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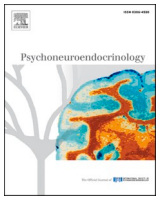

Sex, menstrual cycle, and hormonal contraceptives influences on global–local processing

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ABSTRACT

The effect of sex hormones on global–local tasks has rarely been studied, offering, when done, conflicting results possibly modulated by the congruency between hierarchical stimuli, and by the attentional demands. Here, we examined the global advantage (GA) effect in men (with high testosterone levels), women in the mid-luteal phase (with high levels of estradiol and progesterone), in the ovulatory phase (with high estradiol but low progesterone levels); and in the early follicular phase and with hormonal contraceptive (HC) use (with low sex hormone levels). The level of processing (global–local), the congruency (congruent vs. incongruent), and attentional demands (divided vs. selective) were manipulated. The divided-incongruent condition was sensible to estradiol and progesterone levels and, in this condition, mid-luteal women performed more locally while men performed more globally. The selective-incongruent condition was sensible to the testosterone level and, in this condition, men were faster. The HC group showed a congruency effect in the GA reaction times (RTs) during both, divided and selective conditions. Finally, the GA RTs of the ovulatory group differed from the early follicular and mid-luteal groups only in the congruent-selective condition, but the performance was not related with sex hormone levels. This result is interpreted in relation with the brain effects of estradiol in the absence but not in the presence of progesterone. Thus, sex, menstrual cycle, HC, task difficulty and sex hormones seem to modulate performance in the global–local task. These factors represent an important source of variability in studies focused on the processing of hierarchical stimuli and allow apparently inconsistent data to be explained.

1. Introduction

Most likely, over the course of our lives, we have wondered if we are the type of person who sees the *trees* or the *forest* in our path. In fact, knowing the individual characteristics that determine the processing of the information in a more global (i.e., seeing the *forest*) or in a more local (i.e., seeing the *trees*) style has been a recurrent question in neuroscience. Thus, Navon (1977) proposed a well-known paradigm (the global–local paradigm or Navon task) to study global and local processing during visual stimuli presentation. In this task, global structures that are made up of local parts are presented to participants who have to recognize either just the global structure or just the local parts. Interestingly, this paradigm typically shows that people are faster and more accurate with the processing of global than local hierarchical stimuli, a result called the global advantage (GA) effect (Navon, 1977, 1981).

Global–local tasks induce conflict by providing irrelevant information (e.g., global stimuli during processing of local information or local stimuli during processing of global information). Accordingly, performance is better in congruent trials (e.g., identifying a large square made of small squares) than in incongruent trials (e.g., identifying a large square made of small rectangles), and the GA effect is greater in the latter case (Álvarez-San Millán et al., 2021; Hedden and Gabrieli, 2010; Leaver et al., 2015; Steenbergen et al., 2015).

The GA effect is also modulated by the degree of attentional demand during the task. A selective attention condition is a lower demanding condition where participants are instructed to focus on the processing of one unique type of essay in the same block (global or local). However, the divided attention condition requires the processing of both global and local essays in the same block, which implies more cognitive demand. Interestingly, previous results indicated that performance is

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worse and the GA larger in the highly demanding divided attention condition (Hedden and Gabrieli, 2010; Leaver et al., 2015; Steenbergen et al., 2015).

The performance in the global–local task also seems to be influenced by the sex of the participants. However, few studies have investigated sex differences during the processing of hierarchical stimuli and, when done, very contrasting results have been observed (Álvarez-San Millán et al., 2021; Kimchi et al., 2009; Razumnikova and Volf, 2011; Roalf et al., 2006). Indeed, Roalf et al. (2006) found that women respond faster to local targets (i.e., negative GA effect), and men did not differentially respond to hierarchical stimuli. However, Razumnikova and Volf (2011) observed that men respond faster to global targets (i.e., positive GA effect), while women do not differentially respond to hierarchical stimuli. However, Álvarez-San Millán et al. (2021) observed that both women and men responded faster to global than local targets. In addition, when men and women performance was compared,Kimchi et al. (2009) observed that men respond faster to local stimuli and Álvarez-San Millán et al. (2021) observed that men respond faster to both local and global stimuli.

These contrasting patterns of results could be due to different variables. First, previous studies have shown that sex differences increase with highly demanding tasks, but disappear if the level of demand decreases (e.g., for a review see Coluccia and Louse, 2004). Consequently, the level of demand of the task can be a relevant modulator of sex differences in cognitive tasks. Second, these different patterns could be explained, at least in part, by the possible modulation effects on the brain of endogenous sex hormones (testosterone, estradiol, and progesterone) or synthetic sex hormones. In this context, in men, the release of sex hormones is under tonic control. Levels of testosterone are higher and levels of estradiol and progesterone are lower than in women (for a review, see Keevil and Adaway, 2019). However, in women, the release of sex hormones is under cyclic control (menstrual cycle) during three hormonally different phases: early follicular, ovulatory, and mid-luteal. The menstrual cycle begins with the early follicular phase, with low levels of estradiol and progesterone, which lasts for approximately 7–10 days. Subsequently, a rise in estradiol levels that culminates in a high but short-lived peak lasting about 36 h occurs (ovulatory phase). Following ovulation, 13–15 days before the next menses, the luteal phase begins. Estradiol returns nearly to the early follicular phase values, to increase again, accompanied by increases in the levels of progesterone. Thus, estradiol and progesterone levels have shown a sustained peak during the interval from 10 to 5 days (mid-luteal phase), which is followed by a subsequent drop before onset of the next menses (for a review, see Hampson, 2020). In this way, low levels of estradiol and progesterone, high estradiol but low progesterone, and high levels of both estradiol and progesterone characterized the early follicular, ovulatory and mid-luteal phases, respectively. Additionally, most hormonal contraceptives (HCs) contain synthetic analogues of estrogen and progestins that prevent monthly sex hormone fluctuations and ovulation and reduce the endogenous secretion of sex hormones (Hampson, 2020; Pletzer and Kerschbaum, 2014; Warren et al., 2014).

