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The effects of menstrual-related pain on attentional interference

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## Abstract

Pain-related attentional interference has been found in both chronic pain and laboratory-induced pain settings. However, few studies have examined such interference effects during common everyday painful episodes. Menstrual cycle-related pain is a common pain that affects a large number of women on a regular basis. The purpose of the current study was, therefore, to examine the effects of menstrual pain on attentional interference. Fifty-two healthy adult females were tested during two different phases of their menstrual cycles: once during a non-pain phase (mid follicular), and once whilst experiencing menstrual pain (late luteal/early follicular). On each testing session participants received a battery of four attentional interference tasks that included selective attention (flanker task), attention span (n-back task), attentional switching (switching task), and divided attention (dual task). Greater attentional interference effects were found to occur during the menstrual pain phase compared to the non-pain phase. Interestingly, the nature of this effect was a general worsening in performance (e.g., slowing, less accurate), rather than a specific attentional deficit. These results add to a growing literature that generally indicates that attentional interference occurs across a range of different types of pain, including common painful episodes. However, they also highlight that the specific nature of this interference effect may depend on the type pain under consideration. Implications of these findings are also considered.

## Summary

Menstrual cycle-related pain results in a general attentional interference effect in healthy women.

## 1. Introduction

Pain has a disruptive and interfering effect on attention [6]. However, there are certain situations where aspects of attention are spared these interruptive effects [13; 14; 21]. For example, LeGrain and colleagues [14] found that working memory processes can help direct attention away from pain and towards task performance. Similarly, others have found that pain interference is more likely to occur when the task in question is demanding, with easier tasks escaping interference effects [21]. Such variability is partly because attention is not a unitary construct, but instead can be divided into different types (e.g., early detection, dual processing) [2], and varies in difficulty and/or dependence on executive control [20; 21]. The relationship between pain and attention is therefore complex, and determined by an interplay between top-down (e.g., motivation) and bottom-up (e.g., salience) factors [15; 28; 33].

Much of what is known about pain interruption is derived from investigations with chronic pain patients, or from studies that make use of experimental pain induction techniques [6]. Much less is known about the potential interruptive effects of common everyday pain on attentional performance [23]. There is also a more general need to consider the impact that common pains have on everyday life [5]. This impact is likely to be considerable, especially given that common events such as periodic back pain, headaches and cold-flu symptoms make up a large number of the reasons given for physician visits, as well as days off work [9; 17].

Although there are methods for investigating common acute pain [19], few studies have actually used these methods to directly examine pain interference effects. One recent study examined the effects of spontaneous headache on a

battery of attentional tasks [23]. Unlike laboratory-pain, headache pain resulted in general performance detriments (e.g., slowing, inaccuracy) rather than specific attention impairments. This suggests that common everyday pains might result in different types of interference. However, before any specific conclusions can be made there is a need to examine whether such effects are stable, and generalise to other types of common acute pain.

The primary aim of the current study was therefore to investigate whether pain interference effects found in headache generalise to another type of common pain. We sought to examine attentional interference effects using a menstrual pain model. The rationale was based on a previous review of everyday pain methods [19] that recommended menstrual pain as a potentially useful paradigm; it is not only a common pain, but is also highly predictable. Furthermore, menstrual cycle-related changes in both pain and cognition have been previously reported [7; 8; 10; 24; 26; 27]. A secondary aim was to investigate whether menstrual pain results in a general dampening of performance or is associated with specific attentional deficits.

## 2. Methods

### 2.1. Design

A repeated-measures design was employed in which all participants were testing during two phases of their menstrual cycles. One phase was whilst experiencing menstrual-related pain, whereas the other was during a no-pain phase. Therefore, the within-groups factor was the phase of testing (no pain vs. menstrual pain phase). The primary outcome variables were attentional performance indicators derived from our previous work with cognitive tasks (e.g., reaction times, error rates). Secondary outcomes were pressure pain threshold, self-report pain and mood experience.

## *2.2. Participants*

A total of 65 participants were initially recruited into the study, with a mean age of 22.09 (SD= 5.49; age range 18-46 years). Participants were female students and staff from the University of Bath who identified themselves as experiencing recurring menstrual pain during their monthly cycle. Women were recruited into the study if they reported a regular menstrual cycle (ranging from 25 to 32 days in length), were not taking hormonal contraceptives and had not done so for at least 6 months, were not pregnant, were not menopausal or post-menopausal, and were not taking any fertility medications. Participants were in good general health with no chronic pain condition, and were asked to refrain from taking analgesic medication for at least 12 hours prior to experimental testing sessions.

Of those recruited, 54 completed both phases of the study. Of the remaining 11 participants, 3 completed the no pain phase only, 1 completed the pain phase only, and 7 did not complete either phase. Reasons for non-completion varied, and included not experiencing menstrual pain and not being able to attend for testing. Data from 2 participants who completed the study were excluded from the final analysis due to a computer logging error. The final sample for analysis was 52 participants, with an average age of 21.92 (SD= 5.71; age range 18-46 years). The phase participants were initially tested in was opportunistically determined, and based on where in their cycle they were when recruited.

