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Behavioural measures of frontal lobe function in a population of young social drinkers with binge drinking pattern

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ABSTRACT

Background: Binge drinking may lead to brain damage. The aim of the present study was to compare the cognitive abilities of binge and non-binge drinkers in tasks which test functions linked to discrete areas of the prefrontal cortex.
Methods: Non-binge and binge drinkers were identified according to their binge score derived from the Alcohol Use Questionnaire. Cognitive performance was tested with the Spatial Working Memory task (SWM) linked to the dorsolateral prefrontal cortex, Intra/Extradimensional Shift and reversal task (IED) linked to dorsolateral prefrontal cortex (shift) and to orbitofrontal cortex (reversal), Paired Associates Learning task (PAL) linked to temporal cortex, and Reaction Time Task (RTI) a task measuring motor impulsivity (Inferior frontal gyrus). Personality traits, alcohol outcome expectancies and mood were also evaluated.
Results: Binge drinkers recorded a significantly shorter movement time to target in the RTI, and completed fewer stages on first trial in the PAL, compared with non-bingers. In the IED as well as in the SWM, only female binge drinkers were more impaired than non-binge drinkers.
Conclusions: Functions linked to dorsolateral prefrontal cortex may be more impaired in female, whereas functions linked with the temporal lobe may be impaired in both male and female binge drinkers compared to non-binge drinkers. Functions linked to orbitofrontal cortex were not impaired. The increased speed of response in the RTI in binge drinkers may indicate an increased motor impulsivity in binge drinkers.

1. Introduction

Binge drinking has become increasingly common among adolescents and college students and refers to the excessive drinking of alcohol often with harmful consequences (Midanik et al., 1996; Wechsler et al., 1994). Hunt (1993) suggested that a binge drinking pattern of alcohol consumption may cause brain damage in both humans and animals.

Binge ethanol exposure in adult rats causes necrotic neurodegeneration after as little as two days of exposure (Obernier et al., 2002a). In addition Crews et al. (2000) have found that young adolescent rats show a different pattern of brain damage after binge ethanol administration than that found in adult rats. Damage to the associated frontal cortical olfactory regions was sustained in the adolescent, but not adult rats. Since then several animal studies have confirmed the neurotoxic effects of excessive alcohol drinking in the adolescent brain. More recently, studies with human adolescents and university students, which examined the effects of heavy binge drinking have suggested alcohol-related brain structural (De Bellis et al., 2000, 2005; Medina et al., 2007; Nagel et al., 2005) and functional (Hartley et al., 2004; Tapert et al., 2004; Townshend and Duka, 2005) abnormalities. In humans, the prefrontal lobe continues to mature into the early twenties (Casey et al., 2000; Gogtay et al., 2004). This late developing area may therefore be especially sensitive to heavy alcohol use.

There have been several definitions of binge drinking. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has approved the following definition: 'A 'binge' is a pattern of drinking alcohol that brings BAC to about 0.08 gram-percent or above. For the typical adult, this pattern corresponds to consuming 5 or more drinks (male), or 4 or more drinks (female), in about 2 h' (NIAAA, 2004). In our own studies of binge drinking, we have used a more behavioural approach based on the Alcohol Use Questionnaire (Mehrabian and Russell, 1978), which incorporates speed of drinking, and the behavioural measures, 'numbers of times being drunk in the last 6 months' (with drunkenness defined as loss of coordination, nausea and/or the inability to speak clearly, or blackout) and the percentage of times getting drunk when drinking (Townshend and Duka, 2002). Although differences in definition of binge drinking may give rise to some confusion both in the scientific literature and among the general public, it is likely that the multiple definitions tap into closely related phenomena.

Binge drinking in addition is characterised by repeated bouts of drinking leading to high levels of alcohol in the brain followed by periods in which brain alcohol levels return to zero. We have proposed that binge drinking may lead to brain damage and resultant cognitive

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dysfunction, which may be similar to the neurotoxicity induced by repeated withdrawals from alcohol in dependent animals and humans (Crews et al., 2001; Duka et al., 2004, 2003; Stephens and Duka, 2008; Stephens et al., 2005; Veatch and Gonzalez, 1999).

Previous studies examining the effects of drinking history on frontal lobe tasks have found that binge drinkers are impaired in decision making tasks (e.g. Tower of London task; Hartley et al., 2004). In two consecutive studies we have found that binge drinkers compared to non-binge drinkers are impaired in a Spatial Working Memory task (Townshend and Duka, 2005; Weissenborn and Duka, 2003). However this effect was more pronounced in female binge drinkers in the second study. Similarly only female binge drinkers compared to female non-binge drinkers were impaired in the Gordon Diagnostic Adult Vigilance task, a task that measures the ability to inhibit a pre-potent response (Townshend and Duka, 2005). It is reported that females are more sensitive to the neurotoxic effects of alcohol than males (Mann et al., 2005; Schweinsburg et al., 2003). A recent study has also shown that alcohol use may affect prefrontal neurodevelopment differently in males and females (Nagel et al., 2006).

The aim of the present study was to extend our previous findings with binge drinkers, using tasks from the CANTAB battery, which test additional aspects of frontal lobe functions compared to those used previously ((Townshend and Duka, 2005; Weissenborn and Duka, 2003). The classification of participants as binge drinkers and non-binge drinkers, was based on their completion of the Alcohol Use Questionnaire (AUQ; (Mehrabian and Russell, 1978). A binge drinking score was calculated for each individual using the three questions from the AUQ which evaluate drinking patterns (drinks per hour; times drunk within the last 6 months; % of being drunk when drinking) independent of weekly alcohol consumption (Townshend and Duka, 2002). Thus the score includes measurements of 'drinks in a row' (Wechsler and Austin, 1998) but also frequency of drunkenness.

