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**The relationship between the menstrual cycle, anxiety
and cognitive functioning – the moderating role of oral
contraceptives**

PhD thesis

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Abstract

Women are twice as likely as men to suffer from generalized anxiety disorder. Anxiety symptoms are linked with cognitive deficits, especially with different biases in working memory, interpretation, and attention. Both naturally occurring hormonal fluctuations and hormonal contraception can affect anxiety levels and cognition in women. In Poland, combined oral contraceptives are the most common contraceptive method chosen by women between the ages of 18 and 35. The literature on the relationship between oral contraceptives, anxiety disorders, and cognitive functions reveals a lack of consistency in the results of previous studies. Therefore, it seems crucial to conduct further research on this topic to enhance the treatment of anxiety, one of the most prevalent disorders in women.

This research project aimed to analyze the relationship between the menstrual cycle, anxiety, and executive functioning in women who take oral contraceptives and in those who cycle naturally. The goal was to discover whether there are differences in anxiety levels and executive functioning in oral contraceptive users compared to naturally cycling women, and whether anxiety levels and executive functioning change throughout the menstrual cycle. Three studies were conducted (a meta-analysis, a cross-sectional study, and a daily diary study) and described in four articles presented in this thesis.

The main finding of this research project is that there is no significant difference in anxiety levels between naturally cycling women and women taking oral contraceptives. However, anti-androgenic oral contraceptive users have higher levels of worry than naturally cycling women. Regarding differences in executive functions, the meta-analysis did not show any difference between the two groups, but the composition of the oral contraceptives was not considered, as it was rarely reported in previous studies. The inhibitory control study conducted during my research project concluded that anti-androgenic oral contraceptive users exhibit lower inhibitory control compared to androgenic oral contraceptive users and naturally cycling women. Additional findings presented in this research project indicate that both groups of oral contraceptive users have higher daily levels of depression and lower daily levels of self-esteem than naturally cycling women. The fact that oral contraceptive users, especially anti-androgenic, present higher levels of worry, lower levels of inhibitory control, higher levels of depression, and lower levels of self-esteem than naturally cycling women indicates a need to conduct further studies on this topic to allow healthcare providers to help women choose the most appropriate treatments for their individualized needs.

Streszczenie

Kobiety są dwukrotnie bardziej narażone na uogólnione zaburzenie lękowe niż mężczyźni. Lęk ma negatywny wpływ na funkcje poznawcze, szczególnie w obszarze pamięci roboczej, interpretacji i koncentracji uwagi. Naturalne wahania hormonalne oraz antykoncepcja hormonalna mogą wpływać na poziom lęku i funkcje poznawcze u kobiet. W Polsce złożone doustne środki antykoncepcyjne są najczęściej stosowaną metodą antykoncepcji wśród kobiet w wieku 18-35 lat. Literatura dotycząca związku między doustnymi środkami antykoncepcyjnymi, zaburzeniami lękowymi i funkcjami poznawczymi ujawnia brak spójności w wynikach wcześniejszych badań. Dlatego kluczowe wydaje się prowadzenie dalszych badań w tym temacie w celu udoskonalenia leczenia lęku, jednego z najpowszechniejszych zaburzeń u kobiet.

Zamierzeniem niniejszego projektu badawczego była analiza związku między cyklem menstruacyjnym, lękiem i funkcjami wykonawczymi. Celem było ustalenie, czy występują różnice w poziomie lęku i funkcjach wykonawczych u kobiet stosujących doustne środki antykoncepcyjne w porównaniu z kobietami z naturalnym cyklem menstruacyjnym, a także czy poziom lęku i funkcje wykonawcze zmieniają się w trakcie cyklu menstruacyjnego. Przeprowadzono trzy badania (metaanalizę, badanie przekrojowe oraz badanie dziennikowe), których wyniki przedstawiono w czterech artykułach przedstawionych w niniejszej rozprawie.

Przedstawione badania wykazały brak istotnej różnicy w poziomie lęku między kobietami z naturalnym cyklem menstruacyjnym a tymi stosującymi doustne środki antykoncepcyjne. Jednak kobiety stosujące doustne środki antykoncepcyjne o działaniu antyandrogennym charakteryzują się wyższym poziomem zamartwiania się niż kobiety z naturalnymi cyklami. Jeśli chodzi o różnice w zakresie funkcji wykonawczych, metaanaliza nie wykazała żadnych różnic między obiema grupami, ale skład doustnych środków antykoncepcyjnych nie został wzięty pod uwagę, ponieważ rzadko był on raportowany w analizowanych badaniach. Badanie kontroli hamowania, przeprowadzone w ramach mojego projektu badawczego, wykazało, że kobiety stosujące antyandrogenną doustną antykoncepcję mają niższy poziom kontroli hamowania niż kobiety stosujące antykoncepcję androgenną i kobiety z cyklem naturalnym. Ponadto, dodatkowe wyniki uzyskane w moim projekcie badawczym wskazują, że obie grupy kobiet stosujących doustne środki antykoncepcyjne charakteryzują się wyższym poziomem depresji i niższą samooceną, mierzonymi codziennie, w porównaniu do kobiet z naturalnymi cyklami menstruacyjnymi.

Uzyskane wyniki wskazujące na to, że kobiety stosujące doustne środki antykoncepcyjne, zwłaszcza antyandrogenne, mają wyższy poziom zamartwiania się, niższy poziom kontroli hamowania, wyższy poziom depresji i niższą samoocenę niż kobiety z naturalnym cyklem, wskazują na potrzebę dalszych badań, aby kobiety miały dostęp do jak najlepszego leczenia odpowiadającego ich indywidualnym potrzebom.

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1. Introduction

Generalized anxiety disorder (GAD) has a prevalence of 4.5% worldwide (Stein et al., 2021). Anxiety disorders have a prevalence of 3.9% in Poland (World Health Organization, 2017). According to The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; American Psychiatric Association, 2013), GAD is manifested by excessive worry and anxiety about any given topic, difficulty controlling those worries, and physical symptoms such as constant tiredness. According to Eysenck and Holmes (2020), anxiety symptoms are linked with cognitive deficits, especially with different biases in working memory (Moran, 2016), interpretation, and attention (Shi et al., 2019).

Women are twice as likely as men to suffer from GAD (Kessler et al., 2012). Both naturally occurring hormonal fluctuations and hormonal contraception can affect anxiety levels and cognition in women (Beltz, 2022; Russman Block et al., 2024). Based on the data gathered by the United Nations from 195 countries, 16% of women of reproductive age (15–49 years old) use oral contraceptives (OC) worldwide (United Nations, 2019). In Poland, combined OC are the most common contraceptive method chosen by women between the ages of 18 and 35, with a prevalence of 38% (Zgliczynska et al., 2019).

The literature reviews by Laird et al. (2019) and Beltz (2022) on the relationship between OC, mental disorders, and cognitive functions revealed a lack of consistency in the results obtained in previous studies. Laird et al. (2019) suggested that these inconsistencies might be due to limitations such as the lack of distinction between different kinds of OC and data based mostly on self-reported menstrual cycle phases, with a lack of verification of actual hormone levels in naturally cycling women and women taking OC. The necessity of implementing more study designs, including those with between- and within-subjects variation, such as repeated measures or longitudinal studies, was also emphasized. The current project took into consideration those limitations and suggestions. Since there is a lack of specific biomarkers for GAD and no recent significant advances in the treatment of this disorder (Maron & Nutt, 2017), examining it through the prism of female gonadal hormones constitutes a novel addition to the existing literature and a potential path for further improvement of the anxiety treatment from a transdisciplinary perspective.

1. 1. The menstrual cycle and oral contraceptives

The menstrual cycle of women who cycle naturally is composed of two parts: a follicular phase and a luteal phase (Fehring et al., 2006). As described by Schmalenberger et al. (2021),

the menstrual cycle starts on the first day of menstruation when both estradiol and progesterone levels are low. Menstruation is part of the follicular phase, characterized by low levels of progesterone, while estradiol levels continuously increase until they reach a strong peak before ovulation. The luteal phase starts after ovulation and shows increasing levels of progesterone and estradiol until the mid-luteal phase, during which there is a peak in progesterone and a mild peak in estradiol. Finally, menstruation is triggered by a decline in the levels of estradiol and progesterone. A review conducted by Pinkerton et al. (2010) showed that the luteal phase (i.e., premenstrual phase) has been linked with an exacerbation of numerous disorders, including anxiety disorders.

According to Hampson (2020), there are differences in the levels of estradiol, progesterone, and testosterone between NC women and women using OC. Indeed, OC users see a decrease in those three hormones, sometimes even down to 60% for testosterone, which is a type of androgen. The composition of combined OC is an association between ethinylestradiol and progestins. The progestins are either androgenic or anti-androgenic (Beltz, 2022). Androgenic progestins originate from testosterone and do not induce such a substantial decrease in testosterone levels as anti-androgenic progestins, which block androgen receptors and exacerbate the decrease in testosterone (Raudrant & Rabe, 2003; Zimmerman et al., 2014).

1. 2. Cognitive functions

My research project focuses on executive functions, which are defined as a set of top-down cognitive processes that regulate the cognitive control of behavior (Diamond, 2013; Miyake & Friedman, 2012). According to Miyake and Friedman's model (2012), there are three core executive functions: inhibition, updating, and shifting. Inhibition is a "deliberate overriding of dominant or prepotent responses" (Miyake & Friedman, 2012, p. 2). The inhibitory control of attention enables us to select which stimuli to focus on or direct our attention to other stimuli (Diamond, 2013). Updating is a "constant monitoring and rapid addition/deletion of working-memory contents" (Miyake & Friedman, 2012, p. 2). Working memory involves not only passive storage but also active manipulation of information, such as monitoring information for relevance to the task at hand and replacing old, no longer relevant information with new, more relevant information. Finally, shifting is defined as "switching flexibly between tasks or mental sets" (Miyake & Friedman, 2012, p. 2). It relates to one's cognitive flexibility as it requires switching back and forth between multiple operations.

1. 3. Anxiety, the menstrual cycle, and oral contraceptives

Previous literature has found that even non-anxious women report mental fatigue similar to women suffering from GAD in the mid-luteal phase of the cycle (Li et al., 2020). Welz et al. (2016) showed that women lower in anxiety and rumination experience a more positive mood toward the end of the cycle. In contrast, the opposite is true for women with higher levels of anxiety and rumination. The review by Nillni et al. (2021) indicates that the most consistent findings in the literature are retrospective self-reports of an increase in anxiety symptoms during the premenstrual phase. The systematic review conducted by Green and Graham (2022) concluded that changes in anxiety symptoms are associated with the menstrual cycle, i.e., that symptoms increase before menstruation and at the beginning of menstruation. The review suggests that a decrease in progesterone and estradiol levels could be linked with an increase in anxiety symptoms. Moreover, higher levels of anxiety are experienced by women who have higher average progesterone levels during their entire cycle (Reynolds et al., 2018). The review by Beltz (2022) also described an increase in anxiety symptoms associated with lower estradiol levels, as is the case for women taking OC (Hampson, 2020). However, the review by Laird et al. (2019) highlighted a lack of studies on the link between GAD and OC use; the only cited study found that OC users were less likely to suffer from GAD (Cheslack-Postava et al., 2015). Beltz (2022) emphasized that randomized controlled trials (RCTs) are rare in this field due to ethical concerns, which makes it more challenging to explore the topic as accurately as possible. However, an RCT conducted by Lundin et al. (2017) showed that adult women experienced an increase in anxiety after starting OC, compared to the placebo group, over 3 months of use. Another RCT conducted by Bengtsson et al. (2018) concluded that only women with an ongoing or previous anxiety disorder saw an increase in their symptoms after three months of treatment with an anti-androgenic OC.

1. 4. Executive functions, the menstrual cycle, and oral contraceptives

Estrogen and progesterone receptors have been identified in brain regions associated with cognitive functions, as demonstrated by Hara et al. (2015) for estrogen and Brinton et al. (2008) for progesterone. According to a review by Hampson (2018), the literature is consistent with the fact that 17 β -estradiol (the most prevalent type of estrogen in women of reproductive age) is associated with improved working memory: the higher the level of estradiol, the better the performance in updating tasks. However, the literature review by Le et al. (2020) concluded that the potential impact of hormonal fluctuations during the menstrual

cycle on other executive functions is inconsistent, mainly due to methodological differences between studies. Moreover, the review underlines that studies have primarily focused on estrogen, rather than progesterone. For instance, inhibition was related to inconsistent results: one study showed improved performance in the follicular phase (Hatta & Nagaya, 2009), while another showed impairment in the same phase (Colzato et al., 2010). Regarding updating and shifting tasks, a study by Solís-Ortiz and Corsi-Cabrera (2008) showed that during the follicular phase, performance in updating tasks is enhanced, while performance on shifting tasks is impaired. However, not all studies found a difference in shifting task performance based on the phases of the menstrual cycle (Griksiene & Ruksenas, 2011). Overall, two literature reviews concluded that studies with the most robust methodologies do not show any differences between menstrual cycle phases in executive functions (Le et al., 2020; Sundström-Poromaa, 2018).

