Stress and alcohol: A toxic combination for the teenage brain

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Abstract

Young adult university students frequently binge on alcohol and have high stress levels. Based on findings in rodents, we predicted that heavy current alcohol use and elevated and depression scores would be associated with deficits on high interference memory tasks, while early onset, prolonged binge patterns would lead to broader cognitive deficits on tests of associative encoding and executive functions. We developed the Concentration Memory Task, a novel computerized version of the Concentration card game with a high degree of interference. We found that young adults with elevated depression and alcohol consumption scores were impaired in the Concentration Memory Task, when tested on which location each object was seen in the most recent game. We also analyzed data from a previous study, and found that higher alcohol consumption scores were associated with impaired performance on another high interference memory task, based on Kirwan and Stark's Mnemonic Similarity Test. On the other hand, adolescent onset of binge drinking predicted poorer performance on a more systematic test of spatial recognition memory, and on an associative learning task. Our results are broadly consistent with findings in rodents that acute alcohol and stress exposure suppress neurogenesis in the adult hippocampus, which in turn impairs performance in high interference memory tasks, while adolescent onset binge drinking causes more extensive brain damage and cognitive deficits.

Keywords: Stress, Depression, Alcohol, Binge drinking, memory interference, neurogenesis

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1. Introduction

The vast majority of psychological studies are conducted on university undergraduates [1]. While this may limit the generality of such findings [1], in other respects undergraduates are assumed, by many, to be an ideal participant pool: a homogeneous group of high-functioning, and physically and mentally healthy young adults. However, these assumptions may be called into question, considering the high levels of binge drinking, chronic stress and depression in the undergraduate population. In our own studies involving hundreds of undergraduates over the past 10 years, we find that 25-30% score in the mild to severe range on the Beck Depression Inventory II, and engage in regular binge drinking (where a binge is defined by the National Institute on Alcohol Abuse and Alcoholism to be 4 drinks per 2 hours for a female and 5 drinks per 2 hours for a male); similar binge levels have been reported in the literature for this population [e.g. 2]. Worldwide, rates of binge drinking and dangerous alcohol consumption behaviour are on the rise in adolescents [3, 4, 5]. Given the ongoing brain development that occurs in adolescence to early adulthood [6], it is important to establish the long-term consequences of exposure to binge drinking and stress during this period.

While the neurotoxic effects of chronic, long-term stress, depression and alcohol on the human brain are well established, acute effects have been less studied. Multiple episodes of major depressive disorder and prolonged alcohol abuse both lead to hippocampal / medial temporal lobe volume loss [7, 8, 9, e.g.]; long-term alcohol exposure also affects other brain regions including the prefrontal cortex and fronto-striatal reward circuits [10, 11]. The effects of prolonged heavy drinking are even more pronounced in the adolescent brain [12]. Although less is known about the acute effects on the human brain, there is evidence that periodic binge drinking in adolescence may also cause brain volume loss [13].

In animal models, the acute effects of stress and alcohol exposure have been studied more extensively. In adult rodents, several days of binge alcohol or stress exposure reduces hippocampal neurogenesis [14, 15]. Adolescent animals are especially vulnerable to the effects of binge alcohol exposure on the inhibition of neurogenesis [16]; they also exhibit more widespread brain damage than adult-exposed animals, in regions including the temporal and frontal lobes [17, 18]. Based on these findings, we would expect to see parallel effects of acute stress and binge drinking in the human adolescent brain.

Unfortunately, we lack a means of assaying neurogenesis non-invasively in humans. In rodents, the effects of neurogenesis knockdown versus broader hippocampal pathology can be distinguished behaviourally. Knockdown of neurogenesis results in selective impairments on a wide range of high interference memory tasks, whether the interference arises from overlapping stimuli, time delay between learning and retrieval, context effects, or reversal of previously learned responses [19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29]. In contrast, broader hippocampal pathology leads to more general associative encoding deficits [30, 31, 32, 33, 34, 35].

Consistent with findings from rodent studies, in humans with no current or previous psychiatric diagnosis, elevated depression and stress scores are associated with selective impairments on high interference memory tasks including the CANTAB delayed match to sample at long delays [36], Kirwan and Stark's[37] Mnemonic Similarity Task and variants (MST, formerly called the Behavioural Pattern Separation Task) [38, 39, 40], and recognition memory across a 2-week delay [40]. Conversely, exercise is an established up-regulator of neurogenesis in animal models [41] and of neurogenesis biomarkers in rodents and humans [42]; exercise causes improved human performance on an MST-like task [38]. Thus, data from humans and animal models consistently point to a selective role for hippocampal neurogenesis in mitigating memory interference. In contrast, as in rodents, hippocampal damage in humans causes more generalized episodic and associative memory deficits [43, 44, 45, 46]. Based on the above findings, in the two experiments reported here, we sought to investigate the relationship between binge alcohol patterns, depression and memory performance in university students. We hypothesized that high current alcohol binge and depression levels would be associated with selective deficits on high interference memory tasks, while early onset binge drinking would cause broader deficits in memory and executive functions.

