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Effects of Age and Acute Moderate Alcohol Administration on Electrophysiological Correlates of Working Memory Maintenance

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Abstract

Background—Previous studies suggest older adults may be differentially susceptible to the acute neurobehavioral effects of moderate alcohol intake. To our knowledge, no studies have addressed acute moderate alcohol effects on the electrophysiological correlates of working memory in younger and older social drinkers. This study characterized alcohol-related effects on frontal theta (FTP) and posterior alpha power (PAP) associated with maintenance of visual information during a working memory task.

Methods—Older (55–70 years of age; $n = 51$, 29 women) and younger (25–35 years of age; $n = 70$, 39 women) community-dwelling moderate drinkers were recruited for this study. Participants were given either placebo or an active dose targeting breath alcohol concentrations (BrACs) of 0.04 or 0.065 g/dL. Following absorption, participants completed a visual working memory task assessing cue recognition following a 9s delay. FTP and PAP were determined via Fourier transformation and subjected to 2 (age group) X 3 (dose) X 2 (repeated: working memory task condition) mixed models analysis.

Results—In addition to expected age-related reductions in PAP, a significant age group X dose interaction was detected for PAP such that 0.04 g/dL dose level was associated with greater PAP in younger adults but lower PAP in their older counterparts. PAP was lower in older vs younger adults at both active doses. Further mixed models revealed a significant negative association between PAP and working memory efficiency for older adults. No effects of age, dose, or their interaction were noted for FTP.

Conclusions—Results bolster the small but growing body of evidence that older adults exhibit differential sensitivity to the neurobehavioral effects of moderate alcohol use. Given the theoretical role of PAP in attentional and working memory function, these findings shed light on the attentional mechanisms underlying effects of acute moderate alcohol on working memory efficiency in older adults.

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Key works

alpha; theta; alcohol; aging; working memory; moderate drinking

INTRODUCTION

Recent surveys of alcohol consumption in the United States suggest 53% of adults between 55 and 65 and 41% over 65 years of age have consumed at least one alcoholic beverage in the past 30 days, the majority of whom (65–80%) do not meet criteria for binge drinking or chronic heavy use (SAMHSA, 2014). Thus, most older adults may be considered to be moderate or social drinkers. Despite some controversy, moderate alcohol use is typically assumed to be a healthy lifestyle choice (for review, see Boissoneault et al., 2016). However, a lifestyle including moderate drinking necessarily includes sessions of acute moderate drinking that can have significant effects on neurobehavioral function. Indeed, studies indicate blood alcohol concentrations (BACs) associated with moderate drinking events (i.e., < 0.08 g/dL) may be associated with impairments in higher-order cognitive functions such as decision-making and working memory (Fillmore, 2007). These deficits are more pronounced in the context of dual-tasking or divided attention tasks (Fillmore, 2007), which reflect situations that occur commonly in everyday life.

Unfortunately, little systematic research has addressed how older adults (operationally defined here as being greater than 55 years of age) may differ from their younger counterparts in terms of susceptibility to these effects. Working memory is an important higher-order cognitive process that may be susceptible to interactions between age and alcohol use, especially given a substantial literature indicating working memory deficits in older adults (Drag and Bielauskas, 2010). Age-related reductions in lean muscle mass and total body water (that alter alcohol pharmacokinetics; Vogel-Sprott and Barrett, 1984) and subtle deficits in working memory function may synergistically drive increased working memory impairment from sub-intoxicating alcohol consumption.

We have previously explored differential sensitivity to the effects of acute moderate alcohol doses on working memory efficiency among older adults (55–70) vs. younger adults (25–35) during a working memory task (Boissoneault et al., 2014). We found evidence for an interaction of age group and dose such that older adults showed task- and dose- dependent changes in working memory efficiency that were not evident in their younger counterparts. The directionality of these effects depended on whether probes were present (i.e., hits) or absent (i.e., correct rejections) in preceding sets of stimuli. Furthermore, using electroencephalography (EEG), we have documented increased susceptibility of older adults to the impairing effects of acute moderate alcohol administration on P3 amplitude and latency that are thought to reflect aspects of attentional function (Lewis et al., 2013). However, its effect on the neurophysiological correlates of working memory function in older adults has yet to be examined.

