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Sex and menstrual cycle influences on three aspects of attention



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ABSTRACT

Sex differences and menstrual cycle influences have been investigated in a variety of cognitive abilities, but results regarding attention are comparably sparse. In the present study, 35 men and 32 naturally cycling women completed three attention tasks, which are commonly used in neuropsychological assessment situations. All participants completed two sessions, which were time-locked to the follicular (low progesterone) and luteal cycle phase (high progesterone) in women. The results reveal higher operation speed during sustained attention in men, but no sex differences in selected and divided attention. Menstrual cycle influences were observed on accuracy in all three tasks. During divided and sustained attention, for which a male advantage was previously reported, accuracy was higher during the early follicular compared to the mid-luteal cycle phase. Furthermore, during selected and sustained attention the learning effect from the first to the second test session was higher in women who started the experiment in their luteal cycle phase. These results suggest a possible role of progesterone in modulating the ability to focus on certain stimulus aspects, while inhibiting others and to sustain attention over a longer period of time.

1. Introduction

Sex differences and menstrual cycle influences have been investigated for a variety of cognitive abilities, including spatial and numerical abilities, verbal abilities and memory functions with men typically outperforming women in spatial and numerical abilities, but women typically outperforming men in verbal and memory functions (see [2] for a review). Note however that even though mean performance differs between men and women, there is also substantial variation in performance within each group, causing a wide overlap in the distribution of performances of men and women. These sex differences in cognitive performance have been linked to sex differences in brain activation patterns and brain structure. Several functional imaging studies demonstrate that men and women differ in brain activation patterns, suggesting the use different processing strategies to solve a variety of tasks [24,37,39]. Structural imaging studies agree on larger regional gray matter volumes in the frontal cortex, relevant for verbal and memory processing, in women and larger regional gray matter volumes in parahippocampal areas, relevant for spatial processing in men (e.g. [14,40]).

Several studies attempted to link these sex differences to the actions of sex hormones on the brain. Particularly structural changes across the menstrual cycle are thought to be mediated via estrogen receptors [3,55]. However, reports on the relationship between sex hormones and

cognitive performance are not entirely consistent (see [51] for a review). For example, testosterone has been linked to improved spatial abilities in men, but the exact nature of the relationship remains unclear (e.g. [8,15,16,19,20,33,42]). Across the menstrual cycle it has been suggested that spatial and numerical abilities improve during the early follicular phase, when estradiol (the principal estrogen) and progesterone (the principal progestin) are low, while verbal and memory abilities improve during the luteal phase, when female sex hormones are high (e.g. [17–19,30,45]).

However, while attentional processes play a role in all of these functions, the results regarding sex differences and menstrual cycle influences on attention itself are still comparably sparse. One of the reasons for this lack of findings may lie in the concept of attention itself, which is comprised of a variety of heterogenous functions.

The clinical model of attention [49] distinguishes 5 aspects of attention of increasing complexity: (i) *focused attention*, i.e. discrete responses to specific stimuli; (ii) *sustained attention*, i.e. maintaining these responses over time; (iii) *selective attention*, i.e. maintaining these responses in the face of distracting information; (iv) *alternating attention*, i.e. switching between responses to different stimuli; and (v) *divided attention*, i.e. simultaneously responding to different stimuli. A differentiation can also be made regarding the type (e.g. visuo-spatial), position (e.g. peripheral vs. central) and presentation mode (e.g. auditory vs. visual) of the stimuli to be attended and the distracting information

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(e.g. [7,11,26,41]).

Few studies, including animal studies, have demonstrated a male advantage in tasks of sustained [13] and divided attention [23,28]. The results regarding selective attention were recently reviewed by Stoet [53]. They present a more heterogenous picture and suggest a modulation by stimulus type and position. In tasks of spatial attention it has been demonstrated that women are more strongly distracted by invalid spatial cues [1,4,9,10,32,46,52] and task-irrelevant information [12,53]. However, in the Stroop-task women usually outperform men, i.e. they react faster and show a smaller interference effect, suggesting that during attention to semantic information or colors, they are less distracted by task-irrelevant information (e.g. [31,54]). Finally, in hierarchical scenes or stimuli, women outperform men in responses to peripheral or local-level stimuli, while men outperform women in responses to central or global-level stimuli [38,43,44]. A focus on peripheral information would explain the stronger distractability of women by irrelevant information in tasks of spatial attention.