## *2.3. Determination of menstrual cycle testing phases*

Our primary goal was to measure attentional interference when women were experiencing menstrual-related pain. Since menstrual pain can vary within and between cycles we chose to follow the same testing strategy used previously in spontaneous headache i.e., test participants when they self-reported experiencing

pain [22]. However, pain sensitivity, mood and cognition can vary across the menstrual cycle [7; 10; 24; 26; 27], so we also needed to ensure that each participant was tested at approximately the same two phases of their cycle. As we chose to test participants when they self-reported experiencing menstrual pain, the pain phase was broadly defined as occurring around menstruation, and ranged from late-luteal (e.g., days 26-28, prior to day 1 of a 28 day cycle) to the early-follicular phases (e.g., days 1-5 of a 28 day cycle). This meant that women were not all tested at precisely the same hormonal phase of their cycles (e.g., late luteal only, early follicular only), but were instead tested when experiencing pain. This is an important methodological point, as pain sensitivity studies tend to define phases based on hormonal profile. However, this could have meant not testing women when they were in pain, which would have been inconsistent with our primary research goals. Although the pain phase depended on when women report experiencing menstrual pain, for the majority this was actually the first day of menstruation (day 1 of their cycle). The second phase was a non-pain/pain free day, and was defined as the mid-follicular phase, prior to ovulation. This phase was chosen because previous studies suggest that pain sensitivity is relatively low [24], and was determined by counting from the first day of menstruation i.e., days 5-9 of an average 28-day cycle.

As menstrual cycle lengths can vary between women, there is a need to determine optimal testing phases for each individual. Self-report (e.g., menstruation onset) was the main method used to achieve this goal, and supplemented with home ovulation detection tests. These tests provide a non-invasive objective measure of the surge in luteinizing hormone (LH) within urine, which occurs prior to ovulation [18]. Following standard instructions participants begin home testing during their late follicular phase (e.g., day 11 of a 28 day cycle), and was repeated every day for up

to 7 days until a surge is detected. A positive result indicated ovulation in the next 24 to 36 hours, and was used to help confirm whether testing occurred during the early follicular phase and prior to ovulation, as well as help predict menstrual pain phase.

#### *2.4. Attention tasks*

The tasks used in the current study comprised of modified versions of the Bath Test of Attention to Pain (BathTAP) battery [21; 22], and were selected on the basis that they were successfully used in a previous study on headache-related interference [23]. The tasks were programmed in E-Prime 2 Professional Software and presented on an Iiyama ProLite B1902STFT monitor, powered by a Viglen Genie desktop computer with a 32Hz Pentium Intel Core 2 duo processor and 2GB of RAM. A PST model 200a serial response box was used to record responses. As the tasks are described in detail elsewhere [23], they are briefly outlined here.

##### *2.4.1. Flanker task (selective attention)*

Selective attention was measured using a flanker task. A fixation cross was initially presented centrally on the screen display for 500ms, which was then replaced by either the number 2 or the number 4. Participants were required to indicate which number had been presented. These central targets were flanked by two additional numbers on either side, creating a 5-digit number. These flankers were either congruent, in that they were all the same digit as the central number (e.g., 22222) or they were incongruent, and so different to the central number (e.g., 44244). The congruent or incongruent presentation of stimuli was randomised. There were a total of 80 trials, with 40 congruent and 40 incongruent trials. There was a random inter-stimulus interval of either 500, 1000, or 1500 msec, and the task lasted approximately two minutes.

##### *2.4.2. n-back task (attention span)*

The n-back task is commonly used as a test of attention span. It requires participants to monitor a continuous stream of 90 letters that are presented in the central location of a display screen. Each letter is presented for 500ms, which is then followed by a blank screen for 1500ms. Participants are instructed to indicate whether the current letter was the same as one presented two letters previously. For example, in the sequence A, B, C, B, the correct response to the third letter (C) would be 'no', whereas for the fourth letter (B) it would be 'yes'. Participants made a key press response as to whether the letter was the same (define as a target) or different (a non-target) from the letter presented two items back (2-back). 30 target stimuli and 60 non-target items were presented in a randomised order. The duration of this task was approximately three minutes.

#### *2.4.3. Attentional switching task (switching)*

In this task participants were required to switch between two completing sets of instructions. A series of single digit numbers were centrally presented one at a time for 500 msec, with each item occupying a  $.7^{\circ}$  visual angle of the screen. Prior to each digit presentation, participants were presented with one of two instruction priming screens, which indicating how to respond to the subsequent digit. In one task, participants were instructed to indicate whether an odd or even number was presented, whereas in the second task, they were instructed to decide whether the digit was greater than five (i.e., 6, 7, 8, 9) or less than five (i.e., 1, 2, 3, 4). The priming screen contained either 'odd or even' or 'low or high' to indicate how to respond to the subsequent digit. For each trial, the task instructions could either remain the same as the previous trial (a repeat condition), or switch to the alternative task (a switch condition). Repeat or switch conditions were presented in a

randomised order. A total of 200 trials were presented, with a total duration of around six minutes.

