1. Introduction

Pregnancy-related declines in executive functions, including working memory and attention, are regularly reported anecdotally and have also been documented in controlled experiments (Brett and Baxendale, 2001; Brindle et al., 1991; Crawley et al., 2008; Crawley et al., 2003; Crawley, 2002; Davies et al., 2018; De Groot et al., 2003; Farrar et al., 2014; Galen Buckwalter et al., 1999; Henry and Sherwin, 2012; Raz, 2014; Sharp et al., 1993). This phenomenon became known as “pregnancy brain” or “baby brain”. Selective attention, where the focus is on a distinct, relevant goal at the expense of surrounding, irrelevant stimuli (Gazzaley and Nobre, 2012), is a vital component of the executive functions and seems to be critically impaired in pregnant women (De Groot et al., 2003). In everyday life, this form of attention is used to navigate through complex environments, such as finding a tourist attraction, a distinct store in a shopping mall, or a spelling error in a text. Visuo-spatial attention tasks, where a cue directs spatial attention in a distinct direction and is followed by a target presentation, are regularly used to analyse the neural components underlying the alignment of stimulus–response processing with internal goals (Sauseng et al., 2005; Sauseng et al., 2011). This task reveals a temporal sequence of distinct neural states, like neural activity while expecting a target (endogenous expectations) with neural activity following target presentation (stimulus–response processing). Specifically, in preparation of a jittered, predictive cue, the brain is in a state of general alertness. Increased vigilance to an expected stimulus and its preparation to perceive a predictable enhancement in alpha desynchronisation in a fronto-parietal network might modulate accuracy during a visuo-spatial attention task.
enhanced perceptual performance (Gazzaley and Nobre, 2012). Using cue-dependent bilateral presentation of stimuli also shows induced hemispheric oscillatory cortical activity differences related to visual hemifield in which the stimulus is expected (Kelly et al., 2006).

Selective attention can be seen as an enhancement of relevant and suppression of irrelevant information along the visual pathway (Carrasco, 2018; Gazzaley and Nobre, 2012). A prominent theory on top-down driven control of sensory processing during attentional processing includes long-range alpha desynchronization in a fronto-parietal network (Capotosto et al., 2009; Klimesch et al., 2007; Marek and Dosenbach, 2018; Sauseng et al., 2011). Alpha oscillations (~8–12 Hz) are functionally inhibitory (Bonfond and Jensen, 2012; Jensen and Mazaheri, 2010; Klimesch et al., 2007). Occasionally, lower frequencies starting at 6 Hz are included in studying attention (Klimesch et al., 1998). While an increase in alpha synchronisation indicates an increase in functional inhibition required for suppression of irrelevant information, a decrease in alpha synchronisation indicates relief of inhibition and indicates processing of relevant information (Klimesch et al., 2007).

Accordingly, cortical areas activated by task-irrelevant stimuli show an increase in alpha synchronisation (Klimesch, 2012), like stronger alpha power in the parieto-occipital sulcus when subjects are informed to remember face identity (ventral stream) but not face orientation (dorsal stream) in a “Delayed-match-to-sample task” (Jokisch and Jensen, 2007). Regarding spatial cuing, it has been demonstrated that alpha synchronisation occurs in the contralateral hemisphere of the to-be-ignored visual hemifield (i.e., ipsilateral to the cued direction of attention) and represents an active attentional inhibition mechanism (Bonacci et al., 2020; Deng et al., 2020; Kelly et al., 2006; Sauseng et al., 2009; Schuhmann et al., 2019; Worden et al., 2000). Critical in the interpretation of the impact of alpha oscillations on attention is the temporal sequence of pre- and post-stimulus alpha power. A post-stimulus decrease in alpha power compared to the pre-stimulus power is called an event-related desynchronisation (ERD), while an increase is referred to as an event-related synchronisation (ERS) (Klimesch, 2012). In the EEG-literature, an “event” is not restricted to the presentation of a target, but also includes the presentation of a cue. Previous research suggests that the “anticipatory alpha ERD” (~8–12 Hz) observed during the pre-stimulus period in various cognitive tasks is a marker of the neural mechanisms that contribute to the development of temporal expectations (Capotosto et al., 2009; Klimesch et al., 1998; Rohenkohl and Nobre, 2011; Spadone et al., 2020).

While alpha activity has been mainly investigated in posterior brain areas, in the last decade a fronto-parietal network has gained attention. Importantly, visuo-spatial attention tasks are known to activate a fronto-parietal network (Capotosto et al., 2009; Klimesch et al., 2007; Marek and Dosenbach, 2018; Sauseng et al., 2011). Alpha oscillations (~8–12 Hz) are functionally inhibitory (Bonfond and Jensen, 2012; Jensen and Mazaheri, 2010; Klimesch et al., 2007). Occasionally, lower frequencies starting at 6 Hz are included in studying attention (Klimesch et al., 1998). While an increase in alpha synchronisation indicates an increase in functional inhibition required for suppression of irrelevant information, a decrease in alpha synchronisation indicates relief of inhibition and indicates processing of relevant information (Klimesch et al., 2007).

Accordingly, cortical areas activated by task-irrelevant stimuli show an increase in alpha synchronisation (Klimesch, 2012), like stronger alpha power in the parieto-occipital sulcus when subjects are informed to remember face identity (ventral stream) but not face orientation (dorsal stream) in a “Delayed-match-to-sample task” (Jokisch and Jensen, 2007). Regarding spatial cuing, it has been demonstrated that alpha synchronisation occurs in the contralateral hemisphere of the to-be-ignored visual hemifield (i.e., ipsilateral to the cued direction of attention) and represents an active attentional inhibition mechanism (Bonacci et al., 2020; Deng et al., 2020; Kelly et al., 2006; Sauseng et al., 2009; Schuhmann et al., 2019; Worden et al., 2000). Critical in the interpretation of the impact of alpha oscillations on attention is the temporal sequence of pre- and post-stimulus alpha power. A post-stimulus decrease in alpha power compared to the pre-stimulus power is called an event-related desynchronisation (ERD), while an increase is referred to as an event-related synchronisation (ERS) (Klimesch, 2012). In the EEG-literature, an “event” is not restricted to the presentation of a target, but also includes the presentation of a cue. Previous research suggests that the “anticipatory alpha ERD” (~8–12 Hz) observed during the pre-stimulus period in various cognitive tasks is a marker of the neural mechanisms that contribute to the development of temporal expectations (Capotosto et al., 2009; Klimesch et al., 1998; Rohenkohl and Nobre, 2011; Spadone et al., 2020).

While alpha activity has been mainly investigated in posterior brain areas, in the last decade a fronto-parietal network has gained attention. Importantly, visuo-spatial attention tasks are known to activate a fronto-parietal network (Capotosto et al., 2009; Heinen et al., 2017; Klimesch et al., 2007) and the massive increase in sex hormones in pregnant women (Soldin et al., 2005) is likely to modulate in the prefrontal cortex structure and function, including executive functions. However, the behavioural significance of the volumetric decrease of the prefrontal cortex or its correlation with sex hormones in pregnant women is still unknown.

