



The effects of menstrual cycle stage and hormonal contraception on alcohol consumption and craving: A pilot investigation

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ABSTRACT

Background and aims: Although alcohol research often comments on observed sex differences (i.e. patterns of consumption), there is a lack of investigation into the reasons for these differences. For females, the regular hormonal fluctuations across the menstrual cycle are a potential influencing factor for alcohol consumption. In this pilot we aimed to investigate the relationship between menstrual cycle phase (follicular-phase [FP] and luteal-phase [LP]) and status (naturally-cycling [NC] and hormonal-contraception [HC]) on alcohol consumption and craving of casual drinkers, and identify potential influencing factors in this relationship.

Methods: *Study One:* participants ($n = 28$; 15 HC, 13 NC) were either NC or HC (between subject factor: hormonal status) and attended two lab-based sessions corresponding with their FP and LP (within factor: cycle phase [NC] or time [HC]). Participants completed a mock alcohol taste-test, in addition to pre- and post-consumption measures of craving, anxiety, stress, and mood. *Study Two:* participants ($n = 262$; 144 HC, 118 NC) were either NC or HC (between subject factor) and completed an online study assessing menstrual cycle phase, alcohol use, craving, impulsivity, and stress.

Results: *Study One:* A significant effect of cycle phase was found on alcohol craving ($p = .019$): craving was higher during the FP compared to the LP for NC participants, with HC participants showing no difference across sessions. There was no effect of phase or status on alcohol consumption, stress, or mood ($ps > .05$). *Study Two:* Regression analyses showed that age, craving, impulsivity and stress were significantly associated with alcohol consumption for NC participants ($ps < .05$), however only age and craving were associated with consumption for the HC participants ($ps < .001$).

Conclusions: Alcohol craving was higher during the follicular, compared to the luteal, phase for the naturally cycling group, and different factors may be associated with drinking behaviour across women who are NC and those using HC. Future alcohol research should consider the menstrual cycle and contraceptive status for females.

1. Introduction

Since 2006, the prevalence rates for hazardous and problematic drinking amongst the UK adult population have not declined [1], yet in 2018/19 alcohol-related hospital admissions were 6% higher than the previous year [2]. The need for more effective treatments and interventions has led to interest in identifying population-specific factors (e.g. sex) which may influence drinking behaviour and inform future treatments [3,4]. This may be particularly beneficial given that the sex-gap in the prevalence of alcohol use is decreasing [5], largely due to an increase in female drinking which may involve reduced stigma

surrounding female alcohol use and changes in the gender roles of women [6,7]. In terms of heavy alcohol use, prevalence rates are highest among females aged 16–24 years [1].

Sex differences exist in the motivations for alcohol use, e.g. males are more likely to drink for social reasons whereas females are more likely to use alcohol as a coping strategy [8]. Given that the experience of negative states, and reactivity to such states, can differ across menstrual cycle [9], this is one possible mechanism by which cycle might influence alcohol use [10]. Biological responses to alcohol also show sex differences. For instance, females experience the subjective effects of alcohol at lower doses [3]; progression to alcohol use disorders occurs at lower

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consumption levels [11,12]; and women are particularly susceptible to alcohol-related harm (e.g. risk of breast cancer, a typically female disease, has a dose-dependent relationship [12,13]). Despite evidence of sex-specific alcohol use and harm, most theoretical models and treatments are applied without considering such sex-differences [11]. Sex-specific factors, such as sex hormones may contribute to some of these differences [3], for instance, gonadal-hormones may be an influential factor through their effects on the menstrual cycle [3,11].

The average menstrual cycle is 28 days long and has two phases: Follicular (FP) and Luteal (LP) which are characterised by different levels of gonadal hormones. The FP (day 1 [first day of menses] to day 13) is characterised by a higher oestrogens (i.e. estradiol) to progesterone ratio, whereas the LP (day 15 to day 28) is characterised by a higher progesterone to oestrogens ratio. Ovarian hormones (i.e. oestrogens and progesterone) have been found to affect substance use through various mechanisms in both animal models and human literature [11,14]. For example, oestrogen changes neuronal excitability which affects synaptic transmission [15], and alcohol metabolism is faster in female mice following the administration of an oestrogen (estradiol) by increasing the effects of alcohol degrading enzymes [16]. Overall, estradiol appears to enhance the motivation to take drugs whereas progesterone counteracts this effect [17–19]. See Fig. 1 for hormonal levels across the cycle.

Substances such as alcohol are more rewarding during the FP, perhaps due to increased neural excitability [12,15] which may mean that alcohol's positive effects are experienced more quickly. For instance, higher oestrogen levels during the FP have been associated with enhanced positive effects during substance use [20]. Such effects of ovarian hormones may also explain the finding that during the FP, females may be at greater risk of relapse to alcohol use [21]. A potential role for hormones on substance use is further evidenced by the administration of oral micronized progesterone during the FP, which substantially attenuates the positive subjective effects of substances with respect to the normal LP [22].

Despite these important possibilities, recent reviews have highlighted an insufficient level of research investigating the effects of the menstrual cycle on human alcohol use and the potential factors confounding this relationship, and identified limiting methodological inconsistencies in the existing literature [3,11,23].

Similarly, stress [22], negative mood [24], and impulsivity [25] are all positively associated with drinking and fluctuate over the menstrual cycle. For example, brain activity responses to stress can differ between

menstrual cycle phases [26], and women report greater stress reactivity to psychosocial stressors during the LP [27] (this association has been further evidenced with biological markers such as cortisol [28]).

We can crave alcohol for both its positive (e.g. rewarding) and negative (e.g. stress relief) reinforcing effects. Craving has a well-established relationship with alcohol use; higher craving is positively associated with higher consumption [29,30] and craving for other substances, e.g. nicotine, has been shown to differ significantly between cycle phases [31]. This is important as women may use and/or crave alcohol due to its ability to relieve stress and other negative moods, again, suggesting that such negative states may be a mechanism by which menstrual cycle affects alcohol use. A final factor to consider is age due to the shift in menstrual cycle hormonal patterns. Age is important as there is significantly less cycle variability between ages 20–40, compared to the first few years after menarche or when females approach menopause [25]. Thus, age is likely to affect the relationship between the menstrual cycle and alcohol use.