2. Experiment 1.

We administered a battery of cognitive tests, stress and depression inventories and a lifestyle questionnaire to healthy undergraduate participants. The lifestyle questionnaire included questions about recent and remote drinking patterns. The cognitive battery included a paired associate learning task, a visual reverse digit span test, and a novel high interference test of spatial memory, the Concentration Memory Task. We also analyzed data from a

previous study, parts of which had been published [38], to assess the effects of recent binge drinking on another high interference memory test.

2.1. Methods

Participants were brought into a quiet testing room and seated at a desk in front of a touchscreen computer. After reading the letter of information and providing written consent, they completed computerized versions of the Beck Depression Inventory (BDI), Cohen's Perceived Stress Scale (PSS), and a lifestyle questionnaire developed by our lab. Next, they performed the three memory tests detailed below: a CANTAB-like paired associates learning task, a reverse digit span task, and the Concentration Memory Task.

2.1.1. Participants

We recruited 73 McMaster University students through online recruitment programs used by McMaster University ("www.experimetrix.com/mac" and "http://mcmaster.sona-systems.com"). Participants were enrolled in an Introductory Psychology course and received course credit for their participation. All participants had normal or corrected to normal vision and no history or previous diagnosis of major depression or other psychiatric disorders. The McMaster Research Ethics Board (MREB) approved all aspects of our study.

2.1.2. Questionnaires

To assess stress, depression, and alcohol consumption levels, we administered Cohen's Perceived Stress Scale, the Beck Depression Inventory-II (BDI) (Psychological Corporation) and our own lifestyle questionnaire. The BDI is a widely used, standardized, commercially available test consisting of 21 multiple-choice questions, each on a 4-point scale, about the individual's mood during the past week. We have used our lifestyle questionnaire in several previous studies; it probes a number of different variables. The key measures of alcohol consumption included in the analyses reported here were number of drinks consumed on a typical drinking occasion (typical alcohol consumption) and a series of questions probing frequency of binge drinking at ages 13-22. A binge is defined by the United States National Institute on Alcohol Abuse and Alcoholism to be 4 drinks per 2 hours for a female and 5 drinks per 2 hours for a male.

2.1.3. Paired Associate Learning test

Participants completed a paired associates learning task (PAL) similar to the CANTAB PAL, but implemented in e-prime. The CANTAB PAL is a widely used visuo-spatial associative learning task that was predicted to be sensitive to major hippocampal pathology. However, as it lacks a high-interference component, it was not hypothesized to be sensitive to acute levels of binge drinking or depression. Indeed, we have shown previously that performance on this task does not vary as a function of BDI score [47, 38]. The task involves the presentation of a series of patterns that are unique in shape and colour. The PAL task is designed to assess learning and memory of object-place associations. During a study trial, six white boxes are distributed around the screen and are opened, one at a time, in a random order to reveal a concealed pattern. Once all of the white boxes have revealed what was concealed behind them, a test trial begins. In a test trial, patterns are presented one at a time in the middle of the screen with the white boxes still distributed around the screen as in the study trial. The participant must select the white box where the pattern was originally located in the study trial. If an error is made, the participant is allowed to finish the test trial before the patterns are presented again to remind the participant of their locations. The test becomes progressively more difficult by increasing the number of patterns hidden behind the white boxes on a particular study trial.

2.1.4. Reverse Digit Span Task

To assess working memory, we administered a computerized visual reverse digit span task, implemented in e-prime, . Participants are shown a random series of digits, one digit at a time, at a rate of one second per digit, and are required to remember this series and then input the digits in reverse order using a keyboard. The length of the digit string gets progressively longer.

2.1.5. Concentration Memory Task

The Concentration Memory Task (CMT), illustrated in Figure 1,is a computerized version of the Concentration card game. Participants play multiple games of the CMT interleaved with spatial memory tests. The memory tests require selecting the location where each card appeared in the most recent game. Repetition of the same cards in different locations across games creates proactive interference.

