Higher Olfactory Sensitivity To Coffee Odour

In Habitual Caffeine Users

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Abstract

The present two studies aimed to look at alternative methods of assaying the changes underpinning drug consumption and dependence. Here we focus on whether olfactory differences exist in habitual consumers in the form of recognition and sensitivity tasks to a caffeine-related odour.

In experiment 1, High (n = 18), moderate (n = 23) and non-consumers (n = 21) of caffeine completed a threshold test for a coffee odour, followed by a recognition test for both a coffee and a neutral odour; finally a measure of caffeine craving. In experiment 2, (n=16 consumers/n=16 non-consumers) completed threshold tests for two odours: coffee; control (n-butanol), followed by a caffeine related Implicit Association Test.

In exp 1, recognition to the coffee odour was faster for caffeine consumers versus non-consumers. We also found that high caffeine consumers had greater olfactory sensitivity for the coffee odour compared to the other groups, which was related to craving. In exp 2, again we found greater sensitivity for the coffee odour in consumers but no differences between groups for the control odour. Additionally, craving was greater in consumers who had just been exposed to the coffee odour.

These findings provide evidence for the first time, that regular consumers of coffee have enhanced sensitivity to an odour associated to caffeine. They further suggest that drug associated odours could be a useful tool in furthering theory in drug dependence.

Keywords

Caffeine, Coffee, Addiction, Attentional bias, Odour, Drug cue

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2 **Public Significance Statements**

3 Caffeine is the most widely consumed psychoactive drug. In this study, we found that habitual
4 caffeine (coffee) consumers were more sensitive to a coffee odour than non-consumers, which
5 increased with level of caffeine craving. These findings suggest that changes in odour detection
6 are a useful index of drug dependency.

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1 **Introduction**

2 Caffeine is the world’s most widely consumed psychoactive drug with the main dietary sources
3 coming from coffee, tea and soft drinks. Caffeine dependency has been recognized in research
4 (Hughes et al., 1993; Ogawa & Ueki, 2007) and by clinicians (DSM-5 diagnosis of caffeine
5 dependence, APA 2013). In particular, work has shown that a central aspect of continued caffeine
6 use is the alleviation of withdrawal effects (Hughes et al., 1993). In a study using a ‘drug/money’
7 paradigm, they found that those experiencing headache (common withdrawal effect) following
8 placebo were more likely to forfeit a monetary reward than to again receive placebo (Schuh &
9 Griffiths, 1997). Research has also found that more caffeinated coffee was consumed for
10 individuals following placebo compared to caffeine administration, who also reported higher
11 levels of drowsiness (Stafford & Yeomans, 2005). However, in the wider addiction literature, it
12 is well known that drug users who have undergone a lengthy period of drug abstinence and thus
13 free of withdrawal effects, can still be motivated to consume the relevant drug (Lamb et al., 1991).
14 For these reasons, alternative theories emerged, highlighting the importance of drug related
15 paraphernalia in the maintenance of addiction (e.g. Bindra, 1978; Robinson & Berridge, 1993;
16 Berridge & Robinson, 2003). The idea being that stimuli (e.g. cigarette ‘packet’, alcohol ‘bottle’)
17 repeatedly paired with the drug itself result in a Pavlovian response, whereby the mere presence
18 of that stimuli can induce craving¹ for the relevant drug. These theories help explain how drug
19 relapse can occur even when users are beyond the phase of withdrawal. The most commonly used
20 tools to test this theory have been ‘visual’ tasks taken from the wider attentional domain, such as
21 the modified Stroop and Dot-probe. Due to the inherent differences between the two tasks, they

¹ Subjective craving is an important facet of drug dependency, as demonstrated by its link with heavy drug useage (e.g. alcohol, Charkravorty et al., 2010).

