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# Eye-movements during number comparison: Associations to sex and sex hormones

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# Abstract

Multi-digit numbers are of a hierarchical nature with whole number magnitudes depending on digit magnitudes. Processing of multi-digit numbers can occur in a holistic or decomposed fashion. The unit-decade compatibility effect during number comparison is often used as a measure of decomposed processing. It refers to the fact that performance is reduced when the larger number contains the smaller unit digit (e.g. 73 vs. 26). It has been demonstrated that women show a larger compatibility effect than men, which is in accordance with their general tendency towards focusing on stimulus details during processing of visual hierarchical stimuli (local processing style). Such a local processing style has been related to higher progesterone and lower testosterone levels. One method to study individual processing styles is eye-tracking. The aim of the present study was to examine whether sex and sex hormones (estradiol, progesterone, testosterone) relate to eye movement behavior in the number comparison task. Unlike previous studies we found no evidence for sex differences in the behavioral compatibility effect. Nevertheless, women look more often and longer at individual digits and show a stronger compatibility effect in fixation durations compared to men, while men show more saccades between numbers than women. Estradiol and progesterone were related to fewer fixations and shorter fixation durations and more saccades between numbers in men, but not in women. Furthermore, the compatibility effect in the number of fixations and fixation durations was negatively related to testosterone in women. In summary, this is the first study to demonstrate sex differences and sex hormone influences on eye gaze behavior during number comparison.

#### **Keywords**

Number comparison; Unit-decade compatibility effect; Sex differences; Sex hormones; Eyetracking; Eye movements

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<sup>&</sup>lt;sup>2</sup>This result remained significant, even if all estradiol values exceeding the group mean by more than 2 SD were excluded. Men showed a significant negative association between estradiol and relative fixation duration (r = -.39, p = .023), while no significant association was observed in women (r = .08, p = .65).

<sup>&</sup>lt;sup>3</sup>This result remained significant, even if all estradiol values exceeding the group mean by more than 2 SD were excluded. Men showed a significant negative association between estradiol and relative fixation duration (r = -.38, p = .026), while no significant association was observed in women (r = .09, p = .62).

# 1 Introduction

Arithmetic skills are an important predictor of academic achievement [16]. Accordingly, numerical skills have been extensively researched and various models of number processing have been proposed [15,62]. For instance, both a spatial and verbal involvement in number processing has been postulated ([27]; Dehaene et al., 2003). Number magnitudes are represented on a mental number line with larger numbers to the right and smaller numbers to the left. This representation of number magnitudes constitutes a spatial format, and multiple interactions between numerical and spatial processing have been observed [27]. Most importantly, a strong overlap between brain areas responsible for number magnitude processing and brain areas responsible for spatial processing is observed in the parietal cortex [27]. Arithmetic facts on the other hand are likely stored in a verbal format (Dehaene et al., 2003).

The number comparison task employed in the current study, is a task to assess number magnitude processing [39], which has been related to spatial processing [27]. One of the most prominent results regarding tasks of spatial orientation are robust sex differences favoring men, which are likely the result of sex differences in spatial processing strategies (for reviews see [2,42]). However, less attention has been paid to sex differences in number processing, even though some neuroimaging studies also suggest differences in number processing styles between men and women [6,31,43]. In a recent study we demonstrate that spatial navigation strategies relate to processing styles during the number comparison task [50]. In fact, sex differences in spatial navigation strategies transfer to sex differences in number processing styles [50]. Sex differences in processing strategies are not only reflected in the neural networks utilized to solve a task (e.g. [30]), but also in the way attentional resources are allocated during a task, e.g. by sex differences in the focus on certain stimulus aspects as reflected in eyefixations (e.g. [1,34]). Accordingly, sex differences in eyemovements during spatial tasks have previously been described [1,37]. However, up to date no study has investigated sex differences in eye movements during number processing. Investigating different eye-movement patterns in men and women during number processing is the most direct way to understand, which information men and women focus on when solving numerical tasks.

Multi-digit numbers are of a hierarchical nature with whole number magnitudes being determined by the place and value of individual digit magnitudes (e.g.  $79 = 7 \times 10 + 9$ ). While early models assume that the magnitude of multi-digit numbers is represented holistically (whole number magnitude) [14,25], this account has been questioned by the discovery of the so-called unit-decade compatibility effect during number comparison [39]. The unit-decade compatibility effect describes the fact that number comparison occurs slower and less accurately if the smaller number contains the larger unit digit (*incompatible items*, e.g. 61 vs. 27, 6 > 2, but 1 < 7) than when the smaller number contains the smaller unit digit (*compatible item*, e.g. 67 vs. 21, 6 > 2, and 7 > 1). This suggests an interference of unit digit magnitudes on number comparison performance. If number comparison was based only on the representation of whole number magnitudes, no compatibility effect should occur. Accordingly, a decomposed model of number processing has been formulated, assuming that decade and unit digit magnitudes are represented separately and number

comparison relies on the separate comparison of decade and unit magnitudes. However, newer accounts assume that single digit magnitudes have to be processed separately to form a holistic representation of the whole number magnitude. Accordingly representations of both, the single digit magnitudes and the whole number magnitude are formed and can be used in parallel during number comparison and other arithmetic processes (hybrid models; [41,62]). If this is the case, the unit-decade compatibility effect represents a measure of how much more likely participant's base their comparisons on decomposed rather than holistic magnitude representations. Since, the holistic magnitude representation depends on the representations of digit magnitudes it may be faster during number comparison to base decisions on digit magnitudes. However, during incompatible items, a decision based on digit magnitudes is more prone to error, and the response may be delayed if participants suppress the response tendency elicited by unit magnitudes and refer to holistic or decade magnitudes instead. Accordingly, the more items participants solve based on decomposed magnitude representations, the larger is their compatibility effect. This understanding of multi-digit number processing opens the possibility of assessing intra- and interindividual differences in the compatibility effect to understand, which task conditions and individual characteristics lead to a stronger or weaker likelihood to base number processing on decomposed magnitude representations.

Indeed it has been demonstrated that the unit-decade compatibility effect is affected by stimulus presentation mode [40,46] and by interindividual differences like sex [29,43,48]. For example, the compatibility effect is significantly smaller when the numbers are spaced further apart [46,50]. Furthermore, multiple studies demonstrate a larger compatibility effect in women [21,29,44,50] compared to men, suggesting that women use a more decomposed processing style during number comparison.

In that respect, the number comparison task shares similarities with a task of visual attention, i.e. the Navon paradigm [38], which assesses a person's tendency to process hierarchical stimuli in a global/holistic or local/decomposed fashion. The Navon paradigm consists of global structures (for example the letter O) made up of local parts (for example letters C) and participants are required to identify targets either at the global or local level. During visual processing both global and local level information are processed in parallel [23,24]. Responses are generally faster for targets at the global level (global advantage), but this effect depends on stimulus characteristics and individual differences. A larger global advantage effect suggests that participants process global information faster than local information and/or are more prone to inhibit local compared to global information. Several studies demonstrate sex differences in the Navon paradigm with a stronger tendency towards global processing in men compared to women [4,45,54,55,57].

It has been demonstrated that participants tendency towards global or local processing relates to cognitive processing styles in various tasks including spatial tasks [4,47,48]. For instance during spatial navigation, women tend to use a more egocentric perspective and focus more strongly on landmarks, when they are more prone to a local/decom- posed processing style [48]. Furthermore, participants with a strong focus on landmarks in a navigation task, show a stronger compatibility effect during number comparison [50]. In fact, sex differences in spatial navigation strategies mediate sex differences in the

compatibility effect [50]. Similarly, during number comparison tasks, women show a larger compatibility effect if they are more prone towards a local processing style [47]. In summary, this behavioral evidence suggests, that sex differences in the compatibility effect emerge, because women pay more attention to individual digits than men. However, while for spatial studies, the assumption of women's stronger focus on landmarks has been corroborated by eye-tracking studies [1,37], no study so far has explored sex differences in the number comparison task using eye-tracking.