In each game of CMT, using a touchscreen computer, participants perform an exhaustive search through a grid of 16 face down playing cards to find matching image pairs. After completion of Game 1, three more challenging games are played in which some images from the previous game are repeated at new locations. These repeated images appear in a total of 4 different locations within 2 consecutive games. After each game, participants complete a 2-alternative forced choice (2-AFC) test of their spatial memory. On each trial of the 2-AFC test, an image appears simultaneously in two locations; their task is to indicate in which of they two locations they saw the image most recently, with 1 image having been presented in the most recent game and the other presented in the game immediately prior. Optimal performance on this task requires the avoidance of interference from multiple similar memory representations, requiring the participant to segregate the memories of identical objects experienced in more than one location. We predict that the high potential for memory interference associated with multiple object presentations places a high demand on neurogenesis, consistent with the rodent literature [20, 25, 24, 19, 29]. Participants played a total of 4 games for a total of 32 image pair searches (8 per game) and completed three, 2-alternative forced choice tasks appearing after games 2, 3 and 4. Each 2-AFC spatial memory test included 4 trials for a total of 12 2-AFC trials. It was predicted that those with elevated depression and alcohol consumption scores would have suppressed neurogenesis and exhibit selective performance deficits on the neurogenesis sensitive CMT while maintaining normal performance on the two control tasks predicted to be neurogenesis-independent.

2.2. Results

All statistical analyses were performed using SPSS version 18 (SPSS Inc.). Outlier detection was used [48] to identify participants that may have misunderstood the instructions or did not attend to the main task, the CMT. On this basis, one person's data were removed, resulting in 72 participants' data included in the final analysis (26 males, 46 females; mean age=18.6 years, SD=1.43).

To obtain an estimate of high interference memory performance, percent correct on the CMT 2-AFC was analyzed as a function of depression, stress and drinking scores. During the 2-AFC task, participants were required to select the location where they had seen each image most recently. This proved to be relatively difficult, as evidenced by mean performance of

71.1% (SD=15.1%). Correlation analyses revealed significant, negative relationships between performance on the CMT and both measures of mood including BDI (r_s(72)=-.308, p=.008) and PSS (r(71)=-.356, p=.002) as well as typical alcohol consumption (r_s(52)=-.280, p=.04). Confidence intervals for the bootstrapped correlations can be found in Table 1. Thus, individuals who scored higher on scales of depression, stress and typical alcohol consumption tended to score more poorly on the 2-AFC, a high interference memory test.

Variable	Correlation	p-value (two-tailed)	95% CI
BDI	-.308	.008	[-.595, -.036]
PSS	-.356	.002	[-.584, -.068]
Alcohol Consumption	-.280	.04	[-.451, -.120]

Table 1: Spearmans's rank correlation coefficient used for correlation analysis involving BDI and alcohol consumption scores as they did not follow a normal distribution. Pearson product-moment correlation coefficient used for correlation analysis involving normally distributed PSS scores.

As a means of assessing the reliability of the 2-AFC task, split-half reliability was used. The trials were split into odd and even trial groups. There was a significant positive correlation between performance on the even and odd trials (r(72)=.409, $p < .001$). This reliability estimate was then adjusted for full test length using the Spearman-Brown prediction formula resulting in a predicted reliability (P^*xx') of 0.581.

To further examine the relationship between stress, depression, alcohol consumption and CMT performance, we separated individuals into those scoring either low or high on the BDI, PSS and recent alcohol scores based on median splits on each of these three variables. Significant group differences in percent correct on the CMT were found between the above-median (M=66.7%, SD=15.8%) and below-median (M=75.2%, SD=13.4%) BDI groups using an independent samples t-test (t(70)=2.439,p=.02). Cohen's effect size value (d=.58) suggests a moderate to high effect of depression on performance. Significant group differences in percent correct on the CMT were also found between above-median (M=67.8%, SD=11.2%) and below-median (M=77.1%, SD=14.3%) alcohol consumption groups (t(50)=2.476, p=.02). Cohen's effect size value (d=.7) suggested a moderate to high effect of alcohol on performance. These median split results for BDI and alcohol

consumption are shown in Figure 2.2. Group differences in percent correct on the CMT between above-median (M=67.6%, SD=16.1%) and below-median (M=74.5%, SD=13.6%) PSS groups were close to significance as well (t(69)=1.957, p=.05). Again, Cohen's effect size value (d=.47) suggested a moderate effect of stress on performance.