Menstrual cycle influences have mainly been studied for sustained attention and provide an inconsistent picture of results regarding the luteal cycle phase. In a small sample, Solís-Ortiz and Corsi-Cabrera [50] report an improvement of sustained attention during the mid-luteal phase (days 20-21 of a 28 day cycle) compared to ovulation (days 13-14 of a 28 day cycle). In the late luteal/pre-menstrual phase (2-3 days before onset of next menses) reaction times were comparable to the ovulation phase, while error rates were comparable to the midluteal phase, i.e. women decreased their speed but maintained the same accuracy as during the mid-luteal cycle phase. They interpret their findings as relating to high progesterone levels during the mid-luteal cycle phase. Similar findings were reported by Brötzner et al. [6]. Lord & Taylor [27] however suggest continuously dropping performance throughout the luteal cycle phase from ovulation to next menstruation. Note however that they did not follow the same women along their menstrual cycle, but compared different women, who were at different time points in their menstrual cycle. Comparably, [29] report decreased performance during the late luteal/pre-menstrual phase compared to the pre-ovulatory phase (days 10-14), while Morgan et al. [35] report no changes in sustained attention performance in the late luteal/premenstrual cycle phase. Regarding selective attention it has been demonstrated that sex differences in the processing of hierarchical stimuli are restricted to the luteal cycle phase, when progesterone levels are high [38]. Furthermore, Hausmann [21] reports reduced hemispheric asymmetries, i.e. a smaller performance difference between stimuli presented to the left or right hemifield, during spatial attention in the luteal phase of the menstrual cycle.

In summary, research regarding sex differences and sex hormonal influences on attention is still in its infancy. However, previous findings suggest an important role of progesterone in modulating different aspects of attention. The present study utilized three attention tasks that are commonly used in neuropsychological assessment in men and women during different cycle phases. According to their demands, the tasks were classified as combined selective-divided attention tasks and a sustained attention task. Thereby, we seek to explore sex differences and menstrual cycle influences on different forms of attention. We expect to confirm improved sustained and divided attention performance in men compared to women and hypothesize an improvement of sustained and divided attention performance during the follicular compared to the mid-luteal phase in women.

2. Methods

2.1. Participants

Thirty two healthy young women (mean age: 22.71 years, SD = 3.67 years) and 35 healthy young men (mean age: 23.06 years, SD = 2.25 years) participated in this study. As indicated by self-reports, all participants were right-handed, free of medication and had no

history of psychological, neurological or endocrinological disorders. Female participants were not taking hormonal contraceptives and had a regular menstrual cycle with a mean duration of 29.06 days (SD = 1.71 days, range: 28–33 days). All participants were students, who had achieved a general qualification for University entrance (8–9 years of secondary education), i.e. men and women did not differ in educational status. Age also did not differ between men and women ($t_{(64)} = 0.51$, p = 0.62). All participants gave their informed written consent to participate in the study. All methods comply with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Procedure