We planned to examine attentional processes and cognitive flexibility using the Intra/Extradimensional Shift (IED) a task believed to be dependent on the dorsolateral part of the prefrontal cortex (shift phases) and orbitofrontal cortex (reversal phases; (Dias et al., 1996)). We also added a task that measures aspects of visuospatial associative memory the Paired Associates Learning (PAL), which depends on temporal lobe and hippocampal function as shown in monkeys (Bachevalier and Nemanic, 2008) and human studies (Owen et al., 1995). The Spatial Working Memory (SWM) task, which depends on dorsolateral prefrontal cortex function (Chase et al., 2008), was reintroduced to replicate our previous data and confirm the gender difference effect. We have also added a measurement of impulsivity, the Reaction Time Task (RTI; (Stip et al., 2005)). Because of the gender differences in both the rate of prefrontal neuronal maturation (Nagel et al., 2006) and the neurotoxic effects of alcohol (Mann et al., 2005), and also because of our previous data (Townshend and Duka, 2005), we examined differences in cognitive performance in male and female binge drinkers.

We have included measurements of alcohol expectancy using the Alcohol Expectancy Questionnaire (AEQ (Fromme et al., 1993)) as there is evidence that greater expectation of positive alcohol experiences may be associated with binge drinking episodes (Blume et al., 2003). Certain personality traits (e.g. novelty seeking) have also been associated with heavy drinking (Cloninger, 1994; Gilligan et al., 1987). However, in a previous study we used the Temperament and Character Inventory (TCI; (Cloninger, 1994)) and we found no correlation between different personality types and binge drinking behaviour including novelty seeking (Townshend and Duka, 2005). In the present study, we used the NEO Revised Personality Inventory (NEO PI-R; (McCrae and Costa, 1987). Unlike the TCI, the NEO PI-R measures five main traits: neuroticism, extroversion, openness to experience, agreeableness and conscientiousness. These measures will provide information about trait characteristics which may predispose to binge drinking. In a previous study we have also found that binge drinkers compared to non-binge drinkers show negative mood (composite score from the Profile of Mood States; POMS (McNair et al., 1971)), including depression, irritability and anxiety. Therefore we repeated the POMS to assess mood in the current cohort of participants. The Spielberger State-Trait Anxiety Inventory (STAI (Spielberger et al., 1970) was introduced to further explore the relationship between binge drinking and negative affect.

2. Methods

2.1. Participants

Sixty young, healthy volunteers (30 male and 30 female) moderate to heavy social drinkers between the ages of 18 and 29 (mean 20.6 SEM 0.34) answered an advertisement for social drinkers to take part in a study looking at the relationship between performance on cognitive tasks and drinking patterns. Volunteers with current symptoms or a history of mental illness, neurological diseases, drug or alcohol dependence were not included in the study. Participants had been instructed to abstain from the use of illicit recreational drugs for at least 1 week prior to the experiment, from the use of sleeping tablets or hay fever medication for at least 48 h, and from the use of alcohol for at least 12 h prior to the experiment. All spoke English as their first language, except 4. The NART scores from these 4 volunteers were discarded. The study was approved by the University of Sussex Ethical Committee and all volunteers gave their informed consent and were paid for their time at a rate of approximately £5 per hour.

2.2. Research methods

2.2.1. Population characteristics

Population characteristics were based on information obtained from the participants and included age and smoking information.

2.2.2. Questionnaires

2.2.2.1. Alcohol and drug use

2.2.2.1.1. Alcohol Use Questionnaire (AUQ). A quantity–frequency, beverage-specific index of alcohol consumption for the previous 6 months was obtained using a revised version of the Alcohol Use Questionnaire (AUQ; (Mehrabian and Russell, 1978). The revised questions, by determining brands of liquor, allow for actual alcoholic content (percentage volume) of drinks to be assessed. Subjects were asked to estimate the number of drinking days, the usual quantity consumed and the pattern of drinking. We have previously demonstrated that the AUQ is a reliable measure of drinking quantity and drinking pattern (Townshend and Duka, 2002).

2.2.2.1.1. Binge drinking score. A 'binge drinking' score was calculated for all subjects on the basis of the information given in items 10, 11 and 12 of the AUQ (Mehrabian and Russell, 1978): average drinks per hour (item 10); number of times being drunk in the previous 6 months (item 11); percentage of times getting drunk when drinking (item 12)]. The binge score is calculated using the equation: $[4\times(\text{Item } 10)+\text{Item } 11+0.2\times(\text{Item } 12)]$. This score gives a picture of the drinking patterns of the participants rather than just a measure of alcohol intake. Subjects who have a high 'binge score' and drink frequently but irregularly may have a similar intake of alcohol to those with a lower 'binge score' who drink on a regular basis. Participants were recruited on the basis of their binge score and effort was made during recruitment to separate the participants into a binge drinkers group, if their binge score was close to the upper 33% ($\geq$24) of scores obtained previously in our laboratory, and to a non-binge drinkers group if their binge scores were close to the low 33% ($\leq$16; see, (Townshend and Duka, 2005)). We did not exclude eight participants with binge scores between 16 and 24 and the separation into binge drinkers and non-binge drinkers for the present study was based on

median split. The current participants' binge scores had a median of 31 and the upper and low 33% was 46 and 20 respectively, indicating a significant increase in binge scores among young adults over the years.

2.2.2.1.3. Alcohol Expectancy Questionnaire (AEQ). Based on the Comprehensive Effects of Alcohol Questionnaire (CEOA) (Fromme et al., 1993), the AEQ is a 38-item questionnaire, which assesses positive and negative expected effects of alcohol consumption. There are seven expectancy factors, four positive (sociability, tension reduction, liquid courage and sexuality), and three negative (cognitive and behavioural impairments, risk and aggression, and negative self perception).

2.2.2.1.4. Drug Use Questionnaire. This questionnaire asks for duration of use, time since last use, how often used and dose per session for all the main drug categories. For the purposes of this study as a rough guide to drug use, participants were given a score in which 0 = no drug use; 1 = occasional use of cannabis/hash or marijuana; 2 = regular use of cannabis/hash or marijuana (at least once a week); 3 = use of ecstasy and/or other drugs.

2.2.2.2. Personality Trait measurements. The Revised NEO Personality Inventory (NEO PI-R), is a psychological personality inventory; a 240-question measure of the Five Factor Model: Extraversion, Agreeableness, Conscientiousness, Neuroticism, and Openness to Experience. Additionally, the test measures six subordinate dimensions (known as 'facets') of each of the "Big Five" personality factors (McCrae and Costa, 1987). The NEO PI-R was always given at the start of the testing session, prior to cognitive testing.

