

Interoceptive awareness is associated with acute alcohol-induced changes in subjective effects



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ABSTRACT

Interoception, the sensing of bodily signals, is related to emotional reactivity and may contribute to the pathophysiology of addiction. Evidence is accumulating that individuals with alcohol use disorders and other substance-dependences show altered interoceptive processing, however little is known about the acute effects of alcohol on interoception and how this may influence the perception of drug induced effects.

In a double-blind design, fifty (30 females) healthy young participants were given a beverage containing either a low (0.4 g/kg, n = 18) or high (0.6 g/kg, n = 15) alcohol dose or a placebo (n = 17). After alcohol administration, participants completed two interoceptive paradigms, the heart-beat tracking and heart-beat discrimination tasks, both assessing different accuracy and metacognitive measures of interoception. Subjective feelings elicited by alcohol administration were also measured.

Participants under the low alcohol dose had lower metacognitive interoceptive awareness on the discrimination task compared to placebo. Participants under alcohol experienced feelings of light-headedness, which were positively associated with increased interoceptive awareness in the cardiac discrimination task.

These results provide evidence for a relationship between interoceptive processing and the perception of drug-induced mood changes. This finding, showing how interoceptive awareness of cardiac discrimination contributes to the appraisal of subjective light-headedness generated by alcohol administration, brings novel perspectives to the understanding of drug discrimination and reinforcement mechanisms.

1. Introduction

Interoception refers to the neural and mental representation of internal bodily signals (Craig, 2002; Sherrington, 1948). The processing of this information is implicated in the formation of emotional responses (Critchley and Garfinkel, 2017; Dunn et al., 2010). Internal bodily signals are communicated to the brain via afferent pathways and integrated within the insular cortex (Craig, 2002; Critchley and Harrison, 2013; Schulz, 2016). The insular cortex is associated with addictive processes, as demonstrated using a range of techniques including lesion (Naqvi et al., 2007) and imaging studies (Naqvi and Bechara, 2010).

The role of interoception in addictive behaviours is hypothesized to relate to the perception of bodily sensations induced by substance consumption (Paulus et al., 2009), where neural areas subserving interoception may also contribute to craving states (Gray and Critchley, 2007). Insula activation reflects the sensing of internal bodily states and physiological changes elicited by drug administration (Verdejo-Garcia et al., 2012). This information is then used to extract conscious information about the effects of the drug (Garavan, 2010; Naqvi and

Bechara, 2010). Altered interoceptive processes in the context of emotional appraisals could in turn contribute to the development of addictive disorders (Stewart et al., 2015). In addition, research shows that alcohol-addicted individuals have impaired baseline interoceptive accuracy compared to a control group, as demonstrated using a heart-beat tracking task (Ateş Çöl et al., 2016). That is, individuals with alcohol use disorder are less accurate at counting their own heartbeats compared to their actual heartbeats over different periods of time.

Drug effects encompass strong sensory and mood changes, which can be transformed into interoceptive cues associated with the rewarding properties of drugs. Drug discrimination tasks are used to identify the type of sensations generated by drugs. During drug discrimination procedures, participants initially learn to discriminate a drug given at a low but effective dose from placebo. Once learning is achieved, participants' ability to generalise this discrimination at lower doses of the same drug is tested and the drug effects associated with this ability are evaluated. In an alcohol discrimination task (Duka et al., 1998) it was shown that administration of low alcohol doses generates subjective feelings of light-headedness, which facilitates the discrimination (and generalisation to lower doses) of the drink consumed.

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The mechanisms by which drug-discrimination is established may therefore originate in interoceptive processes (Duka et al., 1999), and examining the contribution of interoceptive awareness to the perception of light-headedness is the main purpose of this report.

It has long been posited that interoception may mediate the detection of reward effects of food or of substances (Paulus et al., 2009), determining their hedonic value even in healthy participants (Cabanac, 1979; Toates and Frederick, 1986), and indicating its possible involvement in addictive processes. To our knowledge there is one only study which looked at how alcohol affects interoceptive accuracy directly (Abrams et al., 2018). The present study examines the acute effects of alcohol on interoceptive processing using different dimensions of interoception, and assesses their relationship to the perception of subjective alcohol-induced effects. Metacognitive interoceptive awareness, also termed interoceptive insight (Khalsa et al., 2017), provides information about conscious interoceptive abilities (Garfinkel et al., 2016a) and might constitute a more suitable predictor of the perception of subjective (conscious) drug effects.

Using a double-blind alcohol-placebo experiment we explored the role of interoceptive awareness of cardiac functioning (heartbeat) in the appraisal of alcohol effects. Interoception was measured using the tracking (Schandry, 1981) and discrimination (Katkin et al., 1983; Whitehead et al., 1977) tasks, which evaluate different facets of interoceptive processing (Garfinkel et al., 2015, 2016a; Garfinkel and Critchley, 2013); the tracking task testing the perception of a subject's own heartbeat, and the discrimination task testing the ability of the subject to assess whether a tone is synchronised or not with their own heartbeat (Betka et al., 2018a).