The responsiveness of attention networks to sex hormones may modulate cortical computations. Hormonal tuning of attention networks can be characterised by correlational studies showing associations between hormone level, performance, and neural activity. Inverted U-relations between estradiol and cognitive abilities (e.g., sustained attention as well as verbal and spatial memory performance; Bean et al., 2014; Foster, 2005, 2012; Marrs et al., 2013) indicate that estradiol levels below or above the optimal level are associated with cognitive impairments (Bean et al., 2014). Furthermore, associations between sex hormones, EEG activity, and cognitive performance have been observed in non-pregnant, naturally cycling women (Becker et al., 1982; Brötzner et al., 2014; Brötzner et al., 2015a, 2015b). Interestingly, alpha oscillations, are sensitive to basal estradiol levels (Brötzner et al., 2014). As endogenous hormonal oscillations during the menstrual cycle correlate with cognitive performance, profound elevations of estradiol and progesterone during pregnancy (Soldin et al., 2005; Tulchinsky et al., 1972) have been suggested to cause cognitive impairments in pregnant women (Brown and Schaffir, 2019; Ouellette and Hampson, 2019).

It is not yet clear whether the observed volumetric decrease of the prefrontal cortex (Carmona et al., 2019; Hoekzema et al., 2017; Luo et al., 2020) and the massive increase in sex hormones in pregnant women (Soldin et al., 2005; Tulchinsky et al., 1972) affects attentional performance in pregnant women. Regarding attention processing, it was shown that alpha activity in a fronto-parietal network underpins attentional processing (Capotosto et al., 2009; Heinen et al., 2017; Marshall et al., 2015; Sauseng et al., 2011) and alpha oscillations are supposed to control the selective processing of visual information in the occipital lobe via a fronto-parietal network (Capotosto et al., 2009; Gaillard et al., 2020; Liu et al., 2016; Wiesman et al., 2019). Capotosto et al. (2009, 2012) demonstrated experimentally by repetitive transcranial magnetic stimulation in frontal and parietal areas not only a functional link between the fronto-parietal network and the occipital cortex but also the crucial impact of alpha activity as transcranial magnetic stimulation impaired target identification. Thus, due to their inhibitory nature and their large power in cortical areas associated with to-be-ignored sensory information, alpha oscillations are known to be a critical mechanism in the suppression of irrelevant sensory information. So far, many studies on attentional performance between pregnant and non-pregnant women revealed inconsistent results. While some findings indicate no difference in attentional performance (processing time and accuracy) between pregnant and non-pregnant women (Crawley et al., 2008; Crawley et al., 2003; Farrar et al., 2014; Henry and Sherwin, 2012) others suggest impaired performance (processing time, response time and accuracy) during pregnancy (Crawley et al., 2008; De Groot et al., 2003; Galen Buckwalter et al., 1999; Raz, 2014). The small number of publications as well as the heterogeneity of attention paradigms used may contribute to the inconsistencies in these studies. However, even when performance on cognitive tasks is similar during pregnancy, there could be differences in neural activity underlying the behavioural outcome. Interestingly, in comparison to non-pregnant women, pregnant women have a smaller volume of the prefrontal cortex (Carmona et al., 2019; Hoekzema et al., 2017; Luo et al., 2020), a central cortical area involved in attentional processing (Heinen et al., 2017; Sauseng et al., 2011). In human prefrontal cortex, estradiol shows next to hypothalamic areas elevated concentrations compared to other cortical areas (Bixo et al., 1995). Estradiol receptor alpha and beta have been localized immunocytochemically (Hwang et al., 2021; Montague et al., 2008), and the cortical thickness correlates with estradiol level (Beltz and Moser, 2020). Furthermore, working memory performance, which relies on an intact prefrontal cortex, correlates with peripheral estradiol level (Hwang et al., 2021). These observations indicate that the prefrontal cortex responds to changes in estradiol level structurally and functionally. Accordingly, elevated estradiol levels in pregnant women (Soldin et al., 2005) are likely to modulate in the prefrontal cortex structure and function, including executive functions. However, the behavioural significance of the volumetric decrease of the prefrontal cortex or its correlation with sex hormones in pregnant women is still unknown.
cortical activity which are known to be associated with attentional performance.

2. Results

2.1. Sexual hormone levels

Mann-Whitney-U-tests revealed that pregnant women show higher estradiol ($Mdn = 38.7$ pg/ml) and progesterone ($Mdn = 1208.4$ pg/ml) concentrations than non-pregnant women (estradiol ($Mdn = 3.7$ pg/ml); progesterone ($Mdn = 45.6$ pg/ml)) (estradiol: $U_{(14)}$ pregnant women $-14$, n non-pregnant women $-15) = 2.000, Z = -4.496, p < 0.001$, $r = 0.835$; progesterone: $U_{(14)}$ pregnant women $-15$, n non-pregnant women $-15) < 0.001, Z = -4.666, p < 0.001$, $r = 0.852$ (Fig. 1). Estradiol levels were not associated with accuracy or response time in valid trials in both groups (cf. Table 1). Furthermore, progesterone levels were not associated with accuracy or response time in valid trials in both groups (cf. Supplementary Material Table S1).

2.2. Attentional performance and correlations with sexual hormone levels

A 2x2 ANOVA with the factors VALIDITY (valid, invalid) and GROUP (pregnant women, non-pregnant women) with the accuracy [RAU] as dependent variable revealed a significant main effect for GROUP ($F(1,28) = 5.361, p = 0.028$, $\eta^2_p = 0.161$) indicating pregnant women reacted more accurately than non-pregnant women (cf. Fig. 2A). The main effect VALIDITY and the interaction between the factors VALIDITY and GROUP was not significant ($p > 0.9$).

To investigate differences in response time between pregnant and non-pregnant women a 2 x 2 repeated measures ANOVA with the factors VALIDITY (valid, invalid) and GROUP (pregnant women, non-pregnant women) was conducted. While there were no group differences for response time ($F(1,28) = 1.419, p = 0.244$, $\eta^2_p = 0.048$) a main effect for VALIDITY ($F(1,28) = 14.399, p = 0.001$, $\eta^2_p = 0.340$) was found, indicating that all women responded significantly faster to valid compared to invalid trials (Fig. 2B). Furthermore, a slower response time was by trend correlated with higher accuracy (valid: $r_{(30)} = -0.352, p = 0.057$; invalid: $r_{(30)} = -0.434, p = 0.016$).

Pregnant women with lower estradiol levels responded more accurately to valid trials ($r_{(14)} = -0.649, p = 0.012$) compared to pregnant women with higher estradiol levels (cf. Fig. 3A). In non-pregnant women, estradiol levels were not associated with accuracy ($r_{(15)} = 0.088, p = 0.756$). Estradiol levels were not associated with response time on valid trials in both groups (cf. Table 1).

2.3. EEG results

2.3.1. Alpha activity during the reference period

A 3x3x2 ANOVA with the factors ELECTRODE (F7, Fz, F8), FREQUENCY (lower alpha1, lower alpha2, upper alpha) and GROUP (pregnant women, non-pregnant women), with the alpha activity in the reference period (mean amplitude [\mu V] between $-1500$ to 0 ms) as dependent variable revealed no differences between pregnant and non-pregnant women ($F_{(1,28)} = 0.779, p = 0.385$, $\eta^2_p = 0.027$). The same ANOVA, calculated for parietal electrodes (P3, Pz, P4), did not show any group differences in the alpha activity during the reference period ($F_{(1,28)} = 0.214, p = 0.647$, $\eta^2_p = 0.008$). Furthermore, main effects and interactions of the ANOVAs are reported in the Supplementary Material (cf. Supplementary Material Table S2A and B and Table S3 for descriptive data). Additionally, it was found that pregnant women had a significantly faster gravity frequency ($M = 10.3 \pm SD = 0.6$ Hz) than non-pregnant women ($M = 9.8 \pm SD = 0.5$ Hz) ($t_{(28)} = -2.371, p = 0.025$, $\eta^2_p = 0.167$).