Recently, the link between OC and cognitive functioning has been evaluated in 4 literature reviews, including three narrative reviews (Beltz, 2022; Gogos et al., 2014; Laird et al., 2019) and one systematic review (Warren et al., 2014). Those literature reviews have shown that most results are significant yet contradictory, with some studies indicating an improvement in executive functions for OC users, while others show a deterioration. The review by Beltz (2022) focuses on studies examining the relationship between hormonal contraceptives and cognition, with an emphasis on spatial skills and verbal memory, both of which are related to updating. The review concluded that the use of androgenic OC is linked to enhanced performance in spatial updating (Bianchini et al., 2018). In contrast, anti-androgenic OC is linked with impaired performance (Griksiene et al., 2018). When it comes to verbal updating, OC use is related to an enhancement in performance, irrespective of androgenicity. This review also refers to one of the rare RCTs conducted on the link between OC and executive functions (Gingnell et al., 2016), which found no difference in inhibition between OC users and NC women but showed that women who were given androgenic OC improved their performance on the task after a few weeks of OC use, contrary to the placebo group. This study suggests that the use of androgenic OC is linked with an improvement in inhibition. On the other hand, the study by Garrett and Elder (1984) found an impairment in inhibition in the performance of OC users compared to NC. When it comes to shifting, the review by Gogos et al. (2014) mentioned a study that showed androgenic OC users performed worse than anti-androgenic OC users (Griksiene & Ruksenas, 2011). Overall, there are few

studies and no consensus in the literature on the relationship between executive functions and the use of OC.

2. Aim of the research project

My research project aimed to analyze the relationship between the menstrual cycle, anxiety, and executive functioning in women who take OC and in those who cycle naturally. Based on the theoretical analyses and results of previous research, the following hypotheses were tested through a meta-analysis, a cross-sectional study, and a diary study. The results of the studies have been described in four articles presented in this thesis. Three of the articles have been published, and one has been accepted for publication.

- **Hypothesis 1:** There are differences in anxiety levels and executive functioning between women taking oral contraceptives and naturally cycling women (Article 1, Article 2, and Article 3).
- **Hypothesis 2:** Women's anxiety levels and executive functioning change throughout the menstrual cycle (Article 1 and Article 4).

All studies were conducted in compliance with the Helsinki Declaration, and the research protocol was approved by the Ethics Committee of SWPS University (decision No. 55/2020/2).

3. Series of articles

Article 1

Kowalczyk, M., Kornacka, M., Wisiecka, K., Młyniec, A., Redeł, A., Szwykowska-Ziemniak, M., & Krejtz, I. (2023). The relationship between the menstrual cycle, oral contraceptives, and executive function – Inhibition, updating, and shifting: A systematic review and meta-analysis. *European Psychologist*, 28(4), 288-304. <https://doi.org/10.1027/1016-9040/a000514>

To my best knowledge, no meta-analysis has ever been conducted on the relationship between the use of OC and the core executive functions described in Miyake and Friedman's model (2012). Due to the inconsistent results found in previous literature reviews (Beltz, 2022; Laird et al., 2019), particularly the fact that some studies found an improvement while others showed an impairment in the performance of OC users compared to NC women, the main aim of this meta-analysis was to get a better understanding of the current results on this topic by systematically reviewing and examining through statistical analysis the available

literature comparing NC women with women taking OC on three main measures of executive functioning: inhibition, updating, and shifting.

The meta-analysis was prepared and conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2015). Three reviewers systematically and independently obtained the articles through the following databases: PubMed, Scopus, Web of Science, Ebsco (including APA PsycInfo and APA PsycArticles, as well as MEDLINE), and Google Scholar. All databases were searched from 2000 to mid-February 2021. We chose to conduct our search starting from 2000, as the systematic review by Warren et al. (2014) already provided a summary of the eight studies done before 2000. Altogether, a total of 674 articles were obtained. After excluding duplicates, analyzing abstracts, and conducting full-text screening, 16 studies were included in the meta-analysis. The inclusion criteria were the following: (1) the participants were women over the age of 18; (2) the study had either a comparison on executive function measures between one group taking OC and one group cycling naturally (cross-sectional) (studies showing the impact of previous OC use on postmenopausal women or comparing one group to men were excluded) OR the study had an experimental design which tested participants on executive functions measures before and after they were given OC and compared them to control participants (RCT) (studies where only women taking OC or only NC women were tested were excluded as they did not allow any comparison); (3) there was at least one measure testing for one of the following executive functions: inhibition, updating (studies testing short-term and long-term memory were excluded), shifting (studies where executive functions tests were used only for distraction purposes and no data were collected were excluded); (4) the studies were published in English; (5) the studies were published in a peer-reviewed journal (theses were excluded). The methodological quality of all the articles was also rated.

The oldest study taken into account in this meta-analysis was conducted in 2002, and the most recent one was published in 2022. The total number of participants included in the meta-analysis was 1,182, with 594 women cycling naturally and 588 taking OC. The average sample size was 32.33 for OC users and 31.34 for NC women, with ranges going from 8 to 144 participants per study. The age range of participants across all studies combined was between 18 years old (the youngest participant) and 50 years old (the oldest participant), with a mean of $M = 21.97$ and a standard deviation of $SD = 2.28$.

The meta-analysis, based on 66 effect sizes retrieved from 16 articles, did not show a significant effect size, indicating no difference between OC users and NC women on core executive functions. It should be noted that there was a high degree of heterogeneity in effect-size estimates from the individual studies, which may reflect a high level of methodological diversity. This high heterogeneity of methods has already been observed in previous literature reviews on the topic. Gogos et al. (2014) demonstrated that results vary across different studies, with significant methodological discrepancies observed between them, for instance, regarding the cycle phases or cognitive tasks tested. Laird et al. (2019) concluded that there is a lack of literature on the effects of OC on executive functions and that the available literature presents methodological limitations, sporadically showing a link between the variables, and only when controlling for the androgenicity of OC.

The heterogeneity of the results was further explored through the analysis of moderators. First, the cycle phases of NC women were examined as potential moderators. Our analysis revealed no difference between OC users and NC women, regardless of the phase of the menstrual cycle in which the NC women were. The second moderator we analyzed was the type of executive functions tested for. This analysis revealed no difference between OC users and NC women, regardless of the type of executive function tested. A separate meta-analysis was conducted for each cycle phase and executive function type, and once more, no difference was found between OC users and NC women. The quality of the studies was the last moderator analyzed, which indicated that studies with lower methodological quality strengthened the differences between the groups. This finding suggests the need to standardize methods when conducting studies comparing the executive functions of OC users and NC women.

Article 2

Kowalczyk, M., Kornacka, M., Kostrzewa, Z., & Krejtz, I. (2024). Differences in anxiety, worry, and perceived stress among naturally cycling women and oral contraceptive users: A cross-sectional study investigating the role of contraceptive types. *Archives of Women's Mental Health*, 27(2), 241-247. <https://doi.org/10.1007/s00737-023-01405-1>

Excessive worrying is one of the main components of GAD (American Psychiatric Association, 2013). According to Borkovec et al. (1983), worry is defined as “a chain of thoughts and images, negatively affect-laden and relatively uncontrollable” (p. 10). However, in the cognitive model of GAD (Wells, 1999), worry can be seen as a positive coping strategy

as the person believes that worrying serves a protective function to anticipate potential future threats. These beliefs may reduce distress in the short term, but they do not resolve it, and the repetition of this strategy only reinforces distress in the long run (Andrews et al., 2010). Additionally, worry can also enhance and maintain the physiological and cognitive activation caused by stress, resulting in higher and perseverative anxiety (Brosschot et al., 2006). Women are particularly susceptible to the effects of excessive worrying (Lal et al., 2014). The present study aimed to test whether the types of OC affect the link between anxiety and its main maintenance factors: worry and perceived stress.

A total of 1,289 women participated in the study; 908 of them were included, with 499 cycling naturally and 409 taking OC. The OC users were further classified according to the androgenicity of their OC (Mathur et al., 2008; Raudrant & Rabe, 2003): 277 participants in the anti-androgenic group and 132 in the androgenic group. The inclusion criteria for participants in the study were as follows: being between 18 and 45 years of age, speaking Polish, taking OC, or being NC. The exclusion criteria were as follows: using other forms of hormonal contraception (Pahnke et al., 2019), using a copper intrauterine device, having undergone sterilization, having stopped taking OC in the past 6 months (Hidalgo-Lopez & Pletzer, 2017), being pregnant or breastfeeding (Welz et al., 2016). We did not consider the phases of the menstrual cycle or the phases of the OC (active versus inactive). To determine the sample size for a fixed effects ANOVA, a power analysis was conducted using G*Power (Faul et al., 2007). With a medium effect size of 0.25, the results of the power analysis indicated that a minimum of 252 participants (84 participants per group) would be required to achieve an appropriate power level for this study.

We used the GAD-7 Scale (Spitzer et al., 2006), the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990), and the Perceived Stress Scale (PSS; Cohen et al., 1983). The GAD-7 is a 7-item scale used to screen for GAD by measuring levels of anxiety. The participants reply to the question “Over the last 2 weeks, how often have you been bothered by the following problems?” regarding different symptoms related to GAD such as “Feeling nervous, anxious, or on edge” and using a scale from 0 (“not at all”) to 3 (“nearly every day”). The Cronbach's alpha in our study was $\alpha = 0.91$, indicating high internal consistency. The PSWQ consists of 16 items that measure trait levels of worry. The instructions for this questionnaire are as follows: “Rate each of the following statements on a scale of 1 (“not at all typical of me”) to 5 (“very typical of me”). An example of an item from the scale is as follows: “Many situations make me worry.” The Cronbach's alpha was high ($\alpha = 0.91$). The

PSS is a 10-item questionnaire and is the most widely used psychological instrument for measuring perceived stress. The instructions indicate that the questions refer to the participants' feelings and thoughts over the last month and require them to express how often they felt or thought a certain way on a scale from 0 ("never") to 4 ("very often"). The Cronbach alpha was high ($\alpha = 0.89$).

In this extensive cross-sectional study, we examined whether women taking different types of OC and NC women differ in their levels of anxiety and its main maintenance factors: worry and perceived stress. We found no differences between groups on all measures. We found a significant difference between the groups in age, with the anti-androgenic OC group being younger than both the androgenic OC group and the NC group. After controlling for age and levels of stress, we discovered that women taking anti-androgenic OC had higher levels of worry than NC women. Nevertheless, a conservative conclusion should be made until the finding is replicated in another independent sample. Worry is an important risk factor for developing anxiety, and it should be monitored, particularly in women taking anti-androgenic OC.

Article 3

Kowalczyk, M., Kornacka, M., & Krejtz, I. (2025a). Anxiety and inhibitory control in women cycling naturally and women taking oral contraceptives. *Journal of Cognitive Psychology*, online first. <https://doi.org/10.1080/20445911.2025.2525254>

According to the Attentional Control Theory by Eysenck and Derakshan (2011), impairments of attentional control are one of the crucial symptoms that lead to the development of anxiety disorders. Anxious participants exhibit longer response times in tasks measuring attentional control, such as the Emotional Stroop Task, the Go/No-Go task, or visual search tasks, without producing errors in accuracy (Shi et al., 2019). They also exhibit attentional biases toward threatening stimuli and tend to react more quickly than control groups to threat-related stimuli, for instance, in the dot-probe task (Eysenck et al., 2007).

The Emotional Stroop task (Smith & Waterman, 2003) is derived from the classic version of the Stroop task (Stroop, 1935) and utilizes words with either emotional or neutral valence. This task assesses the degree of interference caused by the meaning of a word by asking participants to disregard its meaning and focus solely on the color in which the word is written. It tests inhibition deficits towards emotional stimuli and has been used previously to study anxiety disorders (Mogg & Bradley, 2005). Indeed, according to Williams et al. (1996),

participants have slower response times when presented with words whose meaning is related to their psychopathology.