The EEG reflects summated activity of open field neuronal configurations, especially cortical pyramidal cells (Fabiani et al., 2000). Analysis of EEG spectral power (which reflects complex interactions of neuronal networks; Buzsaki and Draguhn, 2004), during

working memory maintenance represents an intriguing vantage point for the examination of older adults' potentially greater susceptibility to acute moderate alcohol effects. The current investigation focused specifically on frontal theta power (FTP; 4–7 Hz) and posterior alpha power (PAP; 8–12 Hz) because these combinations of region and frequency band have been previously demonstrated to be sensitive to task demands (Dias et al., 2015; McEvoy et al., 2001; Wang et al., 2016), older age (Dias et al., 2015; McEvoy et al., 2001), and acute alcohol use (Boha et al., 2009; Ehlers et al., 1989; Ehlers et al., 2012). Both older age and acute alcohol use are associated with attenuated increases in FTP during task performance (Boha et al., 2009; Dias et al., 2015; McEvoy et al., 2001; Kovacevic et al., 2012; Marinkovic et al., 2012). Because FTP has been positively correlated with cognitive performance (Gevins et al., 1997; Sederberg et al., 2003), it has been hypothesized that FTP shifts reflect allocation of resources associated with efficient performance.

The relationship between PAP and task performance is context-dependent. Generally, tasks requiring focus on an internal representation (e.g., working memory maintenance) are associated with increases in PAP posited to reflect decreased excitability of sensory cortices associated with enhancement of inhibitory 'gating' processes that prevent sensory interference. In contrast, tasks requiring visual focus on external objects or events are associated with decreases in PAP reflecting greater excitability of sensory cortices and, by extension, enhanced stimulus processing (for brief review, see Wang et al., 2016). Age may affect alpha-band power during cognitive performance; a study by Dias et al. (2015) indicated 'middle aged' (mean age ~56) and 'older' adults had significantly lower alpha power than younger adults (mean age ~24) both at baseline and during task performance, suggesting less efficient inhibitory control in these groups. In addition, acute alcohol intake (~.07–.08 g/dL) has been documented to affect alpha power during wakeful rest (Ehlers et al., 1989) and phase-locking of alpha band event-related related oscillations during an auditory oddball task (Ehlers et al., 2012) in healthy young men.

To our knowledge, there have not been previous comparisons of the differential effects of moderate alcohol doses (i.e., 0.065 g/dL) on FTP and PAP in older and younger adults. In the current study, we aimed to address this gap in the literature and extend our previous behavioral findings of age-related susceptibility to acute moderate alcohol effects on working memory function by conducting spectral analysis of EEG activity during the maintenance period of the same working memory task. We hypothesized age- and dose-related changes in both theta and alpha power during working memory maintenance. Our primary focus, however, was the predicted interaction of age group and alcohol dose such that alcohol's effects on theta and alpha power would be exaggerated in older adults compared to their younger counterparts.

METHODS

Study Design

A 2 (age: younger, 25–35; older, 55–70) x 3 (alcohol dose group: placebo; low [target = 0.04 g/dl]; and moderate [target = .065 g/dl]) double-blind, placebo- controlled, factorial design was used. A total of 52 older (30 women) and 73 younger (41 women) community-dwelling moderate drinkers were recruited for this study. Of these, behavioral but not

neurophysiological outcomes from 90 have been previously reported (Boissoneault et al., 2014). Four subjects (3 younger, 1 older) were excluded from further analysis due to concerns regarding EEG data quality, resulting in a total N = 121. All procedures were approved by the Institutional Review Board at the University of Florida.

Screening phase

Participants were recruited through advertisements on the radio, in print, and on flyers. Potential participants were informed regarding basic inclusionary criteria. These criteria included: (1) either being between the ages of 25 to 35 or 55 to 70, (2) being a nonsmoker, (3) being in good physical health, (4) having at least 12 years of education (i.e. a high school diploma or GED), (5) having no significant history of head injury or unconsciousness, (6) having prior experience consuming alcohol, and (7) having no history of alcohol or other substance use treatment. Potential participants who remained interested after learning these criteria were scheduled for an in-laboratory screening session. Written informed consent was obtained prior to any data collection.

Screening measures included assessments of basic demographic, history of alcohol and drug use, state anxiety (Spielberger, 1983), and age-appropriate measures of depressive symptomatology (younger: Beck Depression Inventory, 2nd Ed. [BDI-II]; older: Geriatric Depression Scale [GDS]) (Beck et al., 1996; Yesavage et al., 1982–1983). A quantity-frequency index (QFI) of average daily consumption of absolute ethanol in ounces over the 6 months before screening was determined (modified from Cahalan et al., 1969). QFI > 1.2 (approximately 2 drinks/day) was exclusionary for men and a QFI > 0.6 (approximately 1 drink/day) was exclusionary for women.