2.3.2. Alpha ERD

Considering that frontal and parietal areas are involved in visuospatial attention tasks (Heinen et al., 2017; Sauseng et al., 2005; Sauseng et al., 2011), we calculated two ANOVAs for each brain region. A 4x3x2x2 ANOVA with the factors TIME (200 to 300 ms; 300 to 400 ms; 400 to 500 ms; 500 to 600 ms), ELECTRODE (F7, Fz, F8), FREQUENCY (lower alpha1, lower alpha2, upper alpha), HEMIFIELD (attend left, attend right) and GROUP (pregnant women, non-pregnant women) was conducted with alpha ERD [%] as dependent variable. The main effect for GROUP revealed a greater magnitude of the alpha activity in pregnant women compared to non-pregnant women.

Fig. 1. Differences in sexual hormone levels between pregnant and non-pregnant, naturally cycling women. Pregnant women showed significantly higher estradiol (A) ($Mdn = 38.7$ pg/ml) and progesterone (B) ($Mdn = 1208.4$ pg/ml) levels than non-pregnant women (estradiol: $Mdn = 3.7$ pg/ml; progesterone: $Mdn = 45.6$ pg/ml). Horizontal lines represent the medians, boxes the interquartile range (IQR; distance between the 1st [Q1] and 3rd quartile [Q3]), and whiskers extend at most to Q1 $-$ 1.5*IQR (lower whisker) and Q3 $+$ 1.5*IQR (upper whisker). * displays the mean and dots display outliers and represent cases more than one and a half times the IQR away from the lower or upper quartile. ** $p \leq 0.01$. 

C.P. Plamberger et al. 

Brain Research 1798 (2023) 148130
Note: Bonferroni corrected: 0.05/4

Correlations between estradiol levels [pg/ml] and accurate identification of targets [RAU] in valid trials in pregnant women (n = 14). Pregnant women with lower estradiol levels responded with higher accuracy in valid trials. RAU: rationalised arcsin units transform for correct responses.

Table 1
Correlations between estradiol levels [pg/ml] and behavioural data (response time [ms] and accuracy [RAU]) for valid trials. Pregnant women with lower estradiol levels responded with higher accuracy in valid trials.

| Estradiol | Response time [ms] | Accuracy [RAU] |
|-----------|-------------------|---------------|
| Pregnant women | $r_{(14)} = 0.087, p = 0.767$ | $r_{(14)} = -0.649, p = 0.012$ |
| Non-pregnant women | $r_{(15)} = 0.104, p = 0.713$ | $r_{(15)} = 0.088, p = 0.756$ |

Note: Bonferroni corrected: 0.05/4 = 0.0125; * = $p \leq 0.05$; RAU: rationalised arcsin units transform for correct responses.

ERD in frontal areas in pregnant compared to non-pregnant women ($F_{(2,28)} = 13.590, p = 0.001, \eta^2_p = 0.327$; cf. Fig. 4A and B). The same ANOVA, calculated for parietal electrodes (P3, Pz, P4), showed by trend an interaction between ELECTRODE*GROUP ($F_{(1,28)} = 3.955, p = 0.056; \eta^2_p = 0.124$; Bonferroni corrected: 0.05/2 = 0.025). Post-hoc independent sample $t$-tests revealed by trend a greater magnitude of the alpha ERD for pregnant compared to non-pregnant women at P3 ($t_{(28)} = 1.838, p = 0.077, \eta^2_p = 0.108$) and at Pz ($t_{(28)} = 1.946, p = 0.062, \eta^2_p = 0.119$) but not at P4 ($t_{(28)} = 0.866, p = 0.394, \eta^2_p = 0.026$; cf. Fig. 4A and B). Furthermore, main effects and interactions of the ANOVAs are reported in the Supplementary Material (cf. Supplementary Material Table S4A and B and Table S5A and B for descriptive data).

2.3.3. Lateralisation of alpha ERD
To investigate whether the parietal areas show a stronger alpha ERD at contralateral sites to the attended visual hemifield than at ipsilateral sites a 4x2x3x2 ANOVA with the factors TIME (200 to 300 ms; 300 to 400 ms; 400 to 500 ms; 500 to 600 ms), LATERALISATION (ipsilateral, contralateral), FREQUENCY (lower alpha1, lower alpha2, upper alpha), and GROUP (pregnant women, non-pregnant women) was conducted with alpha ERD [%] as dependent variable. Results revealed a significant main effect for LATERALISATION ($F_{(1,28)} = 4.502, p = 0.043, \eta^2_p = 0.139$) indicating a significantly stronger alpha ERD at contralateral sites to the attended visual hemifield than at ipsilateral sites. The interaction between the factors LATERALISATION and FREQUENCY was also significant ($F_{(2,56)} = 4.293, p = 0.040, \eta^2_p = 0.133$) indicating a significant main effect of lateralisation of the alpha ERD solely in the lower alpha2 (i.e., ~8–10 Hz) and the upper alpha band (i.e., ~10–12 Hz) but not in the lower alpha1 band (i.e., ~6–8 Hz) (cf. Supplementary Material Fig. S1). The interaction between the factors LATERALISATION and GROUP ($F_{(1,28)} = < 0.001, p = 0.997, \eta^2_p < 0.001$) and the three-way interaction LATERALISATION, FREQUENCY and GROUP ($F_{(2,56)} = 0.740, p = 0.419, \eta^2_p = 0.026$) were not significant, indicating no group differences for the posterior alpha ERD lateralisation.

2.3.4. Alpha ERD and behavioural performance
With respect to alpha ERD effects on behavioural performance, a stronger parietal alpha ERD was by trend associated with faster response time and a stronger frontal alpha ERD was by trend associated with
5.001) but not in non-pregnant women (cf. Table 3 and Fig. 5). No significant correlations between alpha ERD and progesterone levels were found for both groups (cf. Supplementary Material Table S6).

### 3. Discussion

Alpha power, which has been shown to act inhibitory in fronto-parietal networks, is associated with expectancy and stimulus processing in attentional tasks (Klimesch, 2012; Klimesch et al., 2007; Sauseng et al., 2005; Sauseng et al., 2011). How pregnancy-related changes in attentional performance are indicated by alpha ERD in frontal and parietal areas and a moderate increase in accuracy in the visuo-spatial attention task. Further, in pregnant women,
saliva estradiol level correlated negatively with the magnitude of the alpha ERD and accuracy. Our results therefore replicate earlier findings that an alpha-driven inhibitory network in the fronto-parietal network is associated with attentional processing in a visuo-spatial attention task. All women, regardless of pregnancy, performed well (approximately 95% accuracy). Despite this high level of accuracy, estradiol is still significantly associated with accuracy. Pregnant women having lower estradiol levels had greater than average correct decisions and those with higher estradiol levels showed less than average correct decisions.

Although most self-reports suggest cognitive impairment during pregnancy (Crawley et al., 2003; Logan et al., 2014), standardised experiments on attention are inconclusive (Crawley et al., 2008; Crawley et al., 2003; Farrar et al., 2014; Galen Buckwalter et al., 1999; Henry and Sherwin, 2012; Logan et al., 2014, Raz, 2014). It should be noted that accuracy on valid and invalid trials showed a moderate, statistically significant increase in pregnant women compared to non-pregnant women, while groups did not differ regarding response time. We observed that accuracy showed a ceiling effect in pregnant (Mdn 98.3%) as well as in non-pregnant women (Mdn 96.6%). Evaluating whether accuracy in visuo-spatial attention differs between pregnant and non-pregnant women therefore seems to require either a bigger sample size or a more challenging attention task.