2.2.2.3. Current mood measures. Profile of Mood States (POMS; (McNair et al., 1971)). The POMS consists of 72 mood related adjectives which participants are instructed to rate on a 5-point scale ranging from 'not at all' (0) to 'extremely' (4). Through the process of factor analysis 8-factors have been established: Anxiety, Fatigue, Depression, Anger, Vigour, Confusion, Friendliness, and Elation. In addition, two further composite factors can be derived as follows: Arousal = (Anxiety + Vigour) − (Fatigue + Confusion), and Positive Mood = Elation − Depression. All 10 factors were evaluated for this study.

2.2.2.4. Spielberger State-Trait Anxiety Inventory. Spielberger State-Trait Anxiety Inventory (STAI; (Spielberger et al., 1970)): The STAI differentiates between the temporary condition of "state anxiety" and the more general and long-standing quality of "trait anxiety". The essential qualities evaluated by the STAI are feelings of apprehension, tension, nervousness, and worry.

The questionnaires were given in random order before the other cognitive measures.

2.2.3. Cognitive measures

2.2.3.1. National Adult Reading Test (NART;(Nelson and O'Connell, 1978)). The participants were given the NART in order to provide an estimate of the participants' verbal IQ performance.

2.2.3.2. Paired Associates Learning task (PAL; CANTAB (Cambridge Cognition Ltd.)). The PAL is comprised of eight stages and assesses visual memory and new learning. It is primarily sensitive to changes in medial temporal lobe functioning. For each stage, boxes are displayed on the screen. All are opened in a randomized order. One or more of them will contain a pattern. The patterns shown in the boxes are then displayed in the middle of the screen, one at a time, and the subject must touch the box where the pattern was originally located. Each stage may have up to 10 trials in total (the first presentation of all the shapes, then up to 9 repeat presentations until the subject gets all the locations correctly). If the subject makes an error, the patterns are presented again to remind the subject of their locations. When the subjects get all the locations correctly, they can proceed to the next stage. If the subject cannot complete a stage correctly, the test terminates. There is one pattern to recall in stages 1 and 2, two patterns in stages 3 and 4, and three patterns in stages 5 and 6. The test becomes more difficult in stage 7, where six patterns are displayed; stage 8 is the most complex, with 8 patterns displayed.

The variable 'stages completed on first trial' indicates how many stages the subject is able to complete without errors, on the first attempt.

2.2.3.3. Spatial Working Memory task (SWM; CANTAB (Cambridge Cognition Ltd.). This sub-test of CANTAB is a self-ordered search task that requires subjects to search through a spatial array of boxes in order to collect tokens hidden inside. At any one time there will be one single token hidden. The key instruction is that once a blue token has been found inside a box, then that box will never be used again to hide a token. There are trials of 3, 4, 6 and 8 boxes. There are two types of errors in this task, within- and between-search errors. A 'between-search error' occurs when a participant returns to a box in which a token has previously been found and a 'within search error' occurs when a participant returns to a box within the same search. Results refer to 'between-search errors' and are given only for the 6 and 8 boxes condition as in the 3 and 4 box conditions error rates are very low. A further variable was the "strategy score" which indicates the particular sequence that participants follow in each session. A high score indicates poor strategy. Spatial Working Memory is a test of the subject's ability to retain spatial information and to manipulate remembered items in working memory. It is a self-ordered task, which also assesses heuristic strategy. This test is a sensitive measure of frontal lobe and 'executive' dysfunction.

2.2.3.4. Intra/Extradimensional Shift task (IED; CANTAB (Cambridge Cognition Ltd.)). Intra/Extradimensional Set Shift is a test of rule acquisition and reversal. It features visual discrimination and attentional set formation and the maintenance, shifting and flexibility of attention. This test is primarily sensitive to changes to the fronto-striatal areas of the brain. Two artificial dimensions are used in the test; colour-filled shapes and white lines. Simple stimuli are made up of just one of these dimensions, whereas compound stimuli are made up of both, namely white lines overlying colour-filled shapes. Subjects progress through the test by satisfying a set criterion of learning at each stage (6 consecutive correct responses). If at any stage the subject fails to reach this criterion after 50 trials, the test terminates. The test starts with stage 1, the presentation of two simple, colour-filled shapes. The subject must learn which of the stimuli is correct by touching it, and continue until the criterion is reached. In stage 2, the contingencies are reversed, so that now the previously incorrect stimulus is correct. In stage 3, the second dimension is then introduced, initially lying adjacent to, and then, for stage 4, overlapping, the first dimension. Once the criterion has been reached with the overlapping compound stimuli the contingencies are reversed for stage 5, within the original dimension. It is important to note that the second dimension is entirely redundant to the solution of the problem at this stage. Once the subject has learned the compound discrimination, new compound stimuli are presented (stage 6), still varying along the same 2 dimensions (of shape and of line). Subjects are required to continue to attend to the previously relevant dimension of shape and learn which of the two new exemplars is correct (the 'intradimensional shift'). Once the subject has completed a successful intradimensional shift, followed by a reversal (stage 7), again the compound stimuli are changed. For this stage (stage 8), subjects are required to shift attention to the previously irrelevant dimension and learn which of the two exemplars in this dimension is now correct (the extradimensional shift). In stage 9 the contingencies are again reversed.

2.2.3.5. Reaction Time Task (RTI; CANTAB (Cambridge Cognition Ltd.). The RTI is comprised of two tasks, a simple Reaction Time Task, followed by a 5-choice Reaction Time Task. In the simple Reaction Time Task one circle is presented on the computer screen and subjects are required to hold a press pad button down and only release it to touch the screen at the centre of the circle where a yellow spot appears, neither touching it too soon nor too late. In the 5-choice reaction task, five interconnected circles are presented on the screen and the yellow spot may now appear in the centre of any one of the 5 circles. The dependent variables we used for the RTI test are reaction time, movement time and accuracy score. Reaction time represents the speed with which the subject releases the press pad button in response to the onset of a stimulus whereas movement time is the time taken to touch the stimulus after the press pad button has been released. These measures are recorded separately for the 'simple' and the 'five choice' Reaction Time Tasks.