So far, only one eye-tracking study has been conducted on the number comparison task [35], which included only 10 participants. In accordance with the hybrid model, they found that unit-digits were fixated more often than decade-digits, an effect that was even more pronounced in incompatible items, i.e. unit-decade-incompatibility increased unit-fixations and decreased decade-fixations. However, no study has addressed, whether factors influencing the unit-decade compatibility effect during number comparison also affect participants eye-movements during the task. Specifically, no study so far has investigated individual differences, like sex differences in eye-movement behavior during the number comparison task. If women indeed use a more decomposed processing style, they should show more/longer fixations on individual digits. Particularly, if incompatible items are characterized by more/longer fixations on unit digits [35], a more decomposed processing style in women could lead to a specific focus on unit digits, rather than decade digits. Furthermore, it can be assumed that a holistic processing style, would lead participants to look longer at a multi-digit number until a holistic representation of its magnitude has been formed rather than switching gaze between numbers. If women indeed show a more decomposed processing style, they should show more gaze switches between numbers, while men should show more gaze switches within numbers.

For most sexually dimorphic behaviors, extensive studies assessing organizational and activational effects of sex hormones have been conducted (see e.g. [32] for a review). However, the role of sex hormones has hardly been explored in numerical tasks. For example, several studies have explored the role of testosterone in spatial abilities (e.g. [9,13,22,26], but see [20,17,52]), the role of estradiol in verbal and memory functions (e.g. [11,64,67]) and menstrual cycle effects in spatial and verbal functions (for a review see [61]). However, these studies have often yielded inconsistent results and also suggest that sex hormones may play a different role for cognitive tasks in men and women. For example, a positive association of testosterone to spatial performance has been more often observed in women [8,18], while in men even negative associations have been observed [18,33,63,65]. It should be noted, that most of these studies focused on rather coarse performance measures (like accuracy or RT), rather than measures of cognitive processing styles. If sex differences in cognitive performance are indeed routed in cognitive processing styles, it is reasonable to assume that any sex hormone influences underlying these sex differences, might also be found on these processing styles. Accordingly, if sex differences in cognitive processing styles are indeed routed in participant's attentional focus on global or local stimulus aspects, studies on the association between sex hormones and cognitive processing styles might profit from a direct assessment of participants attentional focus.

Furthermore, hypotheses regarding sex hormone influences in cognitive tasks might be better drawn from sex hormone influences observed during global-local processing.

In the Navon paradigm it has consistently been demonstrated that higher progesterone levels relate to a stronger tendency towards local/ decomposed processing [45,49], while higher testosterone levels relate to a stronger tendency towards global/holistic processing [45]. Given the behavioral link between global-local processing and the compatibility effect, it is reasonable to assume, that sex hormone influences observed during global-local processing, could also be observed for the compatibility effect. However, sex hormone associations to the compatibility effect have hardly been investigated. Two studies assessing sex hormone associations to the compatibility effect, observe only weak associations. In one study, the behavioral compatibility effect was only weakly associated to the progesterone/testosterone ratio, but not to progesterone or testosterone per se [50]. In the second study, no association of progesterone or testosterone to the behavioral compatibility effect was observed [51]. However, sex hormones were related to hemispheric asymmetries during number comparison as investigated with a visual hemifield experiment [51]. Accordingly, it appears that also during number comparison, an association of sex hormones to processing styles is hardly reflected in behavioral measures and might profit from a more direct assessment of participants attentional focus. If sex hormones moderate cognitive processing styles via visual-atten- tional processes (like the focus on global vs. local stimulus aspects), this relationship might be more adequately captured by studying participant's eye gaze rather than reaction times. Given that progesterone relates to a more local and testosterone to a more global processing style during the Navon paradigm, participant's with higher progesterone and lower testosterone levels should also show longer flxation durations on individual digits in the number comparison task.

Accordingly, in the present study, we utilize eye-tracking in a large sample of men and women to address the questions of sex differences and sex hormone influences on eyemovements during number processing. This is the second part of a larger project focusing on sex hormone actions during number comparison (for results of the flrst part, see [51]). In summary, we hypothesize a larger behavioral compatibility effect in women compared to men. We expect these behavioral sex differences to be accompanied by more frequent and longer fixations on (unit) digits in women compared to men. In addition, we expect women to switch more often between numbers and men to switch more often within numbers. Regarding sex hormones, we expect progesterone to relate to a larger behavioral compatibility effect and longer fixation durations on (unit) digits, while we expect testosterone to relate to a smaller behavioral compatibility effect and shorter fixation durations on (unit) digits. While previous studies do not provide enough information to formulate directed hypotheses regarding the role of estradiol, the relationship of eyemovements to estradiol will also be explored. To address these questions, we conducted the first eyetracking study on the number comparison task assessing the effects of sex and sex hormones on eye-movement behavior.

# 2 Methods

#### 2.1 Participants

Participants were the same as described in Pletzer et al. [51]. 41 men and 46 women were recruited for this study. Exclusion criteria were neurological, endocrinological or psychiatric diseases, left-handedness, and hormonal contraception, cycle irregularities as well as cycle related disorders like premenstrual dysphoric disorder (PMDD) in women. Since glasses with a narrow frame or hard contact lenses can interfere with the correct detection of the pupil, participants with glasses or hard contact lenses were also excluded. Since cycle phase has been shown to moderate sex differences in some cognitive tasks (e.g. [44]) and sex differences in the related Navon paradigm are restricted

to the luteal cycle phase [45], all women were tested in their luteal cycle phase (10–3 days before the expected onset of next menses). To calculate the expected onset of next menses the average duration of the last three cycles was added to the onset of the last menses. Onset of next menses was evaluated in follow-up. Four men and two women did not complete the study due to technical issues with the eye-tracker. Five women were excluded because their next menses occurred too early or too late. Accordingly, the final sample included 39 men and 37 women. These participants were between 18 and 32 years old with a mean age of 23.36 years in men (SD = 3.27 years) and 23.27 years in women (SD = 3.59 years). Age did not differ significantly between men and women ( $t_{(74)} = 0.11$ , p = .91, d = 0.03). An intelligence screening using Ravens Advanced Progressive Matrices (APM) as implemented in the Vienna Test System showed a mean intelligence quotient of 110.35 in men (SD = 9.56) and 107.86 in women (SD = 9.20). IQ did not differ significantly between men and women ( $t_{(72)} = 1.13$ , p = .26, d = 0.27). Furthermore, men and women did not differ significantly in education level (Z = -1.61, p = .11) or employment status (Z = -0.58, p= .56). The average cycle duration in women was 29.15 days (SD = 2.40 days) ranging from 24 days to 34 days. Women were on average tested on day 21.53 of their cycle (SD = 3.61days).

# 2.2 Ethics statement

All participants gave their informed written consent to participate in the study. All data were processed in anonymized de-identified form. All methods conform to the code of ethics of the World Medical Association (Declaration of Helsinki).

The institutional guidelines of the University of Salzburg (Statutes of the University of Salzburg<sup>1</sup>) state in §163 (1) that it is necessary to seek ethical approval for research on human subjects if the physical or psychological integrity is affected, the right for privacy or other important rights or interests of the subjects or their dependents are confounded. Paragraph §163 (2) states that it is the decision and responsibility of the PI to decide, whether (1) applies to a study or not. Therefore, no ethical approval for this study was sought out. Non-in- vasive methods were used on healthy adult volunteers, who willingly gave their informed consent to participate. Accordingly, (1) did not apply. Data were

<sup>&</sup>lt;sup>1</sup>This result remained significant, even if all participants with hormone values exceeding the group mean by 2 SD were excluded (resulting in a sample of 32 men and 31 women: F(1,61) = 5.10, p = .027).

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processed in anonymized/de-identified form. Participants were assigned a subject ID (v001, v002, etc.), when physically present at the lab, which was used throughout the study.