Qualifying participants provided a self-report of their medical history and were assessed for probabilistic psychiatric diagnoses using the computerized Diagnostic Interview Schedule IV (American Psychiatric Association, 2000; Robins et al., 1995). Exclusionary psychiatric criteria included: (1) current or lifetime diagnosis of alcohol or other substance dependence, including nicotine; (2) lifetime diagnosis of any psychotic disorder; (3) current diagnosis of major depressive disorder; and (4) lifetime diagnosis of major depressive disorder if electroconvulsive therapy was used for treatment. History of serious medical illness was also exclusionary, including: (1) uncontrolled type 2 diabetes; (2) uncontrolled hypertension; (3) epilepsy; (4) HIV/AIDS; (5) past incidence of powerful electric shock; (6) prolonged periods of unconsciousness; or (7) skull fracture. Pregnant or breastfeeding women were also disqualified.

Laboratory phase

Laboratory sessions were scheduled to begin in the morning between 8 am and 10:30 am, most typically starting at 9 am. Participants were asked to: (1) fast for 4 hours prior to the session; (2) take morning medications as normal; and (3) not take over-the-counter allergy or sinus medications on the morning of the session. Participants verbally confirmed their compliance with these guidelines and that their medication use had not changed between the screening and laboratory sessions. Those who reported noncompliance or change in

medication were rescheduled. Participants provided separate written informed consent for the laboratory session.

Recent abstinence from alcohol consumption was confirmed using standard instruments (Intoxylizer 400PA; CMI, Inc., Owensboro, KY). Initial breath alcohol concentrations (BrACs) were required to be .000 g/dl. Participants were required to produce a negative urine drug screen for benzodiazepines, amphetamines, cocaine, marijuana, and opiates. Women of childbearing potential were also required to produce a negative pregnancy test. Participants were given a light snack (~220 calories) approximately 1 hour before alcohol administration.

Alcohol administration

Doses of medical-grade alcohol needed to achieve BrAC targets for each participant were calculated using a modification of the Widmark formula, taking into account age and weight for men and height and weight for women (Watson et al., 1981). Consistent with standard procedures (Fillmore et al., 2000), calculated doses of alcohol (0 mL for the placebo group) were mixed with ice-cold, sugar-free lemon-lime soda in a 1:3 ratio, misted with alcohol to enhance placebo efficacy, split into two equal portions, and served. Participants consumed both portions within 5 minutes. BrAC measurements were taken at 10, 25, 60, and 75 minutes after alcohol administration. If, after twenty-five minutes, a participant's BrAC was less than or equal to half the target, they were provided a "booster" beverage containing half their initial alcohol dose. 5 subjects (2 older) received an active booster. All remaining participants were provided a placebo booster containing only soda and misted with alcohol. Participants' completed assessments of subjective intoxication before and after the working memory task using a 10-point Likert scale (1="not at all"; 10="most in my life"). Ss were transported home when their BrAC was ≤ 0.01 g/dL.

EEG Recording

Electrophysiological recording was conducted in a sound attenuated, electrically shielded booth (Eckel Industries of Canada Limited, Morrisburg, Ontario). Participants were fitted with an elastic cap containing a 64-electrode array arranged according to an expanded International 10/20 System configuration (Electro-Cap International, Inc., Eaton, OH). Linked earlobe electrodes were used as a reference with a mid-forehead ground. Two electrodes were also placed above and below participants' left eye in order to detect blinks. Impedances were maintained below 10 k Ω for all participants. NeuroScan 4.4 Acquire (Compumedics USA, Charlotte, NC) was used to record continuous EEG data. Amplifier gain was set to 10,000 $\times$ with an on-line bandpass filter of 0.15–50-Hz. Data were sampled at a rate of 500 Hz.