No significant group differences were found between above and below-median BDI groups on either the PAL (t(69)=-.670, p=.505) or reverse digit span task (t(68)=-.114, p=.910). The same is true of above and below-median PSS groups (t(69)=-1.479, p=.144; t(68)=-.195, p=.846) as well as above and below-median alcohol consumption groups (t(50)=.845, p=.402; t(50)=1.047, p=.300) on paired associate learning and reverse digit span respectively.

Linear regression was used to identify variables that would best predict performance on the CMT. Variables were entered into a regression model using SPSS. The model that accounted for the greatest amount of variance in CMT performance was that which included both BDI (Beta=-.397, p=.003) and typical alcohol consumption (Beta=-.274, p=.033) and accounted for 20.7% (adjusted r-squared=.207) of observed variance in CMT performance (F(2,49)=7.655, p=.001). PSS accounted for little variance after BDI. The lower degrees of freedom in this model are due to there being fewer individuals in the sample who reported drinking alcohol (50) compared to the total number of individuals in the sample (72).

In a previously published study [38], we also found a negative relationship between stress and depression scores and performance on another high interference memory task, a version of Kirwan and Stark's Mnemonic Similarity Task [37]. The MST requires participants to study a set of images of distinctive everyday objects, and then perform a 3-alternative recognition memory task in which test items are judged to be "old" (if they are identical to a previously studied item), "similar" to a previously studied item, or "new". The similar lures create a high degree of interference on this task. In that study we also collected data, previously unpublished, using an earlier version of our lifestyle questionnaire which included questions about recent alcohol consumption. We therefore analyzed MST performance on old versus similar items, as well as performance on the "most similar" versus "least similar" of the similar items, as in our previous study [38]. While median split analyses on MST performance of participants with below- versus above-median alcohol consumption scores revealed no significant differences, there was a significant negative correlation between performance on the most similar lures

[bias corrected, as per 38] and participants' typical alcohol consumption levels (Pearson's r = -.215, df = 100, p ¡ .05 two-tailed).

2.3. Discussion

Taken together, our findings in experiment 1 with the Concentration Memory Task (CMT), and our analysis of unpublished data from our previous study with the Mnemonic Similarity Task (MST), are consistent with the hypothesis that performance on high interference memory tests is particularly sensitive to the effects of recent depression and drinking levels. Our failure to observe significant differences in PAL or digit span based on above- versus below-median stress, depression or alcohol consumption scores suggests that participants in this study did not exhibit broader hippocampal or prefrontal pathology that could have accounted for the impairments on the CMT. However, it is possible that with a larger sample including more participants who had higher binge alcohol rates or earlier onset binge drinking, PAL or digit span performance may have been affected also.

Our two high interference tasks, MST and CMT, have different sources of interference. The MST creates interference by testing recognition memory for objects using highly visually overlapping lures, while the CMT creates interference by testing object location memory for identifical copies of the same object when it has appeared in more than one location. However, the CMT did not tax spatial memory at a fine level of detail.

3. Experiment 2.

To assess the impacts of alcohol and depression on spatial recognition memory more systematically, at varying spatial separations, we developed the Spatial Separation Recognition Task. We hypothesized that performance at the finest spatial separations would depend upon high fidelity encoding mechanisms in the hippocampus and would be most vulnerable to the acute effects of stress and alcohol. On the other hand, performance at coarser separations may tax hippocampal coding mechanisms more broadly, and would be impacted by more prolonged or early onset binge drinking. A second goal of our second experiment was to collect data from a larger sample of participants, to more fully assess different aspects of drinking (e.g. early versus late onset) high interference tasks versus more general associative encoding (PAL) and working memory (reverse digit span).

3.1. Methods

We recruited 125 participants in the same manner as in Experiment 1. Participants completed the Spatial Separation Recognition Task (SSRT), detailed below. Participants also completed the BDI-II, our lifestyle questionnaire, and the visual reverse digit span and CANTAB-like PAL tasks as in Experiment 1.

3.1.1. The Spatial Separation Recognition Task

The SSRT is illustrated in Figure 3. During the presentation phase, participants view images of objects, the locations of which vary along the horizontal axis of the computer screen while the vertical axis is held constant at 50 percent of the screen. During the testing phase, participants are shown the same images, one at a time, in either the exact same location as the presentation trial or a different location. The "different" trials are divided into 4 groups consisting of 5 separation each which ranged from 1-20% of the screen. Separations 16-20% were grouped as the large-, 11-15% as the moderate-, 6-10% as the medium-, and 1-5% as the low-separation conditions, each with varying potential for memory interference. Despite being labelled as the high separation trials (therefore trials with relatively weakest potential for interference), the 16-20% trials are still challenging and have a high potential for interference. It is only relative to the low separation trials that these trials are characterized as low-interference. Participants respond by pressing the 1-key if the image is in the same location or the 2-key if the image is in a different location. Optimal performance on this task requires the participant to create distinct memory representations of each image location during the presentation phase so as to avoid interference when presented with the same image during the testing phase. The experiment consists of 24 blocks consisting of 7 presentation and 7 testing trials for a total of 168 trials.

