**Title.** Alcohol use in adolescence and later working memory: findings from a large population-based birth cohort

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**ABSTRACT**

*Aims*. The study aimed to examine the association between adolescent alcohol use and working memory (WM) using a large population sample.

*Methods*. Data from the Avon Longitudinal Study of Parents and Children was used to investigate the association between alcohol use at age 15 years and WM three years later, assessed using the N-back task (N~3,300). A three-category ordinal variable captured mutually exclusive alcohol groupings ranging in order of severity (i.e., low alcohol users, frequent drinkers, and frequent/binge drinkers). Differential dropout was accounted for using multiple imputation and inverse probability weighting. Adjustment was made for potential confounders.

*Results*. There was evidence of an association between frequent/binge drinking (compared to the low alcohol group) and poorer performance on the 3-back task after adjusting for sociodemographic confounding variables, WM at age 11 years, and experience of a head injury/unconsciousness before age 11 years (β=-.23, 95% CI=-.37 to -.09, *p*=.001). However, this association was attenuated (β=-.12, 95% CI=-.27 to .03, *p*=.11) when further adjusted for baseline measures of weekly cigarette tobacco and cannabis use. Weaker associations were found for the less demanding 2-back task. We found no evidence to suggest frequent drinking was associated with performance on either task.

*Conclusions*. We found weak evidence of an association between sustained heavy alcohol use in mid-adolescence and impaired WM three years later. Although we cannot fully rule out the possibility of reverse causation, several potential confounding variables were included to address the directionality of the relationship between WM and alcohol use problems.

**INTRODUCTION**

Alcohol consumption during adolescence is a major public health concern, in particular because the brain is still developing and undergoing considerable structural and functional changes (De Bellis et al. 2000). One area of research that has received considerable attention is the association between alcohol use and working memory (WM) performance. WM is critical to higher-order cognitive functioning, such as decision making and planning (Miller & Cohen 2001) and deficits in WM make it more difficult to respond in a controlled and planned manner to alcohol stimuli (Grenard et al. 2008; Peeters et al. 2012). Furthermore, WM may be more susceptible to damage from heavy alcohol use during adolescence than in adulthood (De Bellis et al. 2000) as it is not fully developed until young adulthood (Boelema et al. 2014; De Luca et al. 2003).

Research using both animal models and human data has provided evidence to suggest a negative association between alcohol use and WM during adolescence. For example, research in animal models has demonstrated lasting consequences of adolescent exposure to alcohol, including alterations in later WM performance (Risher et al. 2013; White et al. 2000). Human brain imaging studies have identified neural functioning correlates of adolescent heavy drinking. Studies using co-twin designs have found that amygdala deficits (Wilson et al. 2015), smaller orbitofrontal cortex volumes, and diminished quality of decision making (Malone et al. 2014) are associated with adolescent alcohol use. Brain imaging studies examining singletons have found that young people with alcohol use disorders have smaller hippocampal volumes (De Bellis et al. 2000; Nagel et al. 2005), prefrontal abnormalities at both the structural (De Bellis et al. 2005) and functional levels (Tapert et al. 2004), and damage to the frontal lobe (Crews et al. 2007). Taken together, these findings suggest that alcohol use during adolescence may be associated with risks for neurocognitive deficits, however the direction of the association is not clear.

Studies that have examined the prospective association between alcohol use and WM functioning using both brain imaging and neuropsychological study designs have largely revealed mixed findings. Some studies found that alcohol use preceded WM functioning (e.g., Peeters et al. 2014; Squeglia et al. 2009; Squeglia et al. 2012); while others found evidence for the opposite direction (e.g., Peeters et al. 2014; Peeters et al. 2015), in that, adolescents with poor WM may be at increased risk of developing alcohol problems.

Evidence from the limited number of prospective community samples that have examined this relationship have shown an equally conflicting pattern of results. For example, (Boelema et al. 2015) found no evidence of an association between heavy drinking in adolescence and maturation of executive functioning. The discrepancies in the literature could be due to a number of factors, including: 1) sample size, 2) study design (high-risk vs community-based samples), 3) the alcohol use phenotype (i.e., binging vs frequency), 4) lack of control for potentially relevant confounding factors, and 5) different follow-up periods.

While acknowledging that it is possible that deficits in cognitive functioning could precede and influence alcohol use, this study sought to expand on previous research by using a large UK birth cohort to examine the possibility that the neurotoxic effects of alcohol during this sensitive developmental period may impact on later cognitive functioning. Focusing on this one potential pathway, we hypothesized that sustained heavy drinking, defined as frequent and binge drinking at age 15 years (peak incidence for alcohol use Melotti et al. 2013), would be adversely associated with WM at age 18 years (as WM matures in late adolescence (Boelema et al. 2014; De Luca et al. 2003) while controlling for potentially relevant confounding factors, including a measure of WM assessed prior to the onset of alcohol use.

**METHOD**

*Participants and Procedure*

We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC), an ongoing population-based study that contains a wide range of phenotypic and environmental measures, genetic information and linkage to health and administrative records. A fully searchable data dictionary is available on the study’s website ([www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/](http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/)). Approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. All pregnant women residing in the former Avon Health Authority in the south-west of England between 1 April 1991 and December 1992 were eligible for the study (Phase I consisted of *n*=14,541). Of the 13,978 offspring alive at one year, a small number of participants withdrew from the study (*n*=24), leaving a starting sample of 13,954. Detailed information about ALSPAC is available online [www.bris.ac.uk/alspac](http://www.bris.ac.uk/alspac) and in the cohort profiles (Boyd et al. 2013; Fraser et al. 2013). A detailed overview of our study population, including attrition at the different measurement occasions, is shown in the Supplementary Material (Figure S1).

*MEASURES*

A timeline for data collection is shown in Supplementary Material (Figure S2).

*Exposures: Adolescent alcohol use.* At approximately 15 years of age (M=15.5; SD=0.35), participants completed a computer-based session at a research clinic, which included questions regarding drinking frequency and binge drinking. The following two binary variables (present vs. absent), as previously defined (Melotti et al. 2013), captured alcohol involvement: 1) frequent drinking (≥20 times in the previous 6 months); and 2) regular binge drinking (consuming more than five drinks in any 24-hour period on ≥20 occasions in the previous 2 years), which adapts a common definition of binge drinking (Masten et al. 2008). An ordinal variable capturing three mutually exclusive groups was created by combining these two measures. Groups consisted of participants who did not meet either criterion, *n*=3,525 (78.9%), from here on referred to as the ‘low’ alcohol group, participants who were frequent drinkers only, *n*=480 (10.8%), and participants who were binge and frequent drinkers *n*=461 (10.3%). High thresholds for alcohol use were used to capture the extreme end of consumption as it has been suggested that the amount of alcohol consumed in community samples might be too low to negatively influence the development of WM (Khurana et al. 2013). For all analyses, the low alcohol group was taken as the reference group.