Working Memory Task

Twenty-five minutes after beverage administration, participants completed the working memory task (Gazzaley et al., 2005). Participants completed counter-balanced trial blocks under each of three instructional sets: 'remember faces', 'remember scenes', or passively view cue stimuli and indicate the direction of an arrow replacing the probe image with a button press. Each block contained 20 trials consisting of four grayscale photographs (two

faces and two scenes). Following cue presentation and before probe image presentation, a 9-second delay occurred during which participants were presented a fixation cross. During this period, participants were instructed to maintain representations of relevant cue stimuli. At the end of the 9-second delay period, the probe image was presented and participants were required to respond whether the probe image was in the preceding set of cue stimuli (50% chance). The task is illustrated in Figure 1. For purposes of this report we restricted our analysis to the ‘remember faces’ and ‘remember scenes’ conditions due to our interest in the electrophysiological correlates of active working memory processes. Reaction time and accuracy was noted after each trial. From these data, proportions of correct responses of “present” to previously presented probes (hits) and correct responses of “absent” to previously absent probes (correct rejections) and their respective average RTs were derived. Accuracy/RT proportions, i.e. efficiency ratios, were constructed for each trial type. These ratios were the focus of our previous investigation of age group differences in the acute neurobehavioral effects of moderate alcohol intake (Boissoneault et al., 2014). The working memory task took approximately 25 minutes to complete.

Spectral Power Analysis

MATLAB 2011b (The MathWorks, INC; Natick, Massachusetts) and the EEGLab toolbox (Delorme & Mekeig, 2004) was used for EEG data cleaning and spectral analysis. Eleven electrodes were selected from frontal and posterior regions in order to topographically target frontal theta and posterior alpha, respectively (Figure 2). Other region/frequency combinations were not examined due to our theoretical focus on FTP and PAP. Rejection of malfunctioning EEG channels was performed automatically based on excessive kurtosis. A 4th-order band pass filter between .01 and 50 Hz was applied to attenuate high frequency noise and low frequency shifts. Artifacts, including eye blinks, eye movements, and general discontinuities, were removed using ADJUST, an automated artifact reduction toolbox based on independent component analysis (ICA; Mognon et al., 2011). EEG data recorded during the 9-second delay period in each trial was split into 3s epochs. Because each run included 20 trials, this resulted in a maximum of 60 3s epochs per condition. The mean number of accepted epochs was 37.06 (SD = 6.78, range: 15–59); repeated measures ANOVA did not indicate differences for age group, dose group, or condition ($ps > .12$; $f^2 < .02$). Note that results were unchanged when the 11 subjects with fewer than 20 epochs for at least one condition were excluded. Thus, these participants were retained in the analysis (described below). The *pop_spectopo* function of EEGLAB was then used to subject epochs to Fast Fourier Transformation (FFT), deriving participants’ average log-transformed absolute spectral power ($10 \cdot \log_{10}[\mu V^2]$, equivalent to dB) in the theta (4–7 Hz) and alpha (8–12 Hz) frequency bands.

Analysis Strategy

SAS Version 9.4 (SAS Institute, Inc., Cary, NC) was used for all statistical analyses. In order to ensure discrepancies in demographic variables did not meaningfully confound our analyses of primary interest, those variables shared by older and younger participants were analyzed using a 2 (age group) x 3 (alcohol dose group) ANOVA (PROC GLM). Significant differences were then followed up by Pearson correlations between specific spectral power bands of interest (PAP and FTP) and the shared demographic variables. Age group specific

demographic variables were analyzed using one-way ANOVA (alcohol dose group). As a conservative approach to identify potential differences in demographic characteristics between age and dose groups, corrections for type I error were not applied.

Separate 2 (age group) x 3 (dose group) x 2 (repeated: working memory task condition) mixed models analyses with random effects (subjects) were used to examine PAP and FTP (PROC MIXED). Although not a primary focus of the current analysis, we were interested in potential main and interactive effects of condition (i.e., ‘remember faces’ vs. ‘remember scenes’) on PAP and FTP. Condition effects were inconsistently detected behaviorally in our previous work (Boissoneault et al., 2014). Inclusion of task condition in the model allowed us to determine whether they may modulate effects of alcohol dose or age group on the neurophysiological correlates of working memory maintenance. Age was treated as a dichotomous factor because individuals between the ages of 35 and 54 were not recruited within the parameters of the larger parent study. Relevant between-group comparisons (i.e., dose effects within age groups) were pre-planned. Extraneous comparisons (e.g. age effects at each working memory task condition) were excluded in order to minimize type I error. Additional type I corrections were not applied. Although not the primary focus of this investigation, potential main and interactive effects of sex were explored using 2 (age group) X 3 (dose group) x 2 (sex) general linear models (GLM). Finally, we explored the relationship between spectral power during the 9-second delay period and previously reported working memory task performance efficiency measures (Boissoneault et al., 2014) using mixed models analysis with random effects (subjects) and type of trial (i.e., correct rejections vs. hits) including the main effect of PAP, and interactions of PAP with dose group, age group, and the three-way combination as factors. Where significant interactions of PAP with age and/or dose group were noted, further mixed models analyses were conducted to decompose them. Effect sizes are reported as Cohen’s f^2 , Cohen’s d , or Pearson’s r as appropriate. A Cohen’s f^2 variant reflecting the unique variance accounted for by each factor of interest (i.e., age group, dose, and their interaction) was utilized (see Selya et al., 2012).

