Psychosocial Stress Increases Craving for Alcohol in Social Drinkers: Effects of Risk-Taking

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Abstract

Background

Exposure to stress and trait impulsivity are independent predictors of relapse in recovering alcoholics, but potential mechanisms that link these two risk-factors in terms of their putative additive or interactive contributions to relapse are not known. The aim of this study was to use a model of stress-induced relapse to test the hypothesis that acute psychosocial stress increases craving for alcohol in social drinkers. We also tested the hypothesis that change in craving could be explained by variability in impulsivity and risk-taking.

Methods

Participants completed questionnaires to assess drinking behaviour (Alcohol Dependence Questionnaire [ADQ]; and an Alcohol Use Disorders Identification Test [AUDIT]), craving (Desires for Alcohol Questionnaire [DAQ] and impulsivity (Barrett Impulsiveness Scale [BIS]). Participants also completed two computer tasks to assess risk-taking and impulsivity, the Balloon Analogue Risk Test (BART) and a continuous performance task (CPT). Participants then underwent the Trier Social Stress Test (TSST), and completed a final DAQ to assess post-stress craving.

Results

Participants showed an increase in craving following exposure to the TSST. In addition, risk-taking was positively correlated with change in craving.

Conclusions

Our data suggested that acute psychosocial stress increases subjective craving in social drinkers, but that the effects may be trait-dependent, with stress-induced increases in craving correlated with risk-taking.

Keywords: alcohol; relapse; risk-taking; impulsivity; stress; craving

1. Introduction

Long-term excessive alcohol use may escalate in some individuals into alcohol addiction ('alcoholism', including tolerance, withdrawal, compulsive alcohol seeking, anhedonia, social/familial problems) (Skinner and Allen, 1982). Like many addictions, alcoholism is a chronic relapsing disorder. Despite decades of accumulating evidence for the need to address chronic relapse in treatment programmes, little cogent progress has been made (Harris and Koob, 2017).

Psychological stress is an important risk factor for relapse in abstinent alcoholics, and the neural mechanisms by which stress induces relapse are fairly well established. Chronic alcohol use results in neuroadaptations, in particular, in stress and reward pathways. Subsequently, alcoholic patients show dysfunction of stress (e.g., sympathetic adrenomedullary axis; SAM; and hypothalamic pituitary adrenocortical axis; HPA) pathways, characterized by (for example) dysregulation of the cortisol response (Kreek and Koob, 1998), and/or deficits in emotional regulation (Sinha, 2001). These neuroadaptations may lead to alcoholic patients showing increases in craving for alcohol in response to stress, and thus being particularly at risk of relapse. However, there is significant variability in risk of relapse within patient groups, making it very difficult to predict the latency to, and likelihood of, relapse in individuals (Sinha et al., 2011).

Trait impulsivity -- the tendency to take risks, or act without adequate forethought or reflection (Dalley et al., 2011) -- is a risk factor in predicting those who develop compulsive (addictive) states and those at high risk of relapse following treatment (Bowden-Jones et al., 2005; Lawrence et al., 2009). In fact, trait impulsivity has been shown, in animal models, to be a potential causative factor for compulsive drug seeking, with drug-naïve animals high in trait impulsivity being more at risk of

developing compulsive drug seeking (Belin et al., 2008; Molander et al., 2011). In addition, impulsivity and cumulative stress interact to predict problem drinking in healthy (social) drinkers (Fox et al., 2010). It may be, therefore, that those high in impulsivity would show increased stress-induced craving.

If we were better able to predict those that were at risk of stress-induced relapse -- for example, by understanding more about underlying traits that put some more at risk -- this would help in the development of stratified interventions to prevent relapse. A logical first step to gaining this increased understanding of how personality traits might influence relapse is to characterize personality traits in relation to stress-induced craving in healthy, social drinkers. This first step will allow us to determine if there exists a generalized mechanism by which personality traits impact upon stress-induced changes in alcohol craving. The first aim of this study was therefore to test the hypothesis that an acute psychosocial stressor (the Trier Social Stress Test; TSST (Kirschbaum et al., 1993)) would increase subjective craving for alcohol in a healthy (non-alcoholic) sample of social drinkers. The second aim was to test the hypothesis that different subtypes of impulsivity and risk-taking would influence stress-induced craving for alcohol, with those high in impulsivity and risk-taking showing higher rates of stress-induced craving.

