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Evidence of deficits in behavioural inhibition and performance monitoring in young female heavy drinkers

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ABSTRACT

Background: New models of the development and maintenance of substance abuse give increasing importance to the role of deficits in inhibitory function. Much of the evidence to support this claim comes from male participants, despite some researchers showing greater disinhibition in females. Clearly, more research on female heavy drinkers is warranted. In this study, we examine behavioural and psychophysiological measures of inhibitory function in female young adults who do and do not regularly drink heavily.

Methods: Participants were thirty female young adults (aged 18–21) who drink heavily (four or more standard drinks per occasion) at least once a month ($n = 13$) or who drink heavily less often than this ($n = 17$); none regularly used any other drugs, including tobacco. They underwent interviews assessing prior use of alcohol, before completing a stop-signal task while brain electrical activity was recorded.

Results: Regular heavy drinkers displayed a longer stop-signal reaction time (the time required to stop an inappropriate response), and a larger P3 increase for successful compared to failed inhibition trials. Heavy drinkers also displayed a smaller error-related negativity (ERN) amplitude, indexing a deficit in performance monitoring.

Conclusion: These results indicate that large deficits in inhibitory processing and performance monitoring occur in young female heavy drinkers, and that heavy drinkers may have to work harder in order to successfully inhibit a response. Future research may determine whether these deficits pre-date or are caused by alcohol abuse.

1. Introduction

Deficits in inhibitory control have attracted a great deal of attention as a factor contributing to both the development and maintenance of substance abuse (Hester et al., 2010; Lubman et al., 2004; Field et al., 2010), such that substance abusers are less able to control use behaviour in the face of an opportunity to use. Disinhibition is known to be present in adult alcohol-dependent groups (e.g., Goudriaan et al., 2005; Kamarajan et al., 2005; Noël et al., 2007), but the effect is less clear with heavy drinkers, with some studies finding significant deficits (e.g., Murphy and Garavan, 2011; Petit et al., 2012; Rubio et al., 2008) and others finding no relationship between inhibition and heavy drinking (e.g., Henges and Marczinski, 2012; López-Caneda et al., 2012; Yan and Li, 2009; Fernie et al., 2010). One experimental paradigm commonly used to study inhibition is the stop-signal task (Logan et al., 1984; Logan, 1994), in which participants press buttons with the left or right hand to different stimuli (Go stimuli). On a random 25% of trials, an auditory 'Stop' stimulus is delivered at variable delays after the Go stimulus, and indicates that participants should withhold the response. Inhibition is more difficult when the stop-signal delay is longer, as response processes to the Go stimulus are closer to completion when the signal to inhibit occurs. The time required to stop a response (the stop-signal reaction time, or SSRT) can be calculated from the probability of inhibition at different delays and is the primary measure of interest in the task.

Several studies using the stop-signal task have found evidence of disinhibition in alcohol-dependent groups, reflected in a significantly or numerically longer SSRT in most studies (Goudriaan et al., 2006; Lawrence et al., 2009; Rubio et al., 2007; van der Plas et al., 2009; but see Li et al., 2009; Schmaal et al., 2013 for the opposite effect). Similarly, comparisons of variously defined heavy and light social drinkers also mostly report numerically longer SSRT (Moreno et al., 2012; Nederkoorn et al., 2009; Rubio et al., 2008; but see Papachristou et al., 2011; Yan and Li, 2009, for the opposite effect). However, it is worth noting that the majority of participants in these studies are male, overwhelmingly so for the studies on dependent groups. Nederkoorn et al. have shown that heavy drinking is associated with disinhibition in females but not males (see also Townshend and Duka, 2005); this may account for the small

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effects observed in some previous studies. Clearly, more research into the possibility of disinhibition associated with heavy alcohol use in women is warranted. In this study, we examine female young adults who report episodic heavy drinking (defined as consumption of four or more standard drinks per occasion) at least monthly, in comparison to those who drink heavily less often than this.