The inconsistencies between self-reports and standardised attention tests are already well-documented in the literature (Crawley et al., 2008; Crawley et al., 2003; Logan et al., 2014, Henry and Sherwin, 2012, Galen Buckwalter et al., 1999; Raz, 2014). For example, Crawley et al. (2003) reported that pregnant women complained about mild impairments in their focused and divided attention ability compared to non-pregnant controls, while these self-reported deficits were not revealed in standardised objective tests, like the “Stroop task” and the “Trail making task”. Similarly, Logan et al. (2014) found more self-reported complaints in memory functioning in pregnant compared to non-pregnant women but groups did not differ in divided attention as measured by the “Trail making task”. Furthermore, no pregnancy related effects were found on divided, focused, sustained and verbal attention, attentional switching (Crawley et al., 2008) and shifting (Crawley et al., 2008; Crawley et al., 2003; Farrar et al., 2014; Henry and Sherwin, 2012). However, other studies found deficits in sustained attention, attentional switching, and response inhibition during pregnancy (Crawley et al., 2008; Galen Buckwalter et al., 1999; Raz, 2014).

Comparing the results of our visuo-spatial attention task with other reports on selective attention in pregnant women are also inconclusive. Crawley et al. (2008) found no differences in selective attention between pregnant and non-pregnant women in the average time to correctly identify a target on the “Telephone search time task” (Robertson et al., 1996). However, this task goes beyond ours because it includes more demands (e.g., a search function) and it does not measure the response time per matched symbols, while our utilised task quantifies accuracy and response time per target. de Groot et al. (2003) assessed selective attention by using the “Spatial finger pre-cuing task” (Miller, 1982). In general, compared to no cues or invalid cues, participants responded faster following valid pre-cues (De Groot et al., 2003; Posner, 1980; Sauseng et al., 2011). Additionally, de Groot et al. (2003) found that in comparison to non-pregnant women, pregnant women show a smaller pre-cuing benefit, which is defined as the difference in response time between conditions with and without informative pre-cues. However, the “Spatial finger pre-cuing task” and our task differ in the nature of the stimuli (e.g., different spatial distributions, a higher cognitive load, symbol (i.e., +) instead of letters (i.e., p and q). Furthermore, de Groot et al. (2003) used a visual cue (a plus sign), while we used acoustic cues. In the present study, we observed a trade-off between accuracy and response time in all women (valid: $r_{(30)} = -0.352$, $p = 0.057$; invalid: $r_{(30)} = -0.434$, $p = 0.016$). Our observation of increased accuracy but at least descriptively slower response time in pregnant compared to non-pregnant women is in agreement with the classical law of Fitts (1954) and could indicate that this trade-off between accuracy and response time might lead to the subjective feeling of impaired performance.

Basal forebrain cholinergic projections to neocortical areas are thought to modulate a fronto-parietal network mediating top-down control on sensory cortices (Donovan et al., 2022; Fernandez-Duque and Posner, 1997; Hasselmo and Mc Gaughy, 2004; Herrera et al., 2008; Jimenez-Martin et al., 2021; Muir et al., 1996; Newhouse and Dumas, 2015; for review see Sarter et al., 2016; Lockhoffen and Mulert, 2021) and are known to be sensitive to estradiol (Milen et al., 2015; Newhouse and Dumas, 2015; Ping et al., 2008; Sarchielli et al., 2020). Relevant to the present study are the findings that cholinergic activity also enhances alpha power during visuo-spatial attention (Bauer et al., 2012; for review see Lozano-Soldevilla, 2018). Thus, considering the findings that estradiol (Brötzer et al., 2014; present study) as well as cholinergic synaptic activity associates with alpha power (for review see Lozano-Soldevilla, 2018), these studies point towards a yet unknown causal link between changes of the sex hormone estradiol, and modulation of alpha power via cholinergic synapses during attentional performance.

A correlation between estradiol and cognitive performance like attention and memory has been described in women across the lifespan, such that improved performance is replaced by impaired performance as the estradiol level either declines or rises (Ali et al., 2018; Bean et al.,...
2014; Foster, 2005, 2012). For example, while higher estradiol levels in young naturally cycling women have been associated with impaired spatial memory (Phillips and Silverman, 1997) and semantic categorisation performance (Brotzner et al., 2015a), a decline in estradiol level in post-menopausal women is associated with age-related memory loss and Alzheimers disease (Janicki and Schupf, 2010). Interestingly, hormone replacement therapy near the onset of menopause can delay the progression of age-related memory impairments (Foster, 2005; Vinogradova et al., 2021). Marrs et al. (2013) indicate that elevated levels of estrogens (estrone, estradiol, estriol) are associated with weak attentional and memory performance in pregnant women. Interestingly, following a drop of estradiol due to parturition, elevated estrogen levels are associated with better recall and verbal learning performance (Marrs et al., 2013). This corroborates the findings of our study, where we observed that elevated estradiol was associated with a mild but statistically significant decline in attentional performance in pregnant women. Furthermore, a quadratic regression analysis using salivary estradiol increase as a predictor and the rationalised aescin units transform (RAU) for correct responses in valid (R2(20) = 0.203, p = 0.052) or invalid trials (R2(20) = 0.244, p = 0.026) as the dependent variable, pointed towards an inverted U-shaped relationship (cf. Supplementary Material Fig. S3A and B). Together, these studies indicate that the direction of estradiol-related modulation on attentional performances might differ between non-pregnant and pregnant women, whereby pregnant women show an impairment in attentional performance when estradiol is elevated.

The neural substrate of the visuo-spatial orienting of attention includes the lateral prefrontal cortex and the dorsal visual stream, which originates from the primary visual cortex, V1, and extends to the dorsolateral occipital cortex and posterior parietal cortex (for review Sciberras-Lim and Lambert, 2017). Visual information processing is modulated by top-down mechanisms acting on V1 as well as on the ventral and dorsal visual stream (for review Gilbert and Li, 2013). Previous studies revealed that alpha oscillations in the fronto-parietal network are critical for the suppression of irrelevant information during attentional processing (Sauseng et al., 2005; Sauseng et al., 2011). Here we observed an alpha ERD in frontal and parietal areas, where frontal alpha ERD was significantly stronger in pregnant compared to non-pregnant women. This observation is consistent with the studies showing that a stronger alpha ERD observed during the pre-target period is a reliable predictor for high attentional performance (Capotosto et al., 2009; Kelly et al., 2009). Previous studies suggest that the ERD in the lower (6–10 Hz) alpha band during the pre-stimulus period reflects alertness and is a marker for neural mechanisms that contribute to the development of temporal expectations (Klimesch et al., 1998). The ERD of the upper alpha band (10–12 Hz) is used as a predictor for sensory semantic processing (Klimesch et al., 1998; for review see Klimesch et al., 2007). Our observation that the lower as well as the upper alpha band equally contribute to a stronger alpha ERD in fronto-parietal areas in pregnant compared to non-pregnant women indicates a general increase of an alerting state. As it is well established that alpha activity describes functional inhibition of cortical networks (Bonfond and Jensen, 2012; Jensen and Mazaheri, 2010; Klimesch et al., 2007), our findings revealed more efficient inhibition of irrelevant sensory input in pregnant women.