*Outcome: Working memory.* A computerised version of the N-back task, including both 2- and 3-back conditions (*N*=4,827), was used to assess WM at the age 18 years research clinic (M=17 years 10 months; SD=5 months). The N-back task, originally introduced by Kirchner (Kirchner 1958) is widely used to measure WM (Wardle et al. 2013; Rossi et al. 2016), and has been shown to activate prefrontal cortex areas (Cohen et al. 1997). Despite being frequently used in brain imaging studies, there have been few psychometric studies of the N-back task. In general, the studies that have examined its psychometric properties have reported reliability coefficients greater than 0.70 (Jaeggi et al. 2010; Schmiedek et al. 2009; Unsworth 2010).

Four metrics were examined for both the 2- and 3-back conditions: 1) hits, or the percentage of matching numbers correctly identified as matches, 2) false alarms, or the percentage of non-matching numbers incorrectly identified as matches, 3) discriminability index (*d'*) which is a signal-detection metric that takes into account both hits and false alarms to derive an overall estimate of signal detection ability, see (McNicol 1972), and 4) median reaction times for hits and false alarms, as an indicator of processing efficiency. A measure of d´ was chosen as the primary outcome measure given it is an overall estimate. The remaining indices were examined for descriptive purposes. High scores on number of hits indicated more accurate identification, while high scores on false alarms indicated less accurate identification. High scores on *d´* therefore indicated a greater ability to distinguish signals from noise.

As we were interested in examining possible enduring effects of alcohol use on WM performance, WM was assessed at age 18 years as it generally shown that WM matures in late adolescence (Boelema et al. 2014; De Luca et al. 2003). Participants were excluded if they did not provide any responses (*n*=373 for the 2-back task; *n*=320 for the 3-back task). In total, *n*=3,141 participants completed both versions of the task, while *n*=3,351 participants had available data for the 2-back task and *n*=3,319 had available data for the 3-back version.

*Potential confounders*

Given the complicated confounding structure, potential confounding variables were included in three steps. First, we examined an unadjusted model (Model 1). Second, a number of sociodemographic measures were considered to be potential confounders of the relationship between alcohol and WM in adolescence (Model 2). These comprised of established risk factors for WM performance for which we felt the assumption of a causal predictive relationship with earlier alcohol use could be justified. Adjustment was made for a number of potential time-invariant confounding variables during pregnancy. These included: income (quintiles), maternal education (<O level: indicating no qualification; O level: indicating completion of school examinations at age 16; and >O level: indicating completion of college or university education at or after age 18), socioeconomic position (SEP, grouped into four categories: 1) unskilled or semiskilled manual; 2) skilled manual or non-manual; 3) managerial and technical; and 4) professional), parity (1st, 2nd, ≥3rd children), housing tenure (mortgaged, subsidised renting, and private renting), sex, and maternal smoking during first trimester in pregnancy (yes/no).

Third, WM at approximately age 11 years and experience of a head injury/ unconsciousness up to age 11 years were included (Model 3). A computerised version of the Counting Span task (Case et al. 1982) was included at approximately age 11 years (M=10 years, 8 months, SD=3 months) to assess WM performance during a focus clinic. A span score was based on the number of correctly recalled sets (maximum score of 5 in increments of 0.5). Further detail is provided in the Supplementary Material. A measure of head injury/ unconsciousness was also included. Since adolescents who have experienced head injury perform poorly compared with age-matched peers (Newsome et al. 2007), we included participants who experienced head injury/ unconsciousness before the age of 11 years *n*=113 (3.4%). The inclusion of both measures, prior to the onset of alcohol initiation, helps to remove the possibility that deficits in WM performance precedes alcohol use, thereby allowing for the temporal order between alcohol use and later WM to be established.

Finally, weekly cigarette smoking and cannabis use at age 15 years (assessed during the same clinic assessment as the alcohol measures) were included (Model 4). Weekly cigarette smoking, assessed using the question ‘do you smoke every week’ (*n*=181/2,659), was included because of evidence suggesting that smoking is associated with cognitive function (Loughead et al. 2009). Cannabis use in the past 12 months, assessed using the question ‘has used or taken cannabis in the past 12 months’ (*n*=442/2,649), was included as evidence suggests that engagement in cannabis use often display deficits in neurocognitive function (Henderson et al. 1999).

*Statistical methods*

A series of univariable and multivariable linear regression models were conducted to examine the association between each of the alcohol exposures and the 2- and 3-back outcome measures. Models unadjusted and adjusted for potential confounding variables were examined. *d´* was chosen *a priori* as the primary outcome as it captures overall signal detection. Number of hits, false alarms, and reaction time for hits and false alarms were used as secondary outcomes allowing for specific effects to be examined. Standardised regression coefficients with 95% confidence intervals were used and can be interpreted as a change in the exposure associated with a one standard deviation change in WM performance assessed using the d´ measure (i.e., our primary outcome). All standardized scores are normalized to have a mean of 0 and a standard deviation of 1, and thus regression coefficients can be interpreted as effect sizes.

*Attrition*

Since using complete case analysis can result in biased estimates (Sterne et al. 2009), we examined possible effects of missing data using a combination of multiple imputation and inverse probability weighting (MI/IPW) (Seaman et al. 2012). In the first step, multiple imputation was based on the 3,351 participants who had information on the 2-back task, and 3,319 participants who had information on the 3-back task. The imputation model contained performance on both versions of the WM task, alcohol exposure variables, and potential confounding variables, as well as a number of additional auxiliary variables known to be related to missingness. Fifty datasets by 10 cycles of regression were generated.

In the second step, inverse probability weighting (IPW) was performed. Estimates of prevalence and associations were weighted to account for probabilities of non-response to attending the clinic. Further information is provided in the Supplementary Material. All analyses were conducted using Stata version 14. Results using weighted estimates are reported as the main results. Table S1 shows strong evidence of a relationship between sociodemographic variables, a measure of WM at age 11 years, cigarette smoking, cannabis use, and alcohol use at age 15 years, and missing data on both conditions of the WM task. Furthermore, individuals who attended the clinic at age 18 years but who did not complete either of the N-back tasks were more likely to be involved in frequent and binge drinking at the earlier age of 15 years (Table S2).