2. Methods

2.1. Participants

Thirty-one undergraduate participants were recruited (11 male; mean age = 21.68 years [SD = 3.4]) following an internal advertisement via email or by word-of-mouth. Participants were initially screened for suitability using a series of self-report measures: exclusion criteria included aged < 18; currently undergoing treatment for

alcoholism; in the past year undergoing any treatment for anxiety or depression. As an additional measure to screen for depression and anxiety, potential participants were also asked to complete the Patient Health Questionnaire for Depression and Anxiety questionnaire (PHQ-4 (Kroenke et al., 2009)). A key exclusion criterion was anyone scoring high (>5) on the PHQ-4; however, no participants in the current study scored >5. The study was approved in its current form by the University of Portsmouth Science Faculty Ethics Board (ref: SFEC 2016-068).

2.2. Alcohol use and Drinking Behaviour

To assess drinking behaviour, participants reported the total units of alcohol usually consumed each day. Participants also completed an adapted 12-item version of the Alcohol Dependence Questionnaire (ADQ; (Skinner and Allen, 1982)) and the Alcohol Use Disorders Identification Test (AUDIT; (Bush et al., 1998)). AUDIT is scored on a scale of 0-40, where scores of >20 would be considered dependent on alcohol, and >30 severely dependent. The ADQ is based primarily on diagnosing the physiological aspects of alcohol dependence (e.g., withdrawal), and has been shown to have good psychometric properties as a test of alcohol dependence, including having cross-cultural and clinical efficacy (Allen et al., 1994; Doyle and Donovan, 2009; Willenbring and Bielinski, 1994). The ADQ is scored on a scale of 0-47, with scores >21 being classified as dependent on alcohol, and >30 as severely dependent.

2.3. Impulsivity and Risk-Taking

Impulsivity and risk-taking were assessed using both questionnaire (explicit) methods and computer based (implicit) measures. The Barratt impulsiveness scale

BIS-11 (Patton et al., 1995) is a validated and reliable questionnaire designed to assess the personality/behavioural construct of "impulsivity". It has been used both in research and clinical settings for many years, and is the most widely used psychometric instrument for assessing impulsivity. Implicit measures of impulsivity and risk-taking involved two computer tasks, the Conners Continuous Performance Test (CPT; impulsivity (Conners et al., 2003; Epstein et al., 2003)) and the Balloon Analogue Risk Task (BART; risk-taking (Lejuez et al., 2002)), respectively (see Fig 1).
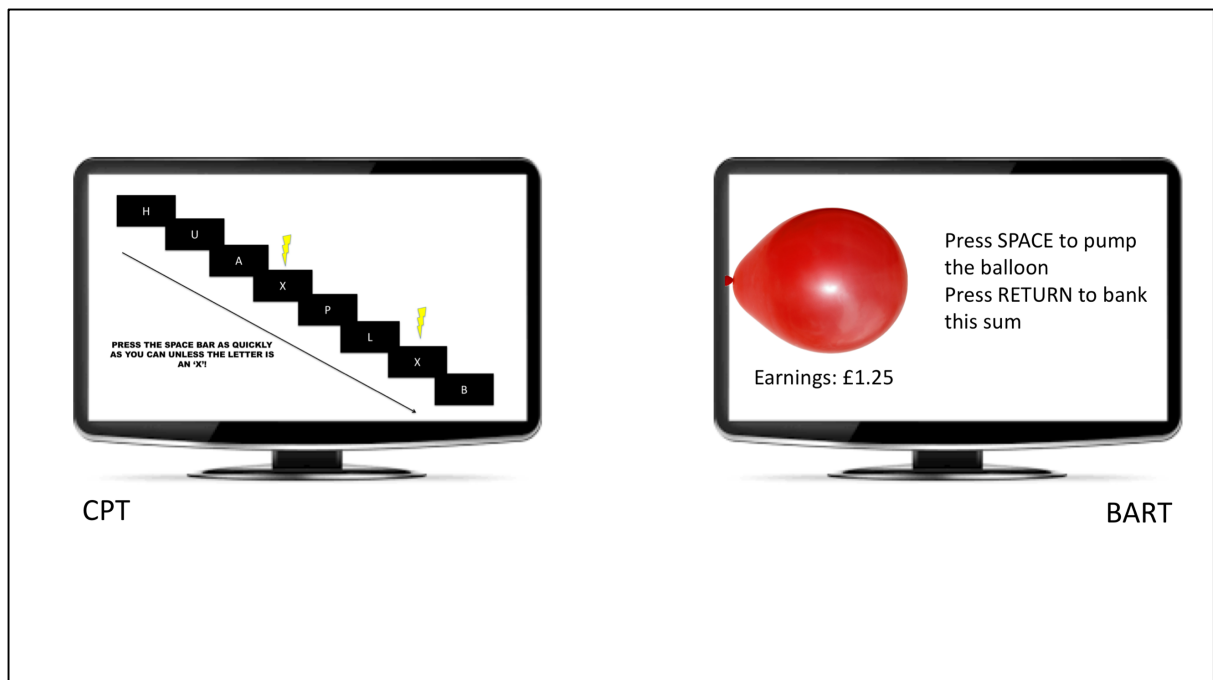