#### 2.3 Procedure

Participants were tested in the eye-tracking laboratories at the faculty of natural sciences of the University of Salzburg. Upon arrival, participants were greeted by the experimenter and asked to rinse their mouth in order to remove any particles before taking saliva samples. Then participants completed the written informed consent as well as screening questionnaires on demographic variables, exclusion criteria and, in the case of female participants, hormonal status. Afterwards, participants were asked to give their first saliva sample. Participants were then seated in front of the computer screen at a viewing distance of 58 cm held constant by a chin-and-forehead rest. After receiving task instructions, the eye-tracker was calibrated and participants completed two number comparison tasks, one described in the present study, the second one in [51]. Each task was preceded by 20 training trials, followed by 200 experimental trials. Participants were asked for a second and third saliva sample after completing each task. The Advanced Progressive Matrices (APM, [53]) was completed in the end of the study. Women additionally also filled out a pre-menstrual symptoms screening tool (PSST, [60]). After the study, participants were debriefed and received either course credit or a small monetary compensation for their participation.

# 2.4 Number comparison task

The same task as in Pletzer et al. [46] was used. Two two-digit numbers were presented vertically above each other at the vertical midline of the monitor in white on a black background. Numbers comprised a visual angle of  $2.96^{\circ}$  in height and were spaced  $6.91^{\circ}$ (dense spacing) or 14.74° (sparse spacing) apart. Trials with dense and sparse spacing were randomized as a manipulation control, since previous studies indicate effects of spacing on the behavioral compatibility effect [46,50]. Participants were asked to decide which number was larger by pressing a response button as quickly and accurately as possible. They were asked to press the upper response button, if the upper number was larger and the lower response button, if the lower number was larger. Numbers remained on the screen until the participant responded, but disappeared after a maximum presentation time of 3 s. Each trial was preceded by a fixation cross, presented for 1.5 s. Among items with dense and sparse spacing, 20 were so called within-decade trials, in which both numbers contained the same decade digit (e.g. 71 vs. 75). These trials were included as recommended by Nuerk et al. [39] to avoid a strategy of focusing only on decade digits. Among the remaining trials half were compatible, i.e. the larger number contained the larger unit digit (e.g. 86 vs. 53; 8 > 5, 6 > 3), the other half was incompatible, i.e. the larger number contained the smaller unit digit (e.g. 83 vs. 56; 8 > 5, 3 < 6). The order of trial presentation was randomized. Problem size, decade distance and parity was matched across conditions as described in Pletzer et al. [46]. Reaction times (RT) and accuracy were recorded for each item.

# 2.5 Eye-tracking

Eye-tracking was performed with EyeLink 1000 desktop mount system (SR Research, Ontario, Canada; sampling rate of 1000 Hz). The eye tracker was calibrated and validated by a 9-point calibration routine. The criterion for successful calibration was an average error of

less than  $0.5^{\circ}$  of visual angle ( $M = 0.35^{\circ}$ , SD = 0.08). The fixation cross at the beginning of each trial (also) served as a fixation control. If the eye tracking system did not detect a fixation on the fixation cross, the system was re-calibrated. This feature ensured constant eye tracking accuracy throughout the experiment. Regions of interest were defined around the unit and decade digit of each number. Dependent variables were the number of fixations on unit and decade digits, fixation duration on unit and decade digits and the number of eye movements (saccades) between digits of the same number, as well as digits of different numbers. All variables were considered in relationship to reaction time, since participants who took longer to respond to items also had more time to look at digits. Accordingly, relative fixation durations are reported in percent reaction time and number of fixations as well as eye movements as number of fixations or number of saccades per second.

# 2.6 Statistical analysis

Statistical analysis was performed via IBM SPSS Statistics (version 26). Behavioral data (RT and accuracy), fixation durations and eye movements (saccades) were analyzed using mixed ANOVAs with the between-subjects factor sex (men vs. women) and within-subjects factors for the different conditions. These are described in detail in the respective paragraphs of the results section. Effects of spacing were replicated for behavioral variables, but not considered further for fixations and eye-movements due to the low number of fixations in items with sparse spacing. To evaluate the relationship of sex hormones to dependent variables and the compatibility effect irrespective of and in interaction with sex, the group-standardized hormone levels were entered as covariates in the ANOVAs described above (for details, see results section). Data are openly available at http://webapps.ccns.sbg.ac.at/OpenData/.

#### 2.7 Hormone analysis

Three saliva samples were collected throughout the study. One in the beginning, after participants rinsed their mouth and filled in the informed consent and screening questionnaires. One between tasks and one in the end. Since the e;min respectively. Prior to analysis the three samples of one participant were pooled, as recommended by the ELISA kit instructions, to obtain a more stable measure of the hormone level throughout the test session. Pooling has the advantage that fluctuations in hormone release and saliva production.are accounted for, but may - in the case of testosterone - have the disadvantage that diurnal changes or pulsatile variations of potential functional relevance are averaged out. The pooled samples were analyzed using the respective DeMediTec (http:// www.demeditec.com) salivary ELISA kits for testosterone, progesterone and estradiol (DES6644, DES6633, DES6622). According to the kit instructions, sensitivity is 1.4 pg/ml for estradiol, 5 pg/ml for progesterone and 2.2 pg/ml for testosterone. As calculated from assay controls, inter-assay CV was on average 2.1% for estradiol, 7.1% for progesterone and 5.6% for testosterone. All samples were assessed in duplicates and assessment was repeated for samples showing coefficients of variation (CV) above 25% or exceeding the group mean by more than 3 standard deviations. As a limitation it should be noted that ELISAs have been discussed to provide inflated estimates in the lower range [58]. Hormone values exceeding the group mean by more than 3 standard deviations were considered outliers and dismissed from analysis. This concerned one female progesterone value and one male

estradiol value. In addition, to ensure that hormonal association were not attributable to outliers, all analyses were rerun, after excluding all hormone values exceeding the group mean by more than 2 standard deviations. This concerned 4 male and 5 female estradiol, as well as 6 male and one female progesterone values. Since the same results were obtained, results of the larger sample are reported, but results of the more stringent outlier correction are added as footnotes.

Mean hormone values for men and women are displayed in Table 1. As outlined in Pletzer et al. [51], estradiol did not differ significantly between men and women ( $t(_{72}) = -1.06$ , p = .29, d = -0.25). This is not unusual, since estradiol levels only reach peak-levels in women during the pre-ovulatory cycle phase [50,59]. Testosterone was significantly higher ( $t_{(73)} = 10.57$ , p < .001, d = 2.44) and progesterone significantly lower ( $t_{(72)} = -6.87$ , p < .001, d = -1.59) in men compared to women. All hormone levels were highly inter-correlated in both men and women (all r > 0.39, all p < .05), with the exception of estradiol and testosterone in men (r = 0.13, p = .44, compare [51]).

# 3 Results

# 3.1 Behavioral results

To evaluate the effects of sex, compatibility and spacing on RT and accuracy,  $2 \times 2 \times 2$ ANOVAs were performed with the within-subjects factors 'compatibility' (compatible vs. incompatible) and 'spacing' (dense vs. sparse) and the between-subjects factor sex (men vs. women). Behavioral data are summarized in Table 2.

**3.1.1 Reaction time**—There was no significant main effect of sex on RT ( $F_{(1,74)}$ ) = 0.39, p = .53,  $\eta^2 = 0.005$ ). We observed highly significant main effects of compatibility ( $F_{(1,74)}$ ) = 128.28, p < .001,  $\eta^2 = 0.63$ ) and spacing ( $F_{(1,74)}$  = 196.64, p < .001,  $\eta^2 = 0.73$ ). Compatible items were solved faster than incompatible items. Items with dense spacing were solved faster than items with sparse spacing. There was a significant interaction of compatibility\*spacing ( $F_{(1,74)} = 5.56$ , p = .02,  $\eta^2 = 0.07$ ). The compatibility effect was larger, when numbers were spaced closer together. All other interactions were non-significant (all F < 1).