Many studies also report gender differences in the effect of alcohol abuse on brain structure and function (e.g., Squeglia et al., 2011; Hommer, 2003). Thus, we also examined brain electrical activity during the inhibitory control task. The P3 is a frontocentrally maximal potential peaking 300–600 ms after the stop-signal, and is reliably larger on trials where inhibition is successful (i.e., no response is made) compared to those where inhibition fails (i.e., a response is made, e.g., Kok et al., 2004), and is considered an index of response inhibition (e.g., Smith et al., 2008). There are no published papers examining failed and successful P3 to stop-signals in heavy drinkers compared to controls, but most prior research using a different motor inhibition task has reported reduced inhibitory P3 in heavy drinkers (Colrain et al., 2011; Kamarajan et al., 2005; Oddy and Barry, 2009; Cohen et al., 1997, but for different results see also Karch et al., 2008; Fallgatter et al., 1998).

We also examined the Error-Related Negativity (ERN), a brain potential peaking 50–100 ms post-response, maximal at the frontal midline site, and arising from the anterior cingulate cortex (Yeung et al., 2004). The ERN is an index of performance monitoring in general, although interpretations vary between the detection of an incorrect motor response (Falkenstein et al., 2000), a signal that outcomes are worse than expected (Holroyd and Coles, 2002), or negative affect related to error commission (Hajcak and Foti, 2008). Previous studies have reported reduced ERN amplitude or anterior cingulate error-related hypoactivity in substance-dependent individuals using a range of experimental tasks (Fein and Chang, 2008; Forman et al., 2004; Franken et al., 2007; Hester et al., 2007; but see Schellekens et al., 2010 for an increased ERN in alcohol dependence). In this study, we examine whether such a deficit in performance monitoring also exists in young female heavy drinkers performing a stop-signal task.

2. Materials and methods

2.1. Participants

Participants were 30 females aged 18–21 years, who were recruited into two groups: those who engaged in heavy drinking (4 or more Australian standard drinks, equal to 40 g alcohol, on one occasion) at least monthly in the preceding 12 month period ('heavy drinkers' group, $n = 13$), and those who engaged in heavy drinking less often than this ('control' group, $n = 17$). Fifteen controls and 10 heavy drinkers were right-handed ($\chi^2 = 0.679$, df = 1, $p = .410$). Participants were recruited via posters displayed on the university campus, and were excluded if they had ever had an epileptic seizure, a serious head injury or period of unconsciousness, uncorrected hearing or vision problems, or regular (at least twice a month) use of other drugs. Additionally, participants reported no use of medication other than the contraceptive pill and/or antibiotics, and one participant in each group reported a prior diagnosis of depression. The pattern of results was unchanged when these participants were removed. All participants gave written informed consent, and the protocol was approved by the University of New South Wales Human Research Ethics Committee before data collection began.

Testing sessions lasting 2 h were scheduled for the vast majority between 9 am and 5 pm, Monday to Friday at a time that suited the participant. Most of the time, participants were completing the study directly before or after a university class, thus it is unlikely that participants were intoxicated at the time of testing. However, we did not perform a check on blood/breath alcohol concentration, nor did we ask participants to refrain from alcohol prior to testing, so we cannot definitively say that no participants were under the influence of alcohol at the time of testing.

The experimenter showed the participant the lab and recording equipment and described the experimental protocol before written informed consent was obtained. Participants then completed a short demographics questionnaire and modified versions of the Alcohol Use Disorders Identification Test (AUDIT, Saunders et al., 1993) and the Drug Use Disorders Identification Test-Extended (DUDIT-E, Berman et al., 2007). Question 3 of the AUDIT was modified from "How often do you have six or more standard drinks on one occasion?" to "four or more standard drinks" to reflect Australian alcohol consumption guidelines (National Health and Medical Research Council, 2009). Participants were requested to reference a standard drinks guide provided while they completed this section. Only the first section of the DUDIT-E was administered, and was used to screen participants for eligibility to the study. That section assesses the frequency of use of a range of drug classes other than alcohol, with the options: Never (score = 0), Tried it once or more (1), Once a month or less often (2), 2–4 times a month (3), 2–3 times a week (4), 4 times a week or more (5). Eighteen participants had a total score of zero, and no participant in this study scored more than 2 for any drug class. Use of tobacco does not contribute to the total score; 8 controls and 9 heavy drinkers had never tried tobacco, 7 controls and 3 heavy drinkers had tried it once or more, and 2 controls and 1 heavy drinker used tobacco once a month or less. Thus, the distribution of tobacco use was matched across groups ($\chi^2 = 1.485$, df = 2, $p = .476$), and controls and heavy drinkers were not regular users of any other drug including tobacco. Table 1 shows the demographic characteristics of the participants included in the study.

