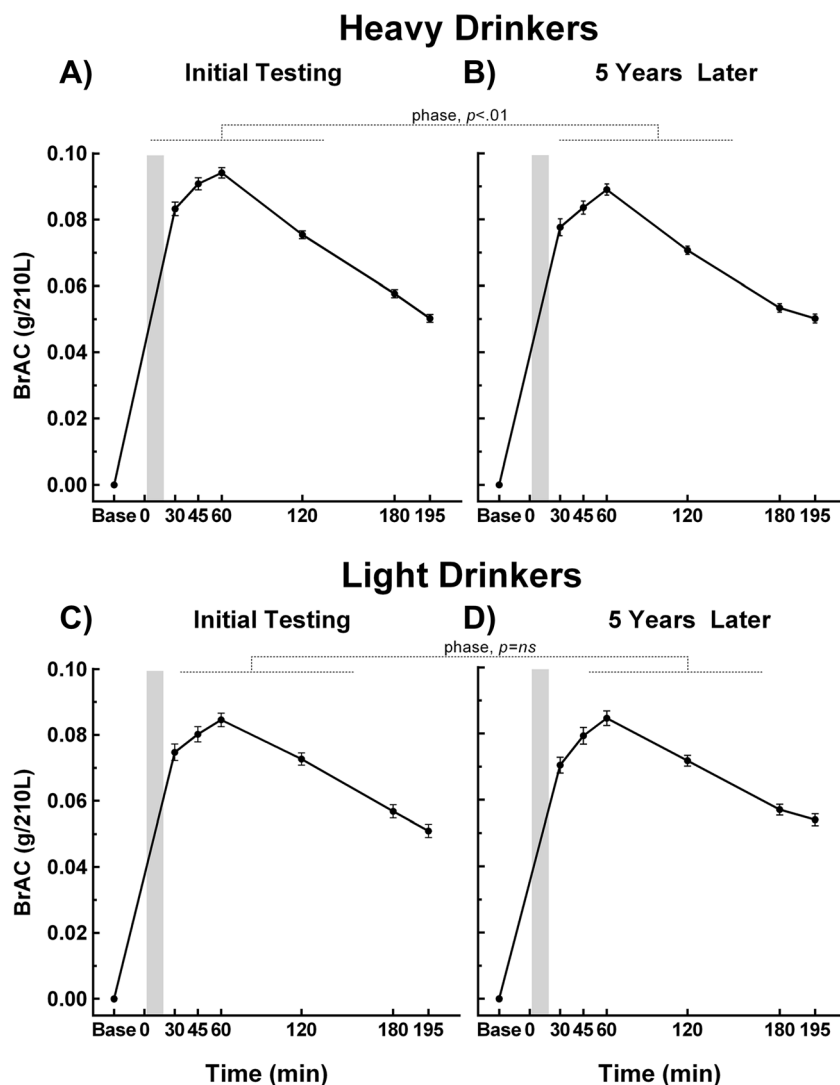
coded items particularly during rising-to-peak BrACs [HD, dose × time  $F(4, 83) = 14.5, p < .001, \eta^2_p = 0.39$ ; LD, dose × time  $F(4, 66) = 15.2, p < .001, \eta^2_p = 0.43$ ]. For both groups, alcohol-induced impairment on the DSST persisted in the re-examination phase to a similar extent as in initial testing (i.e., no dose × phase or dose × phase × time interactions). In each model, BrAC was the only significant covariate. The



**Fig. 1** Boxplots of average drinks per month at initial test phase (left) and over 5-year follow-up period (right) for light drinkers (LDs) and heavy drinkers (HDs). Shaded boxes represent the interquartile range (IQR) and

error bars represent 1.5\*IQR. White lines in the IQR box represent the group means. Data points greater than 1.5\*IQR are plotted with open circles, and data points greater than 3\*IQR are plotted with stars

**Fig. 2** Breath alcohol concentrations (BrACs) over the course of alcohol sessions at initial testing and re-examination testing 5 years later for heavy drinkers (top row) and light drinkers (bottom row). Error bars represent  $\pm 1$  SEM. NOTE: All available BrAC measures are presented here to depict full BrAC curve, but only those that coincide with performance measures (i.e., 30, 60, 120, 180) were included in analyses