Fig 1. Screenshots of computer tasks administered to participants. CPT – continuous performance task; BART – balloon analogue risk task.

The CPT is a neuropsychological test of impulsivity that has regularly been shown to have efficacy in differentiating impulsive clinical (e.g., attention-deficit hyperactivity disorder [ADHD], conduct disorder) and non-impulsive (normative) populations (Epstein et al., 2003). In this task, the participant was faced with a blank computer screen, upon which letters flashed up every 2-seconds, and remained for

0.5-seconds. The participant was asked to press the space bar on the keyboard as quickly as possible after each letter flashed up, except when the letter was 'X', when they should withhold responding. Dependent measures for this task included reaction time (ms), errors of omission (failing to press the space bar on all non-'X' letters), and errors of commission (pressing the space bar following 'X' presentations).

The BART is designed as a proxy measure of real-world 'risk-taking' behaviour by examining balances between potential for reward and loss. During the task, participants were given the opportunity to earn a (virtual) financial reward in return for inflating a balloon by clicking the space bar on the computer. Each click of the space bar inflated the balloon and increased the money on the counter until at some point, the balloon over-inflated and exploded. If the balloon exploded, the participant lost the money accrued on that trial. Alternatively, the participant was free to collect their winnings at any time (prior to the balloon exploding) and bank the money from that trial. The explosion point was withheld allowing for analysis of the early (pre-experience) responses, as well as the changes in responses after learning.

2.4. Craving

Craving was assessed using the 14-item version of the Desires for Alcohol Questionnaire (DAQ; (Kramer et al., 2010)). Participants rated (on a 9-point Likert scale [1 = 'Disagree completely': 9 = 'Agree completely']) a series of statements relating to their desires to drink alcohol at the time they are completing the measure. The questionnaire was scored such that it produced a single measure of craving for each participant, with high scores indicating greater desire for alcohol. Previous research on the psychometric properties of the DAQ have shown that alcoholic

patients have a DAQ score of 40.5, and healthy non-alcoholic drinkers, around 23.1 (Kramer et al., 2010).

2.5.   Procedure

Participants initially completed the BIS-11, DAQ, ADQ, AUDIT. All questionnaires were completed on a computer (Google forms). Participants then carried out the CPT and BART. The order of the two computer tasks and four questionnaires were counterbalanced to avoid order effects. Participants were then introduced to the TSST (Kirschbaum et al., 1993). The TSST protocol is split into three distinct stages: 1) Preparation and anticipation; 2) The speech; 3) The maths test. During stage 1, the preparation and anticipation, participants were told that in 10-minutes they will give a 5-minute speech to a panel of three people about their dream job, and what makes them the ideal candidate. Participants were then told that they would have to deliver this speech with no notes. During stage 2, the participants were led to an adjacent room in which a panel of two people sat at a table wearing lab coats and taking notes. There was also a video camera on a tripod in the room, trained at the position in which the participant was asked to stand (the video camera was a dummy, and no actual video files were kept). Participants were then asked to give their 5-min presentation to the panel. If they stopped speaking for more than 10-seconds, they were encouraged to continue and told how much time was remaining of their 5-minute slot. Finally, in stage 3, participants were asked to count backwards in 13s, starting at 1022, for 5-minutes. If they made an error, they were asked to start again at 1022. Participants then filled in a second DAQ. Finally, all participants were debriefed, during which time they were advised that the videos of their speech were dummy, and no data would be kept.