Given the existing findings that menstrual cycle may influence alcohol use, the present research aimed to explore this relationship in more detail, by taking into account both cycle phase (FP and LP) and hormonal contraception (HC) use (HC leads to a more stable hormonal levels [3,11], see Fig. 2). Additionally, we considered the roles of craving, stress, state-mood, and impulsivity as potential mediators. As the existing literature has not suggested reliable methods for studying this association, the current pilot research employed two methodologies. To address these aims, we conducted two studies, a lab-based study (study one) and an online, observational cross-sectional study (study two). Study one used a mixed design; the within-subjects factor of cycle phase for the Naturally Cycling (NC) group/time for the HC group allowed the comparison of the effects of the FP and the LP as the NC participants attended the lab twice (once during each phase). The between-subjects factor of cycle status (NC vs HC) allowed the HC group to act as a quasi-control condition (as they do not experience traditional menstrual cycle phases) to determine whether any effects were present amongst those without natural hormonal shifts. For study two, factors associated with consumption (age, craving, mood, stress, and impulsivity) were explored with the between-subjects factor being HC use (NC vs HC).

Based on existing literature, for study one we hypothesised that within the NC group, females would consume more alcohol and crave alcohol to a higher degree during the FP compared to LP. We also hypothesised that the HC participants would not differ between the two

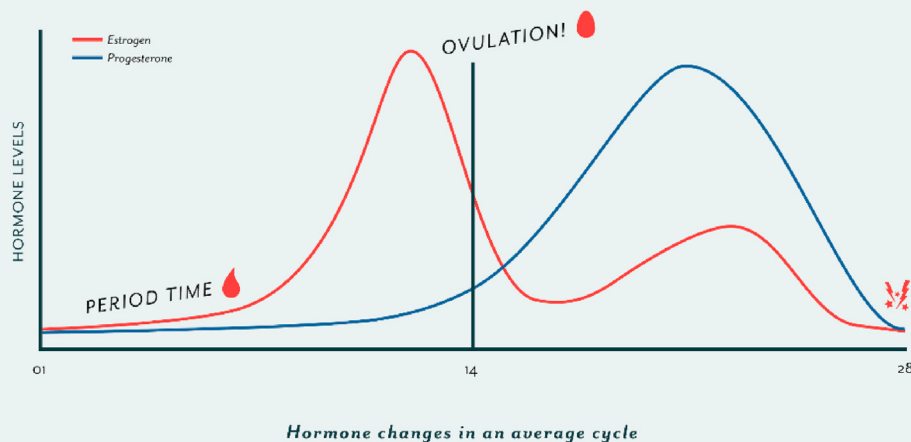


Fig. 1. Diagram of oestrogen and progesterone levels across the menstrual cycle for NC females [46].

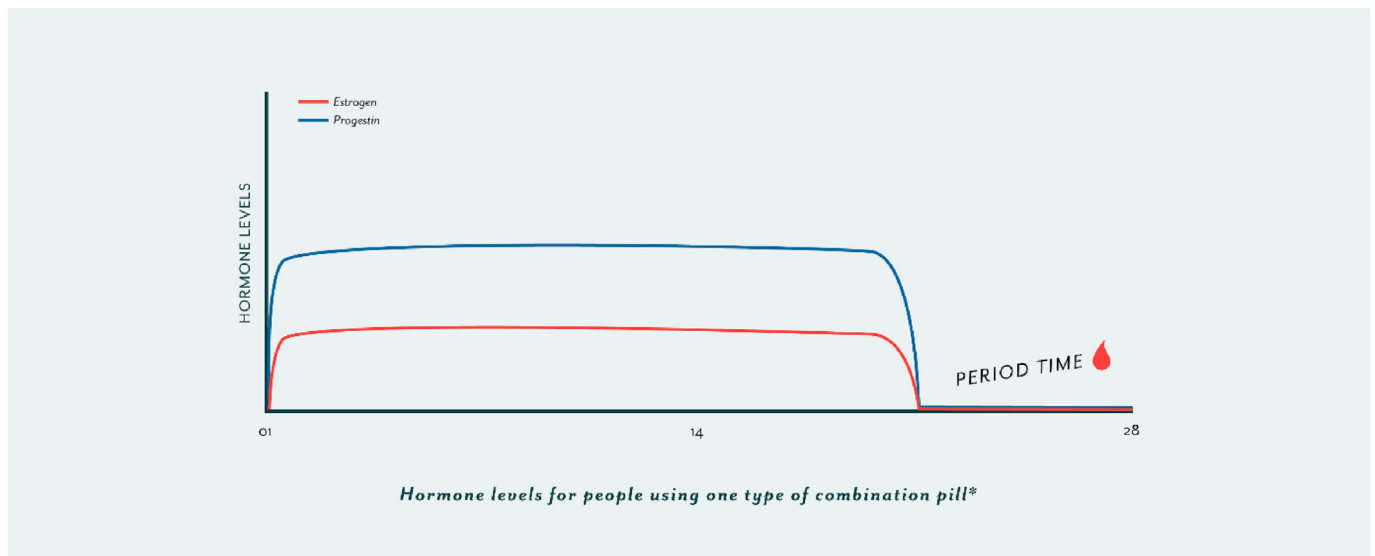


Fig. 2. Diagram of oestrogen and progesterone levels for HC users [46].

sessions as they have more constant levels of ovarian hormones. Finally, we predicted that current craving, state-mood, stress and impulsivity would act as mediating variables for any relationship between menstrual cycle phase and alcohol consumption. For study two, we hypothesised differences in alcohol consumption and craving between the NC and HC groups. Additionally, we predicted that age, craving, impulsivity and stress would be more strongly associated with alcohol use in the NC group, as the NC group experience hormonal fluctuations which these factors may be associated with.

2. Materials and methods – study one

2.1. Participants

Female undergraduate university students ($n = 29$) were recruited via opportunity sampling. Participants were either naturally cycling or using any 'hormonal contraception'. One participant was excluded from the analysis as they reported after the study that they purposefully consumed less in one lab visit due to sickness. The final sample size for analysis ($n = 28$; 14 NC and 14 HC) was sufficient to detect a large effect size while ensuring 80% power at $\alpha = 0.05$, calculated in G*Power 3.1 [32]. Inclusion criteria were: 1) aged 18 years and over; 2) fluent English speaker; 3) consumed alcohol at least once a week; 4) provide a breathalyser reading of 0.0 mg/l at the start of each experimental session; and 5) like the taste of white wine spritzer (the drink provided in the study). Exclusion criteria were: 1) had a child through pregnancy; 2) history of or currently seeking treatment for alcohol use disorder; 3) currently seeking to reduce alcohol use; 4) currently using medication that would affect alcohol consumption e.g. cold/flu medication. This study was approved by the Ethics Committee at the host university.