Considering the gap in the literature, i.e., the lack of comparison between the different components of OC, and the need for more intensive longitudinal studies, the present two studies aimed to compare inhibitory control towards emotional words, including those eliciting anxiety, in NC women, women taking androgenic OC, and women taking anti-androgenic OC. The first study is a cross-sectional study meant to assess the link between levels of anxiety and reaction times on an Emotional Stroop task (Smith & Waterman, 2003). The second study is a daily diary study designed to assess daily levels of anxiety and reaction times on an Emotional Stroop task and then compare these between the phases of the menstrual cycle.

Cross-sectional study

In the first study, 240 participants ($M = 27.09$, $SD = 5.69$) completed an online questionnaire and an Emotional Stroop task. 133 participants were naturally cycling, and 107 were taking OC. The women using OC were further classified according to the androgenicity of their OC: 72 in the anti-androgenic group and 35 in the androgenic group. The inclusion and exclusion criteria were identical to those in the previous study.

We used the GAD-7 scale (Spitzer et al., 2006) to test for anxiety ($\alpha = 0.86$), and the Emotional Stroop task to assess the participants' inhibitory control towards emotional words, including those eliciting anxiety. To test for anxiety, we selected 40 words with the highest mean in the fear category from the Polish adaptation of the Berlin Affective Word List–Reloaded (Riegel et al., 2015; Vö et al., 2009), which is used to study the affective properties of words in German. Then, based on Ben-Haim et al. (2016), we matched the fear words with positive, negative, and neutral words. Words were first matched based on their length in characters and then on their estimated frequency in the Polish language. The mean reaction time differences between the categories of words measured the strength of the interference created by the meaning of the words. The number of correct answers was not considered in our analysis since most of the participants had correct answers, and there was a ceiling effect (out of 200 trials, the mean of correct answers was $M = 194.50$; $SD = 13.79$).

No link was found between anxiety levels and mean response times in the Emotional Stroop task, after conducting a Bonferroni correlation correction. There were also no

differences in anxiety and inhibitory control between the NC women and the OC users in the cross-sectional study.

Daily diary study

For the daily diary study, we invited 103 volunteers from the first study. Welz et al. (2016) noted that, due to the high drop-out rate in daily diary studies, there should be more than 60 participants in total. The final sample included 89 women (M age = 26.60, SD = 4.65) with 41 NC women and 48 taking OC. The women using OC were further classified according to the androgenicity of their OC: 32 in the anti-androgenic group and 16 in the androgenic group. To be selected for the study, participants in the NC group needed to have regular menstrual cycles. According to Fehring et al. (2006), a regular menstrual cycle lasts between 21 and 35 days, with a difference of less than 7 days between cycles. However, to conduct the diary study, the participants needed to have cycles that lasted at least 28 days so that the menstrual cycle phases did not overlap.

Each participant was provided with her own individual menstrual cycle calendar, which was calculated based on the date of her last menstruation onset and the usual length of her menstrual cycle. For the NC participants, the calendar was divided into three phases: early follicular, late follicular, and late luteal phases. In each phase, measures were taken for five consecutive days, totaling 15 days, as per Nezlek's method (2012). The women taking OC were tested on the same days as the NC participants, starting from the first day of their menstruation. The OC users had an average cycle length of 28 days and were tested on the same days as NC participants with a 28-day menstrual cycle. We did not compare active to inactive pill phases, as some participants had 21 days of active treatment while others had 24. Instead, we chose to match the phases of the NC women to compare the results of both groups in parallel throughout the menstrual cycle.

The daily measures consisted of 3 items chosen from the GAD-7 scale, as used in the first study (Spitzer et al., 2006), and adapted for daily administration, following the guidelines discussed in Nezlek (2012). The main question was "How often today have you been bothered by the following problems?". The items chosen from the GAD-7 were items 1 ("Feeling nervous, anxious, or on edge"), 3 ("Worrying too much about different things"), and 7 ("Feeling afraid as if something awful might happen"). Participants provided answers ranging from 1 ("not at all") to 7 ("a lot"). The Emotional Stroop task was similar to the one used in the first study. Participants received a daily email at 8 pm during the 15 days of their

individual menstrual cycle calendar, which included a link to the electronic diary entry on the Qualtrics platform. This link then redirected them to the Inquisit platform to perform a daily Emotional Stroop task. The number of measures collected for the 89 participants was 1120.

No significant differences were found between groups on daily anxiety levels. However, anti-androgenic OC users had lower inhibitory control in all categories of words, whether neutral or related to emotional stimuli, compared to androgenic OC users. To my knowledge, no study has tested for these differences previously, as the studies conducted on response inhibition and OC use were RCTs where participants received either androgenic OC (Gingnell et al., 2016) or anti-androgenic OC (Scheuringer et al., 2020). However, there was no comparison between androgenic and anti-androgenic OC. Anti-androgenic OC users also showed greater interference than NC women in all the categories of words in their late luteal phase, and with negative words in their late follicular phase. These findings underline differences in inhibitory control in women, depending on which menstrual cycle phase they are in, on whether they use OC or not, and on the components of their OC. Further studies could focus on the link between the different components of OC and inhibitory control, which can be linked to anxiety symptoms in women.

Article 4

Kowalczyk, M., Kornacka, M., & Krejtz, I. (2025b). Anxiety, depression and perseverative cognition in women cycling naturally or taking oral contraceptives – a diary study. *BMC Psychology*, online first.

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After conducting the cross-sectional study, I observed that the literature is inconsistent regarding the link between anxiety and OC (Beltz, 2022; Laird et al., 2019), whereas the link between depression and OC is recognized in women who started OC during adolescence (Anderl et al., 2022; Skovlund et al., 2016). I decided to compare depression levels between NC women and OC users at the same time as we were comparing their anxiety levels. Indeed, similar to the higher prevalence of GAD in women, they are also twice as likely as men to suffer from depression (Kuehner, 2017). The premenstrual and menstrual phases are linked with an increase in depression (Handy et al., 2022). The DSM-5 (American Psychiatric

Association, 2013) indicates that depression is accompanied by symptoms such as a depressed mood, a loss of interest and pleasure, feelings of worthlessness, or decreased concentration.

To obtain accurate results, we studied negative variables linked with anxiety and depression, namely perceived stress and perseverative cognition. Higher levels of perceived stress are linked with higher levels of anxiety (Mirón et al., 2019), and stress plays a role in the onset of depression (Tafet & Nemeroff, 2016). According to the literature, one of the key transdiagnostic factors, being a common mechanism to anxiety, depression, and stress, might be perseverative cognition (Watkins, 2008). Our study examined two types of perseverative cognition separately: worry, which, as observed in my cross-sectional study, is characteristic of anxiety (Wells, 1999), and perseverative thinking, typically associated with depression (Nolen-Hoeksema et al., 2008). We also studied variables that are protective against anxiety and depression, namely self-esteem and satisfaction with life. Positive psychology literature points to low self-esteem as a predictor of higher levels of anxiety and depression (Sowislo & Orth, 2013). Lower life satisfaction is associated with a risk of developing depression, and GAD is associated with a higher likelihood of experiencing lower satisfaction with life.

Our study aimed to understand the differences between women taking OC and naturally cycling (NC) women regarding their daily levels of anxiety, depression, related negative factors (perseverative cognition and stress), and protective factors (self-esteem and life satisfaction). This study was conducted on the same sample of participants as in the previous daily diary study, with a final sample including 89 women (M age = 26.60, SD = 4.65), with 41 NC women and 48 taking OC (32 in the anti-androgenic group and 16 in the androgenic group). The inclusion and exclusion criteria, as well as the procedure, were identical.

The following questionnaires were used at the beginning of the study: the GAD-7 Scale (Spitzer et al., 2006), the Perseverative Thinking Questionnaire (PTQ, Ehring et al., 2011), the Penn State Worry Questionnaire (PSWQ, Meyer et al., 1990), the Perceived Stress Scale (PSS, Cohen et al., 1983), and the Self-Esteem Scale (SES, Rosenberg, 1965). Most of the daily measures were taken from existing trait-level scales and adapted for daily administration, as described in the previous article. The daily measures included daily levels of anxiety (based on the GAD-7 scale), depression (Nezlek & Gable, 2001), perseverative thinking (based on the PTQ), worry (based on Thielsch et al., 2015), stress (based on the PSS), self-esteem (based on the SES), and satisfaction with life (Nezlek et al., 2017).

We found a significant link between anxiety and depression levels within the sample. There were no differences between groups in daily levels of anxiety, worry, perseverative thinking, and perceived stress. There were also no differences in daily levels for all the variables tested during the study between the different phases of the menstrual cycle in NC women, and between the three times when OC users were tested. However, there were differences between groups in daily levels of depression, self-esteem, and satisfaction with life. Anti-androgenic OC users had higher daily levels of depression than NC women in all the phases of their menstrual cycle, while androgenic OC users had higher daily levels of depression than NC women who were in their menstrual and follicular phases. Both groups of women taking OC had lower daily levels of self-esteem than NC women in all phases of the menstrual cycle. Androgenic OC users reported higher levels of daily life satisfaction than anti-androgenic OC users in one of the three time points tested. As with the cross-sectional study, there was no relationship between anxiety and OC use, but there was a relationship between depression and OC use.

4. Discussion

My research project aimed to analyze the relationship between the menstrual cycle, anxiety, and executive functioning in women who take OC and in those who cycle naturally. To achieve this, I conducted a meta-analysis, a cross-sectional study, and a daily diary study. In these studies, I have attempted to address some of the limitations identified in literature reviews on the topic of anxiety and cognitive functions in women taking OC and NC women (Beltz, 2022; Laird et al., 2019). These limitations included a lack of distinction between the different components of OC, which I remedied by verifying the androgenicity of the OC taken by the participants in the cross-sectional and daily diary studies. Another limitation was that the data were based on self-reported menstrual cycle phases, whereas participants in the diary study were provided with ovulation tests, allowing for more accurate calculations of the cycle phases. The reviews (Beltz, 2022; Laird et al., 2019) also emphasized the need to conduct studies with repeated measures or a longitudinal design, which was the case in my daily diary study.

4.1. Hypotheses

- **Hypothesis 1:** There are differences in anxiety levels and executive functioning between women taking OC and NC women.

The main finding of my research project is that there is no significant difference in anxiety levels between NC women and women taking OC in any of the conducted studies (cross-sectional and daily diary). These results are in line with some studies, which did not find a difference in anxiety levels between hormonal contraceptive users and NC women (Kecer et al., 2024; Masama et al., 2022). However, the RCT by Lundin et al. (2017) showed that women taking anti-androgenic OC saw an increase in anxiety levels during their treatment, compared to the placebo group. There may be no difference in anxiety levels between OC users and NC women, because women who experience side effects during the treatment are more likely to discontinue it (Frye, 2006). Even though we did not find a difference in anxiety levels between OC users and NC women, we found a difference between groups in levels of worry, which is one of the main components of GAD (American Psychiatric Association, 2013). After controlling for age and levels of stress in the cross-sectional study, we discovered that women taking anti-androgenic OC had higher levels of worry than NC women. Our findings are consistent with those of Louis et al. (2022) in that hormonal contraception is associated with increased levels of worry. According to the literature, women are more likely to be affected by excessive worry than men (Lal et al., 2014). This might explain why the use of anti-androgenic OC, which reduce the levels of male hormones, is linked with higher levels of worry. However, the literature review by Hampson (2023) highlights that the association between ethinylestradiol and certain progestins may also affect neurotransmitters such as serotonin or dopamine in rats, which could explain the difference in worry levels between androgenic and anti-androgenic OC users.

The daily diary study revealed differences in inhibitory control among groups, with anti-androgenic OC users exhibiting lower inhibitory control compared to androgenic OC users and NC women. The meta-analysis did not show any difference in executive functioning (inhibitory control, shifting, and updating) between NC women and OC users; however, it did not take into account the components of the OC, as they were often not reported.

- **Hypothesis 2:** Women's anxiety levels and executive functioning change throughout the menstrual cycle.

The daily diary study examined the differences in anxiety levels and inhibitory control in NC women across three phases of the menstrual cycle (menstrual, follicular, and luteal). There was no difference in anxiety levels or inhibitory control between the phases of the menstrual cycle in NC women. These results are not in line with the existing literature, which suggests that the symptoms of numerous disorders typically increase at the end of the luteal

phase (Pinkerton et al., 2010). However, I did not ask the participants whether they had an anxiety disorder diagnosis, and symptoms of anxiety or inhibitory control performance might not significantly worsen in the luteal phase in healthy participants.

4.2. Additional findings

In the daily diary study, OC users had higher daily levels of depression and lower daily levels of self-esteem than NC women. Our results are in line with the population-based cohort studies (Johansson et al., 2023; Skovlund et al., 2016), which showed higher levels of depression in adult OC users, both in androgenic and anti-androgenic ones. To the best of my knowledge, no study has looked at the levels of self-esteem in OC users and NC women. The fact that OC users fare worse than NC women indicates a need to conduct further studies on this topic.