1 measure the degree to which individuals exhibit either a delayed response (Stroop interference) or
2 faster reactions (dot probe) to drug related words or pictures. Using these tools, a number of
3 studies have provided evidence to support both of these predictions, across a range of different
4 drugs, including caffeine (Field & Cox, 2008; Yeomans et al., 2005). However, more recently,
5 research has demonstrated the low internal reliability of these tasks to measure such cognitive
6 biases (Ataya et al., 2012), in addition to questions on the clinical significance of such paradigms,
7 (Field et al., 2014; Christiansen et al., 2015). One of the aims of the research here was therefore
8 to explore alternative measures of drug biases, beyond purely visual attentional tasks. Our sense
9 of smell is of particular interest in caffeine work, due to its strong association with widely
10 consumed drinks (coffee, tea), but there is also work demonstrating the importance of odours in
11 other drugs. For alcohol dependent users, smelling a drink appears to increase reported cravings
12 (Litt & Cooney, 1999), skin conductance (Glautier et al., 1992) and orienting response (Field &
13 Duka, 2002).

14 The main aim of the current research was therefore to explore for the first time, the relationship
15 between craving drug dependency and our sense of smell. To test this, in experiment 1, we
16 examined differences in odour sensitivity to a caffeine related odour (coffee) in High, Moderate
17 and Non-consumers of caffeine, using a threshold detection task; which provides a reliable
18 measure (Hummel et al., 2007) of the lowest concentration an individual can detect a given odour.
19 We selected coffee as the drug associated odour based on its distinctiveness (as compared to tea)
20 and the fact that it is the primary contributor to the total intake of caffeine (Frary, Johnson & Wang,
21 2005; Mitchell, Knight, Hockenberry, Teplansky & Hartman, 2014). We tentatively predict that
22 individuals with greater habitual consumption would have higher olfactory sensitivity for the
23 coffee associated odour and this would also relate to caffeine craving. As an additional measure

of olfactory function, more related to attention, we designed a novel task which measured the recognition latency to identify the odour of coffee. Based on related research from the visual domain (Yeomans et al., 2005), we predict that reaction times would be faster for higher habitual caffeine consumers. In experiment two, we aimed to verify if the effect in the threshold test was selective to the coffee odour by completing a threshold test to both the same coffee odour as experiment one and a neutral (control) odour.

Experiment One

Method

Participants

Participants ($n = 62$; age $M = 20.39$, $SD = 1.80$ years, range 18 – 25; 33 female, 29 male) were University students and identified through the use of a general health questionnaire as used in previous work (Stafford, Wright & Yeomans, 2010) assessing self-reported caffeine consumption. Of the individuals that signed up only those whose habitual caffeine consumption met the criteria for the three conditions (Non-consumer 0mg/day, Moderate 70-250mg/day, High 300+mg/day) were invited to take part. Given the nature of the study, an additional requirement for the caffeine consumers, was that the majority of their caffeine consumption had to be from coffee. The study was advertised as ‘The Relationship between life style and sense of smell’ and the protocol was given ethical approval from the Psychology department ethics committee (British Psychology Society guidelines).

Design

The study used a between-subjects design, where the independent variable was Group (high, moderate, and non-consumer) and the main dependent variables were odour recognition latency and odour sensitivity (threshold).

Materials

Olfactory Sensory & Threshold Tests

The details for these tests and the Odour Recognition test are described fully in supplementary materials. We used the same procedure for measuring threshold as a previous study (Stafford & Whittle, 2015).

Odour Recognition

This was measured by recognition latency (seconds) to identify two odours (coffee/lavender). Lavender was selected as the control odour on the basis of being a relatively well recognised odour. Participants (blindfolded) were presented with the coffee or lavender odour (counterbalanced order), by squeezing the bottle under the participants nose, and asking them to identify the odour as quickly as possible. The point from when the odour was presented to when the odour was identified was timed using a stopwatch.

Caffeine Craving Questionnaire

The current study used the Questionnaire of Caffeine Craving (QCC; West & Roderique-Davis, 2008) which was based on the Questionnaire of Smoking Urges (QSU) (Tiffany & Drobes, 1991). The QCC is a 21 item measure, yielding three factors: factor 1 (Desires and intention), factor 2 (General reinforcement), factor 3 (Negative reinforcement).

Procedure

Participants were instructed to refrain from consuming any food/drinks that contained the following substances: alcohol, taurine, caffeine, glucose, and aspartame 12 hours before their allocated session; with any who had consumed any caffeine being re-booked. Participants were then presented with the target odour and instructed to rate the pleasantness and intensity of the odour using VAS 100 mm unmarked line scales end-anchored 'not at all' and 'extremely', followed by the olfactory threshold test. Participants were then allowed a short break. Next participants completed the odour recognition test followed by the QCC and were then given a full debriefing.