3.2. Results

The same means of outlier detection [48] was used to identify participants that may have misunderstood the instructions on the main task (SSRT, described below), or did not attend to the task. On this basis, five participants' data were removed resulting in 120 participants' data included in the final analyses (33 males, 87 females; mean age=18.8 years, SD=1.64).

As a means of assessing the reliability of the Spatial Separation Recognition Task (SSRT), split-half reliability was used. The separations were

grouped into odd and even groups (2,4,6, etc. & 1,3,5, etc). There was a significant positive correlation between performance on the even and odd trials (r(10)=.743, $p = .014$). This reliability estimate was then adjusted for full test length using the Spearman-Brown prediction formula resulting in a predicted reliability (P^*xx') of 0.853.

A repeated measures analysis of variance (ANOVA) was used to assess the effect of spatial similarity (separation) on SSRT performance. The assumption of sphericity was found to be violated ($\chi^2(209) = 340.823, p < .001$) therefore degrees of freedom were corrected using Huynh-Feldt estimates of sphericity ($\epsilon = .854$). A main effect of spatial separation was found ($F(17.076, 2032.001) = 106.922, p < .001$) as well as a significant linear trend, ($F(1, 119) = 766.23, p < .001$), indicating that as separation increased, performance increased proportionately. Previous work by [38] showed that performance differences on the MST between high and low BDI groups was restricted to visual stimuli pairs that were relatively less similar in terms of their visual characteristics. These findings are similar to those of Stark et al. [49] looking at performance differences between young and aged participants on a spatial pattern separation task. As a result, we expected to find performance differences between individuals with high and low depression scores, particularly on the relatively less similar trials, those with relatively greater separation. Participants were separated into high (BDI above 8, N = 57, M = 16.16) and low (BDI at or below 8, N = 63, M = 4.67) BDI groups using a median split. Levene's test indicated unequal variances ($F = 24.147, p < .001$) so degrees of freedom were adjusted from 118 to 68.539. These groups differed significantly in BDI score, $t(68.539) = -11.045, p < .001$. While raw BDI score was not significantly correlated with performance, the low BDI group (M = 55.3%, SD = 8.27%) was significantly better at identifying the correct location on "different" trials compared to the high BDI group (M = 51.9%, SD = 8.18%), $t(118) = 2.279, p = .024$. This difference was found to be mainly the result of performance on the large separation trials (16-20% shift) where the low BDI group (M = 71.7%, SD = 10.8%) significantly outperformed the high BDI group (M = 66.2%, SD = 12.2%), $t(118) = 2.635, p = .01$. The same performance differences between high and low BDI groups were not found on PAL (t(110) = $-1.655, p = .101$) and digit span tasks ($t(96) = 1.033, p = .304$).

Of the 120 participants, 75 reported binge drinking with some regularity between the age of 13 and 22. Interestingly, typical alcohol consumption

was not found to be correlated with SSRT performance. Instead, the age of onset of reported binge drinking correlated with SSRT performance but only at the large separations ($r(75) = -.31, p < .01$), and not the smaller separations. Age of onset of binge drinking also correlated with performance on PAL ($r(75) = -.24, p < .05$) but not with digit span performance. Linear regression was used to quantify the amount of variance in SSRT performance that could be accounted for by BDI grouping and binge drinking history. These variables were entered into a stepwise regression model. Together, median-split BDI grouping (Beta = -.315, p = .006) and age of onset of binge drinking (Beta = -.316, p = .006) accounted for 16.5% (adjusted $r^2 = .165$) of observed variance in SSRT performance, $F(2, 65) = 7.621, p = .001$.

3.3. Discussion

The findings in experiment 2 with the SSRT were somewhat surprising in light of those in Experiment 1. In contrast to our findings in Experiment 1, performance on this high interference spatial memory test was not related to current drinking levels. Instead, SSRT memory scores were significantly impacted by age of onset of binge drinking. Also, unlike in Experiment 1, in Experiment 2 performance on the paired associate learning task (CANTAB-like PAL) was negatively related to age of binge onset. This pattern of results is consistent with our original hypothesis that many years of binge drinking and/or early onset of binge drinking will have broader impacts on the hippocampus and other brain regions. We did not, however, see an impact of early binge drinking on the reverse digit span that might be indicative of damage to the prefrontal cortex.