2.6. Data analysis

All data were analysed using SPSS for Macintosh (version 22). Raw data were examined for normality prior to analysis. Initially, all variables were analysed for sex differences using a series of independent-samples t-tests. Change in DAQ scores (pre- vs post-stress) was assessed using a paired-samples t-test. Owing to missing data (incomplete/unreadable questionnaires), two participants' responses (1 male and 1 female) were lost from the DAQ leaving n = 29 for analysis. We examined all data for intercorrelations (Pearson's). Descriptive statistics are reported as mean ± SEM. Statistics are reported with effect sizes (Cohen's *d*), and 95% confidence intervals [95% CIs]). Null-hypothesis statistical tests were evaluated according to an alpha value of *p* = .05.

3. Results

3.1. Sample Characteristics

Table 1 displays the sample characteristics, in terms of alcohol consumption, impulsivity and craving (pre-and post-stress). There were no differences between male and female participants in terms of the variables measured (*t*s < 1.49; *p*s > .15).

Table 1. *Demographic Characteristics of Sample, and Raw Data*

	Male (SD)	Female (SD)	Total
Demographic			
Age	22.09 (4.23)	21.45 (2.95)	21.68 (3.4)
N	11	20	31
Alcohol Use			
ADQ	11.73 (6.86)	8.53 (4.54)	9.79 (5.67)
AUDIT	12.36 (2.29)	11.8 (1.61)	12 (1.86)
Units per day	5.60 (2.87)	5.20 (2.61)	5.37 (2.68)
Impulsivity			
BART	23.56 (10.34)	25.25 (10.82)	24.65 (10.51)
CPT	.57 (.21)	.57 (.16)	.57 (.18)
BIS attention	17.09 (2.63)	16.9 (4.48)	16.97 (3.88)
BIS motor	23.82 (5.4)	21.8 (3.14)	22.52 (4.11)
BIS non-planning	22.09 (4.61)	23.15 (5.25)	22.77 (4.98)
DAQ			
DAQ pre-TSST	34.5 (14.17)	28 (11.73)	30.24 (12.76)
DAQ post-TSST	41.73 (20.48)	39.6 (25.49)	40.35 (23.50)

ADQ – Alcohol Dependence Questionnaire; AUDIT – Alcohol Use Disorders Identification Test; BIS – Barratt Impulsiveness Scale; BART – Balloon Analogue Risk Test; CPT – Conners Continuous Performance Task; DAQ – Desires for Alcohol Questionnaire. n.b., no significant sex effects were found for any variable, *p* > .1

3.2. *Effects of psychosocial stress on craving*

There was a significant effect on alcohol craving, with DAQ scores increased following the TSST (Fig 2), $t(28) = -2.36$, $p = .026$, Cohen's $d = .44$ [95% CI 1.2-17.2]
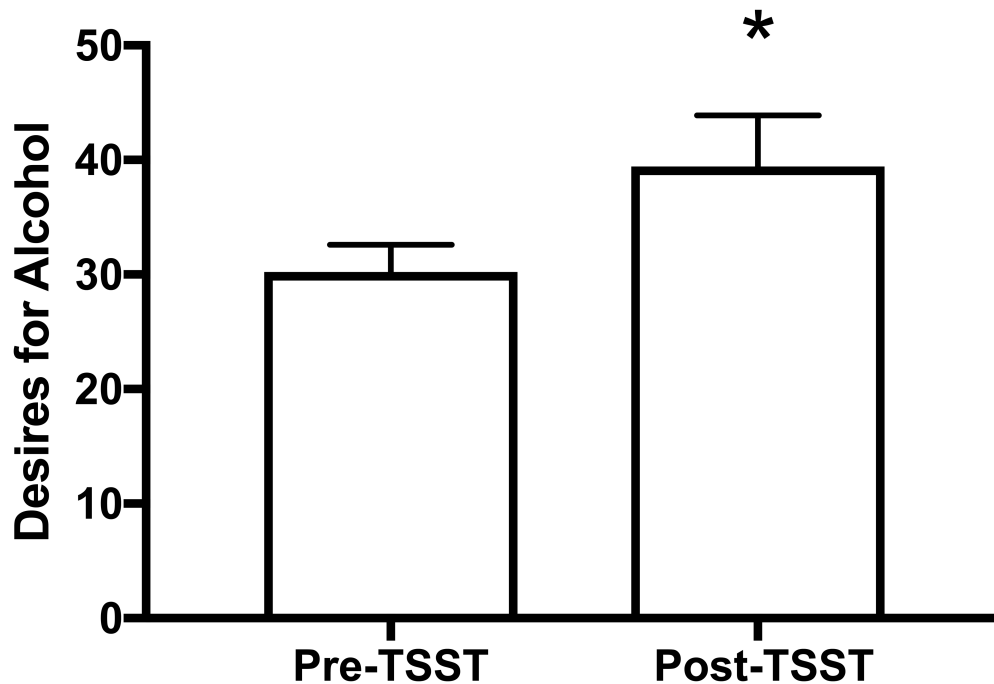
Fig 2. Mean (±SEM) Desires for Alcohol Questionnaire (DAQ) scores (high score = higher desire) prior to, and immediately following, the Trier Social Stress Test (TSST). *$p < .05$