#### *2.4.4. Dual attention task (divided attention)*

Participants were given instructions for two tasks that were run concurrently. For the numbers task, a continuous stream of single digits was presented in the centre of the screen, with each item occupying a  $.7^{\circ}$  visual angle. Participants were required to indicate when three consecutive odd or even numbers were presented by making a single button response. For the lines task, two lines were presented  $14.2^{\circ}$  from the centre of the screen, one to the far left of centre and one to the far right of the screen. The lines could appear in either a horizontal or vertical orientation, with instructions given to indicate when the two lines were presented in different orientation i.e., one horizontal and the other vertical, as opposed to both appearing in either a vertical or horizontal position. Items for both tasks (numbers and lines) were presented concurrently on the computer screen, requiring participants to monitor items for both tasks. There were 8 number and 8 line responses required per 80 displays, with 400 displays in total. A 'numbers' target and a 'lines' target could not occur on the same display. The task dependent responses occurred with equal priority (but never together) and required the same single key press for detection of either target. Each presentation of digits and lines remained on the screen for 1000ms. Task duration was approximately seven minutes.

#### *2.5. Pressure Pain Sensitivity*

Since pain sensitivity is known to vary across the menstrual cycle, we also examined whether this variable changed across the two testing phases [8; 16; 24]. Pain sensitivity was measured using a Somedic Algometer [28], which delivers pressure to soft tissue, muscles and joints, and enables a measure of pressure pain

thresholds. Participants were instructed to place their arm on the table in front of them, palm upright and pressure was applied to 5 equally distanced locations on the volar forearm. Pressure was increased at a rate of 50 kPa/s on a .79 cm<sup>2</sup> pad and participants were instructed to indicate as soon as they felt pain. Approximately five seconds was allowed as an inter-stimulus interval to ensure that thresholds did not reduce during testing as a result of the previous stimulus. Pressure pain threshold for each participant was concluded from an average over the five trials. Pressure pain threshold was measured in both the menstrual pain and pain free conditions.

### *2.6. Self-report measures of menstrual symptoms, pain and mood*

The following self-report measures were also completed.

*Menstrual pain screening (typical menstrual pain):* For the current study a short measure of typical menstrual pain was constructed, and administered during the initial screening phase. It comprised of a series of questions regarding the typical number of days that menstrual pain is experienced each month, a checklist of typical menstrual pain symptoms (e.g., cramps, abdominal swelling, backache headache etc.), as well as an index of typical severity of painful symptoms (none, mild, moderate, severe). Information concerning inclusion and exclusion criteria was also included in this scale to ensure participants were not taking oral contraceptives and were in good general health. Finally, the measure included a 100mm visual analogue scale (VAS) with the words 'no pain' to the left and 'worst imaginable pain' to the right. Participants were instructed to report their typical menstrual pain experience.

*Current menstrual pain:* On the day of menstrual pain phase testing, and before completing the cognitive tasks, all participants completed a measure of current menstrual pain. Participants indicated how long they had currently been in pain for, and completed the brief symptom checklist (as above). Pain intensity was

also measured using a four item descriptor scale (no pain, mild, moderate or severe), and included a question as to whether the current pain interferes with work/daily activities. A 100mm VAS scale was also included to measure current pain experience.

*Pain Catastrophizing Scale (PCS)* [30]: The PCS is a 13 item questionnaire designed to measure the extent to which individuals engage in catastrophic thinking and how this impacts on pain experience. Each item is scored on a five-point Likert-type scale, ranging from 0 (not at all) to 4 (all the time). Items can be combined into three subscales assessing rumination, helplessness and magnification, as well as summed together to form a total score. The total score was used here. This scale was administered once, during the screening session.

*Anxiety Sensitivity Index-3 (ASI-3)* [32]. The ASI-3 is an 18-item multi-dimensional scale designed to assess fear of anxiety-related sensations. Items include assessment of self-reflective concerns about physical responses (e.g., rapidly beating heart) as well as cognitive (e.g., concentration problems) and social concerns (e.g., others noticing signs of anxiety). Each item is scored on a five point scale, ranging from 0 (very little) to 4 (very much), and can be summed to form either three subscales or a total score scale. The total score was used here. This ASI-3 was administered once, during the screening session.

## 2.7. Procedure

Following ethical committee approval, participants attended a screening session. Participants in good general health who did not experience any clinically significant menstrual related symptoms gave their informed consent to participate in the study. Screening was used to obtain menstrual cycle details (e.g., current phase, average length etc.), which informed home ovulation testing. Participants also

completed the menstrual pain screening measure, as well as the PCS and ASI-3. Allocation to either menstrual pain or no-pain as the first testing condition was determined by calculating current menstrual phase and counting onto the next possible testing window; 21 participants were tested in the non-pain phase first, and 31 in the pain phase first. Mid-follicular phase (day 5-9 of the cycle) was determined by counting on from self-reported onset of menstruation. Home ovulation tests were used to confirm testing occurred prior to ovulation, and helped predict menstruation.