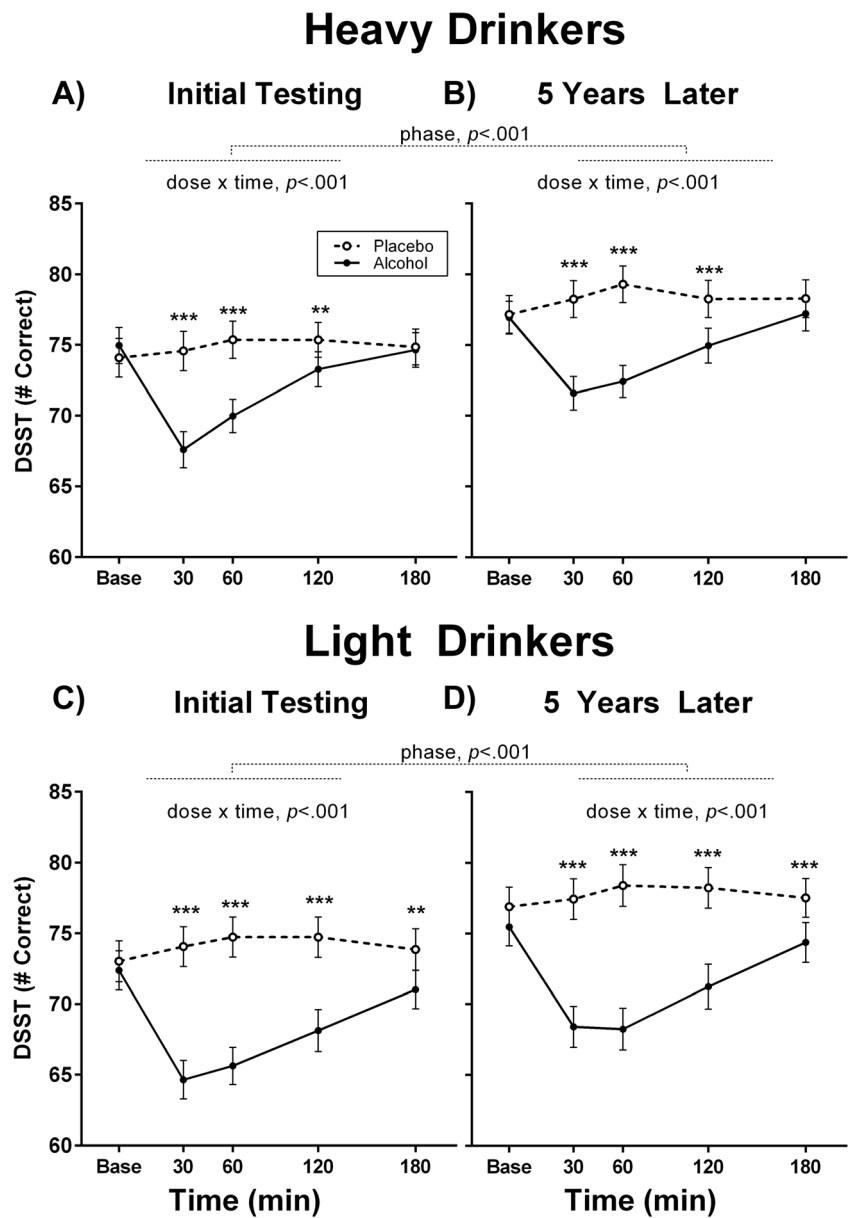
comparison between groups showed no group  $\times$  phase  $\times$  time interaction ( $F(4, 151) = 0.1$ , ns).