In this context, four studies included women at various stages of the menstrual cycle and hormonal contraceptives users (Álvarez-San Millán et al., 2021; Pletzer and Harris, 2018; Pletzer et al., 2014, 2017). Pletzer et al. (2014), using groups of men, early follicular, mid-luteal and oral contraceptive users women; Pletzer et al. (2017), with the same group of participants except for the oral contraceptives group; Pletzer and Harris (2018), who compared a group of men with a group of women during the mid-luteal phase of the menstrual cycle; and Álvarez-San Millán et al. (2021) with follicular and luteal groups and hormonal contraceptive users. Importantly, these studies have also revealed a discrepant pattern of results. In fact, Pletzer et al. (2014) found that mid-luteal women showed reduced GA response times (RTs) when compared with men, early follicular women, and oral contraceptive users in a selective but not in a divided attention condition. Álvarez-San Millán et al. (2021) confirmed the lower global advantage of women during the luteal phase in a selective attention task. However, these behavioral differences among groups were not observed in other studies (Pletzer and Harris, 2018; Pletzer et al., 2017). Moreover, in the 2014 and 2018 studies, but not in Pletzer et al. (2017), progesterone levels negatively correlated with GA RTs during the selective attention condition. Sex hormone levels of the participants were not collected by Álvarez-San Millán et al. (2021). These controversial results could point to a more complex modulation between high levels of estradiol and progesterone during the mid-luteal menstrual cycle phase. This means that progesterone, estradiol, or the joint effect of both hormones could modulate the GA effect on the global–local task. Critically, for the aim of this research, none of the previous studies included a group of women during the ovulatory phase. The inclusion of this phase seems especially relevant because their high levels of estradiol but low levels of progesterone can help to differentiate the contribution of estradiol and progesterone (Bernal et al., 2020) during the processing of hierarchical stimuli.

Therefore, the scope of this study was to evaluate the sex differences, the modulation of the menstrual cycle (early follicular, ovulatory, and mid-luteal phases, hereafter, follicular, ovulatory, and luteal women), and hormonal contraceptives (HCs) (hereafter HC women) in a global–local task, manipulating the level of the attentional demand (divided vs. selective) and the features' congruency of hierarchical stimuli (incongruent vs. congruent).

According to the suggestion that women process the information more locally and men more globally (Heil and Jansen-Osmann, 2008; Peña et al., 2008; Pletzer et al., 2013; Rilea, 2008; for a review, see Pletzer, 2014), a reduced GA effect is expected in women according to Roalf et al. (2006), and an increased GA effect is expected in men according to Razumnikova and Volf (2001). Also, considering the influence of the menstrual cycle, a reduced GA effect in the luteal group is expected (Álvarez-San Millán et al., 2021; Pletzer et al., 2014) associated with progesterone levels (Pletzer and Harris, 2018; Pletzer et al., 2014). More importantly, we sought to explore, for the first time, the GA effect on accuracy data and whether ovulatory women differ in their processing of hierarchical stimuli, as well as the role of estradiol, a sex hormone that appears to have remarkable effects on the brain and on a wide range of different cognitive processes in both humans and rodents (Bernal et al., 2020; Dreher et al., 2007; Hamson et al., 2016; Hussain et al., 2014; Korol and Kolo, 2002; Quinlan et al., 2008; Weis et al., 2008). Finally, we wanted to verify that GA is modulated by the degree of attentional demand and features congruency as previous results have indicated larger GA in highly demanding divided–incongruent conditions (Hedden and Gabrieli, 2010; Leaver et al., 2015; Steenbergen et al., 2015).

2. Materials and methods

2.1. Participants

A total of 97 students from the University of Granada participated in the study. Exclusion criteria were the following: uncorrected visual problems; any kind of hearing, language, neurological, or psychiatric impairment; the use of anabolic steroids or medication for chronic or neurological diseases; and substance abuse (Bernal et al., 2020; Colzato et al., 2010a; Sundström-Poromaa and Gingnell, 2014). Additional exclusion criteria for women were the use of abortion pills in the previous four months and the presence of dysphoric emotional disorder (Dubol et al., 2020), which was based on their responses to a premenstrual dysphoric disorder questionnaire (see below). However, no volunteers were excluded for this reason. The following groups were enrolled: 16 healthy men aged 18–26 years (mean ± *SEM* of 22.2 ± 0.5 yrs); 55 healthy women with a natural menstrual cycle aged 18–31 years (mean of 21.2 ± 0.4 yrs) who constituted the follicular (n = 18), ovulatory (n = 18), and luteal (n = 19) group; and 26 healthy women using HCs aged 18–31 years (mean of 21.5 ± 0.6 yrs). In the current study we use a cross-sectional design in order to avoid possible practice effects previously observed in the global-local task (Dulaney and Marks,

2007), and in other studies (e.g., Hampson, 1990; Maki et al., 2002; Mordecai et al., 2008; for review see Bernal and Paolieri, 2021). As a reward for their participation in the experiment, volunteers obtained university course credits. A total of five participants were excluded from analyses due to high error rates (>50%; for a similar procedure, see Pletzer and Harris, 2018): two men and one follicular, one ovulatory, and one HC woman as well as one woman in the ovulatory group who was also excluded because of a high level of progesterone (see Hampson, 2020). Power analysis using G*Power Version 3.1.9.2 software (Faul et al., 2009) revealed that 85 participants were sufficient for detecting the critical interaction between groups and demands of the task ($\eta^2 = 0.14$; power = 0.80; $\alpha = 0.05$). Similar sample size was employed in previous cross-sectional studies (e.g. Bernal et al., 2020; Hampson et al., 2014; Hussain et al., 2016).

2.2. Determination of menstrual cycle phase in women

Classification of the women's natural menstrual cycle as regular was based on self-reports of the onset date of the last four cycles (Becker et al., 2005; Bernal et al., 2020), only including women with a cycle duration of 28 ± 7 days. The women with a natural menstrual cycle were randomly assigned to one of three experimental groups (follicular, ovulatory, or luteal). Selection of the day of the experiment for participants in each group was determined by calculating the mean duration of their last four menstrual cycles and estimating the onset date for their next cycle. The participants reported the current length of the menstrual cycle after the onset of the new menstrual cycle. Women in the follicular group were tested on days 1–7 of the cycle, those in the ovulatory group were tested on days 16–12 before their next menses, and those in the luteal group on days 9–3 before their next menses (for a review, see Hampson, 2020).

Women in the HC group ($n = 26$) were tested during the active phase, established according to self-reports. HC were combinations of a synthetic estrogen with a progestin (see Supplement A).

2.3. Procedure and materials

Written informed consent was first obtained from all volunteers who participated in the study, which was approved by the Granada University Ethical Committee. Next, women completed the premenstrual dysphoric disorder questionnaire, and salivary samples were obtained from all participants. Finally, participants completed the global–local task followed by the Raven Progressive Matrices Test (Raven et al., 1988) to assess general non-verbal intelligence.

2.3.1. Premenstrual dysphoric disorder questionnaire

Given that premenstrual dysphoric disorder can affect performance during global–local tasks (Gasper and Clore, 2002), we applied a 14-item questionnaire based on the American Psychiatric Association (APA) classification (APA, 2013) to assess the presence of depressive symptoms during the previous premenstrual period, which recurred for at least two consecutive months in the previous year, interfered with daily activities, and disappeared shortly after the onset of menses.