Data Analyses

Any data that were outliers (± 2 SD away from the mean) were corrected to the mean, which affected 2pct of the data, with similar approaches used in previous research (e.g. Wright & Diamond, 2014). For odour recognition latency scores, data for participants that guessed either odour incorrectly were excluded from that analysis. The olfactory data were analysed using separate one way ANOVAs with the between-subjects factor of Group (high, moderate, non-consumer). For recognition latency, we used a RM ANOVA with the within-subjects factor of Odour (coffee/control) and the between-subjects factor of Group (high, moderate, non-consumer). For caffeine craving, a MANOVA was performed using the QCC dependent variables: Desires and intentions, General reinforcement, Negative reinforcement and the between-subjects factor of Group (high, moderate, non-consumer). Preliminary analyses of the data revealed Box's Test of Equality of Covariance Matrices was violated, Box's $M = 31.02$, $F = 2.39$, $p = .004$, which was due

to differences in variability in the Non-consumer group, particularly in the Desire & Intentions factor. In all cases, follow up post hoc comparisons were carried out using Bonferroni correction.

Results

Olfactory Threshold Test And Ratings

Analysis revealed that sensitivity was significantly greater in the high versus moderate and non-consumer groups (Table 1). There were no significant differences in odour pleasantness or intensity ratings between consumer groups.

Odour Recognition

We observed a significant Group x Odour interaction, $F(2, 43) = 3.62$, $p = .035$, $\eta^2 = .14$, with post-hoc comparisons revealing that both High and Moderate consumers had faster reactions to the coffee odour than the non-consumers, with the High/Moderate groups not differing from each other (Table 1). No such differences were observed between groups for the control odour, suggesting the effect was specific for the coffee odour in high and moderate consumers.

Caffeine Craving Questionnaire

Unsurprisingly, caffeine craving was higher for the two caffeine groups compared to Non-users (Table 1). We also found for two of the factors, craving was greater in the high versus moderate consumers.

1 *Correlations*

2 To explore the relationships further, we completed correlations between the key variables for the
3 high and moderate consumers. We found that increases in habitual caffeine consumption were
4 related to higher sensitivity to the coffee odour ($r = 0.39$, $p < .05$) and also higher craving: Desires
5 & intention ($r = 0.50$, $p < .01$); Negative reinforcement ($r = 0.36$, $p < .05$). Habitual caffeine
6 consumption was negatively correlated with recognition times for the coffee odour ($r = -0.46$, p
7 $< .01$), whereby increases in caffeine consumption were associated with faster responses to the
8 coffee odour. We further found that increases in craving (Negative reinforcement) was associated
9 with higher sensitivity to the coffee odour ($r = 0.31$, $p < .05$).

10 **Discussion**

11 The findings, though highly novel, need to be seen in the wider context. In particular, it needs to
12 be acknowledged that even though we found that sensitivity to the coffee odour was greater in the
13 high caffeine group, since we did not use a control odour in that threshold test, we cannot be certain
14 if the finding is specific to the drug associated odour, or would also be found for any odour
15 generally. Hence, if caffeine consumers' sensitivity changes as a result of drug consumption at a
16 level where some tolerance or withdrawal may be expected, we would expect this to be unique to
17 the odour associated to caffeine (coffee). For this reason, in order to verify this finding, we
18 completed a further experiment, where caffeine consumers and non-consumers completed a
19 threshold test to the same coffee odour and separately for a control (neutral) odour. Additionally
20 in experiment two, we explored the relation between odour sensitivity and a more traditional
21 (visual) measure of attention to drug cues using an Implicit Association Test (IAT). In a previous
22 study, it was demonstrated that high caffeine users had faster responses to caffeine/positive words
23 compared to moderate and non-consumers (Stafford, Wright and Yeomans, 2010); and it is

- 1 therefore of theoretical interest to examine whether such visual attention relates to other modalities
- 2 (i.e. olfaction).

