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Cognitive flexibility during breath alcohol plateau is associated with previous drinking measures

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Abstract

Although the biphasic effects of acute alcohol during ascending and descending Breath Alcohol Concentrations (BrACs) are well described, the plateau period between peak and steadily descending BrACs is generally unrecognized and under-studied by researchers. Naturalistic examinations indicate such periods persist for substantial intervals, with a time frame of onset suggesting BrAC plateaus may co-occur with potentially risky behaviors (e.g., driving). The current pilot study examined neurocognitive performance during this period. Participants were healthy, community-residing moderate drinkers ($n=18$). In the first phase of the study, the Digit Symbol Substitution and Trail Making Tasks were administered during BrAC plateau ($M=62$ mg/dL). BrACs were negatively correlated with Digit Symbol performance but unrelated to other tasks. In contrast, performance on a derived Trail Making measure of set-shifting was positively associated with the maximum alcohol doses consumed in the preceding 6 months. Phase 2 analyses demonstrated that relationships between previous alcohol experience and cognitive performance were absent among individuals receiving placebo beverages. Taken together, these data suggest a relationship worthy of investigation between previous drinking experiences and cognitive flexibility during the plateau phase.

Keywords

Alcohol; BAC; Acute administration; Alcohol use history; Digit Symbol Substitution Task; Trail Making Task

Introduction

Analyses of acute alcohol effects often involve rapid consumption following limited food intake (e.g., Gilbertson, Prather, & Nixon, 2010; Ostling & Fillmore, 2010). These procedures produce Breath Alcohol Concentrations (BrACs) which rise quickly and decline steadily. These investigations have revealed limb-dependent differences in attention (Hurst & Bagley, 1972), memory (Jones, 1973; Schweizer et al., 2006), executive function (Pihl, Paylan, Gentes-Hawn, & Hoaken, 2003), and motor coordination (Vogel-Sprott & Fillmore, 1993). However, few studies have been directed toward performance during the BrAC plateau. Although not consistently defined in the literature, plateau can be broadly considered the phase in which absorption and elimination rates interact to produce a relatively stable alcohol concentration in the blood.

Peak BrACs are attained between approximately 10 and 25 min following the last beverage consumed in a drinking episode (Breen, Dang, Jaing, & Boyd, 1998; Ganert & Bowthorpe,

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2000; Winek, Wahba, & Dowdell, 1996), and BrAC plateaus appear to persist for up to 60 min (Ganert & Bowthorpe, 2000). Naturalistic examinations support the relevance of this period. Geller and colleagues observed that intoxicated (> 100 mg/dL) individuals consumed their last beverage approximately 20 min prior to departure from the drinking establishment, suggesting a variety of risk-taking behaviors (e.g., driving) may occur during BrAC plateau. For example, among drivers with positive blood alcohol levels killed in vehicular accidents, approximately 25% crashed during the plateau phase (determined by alcohol ratios in blood/urine; Levine & Smialek, 2000). Given the relatively sparse literature examining this period, there is a clear need for additional research.

The current pilot study was designed to examine cognitive performance at BrAC plateau. Two neurocognitive measures were administered following plateau detection. The Trail Making Task (TMT) and Digit Symbol Substitution Task (DSST) were selected for their brief administrative demand and measurement of relevant cognitive domains. Although the paucity of information concerning performance at plateau precluded more nuanced hypotheses, we predicted BrACs would be negatively associated with task performance, and we asked whether performance would be related to previous alcohol use.

Materials and methods

Experimental design

The current pilot study was conducted in 2 phases (depicted graphically in Fig. 1). In Phase 1, alcohol was acutely administered to 8 participants. Following administration, BrACs were measured, BrAC plateau was identified, and cognitive testing was administered. Retrospective analysis indicated 2 participants were tested following plateau, thus only 6 were included in the data analysis. Phase 1 was conducted as part of an SBIR study examining novel BrAC measurement technologies (Morey et al., 2011).

Based on Phase 1 results, discussed below, Phase 2 participants were selected from a large, double-blind, placebo-controlled acute alcohol administration study. Phase 2 controls were matched on drinking histories to Phase 1 individuals. Two control subgroups ($n = 6/\text{group}$) were selected, based on the effectiveness of the placebo. Placebo Effective [P_E] participants believed they had received alcohol-containing beverages, whereas Placebo Ineffective [P_I] participants endorsed having received no alcohol. This design allowed for consideration of potential alcohol-expectancy effects.