The two interoceptive tasks tap into different cognitive processes (Garfinkel and Critchley, 2013), with the tracking task based on the observation (counting) of internal physiological information. However, this task has also been shown to be amenable to higher order influences such as knowledge about heartrate (Ring and Brener, 1996). The discrimination task requires coupling information proceeding from exteroceptive (the tone) and interoceptive channels (Garfinkel et al., 2016b, 2015). Out these tasks, accuracy measures can be obtained. For the Tracking task that is the difference between perceived heartbeats and actual heartbeats on each trial. For the Discrimination task it is the correct perception of whether the tones are synchronised or not with each heartbeat. Confidence can be taken after each trial, and metacognitive interoceptive awareness can finally be derived from confidence-accuracy correspondence in both tasks in order to grasp the conscious perception of cardiac functioning. Previous work indicates that these subjective (confidence) and objective (performance accuracy) or metacognitive measures do not significantly correlate with each other or with other measures of interoception, such as inspiratory resistance (Davenport et al., 2007) or gastric load (Garfinkel et al., 2015, 2016a; van Dyck et al., 2016), implying that not all the information required for an accurate performance on the task reaches consciousness (Garfinkel et al., 2015).

Trait measurements were taken relative to subjective interoceptive sensibility (ascertained through a questionnaire measure), emotion regulation and impulsivity. The general ability to perceive bodily functions was measured using the awareness section of the Body Perception Questionnaire (BPQ) (Porges, 1993). Alexithymia, the deficit in the perception of one's own emotions, which is shown to relate to addictive processes (Kopera et al., 2015; Thorberg et al., 2009), and to mediate partially the relationship between interoception and alcohol consumption (Betka et al., 2018b), was assessed using the Toronto Alexithymia Scale (TAS-20) (Bagby et al., 1994). Impulsivity which also relates to alcohol consumption (e.g. Caswell et al., 2013) was also measured as a trait, using Barratt's Impulsiveness Scale (BIS-11) (Patton et al., 1995).

We aimed to observe differences in interoception induced by alcohol administration in a low and a high dose compared to a placebo group. We also aimed to observe a dose-dependent induction of

subjective feelings of light-headedness by alcohol, replicating previous results (Duka et al., 1998). We hypothesized that a high ability to consciously perceive internal bodily sensations (metacognitive interoception) would facilitate the detection of subjective light-headedness generated by alcohol administration.

2. Materials and methods

2.1. Participants

Fifty students from the University of Sussex (30 females, age range 18–48, mean age 21.79) took part in this experiment. Exclusion criteria were: being below the legal drinking age, extreme Body Mass Index (BMI < 18 or BMI > 28), current prescribed regular medication and pregnancy or breastfeeding. Participants were asked to report if they had been diagnosed or treated for any mental disorder in the past 2 years and excluded if that was the case. Asian participants were excluded as well due to high probabilities of aldehyde dehydrogenase isoenzyme deficiencies in this population (Wall et al., 1997), which can trigger aversive reactions to alcohol intake. All participants included in the experiment consumed more than six units of alcohol a week (1 unit = 8 g of alcohol).

In addition, participants refrained from drinking alcohol for at least 12 h prior to the test session and were breathalysed at the start of the session to ensure a blood alcohol concentration (BAC) of 0. They also refrained from taking illicit drugs for at least seven days, as well as caffeinated drinks and cigarettes an hour before the test. Participants were also required to have a low-fat meal the evening before testing and a low-fat breakfast on the day of testing.

Ethical approval was granted by the BSMS ethics committee at the University of Sussex.

2.2. Methods

2.2.1. Questionnaires

Participants completed the Alcohol Use Questionnaire (AUQ) (Mehrabian and Russell, 1978) for evaluating drinking habits. The AUQ measures, via 12 items, the amount of alcohol consumed per week as well as the frequency and speed of drinking to obtain an alcohol Binge score (Townshend and Duka, 2002).

Impulsivity traits were measured using Barratt's Impulsiveness Scale (BIS-11) (Patton et al., 1995). This 30-item questionnaire assesses different constructs related with impulsivity, namely attentional, motor and non-planning impulsiveness, in addition to providing an overall impulsivity score.

The awareness subscale of the BPQ (Porges, 1993) measures trait sensibility to bodily changes with 45 items, as ascertained via self-report, by asking participants to rate on a likert scale the extent to which they feel different bodily sensations (i.e. facial twitches).

Finally, the ability to process emotions was assessed using the Toronto Alexithymia Scale (TAS-20) (Bagby et al., 1994), which measures, via a likert scale, difficulties in describing feelings, difficulty identifying feelings and the propensity to engage in externally oriented thinking.