**3.1.2** Accuracy—There was no significant main effect of sex on accuracy ( $F_{(1,74)} = 0.95$ , p = .33,  $\eta^2 = 0.01$ ). We observed highly significant main effects of compatibility ( $F_{(1,74)} = 94.57$ , p < .001,  $\eta^2 = 0.56$ ) and spacing ( $R_{(1,74)} = 7.76$ , p = .007,  $\eta^2 = 0.10$ ). Accuracy was higher for compatible than incompatible items and for sparse compared to dense spacing. There were no significant interactions (all *F*-values 2.26, all *p*-values 0.13).

# 3.2 Eye-tracking results

**3.2.1 Relative number of fixations**—Relative number of fixations refers to how often participants looked at unit or decade digits proportional to their reaction time, i.e. per second. To evaluate whether sex and compatibility affected how often participants looked at unit and decade digits, a  $2 \times 2 \times 2$  mixed ANOVA was performed with the within-subjects

factors 'digit' (unit vs. decade) and 'compatibility' (compatible vs. incompatible) and the between-subjects factor sex (men vs. women). The number of fixations per second is depicted in Fig. 1A.

We observed a significant main effect of sex on relative number of fixations ( $F_{(1,74)} = 5.11$ , p = .03,  $\eta^2 = 0.07$ ) with women looking more often at the digits than men. The main effects of compatibility and digit were not significant (both  $F_{(1,74)} < 0.27$ , both p > .63, both  $\eta^2 < 0.003$ ). There was a significant interaction between compatibility and digit ( $F_{f(1,74)}$ ) = 4.65, p = .03,  $\eta^2 = 0.06$ ). While for compatible items participants looked more often at units than decades, for incompatible items participants looked comparably often at decades and units. The interactions of compatibility\*sex and digit\*sex, as well as the 3-fold interaction of compatibility\*digit\*sex were non-significant (Fs < 1.2).

**3.2.2 Relative fixation duration**—Relative fixation duration refers to how long participants looked at unit or decade digits proportional to their reaction time (in percent). To evaluate whether sex and compatibility affected how long participants looked at unit and decade digits, a  $2 \times 2 \times 2$  mixed ANOVA was performed with the within-subjects factors 'digit' (unit vs. decade) and 'compatibility' (compatible vs. incompatible) and the between-subjects factor sex (men vs. women). Relative fixation durations are depicted in Fig. 1B.

We observed a significant main effect of sex on relative fixation duration ( $F_{(1,74)} = 5.89$ , p = .02,  $\eta^2 = 0.07$ ) with women looking longer at the digits than men. The main effect of compatibility was highly significant ( $F_{(1,74)} = 16.75$ , p < .001,  $\eta^2 = 0.19$ ), with shorter fixation durations for compatible items compared to incompatible items. The main effect of digit was non-significant ( $F_{(1,74)} = 0.17$ , p = .68,  $\eta^2 = 0.002$ ), suggesting that overall fixation duration was comparable for unit and decade digits. There was a significant interaction between compatibility and digit ( $F_{f(1,74)} = 7.04$ , p = .01,  $\eta^2 = 0.09$ ). While for compatible items participants spent a comparable amount of time looking at units and decades, for incompatible items participants looked longer at decades compared to units. Furthermore, there was a significant interaction between compatibility and sex ( $F_{(1,74)} = 5.46$ , p = .02,  $\eta^2 = 0.07$ )<sup>1</sup> with a larger compatibility effect on relative fixation durations in women compared to men. The interaction of digit\*sex as well as the 3-fold interaction of compatibility\*digit\*sex were non-significant (Fs < 1).

**3.2.3 Eye-movements (Relative number of saccades)**—To evaluate eyemovements, the pattern of saccades between digits was addressed. To that end, it was evaluated how often per second participants switched their gaze between unit and decade digit of the same number (switches within) and how often per second they switched their gaze between digits of different numbers (switches between). To evaluate whether sex, compatibility or spacing affected how often participants switched within or between numbers a  $2 \times 2 \times 2$ -ANOVA was performed with the within-subjects factors 'compatibility' (compatible vs. incompatible) and 'switches' (within vs. between) and the between-subjects factor sex (men vs. women). Saccades are depicted in Fig. 2.

There was no significant main effect of sex on saccades ( $F_{(1,74)} = 0.50$ , p = .48,  $\eta^2 = 0.007$ ). The main effects of compatibility ( $F_{(1,74)} = 43.64$ , p < .001,  $\eta^2 = 0.37$ ) and switches ( $F_{(1,74)}$ 

= 277.87, p < .001,  $\eta^2 = 0.79$ ) were highly significant with more saccades in compatible items than in incompatible items and between different numbers than within the same number. The interaction of switches\*sex was significant ( $F_{(1,74)} = 6.35$ , p = .01,  $\eta^2 = 0.08$ ). While women exhibited more saccades within the same number than men, men showed more saccades between different numbers than women. Furthermore, the interaction of compatibility\*switches was significant ( $F_{(1,74)} = 12.53$ , p = .001,  $\eta^2 = 0.15$ ). Saccades within the same number were comparable between compatible and incompatible items, while there were more saccades between different numbers in compatible than in incompatible items. The 2-fold interaction compatibili- ty\*sex ( $F_{(1,74)} = 0.90$ , p = .35,  $\eta^2 =$ 0.01) and the 3-fold interaction ( $F_{(1,74)} = 3.17$ , p = .08,  $\eta^2 = 0.04$ ) were non-significant.

# 3.3 Hormone results

In order to evaluate, whether sex hormones relate to performance, fixations or eye movements during the number comparison task, estradiol, progesterone and testosterone were standardized for each sex and entered as covariates in the ANOVAs described above. Since sex hormone levels differ substantially between men and women, standardization was performed separately for each sex, such that higher values represent higher values relative to the respective sex. That way, the association of sex hormones to performance, eye-movements and the compatibility effect therein, can be assessed independent of and in interaction with sex.

**3.3.1 Relationship of sex hormones to performance**—Neither reaction times nor accuracy were related to sex hormones and sex hormones did not interact with sex or compatibility in their relation to performance (all F = 2.12, all p = .15).

#### 3.3.2 Relationship of testosterone to relative number of fixations—

Testosterone was not significantly related to the relative number of fixations ( $F_{(1,71)} = 0.24$ , p = .63,  $\eta^2 = 0.003$ ), but showed a significant three-fold interaction with the compatibility effect and sex on relative number of fixations ( $F_{(1,71)} = 4.70$ , p = .03,  $\eta^2 = 0.06$ ; Fig. 3A). In women, the compatibility effect was significantly smaller, the higher their testosterone levels ( $r_{75}$ ) = -0.36, p = .03), while in men a nonsignificant association was observed ( $r_{(38)} = 0.11$ , p = .50). Testosterone did not interact with digit or sex and no higher order interactions were observed (all  $F_{2.93}$ , all  $p_{-.09}$ ).

**3.3.3 Relationship of testosterone to relative fixation durations**—Testosterone was not significantly related to relative fixation durations ( $F_{(1,71)} = 0.51$ , p = .48,  $\eta^2 = 0.007$ ), but a trend interaction with the compatibility effect on relative fixation durations was observed ( $F_{(1,71)} = 3.68$ , p = .06,  $\eta^2 = 0.05$ , Fig. 3B). The compatibility effect was significantly smaller, the higher participants testosterone levels ( $r_{(75)} = -0.31$ , p = .007). This relationship was significant in women (r = -0.37, p = .03), but not in men (r = -0.07, p = .69).

**3.3.4 Relationship of estradiol to relative number of fixations**—Estradiol showed no significant relationship to the relative number of fixations across groups ( $F_{(1,70)} = 1.83$ , p = .18,  $\eta^2 = 0.03$ ), but a significant interaction with sex was observed ( $F_{(1,70)} =$ 

4.69, p = .03,  $\eta^2 = 0.06$ ; Fig. 4A). In men, the relative number of fixations was significantly lower the higher their estradiol levels ( $r_{(37)} = -0.42$ , p = .01),<sup>2</sup> while in women a non-significant association was observed ( $r_{(37)} = 0.09$ , p = .59). No other interactions with estradiol were observed (all *F* 0.80, all *p* .37).