RESULTS

Participant Characteristics

Eighty-one percent of participants identified as White, 10% identified as Hispanic, 4% identified as African American, and 5% identified as either another race or multiple races. Means of demographic, affective, and alcohol use-related variables by age group and dose assignment are presented in Table 1.

There was a significant main effect for years of education such that younger adults had more years of education than older adults ($F_{1,114} = 4.12$, $p = .04$; $d = .38$). Years of education were not significantly associated with posterior alpha power or frontal theta power for younger or older adults ($r_s < .21$; $p_s > .08$). No age group x dose interaction was detected ($p = 0.53$; $f^2 = 0.01$). Older adults were more anxious than younger adults ($F_{1,114} = 14.86$, $p = .0002$; $d = .69$). However, anxiety scores did not appear to be associated with FTP for either age group ($r_s < .12$, $p_s > .39$). A small negative correlation between anxiety and PAP was detected for younger ($r = -.27$, $p = .02$) but not older adults ($r = -.005$, $p > .97$). No age group x dose interaction was detected ($p = 0.69$; $f^2 = .006$). Critically, no participant’s anxiety level

indicated significant distress. Among older adults, there was no apparent effect of dose group on GDS scores ($F_{2,38} = 1.12, p = .34; \eta^2 = .06$). Similarly, no differences were detected between dose group for BDI-II scores in younger adults ($F_{2,67} = 1.74, p = .18; \eta^2 = .05$). Depressive symptomatology was within normal limits for all participants. Finally, no main effect of age group or dose group, nor an age group X dose interaction was found for QFI ($ps > .09; \eta^2 < .04$). Taken together, these results indicate it is unlikely that bias in group assignment confounded results of interest.

Breath alcohol concentration measures and subjective intoxication

BrACs achieved in each age group and active dose condition are shown in Figure 3. Two (age group) x 2 (active dose level: .04 g/dl and .065 g/dl) ANOVA revealed significant differences between the two active dose levels at each time point ($F_{1,76} > 44, ps < .0001, d > 1.55$). No significant differences in BrAC between older and younger participants were noted at any point in either active dose group (all $ps > .32; d < .44$). In addition, although expected dose effects were detected for subjective intoxication measures ($ps < .0001; \eta^2 > .34$), no significant age effects or age x alcohol dose interactions were noted ($ps > .46; \eta^2 < .03$). Correlation analyses conducted across age groups for each dose level indicated subjective intoxication measures did not correlate significantly with PAP or FTP ($r < .19, ps > .24$).

FTP During Working Memory Maintenance

Mixed models did not detect significant main or interaction effects for frontal theta spectral power (FTP; $ps > .10; \eta^2 < .03$; Figure 4). In addition, no main or interactive effects of sex on FTP were apparent ($\eta^2 < .04, ps > .10$).