2.3.2. Saliva sample collection and immunoassay protocols and analysis

Participants were asked to avoid alcohol consumption during the 24 h prior to the saliva sample collection, tooth brushing during the 3 h prior to the collection, and food intake for 1 h prior to the collection (Bernal et al., 2020; Colzato et al., 2010a). Saliva samples were collected by passive drool into 10-ml polypropylene tubes, which were then centrifuged and stored at −20 ºC until further analysis. Salivary estradiol, progesterone, and testosterone concentrations were analyzed by an independent laboratory using high-sensitivity salivary enzyme immunoassay kits from Labor Diagnostika Nord GmbH & Co KG (LDN) (Nordhorn, Germany). The sensitivity for estradiol, progesterone, and testosterone was 0.2 pg/ml, 5.0 pg/ml, and 2.2 pg/ml, respectively.

2.3.3. Global–local task

The target stimuli of the global–local task consisted of geometric figures adopted from Colzato et al. (2010b) and Huizinga et al. (2006). Larger (global) stimuli (i.e., squares 93 × 93 pixels or rectangles 41 × 189 pixels) were compounded by smaller (local) stimuli (i.e., squares 21 × 21 pixels or rectangles 8 × 46 pixels). The space between the local elements of a stimulus was 3 pixels. A global square consisted of 16 small squares or 16 small rectangles; a global rectangle consisted of 16 small squares or 16 small rectangles. The "local'' and "global'' cues had the same size as the global and local stimuli and were presented at 189 pixels from the center of the computer screen.

Participants responded to randomly presented rectangles or squares by pressing a left or right response button, respectively. Two cues (a rectangle and a square, congruous in location with the associated response button) indicated to which dimension (global or local) the participants should respond (see Fig. 1). The rectangle or square was associated with a spatially assigned response button. The four possible stimuli were presented with equal probabilities, so that 50% of the trials were congruent (a large square formed by smaller squares or a large rectangle formed by smaller rectangles) and the other 50% were incongruent (a large square formed by smaller rectangles or a large rectangle formed by smaller squares).

Each essay started with the presentation of two cues (400–600 ms) that indicated whether the participant should attend to the global or local features. Next, the target stimulus in red appeared in the center of the screen between these two cues and remained on the screen for a maximum of 2500 ms or until a response was given. The interval between response and presentation of the next cue was 900–1100 ms (see Fig. 1). In total, three blocks of trials were administered. The first two blocks consisted of 50 trials each, in which the dimension to be attended (global or local) was constant across all trials within the block (selective attention condition) and counterbalanced among participants. In the third experimental block of 160 trials, participants had to switch between attending to the global or local dimension (divided attention condition). Participants performed a total of 80 congruent trials (40 global, 40 local) and 80 incongruent trials (40 global, 40 local). Before all the experimental blocks were initiated, practice trials were administered.

2.3.4. Raven standard progressive matrices

This widely used reasoning-based test was applied to determine the general nonverbal intelligence scores of participants (Raven et al., 1988). It consists of 60 incomplete figures arranged according to their complexity (maximum score = 60). Participants had to use a keyboard key to select the option from several alternatives that correctly completed the figure. The duration of this task was 20 min

2.4. Statistical analysis

STATISTICA software was used for data analyses. Accuracy (Acc) and RTs were collected (see Table 1), and, for ease of exposition, a GA index was calculated for these two measures. GA Acc was computed as global Acc minus local Acc and GA RTs as local RTs *minus* global RTs. Therefore, higher scores in these two variables indicated higher global advantage effects. GA Acc and GA RTs were analyzed by means of repeated measures ANOVA using as within-subject factors the congruency between the stimuli (congruent vs. incongruent) and attentional demand (divided vs. selective), and as a between-subject factor the different groups of the study (men, follicular, ovulatory, luteal, and HC groups). To test if the groups differed in their hormone levels, three one-way ANOVAs were carried out using estradiol, progesterone, and testosterone levels as dependent variables and groups as a betwe en-subject factor. When appropriate, significant effects were then analyzed with LSD post hoc tests. In addition, Pearson's correlation coefficients were computed to test whether behavioral differences among groups were linearly related to saliva hormone levels. Correlations were first calculated for the GA effects and, when significant, for

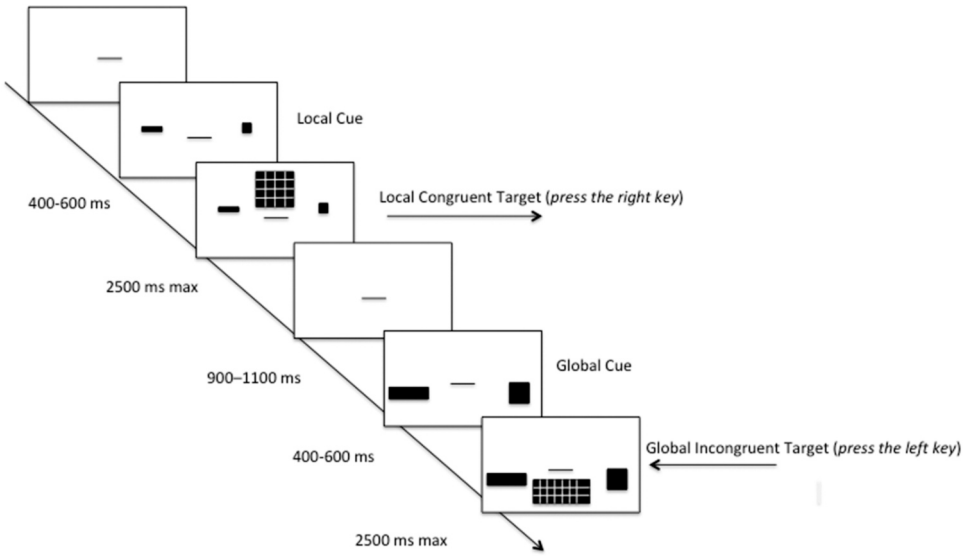

Fig. 1. Example of a sequence of the events in the global–local task. In the first trial, a global square is composed of local squares (Congruent condition). The small cues indicated that participants should respond to the local features: selecting a square using the right key. In the second trial, a global rectangle is composed of local squares (Incongruent condition), and the big cues indicated that participants should respond to the global features: selecting a square using the left key.

the local and global stimuli. Data are presented as mean ± *SEM*, and statistical significance was set at the 5% level.

3. Results

3.1. Demographic data and sex hormone levels

Demographic and sex hormone levels data are exhibited in Table 2. No significant differences were observed among the five study groups in age, $F<1$ or Raven's test result, $F(4, 92) = 1.40$, $p = 0.24$, $\eta_p^2 = 0.057$. No significant difference in menstrual cycle duration was found among the three groups of women with natural menstrual cycles, $F<1$. Women in the follicular group performed their tasks 4.4 ± 0.3 days after the beginning of the menses (M1) and 21.4 ± 2.8 days before the next menstrual cycle (M2). Women in the ovulatory group performed the task 14.8 ± 0.5 days after M1 and 14.1 ± 0.3 days before M2. Women in the luteal group performed the task 21.7 ± 0.4 days after M1 and 6.7 ± 0.3 days before M2.