2.2.2. Current affect and subjective alcohol effects

Affects and subjective alcohol effects were measured using the Positive and Negative Affect Scale, (PANAS) (Watson et al., 1988) and Subjective Alcohol-induced Effects Visual Analogue Scales (Alcohol VAS) (Duka et al., 1998). For the PANAS, participants evaluate their positive and negative affect rating 10 words for each construct. On the Alcohol VAS, participants had to indicate the extent to which they were experiencing a range of states (e.g. 'light-headed', 'stimulated', 'alert', 'relaxed', 'irritated' and 'contented'). Results were converted to an index ranging from 0 to 1, with 0 being 'Not at all' and 1 'Extremely'.

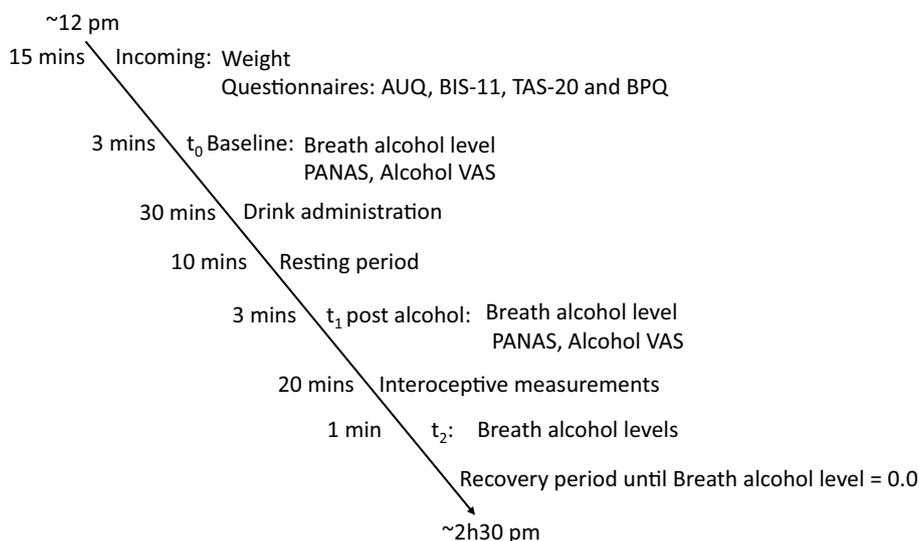


Fig. 1. Figure depicting the experimental procedure followed in this experiment.

2.2.3. Alcohol administration

Breath alcohol levels were measured using a breathalyser (Lion alcoholmeter SD-400, Lion Laboratories Ltd., UK). Following baseline measurements, participants were randomly allocated to receive either an alcoholic or a non-alcoholic beverage in a double-blind design. Two different doses of alcohol were used on this experiment, either a low dose (0.4 g/kg, $n = 18$, 12 females) or a high dose (0.6 g/kg, $n = 15$, 8 females), with 90% v/v alcohol, diluted with sugar-free tonic water (Schweppes, Uxbridge, UK) to make up a 500 ml beverage mixed with 6 drops of Angostura bitters (Garfinkel et al., 2006). The placebo group ($n = 17$, 11 females), was given a beverage consisting of 500 ml of tonic water mixed with an equivalent measure of Angostura bitters. The drink was divided into 10 portions of 50 ml and participants were instructed to consume them at 3 min intervals. The 10 portions were served in small plastic glasses. They were placed on a tray over paper tissues that had previously been sprinkled with a small amount of alcohol so as to increase the olfactory cues. Participants were told they would receive either an alcoholic drink or a placebo.

2.2.4. Interoception tasks

Interoceptive accuracy, operationalized as the objective ability to accurately detect internal bodily sensations using behavioural testing, was measured using the heartbeat discrimination (Katkin et al., 1983; Whitehead et al., 1977) and tracking (Schandry, 1981) tasks. For both tasks, participants' pulse was monitored using an 8000SM finger pulse oximeter (Nonin Medical, Inc., Minnesota, USA). The approximate duration of each task was 15 and 5 min respectively.

In the heartbeat tracking task, participants are instructed to count their heartbeats within their whole body, without putting their hands on their chest or neck. The task started with a practice trial of 20s after which the 6 experimental trials of different time-windows (25, 30, 35, 40, 45 and 50s) occurred in a randomized order. Through a set of speakers, participants heard the word "start" and had to count heartbeats until they heard "stop". At the end of each trial, they indicated to the experimenter the amount of heartbeats they had felt and completed a computerised visual analogue scale to evaluate how confident they are in their responses (0 not confident – 100 extremely confident).

Participants were then administered the heartbeat discrimination task. On each trial, ten auditory tones (100 ms, 440 Hz) were presented either synchronised or asynchronously with the participant's own heartbeat. On non-synchronised trials, a 300 ms delay was introduced between each heartbeat and the tone. After each trial, participants indicated whether tones were synchronised or not with their heartbeat

and again indicated confidence in their responses using a visual analogue scale. In total, 20 trials were presented, randomly allocating synchronised and non-synchronised trials.

The order of the tasks was fixed for all participants.