2.2. Materials

Period Tracker Application: Flo © [33], a period tracker smartphone application was used to monitor cycle phase for NC participants. Participants downloaded the application and were given a user guide during their first visit to the lab. We used average cycle length and day of cycle to determine phase via the countback method [34] and cross-checked this with the application provided by Flo © when the participants visited the lab. Order of sessions was counterbalanced for NC participants.

Alcohol Urge Questionnaire (AUQ [35]): an eight-item Likert scale

(Strongly Disagree-Strongly Agree) measured current alcohol urge across three domains: desire for alcohol; inability to resist drinking available alcohol; and the expectation of positive effect from drinking alcohol.

State Trait Anxiety Inventory (STAI [36]): a 20-item scale measured feelings associated with anxiety (e.g. tension, and nervousness), giving an overall score of state anxiety. Participants indicated on a four-point Likert scale the extent to which they agreed with each statement (e.g. I feel strained; I feel calm).

Profile of Moods Scale (POMS [37]): a 72-item questionnaire measured current mood across eight primary mood states (anxiety, depression, anger, vigour, fatigue, confusion, friendliness and elation) and two composite mood states (arousal and positive mood). Arousal scores were a combination of ([anxiety + vigour] - [fatigue + confusion]) and Positive mood scores were a combination of (elation - depression). Overall, higher scores indicated greater arousal and positive mood.

Stress statement (SS): a 10-point Likert scale measured current stress, with 0 indicating no stress - 10 indicating extreme stress.

Drinks preparation and mock taste test [38]: drinks consisted of TESCO Supermarket's own brand white wine (125 mLs, ABV 12%) mixed with the participants' choice of either 50 mLs of TESCO Supermarket's own brand diet lemonade or TESCO Supermarket's own brand soda water. Two drinks were provided and were served in identical wine glasses (total beverage 350 mLs; 1.2 units of alcohol). Participants were given 10 minutes to complete a mock taste-test where they were instructed to consume as much or as little as they liked to rate the drinks on several taste scales (e.g. Sweet, Bitter). Alcohol consumption (mLs) was the primary outcome measure, calculated by subtracting the post-taste test weight by the pre-taste test weight.

2.3. Procedure

Testing was conducted in lab facilities at the host university, between the times of 1–6 p.m. The NC participants attended a session to download the Flo © application and tracked their period for a minimum of two weeks before the experimental sessions. All participants (NC and HC) attended two identical experimental sessions, approximately two weeks apart allowing for the NC participants to attend the lab once during each cycle phase (determined using the Flo © application). On arrival, participants had to provide a baseline breath alcohol measurement of 0.00 mg/l using the Lion Alcometer 500 © (Lion Laboratories Ltd, Barry, UK) before completing a battery of baseline self-reports: AUQ; STAI; POMS;

and SS. The researcher then provided the participant with the alcoholic beverages before leaving the room to allow completion of the 10 minute mock taste test. At the end of the taste test, the participants completed a second STAI, POMS, and SS before leaving the lab once breathalyser readers were ≤ 0.17 mg/l. At the end of the second session, participants were asked what they thought the aims of the study were before being debriefed (no participants correctly guessed the aims of the study). Each experimental session lasted approximately 45 minutes.

2.4. Statistical analyses

Two 2x2 mixed ANOVAs were conducted to analyse the effects of the within-subjects factor (menstrual cycle phase for NC/time for HC) and the between subjects factor (group/contraception use) on the dependent variables: 1) alcohol consumption; and 2) alcohol craving. Regression analyses were used to determine whether there were relationships between cycle phase/session and the potential mediating factors: craving; stress; and mood. We planned to conduct mediation analyses if relationships were found with phase/session as the independent variable, alcohol craving and alcohol consumption as dependent variables, and craving, stress, and mood as mediators. To test whether the effects of alcohol were different by cycle phase and/or group we calculated change scores (post-alcohol scores – baseline scores) for anxiety, mood disturbance (arousal and positive), and stress. We then conducted four 2x2 mixed ANOVAs with the change scores as the dependent variables and the within-subjects factor (menstrual cycle phase for NC/time for HC) and the between subjects factor (group).

3. Results – study one

3.1. Participant characteristics

Out of the 28 participants, 13 were NC and the remaining 15 were HC users with an overall mean age of 20.47 (± 1.91); NC = 21 (± 2.20) and HC = 19.93 (± 1.62). See Table 1 for baseline measures of craving, anxiety, mood and stress, and taste-test alcohol consumption.

3.2. Baseline craving and taste-test alcohol consumption (mLs)

The analysis revealed a significant main effect of cycle phase/session on craving ($F = 6.24$, $p = .019$, $\eta^2 = 0.19$) with participants craving alcohol more during the FP compared to the LP. There were no main effects of cycle phase/session ($F = 4.13$, $p = .053$, $\eta^2 = 0.14$) or group ($F = 0.62$, $p = .440$, $\eta^2 = 0.02$) on consumption, nor was there an interaction ($F = 2.49$, $p = .126$, $\eta^2 = 0.09$). There was no main effect of group ($F = 4.05$, $p = .055$, $\eta^2 = 0.14$), nor an interaction between cycle phase/session and group on craving ($F = 1.12$, $p = .300$, $\eta^2 = 0.04$).

Table 1
Study One descriptive statistics for Taste-test alcohol consumption and baseline characteristics.

Variable	Mean (SD)			
	NC (n = 13)		HC (n = 15)	
	FP	LP	Session 1	Session 2
Taste-test Consumption (mLs)	180.19 (108.56)	122.69 (89.39)	178.73(75.97)	171.53 (86.29)
Craving (AUQ score)	20.69 (6.13)	15.92 (7.19)	24.73 (9.85)	22.80 (7.97)
Anxiety (STAI score)	36.15 (8.76)	38.92 (12.55)	38.87 (11.48)	37.20 (10.23)
Mood Disturbance (POMS score)	1.01 (2.10)	1.71 (4.15)	3.47 (5.20)	2.57 (3.90)
Stress	4.38 (2.29)	5.31 (2.43)	5.23 (2.19)	4.93 (2.66)

3.3. Mediating variables

The analyses revealed no statistically significant main effects of cycle phase or group, or an interaction of both on baseline measures of anxiety, stress, or mood ($F_s \leq 1.60$, $p_s \geq .217$, $\eta^2 \leq 0.06$). Also, the analyses for the effects of alcohol on measures of anxiety, mood or stress showed no significant main effects of phase or group, nor interactions on change scores ($F_s \leq 4.13$, $p_s \geq .053$, $\eta^2 \leq 0.14$). Given that there were no relationships between phase/time point and any of the potential mediators (craving mood, anxiety, mood, and stress; $p_s > .05$), the planned mediation analysis was not appropriate. (See Fig. 3 and 4)