Regarding spatial cueing tasks, the parieto-occipital areas of the contralateral side of the to be ignored visual field (i.e., ipsilateral to the cued direction of attention) shows a larger alpha power, indicating an active attentional inhibition mechanism (Bonacci et al., 2020; Deng et al., 2020; Kelly et al., 2006; Sauseng et al., 2009; Suhmann et al., 2019; Worden et al., 2000). As reported in the literature, we observed a significant main effect of lateralisation of the alpha ERD, solely in the lower alpha2 (i.e., ~8–10 Hz) and the upper alpha band (i.e., ~10–12 Hz) in parietal areas (P3 and P4) of all participating women when they attended to the ipsilateral visual hemifield but ignored the contralateral visual hemifield as well as when they attended to the contralateral visual hemifield but ignored the ipsilateral hemifield (cf. Supplementary Material Fig. S1). However, we did not find a significant difference in lateralisation between non-pregnant women and pregnant women. The reason why the raw ERD differs between the two groups, whereas the lateralisation does not might be because i) Physiologically, there is no direct relationship between (raw) ERD and lateralisation. ERD reflects cortical ‘tuning’ between inhibition and excitation. Lateralisation is a matter of functional anatomy and hemispheric specialization (Klimesch et al., 2007; Sauseng et al., 2011). (ii) An indirect relationship exists in that strong lateralisation is naturally associated with stronger ‘tuning’, as evidenced by stronger ERD (Klimesch et al., 2007). (iii) Statistically, there may be a direct relationship, e.g., of the type that a stronger ERD is also associated with stronger dispersion, and thus lateralisations in the ERD do not become significant. Some studies suggest that alpha power and frequency are related to cortical thickness (Moretti, 2015; Sander et al., 2020; Woodman et al., 2022). For example, in the clinical context, a high upper (10.9–12.9 Hz) to lower (8.9–10.9 Hz) alpha power ratio correlates with cortical thinning and memory impairment in subjects showing mild cognitive impairment (Moretti, 2015). Interestingly, magnetic resonance imaging studies investigating cortical volumetric changes in pregnant compared to non-pregnant women revealed a decrease in the grey matter volume, indicating a decrease in cortical thickness (Carmona et al., 2019; Hoekzema et al., 2017; Luo et al., 2020). In the present study, we observed a higher gravity frequency in pregnant compared to non-pregnant women. Thus, combining the studies showing a relationship between alpha frequency with cortical thickness and the findings of cortical thinning in pregnant women with our observation of a higher alpha gravity frequency in pregnant women may indicate that the higher alpha frequency in pregnant women relates to a decrease in cortex thickness. Furthermore, thinning of the cortex could go along with a decrease in the number of synapses. Assuming that the decrease in power is due to a decline in synaptic transmission as a consequence of fewer synapses, an increase in alpha frequency could be seen as a compensation for the decline in alpha power (i.e., stronger magnitude of the alpha ERD) in pregnant women.

Beside the above-mentioned pregnancy-related decrease in grey matter volume, pregnancy causes further structural changes in the human brain. In comparison to non-pregnant women, pregnant women show a decrease in brain size by ~ 4–7 % (Oatridge et al., 2002) as well as a decrease in volume in distinct cortical areas. These structural changes are likely associated with an increase in sex hormones during pregnancy (Carmona et al., 2019; Hoekzema et al., 2017; Luo et al., 2020). Sex hormones have transient non-genomic and long-lasting genomic effects. Acute increases in sex hormones cause direct and transient modulation of ion channels via non-genomic mechanisms (Ehring et al., 1998) and neurotransmitter receptors (for review see Barth et al., 2013), while chronic elevation of estradiol affects structure and function of synapses via genomic mechanism (for review see Bean et al., 2014; Foster, 2005, 2012). Due to the prolonged elevation of sex hormones during pregnancy, the gestation-associated changes of the brain are probably due to genomic mechanisms of sex hormones. Accordingly, we assume that the long-lasting consequences of estradiol on synaptic activity, which are relevant for neuronal synchronisation during cognitive processes, dominate in our study, but we cannot exclude additional transient synaptic effects of estradiol.

4. Limitations

(1) This study did not control for mood, anxiety, or quality of life. There is considerable evidence for emotional changes during pregnancy, which in turn modulates attentional functions. Up to 70 % of women experience depressive symptoms during pregnancy, with 10 % – 16 % meeting the criteria for major depressive disorder (Becker et al., 2016). Kataja et al. (2017) found that women experiencing high or moderate levels of psychiatric symptoms during pregnancy had more errors in a
visuo-spatial working memory/executive functioning task than pregnant women with low symptom level. Task performance was predicted by the level of depressive symptoms and concurrent pregnancy-related anxiety symptoms. Further studies should control for these factors to assess whether pregnancy-associated changes in distinct attentional functions are mediated by depressive symptoms. (2) Future studies investigating the neural correlates of attention functions by using EEG should also include an assessment of intelligence, which is known to modulate brain oscillations in the alpha frequency band. Doppelmayr et al. (2002) for example found that more intelligent subjects showed a stronger amplitude in the lower alpha band (~6–8 Hz) compared to less intelligent subjects. (3) Additionally, it must be noted that the socio-economic status (e.g., educational level, occupation, income) of the participants was not collected in this study. Since attention problems (i.e., symptoms of hyperactivity and inattentiveness) are negatively correlated with academic achievement (Forderman et al., 2010), upcoming studies should control for that. (4) Furthermore, sleep-wake rhythms, chronotype as well as sleepiness should be considered in upcoming studies. It is well known that sleep quality is reduced during pregnancy (Garbarzua et al., 2020; Sedov et al., 2018) and evidence that sleep quantity is reduced in the third trimester of pregnancy (Chang et al., 2010). Sleep deprivation and sleepiness are known to negatively affect selective attention performance (Versace et al., 2006) and correlated with a higher alpha amplitude (Kaida et al., 2006). For example, Iemi and colleagues (2019) reported that a stronger pre-stimulus alpha power correlates with higher subjective sleepiness. (5) The current study did not collect any information about subjective attentional complaints, and therefore we are not able to report whether there are inconsistencies between self-reports and standardised attention tests, as it was described in the literature (Crawley et al., 2008; Crawley et al., 2003; Logan et al., 2014; Farrar et al., 2014; Henry and Sherwin, 2012; Galen Buckwalter et al., 1999; Raz, 2014). (6) The significant age difference between the two groups could be a confound for the current data. While some studies have demonstrated that resting state alpha power was smaller in older (65–80 years) compared to younger adults (18–30 years; Barry and De Blasio, 2017; Clements et al., 2021), other studies found no age related effects on alpha oscillations during visuo-spatial attention (22–72 years; Wiesman and Wilson, 2019). Furthermore, older subjects (i.e., 57–84 years) had longer reaction times, and a large magnitude of the cuing effect (Curran et al., 2001; Robinson and Kertzman, 1990; Yamaguchi et al., 1995) but a numerically higher accuracy compared to younger subjects (i.e., 19–49 years) in visuo-spatial attention tasks (Curran et al., 2001). However, note that the mean age difference between the two groups in our study was 3.5 years, while in the above-mentioned studies the age ranged from 18 to 80 years. (7) Finally, it would be interesting to run a longitudinal study to evaluate the development of alpha ERD differences and the associations with sexual hormone levels from early to late pregnancy and from late pregnancy to post-partum, since sexual hormones steadily increase during pregnancy.

4.1. Conclusion

The findings of this study suggest that an enhanced fronto-parietal alpha ERD moderately improves accuracy in a visuo-spatial attention task in pregnant compared to non-pregnant women. Furthermore, we demonstrated that saliva estradiol is related to alpha ERD as well as to performance accuracy in pregnant women. These observations in combination with the well-known modulation of the attention-related networks by basal forebrain cholinergic projections should be used in future studies to delineate the specific neuroendocrine differences in cognition at the neural level between pregnant and non-pregnant women.