Three dimensions of interoception, incorporating interoceptive accuracy, sensibility and metacognitive awareness, were computed for each task (Garfinkel et al., 2015). Interoceptive accuracy is based upon the overall performance on each of the tasks. For the discrimination task, interoceptive accuracy is the percentage of correct responses (hits and correct rejections). For the tracking task, scores are computed based upon the ratio of reported to actual heartbeats, using a formula that accounts for the effect of longer trials (Hart et al., 2013):

$$1 - (|nbeatsreal - nbeatsreported|) / ((nbeatsreal + nbeatsreported) / 2)$$

Interoceptive sensibility is a subjective measure computed from the average confidence in responses stated for both tasks.

For the tracking task, metacognitive awareness was calculated as the relationship between confidence and accuracy using Pearson's correlations. A high correlation implies increased metacognitive awareness. In the discrimination task, an Area Under Receiving Operating Curve (AUROC) (Green and Swets, 1966; Hajian-Tilaki, 2013) provided a measure of the extent to which confidence predicts accuracy accounting for participants' propensity to indicate high levels of confidence. Both these metacognitive measures provide accounts of individual differences in 'interoceptive insight' (Khalsa et al., 2017).

2.2.5. Procedure

Participants came into the lab after 12 pm. Once having read and signed a consent form they completed the AUQ, BIS-11, TAS-20 and BPQ questionnaires and were weighted. Participants then filled PANAS and Alcohol VAS at baseline (t_0) and were breathalysed. Next, they were administered the drink depending on the group they had been assigned to (placebo, low or high dose). After a 10-min resting period, breath alcohol levels were measured (t_1), together with PANAS and Alcohol VAS. Then interoceptive measurements (tracking and discrimination tasks) were finally taken followed by a measurement of breath alcohol levels (t_2). After the experiment, participants were debriefed and remained in a calm area within the lab until their breath alcohol level had fallen below 0.18 mg/L, half the legal driving limit in England, see Fig. 1 for an outline of the procedure. Participants also agreed not to drive or operate any machinery for at least 4 h following the experiment.

Table 1

Descriptive statistics and results comparing questionnaire scores between groups and state changes due to alcohol administration. The only significant interaction was between time and dose in light-headedness, $p = .001$, $n = 50$.

	Placebo		04 ml/kg		0.6 ml/kg				
	n = 17		n = 18		n = 15				
	Mean	SD	Mean	SD	Mean	SD			
One-way ANOVA							<i>F</i> (2,49)	<i>p</i>	η^2
Age	21.06	1.60	21.06	2.38	23.47	6.15	2.098	0.134	0.08
BIS-11	68.12	9.42	74.33	5.81	71.40	15.33	1.502	0.233	0.06
Binge score	22.24	14.44	21.28	11.60	29.33	15.85	1.576	0.218	0.06
AUQ score	29.35	17.14	30.00	14.43	43.40	22.40	3.045	0.057	0.11
Porges	2.79	0.74	2.97	0.70	2.89	0.88	0.240	0.788	0.01
TAS-20	49.88	11.82	49.56	8.93	52.93	11.18	0.483	0.620	0.02
Tracking HR	73.11	11.77	81.08	15.57	71.11	12.46	2.617	0.084	0.10
Discrimination HR	72.47	10.98	79.67	13.41	70.47	12.44	2.608	0.084	0.10
2-way mixed ANOVA time x group							<i>F</i> (2,47)	<i>p</i>	η^2
PANAS Positive t_0	29.59	8.12	31.56	7.31	28.93	7.76	0.085	0.918	0.004
PANAS Positive t_1	27.12	7.86	30.11	8.90	26.93	9.19			
PANAS Negative t_0	16.65	4.85	20.78	7.47	15.73	5.50	0.519	0.599	0.022
PANAS Negative t_1	12.94	3.23	15.61	5.83	12.27	4.45			
2-way mixed ANOVA time x group									
Light-headedness t_0	0.20	0.20	0.16	0.25	0.17	0.17	11.067	0.001	0.320
Light-headedness t_1	0.38	0.25	0.52	0.35	0.81	0.11			
Irritability t_0	0.14	0.15	0.13	0.18	0.12	0.17	0.451	0.640	0.019
Irritability t_1	0.17	0.19	0.11	0.17	0.07	0.13			
Stimulated t_0	0.38	0.19	0.37	0.24	0.53	0.20	1.611	0.210	0.064
Stimulated t_1	0.45	0.24	0.54	0.20	0.54	0.25			
Alertness t_0	0.53	0.24	0.45	0.18	0.57	0.19	2.064	0.138	0.081
Alertness t_1	0.58	0.24	0.52	0.16	0.45	0.26			
Relaxed t_0	0.58	0.20	0.60	0.20	0.50	0.21	0.710	0.497	0.029
Relaxed t_1	0.64	0.25	0.66	0.23	0.65	0.27			
Content t_0	0.63	0.24	0.60	0.17	0.51	0.19	1.698	0.194	0.067
Content t_1	0.64	0.19	0.64	0.22	0.65	0.23			
2-way mixed ANOVA time x group							<i>F</i> (1,31)	<i>p</i>	η^2
BAC t_1		In %	0.053	0.015	0.094	0.005	0.010	0.922	0.000
BAC t_2		In %	0.045	0.010	0.085	0.005			
BrAC t_1			0.23	0.065	0.41	0.021			
BrAC t_2			0.20	0.045	0.37	0.021			

Bold indicates significance at $p < .05$.