*Sensitivity analyses*

As WM is developing across childhood and adolescence, a measure of WM performance, assessed at age 8 years, was included to provide consistency across the findings. The backward digit span task was assessed as part of an in-person standardized assessment of cognitive ability at age 8 years. The backward measure, which requires storage and manipulation of the information prior to recall, is thought to tap into WM capacity see (Alloway et al. 2006). Further information on the measure is provided in Supplementary material. Models using complete cases were included to assess the impact of missing data.

**RESULTS**

*Descriptive results*

*Working memory performance at age 18:* Overall, participants performed better on the 2-back task compared to the 3-back task using all four metrics (Supplementary Material). In terms of WM performance for the specific alcohol groups, frequent and binge drinkers performed worse on the 2-back task, assessed using the *d´*, (M=1.70, SD=1.36) compared to the low alcohol group (M=1.84, SD=1.24) and the frequent drinking only group (M=1.92, SD=1.19). A similar pattern was observed for performance on the 3-back task with frequent and binge drinkers performing worse (M=1.02, SD=1.04) compared to the low alcohol (M=1.19, SD=1.03) and frequent drinking groups (M=1.28, SD=1.04).

Associations between alcohol use at age 15 years and potential confounding variables are presented in Table S3.

*Univariable and multivariable linear regression*

Table 1 presents associations between alcohol use at age 15 years and 2-back task performance (assessed using *d´*) at age 18 years. There was insufficient evidence to suggest an association between frequent drinkers compared to the low alcohol group and WM performance. There was evidence in the unadjusted models that frequent and binge drinking (β=-.17, 95% CI=-.32 to -.03, *p*=.02) was associated with WM performancecompared to the low alcohol group. However, this association was attenuated when adjusting for sociodemographic variables, WM at age 11 years and participants who had a head injury/unconsciousness before age 11 years, weekly cigarette smoking, and cannabis use assessed at age 15 years (β=-.05, 95% CI=-.21 to .10, *p*=.50).

[Insert Table 1 here]

Table 2 presents associations between alcohol use at age 15 years and 3-back task performance at age 18 years. In a similar finding to the 2-back task, there was insufficient evidence to suggest an association between frequent drinking compared to the low alcohol group and WM performance assessed using *d´*. There was however strong evidence that frequent and binge drinking compared to the low alcohol group was associated with WM performance: unadjusted model (β=-.25, 95% CI=-.39 to -.11, *p*<.001), model adjusted for sociodemographic confounders (β=-.22, 95% CI=-.36 to .08, *p*=.001), model further adjusted for WM at age 11 years and participants who had a head injury/ unconsciousness before age 11 years (β=-.23, 95% CI=-.37 to -.09, *p*=.001). However, this association was attenuated when further adjusted for weekly cigarette smoking and cannabis use at age 15 years (β=-.12, 95% CI=-.27 to .03, *p*=.11). All coefficients highlighting the impact of the individual confounding variables are presented in Table S4. For both versions of the N-back task, larger effect estimates for the frequent and binge drinking group (compared to the low alcohol group) indicates stronger evidence of an association with deficits in WM performance, in comparison to effect sizes for the frequent drinking only group.

[Insert Table 2 here]

Given the strength of the association between frequent and binge drinking and performanceon the 3-back task, we examined whether frequent and binge drinking compared to consuming low amounts of alcohol was associated with the specific indices of WM functioning (Table 3). There was evidence to suggest that frequent and binge drinking was associated with the number of false alarms: unadjusted model (β=-.26, 95% CI=-.44 to -.07, *p*=.01), 2), model adjusted for sociodemographic confounders (β=-.42, 95% CI=-.42 to -.05, *p*=.01), 3), model further adjusted for WM at age 11 years and participants who had experienced a head injury/ unconsciousness before age 11 years (β=-.22, 95% CI=-.41 to -.22, *p*=.02). However, this association was attenuated when further adjusted for weekly cigarette smoking and cannabis use at age 15 years (β=-.08, 95% CI=-.26 to .11, *p*=.39). Models examining these associations for the 2-back are presented in Table S5.

[Insert Table 3 here]

*Sensitivity analyses*

Including the backward digit span at age 8 years (Tables S6a and S6b) produced almost identical results demonstrating evidence of an association for frequent and binge drinking and both the 2-and 3-back tasks (stronger associations for the 3-back task) compared to low alcohol users. Repeating the analyses using participants who had complete data on alcohol use, WM measures and all confounding variables produced weaker associations compared to the analyses using the fully imputed data (Tables S7a and S7b). Notably, the estimates for the fully adjusted models (Model 4) were similar.

**DISCUSSION**

In this study, we found weak evidence of a prospective association between alcohol use at age 15 years and impaired WM performance three years later in a general population birth cohort. This association was evident in adolescents who were frequent and binge drinkers for the more demanding 3-back version of the task (assessed using the *d´*)after adjusting for a number of sociodemographic confounding variables, measure of WM at age 11 years and participants who had a head injury/ unconsciousness before age 11 years. However, this association was attenuated when controlling for measures of cigarette smoking and cannabis use. When examining specific indices of WM, false alarms showed the strongest association, suggesting that performance on the task was affected by poor accuracy in rejecting non-targets rather than poor accuracy in detecting targets. There was insufficient evidence for an association between moderate drinking practices (i.e., frequent drinking only) and WM performance three years later for either the 2-back or 3-back versions.

*Limitations*

The present study should be considered in light of a number of limitations. First, the ALSPAC cohort suffers from attrition, which is higher among the socially disadvantaged (Wolke et al. 2009). We attempted to minimise the impact of attrition using sensitivity analyses. Missingness was related to WM at age 11 years, alcohol use at age 15 years and sociodemographic variables. However, the results from the sensitivity analysis suggest that the pattern of missing data did not lead to biased effect estimates. Although we did observe differences in auxiliary measures depending on data availability, the direction and magnitude of the associations were consistent with the weighted models. Second, although alcohol use was self-reported, there is evidence to suggest that self-reported alcohol use is a reliable and valid method (Del Boca & Darkes 2003). Third, as it cannot be ruled out that our findings could be over- or underestimating alcohol use, the inclusion of mutually exclusive alcohol measures ranging in order of severity helped to provide a more accurate account of adolescent drinking practices. Further, focusing on heavy drinking practices among adolescents, rather than more normative aspects of drinking such as frequency of drinking episodes, enables us to examine the hypothesised association in a more robust manner, as it has been suggested that focusing on frequency of drinking episodes may not be extreme enough to adversely impact WM (Khurana et al. 2013). Fourth, an N-back measure assessed prior to alcohol initiation would have been optimal, however, the inclusion of the Counting Span task assessed at age 11 years demonstrate a robust pattern of results.