5. Experimental procedure

5.1. Subjects

Data were collected from 18 healthy non-pregnant women and 18 healthy pregnant women. Note that all of the non-pregnant women were naturally cycling women which indicates that (1) they were cisgender women with a uterus who have naturally occurring menstrual cycles and (2) did not use oral contraceptives. All subjects were Austrians or Germans and had no history of migration. According to previous studies (Sauseng et al., 2005) data of six participants could not be used for analysis due to artefacts caused by eye blinks and/or horizontal eye movements during the visuo-spatial attention task. Finally, a total of 30 women were included in the analyses. Note that pregnant women (age: $M = 26.6 \; SD = 3.0 \; years$) were significantly older than non-pregnant women (age: $M = 23.1 \; SD = 4.3 \; years$) $t(28) = -2.618, \; p = 0.014, \; \rho^2 = 0.197$. One pregnant woman was excluded from analyses including estradiol concentration due to missing estradiol data. Individuals had no history of endocrine, neurological, or psychiatric diseases and were free of taking medications or exogenous hormonal supplementation. Inclusion criteria for non-pregnant women was a menstrual cycle duration between 27 and 34 days and a maximum variation of 7 days between cycles. From the remaining 15 non-pregnant women (age: $M = 23.1 \; SD = 4.3 \; years$, mean cycle length: 29.4 ± 1.9 days), eight were tested during their early follicular phase, three during ovulation, and four during their mid-luteal phase. Early follicular phase ranged from onset of menstruation plus five days. As in other studies (Pletzer et al., 2018), late follicular phase (ovulation) was calculated as 14 days before the expected onset of next menses and confirmed from all participating non-pregnant women by using a commercial ovulation test (Pregnafix®, Austria). Mid-luteal phase spanned from day three post ovulation to five days before the onset of menstruation. Non-pregnant women confirmed prior to participation in the study that they were not pregnant at the time of testing and did not intend to become pregnant during participation. Furthermore, they reported the date of onset of their last period and expect the onset of the next period. From the remaining 15 pregnant women (age: $M = 26.6, \; SD = 3.0 \; years$) 14 were tested during their third trimester (gestational age: six were tested during their 32th, two during their 33th, one during her 34th, two during their 36th and three during their 38th week) and one during the second trimester of pregnancy (gestational age: 14th week). The existing pregnancy was confirmed by a gynaecologist. Two non-pregnant women and three pregnant women were left-handed; all other women were right-handed. Participants had normal or corrected to normal eyesight. All subjects gave written informed consent. The study was performed in accordance with the Declaration of Helsinki and approved by the local ethics committee.

5.2. Visuo-spatial attention task

A modified version of the Posner’s visuo-spatial attention task was used (Posner, 1980; Sauseng et al., 2011). On a computer screen with a visual angle of 1.5° the visual targets (“p” and “q”) were presented (cf. Fig. 6). The fixation cross was presented with a visual angle of 5.5° above the centre of the screen. The targets were 17.2° left or right to the centre, which was labelled by a cross. The distance between the screen and the participant was 80 cm. Each trial consisted of a visual target and an acoustic cue. A 500 Hz tone was used to direct the attention to the left hemifield and a 1000 Hz tone was used to direct the focus to the right hemifield. The eyes had to be always focused on the fixation cross. Following an interval of 600 to 800 ms after the acoustic cue, one of the visual targets (“p” or “q”) was presented on the right or left hemifield for 83 ms. During valid trials (75%), the target was presented on the same side as indicated by the tone; on invalid trials the target was shown on the opposite side of the screen as indicated by the acoustic signal. The whole paradigm consisted of 400 trials that were split equally between trials where the attention had to be shifted to the right and trials where
attention had to be shifted to the left hemifield. The duration of the inter-trial interval varied from 2000 ms to 3000 ms. Participants responded by pressing the right mouse button for “q” with the middle finger of their right hand and for “p” the left mouse button with the index finger of their right hand as fast and as accurately as possible. Before the experiment, all women practiced one block of 50 trials to familiarise themselves with the task. Auditory and visual stimulation were implemented and presented by Presentation® 0.71 software (Version 0.71, 2009, Neurobehavioural Systems Inc., Albany, CA, USA). Median response times of all valid trials (excluding errors) and the percentage of accurate responses were calculated separately for each of the four task conditions (attend left trials valid, attend right trials valid, attend left trials invalid, attend right trials invalid). Since there was a ceiling effect for accuracy (Mdn 98.3 % for pregnant and Mdn 96.6 % for non-pregnant women), we used the rationalised arcsin units (RAU) transform as described in Studebaker (1985) for all accuracy data. Note that “valid trials” (i.e., the averaged response time and accuracy collapsed across the two task conditions: attend left trials valid, attend right trials valid), and “invalid trials” (i.e., the averaged response time or accuracy collapsed across the two task conditions: attend left trials invalid, attend right trials invalid) were used for statistical analyses.

5.3. Salivary sex hormone analysis

Saliva samples were collected from participants via the passive drool method before the EEG-sessions.

The samples were stored at ~20 °C and centrifuged two times at 3000 rpm for 15 min and 10 min, respectively. Estradiol and progesterone levels in saliva were measured by using Demeditec Salivary ELISA (Enzyme-linked Immunosorbent Assay) kits (Demeditec Diagnostics GmBH, Germany).

5.4. EEG recordings and analyses

To record EEG signals, 30 Ag–AgCl electrodes, were applied at the following positions: Fp1, Fp2, F7, F3, Fz, F4, F8, Fc3, Fcz, Fc4, T3, T5, C3, Cz, C4, T4, Cp3, Cpz, Cp4, T5, P3, Pz, P4, T6, PO3, PO4, O1, Oz, O2 using an EasyCap® (EasyCap GmbH, Germany). Signals were online referenced to the signal of an electrode placed on the nose and amplified with a BrainAmp amplifier (Brain Products, Inc., Gilching, Germany) using a sampling rate at 1000 Hz. To eliminate 50 Hz oscillations, a notch filter was applied and recording bandwidth was set from 0.016 to 100 Hz. Two electrodes, set at vertical and horizontal positions near the right eye, controlled eye movements. Impedance was kept below 8 kΩ. BrainVisionAnalyzer (Version 2.0; Brain Products GmbH, Inc., Gilching, Germany) was used to analyse EEG data. Raw EEG data were referenced to earlobe-electrodes (A1, A2) and filtered between 0.5 and 40 Hz using an IIR bandpass filter. EEG data were corrected for eye movement artifacts using ocular correction based on Gratton and Coles (Gratton et al., 1983). Trials containing artifacts (e.g., due to muscle activity, eye movements, blinks, etc..) were rejected after manual visual data inspection.

Because of inter-individual variety in the dominant alpha frequency, gravity frequency was estimated individually for each subject for the alpha ERD analysis (Klimesch, 1997). Individualised gravity frequency is more appropriate than peak individual alpha frequency when multiple peaks are detected in the alpha range (Klimesch, 1999). To calculate the gravity frequency during resting conditions with eyes closed, five minutes were segmented into consecutive 4000 ms epochs. Single epochs were Fourier transformed (frequency resolution 0.244 Hz, 10 % Hann window) and averaged across segments. The gravity frequency was then calculated individually for each subject as the weighted sum of spectral estimates, divided by alpha power with the following formula: (Σ(af(x)f))/Ω(Σa(f)) (Klimesch, 1999). af is the power spectral estimate at frequency f. Summation ranges from f1 to f2 (f1 from 0 – 12 Hz). Gravity frequency data were analysed with a customised script using MATLAB (R2010b) (Brötzner et al., 2014).