There were some important differences in the participant samples in the two experiments that may account for the discrepancies in findings. In Experiment 2 we had a much larger sample of participants, and a much higher proportion of them (about 50%) engaged in binge drinking.

4. General Discussion

It has been reported previously that as many as 44% of college students binge drink every two weeks, while as many as 19% binge more than 3 times per week [2]. In addition to the memory deficits described here, long-term effects of alcohol use during adolescence include increased risk of alcohol dependence, learning deficits, and other memory impairments [50]. Given the

cognitive impacts illustrated here and elsewhere as well as the high prevalence of binge drinking, it is imperative that the risks associated with alcohol consumption become more widely appreciated by youths at an age when they are most impressionable. In this way, it may be possible to reduce the prevalence of this physically and cognitively destructive behaviour. From a research standpoint, it is also important that those dealing with undergraduate populations understand the types of cognitive deficits associated with non-alcoholic adolescents who do tend to binge drink. Researchers may want to screen for drinking behaviour in the future.

A key hypothesis in both of our experiments was that high acute levels of alcohol consumption, stress and depression would lead to selective deficits on high interference memory tasks. This hypothesis was based on past studies, mainly in rodents, indicating that binge drinking and acute stress both potently suppress neurogenesis [14, 15]. While our finidings are consistent with this hypothesis, other explanations cannot be ruled out. A limitation in translating such findings to humans is the lack of a direct measure of neurogenesis. Thus, it is possible that one or more additional variables were affected by stress, depression, or alcohol consumption and that these variables may have caused or influenced the memory deficits observed here. For example, depressive episodes in humans have been shown to be associated with decreased serum levels of brain derived neurotrophic factor (BDNF) [51], a neurotrophin important for plasticity and long-term potentiation [52, 53]. However, given a reduction in BDNF, one might expect to find more widespread learning and memory deficits in domains like working memory and paired associates learning. The results of the current study fail to show such deficits in association with acute drinking, stress and depression levels. Thus, the deficits we observed in Experiment 1 on the CMT are likely not the result of general plasticity changes via BDNF expression. In the future, direct assessment of neurogenesis would be required to dissociate neurogenesis-dependent and -independent effects on memory. On the other hand, the broader memory deficits observed in Experiment 2 on the SSFT and on PAL in association with early onset binge drinking are consistent with broader hippocampal pathology due to early onset drinking.

An important avenue for further research is to determine to what extent the damage caused by early onset binge drinking can be mitigated or reversed. We were hoping to address this question in the present study by comparing those who began binge drinking early and continued this pattern of drinking into their university years to those who began early and then

stopped. Unfortunately, in our sample of university students, there were no participants in the latter group. Perhaps by studying an older more mature sample at mid-life we might find participants who started binge drinking early but gave it up by the time they reached their working years in later adulthood.

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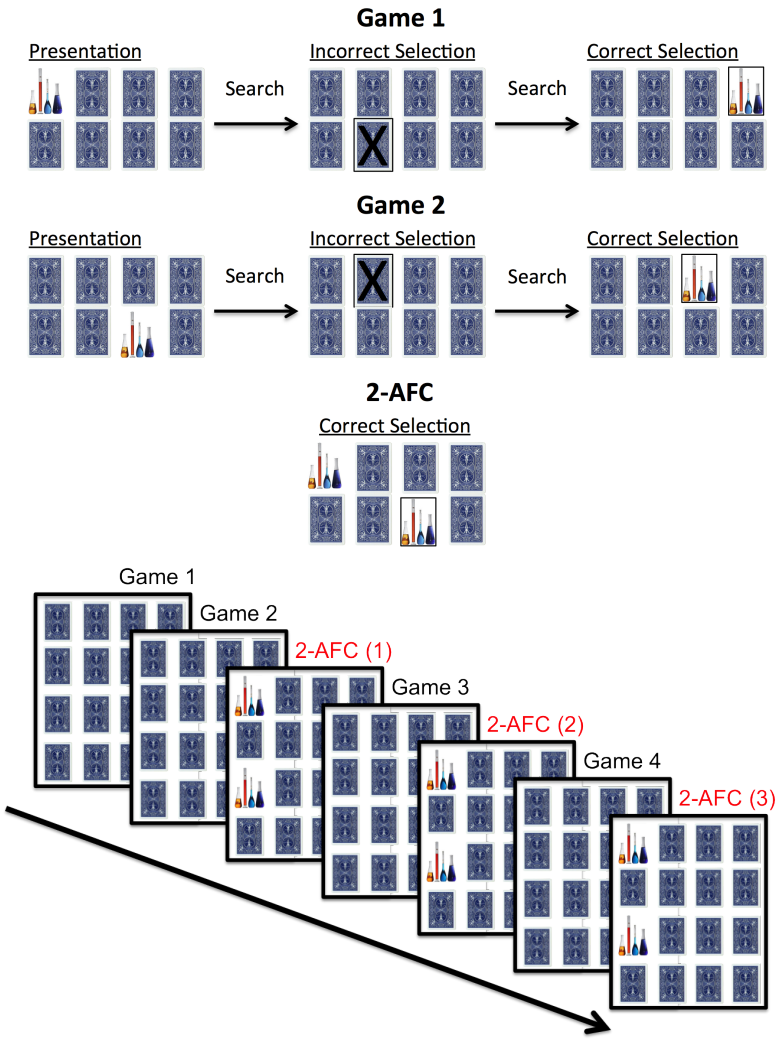