4. Materials and methods – study two

4.1. Participants

Female participants were recruited via opportunity sampling (i.e. online advertisements; posters); those in study one were not excluded from participation. A total of 98 responses were removed (92 incomplete; 4 removed as participants took over 24 hours to complete and the recall period was the previous week; 1 reported at the end of the study that they never consume alcohol; 1 was removed as they were unsure about their use of hormonal contraception). As the data was skewed we report the results both before ($n = 298$) and after removing outliers that were ≥ 3 Standard Deviations from the mean ($n = 261$). The minimum number for analysis was 261 participants which was sufficient to detect a medium effect size while ensuring a minimum of 80% power at $\alpha = 0.05$, calculated in G*Power 3.1 [32]. Participants were 18–24 years old and the median response time to complete the questionnaire was 13.01 minutes. Inclusion criteria were: 1) aged 18 years and over; 2) fluent English speaker. Exclusion criteria were: 1) had a child through pregnancy; 2) history of or currently seeking treatment for alcohol use disorder; 3) currently seeking to reduce alcohol use. More detailed measurement of contraception type showed that, within the HC group, 85.1% used the combined oral contraceptive, 10.6% used the hormonal implant, and 4.3% were using the Marina coil. This study was approved by the Ethics Committee at the host university.

4.2. Materials

Time Line Follow Back (TLFB [39]): this is a retrospective diary that measures daily alcohol use for the previous two weeks and has shown reliability in previous studies [40]. Participants were asked to provide as much information as possible, e.g. quantity and brand, and average

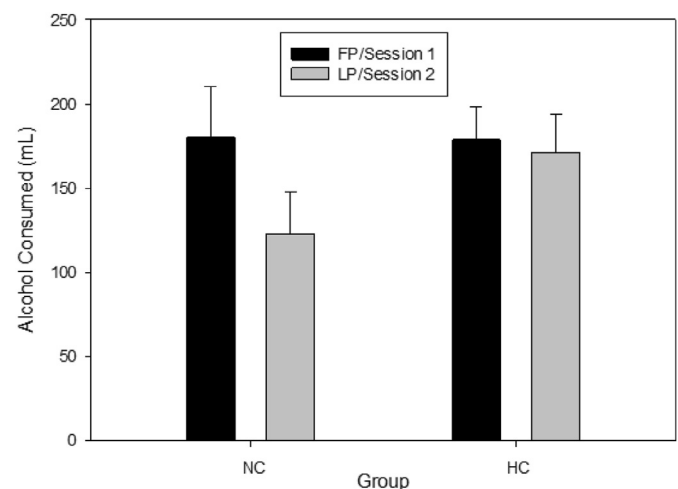


Fig. 3. Bar chart displaying the mean amounts of alcohol consumed (mLs) comparing cycle phase/session and group (including 95% CIs).

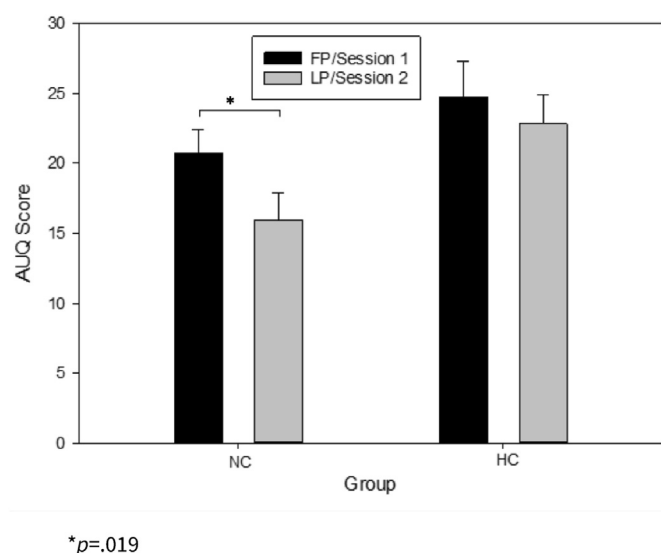


Fig. 4. Bar chart displaying the mean alcohol craving scores (AUQ) comparing cycle phase/session and group (including 95% CIs).

weekly unit consumption was calculated. The TLFB is especially reliable for self-administered web-based methods for reporting drinking behaviour among young adults [41].

Weekly Stress Inventory-Short Form (WSI-S [42]): this was used to measure both the number of stressful events (WSI-Event) as well as their perceived subjective impact (WSI-Impact). Participants were asked to complete the 25-item scale by indicating on a seven-point Likert scale the stress that they experienced if they had a stressful encounter (e.g. Was without privacy). The WSI has high internal consistency and congruent validity [42]. The scale reliability in the present study was very good with an internal consistency of Cronbach's $\alpha = 0.849$.

Barratt's Impulsivity Scale (BIS [43]): this was used to give a total score of impulsivity with higher scores indicating higher impulsivity. The 30-item questionnaire allowed participants to indicate how often they display a behaviour (e.g. I change jobs) ranging from rarely/never to almost always/always. BIS has high internal consistency [44]. The scale reliability in the present study for total BIS scores was acceptable with an internal consistency of Cronbach's $\alpha = 0.638$.

Approach-Avoidance Alcohol Questionnaire (AAAQ [45]): this was used to assess self-reported craving, giving three scores: alcohol-inclination; alcohol-obsessed; and alcohol-avoidance). Participants rated 14 items on eight-point Likert scales the extent to which they agreed with a statement about their alcohol related behaviours in the previous week (e.g. I wanted to drink as soon as I had the chance). The AAAQ gives three scores: inclined (mild inclinations to drink); obsessed (intense inclinations to drink); and avoidant (inclinations to avoid alcohol). Although the AUQ was used in study one, the AAAQ was more suitable for participants recalling the previous week of alcohol craving. The scale reliability in the present study was very good with an internal consistency of Cronbach's $\alpha = 0.812$; inclination $\alpha = 0.757$; obsessed $\alpha = 0.811$; avoidance $\alpha = 0.652$.

4.3. Procedure

The online study was delivered using Qualtrics (online survey software). All participants reported their age, followed by menstrual cycle information (contraception use, type of contraception, and cycle information). NC participants completed cycle questions (average cycle length, length of previous period, date of previous period) in order for us to determine which cycle phase they were in using the countback method [34]. HC participants selected the type of hormonal contraception they used. After this they completed the TLFB, WSI-S, BIS, and AAAQ.