3.3. Intercorrelations of measures

In order to explore the influence of impulsivity/risk taking on stress induced craving, we completed Pearson correlations between the main variables. Analysis revealed that impulsivity (BIS-Motor) was positively related to higher scores in ADQ, AUDIT, Alcohol units consumed. The main finding here however was that whilst a number of variables (ADQ, AUDIT, Alcohol units) were positively associated with baseline DAQ, the only variable to correlate with stress induced craving (i.e. change in DAQ) was risk taking (BART; see Fig 3).

Table 2. *Inter-correlations (Pearson's R values) of Measures*

	1	2	3	4	5	6	7	8	9	10	11	12
1. Age	-											
2. BART	-0.06	-										
3. CPT	0.07	-0.24	-									
4. ADQ	**-0.48***	0.18	-0.16	-								
5. AUDIT	**-0.44***	0.24	-0.13	**0.80****	-							
6. Units per day	**-0.60****	-0.09	0.09	**0.63****	**0.51****	-						
7. PHQ4	0.21	-0.05	**-0.40***	-0.11	-0.13	-0.35	-					
8. DAQ score pre-TSST	-0.23	-0.04	0.04	**0.75****	**0.66****	**0.51****	-0.04	-				
9. DAQ score post-TSST	-0.06	0.32	-0.26	0.28	0.28	0.06	0.19	**0.48****	-			
10. DAQ change (post-pre)	0.08	**0.40***	-0.30	-0.15	-0.09	-0.19	0.24	-0.07	**0.85****	-		
11. BIS (attentional)	0.20	0.05	0.01	0.23	0.04	-0.01	0.27	0.14	0.12	0.05	-	
12. BIS (motor)	**-0.38***	0.18	0.21	**0.61****	**0.54****	**0.51****	-0.33	**0.54****	0.35	0.04	0.20	-
13. BIS (non-planning)	-0.23	0.11	0.28	0.27	0.21	0.37	-0.22	0.03	0.09	0.11	**0.38***	**0.52****

ADQ – Alcohol Dependence Questionnaire; AUDIT – Alcohol Use Disorders Identification; BIS – Barratt Impulsiveness Scale; BART – Balloon analogue risk test; CPT – Conners Continuous Performance Task; PHQ4 - Patient Health Questionnaire for Depression and Anxiety; DAQ – Desires for Alcohol Questionnaire. *$p < .05$; **$p < .01$
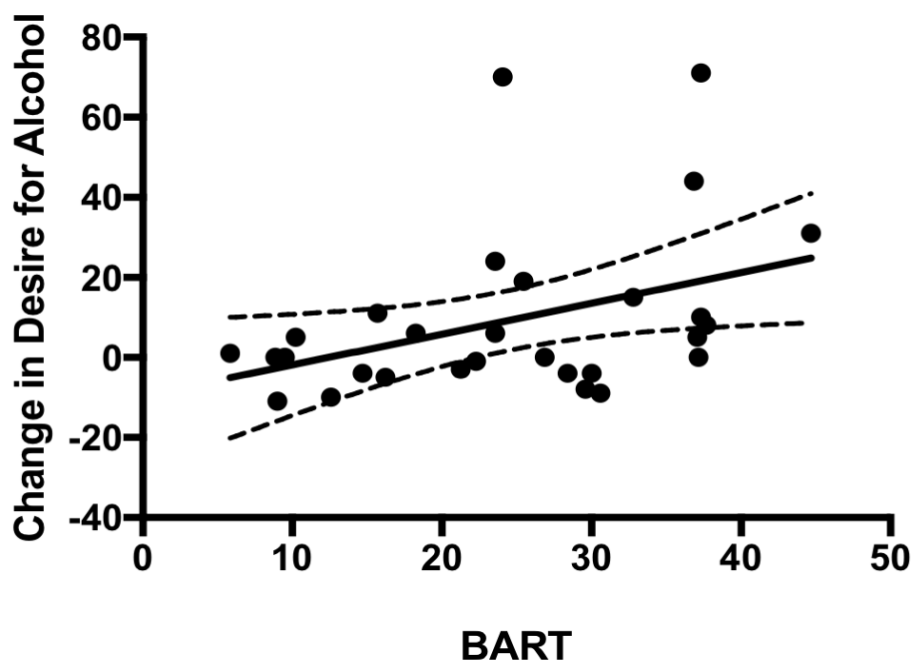