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Experiment Two

Method

Participants

Participants ($n = 35$; age $M = 30.5$, $SD = 11.2$ years, range 21 – 59; 25 females) were University staff and students and identified through the same general health questionnaire as exp 1. Participants were invited to take part in the study if they were moderate/high users (≥ 200 mg of caffeine per day) and that coffee was at least one of the consumed beverages (Moderate/High Caffeine group) or they consumed no more than 30mg of caffeine per day, comprising of soft beverages (e.g. coca-cola) only (Low Caffeine group). We adopted this criteria for the latter group since our main interest was to compare caffeinated coffee users versus non-users and also to help in the difficulty of recruiting individuals who consumed no caffeine from any sources (see also Data Analyses). The study was advertised as ‘examining the relationship between lifestyle and sense of smell’ protocol was given ethical approval from the University Science Faculty Ethics committee (Ref: SFEC 2017-047, British Psychology Society guidelines).

Design

The study used a between-subjects design, where the independent variable was Group (Caffeine or Non/Low Caffeine) and the main dependent variable was odour sensitivity (threshold) for the two odours.

Materials

Olfactory Sensory & Threshold Tests

We used the same coffee odour as in Experiment one. For the control odour, we used N-butanol, with the rationale being that it is a neutral, non-food odour and is the default odour for the threshold

tests used extensively in this research area (e.g. Hummel et al., 2007; Stafford & Wellbeck, 2011). N-butanol was diluted in distilled water, starting at a concentration of 1pct (step 1 strongest) with each successive step diluted by a factor of two to the lowest step (step 16 weakest). For both odours, we used the same method as experiment one to measure sensory (pleasantness/intensity) and threshold aspects.

Implicit Association Test (IAT)

The IAT has been used extensively and has been shown to have relatively high validity and reliability (Greenwald & Nosek, 2001; Nosek, Greenwald, & Banaji, 2005). The task requires individuals to categorize individually presented words on a computer screen as quickly and accurately as possible. The task aims to measure the strength of the association between words of different categories, e.g. (from an example IAT) generally speaking, individuals would be faster at categorizing words associated to ‘flower’ with words associated to ‘good’, in comparison with say words associated to ‘insects’ and ‘good’. The details for the IAT used in this study are described fully in supplementary materials.

Caffeine Craving Questionnaire

We used the same Caffeine Craving Questionnaire (QCC; West & Roderique-Davis, 2008) as experiment one.

Procedure

The study used the same basic procedure as experiment one with the following additions. Following completion of the Sensory and Threshold test for the first odour, they were taken to another room where they completed an IAT. Next, they were returned to the Olfactory lab where

they completed the Sensory and Threshold test for the second odour; where the test order of coffee and control odours was counterbalanced across participants/groups. Participants then completed the Caffeine Craving Questionnaire and were given a full debriefing.

Data Analyses

Data were excluded for participants (n=3) not able to detect the odour at the strongest concentration, resulting in the Caffeine (n=16) and Non/Low Caffeine (n=16) group; the latter were all non-caffeine consumers, except two participants who consumed 30mg caffeine per day in the form of coca-cola); for simplicity, we now refer to this group as the Non-consumers group². Outliers were treated the same way as experiment 1 (affected 1.5pct of the data). The olfactory data were analysed separately using RM ANOVA with the within-subjects factor of Odour (Coffee/Control, N-butanol) and the between-subjects factors of Group (Consumers, Non-consumers) and Odour order (Coffee/Control, Control/Coffee). Caffeine craving was analysed with the same method as exp 1 with the addition of Odour order. Again, we found Box's Test of Equality of Covariance Matrices was violated, Box's $M = 43.42$, $F = 1.93$, $p = .01$, which was again due to differences in variability in the Non-consumer group, particularly in the Desires & Intention factor. For the IAT, since the data did not reveal any significant differences, for conciseness, we have placed the relevant Data Analyses, findings and interpretation in supplementary materials.

Results

² The main findings of experiment 2 were unaffected if these two participants were excluded.

Threshold

We found a significant Group x Odour interaction, $F(1,28) = 5.67$, $p = .02$, $\eta^2 = .17$, with Posthoc comparisons revealing that sensitivity was higher in the Consumers compared to Non-consumers group for the coffee odour but there was no difference for the control odour (Table 2).

Pleasantness & Intensity

The interaction of Group x Odour was significant, $F(1,28) = 4.47$, $p = .04$, $\eta^2 = .14$, where posthoc comparisons demonstrated no differences in groups for the coffee odour but for the control odour, pleasantness was lower in the Consumers versus Non-consumers group (Table 2). It is also worth noting that within each group, pleasantness ratings differed significantly for the Consumers, but not the Non-consumers group. Hence it was only in Consumers, that a clear preference for the coffee compared to control odour was found.