4.4. Statistical analyses

A MANOVA was conducted to analyse whether the between subjects factor (contraception use) influenced the dependent variables (alcohol consumption and alcohol craving). Hierarchical regressions were used for each group (NC and HC) to assess the influence of the variables associated with alcohol consumption. The steps in each regression were: 1) Age; 2) Craving; 3) Impulsivity; and 4) Stress. The number of NC participants who answered the cycle questions correctly was not sufficient to run an analysis comparing cycle phases.

5. Results – study two

5.1. Participant characteristics

Out of the 298 participants, 131 were NC and the remaining 167 were HC users. The mean age of participants in the NC group was 20.04 years (± 3.01) and for the HC group was 19.83 (± 2.68). After outliers were removed there were 262 participants remaining: 118 NC with a mean age of 19.54 (± 2.20) and 144 HC with a mean age of 19.63 (± 2.12). See Table 2 for descriptive statistics for alcohol consumption and associated factors.

5.2. Craving and alcohol consumption (units; 10 mL/8g)

The MANOVA results showed that those in the HC group consumed significantly more alcohol than those in the NC group ($F = 13.40$, $p < .001$, $\eta^2 = 0.04$) and were also more alcohol inclined (according to the AAAQ) ($F = 7.08$, $p = .008$, $\eta^2 = 0.02$). However, there was no significant difference between the groups regarding alcohol obsession ($F = 1.43$, $p = .233$, $\eta^2 = 0.01$) or alcohol avoidance ($F = 3.17$, $p = .076$, $\eta^2 = 0.01$). After outliers (≥ 3 Standard Deviations from the mean) were removed the results showed that those in the HC group still consumed significantly more alcohol than those in the NC group ($F = 8.46$, $p = .004$, $\eta^2 = 0.03$). However, there was no longer a difference between the NC and HC groups for scores on the alcohol inclined dimension of the AAAQ ($F = 3.70$, $p = .056$, $\eta^2 = 0.01$). As before, there was no evidence for a difference between groups for alcohol obsession ($F = 0.31$, $p = .581$, $\eta^2 = 0.00$) or alcohol avoidance ($F = 2.34$, $p = .127$, $\eta^2 = 0.01$).

5.3. Factors associated with consumption in NC group

The hierarchical regression model predicted approximately 29.8% variance in the amount of alcohol consumed in the NC group. The results showed a negative association between age and alcohol consumption. After controlling for age, craving and impulsivity were both positively associated with alcohol consumption. However, stress was not associated with alcohol consumption. After outliers (≥ 3 Standard Deviations from the mean) were removed, the regression model predicted approximately 33.6% variance in the amount of alcohol consumed amongst the NC group. A negative association was found between age and alcohol consumption. Craving and impulsivity were still positively associated. In addition, stress became positively associated with alcohol consumption (Table 3).

Table 2

Study Two descriptive statistics for alcohol consumption and associated factors.

Variable	Mean (SD)	
	NC (n = 118)	HC (n = 144)
Consumption (units of alcohol; 10 mL/8g)	12.87 (11.35)	17.46 (13.66)
Craving (Inclined)	5.83 (2.13)	6.32 (1.88)
Craving (Avoidant)	2.18 (1.21)	1.96 (1.06)
Craving (Obsessed)	1.97 (1.30)	2.07 (1.39)
Impulsivity	69.93 (10.69)	68.90 (11.13)
Stress	64.88 (21.98)	65.81 (21.68)

Table 3

Regression showing the associations between factors and alcohol consumption for the NC group (outliers removed).

Variable	Cumulative		Simultaneous	
	R2-change	F-change	B	P
Step 1				
Age	.104	F(1,115) = 13.33**	-.15	.071
Step 2				
Alcohol Inclined	.117	F(3,112) = 5.63*	.21	.027
Alcohol Obsessed			.12	.199
Alcohol Avoidant			-.11	.204
Step 3				
Impulsivity	.076	F(1,111) = 12.05*	.25	.004
Step 4				
Stress	.039	F(1,110) = 6.38*	.22	.013

**p < .001; *p < .05.

5.4. Factors associated with consumption in HC group

The hierarchical regression model predicted approximately 35.4% in the amount of alcohol consumed amongst the HC group. Similar to the NC group, older participants consumed less alcohol, and higher craving scores predicted higher alcohol consumption. However, neither impulsivity nor stress were significantly associated with alcohol consumption. See Table 4 for regression results. After outliers (≥ 3 Standard Deviations from the mean) were removed, the regression model predicted approximately 33.2% in the amount of alcohol consumed amongst the HC group. The individual associations between factors and consumption remained the same: older participants consumed less alcohol, and higher craving scores predicted higher alcohol consumption. However, impulsivity and stress were not associated with alcohol consumption. See Table 4 for regression results.

6. Discussion

Using both lab- and online-based methods, the current pilot research sought to identify whether differences in alcohol consumption occurred between menstrual cycle phase, between females who were NC or HC, and to explore whether any differences were influenced by factors previously associated with drinking behaviour (craving, stress, mood, and impulsivity). Interestingly, as the studies employed different methods to address these aims, the findings did differ across the two studies. Study one (lab-based) showed that NC and HC participants displayed different alcohol-related behaviours. Contrary to our prediction, NC participants did not consume more alcohol during the FP compared to the LP in the experimental study. However, in line with previous literature [31] the NC group displayed higher alcohol craving during the FP. Further, the quasi-control HC group did not display this shift in craving across the two sessions, supporting our hypothesis that HC participants would not differ between the two sessions. The measures of craving, stress, mood and impulsivity did not appear to be influenced by cycle phase, as such they did not influence the relationship between cycle phase and alcohol consumption. We did not find any effects of alcohol on mood, stress, or anxiety scores for either phase or group. This differed from study two; the online data found that the HC group reported higher alcohol consumption and levels of craving compared to the NC population. Additionally, as hypothesised, the regression model predicted more variance in the alcohol consumed amongst the NC group compared to the HC group. Age, craving, impulsivity, and stress were all significantly associated with alcohol consumption for the NC group, whereas, impulsivity and stress were not associated with consumption for the HC group.

The findings of the present study support previous research which has shown that females may be more susceptible to substance cravings during

Table 4

Regression showing the associations between factors and alcohol consumption for the HC group (outliers removed).