Participants

All participants (ages 21–35; $N = 18$; 11 males) were non-smoking moderate social drinkers, consuming at least one drink/month for the preceding 6 months. Participants' demographic information is presented in Table 1. A multi-tiered screening procedure included pencil/paper questionnaires assessing demographics, affect, and alcohol/substance use histories. Exclusionary psychiatric diagnoses were screened with the computerized Diagnostic Interview Schedule IV (cDIS-IV; Robins, Cottler, Bucholz, & Compton, 1995). Medical conditions that might confound interpretation or contraindicate alcohol administration (e.g., epilepsy or brain trauma) were exclusionary.

Participants arrived at the Neurocognitive Lab at 9:30AM $\pm$ 30 min. Participants were administered urine tests for pregnancy (where appropriate) and recent drug use, as well as breath tested for recent alcohol consumption (Intoxilyzer, Model 400; CMI, Inc., Owensboro, KY). Any positive result on these screens was exclusionary. Participants provided written informed consent prior to screening/testing and received financial reimbursement. All procedures were approved by the University of Florida Institutional

Review Board and were in accordance with the Helsinki Declaration of 1975 (revised, 1983).

Phase 1: materials and methods

Acute alcohol administration

Widmark calculations (Watson, Watson, & Batt, 1981) were employed to produce BrACs of 80 mg/dL in fasting individuals; however, participant food consumption was not regulated until 1 h prior to alcohol administration. Medical grade alcohol (200 proof) was divided into two glasses, each with a non-caffeinated, sugar-free, citrus-flavored soda (183 mL in each glass), and administered at approximately 10:00 AM in a manner similar to published methods (e.g., Ostling & Fillmore, 2010). Consumption of each glass in less than 2 min was required, with a 1 min break in between (total consumption time = 5 min).

Breath Alcohol Concentration (BrAC)

Following beverage administration, BrACs were measured at 5 min intervals. Participants remained blind to BrACs until the conclusion of testing. To eliminate artifactual readings, participants mouth rinsed with water prior to initial measurement. Cognitive tests were initiated following plateau detection, operationally defined as a BrAC measurement less than or equal to the previous 2 measures. Following completion of the experimental session, plateau detection was analyzed retrospectively. If BrAC measures at time of cognitive testing differed from the highest (peak) BrAC measured during the session by ± 10 mg/dL, the data were excluded. This method is depicted in Fig. 2, including examples of participants (A & B) tested both before and after their peak BrAC, and one excluded participant (C). Two participants were determined to have been tested during descending BrACs, and were excluded from further analysis.

When BrACs declined to 10 mg/dL, participants were transported home by laboratory personnel, and advised to avoid consumption of additional alcohol or operation of motor vehicles for the remainder of the day.

Digit Symbol Substitution Task

A standard administration of the DSST was conducted (Wechsler, 1981). The task required the participant to alternate attention between sets of numbers and symbols. A key associating digits 1–9 with simple symbols was provided; participants were given a sequence of digits and required to substitute the appropriate symbols as quickly and accurately as possible, within 90 s. Given the abbreviated length of the task, 2 symbol sets were administered (180 s total). The average of the correct substitutions from each repetition was used as the dependent measure.

Trail making test

A standard administration of the Trail Making Test Forms A and B (TMT-A & TMT-B) was conducted (Reitan, 1955). Both forms required complex visual scanning, as well as a motor component (Shum, McFarland, Bain, & Humphreys, 1990). TMT-A required the participant to draw connections between 25 sequentially numbered dots appearing throughout a single piece of paper. TMT-B was similar; however, TMT-B had greater distances between targets and required alternation between 25 sequentially numbered and lettered dots (i.e., '1' to 'A' to '2' to 'B'). Instructions and brief practice consisting of a sample task (8 practice dots, with appropriate correction when necessary) were provided immediately prior to testing to ensure participants' understanding of the task. Participants were alerted to errors by the examiner and allowed to correct them, thus errors are evidenced in the task by greater latencies to completion. The dependent measure was duration (s) to task completion. Due to

the inclusion of set-shifting demands in TMT-B, the difference between scores [B–A] can be used as an index of set-shifting capability by removing variability associated with visuo-motor aspects of the task (Strauss, Sherman, & Spreen, 2006); specifically, lower scores indicate greater set-shifting ability. Both the TMT-A and TMT-B have high within-subject test–retest reliability ($r_s = .79$ and $.89$, respectively; Dikmen, Heaton, Grant, & Temkin, 1999).