All participants completed 2 test-sessions, which were time-locked to the follicular and luteal cycle phase in women to capture changes in progesterone levels. Follicular sessions were scheduled from the onset of menses up to three days before ovulation, i.e. before the estradiol peak (mean cycle day: 6.06, SD = 3.45). Mid-luteal sessions were scheduled between three days after ovulation and three days before onset of next menses (mean cycle day: 22.35, SD = 4.47). Ovulation was calculated based on participants self-reports of cycle duration and onset of last menses as 14 days before the expected onset of next menses and was confirmed via commercial ovulation tests in cases of uncertainty. Onset of next menses was confirmed by the participants. Although hormone levels were not assessed in the present study for budgetary reasons, this method has proven highly reliable in distinguishing phases of high and low progesterone levels in previous withinsubjects menstrual cycle studies where hormone levels were assessed (e.g. [47]). Note however that this method does not adequately distinguish phases of high and low estradiol levels. Order of cycle phases across test-sessions was counterbalanced. 18 women had their first appointment during the follicular phase, 14 women had their first appointment during the luteal phase. Mean difference between test sessions was 15.21 days (SD = 3.21) in women. Test sessions in men were scheduled approximately two weeks apart (mean = 14.83 days, SD = 3.41 days).

2.3. Tasks

During each test-session participants completed three well-validated attention tasks assessing different aspects of attention, which are commonly used for the psychological assessment of attention in German speaking countries, in the following order: (i) the d2-R [5], (ii) the FAIR-2 [34] and (iii) the DAUF [48]. Order was chosen such that effort increased with each task. Particularly the DAUF, which is extremely effortful, was scheduled last to avoid any depletion effects on the other tasks.

- (i) The d2-R is a paper pencil test, composed of 14 rows with 57 items each (total of 789 items), consisting of the "d"s and "p"s. Each "d" has one to four and each "p" has one to two marks directly below or above them. Aim of the task is to selectively focus on and highlight the "d"s with two marks (two marks above, two below, or one above and one below), all other items are distractors. The participant has 20 s per row to highlight as many "d"s with two marks as possible before moving on to the next row. When only selecting the one goal item two types of errors are possible, first the omission error (to miss a correct item), second confusion error (to mark an incorrect item; [5]). Reliability for concentration and work pace range between 0.89 and 0.95, for accuracy between 0.80 and 0.91.
- (ii) The FAIR-2 (Frankfurter Aufmerksamkeits-Inventar, Engl. Frankfurt attention inventory) is a paper pencil test consisting of two pages, each 16 rows with 20 figures (320 figures per page). All figures consist of three layers: (a) an outside circle, (b) a figure (circle or square) inside that circle, (c) two to three dots within the

figure. The participants are given two targets (e.g. circle with two dots and square with three dots), which have to be marked within three minutes per page. When working on this test, the pencil must be in contact with the paper at all times within a row, meaning the participant positions the pen under the first item, draws a consecutive line under each following item until a target appears or the row ends. The target is marked by drawing into it [34]. Thereby, as in the d2-R, omission errors (failing to draw into a target) and confusion errors (drawing into an item which is not a target) are possible. Reliability ranges between 0.63 and 0.92.

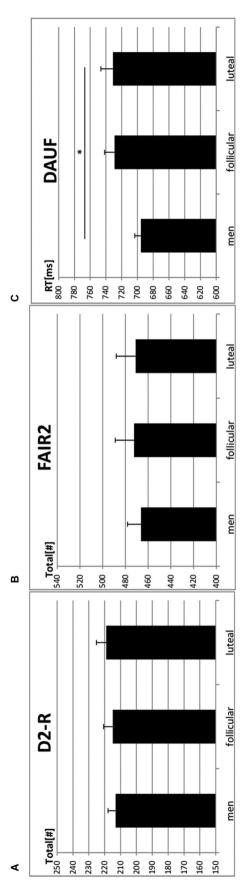
(iii) The DAUF (short for "Daueraufmerksamkeit", Engl. sustained attention) is a computer test within the Wiener Test system catalog. This test was created to measure sustained attention by presenting seven equiangular triangles in a row with their tip pointing up or down for alternating time periods (30 min in total). The participant must press a button only if three of the seven triangle tips point down [48].