Variable	Cumulative		Simultaneous	
	R2-change	F-change	B	P
Step 1				
Age	.095	F(1,142) = 14.97**	-.23	.003
Step 2				
Alcohol Inclined	.226	F(3,139) = 15.47**	.34	<.001
Alcohol Obsessed			.26	.005
Alcohol Avoidant			-.08	.319
Step 3				
Impulsivity	.000	F(1,138) = 0.04	.03	.664
Step 4				
Stress	.010	F(1,137) = 2.04	-.11	.156

**p < .001; *p < .05.

their FP [19], as we found NC individuals displayed increased alcohol craving during this phase. This could be because the sample consisted of young females and younger samples may be driven more by the positive reinforcing effects of alcohol. Interestingly, the HC group showed consistently high levels of craving, which could be because the hormonal content of the contraception is more similar to the FP than the LP, i.e. higher oestrogen levels and/or lower progesterone levels (see Figs. 1 and 2). This hormonal explanation is also supported by previous findings [17, 18,22]. However, there are both monophasic and triphasic methods of hormonal contraception which contain different amounts of oestrogen and, as such, the HC group in this study cannot be considered homogeneous. Additionally, in study one the type of hormonal contraception was not recorded. Future research should consider contraceptive type to control for the differences in hormonal content.

Overall, the results of the present research suggest that NC and HC groups have different patterns of alcohol-related behaviour. One explanation could be hormonal level patterns, as the NC group had cyclical fluctuating levels of oestrogen and progesterone whereas the HC group experienced reduced fluctuations of ovarian hormones. However, this is speculative and more research is needed to investigate causality, particularly research using blood serum samples to measure hormone levels, which would aid our understanding of the potential underlying effects of hormonal level shifts across the cycle. Additionally, these findings suggest that the NC group may have more complex motivations with more factors associated with consumption in comparison to the HC group which, again, could be a result of the fluctuating hormones and the effects of these on the reward system [26,47,48].

To our knowledge, this is the first work to use multiple methodologies to investigate the relationship between the menstrual cycle, alcohol use and potential mediators [3,11,23]. Study one was also the first to use a period tracker to determine cycle phase within this field, use a mixed design, and utilise hormonal contraception users as a quasi-control group. Although we cannot be sure of cycle phase, further studies could verify this method of using a period tracker using blood samples to assess hormone levels (oestrogen and progesterone). The pattern of results across the two studies may be due to the different methodologies used. Alcohol consumption was found to differ between the NC and HC groups in study two but not in study one. There are several potential reasons for this. Firstly, there was a sample size discrepancy between the two studies, with study two having a larger sample, meaning these results may be more reliable. Secondly, study one was conducted in the lab environment which is somewhat artificial, this may then have influenced the participants' responses and behaviour [49]. This could also explain why consumption levels were low overall in study one. We also used different measures of consumption; in study one we measured amount of alcohol consumed in mLs, whereas in study two we relied on participant

recall of alcohol consumption in the previous week. Therefore in study two, participants could recall consumption over a longer period of time which is more representative of overall consumption compared to a 10 minute window. Additionally, participants can underreport alcohol consumption with measures such as the TLFB, as such future research may benefit from an ecological momentary assessment (EMA) design. Regarding the differences in the effects of the other variables measured, again the online study is arguably more ecologically valid as participants can reflect on their experiences within their usual environment. Whereas, those in study one may have felt similar moods and stress levels as they were in the same environment. It must also be noted that the sample in study one comprised mostly of undergraduate students and as such their alcohol consumption and stress levels may be influenced by the time of year (i.e. during exams), although we avoided these periods during data collection. Finally, the studies heavily relied on self-report measures which do not always match with objective behaviour. The cross-sectional method also poses additional issues with regard to reliable measurement of alcohol use. These serve as additional rationales for future studies to adopt EMA methods in order to capture real-time measures which may be more accurate.

This was the first study to encompass the potential role of mediating factors, e.g. stress [3,11]. Although we did not find any relationships between the mediating factors and alcohol use by phase/group in the lab-based study, the online study revealed that factors such as craving, stress, and impulsivity were associated with alcohol consumption amongst NC participants. Perhaps the difference in findings between the studies was due to study one discriminating between menstrual cycle phases, whereas study two simply compared the NC and HC samples. An additional issue arises from cross-sectional methods as it is inherently difficult to ascertain cycle phase using a self-report countback method. As such, future online studies would benefit from a longitudinal design to compare the two cycle phases of individuals. Nevertheless, the findings from the online study suggest that the lack of ovarian hormonal shifts in the HC group may result in alcohol consumption which is less influenced by psychological factors. This is compatible with previous research which has shown that the menstrual cycle influences craving, impulsivity, and stress [31,50,51]. The results from the regression models showed that age was significantly associated with consumption for both NC and HC groups, with older individuals consuming less alcohol. Although such findings might be related to a variety of demographic and socioeconomic factors, e.g. family/work/study responsibilities, oestrogen levels do start to decline after the key reproductive years [52], which may also be linked with lower alcohol use. Further research is needed to establish the factors responsible for this relationship.

Research would benefit from larger sample sizes as, although we used a power calculation to determine the sample size for both studies, the sample was still relatively small for the lab-based study which reduces the reliability of the findings [53]. Additionally, the sample for study one was homogeneous and self-selected (e.g. the age range of 18–25). This was beneficial to control for potential heterogeneous factors that influence the relationship between the menstrual cycle and alcohol use, such as age (as shown in study two). Future research should aim to investigate whether the findings are replicated in different samples (e.g. childbirth history) and cross-culturally as research has shown cross-cultural differences in reports of both somatic, behavioural and psychological pre-menstrual symptoms [54]. It is also important to consider potentially confounding factors in relation to premenstrual syndrome which has been reported to affect alcohol use [55]. A limitation of the studies is that they did not measure baseline consumption. This must be considered in future studies to ensure that the participants usually consume similar amounts of alcohol. Finally, an important limitation to consider is that although using the period tracker for the participants in the present study revealed their cycles were regular, there was no way to ensure that they usually experience regular cycles. As such, future research should ensure that they recruit females with regular menstrual cycles and monitor their cycle for a minimum of two months. Regarding additional factors, more

robust measures of stress (i.e. the Trier Social Stress Test [56]) and impulsivity (i.e. the stop-signal task [57]) could be included in future study designs.

Finally, gonadal-hormones do appear to be an influential factor for sex-specific patterns of alcohol use [3,11]. The menstrual cycle in particular appears to affect factors associated with alcohol use, as such the present research and future work in this field could be used to inform treatments for alcohol use disorder (AUD), e.g. hormonal contraception may influence alcohol consumption in individuals receiving treatment for AUD.