#### 3.3.5 Relationship of progesterone to relative number of fixations—

**3.3.6 Relationship of estradiol to relative fixation duration**—Estradiol showed no significant relationship to relative fixation durations across groups ( $F_{(1,70)} = 1.89$ , p = .17,  $\eta^2 = 0.03$ ), but a significant interaction with sex was observed ( $F_{(1,70)} = 6.93$ , p = .01,  $\eta^2 = 0.09$ ; Fig. 4C). In men, relative fixation duration was significantly lower the higher their estradiol levels ( $r_{(37)} = -0.44$ , p = .007),<sup>3</sup> while in women a non-significant positive association was observed ( $r_{(37)} = 0.15$ , p = .39). No other interactions were observed (all  $F_{(0.75, all p)}$ .

**3.3.7 Relationship of progesterone to relative fixation durations**—Progesterone showed no significant relationship to relative fixation durations ( $F_{(1,70)} = 2.02$ , p = .16,  $\eta^2 = 0.03$ ), but showed a significant interaction with sex ( $F_{(1,70)} = 5.70$ , p = .02,  $\eta^2 = 0.08$ ; Fig. 4D). In men, relative fixation duration was significantly lower the higher their progesterone levels ( $r_{(38)} = -0.42$ , p = .008),<sup>4</sup> while in women a nonsignificant positive association was observed ( $r_{(36)} = 0.11$ , p = .51). Progesterone did not interact with digit or compatibility and no higher order interactions were observed (all F = 1.42, all p = .23).

**3.3.8 Relationship of sex hormones to saccades**—Neither estradiol, nor progesterone, nor testosterone showed a significant relationship to saccades and there were no significant interactions between experimental factors and sex hormones (all F < 3.85, all p > .05), with the exception of a significant 3-fold interaction of switches\*sex\*estradiol ( $F_{(1,70)} = 7.46$ , p = .008,  $\eta^2 = 0.10$ ). Bivariate correlations revealed that this interaction resulted from the fact that in men, there was a negative correlation between estradiol and the number of saccades within the numbers ( $r_{(37)} = -0.39$ , p = .02), but a non-significant positive association to saccades between the numbers ( $\Gamma_{(37)} = 0.27$ , p = .11), while the opposite pattern was observed in women (within:  $r_{(37)} = 0.17$ , p = .31, between:  $r_{(37)} = -0.31$ , p = .06; compare Fig. 5).

<sup>&</sup>lt;sup>4</sup>This result remained significant, even if all progesterone values exceeding the group mean by more than 2 SD were excluded. Men showed a significant negative association between progesterone and relative fixation duration (r = -.36, p = .04), while no significant association was observed in women (r = .11, p = .51).

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# 4 Discussion

The aim of the present study was to examine the effects of sex and sex hormones on eye movement behavior in the number comparison task. The behavioral compatibility effect (faster reactions to compatible compared to incompatible items) is often used as a measure of a decomposed processing style during number processing. It has previously been demonstrated that women show a larger compatibility effect than men, indicating a more decomposed processing style in women than in men. Therefore, it was hypothesized that women show longer fixation durations on individual digits, specifically longer fixations on unit digits than men. Furthermore, it was assumed that saccades in men, who supposedly show a more holistic processing style, would be more frequent between digits of the same numbers. Vice versa, saccades in women were assumed to be more frequent between digits of different numbers. Furthermore, the relationship of sex hormones to these measures was explored. Specifically, we hypothesized that higher progesterone and lower testosterone levels would relate to a longer fixation duration on individual digits, explaining the sex differences in fixation durations.

First of all, it is noteworthy, that unlike previous studies [21,29,44,50], we found no evidence for sex differences in the behavioral compatibility effect in the current study. Likewise, no sex differences were observed in the compatibility effect in the hemifield number comparison task employed in the first part of this study on the same sample [51]. There are two explanations for this finding. On the one hand, there seems to be a ceiling effect in performance, since accuracy is high and reactions are quite fast in both men and women. On the other hand, sex differences in the behavioral compatibility effect seem to be of moderate effect size and may thus only be observed consistently in very large samples [29] or under difficult conditions like in an MRI environment [44].

Nevertheless, women show more fixations and longer relative fixation durations on digits, and a stronger compatibility effect in relative fixation durations than men. This is in line with our hypothesis and the assumption of a more decomposed processing style in women. Longer fixation durations in women have also been reported for other stimulus materials [1,37], supporting the assumption that women take in their visual environment in more detail than men. However, the stronger compatibility effect in fixation durations in women was mostly attributable to decade digits rather than unit digits, which is contrary to our expectation and previous results by Moeller et al. [35]. Unlike Moeller et al. [35] we found more fixations on unit digits in compatible items and longer fixations for decade digits in incompatible items. There are some methodological differences between our study and the study by Moeller et al. [35], which may contribute to the different findings. First, the study by Moeller et al. [35] included only ten participants and did not differentiate between male and female participants. Second, even though the average number of fixations was also low in the study by Moeller et al. [35], it was still higher than in the present study. This may be due to the fact that they did not restrict the presentation time of numbers to a maximum of three seconds, allowing participants to react more slowly and take a closer look at numbers. There is no information on fixation durations in eye fixation behavior in the study by Moeller et al. [35]. Even if the number of fixations on units was larger, they may still have been shorter than fixations on decades. A possible explanation for longer fixations on

decades in incompatible trials may be a compensation mechanism. Participants become aware of the interference between decade and unit information, they know that the decades provide the correct answer and thus deliberately focus on decade digits to solve the trial. This is in line with the overall high accuracy, even on incompatible items.

Furthermore, contrary to our hypothesis, men show more saccades between digits of different numbers, while women show more saccades between digits of the same number. This may be attributable to the same compensation mechanism as women's longer fixations on decades. Saccades within the same number may serve the purpose to resolve the conflict arising from unit and decade information. Likewise, in combination with short fixation durations, saccades between the different numbers may actually serve holistic processing. In that case, men's evenovement behavior suggests that less time is spent on processing the magnitudes of individual digits (short fixation durations on digits), while more time is spent comparing the approximate magnitudes of the whole numbers (more saccades between numbers). However, it is also possible that in fact men do show less holistic processing during number comparison than women. Based on the fact that the compatibility effect relates to global-local processing only in women, we recently argued, that the compatibility effect may represent different cognitive mechanisms in men and women [47]. While the compatibility effect appears to reflect the likelihood of using decomposed over holistic number representations during number comparison in women, it is possible that in men it reflects the likelihood of using unit representations in addition to decade representations without referring to holistic number representations at all. If that is the case, it makes sense that men would spend more time comparing individual differences between numbers rather than within numbers. The assumption that the compatibility effect reflects different mechanisms in men and women, may also explain, why all hormones were differentially related to the number of fixations, relative fixation durations, and estradiol also to saccades, in men and women.

First, testosterone was negatively related to the compatibility effect in the number of fixations and fixation durations. This is in line with our assumptions and previous studies demonstrating that higher testosterone levels relate to a stronger focus on global rather than local aspects of hierarchical stimuli ([45]; Scheuringer & Pletzer, 2017). However this association was observed in women only, which at first sight questions the assumption that men spend less time looking at individual digits in incompatible items due to their higher testosterone levels. One possibility is that testosterone modulates the compatibility effect in fixations only in the lower range, while a ceiling effect is reached in the higher range. This is in line with an increasing literature suggesting that the effects of sex hormones are dose-dependent (e.g. [5,19,28]) and accordingly non-linear (e.g. [36]), often resulting in different associations in men and women (e.g. [8,18]). As an example, a positive association of testosterone to spatial abilities is often only observed in women [8,18], while in men even negative associations have been observed [18,33,63,65].