Caffeine Craving

As expected, we found significantly higher craving for the Consumers versus Non-consumers group on all three measures (all $ps < .01$). For the General reinforcement factor, there was also an approaching Group x Odour order interaction, $F(1,28) = 3.22$, $p = .08$, $\eta^2 = .10$, where posthoc comparisons revealed that interestingly, craving was higher for those Consumers in the control/coffee test order ($p = .02$) and hence who had just experienced the coffee odour; there were no differences for Non-consumers ($p = .68$) (Supplementary Material, Table 3).

General Discussion

1 In experiment one, we found that recognition times were faster to the coffee odour for both
2 high/moderate compared to non-consumers, with no differences for the control odour.
3 Collectively these findings are consistent with previous caffeine research (Yeomans et al., 2005),
4 where a visual attentional bias for caffeine was found in high but not moderate and non-
5 consumers. In terms of threshold sensitivity, the findings from the two experiments revealed that
6 habitual coffee consumers are able to detect the odour of coffee at lower thresholds (i.e. they are
7 more sensitive) compared to non-caffeine users. To our knowledge this is the first study to
8 demonstrate this effect and helps extend our understanding of the sensory changes that
9 accompany drug consumption. An important consideration is whether the effects observed here
10 are simply a product of greater exposure to the odour cue by caffeine consumers and not related
11 to the addictive properties of the drug. However, if that were the case, we would not expect
12 differences between high and moderate users (which were found in exp1), being two groups who
13 have had considerable exposure to the odour. Moreover, we observed that higher sensitivity to
14 the coffee odour was correlated with greater levels of caffeine craving. Hence, it was not simply
15 that coffee consumers were better at detecting the coffee odour but that this ability was directly
16 related to their craving for a caffeinated beverage. It is also interesting to reflect that this
17 relationship was specific to the ‘negative reinforcement’ dimension of craving, which could
18 suggest a close affinity between odour cues and their association with reversing withdrawal
19 symptoms. Though tentative, this would also be consistent with work showing that alleviating
20 negative effects is a central driver in sustaining caffeine consumption (Hughes et al., 1993;
21 Schuh & Griffiths, 1997). More generally, this links with cue exposure work demonstrating the
22 physiological changes that accompany drug dependence, where for instance, skin conductance
23 was greatest when regular alcohol users simply ‘held’ and smelled an alcohol associated

1 beverage compared to when they consumed the drink (Glautier et al., 1992). The work here
2 suggest that such effects may be underpinned by a heightened ability to detect the relevant odour.

3
4 The results from the study here also inform cognitive theories of addiction that have shown
5 heightened attentional bias to drug related stimuli (Robinson & Berridge, 1993, Berridge &
6 Robinson, 2003; Field & Cox, 2008). Whilst we are not suggesting that detecting drug related
7 odours is the same as cognitive bias, we do propose that drug maintenance is likely driven by
8 more than the ability for drug cues to grab ‘visual’ attention; but that other modalities also need
9 to be considered. The results from the work here also offer an alternative method for assaying
10 biases or sensory differences that accompany drug dependency. In addition to theoretical
11 interest, the use of olfactory measures have the potential to be used in interventions to stop drug
12 relapse, just one example being conditioned odour aversion. Using this paradigm, a recent study
13 found that individuals who were trained to receive an odour paired with a mild electric shock
14 showed greater discrimination compared to an unpaired control odour (Cavazzana et al., 2018);
15 hence discrimination in that study was the index of the aversive response. One could envisage a
16 similar methodology being adapted for individuals with a strong drug dependency, especially for
17 those using drugs with widely diffused odours (e.g. tobacco, cannabis).

18
19 It needs to be acknowledged that since both experiments tested caffeine consumers in a caffeine
20 deprived state, it is unclear whether the same effects would emerge in a non-deprived state.