PAP During Working Memory Maintenance

Mixed models for posterior alpha spectral power (PAP) revealed a significant main effect of age group ($F_{1,115} = 13.32, p = 0.0004$), as well as a significant age group x dose interaction ($F_{2,115} = 7.75, p = .0007; \eta^2 = .07$). As predicted, younger participants had higher PAP than older participants ($M_{\text{younger}} = 3.82$ (3.63) dB vs. $M_{\text{older}} = 2.14$ (3.31) dB; $d = .48$). Planned comparisons following the significant Age Group x Dose interaction revealed that for younger participants PAP was higher in the .04 ($M_{0.04} = 4.79$ (3.68) dB) and 0.065 ($M_{0.065} = 4.19$ (3.05) dB) g/dl dose groups versus those younger participants who received placebo ($M_{\text{placebo}} = 2.49$ (3.79) dB; $t_{115} = 3.24, p = .002, d = .68$ and $t_{115} = 2.29, p = .02, d = .56$, respectively). For older participants, PAP was lower in the .04 g/dl dose group ($M_{0.04} = 0.93$ (2.68) dB) versus older participants who received placebo ($M_{\text{placebo}} = 2.96$ (2.72); $t_{115} = 2.42, p = .02; d = .75$) or the .065 g/dL dose ($M_{0.065} = 2.51$ (4.34) dB), although the latter comparison did not achieve significance ($t_{115} = 1.81, p = .07; d = .44$). Comparing between groups, PAP was significantly lower in older versus younger participants at the .04 g/dl dose level ($t_{115} = 4.94, p < .0001; d = 1.20$) and the .065 g/dl dose level ($t_{115} = 1.98, p = .05; d = .45$). No difference was detected between older versus younger participants at the placebo dose level ($p > .54; d = .14$). No other main effects or interaction effects were detected for PAP in mixed linear models analysis ($ps > .35$). These effects are illustrated in Figure 5. Finally, no main or interactive effects of sex on PAP were apparent ($\eta^2 < .017, ps > .39$).

Spectral Power and Task Performance Correlations

Mixed models analysis indicated a significant interaction of PAP with dose group ($F_{1,114} = 25.05$, $p < .0001$; $f^2 = .14$) such that lower PAP was associated with better working memory efficiency for older ($F_{1,49} = 11.28$, $p = .002$; $f^2 = .11$, $r = -.33$), but not younger adults ($F_{1,68} = .21$, $p > .64$; $f^2 = .002$, $r = -.05$). This effect is illustrated in Figure 6. A significant three-way interaction of PAP with age group and dose group ($F_{2,114} = 3.78$, $p = .03$; $f^2 = .03$) was also noted. The main effect of PAP and its interaction with dose group did not achieve significance ($ps > .07$; $f^2 < .02$). Characterization of the three-way interaction indicated the dose group X PAP interaction was significant for older adults ($F_{3,47} = 5.49$, $p = .003$; $f^2 = .16$). However, this interaction was not significant for younger adults ($F_{2,66} = 1.62$, $p > .16$; $f^2 = .03$). Examination of the association between PAP and working memory efficiency by dose level for older adults indicated no significant effects at the placebo ($F_{1,16} = .45$, $p > .51$; $f^2 = .01$, $r = -.10$) or .04 g/dL dose levels ($F_{1,16} = .44$, $p > .51$; $f^2 = .01$, $r = -.10$). However, lower PAP was a significant predictor of better working memory efficiency at the .065 g/dL dose level ($F_{1,13} = 16.57$, $p = .001$; $f^2 = .36$, $r = -.60$). These effects are illustrated in Figure 7.

In order to better characterize the relationship between PAP and working memory efficiency for older adults in the .065 g/dL dose group, additional mixed models *examining* the association between PAP and the measures composing efficiency (i.e., accuracy and reaction time) were constructed. Results indicated lower PAP was a significant predictor of shorter reaction time ($F_{1,13} = 23.19$, $p = .0003$; $f^2 = .44$; $r = .66$), but not accuracy ($F_{1,13} = 3.35$, $p = .09$; $f^2 = .11$; $r = -.33$).

DISCUSSION

These data provide important evidence of older adults' increased susceptibility to the neurobehavioral effects of acute moderate alcohol consumption as reflected by the electrophysiological correlates of working memory function. Consistent with previous literature (e.g., Dias et al., 2015), older adults exhibited roughly half the PAP of younger adults during task performance. Furthermore, the apparent lack of main and interactive effects of task condition was consistent with analyses of behavioral data in our previous report, which indicated isolated effects on working memory efficiency (Boissoneault et al., 2014). Of greater interest the current study, we detected a differential effect of acute alcohol administration on PAP. Compared to placebo, the .04 g/dL dose level was associated with increased PAP in younger adults and decreased PAP in older adults. Increased PAP in younger adults following acute moderate alcohol administration of approximately the same magnitude observed in this study (i.e., an approximate doubling) has been previously observed during wakeful rest (Ehlers et al., 1989). Furthermore, while PAP was equivalent between older and younger adults at placebo, PAP was significantly lower in older adults in both the 0.04 and 0.065 g/dL dose levels. Interestingly, mixed models analysis indicated PAP during the working memory maintenance period was not significantly associated with behavioral efficiency for young adults at any dose level. However, lower PAP was associated with higher efficiency in older adults across dose groups, an effect apparently driven by statistically large correlations at the .065 g/dL dose level.