Fig 3. Relationship between change in Desires for Alcohol (DAQ) and score on risk-taking (BART). Dashed line = 95% CI.

4. Discussion

The primary aim of this study was to test the hypothesis that an acute psychosocial stressor would increase craving for alcohol in social drinkers. We found support for this hypothesis, with self-reported craving for alcohol increasing following exposure to the TSST. The second aim was to test the hypothesis that trait impulsivity and risk-taking would impact upon changes in stress-induced craving for alcohol. We found partial support for this hypothesis, with changes in craving being positively correlated with scores on the BART test of risk-taking. However, there was no correlation between change in craving and any other measures of impulsivity.

Clinical research with alcoholic and cocaine-addicted patients showed increases in craving for alcohol and cocaine, respectively, following exposure to stress-inducing imagery (Sinha et al., 2011). Our data are the first to demonstrate that acute psychosocial stress increases craving for alcohol in a healthy, non-alcoholic sample. Our results are similar to those observed in habitual tobacco smokers, who showed increases in craving for tobacco following psychosocial stress using the TSST (Buchmann et al., 2010). Interestingly, the smokers in the Buchmann et al. (2010) study showing the strongest increase in psychosocial stress-induced craving were not the most 'dependent' individuals (Fagerstrom test for nicotine dependence). Instead, increase in craving was related to individual stress-reactivity (defined by cortisol response). Our findings similarly found no correlation between AUDIT and ADQ (as measures of dependence) and stress-induced increase in craving. Whether our findings were related to individual differences in stress reactivity was not specifically measured in our study, but is deserving of future research.

We found evidence that underlying risk-taking may be an important factor in predicting individual variability in stress-induced craving. Previous research has shown that alcohol consumption (in social drinkers) is predicted by risk-taking (Fernie et al., 2010). In our study, although we found that self-reported alcohol consumption (ADQ, AUDIT and units/week) were all positively correlated with explicit impulsivity (BIS – motor component), alcohol consumption was not correlated with implicit (CPT and BART) measures of impulsivity and risk-taking, respectively. We did, however, find that BIS-motor subcomponent was positively correlated with pre-test craving (DAQ). These data support the theory that there are links between alcohol consumption and impulsivity, but suggest that only risk-taking is predictive of stress-induced increases in craving. We would urge caution, however, in comparing the findings with those of Fernie et al (2010), who found that risk-taking was correated with alcohol preference as there are several differences between our findings and those of other studies; for example, there were considerable differences in the reported alcohol consumption of our sample. In our sample, alcohol consumption was unusually high for social drinkers, especially female participants (male and female ~35 units/week). In the Fernie et al (2010) study, for comparison, while male participants consumed ~30 units/week, females were much lower (~17 units/week). In addition, previous research has found that healthy non-alcoholic participants show a DAQ score of 23.1, and alcoholic participants, 40.5 (Kramer et al., 2010). In our sample, the baseline was much higher, showing 34.5 ± 4.61 for males, and 28 ± 5.25 for females, (overall mean DAQ 30.24 ± 12.76). DAQ was not measured in the Fernie et al. study, but this may have implications on the translational relevance of the two studies.