The four CANTAB tasks were given in random counterbalanced order.

2.3. Target variables

For the purpose of this paper, the target variables for the PAL task were the stages completed on the first trial, the total errors made and the total trials required to complete. In the SWM task, target variables were the between-search errors for 6 and 8 boxes and the strategy score. In the IED shift, target variables were the number of errors made in the discrimination (3 variables), reversal (4 variables) and shift phases (2 variables) of the test. In the RTI task the target variables were movement and reaction time for the simple and the multiple choice task.

Dependent variables in POMS were only the composite factors arousal and positive mood derived from the eight factors of the POMS. In the STAI the main variables were state and trait anxiety ratings.

2.4. Statistical methods

Population characteristics were analysed using univariate ANOVAs with group (binge drinkers versus non-binge drinkers) and gender as a between factors. Measurements of alcohol expectancy, personality, anxiety and mood were analysed using multivariate ANOVAs with the factors from the questionnaires as the dependent variables and group (binge drinkers versus non-binge drinkers) and gender as fixed factors.

With regard to the cognitive tasks the variables between-search errors for 6 and 8 boxes in the SWM were analysed using mixed ANOVAs with difficulty (search 6 versus 8 boxes) as within factors and group (binge drinkers versus non-binge drinkers) and gender as between factors. With the same between factors univariate ANOVAs were performed for the dependent variable 'strategy score' in the SWM and for the dependent variables in the PAL and the RTI task. IED variables in the discrimination (3 variables), reversal (4 variables) and shift phases (2 variables) were analysed using multivariate ANOVAS on the respective dependent variables with group (binge drinkers versus non-binge drinkers) and gender as fixed factors. Where an interaction was found between binge drinking group and gender, further analysis was performed on males and females separately to examine the binge drinking effect separately for each gender.

If group differences were found with regard to any of the population characteristics variable, this variable was entered as covariate where binge drinkers performed differently on cognitive tasks. All procedures were carried out using SPSS software version 14.

3. Results

3.1. Population characteristics, alcohol, drug use and NART

Table 1 shows the characteristics of participants separately for each of the drinking pattern group and for males and females within these groups. Separation to binge drinkers and non-binge drinkers group was based on median split. Although not significant, a different distribution of males and females was found in the binge and non-binge drinking groups, which may reflect real world population ratios. The two groups were different with regard to the binge score and alcohol units with the binge drinkers having a higher binge score and drinking more alcohol units per week ($t(54) = 2.65$; $p = 0.01$) than non-binge drinkers. There were no differences between males and females for any of the demographic characteristics in the Non-Binge Drinker group or the Binge Drinker Group.

3.2. Alcohol Expectancy, NEO personality trait and Anxiety Questionnaire

Data from the 7 factors derived from the self ratings in *Alcohol Expectancy Questionnaire* are presented for each group and for gender within each group in Table 2. Multivariate analysis found a gender × binge group interaction in the multivariate tests approaching significance (F 7,50 = 2.14; $P = 0.055$). Subsequent tests of between-subject effects revealed a significant interaction for the factors 'liquid courage' and Negative perception (F 1,56 = 8.50; $P<0.01$ and F 1,56 = 4.32; $P<0.05$, respectively) indicating high expectancy ratings for 'liquid courage' and 'negative perception' in female binge drinkers. With regard to *NEO personality trait factors* (Table 2) only a significant main effect of gender was found ($F(5,49) = 5.84$, $p<0.001$) with females rating higher than males in Openness to Experience, Agreeableness, and Extraversion (Fs (1,53)>4.9, ps<0.05). There was also a main effect of binge group that only approached significance ($F(5,49) = 2.1$, $p = 0.08$) with binge drinkers rating lower in Openness to Experience than non-binge drinkers ($F(1,53) = 3.50$,

Table 1
Demographic data and alcohol, smoking and drug use information as well as NART scores for non-binge and binge drinkers and for males and females.

	Non-binge drinkers			Binge drinkers		
Group characteristics	Total	Males	Females	Total	Males	Females
Number	30	13	17	30	18	12
Mean age	22.3 (5.24)	24.77 (6.92)	20.47 (2.32)	20.70 (2.97)	21.223.67	19.92 (1.16)
Alcohol units per week[1] mean	21.82* (8.27)	23.63 (9.37)	20.44 (7.32)	32.63 (20.6)	35.15 (12.49)	28.86 (9.26)
Binge drinking score mean	17.96* (7.10)	15.63 (6.67)	19.74 (7.08)	53.47 (15.31)	54.39 (15.61)	52.08 (15.41)
Estimated IQ (NART – verbal)	114.62 (8.96	112.34 (12.35)	116.19 (5.56)	113.15 (3.96)	113.93 (4.30)	111.89 (3.11)
Drug use score	1.43 (1.38)	.92 (1.32)	1.82 (1.33)	1.33 (1.27)	1.22 (1.26)	1.50 (1.31)
Cigarette smokers (n)	7	3	4	13	8	5
Occasional use of cannabis (n)	5	1	4	7	5	2
Regular use of cannabis (n)	1	1	0	3	1	2
XTC and/or other drug use (n)	12	3	9	9	5	4

Data are presented as mean (SEM).
*$p = 0.01$ compared to binge drinkers.
1: one alcohol unit = 8 grams of alcohol.

Table 2
Scores on the 7 factors from the Alcohol Expectancy Questionnaire, the 5 factors from the NEO Personality Inventory and the 2 composite factors from the POMS for non-binge and binge male and female drinkers, mean (SEM).