Second, estradiol was related to fixation durations and eye-movements in men but not in women. In men, higher estradiol levels were related to fewer fixations, shorter fixation durations and fewer saccades between digits of the same number. Instead men with higher estradiol levels showed more saccades between the two different numbers. In sum, estradiol,

but also progesterone, seems to increase the eyemovement pattern observed for men on average. Please note that the association to progesterone was not simply due to a high interrelation between estradiol and progesterone levels in men, as it survived controlling for estradiol via partial correlations. Given the discussion of sex differences in eye-movement patterns above, this may suggest a more holistic processing strategy in men with higher estradiol levels. It may however also suggest that men with higher estradiol levels are less likely to form holistic magnitude representations and thus spend more time comparing the individual digits. The fact that men with higher estradiol levels show more male-typical eyemovement patterns may be explained by the fact that estradiol is a metabolite of testosterone. Accordingly, some testosterone actions are transmitted via estradiol receptors and it has been suggested that some male-typical behaviors are in fact supported by estradiol (e.g. [56]).

However, a multitude of biological mechanisms may contribute to the fact that sex hormones relate differentially to behavioral, neuronal and eye-movement patterns in men and women. First, sex hormone receptors are expressed at different levels between men and women, which may contribute to differential sensitivity for certain hormones and explain the dosedependent effects observed in various studies. Second, a variety of sex differences exist between neurotransmitter systems (e.g. [10,12,66]), which are sensitive to modulation by sex hormones [3]. Given these differences in the neurophysiology of men and women, it cannot be expected that sex hormones show the same effects in men and women. Third, sex hormones are produced in different locations for men and women (e.g. [7]), assigning them differential functionality. Our results also show that we cannot reduce the role of estradiol and progesterone to making someone more "femalelike" and the role of testosterone to making someone more "male-like", since the associations to estradiol and progesterone obviously go in the opposite direction. It is however possible, that we find a modulation by estradiol and progesterone in men and a modulation by testosterone in women, due to differential functionality of these hormones. The fact that estradiol and progesterone are not the primary reproductive hormones in men, may allow them to assume other functions, while the opposite may be the case for testosterone in women.

Importantly, it can be pointed out, that we observed no relationship of sex hormones to overall reaction times or accuracy or the overall behavioral compatibility effect. Rather sex hormones relate to eyemovements during number processing, which were assessed to capture basic visual attentional processes during number processing. It can thus be speculated that sex hormones relate to number processing via at- tentional mechanisms, i.e. by modulating what participants focus on, either by affecting bottom-up mechanisms in the visual system or by affecting top-down mechanisms of attentional control in the brain.

In summary, this is the first study to demonstrate sex differences in eye gaze behavior during number comparison and the first study to show a relationship of sex hormones to eye movement behavior in cognitive tasks. Accordingly, this study adds to the growing evidence that sex differences and sex hormone influences in visual attention contribute to sex differences and sex hormone influences in cognition.

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# References

- Andersen NE, Dahmani L, Konishi K, Bohbot VD. Eye tracking, strategies, and sex differences in virtual nagivation. Neurobiol Learn Mem. 2012; 97:81–89. [PubMed: 22001012]
- [2]. Andreano JM, Cahill L. Sex influences on the neurobiology of learning and memory. Learning & memory. 2009; 16(4):248–266. [PubMed: 19318467]
- [3]. Barth C, Villringer A, Sacher J. Sex hormones affect neurotransmitters and shape the adult female brain during hormonal transition periods. Front Neurosci. 2015; 9:37. [PubMed: 25750611]
- [4]. Basso MR, Lowery N. Global-Local Visual Biases Correspond With Visual-Spatial Orientation. J Clin Exp Neuropsychol. 2004; 26:24–30. [PubMed: 14972691]
- [5]. Bhasin S, Woodhouse L, Casaburi R, Singh AB, Bhasin D, Berman N, Dzekov J. Testosterone dose-response relationships in healthy young men. American Journal of Physiology-Endocrinology and Metabolism. 2001; 281(6):E1172–E1181. DOI: 10.1152/ ajpendo.2001.281.6.E1172 [PubMed: 11701431]
- [6]. Bull R, Cleland AA, Mitchell T. Sex differences in the spatial representation of number. J Exp Psychol Gen. 2013; 142:181. [PubMed: 22545947]
- [7]. Burger HG. Androgen production in women. Fertil Steril. 2002; 77(4):3–5. DOI: 10.1016/ s0015-0282(02)02985-0
- [8]. Burkitt J, Widman D, Saucier DM. Evidence for the influence of testosterone in the performance of spatial navigation in a virtual water maze in women but not in men. Horm Behav. 2007; 51:649–654. DOI: 10.1016/j.yhbeh.2007.03.007 [PubMed: 17462646]
- [9]. Courvoisier DS, Renaud O, Geiser C, Paschke K, Gaudy K, Jordan K. Sex hormones and mental rotation: an intensive longitudinal investigation. Horm Behav. 2013; 63(2):345–351. DOI: 10.1016/j.yhbeh.2012.12.007 [PubMed: 23261859]
- [10]. Cosgrove KP, Mazure CM, Staley JK. Evolving knowledge of sex differences in brain structure, function, and chemistry. Biol Psychiatry. 2007; 62(8):847–855. [PubMed: 17544382]
- [11]. Craig MC, Fletcher PC, Daly EM, Rymer J, Brammer M, Giampietro V, Murphy DG. Physiological variation in estradiol and brain function: a functional magnetic resonance imaging study of verbal memory across the follicular phase of the menstrual cycle. Horm Behav. 2008; 53(4):503–508. [PubMed: 18279872]
- [12]. De Vries GJ. Sex differences in neurotransmitter systems. J Neuroendocrinol. 1990; 2(1):1–13.[PubMed: 19210390]
- [13]. Driscoll I, Hamilton DA, Yeo RA, Brooks WM, Sutherland RJ. Virtual navigation in humans: the impact of age, sex, and hormones on place learning. Horm Behav. 2005; 47:326–335. DOI: 10.1016/j.yhbeh.2004.11.013 [PubMed: 15708762]
- [14]. Dehaene S, Dupoux E, Mehler J. Is numerical comparison digital? Analogical and symbolic effects in two-digit number comparison. J Exp Psychol Hum Percept Perform. 1990; 16:626–641.
  [PubMed: 2144576]
- [15]. Dehaene S, Piazza M, Pinel P, Cohen L. Three parietal circuits for number processing. Cognitive neuropsychology. 2003; 20(3-6):487–506. [PubMed: 20957581]
- [16]. Duncan GJ, Dowsett CJ, Claessens A, Magnuson K, Huston AC, Klebanov P, Pagani LS, Feinstein L, Engel M, Brooks-Gunn J, Sexton H, et al. School readiness and later achievement. Developmental Psychology. 2007; 43(6):1428–1446. DOI: 10.1037/0012-1649.43.6.1428 [PubMed: 18020822]
- [17]. Falter CM, Arroyo M, Davis GJ. Testosterone: activation or organization of spatial cognition? Biol Psychol. 2006; 73:132–140. DOI: 10.1016/j.biopsycho.2006.01.011 [PubMed: 16490297]
- [18]. Gouchie C, Kimura D. The relationship between testosterone levels and cognitive ability patterns. Psychoneuroendocrinology. 1991; 16:323–334. DOI: 10.1016/0306-4530(91)90018-O [PubMed: 1745699]