4.3. Limitations

Although I attempted to address several limitations present in previous studies (small sample sizes, lack of repeated measures, lack of ovulation testing), my project was not without its own limitations. The meta-analysis showed a high level of heterogeneity due to the methodological limitations of the studies, including the differences in sample sizes and tasks used, as well as the lack of distinction between OC types. Moreover, only studies published after 2000 were taken into consideration, which limits the scope of this meta-analysis. We also excluded studies that did not compare groups of NC women with OC users, so studies that tested only one of these groups on executive functions or studies that compared one of these groups with men were excluded. These choices might have impacted the overall results of our meta-analysis.

The limitations present in the other studies in my project were the observational design, which did not allow us to draw any causal conclusions, the use of self-report measures such as questionnaires, which might not always offer the best accuracy, and the recruitment method (social media) which is linked with a selection bias and does not allow to generalize the results to the whole population. The sample size was also relatively small in the daily diary study. Other limitations present in the project are the following: a lack of participants who had an actual anxiety disorder diagnosis, not testing for hormonal levels, not verifying whether the participants were taking the OC for contraceptive or gynecological reasons, and not comparing the different dosages of ethinylestradiol in the OC.

5. Ongoing development of the research project and further directions

Based on the results gathered in the studies presented in this thesis, I conducted a laboratory study to test two more hypotheses.

- **Hypothesis 3:** Oral contraceptives moderate the relationship between the menstrual cycle and anxiety levels, as well as executive functioning.
- **Hypothesis 4:** Women's anxiety levels and executive functioning change according to their levels of estradiol and progesterone.

Fifty-seven women participated in the study (aged 18-45; $M = 29.31$, $SD = 6.96$), comprising one group of NC women ($n = 23$) and one group taking OC ($n = 34$). The inclusion and exclusion criteria for participants in the study were identical to those in previous studies. We could not test the women taking OC according to the androgenicity of their OC, as there were not enough participants taking androgenic OC (5 participants with androgenic OC and 29 with anti-androgenic OC).

The participants were asked to visit the laboratory twice, in two phases of their menstrual cycle, which corresponded to the NC women's peri-ovulatory phase, characterized by low progesterone, and the mid-luteal phase, characterized by high progesterone (Hidalgo-Lopez & Pletzer, 2017). During both sessions, they had to complete questionnaires to assess their anxiety and depression levels and perform eye-tracking tasks to test their executive functions and dynamic emotional expression recognition, as individuals suffering from anxiety disorders (for meta-analysis: Demenescu et al., 2010) and depression (for meta-analysis: Krause et al., 2021) present a broad deficit in emotion recognition. The tasks were performed on the SMI Experiment Centre software with an SMI RED 120 Hz eye-tracking device (SensoMotoric Instruments, Teltow, Germany). Levels of salivary 17β -estradiol, progesterone, and testosterone were assessed with two saliva samples of at least 1 ml each, collected throughout both sessions: one before and one after the task. The procedure was based on the work of Griksiene et al. (2018). Testosterone analysis was added to the study for further exploration of the results, based on the recommendations of Dr. Griksiene, who allowed me to undergo training at her lab at the University of Vilnius, Lithuania, to learn how to analyze hormones in saliva samples. I am currently working on analyzing the results and preparing a publication, with the help of my supervisors, as well as Dr. Griksiene and mgr Erik Ilkevic from Vilnius University.

The research on the link between OC, anxiety, and executive functions is inconsistent and presents many differences in methodologies. Future research on this topic should include more replications and unified methods. It is difficult to obtain consistent results in studies on the topic of contraception, anxiety, and cognition, as RCTs cannot be carried out easily due to ethical concerns. As a result, studies could more often test women before they start taking OC and then again through the course of the treatment, rather than comparing them to NC women (Beltz, 2022). Based on my results and the readings I have done of the literature throughout my project, the following variables should always be tested for to provide a higher accuracy of results when studying the link between OC, anxiety and executive functioning: the phases of the menstrual cycle in NC women, the types of OC, including their androgenicity and the type of estradiol they contain, the phases of the OC (active/inactive) and the actual hormonal levels, both in OC users and NC women.

Finding possible mediators or moderators of the links between mental disorder symptoms, cognitive functions, hormonal levels, and the use of OC might allow better treatment options for women suffering from those symptoms. Getting more information on the interplay between these variables would enable doctors and psychologists to tailor therapy treatment to different phases of the menstrual cycle or to use hormonal supplementation to enhance therapy outcomes. Further research on this topic could be beneficial to create a smartphone application that helps women with mental disorders adapt their lifestyle according to their menstrual cycle, thereby reducing their symptoms. Such applications are already used to help athletes optimize their performance according to the phases of their menstrual cycle (FitrWoman, Encino, CA, USA), or to allow women with ADHD to track their menstrual cycle and possible changes in their symptoms related to hormonal fluctuations (LetterLife, LetterLife AB, Stockholm, Sweden).

The menstrual cycle is a vital indicator of health and observing it can predict the onset of serious diseases later in a patient's life (Vollmar et al., 2025). Moreover, commonly used medications have been proven to be linked with cognition: ibuprofen has a positive relationship with cognition, whereas paracetamol has a negative relationship (Pinilla et al., 2025). OC are also a common medication and should be considered in research. It is currently said that the future of healthcare lies in precision medicine (Kosorok & Laber, 2019), which enables the tailoring of treatments and interventions according to specific individual factors, such as hormones. The more precise the treatment, the better the patients are treated, and the less pressure is placed on the healthcare system.

6. Conclusion

This research project contributes to the literature by studying a topic that is still rarely explored, and which presents inconsistent results, namely the relationship between anxiety and executive functions in NC women and OC users. My studies addressed certain limitations highlighted in the literature by utilizing a large sample size in the cross-sectional study, considering the phases of the menstrual cycle, and incorporating intensive repeated measures in the daily diary study.

To conclude, the main findings of this research project were that OC users, especially anti-androgenic, present higher levels of worry, lower levels of inhibitory control, higher levels of depression, and lower levels of self-esteem than NC women, indicating a need to conduct further studies on this topic to enhance the treatment of anxiety disorders and depression in women.

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The Relationship Between the Menstrual Cycle, Oral Contraceptives, and Executive Function – Inhibition, Updating, and Shifting

A Systematic Review and Meta-Analysis

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Abstract: Previous research suggests a link between oral contraceptives and cognitive functioning in women, yet the results are contradictory and limited by methodological inconsistencies. This is the first meta-analysis of studies comparing naturally cycling women with women taking oral contraceptives on measures testing three executive functions: inhibition, updating, and shifting. We conducted a systematic literature search. Sixteen articles were included which were either cross-sectional or experimental and compared executive functions between women taking oral contraceptives ($n = 588$) or cycling naturally ($n = 594$). The average sample size was $n = 32.33$ for oral contraceptive users and $n = 31.34$ for naturally cycling women with ranges going from 8 to 144 participants per study. The age range of participants in all the studies taken together was between 18 for the youngest participant and 50 years old for the oldest participant with a mean age of $M = 21.97$, $SD = 2.28$. The studies presented a mixture of androgenic and anti-androgenic oral contraceptives which were rarely analyzed as separate groups. We ran a multivariate meta-analysis model to estimate the effect size of 66 comparisons in executive functioning between the groups taking oral contraceptives and the groups of naturally cycling women. Overall, the effect size of differences in executive functioning between groups was not significant: $d = 0.044$, $SE = 0.0713$, 95% CI $[-0.0959, 0.1839]$, $z = 0.62$; $p = 0.54$. The analysis of the cycle phases and types of executive functions as moderators was not significant, however, the studies assessed as having a lower quality increased the overall effect. Our analysis indicates no difference between oral contraceptive users and naturally cycling women on core executive functions but the high amount of heterogeneity might reflect a high level of methodological diversity. Implications for research design and methodology are discussed.

Keywords: executive functions, inhibition, updating, shifting, oral contraceptives

Based on the data gathered by the United Nations from 195 countries, 16% of women of reproductive age (15–49 years old) use oral contraceptives (OC) worldwide (United Nations, 2019). Since such a relatively high number of women rely on OC in daily life, OC should be considered an important factor when exploring women's core executive functions. This systematic review and meta-analysis aimed to quantitatively analyze studies on the relationship between OC and executive functions by comparing naturally cycling (NC) women and OC users.

Executive functions are defined as a set of top-down cognitive processes that regulate the cognitive control of behavior (Diamond, 2013; Miyake & Friedman, 2012). According to Miyake and Friedman's model (2012), there

are three core executive functions: inhibition, updating, and shifting. Inhibition is a “deliberate overriding of dominant or prepotent responses” (p. 2) and refers to the ability to deliberately inhibit automatic or prepotent response (Miyake & Friedman, 2012) and also to the control of interference: selective attention and cognitive inhibition (Diamond, 2013). Updating is a “constant monitoring and rapid addition/deletion of working-memory contents” (p. 2). It refers to working memory because it involves not only passive storage but also active manipulation of information: monitoring information for relevance to the task at hand and replacing old information that is no longer relevant with a new, more relevant one. Finally, shifting, defined as “switching flexibly between tasks or mental sets”

(p. 2), relates to one's cognitive flexibility because it requires switching back and forth between multiple operations, tasks, or mental sets.

NC women experience physiological hormonal fluctuations with their levels of estradiol and progesterone varying through the course of the menstrual cycle. Estrogen levels are at their highest at the end of the follicular phase and then rise again in the middle of the luteal phase. Progesterone levels peak only during the luteal phase. Receptors of these hormones have been found in parts of the brain related to cognitive functioning (progesterone: Brinton et al., 2008; estrogen: Hara et al., 2015). According to a review by Hampson (2018), the literature is consistent with the fact that 17 β -estradiol (the most prevalent type of estrogen in women of reproductive age) is associated with improved working memory: the higher the level of estradiol, the better the performance in updating tasks. However, the literature review by Le et al. (2020) concluded that the potential impact of hormonal fluctuations during the menstrual cycle on other executive functions is inconsistent, due to the differences in methodology between studies. Moreover, the review underlines that studies have mostly focused on estrogen, rather than progesterone. The review indicates that during the follicular phase, performance in updating tasks is indeed enhanced but performance on shifting tasks is impaired (e.g., Solís-Ortiz & Corsi-Cabrera, 2008). However, not all studies found a difference in shifting task performance based on the menstrual cycle phases (e.g., Griksiene & Ruksenas, 2011). Inhibition was also related to inconsistent results: for instance, one study showed an improved performance in the follicular phase (Hatta & Nagaya, 2009) while another showed impairment in the same phase (Colzato et al., 2010). Overall, two literature reviews concluded that the studies with the most robust methodologies do not show any difference between the menstrual cycle phases on executive functions (Le et al., 2020; Sundström-Poromaa, 2018).

The use of OC is linked with a noticeable decrease in levels of estradiol and progesterone (Hampson, 2020). During the periods of active pill use, the levels of these two hormones are similar to the levels of NC women in their menses phase (Elliott-Sale et al., 2013). Moreover, levels of testosterone, a form of androgen, are down by 50–60% in women taking OC compared to NC women (Hampson, 2020). Nevertheless, combined OC contains synthetic steroids, usually ethinylestradiol and progestins which can be androgenic or anti-androgenic. Androgenic progestins are derived from testosterone while anti-androgenic progestins block androgen receptors (Raudrant & Rabe, 2003). The androgenic OC slightly counteracts the effects induced by the decreasing levels of testosterone in OC users but the anti-androgenic OC reinforces them (Zimmerman et al.,

2014). Women taking androgenic and anti-androgenic progestins present differences in their brain structure when compared to the brain structure of NC women (Pletzer et al., 2015). Griksiene and Ruksenas (2011) and Wharton et al. (2008) showed that the efficiency of the performances on cognitive measures depended on the level of androgenicity of the OC: higher androgenicity improved the performance on updating tasks but decreased it on shifting tasks. Previous studies have shown that males usually perform better on updating tasks but worse on shifting ones (Hyde, 2016). If androgenicity becomes higher then updating skills increase and shifting skills decrease. These findings are worthy of attention as Pletzer et al. (2014) showed that women using OC had the same results in numerical tasks as NC women, however, their brains showed patterns of activation similar to those of men. Moreover, the androgenicity of OC determines which parts of the brain are affected by changes during the course of the treatment (Pletzer et al., 2015). Gray matter volume is positively correlated with longer-duration use of OC, especially androgenic ones (Pletzer et al., 2015). Since a larger volume of gray matter is associated with better cognitive functioning (Ramanoël et al., 2018), it seems crucial to explore the link between the use of different types of OC and cognitive functioning, specifically executive functions.