	Non-binge drinkers		Binge drinkers	
	Males	Females	Males	Females
AEQ factors				
Sociable	23.23 (0.79)	22.71 (0.72)	22.72 (0.49)	24.75 (0.88)
Tension reduction	9.85 (0.32)	9.47 (0.35)	9.56 (0.38)	10.58 (0.34)
Liquid courage	13.46 (0.58)	12.82 (0.54)	13.22 (0.45)	15.58 (0.42)*
Sexuality	9.92 (0.52)	8.59 (0.33)	9.17 (0.47)	9.58 (0.71)
Cognitive/behavioural impairment	25.77 (0.77)	26.47 (0.62)	26.28 (0.89)	27.00 (0.95)
Risk/aggression	13.62 (0.58)	12.35 (0.49)	12.50 (0.49)	13.25 (0.65)
Negative perception	10.69 (0.52)	10.29 (0.54)	10.17 (0.43)	11.92 (0.54)*
NEO Personality Inventory				
Neuroticism	86.92 (9.01)	95.87 (5.88)	91.06 (5.35)	104.83 (4.92)
Extraversion[&]	111.25 (4.39)	123.27 (4.03)	117.50 (4.86)	126.83 (5.30)
Openness to experience[&]	122.58 (5.69)	145.40 (8.93)	118.61 (4.51)	125.25 (5.17)
Agreeableness[&]	105.50 (6.33)	121.87 (4.37)	102.83 (4.58)	117.75 (5.07)
Conscientiousness	105.33 (4.19)	103.60 (5.94)	99.06 (5.81)	97.67 (5.47)

*$p<0.05$ compared to female non-binge drinkers and to male binge drinkers. [&]Main effect of gender.

$p=0.06$). *Anxiety ratings* did not show any differences with regard to gender or binge drinking (data not shown).

3.3. Profile of Mood States (POMS)

There was a significant main effect of gender on Arousal (F 2,53 = 3.85; $P<0.05$) with females giving higher ratings of arousal than males (F 1,57 = 6.42; $P<0.05$; data not shown).

3.4. Cognitive measures

3.4.1. Paired Associates Learning (PAL)

A binge drinking effect was found for the variable 'stages completed on the first trial' (F 1,59 = 5.8; $P<0.005$; Fig. 1a;) with binge drinkers completing less stages during the first trial. A marginal binge drinking effect on the number of total errors made and total trials was also found (F 1,59 = 3.23; $P=0.08$ and F 1,59 = 3.85; $P=0.05$; Fig. 1b,c) indicating a tendency in the binge drinkers to make more errors and require more trials to complete the task than non-binge drinkers. There were no other effects of binge drinking, no effect of gender and no interaction between binge drinking group and gender ($Fs = \leq 1$). Units per week entered as covariate did not affect any of the results.

3.4.2. Spatial Working Memory (SWM)

The mixed ANOVA on between trial errors found a binge group by gender by condition (6 or 8 boxes) interaction (F 1,56 = 4.3; $p<0.05$), which indicated a binge group by gender interaction in the 8 boxes condition (F 1,59 = 4.30; $p<0.05$). Consequently the population was split by gender and a binge group effect, approaching significance (F 1,28 = 3.87; $p=0.059$) was found only in females indicating that female binge drinkers made more errors than female non-binge drinkers (Fig. 2).

A binge group by gender interaction (F 1,59 = 4.03; $p<0.05$) was also found for the 'strategy score'. Consequently the population was split by gender and a binge group effect approaching significance (F 1,28 = 3.87; $p=0.08$) was found only in females indicating that female binge drinkers had a worse strategy score (Mean ± SEM: 32.3 ± 1.3) than female non-binge drinkers (Mean ± SEM: 29.1 ± 1.2). Units per week entered as covariate did not affect any of the results.

3.4.3. Intra/Extradimensional Shift (IED)

Multivariate tests revealed a binge group by gender interaction for errors made in the discrimination stages (1, 3 and 4; F 3,54 = 3.03, $p=0.05$) and in the shift stages (6 and 8; F 2,55 = 3.09, $p=0.05$). Subsequent tests of between-subject effects showed a group by gender interaction in the compound discrimination with shapes superimposed (stage 4; F 1,59 = 8.23, $p<0.01$) and in the intradimensional shift (stage 6; F 1,59 = 6.12, $p<0.05$). No main effect of gender ($F<1$), or binge group (F 1,52 = 1.6; $P>0.05$) was found. Consequently the population was split by gender, and males and females examined separately. An effect of binge group was found in females in stages 4 (F 1,28 = 6.78; $p<0.05$; Fig. 3a) and 6 (F 1,28 = 9.38; $P<0.01$; Fig. 3b) indicating that female binge drinkers made more errors than female non-binge drinkers. In males, there was no effect of binge group either in stage 4 or 6 ($Fs<2.30$, $ps>0.1$). For the IED errors in the reversal stages (2, 5, 7 and 9) there were no main effect of gender or of binge group or interactions between binge group and gender found. Units per week entered as covariate did not affect any of the results.