Demographic drinking variables

Drinking behaviors over the previous 6 months were indexed using the Quantity–Frequency Index (QFI; Cahalan, Cissin, & Crossley, 1969), which quantifies average consumption in ounces per day of absolute alcohol over the preceding 6 months. Maximum QFI (MaxQFI) was also obtained, indexing the greatest volume (oz) of single-day alcohol consumption achieved, again over the preceding 6 months. Descriptive statistics for these measures are presented in Table 1.

Phase 1: results

Alcohol administration procedures resulted in a mean peak BrAC of 65 mg/dL (SD = 19; range = 46–93 mg/dL). Plateau detection techniques resulted in a mean BrAC of 62 mg/dL (SD = 17; range = 46–89) at time of cognitive testing. The mean difference between BrAC at testing and peak BrAC was 2.7 mg/dL (SD = 2.6; range = 0–6).

The DSST sets ($M_s = 53.5$ and 57.7) were combined into a composite mean score ($M = 55.6$; SD = 9.4; range = 43.5–67.0) for subsequent examination. The relationships between DSST, QFI, MaxQFI, and BrAC at time of testing were investigated. BrAC was negatively correlated with performance ($r = -.92$, $p = 0.01$; see Fig. 3). No other correlations reached significance. Correlation matrices for DSST and related variables are presented in Table 2.

Correlations between task performance (TMT-A [$M = 24.2$; SD = 8.2; range = 14–38]; TMT-B [$M = 53.3$; SD = 15.5; range = 34–74]; and [B–A] [$M = 29.2$; SD = 11.4; range = 11–44]), and QFI, MaxQFI and BrAC were examined. MaxQFI correlated significantly with [B–A] ($r = -.94$, $p < 0.01$; see Fig. 4); experiences with higher maximum doses of alcohol were associated with better set-shifting abilities during plateau. Correlation matrices for TMT and related variables are presented in Table 2. As the [B–A] measure was derived from TMT-B, their correlation was expected.

MaxQFI and QFI were significantly correlated ($r = .86$, $p = 0.03$), and although not significant, the magnitude of the relationship between QFI and [B–A] ($r = -.71$, $p = 0.11$) was notable. In order to further explore potential associations between drinking history and set-shifting, associations between [B–A] and other measures of previous drinking behavior were examined. Measures included days of sobriety prior to testing, maximum days of continuous sobriety in the preceding 6 months, age of initial alcohol consumption, age of first intoxication, and age at initiation of regular drinking. While failing to meet statistical significance, two interesting relationships were observed. Set-shifting was associated with intoxication age ($r = .73$, $p = 0.10$) and length of sobriety episode ($r = .74$, $p = 0.09$), with earlier ages of intoxication and shorter episodes of sobriety associated with greater set-shifting ability at BrAC plateau.

Phase 2: materials and methods

To further clarify relationships noted in Phase 1, 12 placebo individuals (6 PE; 6 PI) were matched with Phase 1 participants (ALC) on MaxQFI (exact matching was possible for 6 control participants; participants with the closest MaxQFI were selected for the remainder).

Placebo beverages were delivered using standard administration procedures (e.g., Ostling & Fillmore, 2010), including a mist of alcohol (<1 dL) added to the surface of vehicle drinks to provide taste and olfactory cues. TMT tasks were administered at 25 min after beverage consumption.

Results (both phases)

Descriptive statistics for demographic and drinking variables are presented in Table 1. Groups (Phase 1 and 2) were equivalent on age, education, depressive affect, anxiety-related affect, abstracting ability, and body mass index ($F(2,15) = .97, p = 0.40$; $F(2,15) = 1.96, p = 0.17$; $F(2,15) = .89, p = 0.43$; $F(2,15) = 2.97, p = 0.08$; $F(2,15) = 1.12, p = 0.35$; $F(2,15) = .96, p = 0.40$, respectively). QFI measures for all groups indicated moderate consumption (<2 drinks/day for males in each group; <1 drink/day for females), with ANOVA analyses detecting no group differences ($F(2,15) = 1.47, p = 0.26$). Mean MaxQFI scores suggested participants engaged in behavior approaching or exceeding binge-like consumption at least once in the 6 months prior to testing. This finding was unsurprising given the relatively young age of participants and inclusion of college students. MaxQFI scores did not differ significantly between groups ($F(2,15) = .09, p = 0.92$).