Given equivalent task demands, elevated PAP is thought to be involved in the inhibition of attention to irrelevant stimuli, while decreases represent enhancement of attention towards an object or location in the visual field. In the context of working memory maintenance, PAP increases may represent “protection” of an internal representation from interference through inhibition of ongoing visual input (Wang et al., 2016). Thus, lower PAP should theoretically be associated with poorer performance during working memory maintenance. It may be considered counterintuitive that lower PAP might be associated with higher efficiency for older adults at the .065 g/dL dose level, but not the .04 g/dL or placebo levels. The design of the current study does not permit concrete conclusions regarding mechanisms underlying this relationship. However, the results of exploratory mixed models analysis examining the relationship between PAP and working memory performance lead us to speculate regarding several possibilities.

First, this relationship may reflect a compensatory shift in strategy in older adults at the 0.065 g/dL dose level. By prioritizing visual focus on the fixation cross during the working memory maintenance period in anticipation of the probe image, these subjects might optimize behavioral efficiency by reducing reaction time. Vigilance or attention toward external stimuli is associated with reductions in PAP (Wang et al., 2016). Thus, the possibility that older individuals may be shifting attentional strategy (i.e., re-allocating cognitive resources in anticipation of the probe stimulus) to compensate for the higher alcohol dose is supported by the observation that lower PAP was associated with faster reaction times among this group. This effect is consistent with previously documented efficiency decrements in older adults following acute moderate alcohol administration during a covert attention task (Sklar et al., 2012). Indeed, as noted in our earlier report, working memory efficiency was significantly impaired in older adults relative to placebo only at the 0.065 g/dL dose level (Boissoneault et al., 2014), consistent with an age-related compensatory response.

It is also possible that the .065 g/dL dose level met or exceeded a threshold past which a subset of older adults experienced a failure of inhibitory processes such that greater PAP was required to maintain working memory performance at the expense of vigilance for the probe stimulus. Alternatively, the .065 g/dL dose may have made this subgroup of older adults more cautious in their responding. In either case, prolonged reaction times might be expected relative to a less-affected subgroup. The mechanism(s) underlying the relationship between PAP and working memory performance may be better characterized in future studies employing eye tracking technology and manipulating task parameters like difficulty as well as costs inherent in speed/accuracy tradeoffs (i.e., a signal detection theory-based approach).

It is notable that, in contrast to our hypotheses and previous literature, FTP was apparently insensitive to the main and interactive effects of alcohol during working memory maintenance in this study. Although the reasons for this is unclear, studies of the effects of acute moderate alcohol on FTP have been inconsistent with directionality of effects depending on dose and task. Indeed, both FTP decreases (Boha et al., 2009) and increases (Stenberg et al., 1994) during mental arithmetic performance have been observed. Given that FTP has been theorized to reflect mental effort, a possible explanation for the null results in

this study is that the working memory task we employed was insufficiently difficult to challenge participants to the point of needing to recruit additional cognitive resources to the task. Use of a more difficult task in future studies may make acute alcohol effects on FTP more apparent. This interpretation is supported by recent evidence indicating suppression of theta power following alcohol consumption occurred only during the more difficult of two Simon tasks (Rosen et al., 2016).

Study Strengths and Limitations

To our knowledge, this study represents the first demonstration of older adults' increased susceptibility to the impairing effects of acute moderate alcohol administration on the neural correlates of a critical higher cognitive function: working memory maintenance. In turn, the significant correlation between PAP and working memory efficiency in older adults at the higher, yet still sub-intoxicating, dose level provides further evidence that studies of the spectral composition of the EEG during task performance can improve understanding of the neurophysiological underpinnings of acute moderate alcohol's effects in older adults.

Despite these strengths, this study is necessarily limited by its cross-sectional design; replication of these results by future studies using a within-subjects (i.e., repeated measures) design would substantially strengthen conclusions. In addition, while consistent with typical standards for laboratory studies of electrophysiology and neurocognition, the carefully controlled environment in which participants were assessed does not reflect potentially distracting environments where moderate drinking typically occurs. The presence of these additional sensory distractions and/or multi-tasking may significantly alter the profile of the main and interactive effects of acute moderate alcohol use on working memory maintenance, its electrophysiological correlates, and the directionality/magnitude of their relationship. Finally, use of eye-tracking technology in future studies would allow confirmation of participants' focus on cue stimuli and the fixation cross during working memory maintenance, eliminating lack of task engagement as a potential confound.