According to the individual gravity frequency, the non-segmented data were bandpass filtered separately for the following three frequency ranges: (i) the lower alpha1 band (=individual gravity frequency – 4 Hz to individual gravity frequency – 2 Hz), (ii) the lower alpha2 band (= individual gravity frequency – 2 Hz to individual gravity frequency) and (iii) the upper alpha band (= individual gravity frequency to individual gravity frequency + 2 Hz). To calculate event-related desynchronisation (ERD), the data were segmented from −1500 to 1200 ms around cue onset, separately for the four task conditions (attend left trials valid, attend right trials valid, attend left trials invalid, attend right trials invalid, cf. Fig. 4 and Fig. 6). Only trials without responses in the
time window between −1500 and 0 ms were included to avoid that the reference interval was contaminated by responses. Next, phase-locked (evoked) activity was removed to obtain the induced alpha response. Therefore, the inter-trial variance as described in Kalcher and Pfurtscheller (1995) was used, where each participant average ERP for that condition was subtracted from the trial’s time course to isolate the non-phase-locked (induced) activity for each trial. For the alpha ERP calculation, the inter-trial variance was used. The alpha ERD is defined as the percentage change of the inter-trial variance (A, activity period) at each sample point relative to the inter-trial variance (R, reference period) in a reference interval: ERD% = (A − R)/R × 100. Using this formula, ERD or “power decrease” is reflected by negative values, while ERS or “power increase” is reflected by positive values. The reference interval (R) ranged from −1500 to 0 ms prior to cue onset. For statistical analyses alpha ERP data were averaged for the following time windows: 200−300 ms, 300−400 ms, 400−500 ms, 500−600 ms after cue onset (i.e., before target onset; cf. Figs. 4 and 6). For the calculation of Fig. 4B, only the ERD of valid conditions (collapsed across attend left trials valid, attend right trials valid) were used. For data visualization ERP data were smoothed using the option “moving average” as implemented in BrainVisionAnalyzer (Version 2.0; Brain Products GmbH, Inc., Gilching, Germany). Smoothing was done by a centered Simple Moving Average algorithm. A window length of 100 ms was chosen. Similar to other studies (Sauseng et al., 2005) ERD at frontal (F7, Fz, F8) and parietal (P3, Pz, P4) recording sites was used for statistical analysis since findings by (Sauseng et al., 2005; Sauseng et al., 2011) suggest fronto-parietal connectivity at the alpha frequency range to play an important role in top-down processing of visuo-spatial information. Note that in the current study, F7 and F8 were used as our representative electrodes, nevertheless, analysis showed the same effects when using the recording sites F3 and F4.

To better visualise the differences in the alpha power distribution before and following acoustic cue presentation during a visuo-spatial attention task, wavelets presented in Fig. 4A were calculated as follows: After data preprocessing the EEG signal was downsampled to 100 Hz. Next, the data were segmented from −1500 to 1200 ms around cue onset for the valid conditions (collapsed across attend left trials valid, attend right trials valid). Time–frequency analysis was performed using continuous complex Morlet wavelet transformation as implemented in BrainVisionAnalyzer (Version 2.0; Brain Products GmbH, Inc., Gilching, Germany) on individual trials. Wavelet coefficients were calculated for frequencies between 1 and 20 Hz using a wavelet parameter of c = 7 with 1 Hz frequency steps. Time–frequency decompositions were then averaged for each participant. Note that time–frequency power does not only capture purely non-phase-locked (induced) activity but is also influenced by evoked (phase-locked) potentials.

5.5. Statistical analyses

Statistical analyses were performed using SPSS 24 (SPSS Inc. Chicago, Illinois). To test whether the data were normally distributed, Shapiro-Wilk tests were used. Analyses were mainly based on repeated measure analyses of variance (ANOVA) or Mann-Whitney-U-tests, depending on the distribution (normality) of the data. The significance level was set to p ≤ 0.05. P-values < 0.10 were reported as statistical trends. Partial eta squared (η²; for parametric tests) and the correlation coefficient (r; for non-parametric tests) are reported for effect sizes. Greenhouse-Geisser correction was used in case the assumption of sphericity was violated. For post-hoc comparisons of mean values, parametric tests (t-tests) were applied. Multiple comparisons are Bonferroni corrected. Tests that did not survive Bonferroni correction are marked by * (11). For correlations, Spearman rho coefficients (r_s) and Pearson coefficient (r) are reported, depending on the distribution (normality) of the data. To reduce the number of multiple comparisons and given the fact that the 4×3×3×2×2 ANOVAs showed no group effects on TIME, FREQUENCY or HEMIFIELD, the alpha ERD of the four time windows (200 to 300 ms; 300 to 400 ms; 400 to 500 ms; 500 to 600 ms), the three frequency ranges (lower alpha1, lower alpha2, upper alpha) and the two task conditions (attend left trials valid, attend right trials valid) were averaged for correlational analyses. For analysing the parietal alpha lateralisation, the factor LATERALISATION (ipsilateral, contralateral) was calculated as following: “ipsilateral” is the averaged alpha ERP, collapsed across left and right parietal electrodes (P3 and P4) when participants were attending to the ipsilateral hemisphere and ignoring the contralateral hemisphere. Therefore, we averaged together attend-left trials from the P3 electrode and attend-right trials from the P4 electrode. Similarly, “contralateral” is the average alpha ERP, collapsed across left and right parietal electrodes (P3 and P4), when participants were attending to the contralateral side (i.e., ignoring the ipsilateral side). Therefore, we averaged together attend-right trials from the P3 electrode and attend-left trials from the P4 electrode (Bonacci et al., 2020).

We applied a quadratic regression analysis to measure the relationship between estradiol and accuracy. Therefore, we used the logarithmic squared estradiol level as predictor \( y = b_1 \log(\text{estradiol})^2 + b_2 \log(\text{estradiol})^2 + a \). Regression analyses were analysed with RStudio (Version 4.1.0; RStudio Team (2020). RStudio: Integrated Development for R, RStudio, PBC, Boston, MA URL https://www.rstudio.com/). Valid and invalid task conditions belong to two distinct attentional processes (Sauseng et al., 2005; Sauseng et al., 2011). Since we were interested in continuous allocation of attentional processes (valid trials) and not in interruption of and reallocation of attentional processes (invalid trials), we correlated estradiol or alpha ERP only with the valid conditions. Statistical analyses calculated for the invalid task conditions and for progesterone levels are reported separately in the Supplementary Material (Tables S8–S13).

6. Author contributions

C.P.P. collected and analysed the data, performed statistical analyses, interpreted the results and drafted the manuscript. L.M.M. analysed the data. H.H.K. designed the study, interpreted the results and drafted the manuscript. W.K. interpreted the results and drafted the manuscript. K.H. interpreted the results, drafted the manuscript and provided funding. W.G. performed statistical analyses.

7. Financial support

This study was funded by the Centre for Cognitive Neuroscience and the Austrian Science Fund (P32028, W1233).

8. Data and materials availability

All data needed to evaluate the conclusions in the paper are presented in the paper and/or the Supplementary Materials. Additional data (e.g. custom written MATLAB codes) related to this paper can be requested from the authors.