Recently, the link between OC and cognitive functioning has been evaluated in 4 literature reviews including three narrative reviews (Beltz, 2022; Gogos et al., 2014; Laird et al., 2019) and one systematic review (Warren et al., 2014). According to the review by Gogos et al. (2014), improved performance on inhibition tasks was observed for OC users (e.g., Cicinelli et al., 2011). Updating skills showed the greatest contrasts in the results: they were either higher in OC users (e.g., Gogos, 2013), or no difference was found (Vranić & Hromatko, 2008). When the OC users were divided into androgenic and anti-androgenic groups and active/inactive pill phase on an updating task, NC women had better results than anti-androgenic OC users, and OC users in general had better results in the active phase of the pill (Wharton et al., 2008). However, the study by Griksiene and Ruksenas (2011) showed that androgenic OC users performed worse than NC women on updating tasks and worse than anti-androgenic OC users on shifting tasks. This systematic review by Gogos et al. (2014) showed that only some studies controlled for the cycle phases of NC women (Gogos, 2013), the active or inactive phase of OC (Wharton et al., 2008), and the types of OC (Griksiene & Ruksenas, 2011; Wharton et al., 2008). Other limitations underlined by the review were the presence of too many differences in methodologies and limited sample sizes.

The systematic review conducted by Warren et al. (2014) also showed that OC users have better updating skills than

NC women but it added that an impairment in inhibition was found in the performance of OC users compared to NC women (e.g., Garrett & Elder, 1984). This review also cited the study by Wharton et al. (2008) which found better updating abilities depending on the progestin androgenicity. Warren et al. (2014) underlined that visuospatial performance is usually higher in men, which might explain why the levels of androgens present in OC might be related to the performance of OC users. The limitations noted by this review were a high risk of bias, small sample sizes (a mean of $N = 24$ for OC users), a lack of reporting of OC types, and too many differences in methodology, including studies that were not using externally validated testing protocols. The review concluded that the literature is too inconsistent, both in results and in methodology, to draw any firm conclusions. Among recommendations, Warren et al. (2014) suggested that studies should focus on participants using the same kinds of OC. Moreover, it was underlined that the quality of evidence in this field of study might always be weaker compared to fields regularly using randomized controlled trials (RCTs). RCTs would give the most accurate results but are extremely rare due to the practical and ethical implications of blinding participants from the risks of using a placebo contraceptive.

The review by Laird et al. (2019) supported the previous results and concluded that the results of the studies taken into account in the review are inconsistent, methodologies are heterogeneous, sample sizes are too small, and more research is needed, especially on the impact of OC on updating, shifting and a higher order executive function: planning. The review offered multiple interpretations to potentially explain the lack of consistency in the studies' results. For instance, there was not enough control of treatment dose, treatment duration, previous use of OC, or additional pharmacological treatments. Some studies used cognitive tasks that were not intended to test healthy women. The main recommendations were to control for the phases of the menstrual cycle and the active/inactive phases of OC, to verify actual hormonal levels, to collect data on the types of OC, and especially, to separate progestins from estradiol in future studies as it seems that progestins have the strongest impact on cognitive performance in OC users. Moreover, they underlined that more studies with stronger designs are needed, such as repeated measures, longitudinal studies, and RCTs.

The most recent review by Beltz (2022) focuses on the latest studies exploring the link between hormonal contraceptives and cognition with an emphasis on spatial skills and verbal memory, both related to updating. Beltz concluded that the use of androgenic OC is linked to enhanced performance in spatial updating (e.g., Bianchini et al., 2018) whereas anti-androgenic OC is linked with an impaired

performance (e.g., Griksiene et al., 2018). When it comes to verbal updating, OC use is related to an enhancement in performance, irrespective of androgenicity. This review also refers to one of the rare RCTs conducted on the link between OC and executive function (Gingnell et al., 2016) which found no difference between OC users and NC women in inhibition but showed that women who were given androgenic OC improved their performance on the task after a few weeks of OC use, contrary to the placebo group. This study suggests that the use of androgenic OC is linked with an improvement in inhibition. The review by Beltz (2022) also underlines the limitations induced by small sample sizes, the heterogeneity in methods, and the lack of distinction between OC types. However, contrary to the previous reviews, the recommendations were to conduct more within-person studies focusing only on OC users, rather than comparing them to NC women.

Overall, previous literature reviews have shown that most of the results are significant, yet contradictory, with some studies showing an improvement in executive functions for OC users and others showing a deterioration. The results are also limited by methodological inconsistencies and there is still no consensus on the relationship between OC and executive functions. It is important to underline that none of the previous reviews compared the effect sizes of the studies published in the literature. Taking into account all the limitations of the previous studies, the present meta-analysis has also considered the quality of the studies.

To our best knowledge, no meta-analysis has ever been conducted on the relationship between the use of OC and the core executive functions described in Miyake and Friedman's model (2012); executive functions that are implicated in the higher-order executive tasks including reasoning, problem-solving, and planning (Diamond, 2013). Due to the inconsistent results found in previous literature reviews, particularly the fact that some studies found an improvement while others showed an impairment in the performance of OC users, the main aim of this meta-analysis is to have a better understanding of the current results on this topic by systematically reviewing and examining through statistical analysis the available literature comparing NC women with women taking OC on three main measures of executive functioning: inhibition, updating, and shifting.

Method

This study was prepared and conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Moher et al., 2015).

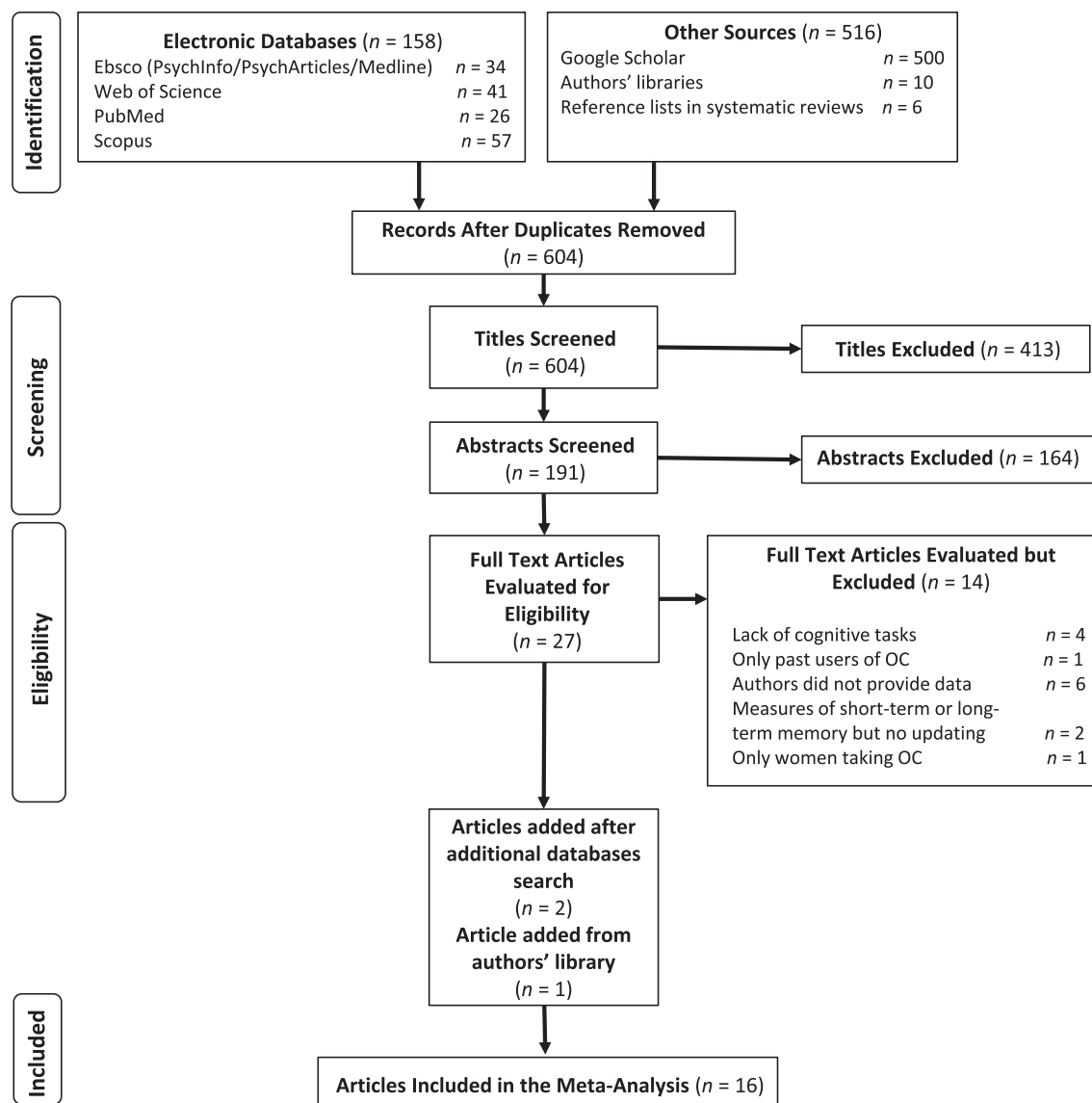


Figure 1. Study selection. Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Search Strategy

The articles were systematically and independently obtained by three reviewers through the following databases: PubMed, Scopus, Web of Science, Ebsco (APA PsycInfo, APA PsycArticles, MEDLINE), and Google Scholar. All databases were searched from 2000 to mid-February 2021. We chose to conduct our search starting from 2000 as the systematic review by Warren et al. (2014) already provided a summary of the 8 studies done before 2000. An additional database search was performed on January 7, 2022. The following search syntax was used for all databases: (“oral contracep*” OR “hormonal contracep*” OR “birth control pill”) AND (“executive control” OR “executive function” OR “executive attention” OR

“working memory” OR (executive AND function*) OR (executive AND shifting) OR (executive AND updating) OR (executive AND inhibition) OR “inhibitory control”). To extend the search scope, we also scanned the reference lists of included studies or relevant reviews identified throughout the search and the authors’ personal files. Only published articles in the English language were selected and duplicates were removed. Figure 1 presents the selection flow.

Selection of Studies

Altogether 658 articles were obtained from the online database search, 10 additional studies were added from the

authors' library and 6 came from the reference lists of systematic reviews found during the database search, which is a total of 674 articles. After the exclusion of duplicates ($n = 70$), 604 publications remained. At the first selection stage, the titles and abstracts were screened by three independent reviewers. A screening of the titles resulted in 191 articles, of which 164 were excluded after abstract screening. The remaining 27 studies were then included in the full-text screening process to establish eligibility for inclusion.

Inclusion Criteria

Studies were included in the meta-analysis if (1) the participants were women over the age of 18; (2) the study had either a comparison on executive function measures between one group taking OC and one group cycling naturally (cross-sectional) (studies showing the impact of previous OC use on postmenopausal women or comparing one group to men were excluded) OR the study had an experimental design which tested participants on executive functions measures before and after they were given OC and compared them to control participants (RCT) (studies where only women taking OC or only NC women were tested were excluded as they did not allow any comparison); (3) there was at least one measure testing for one of the following executive functions: inhibition, updating (studies testing short-term and long-term memory were excluded), shifting (studies where executive functions tests were used only for distraction purposes and no data were collected were excluded); (4) the study was published in English; (5) the studies were published in a peer-reviewed journal (theses were excluded).

Screening Process

Full-text screening process resulted in 13 studies being included in the meta-analysis. If there were discrepancies in the final list of eligible studies for inclusion, the reviewers discussed them and made a unified decision. The authors of 8 studies out of the 27 included before full-text screening were contacted due to missing data in the articles. Out of these 8 authors, two provided additional data on request and were therefore added to the meta-analysis. The additional database search (conducted on January 7, 2022) brought 2 new articles, and an article from the authors' library was also added at this point, bringing the total of studies to 16 (see Figure 1).