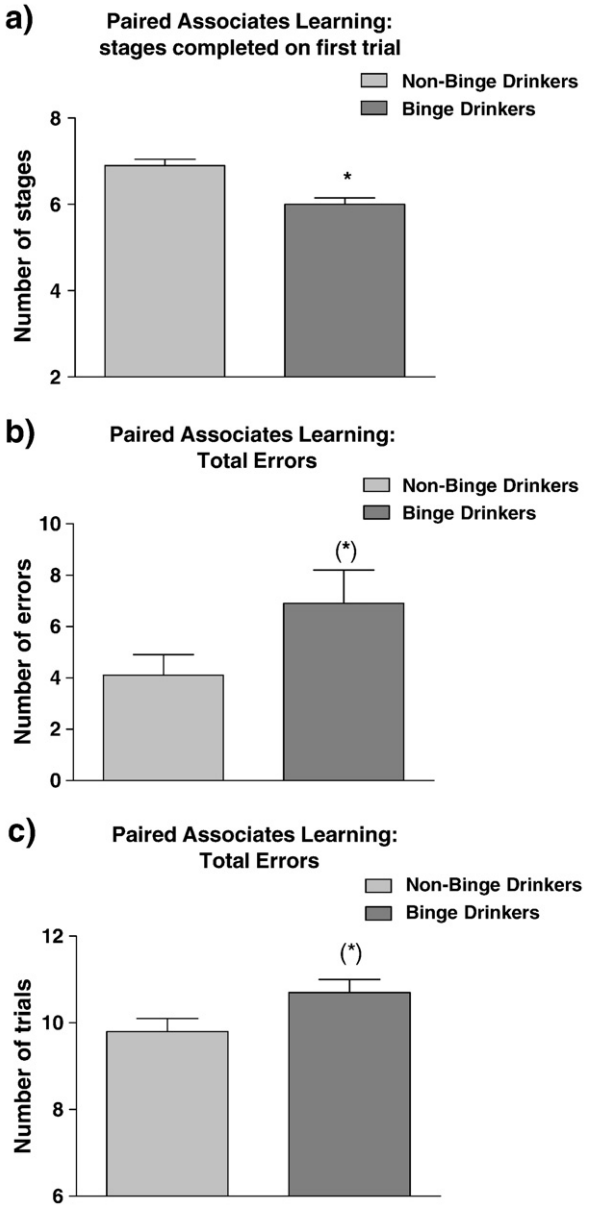

Fig. 1. Mean (±SEM) number of stages completed on first trial (a), total errors made (b) and total trials required for learning (c) for the Paired Associates Learning task for non-binge and binge drinkers. *$p<0.05$, (*) $p<0.08$ compared to non-binge drinkers (independent samples t-test).

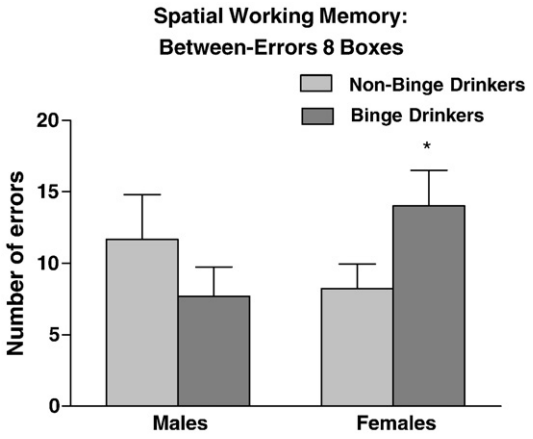

Fig. 2. Between-search errors (8-boxes version; mean ± SEM) measured in the CANTAB Spatial Working Memory task for male and female binge and non-binge drinkers. *$p = 0.06$ compared to female non-binge drinkers (independent samples *t*-test).

3.4.4. Reaction Time (RTI)

Due to technical reasons only 46 participants completed the RTI task. Of those 22 were binge drinkers and 24 were not binge drinkers. Within the binge drinkers group there were 15 males and 7 females whereas within the non-bingers group were 12 males and 12 females.

There was a binge group effect found for the movement time in the simple reaction task (F 1,45 = 4.6, $p<0.05$; Fig. 4) indicating that binge drinkers showed a shorter movement time (time from releasing the press pad to touch the spot on the screen) compared to non-binge drinkers in the simple Reaction Time Task. No effect of binge drinking was found in the reaction time (data not shown). No other effects were found in this task (Fs<1.00) or in the multiple choice reaction task. Units per week entered as covariate did not affect any of the results.

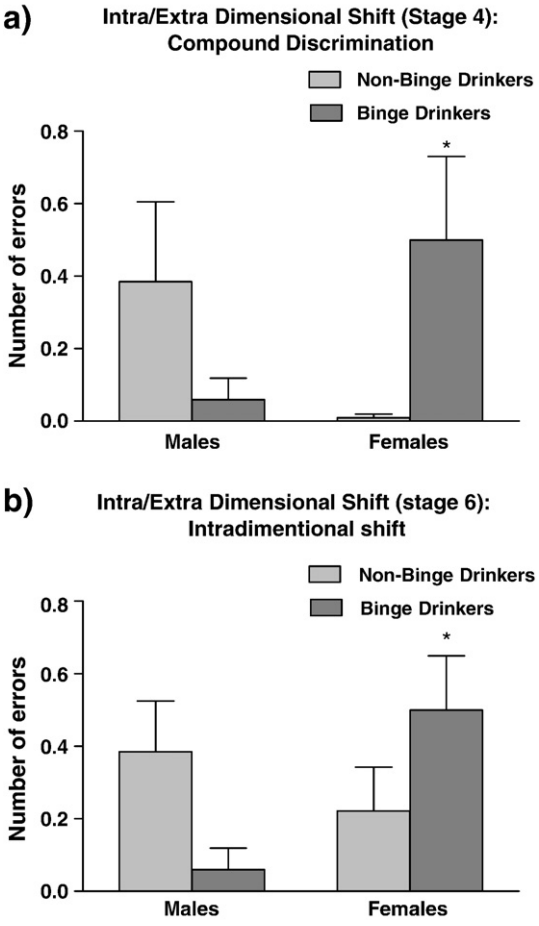

Fig. 3. Number of errors in the compound discrimination (a) and intradimensional shift stage (b; mean + SEM) in the CANTAB extradimensional and intradimensional shifts and reversal task for male and female binge and non-binge drinkers. *$p<0.05$ compared to female non-binge drinkers (independent samples *t*-test).

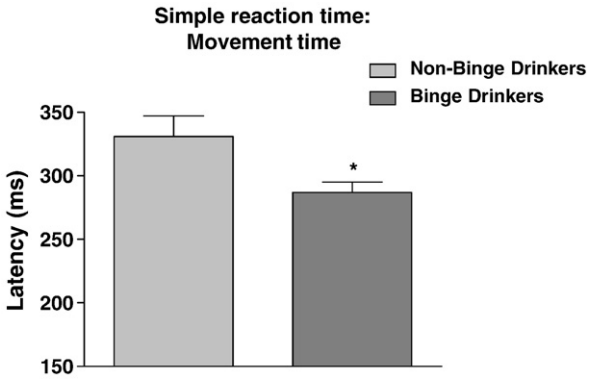

Fig. 4. Movement time (ms; mean ± SEM) for the CANTAB simple choice part of the Reaction Time Task for non-binge and binge drinkers. *$p<0.05$ compared to non-binge drinkers (independent samples *t*-test).

4. Discussion

The present study set out to examine differences in cognitive performance associated with frontal but also temporal lobe and hippocampal function between groups with different drinking patterns. Personality traits, mood and alcohol outcome expectancies were also examined as variables that may predispose individuals to certain drinking patterns. In order to classify the population of young drinkers into those who were and were not binge drinkers, we used a questionnaire, previously developed, which detailed drinking behaviour rather than simply assessing the quantity of alcohol consumed (AUQ, (Townshend and Duka, 2002, 2005). In previous studies we have demonstrated differences in cognitive performance between comparable groups of healthy young adults who differed only in their drinking behaviour patterns.