Thus, the d2-R and the FAIR-2 test selective attention, which is defined as maintaining responses to specific aspects of a task/stimulus in the face of distracting information [49]. However, as the targets have to match in more than one aspect, they also include aspects of divided attention, which is defined as processing and responding to multiple stimuli/stimulus aspects simultaneously [49]. This is more strongly so in the FAIR-2, because participants have to search for two possible target configurations. The DAUF was specifically designed to assess sustained attention, which is defined as maintaining high levels of accuracy over a long period of time, 20 min or longer, with "relatively boring" tasks [49].

For the speeded paper- and pencil tasks, i.e. the d2-R and the FAIR-2, the total number of completed items (i.e. the BZO in the d2-R) was assessed as a measure of operation speed. The percentage of errors among completed items was assessed as a measure of accuracy. For both tasks two error types were evaluated: (i) false alarm errors, i.e. items that were incorrectly marked as targets and (ii) omission errors, i.e. targets that were not marked as such. For the computerized task, i.e. the DAUF, reaction times were assessed as a measure of operation speed. The number of correctly identified targets was assessed as a measure of accuracy.

2.4. Statistical analysis

Power of the sample was estimated using g * Power 3.1.9.2 to be 0.80 for the between subjects comparisons and 0.98 for the withinsubjects comparisons. Statistical analysis was carried out using software R 3.2.2.0. For each task, operation speed and accuracy were analyzed as dependent variables (DV) in the context of linear mixed effects models (lmes) including participant number (PNr) as a random factor. Analyses were performed using the 'lmer' function of the 'lme4' package followed by backwards elimination of non-significant interactions using the 'step' function of the 'lmerTest' package. The lme approach was chosen as contrary to ANOVA-designs - it allows evaluation of the interactive effects of crossed over within-subject factors, such as session and cycle phase. Separate lmes were run to assess the effect of sex across all participants (formula: DV $\sim 1 | PNr + session * sex$) and the effect of cycle phase only in women (formula: DV ~ 1 | PNr + session * cycle). Sex was thereby defined as a three-level factor with men, women in their follicular phase and women in their luteal phase included as separate groups. Due to the automatic dummy coding implemented in R, this results in separate comparisons of men to women in their follicular phase and men to women in their luteal phase within the same model. The effect of session was modeled to control for learning effects. In the analyses of accuracy of the d2-R and the FAIR-2, error type was also modeled as a separate factor. Two women who did not complete the FAIR-2 and the d2-R during the second session were additionally excluded from the analyses of these tasks.



(caption on next page)

Fig. 1. Sex and menstrual cycle effects on the number of items processed in the D2-R and the FAIR2, as well as on reaction times (RT) in the DAUF. Sex and menstrual cycle phase did not affect the number of items processed in the D2-R, a task of selective attention, and in the FAIR2, a task requiring both selective and divided attention. In the DAUF, a task of sustained attention, men responded significantly faster than women in their luteal cycle phase. These effects were irrespective of session. Thus performance is displayed irrespective of session.

3. Results

3.1. Selected attention: d2-R

3.1.1. Items processed

On average, participants completed 215 items (SD = 37 items). There was a significant effect of session on the total number of completed items (b = 0.38, SE_b = 0.08, $t_{(64)}$ = 4.70, p < 0.001). Participants completed significantly more items during the second session (222 items, SD = 37 items) than during the first session (208 items, SD = 36 items). Irrespective of cycle phase, sex did not affect the number of items processed in the d2-R and neither did cycle phase in women (Fig. 1A).