Sex hormone levels differed among the experimental groups: estradiol $F(4, 92) = 5.72$, $p < 0.01$, $\eta_p^2 = 0.20$ progesterone $F(4, 92) = 29.9$, $p < 0.01$, $\eta_p^2 = 0.57$ and testosterone levels $F(4, 92) = 30.7$, $p < 0.01$, $\eta_p^2 = 0.57$. As expected, estradiol levels were higher in the ovulatory and luteal groups when compared with men and the follicular groups (all $ps < 0.02$). Similarly, progesterone levels were higher in the luteal group than in any other group (all $ps < 0.001$). Finally, testosterone levels were higher in the men than in the other groups (all $ps < 0.01$) and lower in HC users than in the follicular ($p < 0.01$) and ovulatory groups ($p < 0.03$).

3.2. Global–local task data and correlations with sex hormone levels

3.2.1. GA Acc

A Group (men, follicular, ovulatory, luteal, and HC women) x Attention (selective and divided) x Congruency (congruent and incongruent) ANOVA with GA Acc as the dependent variable failed to show an effect of Group, $F(4,92) = 1.27$, $p = 0.29$, $\eta_p^2 = 0.052$; Attention, $F < 1$; Congruency, $F(1,92) = 3.69$; $p = 0.058$, $\eta_p^2 = 0.039$; Attention x Congruency $F < 1$; or Congruency x Group, $F < 1$. A significant effect of Attention x Group $F(4, 92) = 2.60$, $p = 0.04$, $\eta_p^2 = 0.10$ and a trend toward significance of the Group x Attention x Congruency $F(4, 92) = 2.45$; $p = 0.051$, $\eta_p^2 = 0.10$ interaction were found.

When focused on the divided attention condition (see Fig. 2A), post hoc analyses revealed a GA Acc congruency effect (i.e., higher GA Acc in the incongruent condition than in the congruent condition) in men ($p < 0.014$) but not in the remaining groups (all $ps > 0.13$). Moreover, in the incongruent essays of this divided condition, men showed a high GA Acc effect when compared with the luteal ($p < 0.01$) and HC ($p < 0.012$) groups; conversely, the luteal group showed the lowest GA Acc when compared with the other groups (all $ps < 0.05$).

In our analysis of these behavioral results, we observed insightful correlations between hormone levels and GA effects in the most demanding divided–incongruent condition.[2] First, estradiol levels negatively correlated with GA Acc in this condition ($r = –0.25$, $p < 0.02$; see Fig. 2B).[3] Second, similar to what was observed with estradiol, there was a negative correlation between progesterone levels and GA Acc ($r = –0.24$, $p = 0.016$; Fig. 2C)[4] in this divided–incongruent condition.

When focused on the selective attention condition (see Fig. 3), a significant congruency effect in the HC group ($p < 0.041$) but not in the remaining groups was observed (all $ps > 0.21$). Additionally, in the incongruent essays of this condition, women in the ovulatory group showed a lower GA Acc effect in comparison with the follicular ($p < 0.015$) and HC ($p < 0.01$) groups and a trend when compared to luteal group ($p = 0.077$). In addition, a trend towards significance that indicated a lower GA Acc effect in men in comparison with HC users ($p = 0.059$) was also observed.

3.2.2. GA RTs

A Group (men, follicular, ovulatory, luteal, and HC women) x Attention (selective and divided) x Congruency (congruent and incon-

[2] All the significant correlations reported in the study reached also statistical significance when corrected by the algorithm described by Benjamini-Hochberg (B-H correction; Benjamini and Hochberg, 1995; Benjamini and Yekutieli, 2001).

[3] Notice that this inverse correlation between estradiol and the GA Acc in the most demanding attentional condition could be related to the positive correlation between the levels of this hormone and the accuracy for the local divided–incongruent condition ($r = 0.23$, $p < 0.025$; Fig. 2D).

[4] This effect could be related to the positive correlation between the levels of progesterone and the accuracy for the local divided–incongruent condition ($r = 0.22$, $p < 0.04$; Fig. 2E).

Table 1
Accuracy and RT means (*SEM* in brackets) of the five groups in the experimental conditions.

		Accuracy								Response times (ms)							
		Divided				Selective				Divided				Selective			
		Congruent		Incongruent		Congruent		Incongruent		Congruent		Incongruent		Congruent		Incongruent	
	N	Global	Local	Global	Local	Global	Local	Global	Local	Global	Local	Global	Local	Global	Local	Global	Local
Men	16	0.99 (0.004)	0.99 (0.004)	0.94 (0.016)	0.89 (0.021)	0.99 (0.006)	0.99 (0.006)	0.96 (0.012)	0.96 (0.013)	442.7 (23.2)	481.6 (22.8)	466.4 (23.9)	533.2 (23.4)	410.8 (13.9)	443.3 (18.3)	421.3 (18.3)	452.3 (16.8)
Follicular	18	0.99 (0.004)	0.98 (0.010)	0.93 (0.012)	0.92 (0.016)	0.99 (0.005)	0.98 (0.011)	0.97 (0.007)	0.95 (0.014)	475.3 (18.6)	525.3 (21.4)	506.9 (21.5)	557.8 (22.6)	443.2 (16.6)	472.6 (18.5)	449.5 (14.3)	511.4 (18.6)
Ovulatory	18	0.99 (0.005)	0.98 (0.004)	0.94 (0.02)	0.91 (0.01)	0.98 (0.006)	0.98 (0.007)	0.95 (0.012)	0.97 (0.009)	496.5 (25.8)	541.0 (26.9)	524.6 (29.6)	571.5 (21.6)	418.0 (13.5)	486.5 (15.7)	433.5 (16.8)	508.5 (16.3)
Luteal	19	0.98 (0.01)	0.99 (0.01)	0.93 (0.01)	0.95 (0.01)	0.99 (0.01)	0.99 (0.01)	0.97 (0.01)	0.96 (0.01)	473.3 (21.9)	522.4 (20.1)	507.7 (28.3)	553.6 (22.7)	440.0 (21.1)	468.9 (19.2)	436.3 (19.1)	499.6 (18.3)
HC user	26	0.98 (0.006)	0.98 (0.004)	0.93 (0.009)	0.93 (0.01)	0.98 (0.005)	0.98 (0.004)	0.97 (0.007)	0.94 (0.01)	468.8 (18.4)	510.1 (19.8)	500.0 (20.3)	561.0 (24.7)	418.7 (14.2)	458.0 (15.5)	429.2 (16.5)	488.9 (15.8)
Mean (SEM)		0.99 (0.003)	0.99 (0.003)	0.93 (0.006)	0.92 (0.006)	0.98 (0.002)	0.98 (0.003)	0.97 (0.004)	0.95 (0.006)	471.7 (9.5)	516.4 (9.9)	501.8 (11.0)	556.3 (10.5)	426.0 (7.2)	465.7 (7.8)	433.9 (7.6)	492.8 (7.8)