Fifth, although there is some debate in the literature surrounding the construct validity of performance on the N-back task as an indicator of WM ability, it has been argued that by using N-back performance indices from a signal detection framework (i.e., d’) may reveal clearer insights about its validity as a measure of WM performance (Meule 2017; Kane et al. 2007; Haatveit et al. 2010). Sixth, it is also possible that a number of higher-order functions could influence this relationship since important maturational changes in brain organization and function continue well into late adolescence. For example, alcohol induced damage to the prefrontal cortex (PFC) and hippocampus could increase impulsive behaviour (Finn 2002), lead to poor decision making (Crews & Boettiger 2009) and motivation (Chambers et al. 2003).

Finally, as we examined one potential causal pathway, it is possible that the direction of the association could work in both ways, that is, impairments in WM may precede (and increase the risk of developing) alcohol problems (see Peeters et al., 2014). We were however able to include a number of measures to maximise the robustness of our findings: i) ascertain the time order of exposure and outcome in our study, enabling the potential temporal associations between alcohol use and WM to be examined, ii) controlling for a measure of WM prior to the onset of alcohol use and participants who had a head injury helped to remove the possibility of deficits in WM influencing alcohol use, and iii) although we cannot exclude the possibility of residual confounding, we have made adjustment for a number of confounding variables, including weekly smoking status, which was shown to have the strongest asscoiation with WM perfromance. Future work aims to follow up large prospective cohorts should take the possibly of reverse causality into account by including measures of alcohol use and WM at every assessment wave.

*Comparison with previous studies*

To the best of our knowledge, this is the largest study to date to assess the prospective relationship between alcohol use and WM in adolescents. Our findings are consistent with the majority of research from neuropsychological and brain imaging that have demonstrated deficits in WM functioning in adolescents exhibiting problematic patterns of alcohol use (Peeters et al. 2014; Squeglia et al. 2009; Squeglia et al. 2012). In terms of findings from community samples, a longitudinal cohort study of Dutch adolescents (aged 11-19 years) found no evidence of an association between heavy drinking in adolescence and maturation of executive functioning (Boelema et al. 2015). The contrast in findings could be due to a number of possibilities. First, our study used the N-back task as opposed to the use of WM measured with the Amsterdam Neuropsychological Task (de Sonneville 1999). Second, Boelema and colleagues examined change in WM performance across adolescence (examining maturation), while in our study WM performance was assessed at age 18 years (which is generally regarded as when WM matures). Finally, WM performance was measured in reaction times only, as opposed to the more comprehensive approach used in our study (e.g., identifying the correct number of hits, number of false alarms, discriminability index, and mean reaction times for hits and false alarms).

The inclusion of tobacco and cannabis use had a sizeable impact on associations between alcohol use and WM. This is perhaps unsurprising as there is substantial evidence from animal studies linking cannabis use in adolescent with deficits in WM performance (Renard et al. 2014; Rubino et al. 2009; Verrico et al. 2014). The association is further complicated as nicotine withdrawal has been shown to be associated with reductions in WM efficiency in animal studies (Levin et al. 2006; Levin et al. 1990). Evidence from human studies reveal a similar pattern of findings for adolescent tobacco and cannabis use on WM performance (Hanson et al. 2010; Harvey et al. 2007; Jacobsen et al. 2005; Jacobsen et al. 2007; Musso et al. 2007; Ilan et al. 2004).

Given that cannabis and tobacco use at the same time is popular among adolescents (Amos et al. 2004), it is of interest to try to disentangle the independent and combined effects. A recent study examining the independent and combined impact of cannabis and nicotine on WM performance suggested that WM performance decreased with acute cannabis use and increased with tobacco use, while cannabis use was not associated with diminished WM when used with tobacco, suggesting that tobacco use may compensate for deficits in WM from cannabis (Schuster et al. 2016).

*Implications and Conclusions*

Our findings contribute to the understanding of the relationship between alcohol use and WM in adolescents, and provide evidence that regular binge drinking in mid-adolescence is associated with impaired WM three years later, after adjusting for confounding variables. These findings have clinical and public health implications. For example, interventions aimed at preventing alcohol use in adolescents (e.g., Koning et al., 2009) might be effective in reducing impairments in WM. In particular, a combined parent and student intervention was the most effective in reducing the onset of weekly alcohol use and frequency of drinking. One advantage is that interventions can yield beneficial effects on alcohol related outcomes for adolescents even when delivered at young ages (Tanner-Smith & Lipsey 2015). Although it is difficult to quantify the meaning of the deficit in WM in practical terms, deficits in WM have been shown to be related to academic achievement (Gathercole et al. 2004), and impulsivity and risk-taking behaviours (Khurana et al. 2013; Khurana et al. 2015) in adolescents. Given the impact that cigarette and cannabis use had on the association between alcohol use and WM, it may be important to include these in future studies. Future research should explore possible mechanisms underlying this association and examine whether these associations persist into adulthood.