21 From a visual attentional bias perspective, there is reason to believe that results would be
22 unaffected by deprivation state, as shown in previous caffeine work (Stafford & Yeomans,
23 2005), however from that same study, consumption of coffee was found to be greater in a

1 deprived versus non-deprived state which might imply that the sensory characteristics were
2 valued more highly when drug deprived. In terms of the control odours used in both studies, it
3 could be argued that using more widely recognised food odours would have provided a more
4 effective control and is something to consider for future research. We also recommend the use
5 of additional measures of caffeine dependency, beyond the craving (QCC) questionnaire used
6 here, that are able to detect clinical dimensions (i.e. as referred to in DSM-5).

7
8 In summary, using a drug with mildly addictive properties, we found that habitual caffeine
9 consumers were faster to identify the odour of coffee and had higher sensitivity to a coffee
10 related odour than non-consumers. These effects suggest that for habitual users, drug associated
11 sensory cues command enhanced olfactory attention and detection.

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8

Table 1. Mean (SE) Participant Characteristics (Study 1)

	High consumers	Moderate consumers	Non consumers	Group Differences
Age	21.39 ±0.45 ^a	20.17 ±0.31	19.76±0.36 ^b	F=4.76, p=.012
Gender (F/M)	7/11	10/13	15/6	$\chi^2= 5.08$, p = .08
Caffeine (mg per day)	419.4 ±27.4	168.8 ±11.8	0	-
Threshold*	10.37 ±0.34 ^a	8.51 ±0.30 ^b	8.06 ±0.31 ^b	F= 11.26, p < .001
Odour Pleasantness	47.3 ±5.9	44.4 ±5.1	37.8 ±4.9	F=0.83, p=.443
Odour Intensity	52.1 ±5.4	53.5 ±4.1	54.4 ±3.6	F=0.07, p=.936
Odour Recognition				
Coffee	1.17 ±0.18 ^a	1.45 ±0.14 ^a	2.80 ±0.17 ^b	F= 26.92, p < .001
Lavender	5.09 ±0.80	4.69 ±0.66	3.92 ±0.77	F= 0.58, p = .564
Craving				
Desires &Intention	3.51 ±0.25 ^a	2.54 ±0.19 ^b	1.39 ±0.08 ^c	F=31.91, p< .001
General Reinforcement	5.07 ±0.26 ^a	4.97 ±0.21 ^a	3.90 ±0.26 ^b	F=6.94, p= .002
Negative Reinforcement	4.63 ±0.16 ^a	3.87 ±0.21 ^b	3.17 ±0.16 ^c	F=14.92, p< .001

*Higher numbers represent greater odour sensitivity

Notes: Means with different superscript letters represent significant differences (p< .05) ‘between’ groups

Table 2. Mean (SE) Participant Characteristics (Study 2)

	Consumers	Low-Non consumers	Group Differences
Age	34.06 ±2.94	26.82 ±2.03	F=4.00, p=.054
Gender (F/M)	13/5	12/5	$\chi^2 = .011$, p = .60
Caffeine (mg per day)	368.61 ±26.23	5.29 ±2.86	-
Threshold			
Overall (both odours)	9.41 ±0.36	8.14 ±0.36	F=6.33, p=.02
Coffee	9.42 ±0.51	7.40 ±0.51	F=7.94, p=.009
N-butanol	9.40 ±0.31	8.88 ±0.31	F=1.41, p=.24
Odour Pleasantness			
Overall (both odours)	41.5 ±3.4	46.6 ±3.4	F=1.13, p=.29
Coffee	58.5 ±5.4 ^c	51.6 ±5.4 ^c	F=0.82, p=.37
N-butanol	24.4 ±5.2 ^d	41.2 ±5.1 ^c	F=5.54, p=.03
Odour Intensity			
Overall (both odours)	62.2 ±3.1	60.1 ±3.1	F=0.23, p=.64
Coffee	55.3 ±4.7	47.1 ±4.6	F=1.55, p=.22
N-butanol	69.1 ±4.1	73.1 ±4.1	F=0.45, p=.50
Craving			
Desires &Intention	3.27 ±0.36	1.60 ±0.36	F=10.74, p=.003
General Reinforcement	4.63 ±0.28	2.61 ±0.28	F=26.52, p<.001
Negative Reinforcement	4.23 ±0.34	2.67 ±0.33	F=10.98, p=.003

Notes: For odour pleasantness, means with different superscript letters represent significant differences (p< .05) ‘within’ that group