- [19]. Gray PB, Singh AB, Woodhouse LJ, Storer TW, Casaburi R, Dzekov J, Bhasin S. Dosedependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. The Journal of Clinical Endocrinology & Metabolism. 2005; 90(7):3838–3846. [PubMed: 15827094]
- [20]. Halari R, Hines M, Kumari V, Mehrotra R, Wheeler M, Ng V, Sharma T. Sex differences and individual differences in cognitive performance and their relationship to endogenous gonadal hormones and gonadotropins. Behavioral neuroscience. 2005; 119(1):104. [PubMed: 15727517]
- [21]. Harris T, Scheuringer A, Pletzer B. Sex differences and functional hemispheric asymmetries during number comparison. Biology for Sex Differences. 2018; 9:3. doi: 10.1186/ s13293-017-0162-6
- [22]. Hausmann M, Schoofs D, Rosenthal HE, Jordan K. Interactive effects of sex hormones and gender stereotypes on cognitive sex differences - a psychobiosocial approach.
  Psychoneuroendocrinology. 2009; 34:389–401. DOI: 10.1016/j.psyneuen.2008.09.019 [PubMed: 18992993]
- [23]. Heinze, HJ, Johannes, S, Münte, TF, Mangun, GR. The order of global-and locallevel information processing: electrophysiological evidence for parallel perceptual processes. Cognitive Electrophysiology, Birkhäuser; Boston, MA: 1994. 102–123.
- [24]. Heinze HJ, Hinrichs H, Scholz M, Burchert W, Mangun GR. Neural mechanisms of global and local processing: a combined PET and ERP study. J Cognitive Neurosci. 1998; 10:485–498.
- [25]. Hinrichs JV, Yurko DS, Hu J. Two-digit number comparison: use of place information. J Exp Psychol Hum Percept Perform. 1981; 7(4):890–901.
- [26]. Hooven C, Chabris KFC, Ellison PT, Kosslyn SM. The relationship of male testosterone to components of mental rotation. Neuropsychologia. 2004; 42:782–790. DOI: 10.1016/ j.neuropsychologia.2003.11.012 [PubMed: 15037056]
- [27]. Hubbard EM, Piazza M, Pinel P, Dehaene S. Interactions between number and space in parietal cortex. Nat Rev Neurosci. 2005; 6(6):435. [PubMed: 15928716]
- [28]. Huang G, Wharton W, Travison TG, Ho MH, Gleason C, Asthana S, Basaria S. Effects of testosterone administration on cognitive function in hysterectomized women with low testosterone levels: a dose–response randomized trial. J Endocrinol Invest. 2015; 38(4):455–461. [PubMed: 25430996]
- [29]. Huber S, Nuerk H-C, Reips U-D, Soltanlou M. Individual differences influence two-digit number processing, but not their analog magnitude processing: a large-scale online study. Psychol Res. 2017; :1–21. DOI: 10.1007/s00426-017-0964-5 [PubMed: 26586290]
- [30]. Jordan K, Wüstenberg T, Heinze HJ, Peters M, Jäncke L. Women and men exhibit different cortical activation patterns during mental rotation tasks. Neuropsychologia. 2002; 40(13):2397– 2408. [PubMed: 12417468]
- [31]. Keller K, Menon V. Gender differences in the functional and structural neuroanatomy of mathematical cognition. NeuroimageNeuroimage. 2009; 47:342–352.
- [32]. Kimura D. Sex hormones influence human cognitive pattern. Neuroendocrinology Letters. 2002; 23(4):67–77.
- [33]. Martin DM, Wittert G, Burns NR, McPherson J. Endogenous testosterone levels, mental rotation performance, and constituent abilities in middle-to-older aged men. Horm Behav. 2008; 53:431– 441. DOI: 10.1016/j.yhbeh.2007.11.012 [PubMed: 18190916]
- [34]. McGivern RF, Huston JP, Byrd D, King T, Siegle GJ, Reilly J. Sex differences in visual recognition memory: support for a sex-related difference in attention in adults and children. Brain Cogn. 1997; 34(3):323–336. [PubMed: 9292185]
- [35]. Moeller K, Fischer MH, Nuerk H-C, Willmes K. Sequential or parallel decomposed processing of two-digit numbers? Evidence from eye-tracking. Q J Exp Psychol. 2009; 62(2):323–334.
- [36]. Moffat SD, Hampson E. A curvilinear relationship between testosterone and spatial cognition in humans: possible influence of hand preference. Psychoneuroendocrinology. 1996; 21:323–337. DOI: 10.1016/0306-4530(95)00051-8 [PubMed: 8817730]
- [37]. Mueller SC, Jackson CPT, Skelton RW. Sex differences in a virtual water maze: an eye tracking and pupillometry study. Behav Brain Res. 2008; 193(2):209–215. [PubMed: 18602173]

- [38]. Navon D. Forest before trees: The precedence of global features in visual perception. Cognitive psychology. 1977; 9(3):353–383.
- [39]. Nuerk H-C, Weger U, Willmes K. Decade breaks in the mental number line? Putting the tens and units back in different bins. CognitionCognition. 2001; 82:B25–B33.
- [40]. Nuerk H-C, Weger U, Willmes K. On the perceptual generality of the unit-decade-compatibility effect. Exp Psychol. 2004; 51:72–79. DOI: 10.1027/1618-3169.51.1.72 [PubMed: 14959508]
- [41]. Nuerk H-C, Willmes K. On the magnitude presentation of two-digit numbers. Psychology Science. 2005; 47(1):52–72.
- [42]. Pletzer B. Sex-specific strategy use and global-local processing: a perspective toward integrating sex differences in cognition. Front Neurosci. 2014; 8:245. doi: 10.3389/fnins.2014.00425
  [PubMed: 25157217]
- [43]. Pletzer B. Sex differences in number processing: differential systems for subtraction and multiplication were confirmed in men, but not in women. Sci Rep. 2016; 6:39064. doi: 10.1038/ srep39064 [PubMed: 27966612]
- [44]. Pletzer B, Kronbichler M, Nuerk H-C, Kerschbaum H. Sex-Differences in the Processing of Global vs. Local Stimulus Aspects of Two-Digit Number Comparison Task - An fMRI Study. Plos One. 2013; 8(1) e53824 [PubMed: 23335976]
- [45]. Pletzer B, Petasis O, Cahill L. Switching between forest and trees: opposite relationship of progesterone and testosterone to global-local processing. Horm Behav. 2014; 66:257–266.
  [PubMed: 24874173]
- [46]. Pletzer B, Scheuringer A, Harris T. Spacing and Presentation Modes Affect the Unit-Decade Compatibility Effect During Number Comparison. Exp Psychol. 2016; 63(3):189–195. [PubMed: 27404987]
- [47]. Pletzer B, Scheuringer A, Harris T, Scherndl T. The missing link: Global-local processing relates to number-magnitude processing in women. Journal of Experimental Psychology: General.
- [48]. Pletzer B, Scheuringer A, Scherndl T. Global-local processing relates to spatial and verbal processing: implications in sex differences in cognition. Sci Rep. 2017; 7 doi: 10.1038/ s41598-017-11013-6
- [49]. Pletzer B, Harris T. Sex hormones modulate the relationship between global advantage, lateralization, and interhemispheric connectivity in a navon paradigm. Brain Connect. 2018; 8(2):106–118. [PubMed: 29226703]
- [50]. Pletzer B, Harris T, Scheuringer A. Sex Differences in Number Magnitude Processing Strategies Are Mediated by Spatial Navigation Strategies: evidence From the Unit-Decade Compatibility Effect. Front Psychol. 2019; 10:229. doi: 10.3389/fpsyg.2019.00229 [PubMed: 30809169]
- [51]. Pletzer B, Jäger S, Hawelka S. Sex hormones and number processing. Progesterone and testosterone relate to hemispheric asymmetries during number comparison. Horm Behav. 2019; 115 104553 [PubMed: 31279702]
- [52]. Puts DA, Cárdenas RA, Bailey DH, Burriss RP, Jordan CL, Breedlove SM. Salivary testosterone does not predict mental rotation performance in men or women. Horm Behav. 2010; 58(2):282– 289. DOI: 10.1016/j.yhbeh.2010.03.005 [PubMed: 20226788]
- [53]. Raven, JC, Raven, JC, Court, John Hugh. Advanced progressive matrices. HK Lewis; London: 1962.
- [54]. Razumnikova OM, Vol'f NV. Selection of visual hierarchical stimuli between global and local aspects in men and women. J Physiol. 2011; 37:14–19.
- [55]. Roalf D, Lowery N, Turetsky BI. Behavioral and physiological findings of gender differences in global-local visual processing. Brain Cog. 2006; 60:32–42.
- [56]. Russell N, Grossman M. Estradiol as a male hormone. Eur J Endocrinol. 2019; 181:R23–R43.[PubMed: 31096185]
- [57]. Scheuringer A, Pletzer B. Sex differences in the Kimchi-Palmer task revisited: global reaction times, but not number of global choices differ between adult men and women. Physiol Beh. 2016; 165:159–165.
- [58]. Schultheiss OC, Dlugash G, Mehta PH, Schultheiss OC, Dlugash G, Mehta PH, Mehta PH. Hormone measurement in social neuroendocrinology: a comparison of immunoassay and mass spectrometry methods.