**Pegboard** Similar to the DSST, Pegboard performance improved from initial to re-examination testing regardless of beverage type, for both HD and LD [HD, phase  $F(1, 83) = 24.6$ ,  $p < .001$ ,  $\eta^2_p = 0.25$ ; LD, phase  $F(1, 66) = 27.0$ ,  $p < .001$ ,  $\eta^2_p = 0.29$ ; Fig. 4]. At both phases, alcohol impaired performance as more time was needed to complete the Pegboard, with highest impairment on rising to peak BrACs [HD, dose  $\times$  time  $F(4, 83) = 5.4$ ,  $p < .001$ ,  $\eta^2_p = 0.28$ ; LD, dose  $\times$  time  $F(4, 66) = 4.5$ ,  $p < .001$ ,  $\eta^2_p = 0.33$ ]. Importantly, for HDs, alcohol produced less impairment on Pegboard at re-examination relative to initial testing as evidenced by a significant three-way interaction [dose  $\times$  time  $\times$  phase  $F(4, 83) = 2.7$ ,  $p < .05$ ,  $\eta^2_p = 0.04$ ], with less impairment evident during the rising limb to peak BrAC interval (Tukey's HSD  $t(81) \geq 4.0$ ,  $ps < .05$ ). This was not the case for LDs as they showed similar impairment between phases [dose  $\times$  phase  $\times$

time  $F(4, 66) = 1.25$ , ns]. As with analyses of the DSST, BrAC was the only significant covariate for Pegboard models. Unlike DSST, the comparison between groups showed a group  $\times$  phase  $\times$  time interaction ( $F(4, 151) = 2.6$ ,  $p < .05$ ,  $\eta^2_p = 0.06$ ), which appeared to be driven by better HD compared to LD performance at re-examination rising limb BrAC interval (30 min: Tukey's HSD  $t(151) = 4.5$ ,  $p < .01$ ).

**Interim drinking and performance change** While drinking level over the 5-year interval was not a significant covariate in the prior mixed models within each group, additional analyses including all participants assessed the association between drinking over the interim period (average drinks per month) and changes in peak impairment, controlling for sex and BrAC. The analyses revealed that individuals who drank more on average over the follow-up period tended to exhibit less impairment on the Pegboard task ( $\beta$  (se) = 0.16 (.02),  $p = .06$ ) but not the DSST ( $\beta$  (se) = 0.07 (.02), ns). As expected,

**Fig. 3** Performance on the Digit-Symbol Substitution Task (DSST); items correctly coded, at initial testing and re-examination testing 5 years later for placebo and alcohol (0.8 g/kg) beverages in heavy drinkerS (top row) and light drinkers (bottom row). Lower scores indicate greater impairment from alcohol. Error bars represent  $\pm 1$  SEM.  $**p < .01$ ,  $***p < .001$ , for post hoc pairwise comparisons



decreases in peak BrAC at re-examination relative to initial testing was significantly associated with lower peak impairment on both tasks [Pegboard: ( $\beta$  (se) =  $-0.19$  (.03),  $p < .05$ ; DSST ( $\beta$  (se) =  $-0.18$  (.03),  $p < .05$ ].