Figure 1: The Concentration Memory Task (CMT). Top row: Progression through several trials in one game of the CMT using a single image as an example. A target is briefly revealed at the start of a trial and then hidden. Participants must search the grid until they find the correct match. Second row: Progression through several trials in game 2. Importantly, some images are repeated between games so that these images are experienced in different spatial locations. Third row: Following completion of two full games participants complete a 2-alternative forced choice task in which they select the location they have experienced an object in most recently. Bottom: Participants complete a total of 4 games in which they search for 8 image pair matches within a 4x4 grid of playing cards. Following games 2, 3 and 4, participants complete 2-alternative forced choice tasks consisting of 4 trials each for a total of 12 trials (Game 1 - Game 2 - 2AFC1 - Game 3 - 2AFC2 - Game 4 - 2AFC3).

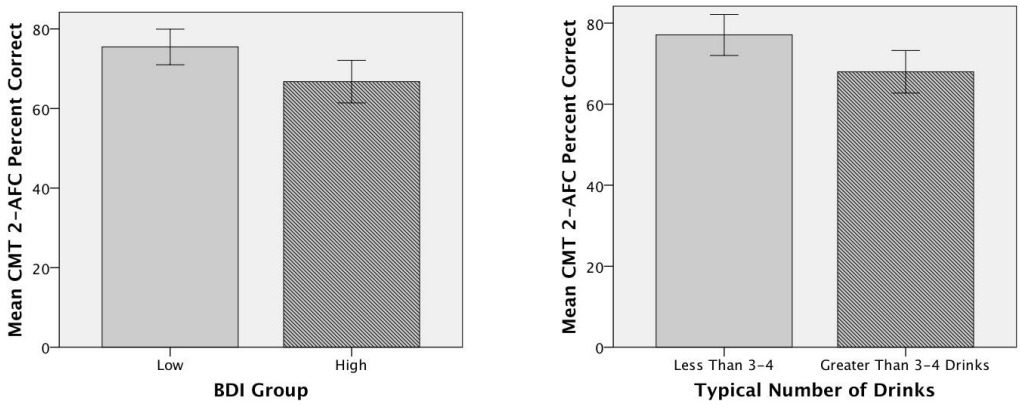


Figure 2: Left: Comparison of CMT performance for those scoring at or below the median on the BDI and those with above median BDI scores. Right: CMT performance of those scoring at or below the median on typical alcohol consumption and those scoring above the median.