All participants also underwent structured interviews assessing lifetime alcohol use and lifetime cannabis use (collected for a separate study) using a modified version of the Lifetime Drinking History interview (Skinner, 1977). This assesses the frequency and quantity of alcohol consumption in relatively homogenous phases from the age of first regular drinking (one standard drink per month), and can be used to assess the number of standard drinks consumed in the participant's lifetime. Participants referred to the standard drinks guide during the alcohol section of the interview.

2.2. Stimuli and procedure

The Go stimuli were green arrows pointing to the left and right, which appeared above a grey central fixation cross on a black background. The fixation cross was continuously present throughout the experiment, while Go stimuli were presented for 1000 ms with a mean 1500 ms SOA (range 1200–1800 ms). Participants were required to press the 'S' button on a computer keyboard with their left index finger on presentation of the leftward arrow, and press the 'L' button with their right index finger to the right arrow. On a random 25% of trials a stop signal was presented indicating that the participants should attempt to inhibit their response. The stop-signal was a 1500 Hz pure tone lasting 200 ms with 20 ms rise and fall time, presented binaurally via headphones at a comfortable loudness which was the same for all participants. Participants completed 4 blocks of 120 trials each, as well as 50 practice trials.

The stop-signal delay was varied relative to each subject's mean reaction time (MRT) to Go stimuli in the preceding block. This procedure allows for theoretically equivalent calculation of the SSRT (Logan et al., 1984; Logan, 1994) compared to other methods (such as the staircase method used by Papachristou et al., 2012), but additionally counteracts strategic slowing by the participant. MRT was calculated from correct no-stop-signal trials only, and stop-signals were presented at fixed intervals prior to MRT (here, around 480 ms), at either (MRT – 450) ms (i.e., shortly after the Go stimulus, so that inhibition is easy), (MRT – 350) ms, (MRT – 250) ms, (MRT – 150) ms, and (MRT – 50) ms (i.e., a long time after the Go stimulus and relatively close to the expected response time, so that inhibition is difficult). Where the above formula would result in stop-signals being presented before the Go stimulus, stop-signals were instead presented simultaneously with the Go stimulus (Dimoska and Johnstone, 2007; Dimoska et al., 2006). There were three presentations of each delay for each (left and right) Go signal per block. Go MRT from the practice block was used to set the delay for the first experimental block. In the practice block, stop-signals were set to occur at delays of 100 ms, 200 ms, 300 ms, 400 ms, and 500 ms after the Go stimulus, with one presentation at each delay for both left and right arrows.

This method counteracts strategic slowing (i.e., participants slowing responses to the Go stimulus in order to increase the chances of inhibition should a stop-signal occur) by delaying stop-signals by an equivalent amount in the subsequent block, so that the probability of inhibition is kept relatively constant over time. To further counteract slowing, participants were instructed not to wait for the tone as they would be unable to stop their response on every trial, and the experimenter noted changes in mean RT displayed at the end of the block and notified participants if this was variable. Furthermore, if participants did not respond within 1000 ms, the Go stimulus was replaced with the words 'TOO SLOW' for 500 ms, and participants were advised to avoid this.

Following the questionnaires and interviews (together lasting approximately 30 min), the EEG cap was fitted (taking 30 min), and participants completed the stop signal task, described above, within the 20 min interval in a modified Rey Auditory Verbal Learning Test, followed by a decision making task and an attentional bias task, not reported here, with the four experimental tasks taking a further hour. Participants were given short rest breaks between blocks and tasks. At the end of the study, participants received a $20 iTunes voucher and $10 cash for their participation, and advertising fliers to pass on to friends who may be eligible and interested to participate.

2.3. Electrophysiological recording

Continuous monopolar EEG was recorded from 58 scalp sites using an elasticised cap with tin electrodes. Additional tin cup electrodes recorded activity from the left and right mastoid as well as vertical and horizontal EOG. All electrodes were