For each testing phase (pain vs. no pain), participants confirmed that no analgesic medication had been taken for at least 12 hours. Participants completed the battery of cognitive tasks, followed by the pressure pain threshold task. For the menstrual pain phase, the current menstrual pain measure was also administered. The duration of each testing session was around 40 minutes. On completion of both phases of testing participants were debriefed and paid a modest sum.

### 3. Results

#### *3.1 Data screening*

Data screening was conducted on the questionnaire scores and attentional response data. There was very little missing data from the questionnaires (<5%), and so a mean substitution method was employed for the few missing data points identified [31]. Data filtering was conducted for extreme scores for each of the attention tasks, and followed the same procedures used in previous studies [23]. Reaction time data for the Flanker task were filtered to exclude responses below 200 msec and above 1500 msec, whereas for the switching task responses below 200 msec and above 3000 msec were removed.

Correct mean response times were calculated for each participant under both conditions of the study. These data were further screened to ensure they were

normally distributed. With the exception of the flanker task reaction time data, all data were normally distributed with acceptable skewness values between -2.56 and 2.56 [23]. Transformations were carried out on the Flanker data, but since this did not correct skewness untransformed data was analysed [31]. Data were examined for outliers, and defined as scores greater than three standard deviations above or below the group mean. Outliers were found in the flanker (reaction times n=3, accuracy n=4), n-back (false alarms n=2) and switching tasks (reaction times n=1, accuracy n=2); these participants were respectively removed from the analysis of each task.

### *3.2 Confirmation of phase of testing*

Of the 54 participants who completed both study phases, 29 participants detected an LH surge, whereas 22 participants were unable to detect an LH surge and 3 participants did not use the ovulation kits. This failure to successfully detect a LH surge in some participants was a surprise, and could be considered potentially problematic. However, in this study having successful ovulation tests were considered to be a useful marker of phase and guide as to when to test (hence their inclusion), but were not considered essential to the study objectives. Indeed, our primary goal was to test women when in subjective menstrual pain and when pain free, rather than pinpoint a particular hormonal phase of the cycle. Therefore, the low success rate was not considered a fatal flaw in study process for our purposes.

Even so, we acknowledge that this may not be a shared view, and as a precaution we conducted exploratory analysis to address whether typical and current pain sensitivity (VAS) levels were different between those where ovulation was confirmed, and those where it was not. No significant differences were found between groups. We also conducted analyses on the attention tasks with ovulation

confirmation as an additional between-groups factor. No overall difference was found in the general pattern of results found to those reported below, with the expectation of one additional effect within the switching task accuracy analysis. In light of this, we included all participants in the main analyses, and only included ovulation confirmation as a factor where it significantly contributed to any effects found.

### *3.3 Pain intensity and sensitivity*

#### *3.3.1 Self-report menstrual pain intensity*

The mean VAS score for reported typical menstrual pain intensity was 61.03 (SD= 20.20), and for current pain it was 53.04 (SD= 20.84). In terms of the four-item pain descriptors, moderate severity was most commonly reported for both the typical menstrual pain (n=34) and current menstrual pain (n=37) versions, with relatively fewer participants reporting severe painful symptoms (typically n=10; current n=3). In terms of specific menstrual pain symptoms reported on the critical day of testing, most reported more than one (mean = 2.67), of which cramps and fatigue were the most frequent. Taken together this confirms that participants reported regular menstrual pain, and that for most this was of moderate magnitude on the critical day of testing.

Following previous studies [12; 23], VAS scores for current pain were used to categorize participants into low (VAS score <50mm) or high current intensity pain groups (VAS score >49mm). There were 20 participants in the low intensity group (mean VAS=29.47; SD=9.09) and 32 in the high intensity group (mean VAS=67.70; SD = 9.03). Table 1 displays the means between these groups on the various self-report measures, and as can be seen there were no significant differences on either PCS or ASI-3 scales. Pain intensity group was used as a between-groups variable within all subsequent analysis.

### 3.3.2 Pressure pain sensitivity

A mixed-groups ANOVA was conducted on pressure pain sensitivity responses (for means see Table 1). The within-groups factor was menstrual pain condition (menstrual pain vs. no menstrual pain), and the between-groups factor was menstrual pain intensity (high vs. low). Analysis identified no significant effects. This indicates that although participants were in pain during the pain testing phase, this did not result in increased pain sensitivity to pressure pain.

[Table 1 & 2 about here]

### 3.4 Cognitive tasks

Table 2 presents the means and standard deviations for the cognitive tasks under pain and non-pain conditions.

#### 3.4.1 Flanker task

To investigate whether menstrual pain had an effect on flanker task performance, mean reaction times and accuracy data were subjected to 2 mixed-groups ANOVAs. The within-groups factors were menstrual pain condition (menstrual pain vs. no menstrual pain) and flanker task congruence (congruent vs. incongruent), whereas the between-groups factors was menstrual pain intensity (high vs. low).