In the present study, the groups were well matched for age and IQ, but binge drinkers consumed more alcohol than the non-binge drinkers. Drug use and smoking habit did not differ between the two groups. Impairment in performance was found in most of the tasks in binge drinkers when compared to non-binge drinkers. This impairment was mostly associated with tasks testing frontal lobe function, in particular dorsal and medial parts of the prefrontal cortex. Although binge drinkers consumed more alcohol per week than non-binge drinkers, units of alcohol drunk per week did not significantly interact with the impairments found in binge drinkers when compared to non-binge drinkers. Thus it appears that the binge pattern of drinking is the main factor associated with frontal lobe dysfunction seen in young heavy social drinkers.

The Profile of Mood States Questionnaire showed higher arousal ratings in females (both binge drinkers and non-binge drinkers) than males. The negative mood state found in binge drinkers in a previous study (Townshend and Duka, 2005) was not seen in the current study. The populations in the two studies were equal with regard to their age and drinking habits; however there were more cannabis users among the binge drinkers in the previous study (22 out of 38) compared to cannabis users among the binge drinkers in the present study (10 out of 30). We do not know how cannabis use might have contributed to the negative mood found among binge drinkers in the previous study. There are reports suggesting a higher incidence of depressive mood among cannabis users especially at a period of abstinence (Hasin et al.,

2008). The participants in our studies (both the present and the previous one (Townshend and Duka, 2005)) are asked to abstain for at least one week from recreational drug use.

An important factor, which may contribute to binge drinking behaviour may be positive alcohol expectancies ((Blume et al., 2003; Mooney et al., 1987). In the present study, female binge drinkers gave a high rating on the positive alcohol expectancy rating ("liquid courage") compared to female non-binge drinkers. Female binge drinkers gave also high ratings for the questions which combined to give the expectancy factor "Negative Perception". Therefore female binge drinkers judged alcohol to give liquid courage, but also expected alcohol consumption to result in negative consequences. The ratings for the two factors were associated positively. To our knowledge there are no reports of the impact that negative expectancies may have on alcohol binge drinking behaviour. One study has looked at the effect that possible expected losses from alcohol, as a measure of negative alcohol expectancy, has on future changes of established binge drinking behaviour (Blume et al., 2003). Negative expectancies in the form of alcohol-related losses had no predictive value for reduction of binge drinking overtime, whereas low positive alcohol expectancies did.

Another study looking at the evaluation of expected alcohol problems found a positive relationship between the number of binge drinking sessions and expected alcohol-related problems (Gaher and Simons, 2007). As in the current study, Caher and Simons found that male heavy drinkers evaluated alcohol consequences less negatively than females. Thus high alcohol expectancies, either positive or negative may relate to binge drinking behaviour; low positive expectancies from alcohol seem to contribute to changing an established binge drinking to non-binge drinking behaviour, whilst high negative expectancies do not contribute to a change in behaviour.

As in our previous studies with young social drinkers we could not establish a relationship between personality characteristics and binge drinking behaviour.

The current study has replicated previous findings that binge drinkers make more between-search errors in the Spatial Working Memory task compared to non-binge drinkers (Townshend and Duka, 2005; Weissenborn and Duka, 2003). In accordance with the finding in one of the two previous studies (Townshend and Duka, 2005) impaired performance in the task showed a tendency to be present only in the female population. Similarly only female drinkers showed a tendency for an impaired strategy in this task. We have argued that female drinkers, although they consume less alcohol, may become drunk more often when drinking, experiencing more of the neurotoxic effects of alcohol. The Spatial Working Memory task reflects frontal lobe function and in particular dorsolateral prefrontal cortex (e.g. (Johnston and Everling, 2009)). The prefrontal cortex is an area most vulnerable to the neurotoxic effects of alcohol use. Studies on brain morphometry have shown that sufferers from alcohol use disorders have smaller PFC total volume (Kubota et al., 2001), and reduced gray (Chanraud et al., 2007) and white (Pfefferbaum et al., 1997) matter volume compared with controls. The PFC is an area of the brain which continues to mature until individuals reach their early twenties. There are studies showing active pruning of gray matter (Gogtay et al., 2004; Lenroot and Giedd, 2006) in the PFC during late adolescence. White matter increases in volume (Giedd et al., 1999) and presents with increased axonal fiber organization (Ashtari et al., 2007) also during late adolescence (see also (Crews et al., 2007)).

Especially relevant to the present study is the finding of a gender difference in neuromaturation (Nagel et al., 2006), which may underlie different gender responses to the neurotoxic effects of alcohol; during the years of age from 15 to 18, PFC gray matter was shown to decrease in females but increases in males. Furthermore, females with alcohol use disorders demonstrated less PFC response (suggestive of reduced function) when performing a Working Memory Task than female controls, whilst males showed an opposite pattern (Caldwell et al., 2005). A recent study (Medina et al., 2008) has reported smaller PFC volumes in young females (between 15 and 17 years of age) with alcohol use disorders compared with same gender controls. Participants in our study were over 18 years of age. However, although the studies mentioned above were carried out with younger participants, recent reports confirm that PFC maturation continues for some years after 18 years of age (Casey et al., 2000; Gogtay et al., 2004). These data taken together suggest that females may be more vulnerable to neurotoxic effects of alcohol.

In the present study, female binge drinkers were also found to be more impaired compared to female non-binge drinkers in the IED task, whereas no difference was found between male binge and non-binge drinkers in this task.