3.1.2. Error rate

On average, participants made 6.35% Errors (SD = 5.74%). There was a significant effect of error type on error rate (b = 0.70, $SE_b = 0.18$, $t_{(184)} = 3.96$, p < 0.001). Omission errors were significantly more frequent (5.6%, SD = 5.6%) than confusion errors (0.7%, SD = 1.0%). Session did not affect the error rate of participants (b = 0.04, $SE_b = 0.18$, $t_{(184)} = 0.21$, p = 0.83). There was however a significant interaction between session and error type (b = 0.73, $SE_b = 0.24$, $t_{(184)} = 2.93$, p = 0.004). Omission errors decreased from the first (6.8%, SD = 6.3%) to the second test session (4.5%,SD = 4.6%), while confusion errors increased from the first (0.6%, SD = 0.7%) to the second test session (0.8%, SD = 1.3%). Irrespective of cycle phase, sex did not affect the error rate in the d2 and did not interact with error type or session (all |b| < 0.14, all $SE_b > 0.24$, all $|t_{(184)}| < 1.48$, all p > 0.14). There was however, a significant 3-fold interaction between sex, error type and session for women in their luteal cycle phase (follicular: b = 0.11, $SE_b = 0.46$, $t_{(184)} = 1.68$, p = 0.10; luteal: b = 0.51, $SE_b = 0.23$, $t_{(64)} = 2.27$, p = 0.03). Also, in women, there was no significant effect of cycle on error rates and cycle did not interact with error type or session (all b < 0.03, all $SE_b > 0.013$, all t < 1.72, all p > 0.08). There was however a significant three-fold interaction between cycle phase, error type and session (b = 0.05, $SE_b = 0.02$, $t_{(84)} = 2.33$, p = 0.02). From the first to the second test session, omission errors decreased more in women who had their first session during their luteal phase compared to women who had their first session during their follicular phase. Conversely, confusion errors decreased more in women who had their first session during the follicular phase compared to women, who had their first session during their luteal phase (Fig. 2A).

3.2. Selected/divided attention: FAIR-2

3.2.1. Items processed

On average, participants completed 469 items (SD = 94 items). There was a significant effect of session on the total number of completed items (b = 0.19, SE_b = 0.10, $t_{(63)}$ = 3.86, p < 0.001). Participants completed significantly more items during the second session (488 items, SD = 90 items) than during the first session (450 items, SD = 96 items). Irrespective of cycle phase, sex did not affect the number of items processed in the FAIR and neither did cycle phase in women (Fig. 1B).

3.2.2. Error rate

On average, participants made 1.2% Errors (SD = 1.4%). There was

a significant effect of error type on error rate (b = 0.28, SE_b = 0.10, $t_{(191)} = 2.75$, p = 0.006). Confusion errors were significantly more frequent (1.4%, SD = 1.5%) than omission errors (1.0%, SD = 1.4%). Session did not affect the error rate of participants. Irrespective of cycle phase, sex did not affect the error rate of participants in the FAIR-2 and did not interact with error type or session. Nevertheless, in women, we observed a significant effect of cycle on error rate (b = 0.004, SE_b = 0.002, $t_{(88)} = 2.22$, p = 0.03), which did not interact with error type or session. Irrespective of error type, error rate was significantly higher during the luteal cycle phase (1.3%, SD = 1.6%) compared to the follicular cycle phase (0.8%, SD = 1.1%) (Fig. 2B).

3.3. Sustained attention: DAUF

3.3.1. Speed

In the DAUF, participants had an average reaction time of 712 ms (SD = 78 ms). A significant main effect of session on reaction times (b = -0.47, SE_b = 0.08, $t_{(64)}$ = 5.89, p < 0.001) indicated faster reactions during the second compared to the first test session. A significant effect of sex was observed, when women were in their luteal cycle phase (follicular: b = 0.38, SE_b = 0.23, $t_{(64)}$ = 1.68, p = 0.10; luteal: b = 0.51, SE_b = 0.23, $t_{(64)}$ = 2.27, p = 0.03), indicating faster reactions in men (696 ms, SD = 66 ms) compared to women (follicular: 729 ms, SD = 72 ms; luteal: 731 ms, SD = 87 ms). Sex did not interact with session in either cycle phase. In women, there was no effect of menstrual cycle phase on reaction times (Fig. 1C).