Analysis of the reaction time data resulted in a significant main effect of menstrual pain condition  $F(1,47)=9.34$ ,  $p<.005$ , with participants responding more slowly during the pain phase (mean=467 msec) compared to the no pain phase (mean=420 msec). A significant main effect of flanker condition was also found  $F(1,47)=223.93$ ,  $p<.001$ , with participants responding faster to congruent stimuli (mean=424 msec) compared to incongruent stimuli (mean=462 msec). No other significant effects were found.

For the accuracy data, a significant main effect of flanker congruence condition was found  $F(1,46)=34.35, p<.001$ . This indicated participants were more accurate in the congruent condition (mean=.99) compared to the incongruent condition (mean=.96). All other effects were non-significant.

#### *3.4.2 n-back task*

The number of times a participant correctly identified a letter which was presented two letters previously (hits) was analysed using a mixed-groups ANOVA. The within-groups factor was menstrual pain condition (menstrual pain vs. no pain), and the between-groups factor was menstrual pain intensity (high vs. low). No significant effects were found.

A similar analysis was conducted on the number of false alarms generated, which was where a participant responded inaccurately to a letter that was not presented two letters back. A significant effect of pain intensity was found  $F(1,48)=5.54, p<.05$ , indicating that participants responded with more false alarms when they were in pain (mean=3.52) than when they were not in pain (mean=2.05). No other significant effects were found.

#### *3.4.3 Switching task*

Two separate mixed-groups analysis were conducted on the switching task data. The within-groups factors were menstrual pain condition (menstrual pain vs. no pain) and switching condition (switch vs. repeat), and the between-groups factor was menstrual pain intensity (high vs. low). For the reaction time data a significant main effect of switch condition was found  $F(1,49)=56.25, p<.001$ , with faster responses for repeat trials (mean=731 msec) compared to switch trials (mean=803 msec). All other effects were non-significant.

For accuracy, a significant main effect of pain condition was found  $F(1,49)=6.56, p<.05$ , with participants responding less accurately when experiencing menstrual pain (mean=.91) compared to when not (mean=.93). A significant main effect of switching condition was also identified  $F(1,49)=79.63, p<.001$ , with participants responding more accurately in repeat trials (mean=.94) compared to switch trials (mean=.90). No other significant effects were found.

When ovulation confirmation was added as an additional between-groups factor, this resulted in a number of additional higher-order interactions, including a four-way interaction between pain condition, switching condition, pain intensity and ovulation confirmation  $F(1, 47) = 8.38, p<.01$ ). However, exploratory analysis indicated that this higher-order effect not only occurred within women who did not confirm ovulation, but it did not make conceptual sense (those reporting low menstrual pain intensity during the pain phase exhibited greater switch costs when tested in the non-pain phase). It was not considered any further.

#### *3.4.4 Dual task*

Accuracy data were subjected to mixed-groups ANOVA, with menstrual pain condition (menstrual pain vs. no pain) and task (numbers vs. lines) as the within-groups factors, and pain intensity (high vs. low) as the between-groups factor. A significant main effect of pain condition was found  $F(1,50)=7.78, p<.01$ , showing that participants were less accurate when experiencing menstrual pain (mean=.60), compared to when not in pain (mean=.66). All other effects were non-significant.

#### *3.5 Correlation analysis between self report measures and attention tasks*

Given that attentional performance may be related to self-reported pain and anxiety, we conducted a series of correlations separately for the pain and non-pain phases. For the n-back and dual tasks we simply included the same variables used

in the main analysis. For the flanker and switching tasks, which were more complex, we calculated the following indexes of attentional performance: average reaction time, average accuracy scores, flanker indexes (flanker - no flanker) for both reaction times and accuracy, and switch cost indexes (switch - repeat) for reaction times and accuracy. These variables were then correlated with the self-report scales and pain sensitivity scores, separately for the pain and pain free phases of testing. Given the large number of correlations conducted, we adjusted the alpha level to  $p < .01$ , to prevent Type 2 errors. This analysis proved to be largely uninformative, with most relationships failing to reach significance. In fact the only significant relationship found was a positive correlation between typical pain intensity and the switch cost (accuracy) during the pain free phase ( $r = .47$ ,  $p < .001$ ).

#### 4. Discussion

These results are amongst the first to demonstrate that menstrual cycle-related pain is associated with attentional interference. Pain-related interference, which is well established within laboratory pain settings, also occurs within common everyday pains, such as the menstrual cycle. However, these data also highlight potentially important differences between types of pain and how such interference effects manifest themselves.