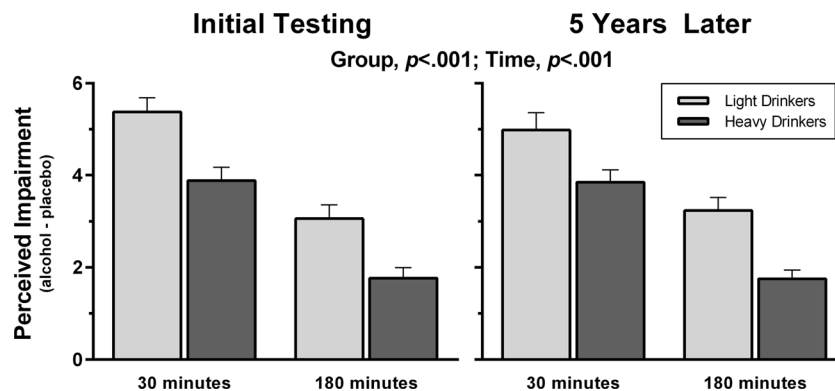
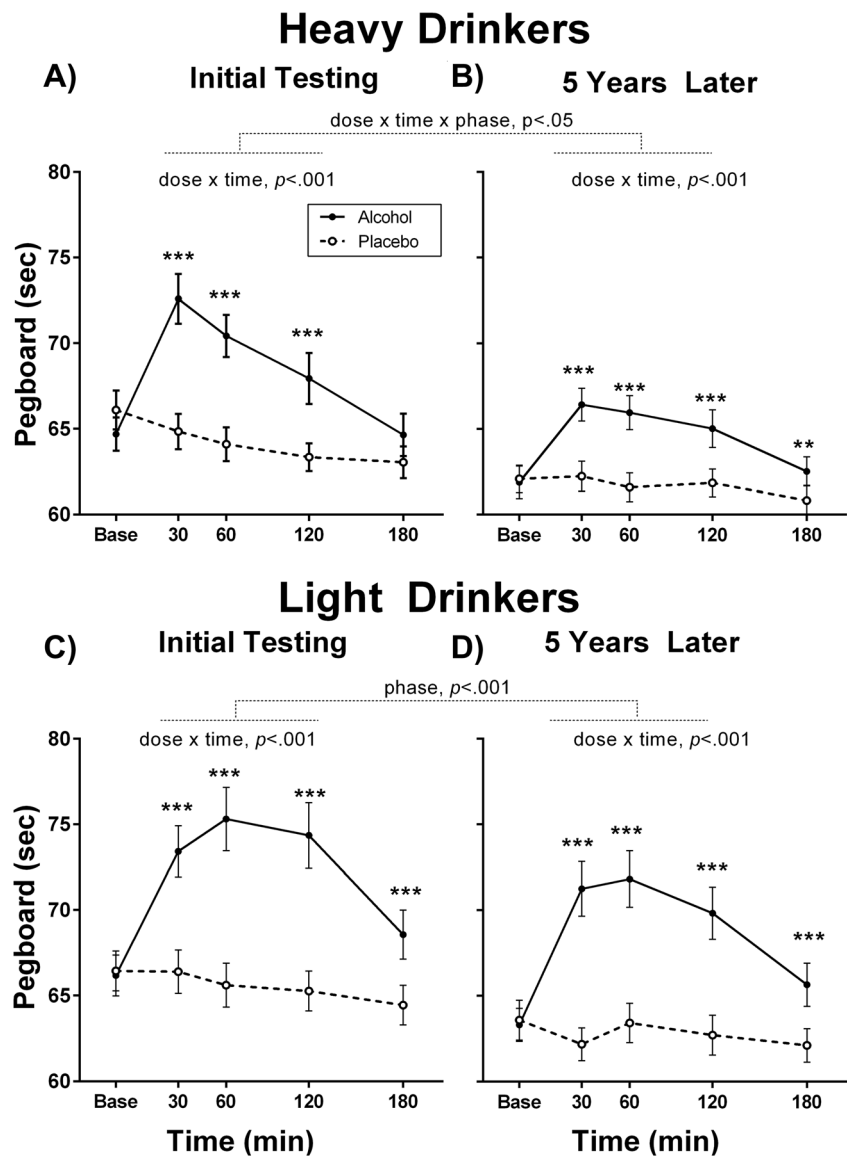
**Perceived impairment and associations with alcohol-induced performance responses**

At both phases and for both groups, alcohol increased perceived impairment ratings to a greater extent during the rising BrAC limb (30 min) than during the declining BrAC limb (180 min) [time:  $F(1, 151) = 44.9$ ,  $p < .001$ ,  $\eta^2_p = 0.49$ ; Fig. 5]. HDs reported lower perceived impairment than did LDs (group:  $F(1, 151) = 12.7$ ,  $p < .01$ ,  $\eta^2_p = 0.13$ ), and higher BrAC was associated with higher perceived impairment ( $F(1,$

$151) = 34.4$ ,  $p < .001$ ,  $\eta^2_p = 0.24$ ), but there were no BrAC by group interactions.

In models comparing perceived and actual performance impairment, greater perceived impairment was associated with greater Pegboard impairment in both groups ( $F(1,151) = 4.1$ ,  $p = .03$ ). However, for the DSST, perceived impairment interacted with group, phase, and time [perceived impairment  $\times$  group  $\times$  phase  $\times$  time:  $F(1, 151) = 5.0$ ,  $p < .05$ ,  $\eta^2_p = 0.05$ ]. A series of post hoc correlations to disentangle this interaction revealed that, in LDs, greater perceived impairment and actual DSST impairment was evident at both time points and at both phases ( $r_s = .25-.46$ ,  $p_s < .01$ ), but for HDs, perceived impairment was not associated with actual DSST impairment at initial testing ( $r_s = .05-.06$ , ns), but it was positively associated with DSST impairment at re-