gruent) ANOVA with GA RTs as the dependent variable failed to show an effect of Group, $F < 1$; Attention, $F < 1$; Attention x Group, $F(4, 92) = 1.28$, $p = 0.29$, $\eta_p^2 = 0.05$; Congruency x Group, $F < 1$; or Attention x Congruency $F(1, 92) = 1.82$, $p = 0.18$, $\eta_p^2 = 0.02$. However, the results showed a main effect of Congruency, $F(1, 92) = 19.67$, $p < 0.001$, $\eta_p^2 = 0.17$, with a higher GA RTs effect for incongruent stimuli (496.2 ± 8.5 ms) in comparison with congruent ones (470.0 ± 7.8 ms), and, interestingly, a significant interaction of Group x Attention x Congruency $F(4, 92) = 3.08$, $p < 0.01$, $\eta_p^2 = 0.12$ (see Fig. 4A).

Results in the divided attention condition revealed a significant congruency effect for men ($p < 0.016$) and HC ($p < 0.03$) but not for the other groups (all *ps* >0.76). In addition, during the divided-incongruent condition, a trend for higher GA RTs of men in comparison with the luteal ($p < 0.059$) and the ovulatory ($p < 0.074$) groups was observed (*ps* >0.12 for all the other pair-comparisons). However, when focused on the selective attention condition, a congruency effect for the follicular ($p < 0.01$), luteal ($p < 0.01$), and HC ($p < 0.03$) women emerged that disappeared in the other groups (all ps >0.54). Moreover, the GA RTs of men in the Selective Incongruent condition were lower in comparison with the other groups (all *ps* < 0.01) and the GA RTs of the ovulatory group in the selective–congruent condition was higher in comparison with the other groups (all *ps* < 0.01).

Additionally, estradiol levels negatively correlated with GA RTs in the divided–incongruent condition ($r = –0.32$, $p < 0.01$; see Fig. 4B), and testosterone levels negatively correlated with GA RTs in the selective–incongruent condition ($r = –0.21$, $p < 0.043$; Fig. 4C).[5]

4. Discussion

This study investigated the processing of hierarchical stimuli (geometric forms) in a global–local task. The results confirmed the *global advantage* effect (Navon, 1977, 1981), enhanced during divided attention and with incongruent stimuli (Hedden and Gabrieli, 2010; Leaver et al., 2015; Steenbergen et al., 2015). However, more importantly, the current results showed that these effects differed according to sex, menstrual cycle, use of HCs, and in relation to the sex hormone levels of the participants (see Table 3 for a summary of the main correlation data and behavioral differences among groups).

4.1. Men, follicular, and luteal groups

It is assumed that women process information in a more local/analytic way than men, that they are more global/holistic (Heil and Jansen-Osmann, 2008; Peña et al., 2008; Pletzer et al., 2013; Rilea, 2008; see Pletzer, 2014 for review), and that tasks with high cognitive load favor the emergence of sex (Coluccia and Louse, 2004) and menstrual cycle (Hampson et al., 2014; for a review, see Bernal and Paolieri, 2021) differences. In line with these ideas, when focused on the more demanding *divided–incongruent condition*, our data indicated that the men group showed a higher GA Acc effect (i.e., better accuracy during the processing of global vs. local stimuli) in comparison with the luteal group and that the luteal group had a lower GA Acc effect in comparison with the remaining groups. Additionally, the GA Acc was negatively related with estradiol and progesterone levels, and the luteal group, with high levels of both hormones (present data; for a review, see also Hampson et al., 2020), showed a negative GA Acc effect (i.e., better accuracy during the processing of local vs. global stimuli) during this divided–incongruent condition. The results of the GA RTs during the divided-incongruent condition point to the same direction, with a negative correlation between GA RTs and estradiol levels and a trend for

[5] This effect may be related to the negative correlation between the levels of testosterone and the RTs for the local selective–incongruent condition ($r = –0.25$, $p < 0.014$; Fig. 4D).

Table 2
Means of demographic data and sex hormone concentrations (*SEM* in brackets).

	N	Age	Raven	Testosterone (pg/ml)	Estradiol (pg/ml)	Progesterone (pg/ml)	Days from M1	Days to M2	Menstrual cycle duration (days)
Men	16	22.2 (0.5)	50.8 (1.3)	161.3 (15.5)	2.4 (0.3)	87.9 (12.9)			
Natural cycle women									
Follicular	18	21.7 (0.8)	48.4 (1.1)	81.8 (5.7)	2.8 (0.1)	107.1 (14.5)	4.4 (0.3)	21.4 (2.8)	28.6 (0.5)
Ovulatory	18	20.9 (0.6)	46.3 (2,2)	77.6 (3.5)	3.7 (0.3)	106.3 (8.2)	14.8 (0.5)	14.1 (0.3)	28.9 (0.5)
Mid-luteal	19	20.9 (0.6)	47.0 (1.6)	65.5 (4.2)	3.6 (0.3)	284.9 (24.3)	21.7 (0.4)	6.7 (0.3)	28.5 (0.5)
HC user	26	21.5 (0.6)	47.4 (0.6)	55.8 (4.9)	3.3 (0.2)	100.0 (10.8)			

a higher GA RTs effect of males compared to the luteal group. Moreover, ovarian hormone levels were positively related with the accuracy on local-, but not global-, divided-incongruent stimuli (see Footnotes 2 and 3), suggesting that these GA Acc effects are related with the positive influence of ovarian hormones on the processing of local stimuli.

In addition, during the divided attention condition, men, but not women in the follicular and luteal groups, showed a *congruency effect* for both GA Acc and GA RTs. According to this, the global processing bias of men is accompanied by a stronger global-to-local interference (Navon, 1977, 1981).

To sum up, the pattern observed in men (congruency effect and higher GA Acc during the divided–incongruent condition) suggests a higher vulnerability to the interference produced by irrelevant features of the incongruent stimuli, especially in the demanding divided condition that requires attentional switching (Hedden and Gabrieli, 2010). However, the pattern observed in women (absence of a congruency effect in follicular and luteal women and lower GA Acc in the last group) reflected a reduced interference of irrelevant (incongruent) features that needed to be inhibited in switching (divided) attentional contexts. This last result is consistent with previous research that showed greater cognitive flexibility of women in different tasks (Gurvich and Rossell, 2015; Müller et al., 2007; Thakkar et al., 2014), especially during the luteal phase of the menstrual cycle (Hidalgo-Lopez and Pletzer, 2017).