The pattern of effects found here suggest that menstrual pain may be associated with a general reduction in task performance; a dampening of cognition when experiencing pain. When experiencing menstrual pain, women were generally slower or less accurate on the flanker and switching task. This is in contrast to results reported in pain induction studies, where pain seems to have specific attentional interference effects [21]. It is more difficult to directly ascertain specificity of effects for the dual (both tasks are given equal priority) and n-back tasks (no

control condition). However, for the dual task there was indirect evidence for a general pain-related effect. Here, pain produced a general decline in accuracy across both tasks, whereas in our laboratory study [21] a specific decrease in accuracy was found on the lines task, and a relative improvement on the numbers task. Overall, this would seem to suggest a general pain-related dampening effect on performance. If so, then it may be interesting to consider a potential mechanism for this dampening effect. Answers may stem from research into the cognitive effects of sleep deprivation, where it has been suggested that a general decline in performance is due to brief inattentiveness [1], possibly due to disruptions in executive control. It is possible therefore that pain causes intermittent disruptions in attention by impairing executive control processes, resulting in a generalized decline in performance.

Importantly, the pattern of effects found here are not in isolation, but consistent with at least one other study to have considered these tasks within the context of common acute pain. Moore et al. [23] found that spontaneous headaches resulted in a general decrement in attentional interference. Table 3 directly compares the results found in the current study with those reported by Moore et al. [23], where a similarity is found. Of course both studies stem from the same research group, and we need to be careful about drawing definite conclusions before such effects are ratified within other laboratories. However, if reliable, then it certainly suggests that the type of pain may impact on the nature of interference effects found.

[Table 3 about here]

What is striking about the comparative results presented in Table 3 relates to the consistency of effects found for the flanker and switching tasks, both of which include speed and accuracy as outcome variables. For the flanker task, there was a

general decrease in speed, but maintenance in levels of accuracy, whereas for the switching task the opposite was found; speed of performance was not affected, whereas accuracy declined when in pain. These differences may partly reflect task demands, including instructions given to participants [3]. Indeed, we have argued that the flanker task may be less complex, and less demanding on executive functions, than the switching task [21]. However, this pattern may also reflect different processing strategies being employed by participants when in pain, which may depend on the type or complexity of task being performed.

If everyday pain results in general attentional dampening, whereas laboratory-induced pain has more specific effects, a key question to ask is why? One possibility is that there are shared or overlapping experiences in the type of everyday pains we have examined, and it is these common symptoms that are resulting in cognitive dampening. For example, a number of women in the current study reported headache as a symptom they were experiencing within the general profile of menstrual pain. Whilst headache may be a possible common factor, for the current study there were fewer women who report this symptom ( $n = 18$ ) than did not ( $n = 34$ ), and of those that did report it, all experienced at least two other symptoms as well. An alternative explanation may be that the type of pain is an important factor. Although a benefit of laboratory-induced pain is that controlled nociceptive insult is short-lived, these features may also affect how people perform tasks. It could be that the relative novelty of induced pain may have resulted in more specific effects. For example, if pain is short-lived and/or novel then a temporary increase in effort or concentration may be possible, e.g., a form of competitive recruitment of effort, whereas for longer types of pain, this may not be sustainable and so alternative approaches may be required.

As with all research a number of issues that emerged during the study that need to be considered before drawing definite conclusions. One of the more unexpected outcomes reported here was the relatively large number of participants who failed to report a positive ovulation test during the study. Reasons are varied, and could be due to both participant (e.g., motivation, missed ovulation) and study characteristic (e.g., instructions, incorrect estimation of ovulation). Fortunately, for the current study, pinpointing and confirming the specific phase of the cycle was less important than ensuring participants were tested when in pain, and when pain free. A second issue is that we assume that menstrual pain is producing attentional interference. However, women often reported multiple complaints (rather than just pain), which means other symptoms could account for the attention-related effects found here. Unfortunately, although women were recruited for the active presence of menstrual pain, we did not ask participants to indicate which other symptoms they were experiencing as strong, and so it not possible to tease out which menstrual symptoms are most disruptive. Similarly, other menstrual symptoms, which were not measured, such as fatigue, may have resulted in this generalized dampening effect.

Interestingly, catastrophizing, anxiety sensitivity and pain intensity were unrelated to attentional performance. This was surprising given that perceptions around the nature of the pain experienced are considered to influence the attentional effects of pain [15]. However, scores on these self-report measures were not particularly high, and most participants reported moderate, rather than highly intense levels of pain. This suggests that the sample did not find their pain experiences particular threatening. Grouping the sample into high and low levels of pain intensity also failed to find any consistent differences. Whilst it is important not to draw too many conclusions from null results, this is similar to the results reported by Moore et

al. [23] who failed to find an effect of current pain intensity using the same task battery. Others have reported mixed results with pain intensity [4; 25], suggesting that such effects are inconsistent. However, it should also be acknowledged that there have been few examples where intensity of pain has been systematically examined within the context of a pain-interference, and so it would be interesting to see a programme of research that examines this issue in detail.