The IED task from the CANTAB is based on the Wisconsin Card Shorting Test but it offers a better separation of ID and ED shifts and rule acquisition as it separates into blocks the trials that require distinct types of discrimination learning. The task also measures reversal i.e. the ability to withhold a response from a previous rewarded stimulus and to direct a response to a previously not rewarded stimulus. In the current study the impairments of performance in the female binge drinkers were seen in discriminations based on attentional processes (discrimination and shift trials) and not in reversal trials. As shown previously from lesion studies with primates, shift learning performance is based on intact dorsolateral prefrontal cortex whereas reversal learning is based on intact orbitofrontal cortex (Dias et al., 1996). A further dissociation of binge drinking effect in females was found for the ID and ED shift. Female binge drinkers were impaired in ID but not in ED shift. ED and ID shift have been shown to relate to different functional systems in the brain with, for instance, ED shift requiring fronto-striatal pathways and ID relying mainly on PFC function (Rogers et al., 2000; Watson et al., 2006). Furthermore, the impairments seen in the task in the present study were not restricted to ID shift phase but were also present during the compound discrimination phase (stage 4). We would like to suggest that attentional processes associated with rule acquisition might be the cognitive processes that are vulnerable to binge drinking effects in this task. Indeed the compound discrimination trials require the subject to continue with a discrimination according to a rule (for example shapes) whilst lines are superimposed upon them (i.e. interference from irrelevant stimuli is increased). Similarly in the ID shift trials, participants must now learn a new rule relating to novel shapes, and continue to ignore the white lines. Thus in both sets of trials (compound discrimination and ID shift), a new rule acquisition is required; from then on, the general rule of the task must be well established. Thus performance in stages 4 and 6 is especially based on working memory (i.e. monitoring and manipulating information held online), which is related to dorsolateral prefrontal cortex function (D'Esposito et al., 2000). Thus the data from the Spatial Working Memory and the IED task suggest that the binge drinking effect on female social drinkers may be associated with damage to dorsolateral prefrontal regions.

Binge drinking was found to affect both males and females with regard to the PAL, a spatial memory task in which binge drinkers made more errors on the first trial, than non-binge drinkers. On the second repetition of the task, the two groups were not significantly different in their ability to identify the locations, although total number of errors and number of trials were marginally higher in binge drinkers when compared to non-binge drinkers. PAL is a task that relies on prefrontal function but it also depends on temporal lobe and hippocampal function (Owen et al., 1995). It has been suggested that prefrontal function is important for the development of strategies in learning (e.g. elaboration of objects), whereas temporal lobe and hippocampal function are related to mnemonic processes. The present findings are in accordance with previous data, which demonstrated that adolescents with AUD suffer memory deficits and show reduced left hippocampal volumes when compared to their control counterparts (Nagel et al., 2005). Thus the data from the present study indicate that binge drinking is associated not only with frontal lobe, but also with temporal lobe and hippocampal dysfunction. Furthermore the present data suggest that

male binge drinkers are more susceptible to temporal lobe and hippocampal dysfunction than to PFC dysfunction. These different patterns of dysfunction related to binge drinking may derive from the differential time of neuronal development of these structure with age (e.g. (Gogtay et al., 2004) and gender (Nagel et al., 2006).

Binge drinkers compared to non-binge drinkers were faster on a simple Reaction Time Task. However it was the movement time and not the reaction (thinking) time that was consistently faster, more suggestive of a motor impulsivity in binge drinkers. Similar data were obtained previously with the matching to sample task (Townshend and Duka, 2005) and again binge drinkers were faster than non-binge drinkers with regard to the movement rather than to the thinking time. As the task was quite easy and there were very few errors overall, it is possible that errors may have been higher in the binge drinking group had they been given a more difficult task. However there were no differences between binge and non-binge drinkers in the more complex version of the task, in the 5-choice Reaction Time Task in the present study. Paradoxically it appears that binge drinkers might perform better in response execution with regard to a visuospatial task. However, we would like to propose that it is impulsivity and motor disinhibition that possibly accounts for the binge drinkers' performance in this task. Further studies should address this question further. The data on the RTI task are in contrast to the findings by (Kokavec and Crowe, 1999), who showed no differences between two subgroups (a "binge" and a "non-binge" drinkers group) of alcohol dependent individuals in a visuomotor speed and a visuospatial search task. However, their study cannot be directly compared to ours, because their method of classifying individuals as binge drinkers was different. Kokavec and Crowe's did not take into account the incidence of drunkenness as a component of binge classification. In addition the tasks used were different; the visual search and motor speed were taken from the Trail making test (Part A and B) from the Wechsler Memory Scale Revised. The trail making task does not separate reaction (thinking) from movement time of response as the Reaction Time Task in our study does. These differences in the procedure between our study and that of Kokavec and Crowe may account for the discrepancy of the findings.

Previous studies examining drinking habits (Deckel et al., 1995) or the adverse consequences of drinking (Giancola et al., 1996) in young adult social drinkers, have shown a relationship between impaired executive function and both the frequency of drinking to "get high/drunk" (Deckel et al., 1995) or the severity of drinking consequences (Giancola et al., 1996). Some of the impairments in certain cognitive tasks, including those found in the present study, may be premorbid and may contribute to the aberrant drinking patterns (including binge drinking) reported in the above studies. Further, it cannot be excluded that the females in the present study showing higher ratings both in "liquid courage" and "negative perception" alcohol expectancy represent a group predisposed to binge drinking and with impaired performance in certain frontal lobe tasks. Nevertheless, data from animals suggest that binge drinking can induce cortical damage and lead to cognitive deficits including perseverative responding in a spatial learning task (Obernier et al., 2002b) that cannot reflect pre-existing changes. It is acknowledged however that only a prospective study investigating cognitive performance in adolescents before and after they start binge drinking would clarify these questions. Further studies incorporating structural and functional MRI during adolescence would also help to establish cause and effect.

In summary, these results suggest that binge drinking is related to differences in cognition in non-dependent young healthy social drinkers. Using a sensitive battery of tasks from the CANTAB it was possible to demonstrate the effects of binge drinking on frontal and temporal lobe as well as hippocampal function. Since these effects were not associated with total alcohol consumption, we can conclude that patterns of drinking may reveal differences that quantity of alcohol consumed does not, and may be more analogous to the effects of repeated detoxification seen in alcoholic patients (intermittent alcohol intoxication; see for a review (Stephens and Duka, 2008)). In particular the results have revealed that binge drinking is associated with impaired performance in cognitive tasks to a greater extent in females than males, especially in tests of frontal lobe function.

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