7. Conclusions

Overall, the findings showed that females who were NC craved alcohol more during their FP compared to their LP, whereas hormonal contraception users did not display this shift. However, these findings did not translate to subsequent alcohol consumption, nor did we find craving, stress or mood to be mediating variables. The findings also revealed that age, craving, impulsivity, and stress were all associated with alcohol consumption in a NC sample, whereas impulsivity and stress were not associated in a HC sample. These findings highlight that future alcohol research should consider menstrual cycle and hormonal contraception, and the corresponding hormonal patterns.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- [1] NHS England, NHS statistics on alcohol, England, Available at, <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-alcohol/statistics-on-alcohol-england-2017>, 2017.
- [2] NHS England, Statistics on alcohol, England 2020, Available at, <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-alcohol/2020/part-1>, 2020.
- [3] A. Erol, V.M. Karpyak, 'considerations', Drug and Alcohol Dependence, Elsevier Ireland Ltd, 2015, <https://doi.org/10.1016/j.drugalcdep.2015.08.023>.
- [4] M.D. Niño, et al., Gender differences in trajectories of alcohol use from ages 13 to 33 across Latina/o ethnic groups, Elsevier, Drug Alcohol Depend. 180 (2017) 113–120, <https://doi.org/10.1016/j.drugalcdep.2017.08.008>. September.
- [5] A. White, et al., Converging Patterns of Alcohol Use and Related Outcomes Among Females and Males in the United States, 2002 to, vol. 39, 2015, pp. 1712–1726, <https://doi.org/10.1111/acer.12815>, 9.
- [6] G. Rahav, et al., The influence of societal level factors on men's and women's alcohol consumption and alcohol problems 41 (2006), <https://doi.org/10.1093/alcalc/agl075>.
- [7] R.W. Wilsnack, et al., Gender and Alcohol Consumption: Patterns from the Multinational GENACIS Project, 2009, pp. 1487–1500, <https://doi.org/10.1111/j.1360-0443.2009.02696.x>.
- [8] E. Kuntsche, et al., Why do young people drink? A review of drinking motives 25 (2005) 841–861, <https://doi.org/10.1016/j.jcpr.2005.06.002>.
- [9] M.K.B. Lustyk, et al., Psychophysiological and neuroendocrine responses to laboratory stressors in women: implications of menstrual cycle phase and stressor type, Biol. Psychol. 83 (2) (2010) 84–92, <https://doi.org/10.1016/j.biopsycho.2009.11.003>.
- [10] M. Holmila, K. Raitasalo, Gender Differences in Drinking: Why Do They Still Exist?, 2005, pp. 1763–1769, <https://doi.org/10.1111/j.1360-0443.2005.01249.x>.
- [11] J.B. Becker, G.F. Koob, Sex Differences in Animal Models: Focus on Addiction, 2016, pp. 242–263. April.
- [12] M. Graziani, P. Nencini, R. Nisticò, Genders and the concurrent use of cocaine and alcohol: pharmacological aspects, Pharmacol. Res. 87 (2014) 60–70, <https://doi.org/10.1016/j.phrs.2014.06.009>. Elsevier Ltd.
- [13] K.D. Shield, I. Soerjomataram, L. Building, Alcohol use and breast cancer, Crit. Rev. 40 (6) (2016) 1166–1181, <https://doi.org/10.1111/acer.13071>.