CRediT authorship contribution statement

C. Plamberger: Project administration, Investigation, Formal analysis, Writing – original draft. L.M. Mayer: Formal analysis. W. Klimsch: Writing – review & editing. W. Gruber: Software. H. Kerschbaum: Resources, Conceptualization, Writing – original draft, Writing – review & editing, Funding acquisition. K. Hoedlmoser: Resources, Writing – original draft, Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial
C.P. Plamberger et al.

Klimesch, W., Sauseng, P., Hanslmayr, S., 2007. EEG alpha oscillations: the Lockhofen, D.E.L., Mulert, C., 2021. Neurochemistry of Visual Attention. Front. Neurosci.

Liu, Y., Bengson, J., Huang, H., Mangun, G.R., Ding, M., 2016. Top-down Modulation of Lockhofen, D.E.L., Mulert, C., 2021. Neurochemistry of Visual Attention. Front. Neurosci.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.

Klimesc, W., Klimesch, W., Klasen, K., Gasser, G., Plenk, A., Born, J., 2010. Modulation of alpha and gamma activity during a working memory task engaging the dorsal or ventral J. Neurosci. 30 (12), 4424–4429. https://doi.org/10.1523/jneurosci.4393-13.

Kida, K., Takahashi, M., Akertstedt, T., Nakata, A., Otuka, Y., Haratani, T., Fukasawa, K., 2006. Validation of the kallikrein sleepiness scale against performance and EEG variables. Clin. Neurophysiol. 117 (7), 1574–1581.

Kalcher, G., Pfurtscheller, G., 1995. Discrimination between phase-locked and non-phase-locked event-related EEG activity. Electroencephalogr. Clin. Neurophysiol. 94 (5), 381–384. https://doi.org/10.1016/0305-3071(95)90040-6.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.

Klimesc, W., Klimesch, W., Klasen, K., Gasser, G., Plenk, A., Born, J., 2010. Modulation of alpha and gamma activity during a working memory task engaging the dorsal or ventral J. Neurosci. 30 (12), 4424–4429. https://doi.org/10.1523/jneurosci.4393-13.

Kida, K., Takahashi, M., Akertstedt, T., Nakata, A., Otuka, Y., Haratani, T., Fukasawa, K., 2006. Validation of the kallikrein sleepiness scale against performance and EEG variables. Clin. Neurophysiol. 117 (7), 1574–1581.

Kalcher, G., Pfurtscheller, G., 1995. Discrimination between phase-locked and non-phase-locked event-related EEG activity. Electroencephalogr. Clin. Neurophysiol. 94 (5), 381–384. https://doi.org/10.1016/0305-3071(95)90040-6.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.

Klimesc, W., Klimesch, W., Klasen, K., Gasser, G., Plenk, A., Born, J., 2010. Modulation of alpha and gamma activity during a working memory task engaging the dorsal or ventral J. Neurosci. 30 (12), 4424–4429. https://doi.org/10.1523/jneurosci.4393-13.

Kida, K., Takahashi, M., Akertstedt, T., Nakata, A., Otuka, Y., Haratani, T., Fukasawa, K., 2006. Validation of the kallikrein sleepiness scale against performance and EEG variables. Clin. Neurophysiol. 117 (7), 1574–1581.

Kalcher, G., Pfurtscheller, G., 1995. Discrimination between phase-locked and non-phase-locked event-related EEG activity. Electroencephalogr. Clin. Neurophysiol. 94 (5), 381–384. https://doi.org/10.1016/0305-3071(95)90040-6.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.

Klimesc, W., Klimesch, W., Klasen, K., Gasser, G., Plenk, A., Born, J., 2010. Modulation of alpha and gamma activity during a working memory task engaging the dorsal or ventral J. Neurosci. 30 (12), 4424–4429. https://doi.org/10.1523/jneurosci.4393-13.

Kida, K., Takahashi, M., Akertstedt, T., Nakata, A., Otuka, Y., Haratani, T., Fukasawa, K., 2006. Validation of the kallikrein sleepiness scale against performance and EEG variables. Clin. Neurophysiol. 117 (7), 1574–1581.

Kalcher, G., Pfurtscheller, G., 1995. Discrimination between phase-locked and non-phase-locked event-related EEG activity. Electroencephalogr. Clin. Neurophysiol. 94 (5), 381–384. https://doi.org/10.1016/0305-3071(95)90040-6.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.

Klimesc, W., Klimesch, W., Klasen, K., Gasser, G., Plenk, A., Born, J., 2010. Modulation of alpha and gamma activity during a working memory task engaging the dorsal or ventral J. Neurosci. 30 (12), 4424–4429. https://doi.org/10.1523/jneurosci.4393-13.

Kida, K., Takahashi, M., Akertstedt, T., Nakata, A., Otuka, Y., Haratani, T., Fukasawa, K., 2006. Validation of the kallikrein sleepiness scale against performance and EEG variables. Clin. Neurophysiol. 117 (7), 1574–1581.

Kalcher, G., Pfurtscheller, G., 1995. Discrimination between phase-locked and non-phase-locked event-related EEG activity. Electroencephalogr. Clin. Neurophysiol. 94 (5), 381–384. https://doi.org/10.1016/0305-3071(95)90040-6.

Kataja, E.-L., Karlsson, L., Huizink, A.C., Tolvanen, M., Parsons, C., Nolvi, S., Karlsson, H., 2017. Pregnancy-related anxiety and depressive symptoms are associated with increased basal synaptic activity during in vivo Magnetic. Neurosci. 22 (11), 2917–2926. https://doi.org/10.1016/j.neuroscience.2015.05.011.
Tulchinsky, D., Hobel, C.J., Yeager, E., Marshall, J.R., 1972. Plasma estrone, estradiol, estriol, progesterone, and 17-hydroxyprogesterone in human pregnancy I. Normal pregnancy. Am. J. Obstet. Gynecol. 112 (8), 1095-1100.

Versace, F., Cavallero, C., De Min Tona, G., Mozatto, M., Stegagno, L., 2006. Effects of sleep reduction on spatial attention. Biol. Psychol. 71 (3), 248-255.

Vinogradova, Y., Dening, T., Hippisley-Cox, J., Taylor, L., Moore, M., Coupland, C., 2021. Use of menopausal hormone therapy and risk of dementia: nested case-control studies using QResearch and CPRD databases. BMJ 374. https://doi.org/10.1136/BMJ.N2182.

Wiesman, A.I., Wilson, T.W., 2019. The impact of age and sex on the oscillatory dynamics of visuospatial processing. NeuroImage 185, 513-520. https://doi.org/10.1016/J.NEUROIMAGE.2018.10.036.

Woodman, G.F., Wang, S., Sutterer, D.W., Reinhart, R.M.G., Fukuda, K., 2022. Alpha suppression indexes a spotlight of visual-spatial attention that can shine on both perceptual and memory representations. Psychon. Bull. Rev. 29 (3), 681-698.

Worden, M.S., Foxe, J.J., Wang, N., Simpson, G.V., 2000. Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. J. Neurosci. 20 (6) https://doi.org/10.1523/JNEUROSCI.20-06-J0002.2000.

Hasselmo, M. E., & Mcgaughy, J. (2004). High acetylcholine levels set circuit dynamics for attention and encoding and low acetylcholine levels set dynamics for consolidation. Progress in Brain Research, 145. https://doi.org/10.1016/S0079-6123(03)45015-2.

Yamaguchi, S., Tsuchiya, H., Kobayashi, S., 1995. Electrophysiologic correlates of age effects on visuospatial attention shift. Cognit. Brain Res. 3 (1), 41-49. https://doi.org/10.1016/0926-6410(95)00017-8.