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**Table 1.** **Associations between alcohol use at age 15 years and *d'* at age 18 years for the 2-back task (*n*=3,351) in 50 multiply imputed datasets (standardized coefficients)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Model 1 | | Model 2 | Model 3 | | Model 4 | |
|  | *n (%)* | *b* (*95% CI)* | *p* | *b* (*95% CI) p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Low alcohol use* |  | ref |  | ref | ref |  | ref |  |
| *Frequent drinking only* | 397 (11.7) | -.00 (-.15, .14) | .96 | -.03 (-.16, .10) .76 | -.02 (-.15, .11) | .72 | .03 (-.11, .17) | .67 |
| *Frequent and binge* | 368 (10.8) | -.17 (.32, -.03) | .02 | -.15 (-.30, .00) .05 | -.16 (-.30, -.01) | .03 | -.05 (-.21, .10) | .50 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, and maternal smoking in pregnancy; Model 3: further adjusted for working memory assessed at approximately age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table 2. Associations between alcohol use at age 15 years and *d'* at age 18 years for the 3-back task (*n*=3,319) in 50 multiply imputed datasets (standardized coefficients)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Model 1 | | Model 2 | Model 3 | | Model 4 | |
|  | *n (%)* | *b* (*95% CI)* | *P* | *b* (*95% CI) p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Low alcohol use* |  | ref |  | ref | ref |  | ref |  |
| *Frequent drinking only* | 399 (11.8) | -.02 (-.16, .11) | .74 | -.04 (-18, .08) .50 | -.04 (-.17, .09) | .57 | .02 (-.11, .15) | .75 |
| *Frequent and binge* | 354 (10.5) | -.25 (-.39, -.11) | <.001 | -.22 (-.36, -.08) .001 | -.23 (-.37, -.09) | .001 | -.12 (-.27, .03) | .11 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, and maternal smoking in pregnancy; Model 3: further adjusted for working memory assessed at approximately age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table 3. Associations between frequent and binge drinking (compared to low alcohol users) at age 15 years and WM indices at age 18 years for the 3-back task (*n*=3,319) in 50 multiply imputed datasets**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Model 1 | | Model 2 |  | Model 3 | | Model 4 | |
|  | *b* (*95% CI)* | *P* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Number of hits* | -.15 (-.28, -.01) | .05 | -.13 (-.27, .01) | .06 | -.13 (-.26, .00) | .05 | -.10 (-.25, .06) | .22 |
| *Number of false alarms* | -.26 (-.45, -.05) | .002 | -.23 (-.41, -.04) | .005 | -.22 (-.40, -.04) | .004 | -.09 (-.28, .11) | .30 |
| *Reaction time-hits* | -.03 (-.17, .12) | .73 | .00 (-.14, .14) | .99 | -.00 (-.14, .14) | .98 | .07 (-.10, .23) | .42 |
| *Reaction time-false alarms* | .01 (-.14, .16) | .91 | .04 (-.11, .19) | .64 | .03 (-.12, .18) | .68 | .11 (-.06, .27) | .23 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, and maternal smoking in pregnancy; Model 3: further adjusted for working memory assessed at approximately age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

13,954 live born offspring who survived to one year – 47.8% female

9,432 participants invited to clinic (mean age: 17y 10m) – 50.2% female

4,827 participants attended clinic – 56.1% female

3,721 participants had available data – 57.3% female

3,319 participants had available data for the 3-back task – 56.4% female (**sample used in analyses**)

3,351 participants had available data for the 2-back task – 56.9% female (**sample used in analyses**)

2,632 participants had available data for the 3-back task and alcohol measures – 56.6% female

2,677 participants had available data for the 2-back task and alcohol measures – 56.5% female

1,919 participants had complete data on outcome, exposures and confounders – 56.3% female

1,896 participants had complete data on outcome, exposures and confounders – 56.3% female

Figure S1. Sample attrition in ALSPAC



**Working memory – N-back task**

Participants continuously monitored a series of numbers presented on a computer screen, and pressed ‘1’ if the number was the same as the number presented N numbers ago, or ‘2’ if it was not. Stimuli were numbers 0–9, presented in black on white background with a random spatial jitter of 180 pixels in y-axis and 200 pixels in x-axis. Each target was presented for 500 ms, followed by a 3,000 ms response window. The practice block consisted of 12 trials containing two targets. Each experimental block was randomized and consisted of 48 trials, containing eight targets, with a single block for each of the 2- and 3-back conditions. In the 2-back condition, the target was the number that was identical to the one presented 2 trials back; while in the 3-back condition was identical to the one presented 3 trials back.

**Working memory – counting span task**

Children were presented with a number of red and blue dots on a white screen and asked to count the red dots out loud. The child was asked to recall the number of red dots seen on each screen with that set in the order they were presented. There were two practice sets and three sets with displays ranging from 2 to 5 screens. A total of 12 blocks were completed with three per load level.

**Inverse probability weighting**

Weights were derived from logistic regression models using variables associated with nonresponse, including maternal age, grandmother having a history of severe depression, maternal alcohol use in pregnancy, financial problems, maternal cannabis use and affordability problems. There was evidence of an association between all of the early-life exposures to adversity and loss to follow-up comparing complete cases and WM outcome data for all participants (*n*=9,432) invited to the clinic. We weighted the included respondents by the inverse of the probability of attending and used the Hosmer-Lemeshow test to assess model fit.