ANOVA analyses conducted between groups for TMT-A, TMT-B and [B–A] failed to detect group differences ($F(2,15) = 1.54, p = 0.25$; $F(2,15) = 2.26, p = 0.14$; $F(2,15) = 1.70, p = 0.22$, respectively). TMT performance is depicted in Fig. 5.

Correlations between set-shifting and measures of drinking experience among Phase 2 individuals were of primary interest. In contrast to ALC participants, no significant correlation between setshifting and either QFI ($r = -.19$) or MaxQFI ($r = -.16$) was detected.

To characterize potential expectancy effects, associations between MaxQFI and set-shifting were re-analyzed among P_E and P_I groups, individually. Although neither was significant, the opposing patterns of the association in these groups were notable ($r = -.57, p = 0.24$ and $r = .48, p = 0.33$, respectively). When set-shifting and previous drinking measures (i.e., QFI and MaxQFI) were analyzed among an “expectation-positive” group (ALC + P_E), set-shifting appeared associated with both measures ($r = -.67, p = 0.02$ and $r = -.75, p < 0.01$, respectively).

Discussion

This pilot study was designed to explore the correlates of cognitive/behavioral performance during the plateau phase of the BrAC curve. Participants receiving alcohol achieved a mean peak BrAC of 65 mg/dL, and were administered the TMT and DSST tasks at a mean BrAC of 62 mg/dL. Numerous investigations (e.g., Fillmore, Ostling, Martin, & Kelly, 2009; for review see Holloway, 1994) have noted the negative influence of alcohol on performance in a variety of cognitive/behavioral tasks; the correlation between BrAC and DSST performance in this project was consistent with these observations. Results from the TMT were intriguing, suggesting a previously unappreciated relationship.

The TMT involves two exercises; TMT-A engages visual search and psychomotor skills. TMT-B further incorporates working memory and set-shifting components. The difference in time-to-completion between these tasks is thought to reflect a more precise measure of set-shifting ability than do raw TMT-B scores (Strauss et al., 2006). At plateaued BrACs, set-shifting ability [B–A] was strongly correlated with the highest alcohol dose experienced in the previous 6 months (MaxQFI). Importantly, when this associations was analyzed among all placebo-treated individuals, no such relationship was apparent.

Only the [B–A] and MaxQFI relationship reached significance. However, several correlations between set-shifting and previous drinking measures appeared notable given the small number of participants. These included QFI, age of initial intoxication, and maximum length of previous episodes of sobriety. Taken together, these findings indicate a generalized positive association between previous alcohol experience and cognitive ability during BrAC plateau. Importantly, the absence of similar relationships between previous drinking measures and either DSST or TMT-A performance suggests previous alcohol experiences may be associated with behavioral advantages only in specific domains. However, these associations were observed early in the plateau, thus their persistence through more extended plateau periods remains unclear. The use of alternative methods to establish and extend BrAC plateaus such as intravenous clamping procedures (e.g., O'Connor, Morzorati, Christian, & Li, 1998) would be well-suited to pursue these questions.

These data were also examined considering alcohol-expectancy effects. When set-shifting associations were re-examined among participants who believed they had received alcohol (ALC + P_E groups), the correlations between set-shifting and both MaxQFI and QFI remained consistent. These relationships were absent in the P_I group, suggesting a substantial expectancy effect. Future consideration of this issue should examine expectancy in a more nuanced manner, including incorporation of an alcohol-expectancy effect questionnaire and subjective intoxication scales.

These data raise new questions, but they should be considered preliminary, and considered with several caveats. Although MaxQFI appeared strongly associated with performance in both ALC and P_E individuals, the recency of the drinking episode with the highest BrAC was not assessed, and should be considered in future work. An additional consideration involves participant BrACs. Participant fasting was regulated only during the hour prior to beverage administration, although variation in BrACs was no greater than would be expected due to absorption kinetics alone (Ramchandani, Plawecki, Li, & O'Connor, 2009). It is possible that the BrAC range in the current study obscured detection of other significant associations. Constraint of BrACs in future work (e.g., extended fasting duration, limiting age/BMI ranges) might allow for greater isolation of the observed relationships or improve detection of additional associations. Sample sizes in the current study were notably small, precluding several important analyses (i.e., gender or age effects). The use of a within-subjects, repeated-measures, placebo-controlled design would be well-suited to address these issues in a future study. Examining the relationships between previous drinking measures and set-shifting capabilities during ascending, descending, and various plateau time points would allow for a particularly nuanced analysis.