2.3. Data analysis

All data were examined for normality of distribution and homogeneity of variance before being entered into statistical analyses.

2.3.1. Questionnaires, subjective alcohol effects and blood alcohol concentration

Age and questionnaire scores on AUQ and Binge drinking measure, BPQ, BIS-11 and TAS-20 were compared between groups (placebo vs. low vs. high dose) with a series of One-way ANOVAs. We also compared heartrate scores both during the tracking and discrimination tasks between groups.

Positive and negative affect (PANAS) and Alcohol VAS scores were analysed using Two-way mixed ANOVAs with time (t_0 vs. t_1) as a within subjects' factor and group (placebo vs. low vs. high-dose) as a between subjects' factors.

Blood alcohol concentration (BAC) was calculated from breath alcohol measurements by multiplying breath alcohol levels by 2.3 and dividing them by 10. BAC levels were compared between groups (low vs. high-dose) and time (t_1 vs. t_2) with a Two-way ANOVA.

2.3.2. Correlation between alcohol and interoception on subjective light-headedness

For participants who consumed alcohol, a planned linear regression examined light-headedness at t_1 as DV, with BAC at t_1 , metacognitive interoceptive awareness, interoceptive accuracy and sensibility on the discrimination task, age and mean heartrate as predictors. An

equivalent analysis was also performed using the tracking task. The regression aimed at providing evidence for the role of interoception in the perception of alcohol-induced effects.

2.3.3. Effects of alcohol on interoception

A series of One-way ANOVAs examined group differences (placebo vs. low vs. high-dose) in interoceptive performance after alcohol consumption, incorporating as dependent measures metacognitive interoceptive awareness, interoceptive accuracy and sensibility for both the discrimination and tracking tasks. Interoceptive accuracy has been seen to decrease with age (Khalsa et al., 2009) and heartrate can be affected by alcohol administration (Conrod et al., 2001; Sayette, 1993). There is also an ongoing debate regarding the influence of heartrate on interoceptive accuracy, in particular during the tracking task (Zamariola et al., 2018). For those reasons these variables were included as covariates. Age data for one participant was missing and hence not accounted for on the interactions with list-wise deletion.

2.3.4. Exploratory analysis on gender effects

Data published during the write up of this manuscript indicated that alcohol administration decreased accuracy in the tracking task, albeit only in males (Abrams et al., 2018).

A post-hoc analysis explored this with a Two-way ANOVA with gender and group (placebo vs. low vs. high-dose) as a between subjects' factors on tracking accuracy.

3. Results

3.1. Questionnaires, subjective alcohol effects and BAC

Regarding questionnaire scores, there were no significant differences between groups ($F_s < 2.100$, $p_s > 0.05$).

In terms of the Alcohol VAS, a significant interaction between group and time was observed for ratings of light-headedness, $F(2,47) = 11.067$, $p < .001$, $\eta^2 = 0.320$, with participants in the low-dose group having lower levels of light-headedness than those in the high-dose group, $t(20.992) = 3.369$, $p = .003$, $d = 1.47$, who were also experiencing more light-headedness than the placebo group, $t(22.823) = 6.489$, $p < .001$, $d = 2.72$, post alcohol consumption. As expected there was a dose-dependent effect of alcohol on light-headedness.

The expected main effect of group, $F(1,31) = 142.086$, $p < .001$, $\eta^2 = 0.821$ and of time, $F(1,31) = 61.257$, $p < .001$, $\eta^2 = 0.664$, on BAC was also found.

No other significant effects were found. See Table 1 for full descriptive statistics and results.

3.2. Correlation between alcohol and interoception on subjective light-headedness

Factors entering the regression were normally distributed, with the exception of age; regression assumptions were also met prior to factors' entry. The regression examining the factors contributing to subjective ratings of light-headedness at t_1 was significant, $R^2 = 0.463$, $F(6,31) = 3.805$, $p = .008$, see Table 2.

Metacognitive interoceptive awareness for the discrimination task was the best predictor of light-headedness following alcohol administration within the model accounting for BAC, age, mean heartrate and accuracy and sensibility on the discrimination task. Fig. 2(a-b) presents the relationship of Light-headedness scores with BAC (Fig. 2a) and with metacognitive interoceptive awareness for the discrimination task (Fig. 2b).

The regression using tracking scores was significant, $R^2 = 0.415$, $F(6,31) = 2.959$, $p = .025$, albeit the only significant predictor was BAC, $p = .031$.