**Fig. 4** Performance on the pegboard (in seconds) at initial testing and re-examination testing 5 years later for placebo and alcohol (0.8 g/kg) beverages in heavy drinkers (top row) and light drinkers (bottom row). Higher scores indicate greater impairment from alcohol. *Error bars* represent  $\pm 1$  SEM. \* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ , for post hoc pairwise comparisons



**Fig. 5** Perceived impairment ratings for heavy drinkers and light drinkers during the rising limb of the BrAC curve (30 min) and the descending limb of the BrAC curve (180 min) at initial testing (left

frame) and re-examination testing 5 years later (right frame). Perceived impairment ratings represent the change score between alcohol and placebo sessions. *Error bars* represent  $\pm 1$  SEM



examination ( $r_s = .29-.31, p_s < .01$ ). Thus, overall LD reported perceived impairment that was correlated with actual impairment, while HD exhibited this relationship only at re-examination testing.

## Discussion

This study provided a unique longitudinal examination of alcohol-induced psychomotor performance impairment over a 5–6-year interval in habitual heavy and light drinkers examined from early to mid-adulthood. HDs exhibited decreases over time in alcohol impairment on a task of fine motor skill and speed (Pegboard) and performed better than LDs did during the rising limb of the BrAC, but they did not show decreases in impairment on a task requiring more complex motor processing skills, frontal lobe-mediated executive processing of short-term memory, and encoding, i.e., the DSST (Glosser et al. 1977; Lezak et al. 2004). Thus, HDs demonstrated signs of behavioral tolerance on more circumscribed fine motor skills than in more complex integrative neurocognitive and motor skills over the interval from their mid-20s to early-30s. In contrast, LDs showed similar alcohol-induced psychomotor impairment on both tasks during the same developmental phase.

Prior work has shown that chronic heavy alcohol consumption alters brain structure and circuitry (Crews et al. 2005; Jacobus and Tapert 2013), particularly in frontocerebellar circuits underlying working memory and visuospatial functioning (Chanraud et al. 2010). Given that both drinking groups improved in performance on both tasks from initial testing to re-examination, it is highly unlikely that participants in these samples exhibited performance decrements due to neural atrophy associated with pronounced excessive drinking typical of long-term alcohol dependence (Crews et al. 2005; Sullivan et al. 2010; Sullivan 2003). Therefore, it appears that moderate levels of drinking (interquartile range of 50–75 drinks per month for HD) in early to middle adulthood may lead to increased behavioral tolerance for routine motor tasks, perhaps through learning of the repetitive behavior, which is not evident on psychomotor tasks that require more mental manipulation and short-term memory. Procedural memory tasks (i.e., repetitive psychomotor task requiring little working memory) show fewer deficits compared to neuropsychological tasks requiring more integration of frontal lobes and motor cortex in chronic alcoholics (Oscar-Berman and Marinković 2007; Parsons and Nixon 1993; Robbins et al. 2008). Thus, it is possible that tolerance develops more readily for repetitive tasks like the pegboard that require less working memory engagement and more procedural execution, as the brain regions underlying such processes are not as sensitive to insults associated with chronic alcohol use.

While acquired behavioral tolerance is the primary theory proposed to explain the neurobehavioral mechanisms of alcohol's effects on psychomotor and cognitive functioning, other

theories may explain some of the results in the current study. For example, state-dependent learning theory purports that habitual drinkers are able to retrieve information better when their physiological and sensory context is the same as during the encoding memory (Petersen 1977). Evidence for facilitated memory retrieval under the influence of alcohol has been mixed in human research (Duka et al. 2001; Moulton et al. 2005) and argues for a small effect on basic memory retrieval that does not readily transfer to more complicated memory or psychomotor tasks (Weissenborn and Duka 2003). Both groups improved on both tasks over time, so it is possible that repeated exposure to these tasks while under the influence of alcohol contributed to improved performance. However, since overall performance improved in both alcohol and placebo conditions, learning and practice likely led to the phase effects rather than learning the task while intoxicated.