3.3.2. Accuracy

On average participants responded correctly to 263 items (SD = 20 items). There was a significant effect of session on accuracy (b = 0.69, $SE_b = 0.17$, $t_{(62)} = 4.09$, p < 0.001), indicating higher accuracy during the second (269 items, SD = 12 items) compared to the first test session (257 items, SD = 23 items). A significant effect of sex was observed, when women were in their luteal cycle phase (follicular: b = 0.41, SEb = 0.26, $t_{(62)} = 1.53$, p = 0.13; luteal: b = -0.59, $SE_b = 0.29$, $t_{(62)} = -2.02$, p < 0.05), indicating more correct responses in men (263 items, SD = 19 items) compared to women in their luteal phase (260 items, SD = 25 items). These effects were qualified by a significant interaction between sex and session for women in their follicular cycle phase (follicular: b = -0.75, SEb = 0.37, $t_{(62)} = -2.01$, p < 0.05; luteal: b = 0.62, $SE_b = 0.37$, $t_{(62)} = 1.68$, p = 0.10). Women who were in their follicular phase in the first session performed better than men, while women who were in their follicular phase in the second session performed worse than men. In women, there was a significant main effect of cycle phase on accuracy (b = -19.35, SE_b = 6.54, $t_{(42)} = -2.96$, p = 0.005), which did furthermore interact with session (b = 26.03, $SE_b = 12.01$, $t_{(31)} = 2.17$, p = 0.04). On average, accuracy was higher during the follicular cycle phase (264 items, SD = 14 items) compared to the luteal cycle phase (260 items, SD = 25 items). The improvement from the first to the second test session was significantly stronger in women, who started during their luteal cycle phase compared to women who started during their follicular cycle phase (Fig. 2C).

4. Discussion

The present study was designed to investigate sex and menstrual cycle influences on three aspects of attention using standardized tests. These tests allow the gradual assessment of the ability to select certain stimuli for information processing while suppressing other stimuli (D2 and FAIR) and to sustain attention over a longer period of time (DAUF). We observed no sex differences in the d2-R and FAIR-2, tasks designed to assess both selected and divided attention. However, performance on the d2 improved more from the first to the second test session in men compared to women. Furthermore, women during their luteal cycle phase (high progesterone) showed increased error rate in the FAIR-2