3.3. Effects of alcohol on interoception

When examining the effect of alcohol on metacognitive interoceptive awareness for the discrimination task, a marginal main effect of dose was observed $F(2,48) = 3.144$, $p = .053$, $\eta^2 = 0.125$. Accounting for covariates, metacognitive interoceptive awareness under the low dose of alcohol was significantly reduced relative to the placebo group, $F(1,33) = 5.479$, $p = .026$, $\eta^2 = 0.154$, demonstrating a deleterious effect of alcohol that was not found in the high-dose group, $F(1,31) = 0.506$, $p = .483$, $\eta^2 = 0.018$, see Fig. 3(a).

There were no significant effects of group regarding discrimination accuracy, $F(2,48) = 0.314$, $p = .732$, $\eta^2 = 0.014$, or sensibility F

Table 2

Regression table for Light-headedness at t_1 . Reported light-headedness was significantly explained by Metacognitive interoceptive awareness for the Discrimination task and marginally by Blood Alcohol Concentration, $n = 33$.

Predictor	B	SE B	β	t	p
Blood Alcohol Concentration t_1	4.65	2.28	0.34	2.04	0.052
Metacognitive Discrimination	0.82	0.29	0.47	2.86	0.008
Accuracy Discrimination	0.32	0.48	0.11	0.67	0.507
Sensibility Discrimination	-0.16	0.24	-0.10	-0.65	0.522
Age	0.00	0.00	0.04	0.26	0.798
Mean Heart-rate	0.00	0.01	0.02	0.13	0.900

$R^2 = 0.477$. Dependent variable: Light-headedness at t_1

(2,48) = 1.432, $p = .250$, $\eta^2 = 0.061$, see Fig. 3(b-c).

Regarding the tracking task, there were no significant group effects on metacognitive interoceptive awareness, $F(2,48) = 0.347$, $p = .709$, $\eta^2 = 0.016$, accuracy, $F(2,48) = 1.321$, $p = .277$, $\eta^2 = 0.057$, or sensibility, $F(2,48) = 0.588$, $p = .560$, $\eta^2 = 0.026$ (data not shown).

3.4. Exploratory analysis on gender effects

Post-hoc analyses, including gender, show a marginal Two-way interaction between gender and dose for tracking accuracy, $F(2,48) = 3.186$, $p = .052$, $\eta^2 = 0.135$. This was explained by lower accuracy for males ($mean = 0.42$, $SD = 0.44$) compared to females ($mean = 0.72$, $SD = 0.16$) in the high-dose group, $F(1,14) = 11.044$, $p = .007$, $\eta^2 = 0.501$, which were not found in the other groups ($F_s < 0.8$, $p_s > 0.39$). No other effects including gender were found, $F_s < 1$, $p_s > 0.4$.

4. Discussion

This report assesses the role of interoceptive processes in the appraisal of drug-induced effects on mood states. Empirical evidence is provided for the effect of acute alcohol administration on the perception of internal bodily sensations and their relationship to drug effect experiences.

Our main finding is that, as predicted, there was a relationship between metacognitive interoceptive awareness and the subjective states alcohol induces in participants, specifically light-headedness. According to previous research, alcohol discrimination at very low doses is based on the influence the drink has on subjective light-headedness, an effect resembling "high" (Duka et al., 1998). Our findings demonstrate that metacognitive cardiac awareness correlates with higher acuity in the perception of substance-induced responses, meaning the greater one's ability to recognise how well they perceive their internal bodily sensations, the more they experience substance effects. Insight in interoceptive abilities can therefore constitute the basis of substance discrimination, which in turn can act as an interoceptive substance-related cue.

Such a relationship should play a relevant role in the development of associations between stimuli and drug effects supporting conditioning models of addiction (Stewart et al., 1984). Furthermore, it is possible that increased interoceptive awareness enhances the detection of low-intensity physiological responses, exemplifying again the function interoception has on the processing of emotional cues which are not explicitly accessible with ease (Damasio, 2000; Leganes-Fonteneau et al., under review). This could be crucial for understanding the mechanisms underlying drug discrimination (Duka et al., 1999) and alcohol priming effects (Rose and Duka, 2006), as well as emotional biases to alcohol related stimuli.

In the present study, lower metacognitive interoceptive awareness in the discrimination task was found for the low-dose group, highlighting that a low dose of alcohol may leave interoceptive accuracy and sensibility relatively unimpaired, but instead influence the capacity for metacognitive interoceptive insight. This effect was maintained after accounting for age differences and heartrate during the tasks. It is possible that only the low dose of alcohol impaired interoceptive metacognition as participants at that dose did not yet have insight into their own intoxicated state.