The current findings also have interesting implications. For example, the attention dampening effects seen here could be considered as part of a wider cognitive response to attentional interruption from pain. If the adaptive function of pain is to penetrate awareness and demand attention, this is most likely to occur when the pain is unexpected, unpredictable, and/or perceived as threatening. However, even after short periods of time (e.g., hours, days), we start to habituate to pain, and so it would be interesting to track the time course of attentional interruption. It could also be that such habituation is actually due to a general dampening down of the attentional system, or some form of attentional fatigue. It would also be interesting to know whether attentional dampening occurs for other types of common acute pains. Would we get the same attentional dampening effects if we examined post-operative pain or dental pain? Placing this research within the context of upper respiratory tract infections would be interesting, not only given the frequency of occurrence, but also the mixture of muscular and headache symptoms that often accompany it. We also need to know how such attentional interference actually affects people's everyday lives. The tasks used here are thought to reflect core processes which are often used in combination in many real world activities. For example, we often find ourselves multitasking, switching between tasks, during a range of real world activities, such as when driving, shopping etc. The next challenge

is to consider attentional interruption out of the lab and in the real world. We have already advocated looking at real world pain [19], so it also makes sense to think about real world cognition [11].

In conclusion, the current study is one of the first to show that variation in pain-related interference occurs across the menstrual cycle. It confirms that common acute pain not only disrupts cognitive performance, but that the type of interruption is different from that found in pain-induction studies. It highlights the need for careful investigations that consider how and in what way attentional interruption translates to everyday pain settings.

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## 6. References

- [1] Alhola P, Polo-Kantola P. Sleep deprivation: Impact on cognitive performance. *Neuropsychiatr Dis Treat* 2007;3(5):553-567.
- [2] Chun MM, Golomb JD, Turk-Browne NB. A taxonomy of external and internal attention. *Annu Rev Psychol* 2011;62:73-101.
- [3] Dambacher M, Hubner R. Investigating the speed-accuracy trade-off: Better use deadlines or response signals? *Behav Res Methods* 2013;45(3):702-717.
- [4] Eccleston C. Chronic pain and distraction: An experimental investigation into the role of sustained and shifting attention in the processing of chronic persistent pain. *Behav Res Ther* 1995;33(4):391-405.
- [5] Eccleston C. A normal psychology of everyday pain. *Int J Clin Pract* 2013;67:47-50.
- [6] Eccleston C, Crombez G. Pain demands attention: A cognitive-affective model of the interruptive function of pain. *Psychol Bull* 1999;125(3):356-366.
- [7] Farage MA, Osborn TW, MacLean AB. Cognitive, sensory, and emotional changes associated with the menstrual cycle: A review. *Arch Gynecol Obstet* 2008;278(4):299-307.
- [8] Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL, 3rd. Sex, gender, and pain: A review of recent clinical and experimental findings. *J Pain* 2009;10(5):447-485.
- [9] Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain* 2012;13(8):715-724.
- [10] Hampson E. Variations in sex-related cognitive-abilities across the menstrual-cycle. *Brain Cognition* 1990;14(1):26-43.

- [11] Keogh E, Moore DJ, Duggan GB, Payne SJ, Eccleston C. The disruptive effects of pain on complex cognitive performance and executive control. *PLoS One* 2013; 8(12): e83272.
- [12] Kuhajda MC, Thorn BE, Klinger MR, Rubin NJ. The effect of headache pain on attention (encoding) and memory (recognition). *Pain* 2002;97(3):213-221.
- [13] Legrain V, Crombez G, Mouraux A. Controlling attention to nociceptive stimuli with working memory. *PLoS One* 2011;6(6):e20926.
- [14] Legrain V, Crombez G, Plaghki L, Mouraux A. Shielding cognition from nociception with working memory. *Cortex* 2013;49(7):1922-1934.
- [15] Legrain V, Van Damme S, Eccleston C, Davis KD, Seminowicz DA, Crombez G. A neurocognitive model of attention to pain: Behavioral and neuroimaging evidence. *Pain* 2009;144(3):230-232.
- [16] LeResche L, Mancl L, Sherman JJ, Gandara B, Dworkin SF. Changes in temporomandibular pain and other symptoms across the menstrual cycle. *Pain* 2003;106(3):253-261.
- [17] McAteer A, Elliott AM, Hannaford PC. Ascertaining the size of the symptom iceberg in a UK-wide community-based survey. *Brit J Gen Pract* 2011;61(582):12-17.
- [18] Miller PB, Soules MR. The usefulness of a urinary LH kit for ovulation prediction during menstrual cycles of normal women. *Obstet Gynecol* 1996;87(1):13-17.
- [19] Moore DJ, Keogh E, Crombez G, Eccleston C. Methods for studying naturally occurring human pain and their analogues. *Pain* 2013;154(2):190-199.
- [20] Moore DJ, Keogh E, Eccleston C. Identifying experimental methods to determine the effect of pain on attention: A review of pain, caffeine, alcohol and nicotine studies. *Hum Psychopharmacol* 2009;24(8):601-618.