Data Extraction

Data were extracted by three authors and included (1) authors and year of publication; (2) number of participants

in total and for each group (OC and NC women); (3) characteristics of the participants including age; (4) study design; (5) type of executive function measured and the tasks used to determine them; (6) OC type; (7) whether the sample was healthy or suffered from some disorders; (8) the phase(s) of the menstrual cycle when the tests were conducted; (9) the level of hormones; (10) the treatment time for OC users; (11) means and standard deviations of each group. The cognitive tasks used in the studies included in the meta-analysis were classified into three categories according to the executive function they measured: inhibition, updating, and shifting. However, despite testing the difference in cognitive measures between OC users and NC women, the studies did not follow the same methods, did not control for the same variables, and did not reach the same conclusions. Some studies that appeared in our search were not aimed at testing the difference in executive measures between OC users and NC women but they were using tasks measuring executive functions. The results of those cognitive tasks were included in our meta-analysis. Those studies include Bradshaw et al. (2020) who found a lack of perseverance in pursuing cognitive tasks for OC users; Cohen et al. (2020) who tested how sex hormones influence the action of stress on the results of visuospatial tasks; and Kuhlmann and Wolf (2005) who showed that OC use diminishes the brain reaction to elevated levels of cortisol. Due to the rarity of research studies that controlled for active and inactive phases of OC, we decided to calculate the results of both phases together for OC users when these data were available. The measures we took into account in our analysis were: (1) the accuracy, (2) the errors, and (3) the reaction times (RT) of NC women and OC users on tasks testing for executive functions. Based on the literature review conducted by Soveri et al. (2018), the test-retest reliability of the various executive functions tasks cited in our meta-analysis ranges from $r = .30$ to $r = .90$ for RT measures (with most r s $> .7$, which means adequate test-retest reliability) and from $r = .15$ to $r = .92$ for accuracy measures (with most r s $> .7$). The details of the selected studies can be found in the Appendix.

Quality Assessment

The methodological quality of all the studies included in the analysis was rated based on criteria from the literature (Downes et al., 2016; Feeley, 2020; Hohn et al., 2019; Ma et al., 2020; Sanderson et al., 2007; Valentine, 2009; Zeng et al., 2015). The quality scores of the studies are displayed in Figure 2. The rating consists of 16 criteria that are rated as 0 = *absent*, 0.5 = *not fully present*, and 1 = *present*, resulting in a maximum quality score of 16 points. Some items were created specifically for studies focused on the menstrual cycle and OC, based on the reported variables

No	Author	Q1. Sample	Q2. Exclusion criteria	Q3. Equal groups	Q4. Groups similarity	Q5. Androgenicity	Q6. Types of OC	Q7. Level of hormones	Q8. OC phases	Q9. Phases in NC group	Q10. Sample size calculation	Q11. Standard measures	Q12. Statistical significance	Q13. Replication possibility	Q14. Data analysis	Q15. Selective reporting	Q16. Ethics	Mean score
1	Beltz et al. (2015)	1	1	0	1	0.5	1	0	0	0	0	1	1	1	1	1	1	0.59
2	Bradshaw et al. (2020)	1	1	0	1	0	0	0	0	0	1	0	1	1	1	1	1	0.5
3	Cohen et al. (2020)	1	1	1	1	0.5	0.5	1	0	0.5	0	1	1	1	1	1	1	0.78
4	Gingnell et al. (2015)	1	1	1	1	0.5	0.5	0	0	0	0	1	1	1	1	1	1	0.69
5	Gogos (2013)	1	1	1	1	0.5	0.5	0	0	1	0	1	1	1	1	1	1	0.75
6	Gravelins et al. (2021)	1	1	1	1	0.5	0.5	0	0.5	1	0	1	1	1	1	1	1	0.78
7	Griksiene & Ruksenas (2011)	1	1	1	1	1	0.5	1	0.5	1	0	1	1	1	1	1	1	0.88
8	Griksiene et al. (2018)	1	1	1	1	0.5	0.5	1	0.5	0.5	0	1	1	1	1	1	1	0.81
9	Högsted et al. (2021)	1	1	0	1	0.5	0.5	1	0	0	0	1	1	1	1	1	1	0.69
10	Kuhlmann & Wolf (2005)	1	0	1	1	0	0.5	1	0.5	1	0	1	1	1	1	1	1	0.75
11	Louis et al. (2022)	1	0	1	1	0	0.5	0	0.5	0.5	1	1	1	1	1	1	1	0.72
12	Mordecai et al. (2008)	1	1	1	1	0	0.5	1	1	1	0	1	1	1	1	1	1	0.84
13	Person et al. (2019)	1	1	0	1	0	0.5	0	0	0.5	0	1	1	1	1	1	1	0.63
14	Rosenberg & Park (2002)	1	1	1	1	0	0.5	0	0	1	0	0.5	1	0	1	1	1	0.63
15	Vranić & Hromatko (2008)	1	1	1	1	0	0.5	0	1	1	0	0	1	1	1	1	0	0.66
16	Wharton et al. (2008)	1	1	0	1	1	1	0	0.5	1	1	1	1	1	1	1	0	0.78



Figure 2. Quality assessment criteria of all the studies.

found in the articles we reviewed. The full list of study quality evaluation criteria is available in ESM 1. If one of these criteria was mentioned but not controlled for, then it was given a score of 0.5. The final score is based on the mean of the 16 criteria. The closer the final score is to 1, the higher the quality of the study. The included items cover: participants’ characteristics, OC-specific questions, study design, statistics, and ethics. The studies obtained scores between 0.5 and 0.88. None of the included studies met all the quality criteria. Three authors independently conducted the quality assessment and disagreements were discussed until consensus was reached.

Analytical Plan

The analyses were conducted in R language for statistical computing (R Core Team, 2021) using metaphor (Viechtbauer, 2010) and tidyverse packages (Wickham et al., 2019). In total, the database included 70 effect sizes of differences between the groups of OC users and NC women in executive function tests gathered from 16 studies. Prior to the analysis, the group differences in reaction times and errors were reversed so their interpretation would correspond to the between-group differences in accuracy. The random effects multivariate meta-analytical model was run using a restricted maximum likelihood method to calculate the overall effect size. The multivariate meta-analysis models jointly the effects from each study and account for their dependence. We then checked outliers using standardized residuals of correlations and the Cook’s distance (Cook, 2011) which is a commonly used estimate of the influence of a data point when performing a regression analysis.

The Cook’s plot revealed that the database included four outlying effects. Therefore, we created a new data frame with outliers removed and re-ran the main meta-analytic model.

Results

The oldest study was from 2002 and the most recent one was from 2022. As can be seen in the Appendix, out of 16 studies included in the meta-analysis, 14 used a group comparison study design, one used pre-post stress intervention where we chose only the pre-intervention group results, and one used RCT (pre-post treatment) with placebo versus OC groups. Regarding study samples, in 10 studies participants were college or university students (one of the studies included also working professionals and two community volunteers), in one study the participants were women from the Department of Psychology, in another one, women from a Brain Imaging database, and 3 studies did not provide information on the participants’ characteristics. The total number of participants included in the meta-analysis was $N = 1,182$ with 594 cycling naturally and 588 taking OC. Some studies had different numbers of participants in each cognitive task, we are here referring to the highest number of participants present in the 16 studies taken together. The average sample size was $n = 32.33$ for OC users and $n = 31.34$ for NC women with ranges going from 8 to 144 participants per study. The age range of participants in all the studies taken together was between 18 for the youngest participant and 50 years old for the oldest participant. Only 10 studies provided a mean age for their

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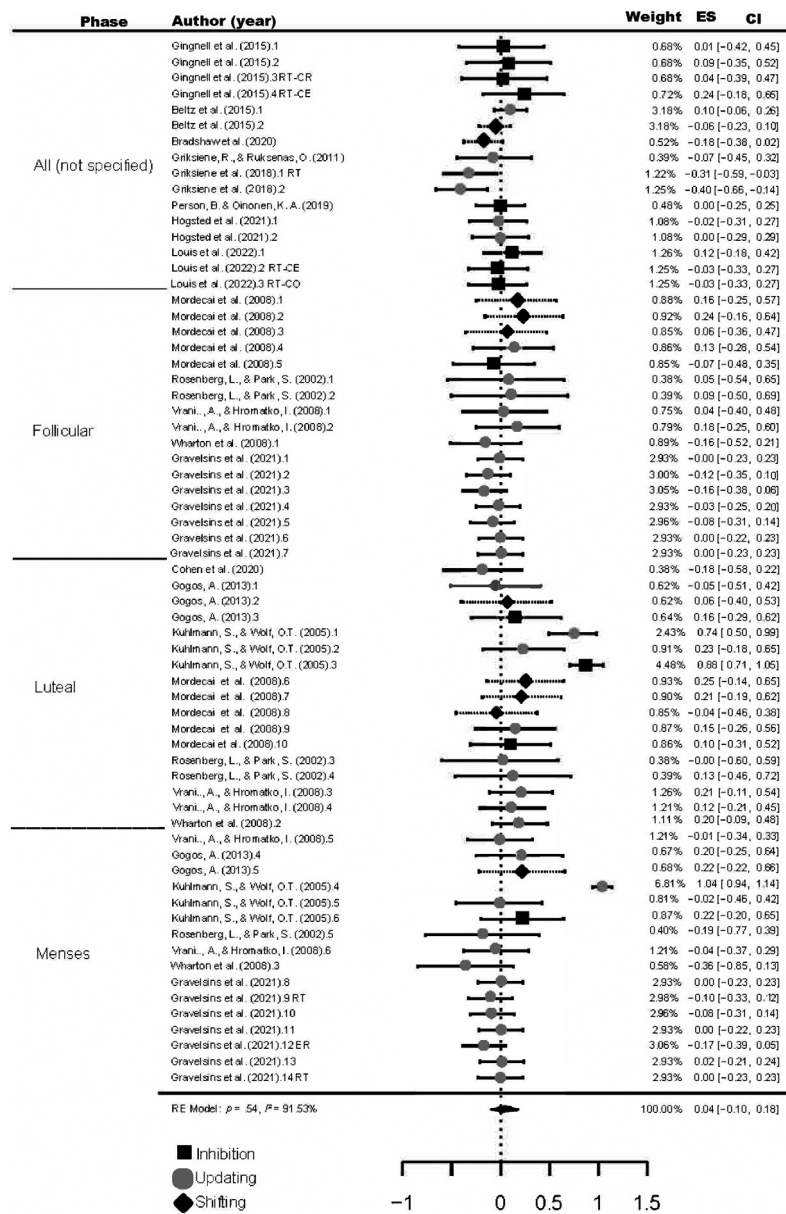


Figure 3. The random effects model multivariate meta-analysis of the difference between oral contraceptive users and naturally cycling groups in executive functioning. Types of executive functions are marked by different shapes. Effects are sorted by cycle phase. RT = reaction time. RT-CR = reaction time-correct response. RT-CO = reaction time-correct omission. RT-CE = reaction time-commission error. ER = error.

participants and the overall mean age of those 10 studies was $M = 21.97, SD = 2.28$. Most studies did not accept participants with mental illnesses, however, some studies did not indicate whether the participants were tested for them. Eight studies did not differentiate between cycle phases and one study tested participants only in the luteal phase. In 7 studies, cognitive task performances were compared between OC and NC groups in different cycle phases: menses, follicular and luteal phases in 3 studies, menses and follicular phases in one study, luteal and menses phases

in 2 studies, follicular, and luteal in one study. Only Mordecai et al. (2008) indicated randomizing the test sessions depending on the phases of the menstrual cycle whereas Gravelsins et al. (2021) counterbalanced the order of the sessions for both the OC and NC groups. Six studies tested for actual levels of hormones to ensure that the phases of the menstrual cycle were adequately defined and to compare levels of hormones between NC women and OC users. Those studies were too rare for us to be able to include this variable in the meta-analysis. Moreover, they did not use the

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same testing methods, some used salivary samples while others chose serum, making the results difficult to compare. Seven studies did not provide any information regarding the androgenicity of the OC taken by the participants, 2 studies had only androgenic OC users, 2 studies had only anti-androgenic OC users, 3 studies had both androgenic and anti-androgenic OC users and analyzed the results together while 2 studies had both androgenic and anti-androgenic OC users and analyzed them separately. Inhibition was measured in 7 studies, updating in 12 studies, and shifting in 5 studies.

Overall Effect

Starting from the main result of the meta-analysis, we calculated the effect size of the 66 comparisons in executive functions between the group taking OC and the group of NC women using a multivariate meta-analysis model. The more positive the value, the higher the advantage of the OC group. The overall result was not significant: $d = 0.044$, $SE = 0.0713$, 95% CI $[-0.0959, 0.1839]$, $z = 0.62$; $p = 0.54$. The descriptive statistics showed that the group taking OC tended to have higher accuracy in tasks measuring executive functions (56 effects, $M = 31.3$, $SD = 26.5$) than the group of NC women ($M = 28.6$, $SD = 22.4$), but the difference was not significant. Analogously, the OC women tended to make more errors and had longer RT ($M = 42.2$, $SD = 16.7$), than the NC group (6 effects, $M = 38.5$, $SD = 14.9$). The results of individual effect sizes are illustrated in the forest plot in Figure 3.