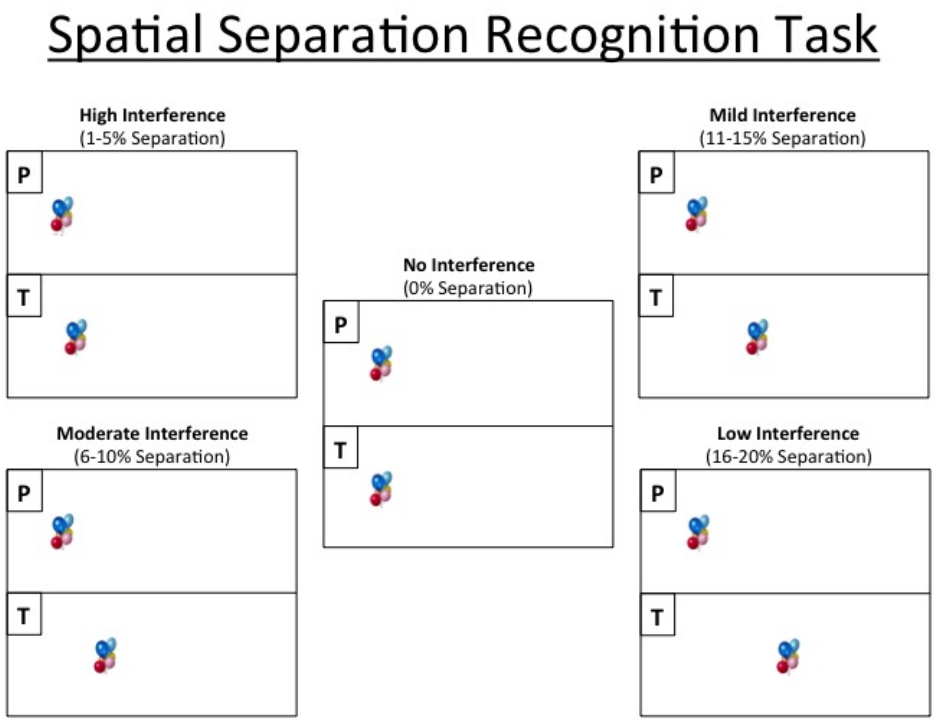
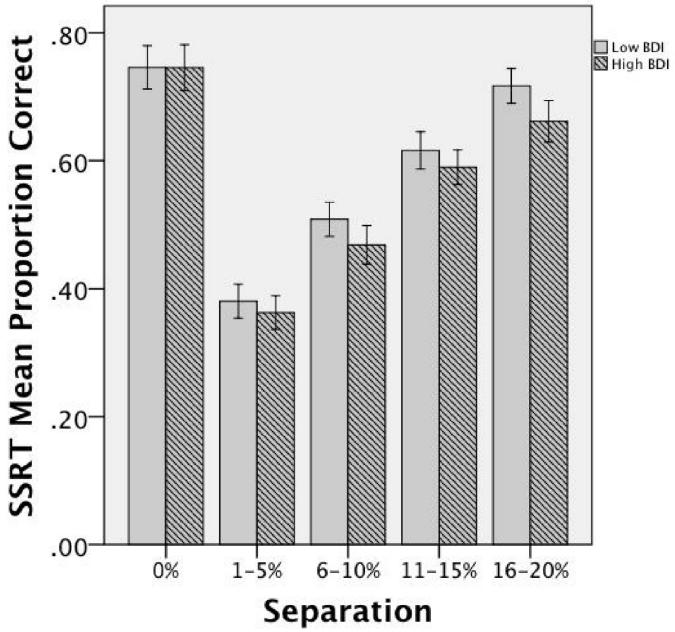


Figure 3: The Spatial Separation Recognition Task (SSRT). The two trial types, **same** (separation of 0%) and **different** (separations of 1-5%, 6-10%, 11-15%, 16-20%), for the Spatial Separation Recognition Task. "**P**" represents the presentation phase. "**T**" represents the test phase.



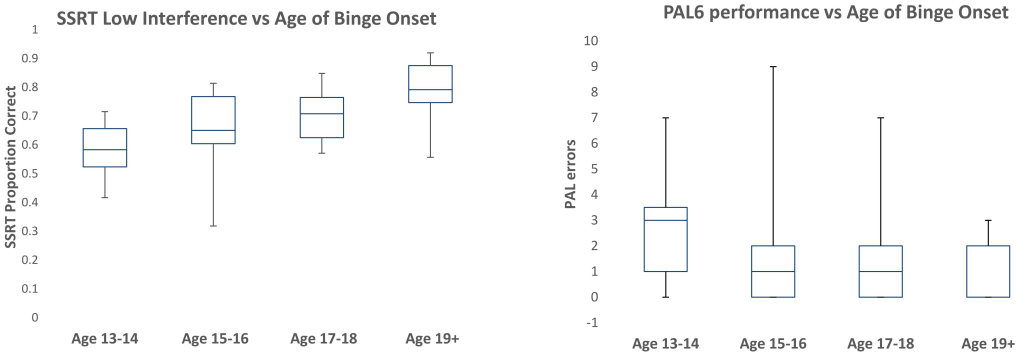


Figure 4: Experiment 2 results. Top: SSRT performance versus spatial separation for those with below- and above-median depression (BDI) scores. Bottom left: Performance on the low interference SSRT trials versus age of onset of binge drinking. Bottom right: Performance on paired associate learning (PAL) versus age of onset of binge drinking.