- [21] Moore DJ, Keogh E, Eccleston C. The interruptive effect of pain on attention. *Q J Exp Psychol* 2012;65(3):565-586.
- [22] Moore DJ, Keogh E, Eccleston C. The effect of threat on attentional interruption by pain. *Pain* 2013;154(1):82-88.
- [23] Moore DM, Keogh E, Eccleston C. Headache impairs attentional performance. *Pain* 2013;154(9):1840-1845.
- [24] Riley JL, Robinson ME, Wise EA, Price DD. A meta-analytic review of pain perception across the menstrual cycle. *Pain* 1999;81(3):225-235.
- [25] Seminowicz DA, Davis KD. Interactions of pain intensity and cognitive load: The brain stays on task. *Cereb Cortex* 2007;17(6):1412-1422.
- [26] Sherwin BB. Estrogen and cognitive functioning in women. *Endocr Rev* 2003;24(2):133-151.
- [27] Sherwin BB. Estrogen and cognitive functioning in women: Lessons we have learned. *Behav Neurosci* 2012;126(1):123-127.
- [28] Solberg Nes L, Roach AR, Segerstrom SC. Executive functions, self-regulation, and chronic pain: A review. *Ann Behav Med* 2009;37(2):173-183.
- [29] Somedic. Manual for Algometer type II. Sollentuna, Sweden: Somedic AB, 2004.
- [30] Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. *Psychol Assessment* 1995;7(4):524-532.
- [31] Tabachnick BG, Fidell LS. Using multivariate statistics. London: Allyn and Bacon, 2007.
- [32] Taylor S, Zvolensky MJ, Cox BJ, Deacon B, Heimberg RG, Ledley DR, Abramowitz JS, Holaway RM, Sandin B, Stewart SH, Coles M, Eng W, Daly ES, Arrindell WA, Bouvard M, Cardenas SJ. Robust dimensions of anxiety

sensitivity: Development and initial validation of the Anxiety Sensitivity Index-

3. *Psychol Assess* 2007;19(2):176-188.

[33] Van Damme S, Legrain V, Vogt J, Crombez G. Keeping pain in mind: A

motivational account of attention to pain. *Neurosci Biobehav R*

2010;34(2):204-213.

Table 1: Means and standard deviations for age and self-report measures by low and high pain intensity groups.

	Low pain intensity		High pain intensity		t-value
Age	22.90	(6.06)	21.31	(5.50)	.97
PCS	19.50	(8.44)	22.22	(11.27)	-.93
ASI-3	21.85	(14.89)	21.34	(13.03)	.13
Typical Menstrual Pain Intensity (VAS)	51.60	(21.58)	66.94	(17.12)	-2.84*
Current Menstrual Pain Intensity (VAS)	29.47	(9.10)	67.78	(9.03)	-14.84*
Pressure Pain Index					
No pain control	272.65	(111.03)	256.48	(97.72)	
Menstrual pain	250.40	(109.17)	246.44	(108.76)	

Note: PCS = Pain Catastrophizing Scale; ASI-3 = Anxiety Sensitivity Index - 3; VAS = visual analogue scale; \*p<.05.

Table 2. Means and standard deviations for cognitive tasks by pain intensity and menstrual pain conditions.

	Low pain intensity		Menstrual Pain		High pain intensity		Menstrual Pain	
	No pain				No Pain			
Flanker Task								
Congruent RT	399	(37)	440	(84)	411	(76)	469	(138)
Incongruent RT	439	(38)	485	(86)	441	(62)	483	(110)
Congruent Accuracy	.99	(.02)	.99	(.02)	.99	(.03)	.99	(.01)
Incongruent Accuracy	.95	(.04)	.95	(.05)	.94	(.07)	.96	(.05)
N-Back task								
Hits	21.65	(5.47)	21.20	(4.88)	22.72	(5.44)	22.50	(3.61)
False Alarms	2.70	(4.04)	2.21	(1.81)	3.42	(3.03)	3.61	(2.87)
Switching Task								
Switch RT	838	(190)	835	(186)	731	(169)	806	(218)
Repeat RT	761	(170)	756	(147)	665	(149)	738	(191)
Switch Accuracy	.92	(.06)	.90	(.06)	.91	(.07)	.90	(.08)
Repeat Accuracy	.96	(.03)	.92	(.07)	.94	(.05)	.93	(.07)
Dual Task								
Number task	.61	(.19)	.54	(.25)	.68	(.17)	.62	(.17)
Line task	.64	(.22)	.60	(.20)	.70	(.17)	.65	(.20)

Note: RT = response time

Table 3: Comparison of effects found in current study with those reported for headache by Moore et al. [22].

	General cognitive effects		Specific cognitive effects	
	Headache	Menstrual Cycle	Headache	Menstrual Cycle
Flanker Task				
RT	✓	✓	✗	✗
Accuracy	✗	✗	✗	✗
N-Back task				
Hits	? ✓	✗	? ✓	✗
False Alarms	✗	? ✓	✗	? ✓
Switching				
RT	✗	✗	✗	✗
Accuracy	✓	✓	✗	✗
Dual Task				
Accuracy	✗	✓	✗	✗

Note: RT = response time