When focused on the *selective–incongruent condition*, testosterone levels were negatively related with the GA RTs and men showed a lower GA RTs in comparison with women groups. This decrease of men's GA RTs during the selective–incongruent condition was accompanied by a reduction of the global-to-local interference and, as a result, no effect of congruency appeared during this selective condition. Conversely, in follicular and luteal women, with lower testosterone levels, the GA RTs during the selective–incongruent condition were higher in comparison with men, and they were accompanied by a significant congruency effect during the selective condition.

In summary, these results indicate that the GA effect depends on the task attentional demand and hormone levels. Thus, while divided attention (higher demand) seems to be more sensitive to estradiol and progesterone, selective attention (lower demand) mainly depends on the effects of testosterone. The congruency effect associated with the GA also shows a reversed pattern in men and women depending on the attentional demand of the task (congruency effect in men in the divided condition that disappears in the selective condition, and the opposite pattern in women). Therefore, these results indicate that both the hormone levels and the level of demand of the task play a joint role in the modulation of the GA effect; therefore, the interaction between these two variables could explain divergent results previously observed in the literature (Álvarez-San Millán et al., 2021; Kimchi et al., 2009; Razumnikova and Volf, 2011; Roalf et al., 2006). Thus, in Roalf et al. (2006), who used a divided attentional paradigm more sensitive to female sex hormones, the differences during the processing of local and global stimuli were observed in women but not in men. Conversely, in Razumnikova and Volf (2011), who used a selective paradigm more responsive to male sex hormones, the global vs. local differences were observed in men but not in women. Moreover, with a selective paradigm, Álvarez-San Millán et al. (2021) observed that men were faster than women in both global and local task, as we observed in the current study (see Table 1). Interestingly, the results of Kimchi et al. (2009) suggested that local essays were more sensitive to sex differences in selective paradigms than global essays (i.e., men were faster than women in local classification), which is consistent with current negative correlation between testosterone and RTs during the processing of local incongruent stimuli (see Footnote 3), and with the lower RTs previously observed in men during different selective attentional tasks (Evans and Hampson, 2015; Gurvich and Rossell, 2015; Stoet, 2017).

In addition, our results showed a more local processing for the luteal group (Álvarez-San Millán et al., 2021; Pletzer et al., 2014; see Pletzer and Harris, 2018; Pletzer et al., 2017) that can be related to progesterone levels (Pletzer and Harris, 2018; Pletzer et al., 2014). However, while in Álvarez-San Millán et al. (2021) and the current study, this effect emerged during the selective condition, in Pletzer et al. (2014) it was observed during the divided but not during the selective condition. This dissimilarity can be explained by the relevant methodological differences between Pletzer's and the current study. For example, the selective condition in Pletzer et al. (2014) involved switching between targets and non-targets, similarly to a divided condition (note also that the GA RTs were significantly larger for their selective attention condition than for their divided attention condition, suggesting greater difficulty for the former).

4.2. Inclusion of the HC group

The performance of the HC group strengthens the above explanation on the influence of sex hormones on the divided and selective conditions. Thus, if the congruency effect of both men during divided and women during selective conditions are related to the low levels of the female and male sex hormones, respectively, we would expect similar effects in the HC because of their reduced endogenous sex hormone levels (Hampson, 2020). According with this possibility, a congruency GA RTs effect in both divided and selective conditions was observed in the HC group. In a similar line, a recent study examining egocentric navigation ability showed that the performance of HC women is related to their endogenous sex hormone levels (Bernal et al., 2020). However, the lower estradiol levels in our HC group did not significantly differ from the ovulatory and luteal groups. Thus, it is also possible that the synthetic hormones contained in HC could have caused these differential findings. In this context, previous studies examining spatial ability have observed a behavior-modulating role of the ethinyl estradiol (Beltz et al., 2015), and of the androgenicity of the synthetic progestins contained in the HC (Griksiene and Ruksenas, 2011; Wharton et al., 2008).

Most importantly, previous studies reported that both, HCs and endogenous sex hormones cause structural changes in brain regions such