The analysis of the multiple moderator model was performed to verify which moderator affects the overall result and if the combination of moderators is influential. To this aim, we used the meta-CART method which provides Classification and Regression Trees (CART) in the meta-analysis (Li et al., 2020). The method identifies the interaction effects between influential moderators, partitions the studies into more homogeneous subgroups, and estimates the summary effect size in each subgroup. We fitted the random effects meta-CART model which did not detect any significant moderator or interaction between them. The overall random effect meta-analysis results were confirmed to be insignificant, $g = 0.05$, 95% CI $[-0.04, 0.16]$, $SE = 0.6$, $z = 1.13$, $p = 0.23$.

Heterogeneity

The heterogeneity was calculated with the I^2 statistic (Higgins & Thompson, 2002) for a standard random-effects model, and Cochran's Q test examined the heterogeneity of effect size estimates from the individual effects (Cochran, 1954; Lipsey & Wilson, 2001). There was a large

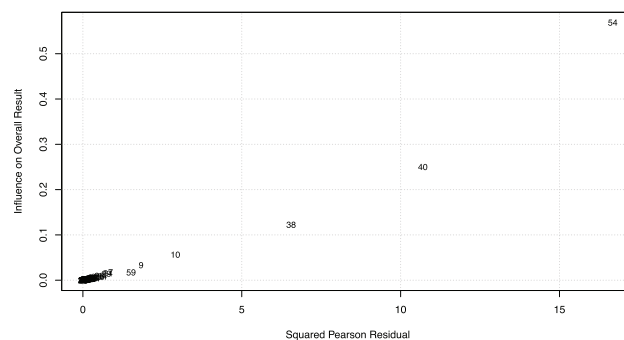


Figure 4. Baujat plot – numbers contribute to individual side effects. Most of the effects are located in the left corner as they had a similar impact on the result.

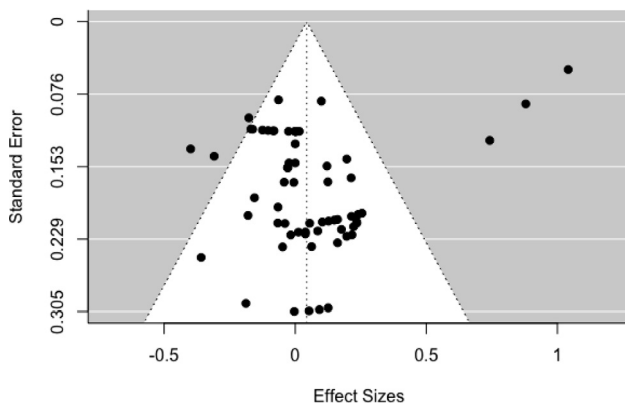
amount of heterogeneity in the calculated model: $I^2 = 77.41\%$; $Q(65) = 525.89$, $p < .001$. Baujat's diagnostics were then run to detect sources of this heterogeneity in meta-analytic data (Baujat et al., 2002). The Baujat plot shows the contribution of each individual effect to the overall Q -test statistic for heterogeneity on the horizontal axis versus the influence of each individual effect on the vertical axis. Therefore, effects that fell to the top right quadrant of the Baujat plot contributed the most to the overall heterogeneity and the overall effect size (see Figure 4). Such heterogeneity suggested that there might be meaningful differences among studies that can be further explored through moderator analyses. The moderator analyses also indicate the variables that contribute the most to the observed difference between the group taking OC and the group of NC women, lowering or increasing the overall effect size.

Moderators

We performed additional, separate moderation analyses to verify if the phase of the cycle (follicular, luteal, menses, or not specified) or the kind of executive function (inhibition, updating, shifting) had an influence on the overall outcome. The moderation analysis of the menstrual cycle phases was not significant, $QM(4) = 3.7139$, $p = 0.45$. The moderation effect of the executive functions was also not significant, $QM(2) = 0.4842$, $p = 0.78$. Separate meta-analyses were also conducted for each cycle phase and each executive function (inhibition, updating, and shifting). None of the separate meta-analyses were significant (see Table 1). We did not examine OC types as a moderator because only 9 out of the 16 studies reported this information. Among those 9 studies, 3 analyzed the results by grouping both OC types together and keeping only a distinction between OC users and NC women, 2 studies analyzed the results separately but did not provide the data in the article, and 4 studies tested only one type of OC (see Appendix).

Table 1. The separate meta-analyses results for all cognitive functions and phases.

	β	SE	95% CI	z	p
Phases					
All	-.06	0.05	[-0.16, 0.05]	-1.07	0.29
Follicular	-.01	0.05	[-0.10, 0.10]	-0.05	0.96
Luteal	.20	0.12	[-0.03, 0.43]	1.69	0.09
Menses	.12	0.20	[-0.27, 0.51]	0.62	0.54
Cognitive functions					
Updating	.06	0.10	[-0.12, 0.25]	0.66	0.55
Shifting	.01	0.08	[-0.16, 0.16]	0.03	0.97
Inhibition	.16	0.12	[-0.07, 0.39]	1.37	0.17

**Figure 5.** The funnel plot with trim fill correction estimates missing studies and adds missing studies to plot. The dashed lines that create a triangular area indicate the 95% confidence limits, and the vertical solid line represents the overall effect size.

Quality Assessment

The moderation effect of the quality of the studies indicated a significant result, $QM(8) = 41.4776$, $p < .01$. The moderation test showed that studies with relatively lower scores (0.63) significantly and positively moderated the observed effect size ($\beta = 1.0$, $SE = 0.35$, 95% CI [0.31, 1.70], $z = 2.83$, $p = .01$). It means that studies of a lower quality boosted the overall effect.

Publication Bias

We used two methods to assess potential publication bias: Egger's regression test (Egger et al., 1997) and the rank correlation for funnel plot asymmetry (Kendall, 1948). The funnel plot is shown in Figure 5. The rank correlation test for funnel plot asymmetry did not indicate a significant result, Kendall's $\tau = 0.319$, $p = .21$. Similarly, the regression test for funnel plot asymmetry with a standard error ($\beta = .21$, $z = -0.76$, $p = .45$) and sample variance ($\beta = .14$, $z = -0.57$, $p = .57$) as predictors showed that there was no significant effect on the summary estimate. Similarly, the age

of participants and year of publication did not influence publication bias. Taken together, the analyses showed that neither the sample size nor the standard error may have contributed to a risk of publication bias. In the end, the analysis for funnel plot asymmetry was conducted with study quality as a predictor. The results showed that the quality of the studies did not influence the asymmetry of the funnel plot ($z = -0.99$, $p = .32$).

Discussion

To our knowledge, this is the first meta-analysis examining the relationship between the use of OC and executive functions. The goal was to compare the executive functioning of women taking OC and NC women on three executive functions, namely inhibition (control of attention), updating (working memory), and shifting (cognitive flexibility). Additionally, we tested three potential moderators of this difference: the cycle phases of NC women, the types of executive functions measured, and the quality of the studies. Sixteen articles were included in the meta-analysis after the literature retrieval and screening, yielding 70 effect sizes. After excluding the four outliers, our analysis did not show a significant effect size, indicating no difference between OC users and NC women on core executive functions. It should be underlined that the analysis found a high amount of heterogeneity of effect-size estimates from the individual studies which might reflect a high level of methodological diversity. These results showing a high heterogeneity of methods are consistent with literature reviews published previously on the topic. Gogos et al. (2014) showed that results vary among different studies and that wide discrepancies can be observed between them, regarding the cycle phases or the cognitive tasks that were tested. Warren et al. (2014) underlined that the literature on the topic is inconsistent and that the methodology should be improved. Laird et al. (2019) concluded that there is a lack of literature on the effects of OC on executive functions and that the

available literature presents methodological limitations, sporadically showing a link between the variables, and only when controlling for the androgenicity of OC. Finally, Beltz (2022) also emphasized that there is too much heterogeneity in the methods used by the different studies. By gathering data from previous studies published on the topic of OC and executive functions, our meta-analysis offers a quantitative review of the contradictory results previously explored only in qualitative reviews. Moreover, none of the reviews published on the topic considered the quality of the articles. Our overall analysis indicates no difference in core executive functions performance between OC users and NC women, which is an important indication for practitioners prescribing OC and women wishing to take them, but the heterogeneity of the results raises the question of the necessity to create guidelines for future studies in this field.

We further explored the heterogeneity of our results through the analysis of moderators. We first tested the cycle phases of NC women as a potential moderator since they were often cited as having an impact on the results of cognitive tasks. For instance, Rosenberg and Park (2002) and Vranić and Hromatko (2008) found that updating was improved in NC women during periods of high estrogen levels (the follicular and the mid-luteal phases) while Gogos (2013) showed that OC users performed better on updating and inhibition tasks but only when compared to NC women in their luteal phase. During the periods of active pill use, the levels of estradiol and progesterone in OC users are similar to the levels of NC women in their menses phase (Elliott-Sale et al., 2013) and overall, OC users tend to have lower levels of estradiol and progesterone than NC women (Hampson, 2020). The differences found by Rosenberg and Park (2002), Vranić and Hromatko (2008), and Gogos (2013) might have been explained by the fact that NC women in their follicular and luteal phases have higher levels of hormones than OC users. However, our analysis of cycle phases as a moderator showed that there was no difference between OC users and NC women, no matter which phase of the menstrual cycle the NC women were in.

The second moderator we analyzed was the type of executive functions tested for. The latest review by Beltz (2022) showed that OC users have significantly different results than NC women on updating tasks, however, those results are contradictory, with some studies showing an improved performance for OC users and some studies showing an impaired performance. Shifting performance also demonstrated different results depending on the study and the OC type: the literature review by Laird et al. (2019) did not find any differences in performances between OC users and NC women but the study by Griksiene and Ruksenas (2011) indicated that the higher the androgenicity of the

OC the lower the performance on a shifting task. Regarding inhibition, in previous literature reviews, Gogos et al. (2014) showed that OC users performed better than NC women, however, the review by Warren et al. (2014) indicated that the results were contradictory depending on the study. Finally, the most recent review by Beltz (2022) refers to the RCT conducted by Gingnell et al. (2016) which showed that women who were given androgenic OC improved their results on a response inhibition task compared to the placebo group. Our analysis of executive function types shows no difference between OC users and NC women, no matter the type of executive function tested for. We also conducted a separate meta-analysis for each cycle phase and executive function type and found no difference between OC users and NC women.

The last moderator we analyzed was the quality of the studies, which showed that the studies with a lower methodological quality strengthened the differences between the groups. This result is similar to the reviews on the link between the menstrual cycle phases and executive functions which concluded that the studies with the most robust methodologies did not show any differences in executive functions between phases (Le et al., 2020; Sundström-Poromaa, 2018). This finding indicates a need to homogenize methods when conducting studies comparing the executive functions of OC users and NC women.

Limitations

The limitations of our meta-analysis are similar to the ones underlined by the previous literature reviews on the topic of the link between OC and executive functions. The meta-analysis shows a high level of heterogeneity due to the methodological limitations of the studies, including the differences in sample sizes and in tasks used as well as the lack of distinction between OC types. Moreover, only studies published after 2000 were taken into consideration which limits the scope of our meta-analysis. We also did not include studies that did not compare groups of NC women with OC users: studies that tested only one of those groups on executive functions or studies that compared one of those groups with men were excluded. These choices might have impacted the overall results of our meta-analysis.

However, contrary to the qualitative reviews already published on the topic, we were able to quantitatively compare the results of previous studies and the methodological qualities of those studies. This allowed us to find that the quality of the studies is a moderator and that a lower methodological quality is linked with a larger difference between the NC women group and the OC users group on tests examining inhibition, updating, and shifting.

Conclusion

Overall, the results of our meta-analysis reinforce the conclusions of previous literature reviews. Additionally, our study is the first to systematically search the literature and quantitatively compare the effect sizes of the previous studies while considering the moderators and quality of the studies. The research on the link between OC and executive functions is inconsistent and presents many differences in methodologies. Future research on this topic should include more replications and unified methods. It is difficult to obtain consistent results in studies on the topic of contraception and cognition as RCTs cannot be carried out easily due to ethical concerns. As a result, and as suggested by the latest literature review by Beltz (2022), studies could more often test women before they start taking OC and then again through the course of the treatment. Based on our observations, we underline that the following variables should always be tested for to provide a higher accuracy of results when studying the link between OC and executive functioning: the phases of the menstrual cycle in NC women, the types of OC, including their androgenicity, the phases of the OC and the actual hormonal levels. Reporting these data in studies will allow for testing these variables as moderators in a future meta-analysis.