Both animal models and human clinical research have demonstrated that high-impulsivity predicts relapse (Economidou et al., 2009; Erblich and Michalowski, 2015; Potvin et al., 2015). Our data, however, are the first to demonstrate that risk-taking appears to modulate stress-induced craving in a healthy sample of social drinkers. BIS-11, risk-taking (as defined by the Character and Temperament Score) and craving are intercorrelated in relapsed alcoholic patients (Evren et al., 2012). Here, we found that the motor sub-component of BIS-11, implicit risk-taking (as operationally defined by the BART) and pre-stress craving (DAQ scores) were intercorrelated. However, we did not find any evidence that BIS-subtype impulsivity remained important following the stressor, with only the BART (risk-taking) performance showing a relationship with stress-induced craving. We also found no evidence that implicit measures of motor impulsivity (the CPT) were related to stress-induced craving. The fact that we found no links between impulsivity and increase in craving is somewhat at odds with evidence that high-impulsive rats (as characterized by the 5-CSRTT) are more prone to punishment-induced relapse (Economidou et al., 2009). This may, however, reflect differences in cue-induced (as was the case with the rats in the Economidou et al. (2009) paper), as opposed to stress-induced, relapse. In addition, the specific psychosocial nature of the TSST should be considered. For example, it may be that other stressors (e.g., physical stressors), would indeed be influenced by impulsivity as well as risk-taking. Future research may help to tease apart the specific roles of impulsivity, risk-taking and stress-induced relapse by fractionating different types of stressor and impulsivity subtype, and examining their modulatory effects on craving.

Much is known about the neural circuits underlying various subtypes of impulsivity (Bourque et al., 2013; Winstanley et al., 2004). Despite there being

correlations between impulsivity (various subtypes) and risk-taking, the two are behaviourally, genetically, neurophysiologically and pharmacologically dissociable (Fernie et al., 2010; Winstanley et al., 2004). What is not currently understood is the functional neural circuitry underlying risk-taking. Indeed, there is evidence that risk-taking may be fractionated into different subtypes (Lejuez et al., 2002). The D_4 dopamine receptor (*DRD4*), variable numbers of tandem repeats (DRD4 VNTR) polymorphism has been variously linked to risk-taking and to propensity for addiction. Recently, a study revealed that healthy (non-alcoholic) participants (social drinkers) carrying the 7-repeat long (DRD4L) allele (rather than the short [DRD4S] allele) were more prone to crave alcohol after an alcoholic drink, suggesting that this polymorphism may be important in cue-induced relapse as well as addiction propensity (Hutchison et al., 2002). There is not currently any evidence for the links between DRD4 VNTR polymorphism and stress-induced relapse, and this might be an interesting area for future research.

There were several limitations in this study that should be considered. First, our sample size was relatively low, and this may have reduced our ability to detect smaller effect-size differences in (for example) links between impulsivity sub-types and craving. Second, it would have been useful to include physiological stress measures in order to control for individual differences in reactivity to the TSST. Third, our sample was limited to undergraduate students, and as mentioned previously, a sample that were perhaps unusually heavy drinkers (particularly the females). Finally, our study is essentially correlative in nature, and it is important to be clear that association (i.e., between risk-taking and change in DAQ) does not imply causation. Indeed, it may be (in the light of previous research from Fernie et al., 2010) that a common factor is the impact on risk-taking on drinking behaviour in

general. Although we did not find such a correlation, it may be that and such association was masked by ceiling effects of our sample's high baseline drinking levels.

A goal of biological psychiatry is to be able to identify measurable risk factors and biomarkers, such that stratified treatment approaches can be introduced based on individual patient profiles. Our study, by examining personality traits that predict stress-induced craving, may be a first step towards identifying a biomarker for stress-induced relapse, i.e., risk-taking. Future work should extend the present study to examine different types of risk-taking, and how this related to both stress-reactivity and craving. In addition, future studies should include incentive motivation for alcohol (e.g., a voluntary drinking paradigm; (Field et al., 2005)) as an explicit outcome measure of craving. It would also be useful to carry out an analysis of stress biomarkers, including alpha-amylase (as a measure of SAM activity) and cortisol (as a measure of HPA activity) (alpha-amylase: (Nater and Rohleder, 2009); cortisol: (Hellhammer et al., 2009)) in order to examine the contribution of individual differences in acute (alpha amylase) and prolonged (cortisol) stress reactivity to changes in craving.

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