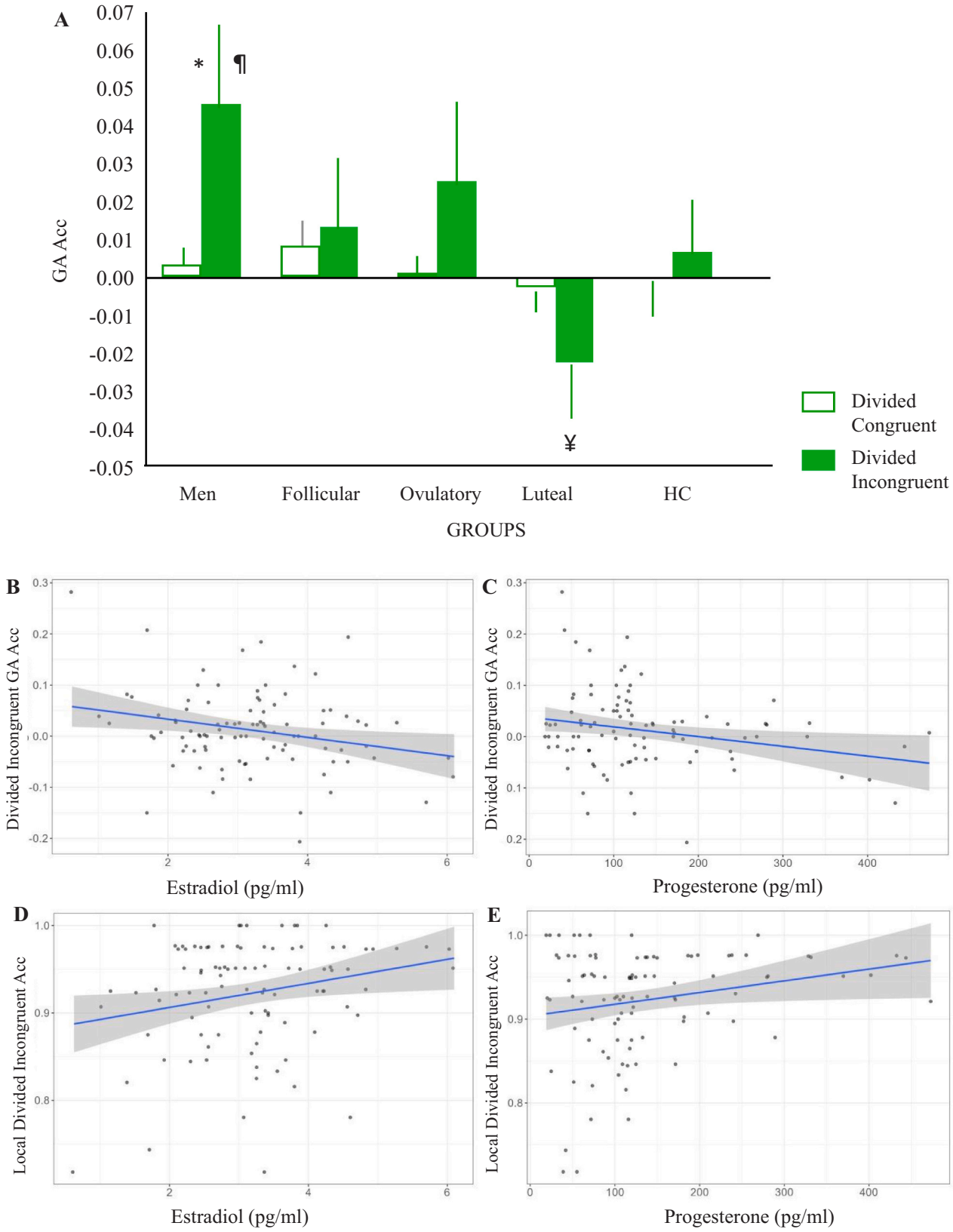

Fig. 2. Global Advantage Accuracy (GA Acc) of the different groups in divided conditions (A). Correlations between divided–incongruent GA Acc and estradiol (B) and progesterone (C) levels. Correlations between local divided–incongruent accuracy and estradiol (D) and progesterone (E) levels. GA Acc is computed as global accuracy *minus* local accuracy
(*$p < .05$ incongruent vs. congruent stimuli; $p < 0.05$ vs. divided–incongruent of mid-luteal and HC groups; ¥ $p < 0.05$ vs. divided–incongruent of all the other groups).

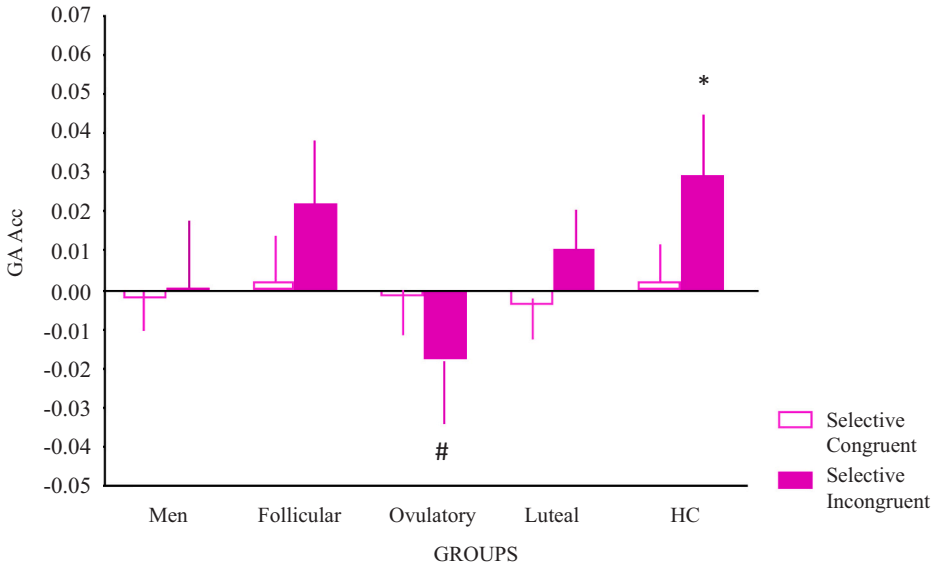

Fig. 3. Global Advantage Accuracy (GA Acc) of the different groups in selective conditions. GA Acc is computed as global accuracy *minus* local accuracy (*$p < 0.05$ incongruent vs. congruent stimuli; #$p < 0.025$ vs. selective–incongruent of follicular and hormonal contraceptive groups).

as the prefrontal cortex, anterior cingulate cortex, and basal ganglia (for a systematic review, see Rehbein et al., 2021), the same structures involved in a global–local task in which congruency between stimuli and attentional switching were manipulated (Hedden and Gabrieli, 2010). Further studies are needed to elucidate how these effects interact and modulate the processing of hierarchical stimuli in HC users women.

4.3. Inclusion of an ovulatory group to study the role of estradiol

To the best of our knowledge, this is the first study that has included an ovulatory group to explain how the menstrual cycle modulates global–local processing. The most important behavioral differences among this group and the follicular and luteal groups were related to their performance in the *selective condition*. First, when we focused on the selective–incongruent condition, the ovulatory group showed a GA Acc with a negative value (this is, the performance of this group was better with local stimuli than global) that statistically differed from the standard GA Acc of the follicular group. Second, in the follicular and luteal but not ovulatory group, the typical congruency effect was observed on GA RTs during the selective condition. Third and most important, when we focused on the selective–congruent condition, we observed that GA RTs in the ovulatory group were higher in comparison with the other groups. The source of this increase in the GA seemed to be the faster RTs to the global selective–congruent stimuli (418 ± 13.5 ms; see Table 1). Thus, ovulatory women benefited more from the congruency between the stimuli in this global selective–congruent condition. However, no significant correlations were observed between estradiol levels and GA RTs during the selective–congruent condition.

A deeper analysis of the overall pattern of the GA RTs effect enabled us to suggest an alternative hypothesis about the possible influence of ovarian sex hormones on this measure (see Fig. 4). The GA RTs effect of the ovulatory group increased during the selective–congruent condition, this being the only difference among the three groups of women with natural menstrual cycles. Thus, one possibility is that estradiol (ovulatory group) increased the GA RTs effect and progesterone countervail it in a non-linear way causing that the similar behavior of the luteal group to the low estradiol and progesterone-follicular group (for a review see Bernal and Paolieri, 2021). This possibility is compatible with studies showing that some brain (Barth et al., 2015; Pletzer et al., 2019) and behavioral (Bernal et al., 2020; Dreher et al., 2007; Jackson et al., 2006) effects of estradiol in the absence of progesterone (i.e., in the ovulatory phase) differ in the presence of progesterone (i.e., in the luteal phase). For example, the prefrontal cortex is involved during the execution of a global–local task in which congruency between stimuli and attentional switching were manipulated (Hedden and Gabrieli, 2010); and estradiol induces dendritic expansion of this structure in the absence but not in the presence of progesterone (Chisholm and Juraska, 2012; Marrocco and McEwen, 2016).