- [14] C. Buccelli, et al., Gender differences in drug abuse in the forensic toxicological approach, *Forensic Sci. International* 265 (2016) 89–95, <https://doi.org/10.1016/j.forsciint.2016.01.014>. Elsevier Ireland Ltd.
- [15] C.S. Woolley, Acute Effects of Estrogen on Neuronal Physiology, 2007, <https://doi.org/10.1146/annurev.pharmtox.47.120505.105219>.
- [16] R. Kishimoto, et al., Differences in Mouse Hepatic Ethanol Metabolism, and CYP2E1 which is induced in mice by ethanol Ethyl alcohol (ethanol) is used in alcoholic beverages exposure, shows high aniline hydroxylase (ANH) active or as an ingredient in cooking contain 9 (2002) 216–224.
- [17] J.B. Becker, M. Hu, Sex differences in drug abuse, *Front. Neuroendocrinol.* 29 (1) (2008) 36–47, <https://doi.org/10.1016/j.yfrne.2007.07.003>.
- [18] V. Quinones-jenab, S. Jenab, Influence of Sex Differences and Gonadal Hormones on Cocaine Addiction, 2010, pp. 14–22.
- [19] R.R. Wetherill, T.R. Franklin, et al., Ovarian Hormones, Menstrual Cycle Phase, and Smoking: a Review with Recommendations for Future Studies, 2016, <https://doi.org/10.1007/s40429-016-0093-z>.
- [20] J.J. Anker, M.E. Carroll, Females are more vulnerable to drug abuse than males: evidence from preclinical studies and the role of ovarian hormones, in: J.C. Neill, J. Kulkarni (Eds.), *Biological Basis of Sex Differences in Psychopharmacology*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2011, pp. 73–96, https://doi.org/10.1007/978-1-4419-9303-2_3.
- [21] R.R. Wetherill, K. Jagannathan, et al., Influence of Menstrual Cycle Phase on Resting-State Functional Connectivity in Naturally Cycling, Cigarette-dependent Women, 2016, pp. 1–9, <https://doi.org/10.1186/s13293-016-0078-6>.
- [22] S.M. Evans, R.W. Foltin, Exogenous Progesterone Attenuates the Subjective Effects of Smoked Cocaine in Women, but Not in Men, 2006, pp. 659–674, <https://doi.org/10.1038/sj.npp.1300887>.
- [23] J.M. Turner, H. De Wit, Menstrual Cycle Phase and Responses to Drugs of Abuse in Humans, vol. 84, 2006, pp. 1–13, <https://doi.org/10.1016/j.drugalcdep.2005.12.007>.
- [24] E. Montero-López, et al., The relationship between the menstrual cycle and cortisol secretion: daily and stress-invoked cortisol patterns, Elsevier, *Int. J. Psychophysiol.* 131 (2018a) 67–72, <https://doi.org/10.1016/j.ijpsycho.2018.03.021>. April 2017.
- [25] A. Treloar, et al., Variation of the human menstrual cycle through reproductive life, *Int. J. Fertil.* (1967) 77–126.
- [26] S. Banis, M.M. Lorst, The combined effects of menstrual cycle phase and acute stress on reward-related processing, *Biol. Psychol.* 125 (2017) 130–145, <https://doi.org/10.1016/j.biopsycho.2017.02.005>. Elsevier B.V.
- [27] L. Espin, et al., Effects of sex and menstrual cycle phase on cardiac response and alpha-amylase levels in psychosocial stress, Elsevier, *Biol. Psychol.* 140 (2019) 141–148, <https://doi.org/10.1016/j.biopsycho.2018.12.002>. December 2018.
- [28] E. Montero-López, et al., The relationship between the menstrual cycle and cortisol secretion: daily and stress-invoked cortisol patterns, Elsevier, *Int. J. Psychophysiol.* 131 (2018b) 67–72, <https://doi.org/10.1016/j.ijpsycho.2018.03.021>. April 2017.
- [29] R.F. Anton, What is craving, *Alcohol Res. Health* 23 (3) (1999) 165–173.
- [30] R. West, J. Brown, *Theory of Addiction*, John Wiley & Sons, 2013.
- [31] T.R. Franklin, et al., Retrospective Study: Influence of Menstrual Cycle on Cue-Induced Cigarette Craving, vol. 6, 2004, pp. 171–175, <https://doi.org/10.1080/14622200310001656984>, 1.
- [32] C. Kiel, G * Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences 39 (2) (2007) 175–191.
- [33] J. Grieger, R. Norman, Menstrual cycle length and patterns in a global cohort of women using a mobile phone app: retrospective cohort study, *J. Med. Internet Res.* 22 (6) (2020).
- [34] E. Hampson, A brief guide to the menstrual cycle and oral contraceptive use for researchers in behavioral endocrinology, *Horm. Behav.* 119 (2020) 104655, <https://doi.org/10.1016/j.yhbeh.2019.104655>. December 2019.
- [35] J. MacKillop, Factor structure of the alcohol urge questionnaire under neutral conditions and during a cue-elicited urge state, *Alcohol Clin. Exp. Res.* 30 (8) (2006) 1315–1321, <https://doi.org/10.1111/j.1530-0277.2006.00159.x>.
- [36] L.D. Grunebaum, et al., No Title 10 (2) (2011) 89–93, <https://doi.org/10.1111/j.1473-2165.2011.00554.x>.
- [37] L.A. Ray, et al., Catching the alcohol buzz: an examination of the latent factor structure of subjective intoxication, *Alcohol Clin. Exp. Res.* 33 (12) (2009) 2154–2161, <https://doi.org/10.1111/j.1530-0277.2009.01053.x>.
- [38] A. Jones, et al., 'The ad-libitum alcohol "taste test": secondary analyses of potential confounds and construct validity', *Psychopharmacology* 233 (5) (2016) 917–924, <https://doi.org/10.1007/s00213-015-4171-z>.
- [39] L.C. Sobell, M.B. Sobell, Timeline follow-back, in: R.Z. Litten, J.P. Allen (Eds.), *Measuring Alcohol Consumption: Psychosocial and Biochemical Methods*, Humana Press, Totowa, NJ, 1992, pp. 41–72, https://doi.org/10.1007/978-1-4612-0357-5_3.
- [40] A.K. Rose, et al., The Contributions of Value-Based Decision-Making and Attentional Bias to Alcohol-Seeking Following Devaluation, 2013, pp. 1241–1249, <https://doi.org/10.1111/add.12152>.
- [41] S. Yu Rueger, et al., Self-administered web-based timeline followback procedure for drinking and smoking behaviors in young adults, *J. Stud. Alcohol Drugs* 73 (5) (2012) 829–833.
- [42] P.J. Brantley, et al., Development and validation of the weekly stress inventory-short form, *J. Psychopathol. Behav. Assess.* 29 (1) (2007) 54–59, <https://doi.org/10.1007/s10862-006-9019-8>.
- [43] J. Patton, M. Stanford, E. Barratt, Factor structure of the Barratt impulsiveness scale, *J. Clin. Psychol.* 51 (6) (1995) 768–774.
- [44] D.M. Dougherty, et al., Fifty years of the barratt impulsiveness scale: an update and review, *Pers. Individ. Differ.* 47 (5) (2009) 385–395, <https://doi.org/10.1016/j.paid.2009.04.008>. Elsevier Ltd.
- [45] A.R. Lang, et al., Comparison of three models of alcohol craving in young adults: a cross-validation, *Addiction* 99 (4) (2004) 482–497, <https://doi.org/10.1111/j.1360-0443.2004.00714.x>.
- [46] *Clue, Cycle Science: Hormonal Contraception and Your Body*, 2019.
- [47] J. Bayer, P. Bandurski, T. Sommer, Differential modulation of activity related to the anticipation of monetary gains and losses across the menstrual cycle, *Eur. J. Neurosci.* 38 (10) (2013) 3519–3526, <https://doi.org/10.1111/ejn.12347>.
- [48] J. Dreher, et al., Menstrual cycle phase modulates reward-related neural function in women 104 (7) (2007) 2465–2470.
- [49] D. McKay, M.L. Schare, The effects of alcohol and alcohol expectancies on subjective reports and physiological reactivity: a meta-analysis, *Addict. Behav.* 24 (5) (1999) 633–647.
- [50] K.J. Pine, Women's Spending Behaviour Is Menstrual-Cycle Sensitive, 2010, 0.
- [51] J. Studd, N. Panay, Hormones and Depression in Women, 2010, p. 7137, <https://doi.org/10.1080/13697130400012262>, 2004.
- [52] E.R. Velde, P.L. Pearson, The variability of female reproductive ageing 8 (2) (2002) 141–154.
- [53] K.S. Button, et al., Nature Publishing Group, Power Failure: Why Small Sample Size Undermines the Reliability of Neuroscience, vol. 14, Nature Publishing Group, 2013, pp. 365–376, <https://doi.org/10.1038/nrn3475>, 5.
- [54] M. Hasin, L. Dennerstein, G. Gotts, Menstrual cycle related complaints: a cross-cultural study, *J. Psychosom. Obstet. Gynecol.* 9 (1) (1988) 35–42.
- [55] S.E.T. Al, et al., And Family History of Alcoholism in Women with Premenstrual Syndrome *, 1994.
- [56] C. Kirschbaum, 'Trier Social Stress test.', *Encyclopedia of Psychopharmacology*, 2015, pp. 1755–1758.
- [57] A. Jones, et al., The effects of priming restrained versus disinhibited behaviour on alcohol-seeking in social drinkers, *Drug Alcohol Depend.* 113 (1) (2011) 55–61, <https://doi.org/10.1016/j.drugalcdep.2010.07.006>. Elsevier Ireland Ltd.