Under this low dose, interoceptive confidence seemed to be marginally higher than in the other conditions, in line with the general effects of alcohol on performance confidence (Earleywine and Martin, 1993; Ray et al., 2006) while accuracy was slightly lower than for the high dose and placebo. While neither of these results were significant in their own right, it is possible that their modulation at this low dose resulted in a disruption of confidence-accuracy mapping, leading to a selective impairment in metacognitive interoception. It is interesting to note that despite the lower levels of metacognitive discrimination in the

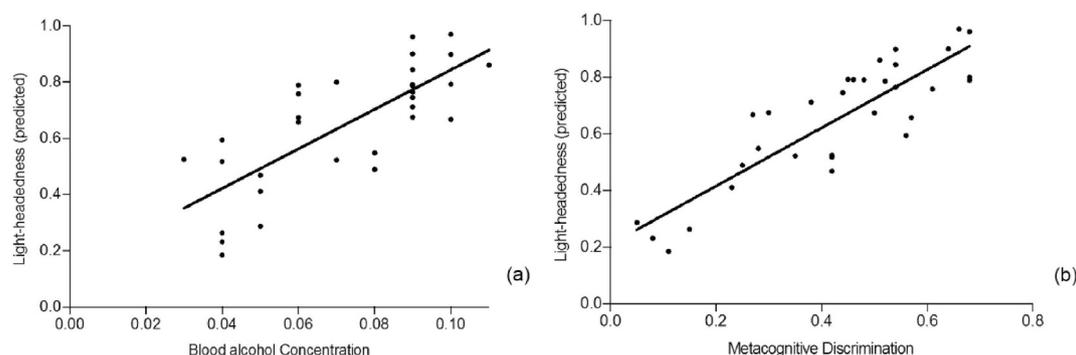


Fig. 2. Scattergrams depicting the relationship of Unstandardized Predicted Light-headedness scores at t_1 with Blood Alcohol Concentration (a) and Metacognitive Interoceptive Awareness for the Discrimination task (b). Increased levels of Blood Alcohol Concentration and Metacognitive Discrimination positively correlate with feelings of light-headedness, $n = 33$.

low alcohol dose compared to placebo, this measure still served as the best predictor of feelings of light-headedness in the two groups who had consumed alcohol.

It is worth noting as well that acute administration of low alcohol doses affects general error monitoring (Ridderinkhof et al., 2002), a type of metacognitive ability, thus supporting the deleterious effect of the low dose on metacognitive interoception. Lack of such an effect in the high dose may be due to a compensatory mechanism mobilised when drug effects are experienced (e.g. Marczinski and Fillmore, 2005) or expected (Caswell et al., 2013).

We did not find significant effects of alcohol administration on overall accuracy or sensibility for the discrimination task; or on any of the interoceptive indexes for the tracking task. An exploratory analysis did, however, replicate recently published data (Abrams et al., 2018). Males had lower accuracy in the tracking task than females, albeit results were restricted to the high-dose group. This replication highlights once more the role of interoception in addictive processes and brings further evidence towards the effects of acute alcohol administration in proprioception and other forms of perception (Stock et al., 2017).

Physiological disparities between males and females could explain the differences observed in the tracking task (Ehlers et al., 2000). In males, alcohol administration may have affected interoceptive pathways, leading to the effects observed in tracking accuracy, which were not altered in females. Gender differences in cardiac functioning, notably in heart-rate variability (Bates et al., 2011; Koenig and Thayer, 2016) have already been reported, explaining disparities in emotional processing after alcohol administration (Udo et al., 2009). Further research should therefore examine the role of interoception in emotional responses and their relationship with heart-rate variability and gender differences.

The use of metacognitive measures of interoceptive awareness over simple indices of accuracy brings a novel approach towards the study of interoceptive processes (Garfinkel et al., 2016a; Garfinkel and Critchley, 2013) that is relatively unexplored (see Canales-Johnson et al., 2015; Forkmann et al., 2016 and Garfinkel et al., 2015 for notable exceptions). The way metacognitive interoceptive awareness is computed, particularly using AUROC for the discrimination task, creates a measure which is less affected by individuals' dispositional or situational interoceptive sensibility (i.e. subjective measures such as confidence) on that particular task (Fleming and Lau, 2014), and thus may provide an unbiased account of their interoceptive ability in the metacognitive domain. In our case, metacognitive discrimination did not differ between males and females but was affected by alcohol administration. Moreover, the predictive power of metacognitive interoception on light-headedness was still present when accounting for accuracy and confidence scores, pointing towards the unique role of metacognitive interoception in the appraisal of drug effects. Metacognitive indices of interoception might therefore constitute a better measure of the interoceptive correlates of addiction.

Different tasks and measures assessing interoception share similar and distinct functional architecture (Schulz, 2016) and reflect different cognitive processes (Garfinkel et al., 2016b). Given that each of the tasks and measures evaluates different aspects of interoception (Garfinkel et al., 2016a), observing which measures are particularly sensitive to alcohol effects can provide insight into the specific processes implicated.