4.4. Limitations

Within-subject designs are frequently used in menstrual cycle studies because allows the determination of the hormonal data at different times of the menstrual cycle, reducing the inter-individual variability. However, our cross-sectional design has the advantage of avoiding the practice effects that difficult data interpretation in some previous menstrual cycle studies (Hampson, 1990; Maki et al., 2002; Mordecai et al., 2008; for a review see Bernal and Paolieri, 2021). In addition, the sex hormone concentrations observed in present study are similar to the levels observed in other studies (Bernal et al., 2020; Hampson et al., 2014; Kozaki and Yasukouchi, 2009; Pletzer et al., 2019; Scheuringer and Pletzer, 2017), and present data are compatible with the typical increases in estradiol levels during the ovulatory and the mid-luteal phases as well with the increase in progesterone levels during mid-luteal phase (see Hampson, 2020 for a review).

A related limitation is that data from cross-sectional studies with a reduced number of participants (especially important for correlations) should be interpreted with caution. We have to mention, however, that other cross sectional studies used a similar number of participants (e.g. Bernal et al., 2020, Hampson et al., 2014; Hussain et al., 2016), and the power analysis seems to indicate that the number of participants is appropriate.

5. Conclusion

In conclusion, global–local tasks are widely used in neuroscience and experimental psychology research through experiments in which men and women are often included in the same experimental group. Also, studies examining the influence of the menstrual cycle often include early follicular and mid-luteal phases, but not ovulatory phase. Our data

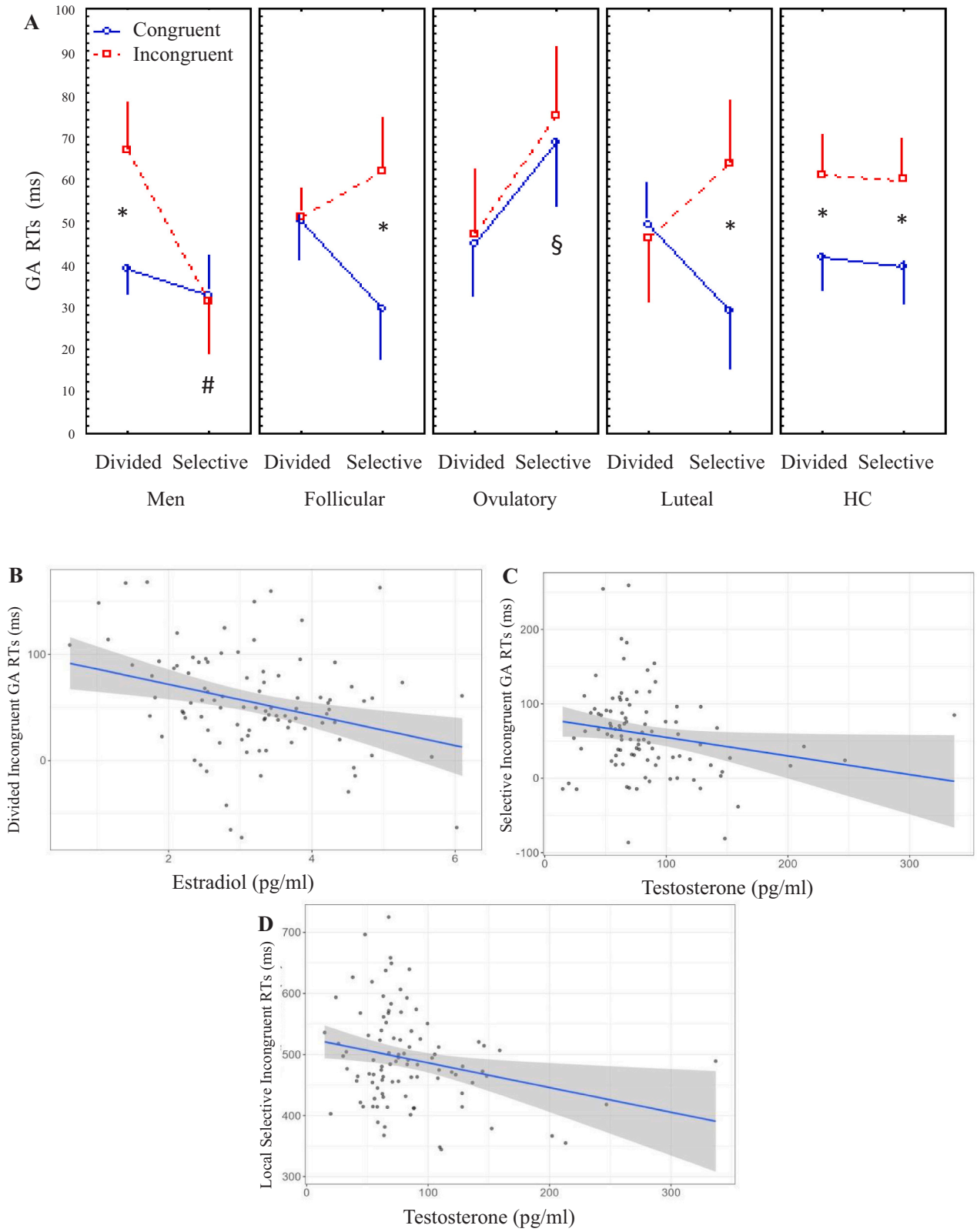

Fig. 4. Global Advantage reaction times (GA RTs) of the different groups and conditions (A). Correlation between estradiol levels and divided–incongruent GA RTs (B). Correlations between testosterone level and selective–incongruent GA RTs (C) and local selective–incongruent RTs (D). GA RTs were computed as local RTs *minus* global RTs (*$p < 0.03$ congruent vs. incongruent; #$p < 0.01$ vs. selective–incongruent of all the other groups; §, $p < 0.01$ vs. selective–congruent of all the other groups).

Table 3
Summary of the main differences observed among groups.

	Divided Attention		Selective Attention	
	GA Acc	GA RTs	GA Acc	GA RTs
Incongruent condition	Negatively correlated with estradiol and progesterone levels. Men were more global than luteal and HC women. Luteal women were the most local.	Negatively correlated with estradiol levels.	Ovulatory women were more local than follicular and HC women.	Negatively correlated with testosterone levels. Men had the lowest GA RTs.
Congruent condition	–	–	–	Ovulatory women had the highest GA RTs
Congruency effect	Significant in men but not in the other groups	Significant in men and HC but not in the other groups	Significant in HC but not in the other groups	Significant in follicular, luteal and HC but not in the other groups

GA: Global Advantage; Acc: accuracy; RTs: reaction times.

suggest that sex, menstrual cycle, including the ovulatory phase and HC use, and the level of demand of the task could constitute an important source of variability in these studies, causing apparently contradictory results.

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Conflict of Interest

The authors declare no conflicts of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2021.105430.

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