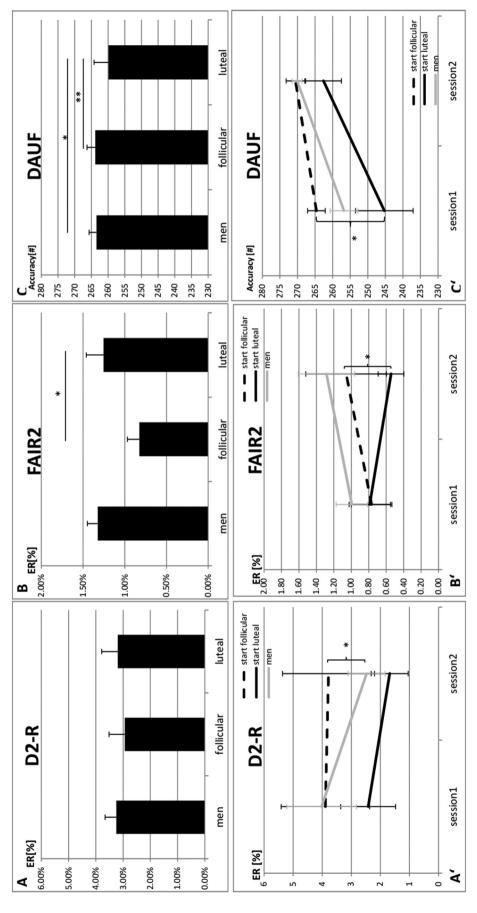


Fig. 2. Sex and menstrual cycle effects on accuracy in 3 attention tasks. The upper panels A-C display performance in men, women during their follicular and women during their luteal cycle phase, irrespective of test session. The low panels display performance, separately by test session A'-C'. Women, who were in their follicular cycle phase during the first session (start follicular), were in their luteal cycle phase during the second session. Women who were in their luteal cycle phase during the first session (start luteal), were in their follicular cycle phase during the second session. In the D2, a task of selective attention, sex and menstrual cycle phase did not affect accuracy (A). However, in men, accuracy improved significantly more between the first and the second test session than in women (A'). In the FAIR2, a task requiring both selective and divided attention, error rate was significantly higher in the luteal compared to the follicular cycle phase (B). Accordingly, error rate increased significantly from the follicular to the luteal cycle phase in women who started during their follicular phase, but decreased from the luteal to the follicular phase in women who started during their luteal phase (B'). In the DAUF, a task of sustained attention, women during their luteal phase showed decreased accuracy compared to men and women during their follicular phase (C,C'). Accordingly, accuracy did not increase significantly from the follicular to the luteal cycle phase in women who started during their follicular phase, but increased significantly from the luteal to the follicular phase in women who started during their luteal phase (B').

compared to women in their follicular cycle phase (low progesterone). In the DAUF, a task of sustained attention, women during their luteal cycle phase showed reduced performance compared to men (RT and accuracy), as well as women during their follicular cycle phase (accuracy).

Regarding sex differences, the results of the DAUF are in line with previous findings demonstrating a male advantage in sustained attention [13]. However, contrary to previous findings of a male superiority during divided attention has previously been reported [23,28], we did not observe any sex differences in the FAIR-2. However, the FAIR-2 is not a pure divided attention task.

Regarding menstrual cycle differences, an improvement of sustained attention in phases of high progesterone has previously been suggested [50]. Although we did not measure exact hormone levels, the results of the present study suggest the opposite. The reasons for these differences may lie in the different tasks employed or in different definitions of cycle phases. A lacking consensus regarding the relevant time windows has been suggested as the most important reason for inconsistencies among menstrual cycle studies [51]. In line with that assumption, Lord and Taylor [27] report increased concentration accuracy during midcycle (pre-ovulatory to early luteal phase), but decreasing concentration accuracy approaching menses, i.e. during the late luteal phase. Also in line with the results of the present study, Matthews and Ryan [29] report reduced performance on sustained attention tasks in the luteal cycle phase. Note however, that their findings concern response times rather than accuracy and were observed in the late luteal rather than the mid-luteal cycle phase.

Contrary to sustained attention, results on menstrual cycle influences regarding selected and divided attention are sparse in the literature and concern specific tasks testing e.g. spatial attention [21] or global-local attention [38]. It is notable that during the sustained attention task, as well as during the FAIR, which includes aspects of divided attention more strongly than the d2, performance worsens during the high progesterone luteal cycle phase. Both tasks include aspects of attention for which a male advantage was previously reported [13,23,28]. On the contrary for selected attention, for which results regarding sex differences are less conclusive, no main effect of menstrual cycle was observed. Rather, women during their luteal cycle phase had an advantage regarding their improvement towards the second test session.

The finding of a modulatory effect of cycle phase on test session in two of the tasks can be attributed to a variety of reasons. During sustained attention for instance, luteal women start off with worse performance, which is likely followed by a stronger improvement than in follicular women, whose performance is already high. However, no performance differences between follicular and luteal women were observed during the first session in the selective attention task. Rather, luteal women already showed slightly better performance than follicular women during the first session in that task. It is thus possible that progesterone levels have different effects on a task that was already trained. The learning effect may also be a result of improved memory functions during the luteal cycle phase (e.g. [17,18,25]).

In summary, the present study is among the first to demonstrate menstrual cycle influences on various forms of attention in a reasonably large sample. Noteworthy, these effects were observed on three well validated tasks commonly utilized for neuropsychological assessment. We found sex differences in a task of sustained attention with better performance in men compared to women. Furthermore, we observed menstrual cycle differences in sustained attention and a task involving divided attention with better performance during the follicular phase compared to the luteal phase. While these data demonstrate a role of hormonal fluctuations along the menstrual cycle in modulating attention, the respective roles of progesterone and estradiol still need to be disentangled. Nevertheless, sex and menstrual cycle phase are factors to be considered in the assessment of attention.

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