These data suggest an interesting relationship between drinking history and cognitive flexibility at an important, yet under-studied, period in the BrAC curve. These findings may augment our understanding of functional tolerance. Specifically, at moderate BrAC plateaus, performance in some cognitive domains (i.e., set-shifting) may be particularly sensitive to previous experience. Although the current work provides only an initial step toward examining this hypothesis, given the paucity of previous empirical study and general lack of awareness about this plateau period, these observations suggest further investigation is warranted.

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Fig. 1.

Experimental design. Based on the observed peak times and variables of interest following behavioral analyses, placebo controls were recruited from a large double-blind, placebo-controlled study, and matched to Phase 1 participants based on MaxQFI. Two placebo individuals were matched for each Phase 1 participant, including one for whom placebo was effective, and one for whom placebo was ineffective.

Fig. 2.

Inclusion/exclusion examples based on retrospective peak analysis. Participant BrAC curves, including one excluded due to BrAC at time of testing which differed from peak by >10 mg/dL. Black arrows indicate time of testing.

Fig. 3. Mean DSST score and BrAC. Correlation between mean DSST scores and BrAC at time of testing. A negative relationship was noted, such that lower BrACs were associated with higher DSST scores ($r = -.92$, $p = 0.01$).

Fig. 4. Set-shifting and maximum alcohol consumption over previous 6 months. Correlation between set-shifting and maximum alcohol consumed in a past drinking episode (previous 6 months). A negative relationship was noted, such that experience with higher doses of alcohol was associated with greater set-shifting ability during the BrAC plateau period ($r = -.94$, $p < 0.01$).

Fig. 5.

Trail Making Task performance and set-shifting measures, by group. ANOVA revealed no significant differences on TMT-A, TMT-B or [B-A] measures.

Table 1

Demographic and drinking measures.

	<u>Alcohol received (n = 6; 3 m)</u>	<u>Placebo effective (n = 6; 4 m)</u>	<u>Placebo ineffective (n = 6; 4 m)</u>
	<i>M</i> (SD) [range]	<i>M</i> (SD) [range]	<i>M</i> (SD) [range]
Demographic measures			
Age (yrs)	25.67 (4.88) [21–35]	28.66 (2.34) [26–31]	27.00 (3.52) [25–34]
Education (yrs)	16.17 (1.17) [15–18]	16.17 (1.83) [13–18]	17.50 (.84) [16–18]
BDI ^a	2.00 (1.41) [0–4]	3.50 (3.78) [0–10]	1.50 (2.34) [0–6]
AI ^b	41.50 (6.89) [34–53]	44.33 (4.22) [36–48]	37.00 (4.19) [34–45]
SILS-V ^c	18.53 (1.81) [16.2–20.6]	18.60 (1.01) [17.4–20.2]	17.60 (1.21) [17.0–19.0]
BMI (kg/m ²)	24.58 (3.98) [20.4–29.7]	25.47 (2.56) [18.6–35.2]	28.47 (2.48) [24.3–31.1]
Drinking measures			
QFI ^d	.67 (.62) [.1–1.8]	.55 (.34) [.2–1.1]	.27 (.11) [.1–.4]
MaxQFI ^e	5.15 (3.02) [1.8–10.2]	4.75 (2.54) [1.8–8.9]	4.54 (2.09) [1.8–6.7]

^aBeck Depression Inventory, 2nd ed. (Beck, Steer, & Brown, 1996).^bAnxiety Inventory (Spielberger, 1983); age corrected.^cShIPLEY Institute of Living Scale (Zachary, 1986); mental age.^dQuantity Frequency Index (Cahalan et al., 1969).^eMaximum Alcohol (oz) in single 24 h period (previous 6 months).

Table 2

Correlations: task performance, drinking behavior and BrAC.

r (p)	DSM	TMT-A	TMT-B	[B-A]	MaxQFI	QFI
TMT-A	-.347 (0.499)					
TMT-B	-.009 (0.986)	.694 (0.125)				
[B-A]	.237 (0.650)	.222 (0.671)	.855 (0.029)			
MaxQFI	-.058 (0.912)	-.088 (0.867)	-.743 (0.090)	-.944 (0.004)		
QFI	.001 (0.999)	.179 (0.734)	-.429 (0.394)	-.711 (0.112)	.861 (0.027)	
BrAC	-.921 (0.009)	.302 (0.560)	.118 (0.822)	-.056 (0.915)	-.167 (0.751)	-.152 (0.772)

Bolded correlation measures denote *p* values < 0.05.