Conclusions

This study bolsters the small but growing body of evidence that older adults exhibit differential sensitivity to the neurobehavioral effects of doses of alcohol consistent with moderate social use (for review, see Boissoneault et al., 2016). Specifically, results suggest older adults at sub-intoxicating BACs have shifts in PAP during working memory maintenance consistent with lower efficiency, with lower PAP (indicating increased focus on an object or representation in the visual field) correlating with decreased reaction time. Given that effective working memory is dependent on top-down processing, including attentional control, it appears that older adults may engage lower degrees of neurophysiological inhibition in an effort to avoid compromises in behavioral performance. Taken together, these findings shed light on the attentional mechanisms underlying previously reported effects of acute moderate alcohol administration on working memory efficiency in older adults (Boissoneault et al., 2014).

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Figure 1. Diagram depicting the working memory task (Gazzaley et al., 2005). Underlines indicate which images Ss were instructed to remember within a stimulus block. Cue stimuli were presented within trials in pseudo-random order. Following the delay period, participants were asked to indicate whether the probe stimulus was present in the original set of cue stimuli. Reprinted by permission from Macmillan Publishers Ltd: Nature Neuroscience (Gazzaley et al., 2005), copyright 2005.

Figure 2.
Map of electrodes contributing to measures of mean theta and alpha spectral power.

Figure 3.

Breath alcohol concentrations (BrACs) achieved by age and dose group. As expected, mean BrACs were higher in the 0.065 than 0.04 g/dL dose group ($F_{1,76} > 44$, $p < .0001$). No differences in BrAC between older and younger participants were noted at any point ($ps > .20$).

Figure 4.

Bar chart depicting FTP by age group and dose. No main or interactive effects were observed ($p > .10$).

Figure 5.

Bar chart depicting the significant age group by alcohol dose interaction on PAP ($F_{2,115}=7.75$, $p=.0007$). For younger adults, PAP was higher in the .04 g/dl dose group than the placebo ($t_{115} = 3.24$, $p = .002$) and .065 g/dL dose groups ($t_{115}=2.29$, $p = .02$). For older adults, PAP was lower in the .04 g/dl dose group than those who received placebo ($t_{115} = 2.42$, $p = 0.02$) or the .065 g/dL dose, although the latter effect did not achieve significance ($t_{115} = 1.81$, $p=.07$). In addition, PAP was significantly lower in older versus younger participants at the .04 g/dl dose level ($t_{115} = 4.94$, $p < .0001$) and the .065 g/dl dose level ($t_{119} = 1.98$, $p = 0.05$). Error bars reflect standard deviation.

Figure 6.

Scatterplot illustrating the correlation between PAP and working memory efficiency for older ($r = -.33$; dashed line) and younger adults ($r = -.05$; solid line) across dose levels.

Figure 7.

Scatter plot illustrating the correlation between PAP and working memory efficiency in older adults at the placebo ($r = -.10$; dotted line), .04 g/dL ($r = -.10$; solid line) 0.065 g/dL dose levels ($r = -.60$; dashed line).

Table 1

Participant Characteristics

	Younger Ss.		Older Ss.	
	Placebo n = 25 Mean (SD)	04 g/dl n = 24 Mean (SD)	Placebo n = 18 Mean (SD)	04 g/dl n = 18 Mean (SD)
Age *	27.48 (2.4)	28.00 (2.89)	61.83 (4.38)	60.76 (3.91)
Education	16.80 (1.15)	16.83 (1.09)	16.22 (1.77)	15.94 (1.47)
Female %	64	50	61.11	50
BDI-II/GDS	2.08 (2.55)	2.46 (3.56)	2.8 (2.37)	1.63 (2.02)
STAI *	39.64 (4.95)	40.54 (4.39)	42.61 (5.48)	44.82 (7.49)
QFI	0.32 (0.19)	0.38 (0.25)	0.47 (0.36)	0.33 (0.38)
Pre-WM Subjective Intoxication	1.95 (1.13)	3.96 (1.63)	2.59 (2.03)	4.12 (1.58)
Post-WM Subjective Intoxication	1.68 (1.21)	3.26 (1.57)	2.47 (2.18)	3.29 (1.90)

* Significant differences between older and younger participants ($p < .01$).