The present results suggest that the effects of alcohol appear to be more sensitive to an interoception paradigm that requires internal-external integration of stimuli. Interestingly both oxytocin (Betka et al., 2018a) and stress (Schulz and Vögele, 2015) also selectively affect

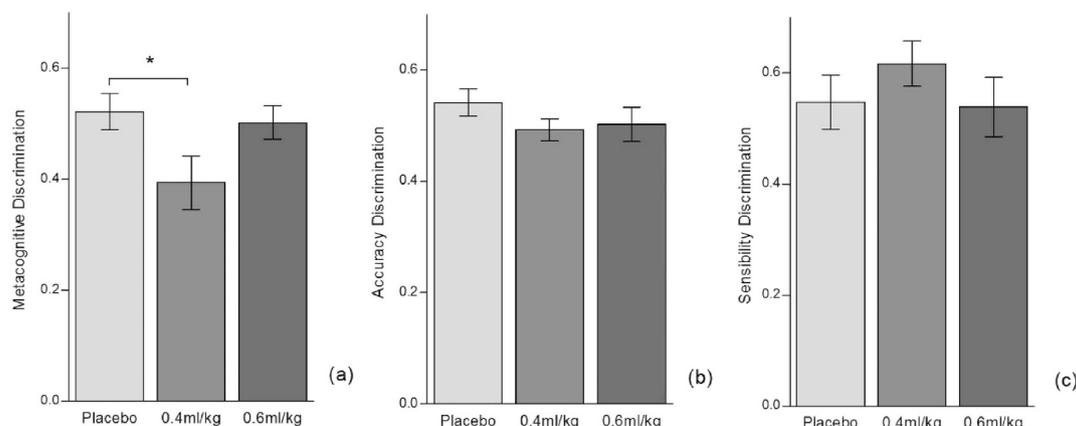


Fig. 3. Metacognitive Interoceptive awareness (a), accuracy (b) and sensibility (c) obtained in the discrimination task across experimental groups (mean scores and SEM). *Metacognitive interoceptive awareness was higher for the placebo group than for the 0.4 ml/kg group, $p = .026$, $n = 50$.

interoception as measured with the discrimination task, though the effects on this task were seen on accuracy rather than on the metacognition of interoception.

5. Limitations

The lack of baseline measurements of interoception in the present study limits the clear conclusion that our findings are solely due to the direct effect of alcohol on interoception and not influenced also by individual differences on that measure. A baseline measurement of interoception, before the administration of any substance, would provide a clearer account of the effects of alcohol on interoception. However, repeated measures of the tasks could lead to learning effects, which could be a confound for the influence of alcohol. Future research should examine the role of interoception as a trait, and not as the result of an experimental manipulation, on alcohol discrimination abilities. Without an improved replication, the differences in interoceptive indexes between groups obtained in this study have to be considered with caution.

Measurements of alcohol use were only taken for the period of the 6 months preceding the study and no information about recreational drug taking was registered. There was a marginal difference in the measure of AUQ with the group that had the higher dose showing higher AUQ scores. Adding AUQ into the regression analysis did not change core findings with respect to interoceptive metacognition and light-headedness, and AUQ was not a significant predictor ($p = .810$). Future studies should examine the effects of alcohol on interoception using groups with different alcohol consumption levels, and should also register recreational drug use.

The present study did not directly assess participants' knowledge about the nature of the substance administered (placebo or alcohol) as a single administration does not allow sensitive measures of drug-discrimination accounting for chance identifications (50% probabilities of being accurate) (Jackson et al., 2001). Taste or liking ratings of the drink were not measured either. We also did not assess a range of physiological responses (e.g. blood-pressure) both before and after alcohol administration. Although as mentioned above, light-headedness was previously found to best predict alcohol dose discrimination (Duka et al., 1998), or to be the sole index varying after the administration of 0.6 g/kg of alcohol (George et al., 2005), other studies found differences as well in relaxation and content in the presence of stimuli conditioned with alcohol (Field and Duka, 2002). It is somewhat surprising that no other indexes in the Alcohol VAS were affected by alcohol (i.e. stimulation), maybe alternative measures of alcohol effects could have provided a more accurate examination of induced subjective effects (Rueger and King, 2013). Future studies should expand and improve our novel findings by incorporating these additional measures.

6. Conclusions

Taken together, our findings show that alcohol consumption can alter interoceptive processes, particularly in the metacognitive domain. Our findings also show that cardiac interoceptive abilities can lead to a higher perception of the effects of alcohol possibly associated with feelings of “high”. This could help understand the interoceptive mechanisms underlying the perception of reward values, a phenomenon previously hypothesized in the reward learning literature (Cabanac, 1979; Paulus et al., 2009; Toates and Frederick, 1986). It also could help explain how light-headedness acts as an interoceptive cue to facilitate alcohol discrimination (Duka et al., 1999) and the mechanisms by which low-dose alcohol priming effects can participate in the generation of craving and cognitive biases (Duka and Townshend, 2004; Schoenmakers et al., 2008). Thus, the present study highlights a possible interplay between interoceptive processing and the perception of drug-induced mood changes, and opens a series of pathways for future research into how interoception relates to processes underlying

addiction. Uncovering the interoceptive correlates of alcohol administration could shed light onto the link between bodily responses and different phenomena associated with alcohol and addiction, the implications of which could shape novel intervention programs.

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