- [59]. Shultz SJ, Sander TC, Kirk SE, Perrin DH. Sex differences in knee joint laxity change across the female menstrual cycle. The Journal of sports medicine and physical fitness. 2005; 45(4):594– 603. [PubMed: 16446695]
- [60]. Steiner M, Macdougall M, Brown E. The premenstrual symptoms screening tool (PSST) for clinicians. Archives of Women's Mental Health. 2003; 6(3):203–209.
- [61]. Sundström Poromaa I, Gingnell M. Menstrual cycle influence on cognitive function and emotion processing—From a reproductive perspective. Front Neurosci. 2014; 8:380. [PubMed: 25505380]
- [62]. Verguts T, De Moor W. Two-digit Comparison Decomposed, Holistic, or Hybrid? Experimental Psychology. 2005; 52(3):195–200. [PubMed: 16076067]
- [63]. Vuoksimaa E, Kaprio J, Eriksson CJP, Rose RJ. Pubertal testosterone predicts mental rotation performance of young adult males. Psychoneuroendocrinology. 2012; 37:1791–1800. DOI: 10.1016/j.psyneuen.2012.03.013 [PubMed: 22520299]
- [64]. Wolf OT, Kudielka BM, Hellhammer DH, Törber S, McEwen BS, Kirschbaum C. Two weeks of transdermal estradiol treatment in postmenopausal elderly women and its effect on memory and mood: verbal memory changes are associated with the treatment induced estradiol levels. Psychoneuroendocrinology. 1999; 24(7):727–741. [PubMed: 10451908]
- [65]. Yonker JE, Eriksson E, Nilsson LG, Herlitz A. Negative association of testosterone on spatial visualization in 35 to 80 year old men. Cortex. 2006; 3:376–386. DOI: 10.1016/ s0010-9452(08)70364-2
- [66]. Young, EA, Korszun, A, Altemus, M. Sex differences in neuroendocrine and neurotransmitter systemsWomen's Mental Health, A Comprehensive Textbook. Guilford Press; New York: 2002. 3–30.
- [67]. Zimmerman ME, Lipton RB, Santoro N, McConnell DS, Derby CA, Katz MJ, Saunders-Pullman R. Endogenous estradiol is associated with verbal memory in nondemented older men. Brain Cogn. 2011; 76(1):158–165. [PubMed: 21354686]



#### Fig. 1.

Number of fixations per second (A) and relative fixation duration (in% reaction times, B) for unit and decade digits in men and women. Women looked more often and longer at any digits than men, particularly at decade digits in incompatible items. Error bars represent standard errors. RT = reaction times.



#### Fig. 2.

Number of saccades within and between numbers per second. There were more saccades between than within numbers. Men showed more saccades between numbers, women more saccades within numbers. Error bars represent standard errors.

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# Fig. 3.

Relationship of testosterone to the compatibility effect in the number of fixations per second (A) and relative fixation durations (B). The higher the testosterone levels, the lower was the compatibility effect in the number of fixations and relative fixation durations, in women, but not men. The compatibility effect was calculated by subtracting relative fixation durations for compatible items from relative fixation durations for incompatible items.

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# Fig. 4. Relationship of estradiol and progesterone to number of fixations per second and relative fixation durations in men and women.

In men, estradiol and progesterone were negatively related to number of fixations and relative fixation duration. The higher estradiol and progesterone levels, the less and the shorter did men look at numbers. In women, a non-significant positive association was observed. Note that all hormone outliers, exceeding the group mean by more than two standard deviations, were removed from the figure for illustrative purposes.

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# Fig. 5. Relationship of estradiol to saccades in men and women.

In men, estradiol was negatively related to saccades within numbers, but positively to saccades between numbers. In women, non-significant associations were observed. The higher estradiol levels, the less did men switch their gaze between digits of the same number and the more they switched between the two different numbers. Note that all estradiol outliers, exceeding the group mean by more than two standard deviations, were removed from the figure for illustrative purposes.

					Table 1
mean hormone	values	in	men	and	women

	Men Mean	SD	Women Mean	SD
Estradiol [pg/ml]	4.06	1.13	4.48	2.14
Progesterone [pg/ml]	86.65 ***	63.28	220.17	100.72
Testosterone [pg/ml]	120.82 ***	29.78	59.19	19.51

\*\*\* significantly different from women *p* < .001

	Table 2			
Reaction time and accuracy	y for each categ	ory in men and women		

	Reaction times compatible	incompatible	Compatibility effect	Accuracy compatible	Incomp.	Comp. effect
dense	$667.07 \pm 174.72$	$720.14\pm202.84$	$53.07\pm57.65$	$.99\pm0.02$	$.96 \pm 0.04$	$.04\pm0.04$
sparse	$714.89 \pm 204.95$	$745.94 \pm 185.94$	$31.05\pm37.12$	$.99\pm0.01$	$.97\pm0.03$	$.03\pm0.03$
dense	$690.04 \pm 110.60$	$744.01 \pm 113.35$	$53.98 \pm 45.43$	$.99\pm0.02$	$.95\pm0.04$	$.04\pm0.04$
sparse	$730.86 \pm 122.76$	$774.37 \pm 115.67$	$43.51\pm41.18$	$1.00\pm0.01$	$.96\pm0.04$	$.04\pm0.04$
	dense sparse dense sparse	Reaction times compatible       dense     667.07 ± 174.72       sparse     714.89 ± 204.95       dense     690.04 ± 110.60       sparse     730.86 ± 122.76	Reaction times compatible     incompatible       dense     667.07 ± 174.72     720.14 ± 202.84       sparse     714.89 ± 204.95     745.94 ± 185.94       dense     690.04 ± 110.60     744.01 ± 113.35       sparse     730.86 ± 122.76     774.37 ± 115.67	Reaction times compatible     incompatible     Compatibility effect       dense     667.07 ± 174.72     720.14 ± 202.84     53.07 ± 57.65       sparse     714.89 ± 204.95     745.94 ± 185.94     31.05 ± 37.12       dense     690.04 ± 110.60     744.01 ± 113.35     53.98 ± 45.43       sparse     730.86 ± 122.76     774.37 ± 115.67     43.51 ± 41.18	Reaction times compatible     incompatible     Compatibility effect     Accuracy compatible       dense     667.07 ± 174.72     720.14 ± 202.84     53.07 ± 57.65     .99 ± 0.02       sparse     714.89 ± 204.95     745.94 ± 185.94     31.05 ± 37.12     .99 ± 0.01       dense     690.04 ± 110.60     744.01 ± 113.35     53.98 ± 45.43     .99 ± 0.02       sparse     730.86 ± 122.76     774.37 ± 115.67     43.51 ± 41.18     1.00 ± 0.01	Reaction times compatible     incompatible     Compatiblity effect     Accuracy compatible     Incomp.       dense     667.07 ± 174.72     720.14 ± 202.84     53.07 ± 57.65     .99 ± 0.02     .96 ± 0.04       sparse     714.89 ± 204.95     745.94 ± 185.94     31.05 ± 37.12     .99 ± 0.01     .97 ± 0.03       dense     690.04 ± 110.60     744.01 ± 113.35     53.98 ± 45.43     .99 ± 0.02     .95 ± 0.04       sparse     730.86 ± 122.76     774.37 ± 115.67     43.51 ± 41.18     1.00 ± 0.01     .96 ± 0.04