**Table S1. Selective attrition for working memory performance at age 18 years**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | 2-back |  |  | 3-back |  |
|  | Available | Not available |  | Available | Not available |  |
|  | *n* (%) | *n* (%) | OR (95% CI) | *n* (%) | *n* (%) | OR (95% CI) |
| **Gender:** |  |  |  |  |  |  |
| Males | 1,408 (43.7) | 3,163 (54.4) | 0.65 (.60, .71) | 1,384 (43.7) | 3,187 (54.4) | 0.65 (.60, .71) |
| **Income:** |  |  |  |  |  |  |
| Low 20% | 351 (12.3) | 933 (21.8) | ref | 349 (12.4) | 935 (21.6) | ref |
| 40% | 512 (17.9) | 884 (20.6) | 0.65 (.55, .77) | 506 (17.9) | 890 (20.6) | 0.65 (.56, .77) |
| 60% | 559 (19.5) | 836 (19.5) | 0.56 (.48, .66) | 553 (19.6) | 842 (19.5) | 0.57 (.48, .67) |
| 80% | 679 (23.7) | 834 (19.5) | 0.46 (.39, .54) | 665 (23.5) | 848 (19.6) | 0.47 (.41, .56) |
| Highest % | 764 (26.7) | 798 (18.6) | 0.39 (.34, .46) | 752 (26.6) | 810 (18.7) | 0.40 (.34, .47) |
| **Maternal education:** |  |  |  |  |  |  |
| <O level | 1,567 (50.1) | 1,726 (33.2) | ref | 1,543 (50.1) | 1,750 (33.4) | ref |
| O level | 1,048 (33.5) | 1,826 (35.1) | 1.58 (1.42, 1.75) | 1,035 (33.6) | 1,839 (35.1) | 1.57 (1.41, 1.74) |
| >O level | 513 (16.4) | 1,646 (31.7) | 2.91 (2.58, 3.29) | 505 (16.4) | 1,654 (31.6) | 2.89 (2.56, 3.25) |
| **Social**: |  |  |  |  |  |  |
| iv-v | 102 (3.4) | 301 (6.3) | ref | 102 (3.4) | 301 (6.2) | ref |
| iii | 890 (29.5) | 1,935 (40.4) | 0.74 (.58, .93) | 871 (29.3) | 1,954 (40.4) | 0.76 (.60, .97) |
| ii | 1,420 (47.1) | 1,995 (41.6) | 0.48 (.38, .60) | 1,403 (47.2) | 2.012 (41.6) | 0.49 (.38, .61) |
| Professional | 601 (20.0) | 564 (11.8) | 0.31 (.25, .41) | 596 (20.1) | 569 (11.8) | 0.32 (.25, .42) |
| **Parity:** |  |  |  |  |  |  |
| First | 1,518 (48.5) | 2,339 (43.4) | ref | 1,496 (48.5) | 2,361 (43.4) | ref |
| Second | 1,113 (35.6) | 1,910 (35.4) | 1.11 (1.01, 1.22) | 1,099 (35.7) | 1,924 (35.4) | 1.11 (1.01, 1.22) |
| Third+ | 497 (15.9) | 1,147 (21.3) | 1.50 (1.32, 1.69) | 488 (15.8) | 1,156 (21.3) | 1.50 (1.33, 1.70) |
| **Tenure:** |  |  |  |  |  |  |
| Mortgaged | 2,719 (86.7) | 3,903 (72.0) | ref | 2,679 (86.8) | 3,943 (72.1) | ref |
| Private rent | 215 (6.9) | 589 (10.9) | 1.91 (1.62, 2.25) | 212 (6.9) | 592 (10.8) | 1.90 (1.61, 2.23) |
| Sub rent | 201 (6.4) | 928 (17.1) | 3.21 (2.74, 3.78) | 196 (6.4) | 933 (17.1) | 3.23 (2.75, 3.80) |
| **Maternal smoking:** |  |  |  |  |  |  |
| Yes | 341 (11.4) | 1,116 (22.0) | 2.19 (1.92, 2.49) | 336 (11.4) | 1,121 (21.9) | 2.17 (1.90, 2.48) |
| **WM at age 11:** |  |  |  |  |  |  |
| Linear term | 3.51 (0.83) | 3.36 (0.86) | 1.23 (1.16, 1.31) | 3.51 (0.84) | 3.35 (0.85) | 1.23 (1.17, 1.31) |
| **Head injury:** |  |  |  |  |  |  |
| Yes | 121 (3.4) | 217 (3.3) | 1.01 (.80, 1.27) | 118 (3.3) | 220 (3.4) | 0.99 (.79, 1.24) |
| **Cigarette smoking:** |  |  |  |  |  |  |
| Yes | 187 (6.9) | 277 (15.0) | 0.42 (.35, .51) | 181 (6.8) | 283 (14.9) | 0.42 (.34, .51) |
| **Cannabis use:** |  |  |  |  |  |  |
| Yes | 66 (2.5) | 97 (5.4) | 0.44 (.32, .61) | 63 (2.4) | 100 (5.4) | 0.43 (.31, .59) |
| **Adolescent alcohol use:** |  |  |  |  |  |  |
| Low alcohol use | 2,191 (81.9) | 1,334 (74.6) | ref | 2,160 (82.1) | 1,365 (74.4) | ref |
| Frequent drinking only | 283 (10.6) | 197 (11.0) | 0.88 (.72,1.06) | 280 (10.6) | 200 (10.9) | 0.88 (.73, 1.07) |
| Frequent and binge | 203 (7.6) | 258 (14.4) | 0.48 (.39, .58) | 192 (7.3) | 269 (14.7) | 0.45 (.37, .55) |

Note: Maternal education: <O level indicating no qualification; O level: indicating completion of school examinations at age 16; and >O level: indicating completion of college or university education at or after age 18; SEP grouped into 4 categories: iv-v: unskilled or semiskilled manual; iii: skilled manual or nonmanual; ii: managerial and technical; and i: professional

**Table S2. Selective attrition for alcohol use at age 15 years and WM at age 18 years**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 2-back task | | | 3-back task | | |
|  | Available | Not available | OR (95% CI) | Available | Not available | OR (95% CI) |
|  | *n* (%) | *n* (%) |  | *n* (%) | *n* (%) |  |
| *Low alcohol use* | 2,191 (81.9) | 556 (76.3) | ref | 2,160 (82.1) | 587 (75.6) | ref |
| *Frequent drinking only* | 283 (10.6) | 76 (10.4) | 1.06 (.80, 1.39) | 280 (10.6) | 79 (10.2) | 1.04 (.80, 1.35) |
| *Frequent and binge* | 203 (7.6) | 99 (13.4) | 1.92 (1.49, 2.49) | 192 (7.3) | 110 (14.1) | 2.11 (1.64, 2.71) |

**Working memory performance at age 18 years**

Overall, participants performed better on the 2-back task compared to the 3-back task using all four metrics: indicated by higher *d´* scores on the 2-back version (M=1.78, SD=1.25) compared to the 3-back version (M=1.16, SD=1.03); recording more correct hits: 2-back version (M=0.72, SD=0.21) compared to the 3-back version (M=0.27, SD=0.22); fewer false alarms: 2-back version (M=0.80, SD=0.22) compared to the 3-back version (M=0.79, SD=0.17), whilst also recording quicker reaction times for hits: 2-back version (M=706.2, SD=236.3) compared to the 3-back version (M=744.2, SD=303.2); and false alarms: 2-back version (M=677.1, SD=211.9) compared to the 3-back version (M=702.7, SD=264.3).

**Cognitive measure: digit span task**

To assess backwards digit span, the fieldworker gave a series of numbers out loud and asked the participant to recall them backwards with no time for pause. There were two practise items and seven test items (each item having two trials). Each item had one more number to recall than the preceding item (item 1 had two digits, item 7 had eight digits). The test was discontinued if a participant scored 0 on both trials of any item. For each item, the child gets 1 point for each number sequence correctly recalled resulting in a range from 0 to 7.