Perceived impairment was associated with actual impairment on both tasks to some degree, though to a greater extent for the DSST. It is unclear why perceived impairment was associated with subsequent performance on this more cognitively demanding task. It is possible that, at least at the later time points after participants completed the task several times, performance impairment on the DSST may be more readily perceived because participants may notice they achieved fewer items coded over the 90-s task duration. In contrast, for Pegboard, the time to complete the board may provide less noticeable feedback on slowing of motor skills. Alternatively, it may be that the assessment of perceived impairment reflects more global and ecologically valid complex tasks (e.g., driving a car) rather than general psychomotor impairment specifically.

As intoxication is an infrequent state for LDs, it was not surprising that they continued to rate a higher intensity of perceived impairment than did HDs, as we previously showed at initial testing (Brumbach et al. 2007). HDs persisted in reporting lower levels of perceived impairment compared to LDs even though they appeared to rate perceived impairment more in line with performance at re-examination compared to initial testing (e.g., HD perceived impairment was unrelated to DSST performance at initial testing). Lower perceived impairment coupled with higher sensitivity to stimulating and rewarding effects of alcohol among HDs (King et al. 2016) may increase their likelihood of alcohol harm. For HDs, in terms of executive functioning under the influence of alcohol, we may speculate there may be “cognitive dissonance,” in that self-perception of low alcohol impairment may justify engagement in potentially risky behaviors while intoxicated. This would need further empirical testing, but if research supports this contention, then personalized feedback and targeted psychoeducation on perceived versus actual impairment in young binge drinkers may be indicated (e.g., Scott-Sheldon et al. 2012). In addition to behavioral tolerance, we also examined pharmacokinetic tolerance related to changes in speed of absorption and metabolism of alcohol. In this case, HDs'

BrACs decreased from initial testing to re-examination after consuming the same doses of alcohol, which likely indicates faster elimination of alcohol out of the blood stream (Whitfield and Martin 1994). Thus, it appears that chronic excessive drinking can yield increased pharmacokinetic tolerance over a 5-year period. BrAC was a significant predictor of both performance impairment and perceived impairment in both groups as expected; however, HDs' increased speed of absorption and metabolism did not result in an advantage in performance on the more complex psychomotor task.

The current study represented the first longitudinal examination of alcohol response using a placebo-controlled paradigm in 620 individual laboratory sessions in a large sample of well-defined drinking groups with outstanding follow-up (i.e., 98% retention and 88% re-examination participation in those eligible for alcohol challenge). However, there are several limitations that should be acknowledged. First, as this study was part of a larger investigation examining other alcohol responses (King et al. 2006, 2011, 2016; Roche and King 2010) and tasks needed to be of short duration to avoid affecting participants' experiences of intoxication, data were collected on two circumscribed psychomotor tasks of varying cognitive complexity. However, this limited our assessments and implications to a wider range of neurocognitive skill assessment. Second, the alcohol dose was chosen at an intoxicating level for ecological validity to simulate a binge drinking episode resulting in BrACs above the legal limit for driving in the USA. Given the absence of other doses which would have been time- and cost-prohibitive in a study of this scale, ascertainment of alcohol dose-ranging behavioral tolerance effects was not possible. Third, HDs showed more variability in their drinking patterns over time than did the LDs. While in animal models experimental manipulations can titrate alcohol exposure across time, in human heavy drinkers, variations in drinking patterns were evident and did not occur at random; however, the threshold for tolerance may have been surpassed even in the least affected HDs who drank at levels at least twice that of the LDs on average over the follow-up phase.

In sum, this study provided evidence of heavy drinkers' acquired behavioral tolerance over a 5-year period on a task of fine motor speed but not on a cognitively more complex task requiring motor speed but also executive functioning skills of encoding, set-shifting, and short-term memory. Our unique longitudinal dataset enabled elucidation of the changes accompanying persistent excessive drinking in humans, with results showing that neurobehavioral skills associated with frontal lobe functioning are less likely to undergo acquired behavioral tolerance in excessive drinkers than are fine motor skills. Given that HDs persist in low perception of alcohol-induced impairment over time, coupled with continued alcohol impairment of complex neurocognition, such drinkers remain at risk for alcohol harm as they continue to engage in chronic binge drinking over time. Future studies are needed to examine

behavioral tolerance and alcohol-induced impairments across a wider range of performance tasks to gain further understanding of neurobehavioral changes in risky drinkers.

#### Compliance with ethical standards

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