**Table S3.** **Associations between alcohol consumption at age 15 years and potential confounding variables**

**(multivariable analysis)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | *Low alcohol use Frequent drinking only Frequent and binge drinking* | | | | | | | | |
|  | *Reference group* | | *OR* | *95% CI* | *Wald/ p* | *OR* | | *95% CI* | *Wald/ p* |
| **Gender:** |  |  |  |  |  |  | |  |  |
| Males | -  -  -  -  - | | 1.32 | 0.99, 1.78 | .08 | 0.96 | | 0.64, 1.42 | .70 |
| **Income:** |  |  |  |  | |  |  |
| Low 20% | 0.88 | 0.47, 1.67 |  | 0.89 | | 0.43, 1.84 |  |
| 40% | 1.19 | 0.65, 2.19 |  | 0.82 | | 0.39, 1.72 |  |
| 60% | 1.22 | 0.67, 2.23 |  | 0.94 | | 0.45, 1.96 |  |
| 80% | 1.36 | 0.73, 2.53 | .19 | 1.37 | | 0.65, 2.90 | .31 |
| Highest % | - | | ref |  | | ref |  | | |  |
| **Maternal education:** |  |  |  |  |  |  | |  |  |
| <0 level | -  - | | 0.99 | 0.68, 1.44 |  | 1.10 | | 0.67, 1.78 |  |
| 0 level | 0.88 | 0.50, 1.55 | .57 | 0.82 | | 0.42, 1.67 | .55 |
| >0 level | - | | ref |  | | ref |  | | |  |
| **Social**: |  |  |  |  |  |  | |  |  |
| iv-v | -  -  - | | 2.51 | 0.58, 10.82 |  | 0.58 | | 0.19, 1.74 |  |
| iii | 2.42 | 0.55, 10.51 |  | 0.74 | | 0.24, 2.25 |  |
| ii | 2.29 | 0.51, 10.28 | .93 | 0.46 | | 0.13, 1.56 | .51 |
| Professional | - | | ref |  | | ref |  | | |  |
| **Parity:** |  |  |  |  |  |  | |  |  |
| First | - | | ref |  | | ref |  | | |  |
| Second | -  - | | 1.44 | 1.04, 1.99 |  | 1.62 | | 1.06, 2.47 |  |
| Third+ | 1.17 | 0.73, 1.85 | .31 | 1.07 | | 0.59, 1.99 | .39 |
| **Tenure:** |  |  |  |  |  |  | |  |  |
| Mortgaged | - | | ref |  | | ref |  | | |  |
| Private rent | -  - | | 1.85 | 1.03, 3.32 |  | 1.44 | | 0.66, 3.13 |  |
| Sub rent | 0.67 | 0.27, 1.71 | .94 | 0.94 | | 0.38, 2.30 | .73 |
|  |  |  |  |  |  |  | |  |  |
|  |  |  |  |  |  |  | |  |  |
| **Maternal smoking:** |  |  |  |  |  |  | |  |  |
| Yes | - | | 0.74 | 0.42, 1.32 | .26 | 1.69 | | 0.96, 3.01 | .11 |
| **WM at age 11:** |  |  |  |  |  |  | |  |  |
| Linear term | - | | 1.09 | 0.90, 1.33 | .32 | 1.24 | | 0.97, 1.61 | .08 |
| **Head injury:** |  |  |  |  |  |  | |  |  |
| Yes | - | | 1.15 | 0.64, 2.07 | .68 | 0.69 | | 0.25, 1.86 | .51 |
| **Cigarette smoking:** |  |  |  |  |  |  | |  |  |
| Yes | - | | 2.33 | 1.45, 3.74 | <.001 | 3.54 | | 2.17, 5.79 | <.001 |
| **Cannabis use:** |  |  |  |  |  |  | |  |  |
| Yes | - | | 3.06 | 2.15, 4.36 | <.001 | 7.09 | | 4.62, 10.86 | <.001 |

Note: Maternal education: <O level indicating no qualification; O level: indicating completion of school examinations at

age 16; and >O level: indicating completion of college or university education at or after age 18; SEP grouped into 4

categories: iv-v: unskilled or semiskilled manual; iii: skilled manual or nonmanual; ii: managerial and technical; and i:

professional

**Table S4. Associations between alcohol use at age 15 years and *d'* at age 18 years for the 3-back task (*n*=3,319) in 50 multiply imputed datasets including covariates**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | *Low alcohol use* | *Frequent drinking only* | | | *Frequent and binge drinking* | | |
|  |  | *3-back d’* | | | *3-back d’* | | |
|  | *Reference* | *β* | *95% CI* | *p* | *β* | *95% CI* | *p* |
| **Alcohol use:** |  | 0.02 | -.11, .15 | .75 | -0.12 | -.27, .03 | .11 |
| **Gender:** |  |  |  |  |  |  |  |
| Males | - | 0.46 | -.02, .11 | .16 | .05 | -.02, .11 | .15 |
| **Income:** |  |  |  |  |  |  |  |
| Low 20% | - | ref |  |  | ref |  |  |
| 40% | - | 0.07 | -.06, .19 | .27 | .07 | -.05, .19 | .26 |
| 60% | - | 0.11 | -.01, .23 | .07 | 0.11 | -.01, .23 | .07 |
| 80% | - | 0.12 | .00, .25 | .05 | 0.13 | .00, .25 | .05 |
| Highest % | - | 0.14 | .01, .27 | .03 | 0.14 | .02, .27 | .03 |
| **Maternal education:** |  |  |  |  |  |  |  |
| <0 level | - | ref |  |  | ref |  |  |
| 0 level | - | -0.18 | -.26, -.10 | <.001 | -0.18 | -.26, -.10 | <.001 |
| >0 level | - | -0.23 | -.34, -.13 | <.001 | -0.23 | -.34, -.14 | <.001 |
| **Social**: |  |  |  |  |  |  |  |
| iv-v | - | ref |  |  | ref |  |  |
| iii | - | -0.03 | -.21, .16 | .77 | -.03 | -.21, .16 | .76 |
| ii | - | -0.00 | -.19, .18 | .97 | -.01 | -.19, .18 | .95 |
| Professional | - | 0.11 | -.09, .31 | .30 | .10 | -.10, .31 | .31 |
| **Parity:** |  |  |  |  |  |  |  |
| First | - | ref |  |  | ref |  |  |
| Second | - | 0.07 | -.00, .14 | .07 | .07 | .00, .14 | .05 |
| Third+ | - | 0.07 | -.02, .16 | .15 | .07 | -.02, .17 | .13 |
| **Tenure:** |  |  |  |  |  |  |  |
| Mortgaged | - | ref |  |  | ref |  |  |
| Private rent | - | 0.07 | -.06, .20 | .31 | .07 | -.06, .20 | .28 |
| Sub rent | - | -0.14 | -.29, .00 | .05 | -.15 | -.30, -.01 | .04 |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Maternal smoking:** |  |  |  |  |  |  |  |
| Yes | - | -0.07 | -.17, .04 | .21 | -.06 | -.17, .04 | .24 |
| **WM at age 11:** |  |  |  |  |  |  |  |
| Linear term | - | 0.13 | ,10, .16 | <.001 | .13 | .10, .16 | <.001 |
| **Head injury:** |  |  |  |  |  |  |  |
| Yes | - | 0.08 | -.07, .22 | .31 | 0.07 | -.07, .22 | .32 |
| **Cigarette smoking:** |  |  |  |  |  |  |  |
| Yes | - | -0.37 | -.49, -.25 | <.001 | -0.34 | -.47, -.22 | <.001 |
| **Cannabis use:** |  |  |  |  |  |  |  |
| Yes | - | 0.07 | -.02, .16 | .12 | .10 | .01, .19 | .03 |

Note:Maternal education: <O level indicating no qualification; O level: indicating completion of school examinations at age 16; and >O level: indicating completion of college or university education at or after age 18; SEP grouped into 4 categories: iv-v: unskilled or semiskilled manual; iii: skilled manual or nonmanual; ii: managerial and technical; and i: professional

**Table S5. Associations between frequent and binge drinking (compared to low alcohol users) at age 15 years and WM indices at age 18 years for the 2-back task (*n*=3,319) in 50 multiply imputed datasets**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Model 1 | | Model 2 |  | Model 3 | | Model 4 | |
|  | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Number of hits* | -.15 (-.30, .01) | .07 | -.13 (-.28, .03) | .12 | -.13 (-.28, .03) | .10 | -.06 (-.23, .11) | .50 |
| *Number of false alarms* | -.13 (-.27, .02) | .10 | -.14 (-.29, .03) | .15 | -.12 (-.28, .03) | .12 | -.02 (-.18, .14) | .87 |
| *Reaction time-hits* | .05 (-.09, .20) | .48 | .06 (-.09, .21) | .42 | -.06 (-.09, .21) | .42 | .10 (-.07, .27) | .24 |
| *Reaction time-false alarms* | .01 (-.14, .15) | .92 | .02 (-.13, .17) | .79 | .02 (-.13, .17) | .81 | .08 (-.09, .25) | .34 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, and maternal smoking in pregnancy; Model 3: further adjusted for working memory assessed at approximately age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table S6a.** **Associations between alcohol use at age 15 years and *d'* at age 18 years for the 2-back task (*n*=3,351) in 50 multiply imputed datasets**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Model 1 | | Model 2 | Model 3 | | Model 4 | |
|  | *n (%)* | *b* (*95% CI)* | *p* | *b* (*95% CI) p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Low alcohol use* |  | ref |  | ref | ref |  | ref |  |
| *Frequent drinking only* | 397 (11.7) | -.00 (-.15, .14) | .96 | -.03 (-.16, .10) .76 | -.04 (-.17, .10) | .58 | .02 (-.11, .16) | .79 |
| *Frequent and binge* | 368 (10.8) | -.17 (.32, -.03) | .02 | -.15 (-.30, .00) .05 | -.14 (-.29, .01) | .06 | -.04 (-.19, .12) | .66 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, maternal smoking in pregnancy; Model 3: further adjusted for WM at age 8 years and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table S6b.** **Associations between alcohol use at age 15 years and *d'* at age 18 years for the 3-back task (*n*=3,319) in 50 multiply imputed datasets**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Model 1 | | Model 2 | Model 3 | | Model 4 | |
|  | *n (%)* | *b* (*95% CI)* | *p* | *b* (*95% CI) p* | *b* (*95% CI)* | *p* | *b* (*95% CI)* | *p* |
| *Low alcohol use* |  | ref |  | ref | ref |  | ref |  |
| *Frequent drinking only* | 399 (11.8) | -.02 (-.16, .11) | .74 | -.04 (-18, .08) .50 | -.05 (-.18, .08) | .44 | .01 (-.12, .14) | .88 |
| *Frequent and binge* | 354 (10.5) | -.25 (-.39, -.11) | <.001 | -.22 (-.36, -.08) .001 | -.22 (-.36, -.08) | .002 | -.11 (-.26, .04) | .16 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, maternal smoking in pregnancy; Model 3: further adjusted for WM at age 8 years and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table S7a. Associations between alcohol use at age 15 years and WM at age 18 years (2-back task) – complete cases (*n*=1,919)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **2-Back *d'*** | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|  | β (*95% CI)* | *p* | β (*95% CI)* | *p* | β (*95% CI)* | *p* | β (*95% CI)* | *p* |
| *Low alcohol use (82.5%)* | ref |  | ref |  | ref |  | ref |  |
| *Frequent drinking only (10.8%)* | .07 (-.05, .19) | .27 | .07 (-.05, .19) | .27 | .01 (-.12, .14) | .90 | .01 (-.13, .15) | .91 |
| *Frequent and binge (6.8%)* | -.11 (-.25, .03) | .13 | -.11 (-.25, .03) | .13 | -.14 (-.30, .02) | .08 | -.10 (-.27, .08) | .29 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, maternal smoking in pregnancy; Model 3: further adjusted for WM at age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years

**Table S7b. Associations between alcohol use at age 15 years and WM at age 18 years (3-back task) – complete cases (*n*=1,896)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **3-back *d'*** | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|  | β (*95% CI)* | *p* | β (*95% CI)* | *p* | β (*95% CI)* | *p* | β (*95% CI)* | *p* |
| *Low alcohol use (82.6%)* | ref |  | ref |  | ref |  | ref |  |
| *Frequent drinking only (10.8%)* | .08 (-.04, .20) | .20 | .03 (-.10, .17) | .62 | .02 (-.13, .16) | .79 | .05 (-.10, .19) | .54 |
| *Frequent and binge (6.7%)* | -.16 (-.31, -.02) | .03 | -.16 (-.33, .00) | .05 | -.20 (-.36 -.03) | .02 | -.16 (-.35, .02) | .08 |

Model 1: unadjusted; Model 2: adjusted for sex, income, social economic position, maternal education, housing tenure, parity, maternal smoking in pregnancy; Model 3: further adjusted for WM at age 11 years, and head injury/unconsciousness up to age 11 years; Model 4: further adjusted for young person cigarette and cannabis use assessed at age 15 years