Electronic Supplementary Materials

The electronic supplementary materials are available with the online version of the article at <https://doi.org/10.1027/1016-9040/a000514>

ESM 1. Quality assessment questions.

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Open Data

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Appendix

Table A1. Characteristics and key findings of studies evaluating the impact of OCs on executive functions

No.	Author	Study design	Type of sample	Androgenicity	Level of hormones	Age	Cycle phase	Measure	EF	Index	OC n	OC Mean (SD)	NC n	NC Mean (SD)
1	Beltz et al. (2015)	Group comparison	Undergraduate students	Androgenic and anti-androgenic, analyzed together	No data	18–30 M = 19.28 SD = 1.30	All	Mental rotation	U	Accuracy	142	27.32 (6.37)	87	26.29 (6.46)
2	Bradshaw et al. (2020)	Group comparison	Undergraduate students	No information about androgenicity	No data	M = 20.24 SD = 2.86	All	Solvable anagram	S	Accuracy	63	0.17 (0.46)	86	0.34 (0.68)
3	Cohen et al. (2020)	Pre-post stress intervention	College students	Androgenic	Estradiol OC: 2.57 pg/ml (0.80) NC: 3.23 pg/ml (1.13) Progesterone OC: 20.48 pg/ml (17.82) NC: 136.12 pg/ml (177.14)	M = 24.47 SD = 2.63	Luteal	Mental rotation	U	Accuracy	20	7.24 (4.86)	17	8.58 (4.60)
4	Gingnell et al. (2016)	RCT (pre-post treatment) Placebo vs. OC	Healthy women with regular menstrual cycles (25–31 days)	Androgenic	No data	18–45	All	Go/no-go	I	CR CO RT-OR RT-OE	17	213.9 (31.2) 13.5 (5.4) 281 (56) 270 (55)	16	213.4 (19.6) 12.8 (5.1) 278 (42) 251 (47)
5	Gogos (2013)	Group comparison	Healthy participants	Androgenic and anti-androgenic, analyzed together	No data	20–43	Menses Luteal	RBANS visuospatial ab.	U	Accuracy	16	96 (11.5)	14	93 (15.7)
							Menses Luteal	RBANS language	S	Accuracy	16	96 (11.5) 110 (9.2)	13 14	97 (15.6) 105 (10.4)
							Menses Luteal	RBANS attention	I	Accuracy	16	110 (9.2) 108 (11.3)*	13 14	109 (11.6) 97 (17.9)*
6	Gravelsins et al. (2021)	Group comparison	University students and women recruited through community advertisement	Androgenic and anti-androgenic, analyzed together	No data	18–30	Menses Follicular Menses Follicular Menses Follicular Menses Follicular Menses Follicular Menses Follicular	N-back Digit span forward Digit span backward Digit ordering task AX-CPT	U U U U U U U U U U U U	Accuracy Accuracy Accuracy Errors Accuracy	57 720 (159.05) 695.5 (137.4) 672 (1.35) 6.88 (1.35) 5.34 (1.58) 5.35 (1.37) 10.7 (7.2) 10.7 (7.2)	62 720 (159.05) 726 (166.93) 6.72 (1.35) 6.88 (1.35) 5.34 (1.58) 5.41 (1.58) 12.8 (8.29) 11.7 (8.26)		

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Table A1. (Continued)

No.	Author	Study design	Type of sample	Androgenicity	Level of hormones	Age	Cycle phase	Measure	EF	Index	OC n	OC Mean (SD)	NC n	NC Mean (SD)
7	Griksiene & Ruksenas (2011)	Group comparison	Students	Androgenic and anti-androgenic, analyzed separately	Estradiol	20–44	All	Verbal fluency	S	Accuracy	22	73.5 (2)*	19	79.7 (3)*
								Mental rotation	U	RT	22	1,845 (41)*	20	1,730 (44)*
8	Griksiene et al. (2018)	Group comparison	University & students & working professionals	Anti-androgenic	Estradiol	M = 24.15 SD = 2.90	All	Mental rotation	U	RT	35	1,135 (261)	33	1,285 (335)
										Accuracy		68.6 (12.3)		76.3 (10.9)
9	Hegsted et al. (2021)	Group comparison	Women from the Center for Integrated Molecular Brain Imaging (CIMBI) database	Anti-androgenic	Estradiol	18–50	All	Letter number sequencing	U	Accuracy	25	12.5 (2.6)	53	12.6 (2.6)
								Symbol digit modalities test	U	Accuracy		68.2 (9.8)		68.2 (10)
10	Kuhlmann & Wolf (2005)	Group comparison	Students	No information about androgenicity	Estradiol	20–34	Menses	Digit span forward	U	Accuracy	20	9 (0.28)	13	8 (0.51)
												9 (0.28)		8.42 (0.54)
					Progesterone	M = 24.81 SD = 0.59	Luteal	Digit span backward	U	Accuracy	20	7.4 (0.31)	13	7.69 (0.41)
												7.4 (0.31)		7.28 (0.34)
					Progesterone	OC: 23.07 pg/ml (7.45)	Menses	d2 test of attention	I	Accuracy	20	194.3 (9.75)	13	171.23 (12.6)
												194.3 (9.75)		174 (11.83)

(Continued on next page)

Table A1. (Continued)

No.	Author	Study design	Type of sample	Androgenicity	Level of hormones	Age	Cycle phase	Measure	EF	Index	OC n	OC Mean (SD)	NC n	NC Mean (SD)
11	Louis et al. (2022)	Group comparison	Undergraduate students	No information about androgenicity	No data	18–21	All	Flankers task	I	Accuracy RT-CE	30	0.91 (0.04) 362.54 (32.41)	38	0.9 (0.06) 364.42 (50.04)
12	Mordecai et al. (2008)	Group comparison	No description	No information about androgenicity	Estradiol OC: M = 16.96 pg/ml (14.73) NC: M = 62.93 pg/ml (25.56) Progesterone OC: M = 0.55 pg/ ml (0.19) NC: M = 3.93 ng/ ml (2.74)	18–40 M = 24.93 SD = 5.28	Follicular Luteal	Verbal fluency (phon.) Verbal fluency (rhyme)	S S	Accuracy	20	28.4 (8.15) 28.4 (8.15) 17.3 (3.73)	16	26.5 (6.57) 25.25 (7.3) 15.88 (3.74)
13	Person & Oinonen (2019)	Group comparison	University students and community volunteers	No information about androgenicity	No data	16–35 M = 20.16 SD = 3.82	Follicular Luteal	Mental rotation	U	Accuracy	58	20.73 (10.3) 20.73 (10.3)	40	18.61 (11.11) 18.31 (10.46)
14	Rosenberg & Park (2002)	Group comparison	University students	No information about androgenicity	No data	M = 19.40 SD = 0.17	Follicular Luteal	Brief test of attention	I	Accuracy	10	17.9 (2.07) 17.9 (2.07)	8	18.11 (1.98) 17.58 (1.87)
15	Vranic & Hromatko (2008)	Group comparison	No description	No information about androgenicity	No data	M = 20.8 SD = 1.40	Menses Follicular Luteal	Verbal task Memory game 1	U U	Accuracy	27 27	81.2 (0.08) 78.8 (0.053) 66.8 (0.062) 81.2 (0.036) 82.9 (0.026) 77.9 (0.022)*	10 28 29	76.3 (0.093) 79.1 (0.089) 76.2 (0.105) 77.6 (0.039) 77.1 (0.046) 72.9 (0.039)*
16	Wharton et al. (2008)	Group comparison	Women from the Department of Psychology at the University	Androgenic and anti-androgenic, analyzed separately	No data	No data	Follicular Luteal	Memory game 2 Mental rotation	U U	Accuracy	27 27	–0.012 (0.796) –0.012 (0.796) –0.012 (0.796)	10 28 22	–0.23 (0.59) –0.17 (0.81) 0.048 (1) 20.52 (4.77) 22.34 (6)
							Menses				9	19.16 (5.36)	13	22.92 (7.25)

Note. Only analyzed measures are included. OC = oral contraceptive users; NC = naturally cycling women; I = Inhibition; U = Updating; S = Shifting; EF = Executive Function; CR = correct response; CO = correct omission; RT = reaction time; RT-CR = reaction time-correct response; RT-CO = reaction time-correct omission; RT-CE = reaction time-commission error; Accuracy = Performance accuracy; RBANS = The Repeatable Battery for the Assessment of Neuropsychological Status; (phon.) = phonemic; (ideat.) = ideational; * = outliers.

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I also declare that my estimated quantitative contribution to this article was 60%.


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I declare that the authors' contribution to the manuscript, according to the CRediT classification, comprised the following:

Melanie Kowalczyk: data curation, funding acquisition, investigation, project administration, writing – original draft, writing – review & editing.

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Differences in anxiety, worry, and perceived stress among naturally cycling women and oral contraceptives users: a cross-sectional study investigating the role of contraceptive types

Melanie Kowalczyk¹ · Monika Kornacka² · Zofia Kostrzewa¹ · Izabela Krejtz¹

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Abstract

The goal of our study was to test whether the types of OC affect the link between anxiety and its main maintenance factors: worry and perceived stress. Women are particularly at risk of being affected by excessive worrying, a core component of generalized anxiety disorder (GAD), and they are twice as likely as men to suffer from GAD. The literature suggests that gonadal hormones and types of oral contraceptives (OC) should be taken into account when exploring anxiety disorders in women, but the precise mechanism of this link remains understudied. We performed an observational cross-sectional study on a sample of 908 women, including 499 women naturally cycling (NC) and 409 taking OC (277 in the anti-androgenic group, 132 in the androgenic group). The participants filled in a battery of online questionnaires. Anxiety positively correlated with worry and perceived stress in the whole sample and in the three groups: androgenic OC, anti-androgenic OC, and NC. There was no significant difference between the groups on all the variables apart from the age of the participants. However, we found that women taking anti-androgenic OC had significantly higher levels of worry than NC women (after controlling for stress and age). The differences in OC types should be taken into account in future studies which might also lead to a better choice of OC based on women's individual needs.

Keywords Anxiety · Worry · Stress · Oral contraceptives · Menstrual cycle

Introduction

Generalized anxiety disorder has a prevalence of 4.5% worldwide (Stein et al. 2021). According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association 2013), GAD is manifested by excessive worry and anxiety about any given topic, a difficulty to control those worries and physical symptoms such as constant tiredness. GAD is related with higher levels of worry than any other anxiety disorder or psychiatric disorder (Olatunji et al. 2010). According to Borkovec et al. (1983), worry is defined as “a chain of thoughts and images, negatively affect laden and relatively uncontrollable” (p. 10). However, in the cognitive model of GAD (Wells 1999), worry can be seen as a positive coping

strategy as the person believes that worrying serves a protective function to anticipate potential future threats. These beliefs reduce distress in the short-term but do not solve it, and the repetition of this strategy only reinforces distress in the long run (Andrews et al. 2010). Women are particularly susceptible to being affected by excessive worrying (Lal et al. 2014), they are twice as likely as men to suffer from GAD (Howell et al. 2001), and they are more likely to develop comorbid disorders (Howell et al. 2001; McLean et al. 2011).

One of the factors affecting both anxiety levels and physical symptoms might be naturally occurring hormonal fluctuations since women's levels of estradiol and progesterone vary through the course of the menstrual cycle. Those hormonal fluctuations happen every month from women's teenage years to middle age, and their impact should be considered to understand the onset and maintenance of anxiety disorders. Moreover, women in their reproductive years are susceptible to using hormonal contraceptives which also might have an impact on their anxiety levels (Beltz 2022; Laird et al. 2019). To understand the link between hormones

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and anxiety, it is also necessary to take into account the main trait dispositions involved, according to the literature, in the maintenance of anxiety: worry, and perceived stress, which positively correlates with levels of anxiety (Mirón et al. 2019). According to the preponderant models of GAD, the cognitive-behavioral model (Dugas et al. 2005), the cognitive model (Wells 1999), and the metacognitive model of GAD (Wells 2005), pathological worry can cause GAD (Behar et al. 2009). Additionally, worry can also enhance and maintain the physiological and cognitive activation caused by stress, resulting in higher and perseverative anxiety (Brosschot et al. 2006). The aim of the present study was to test whether the types of OC affect the link between anxiety and its main maintenance factors: worry and perceived stress.

The menstrual cycle and the use of oral contraceptives

The menstrual cycle of women who cycle naturally usually lasts between 21 and 35 days and is divided into two parts: a follicular phase and a luteal phase (Fehring et al. 2006). The menstrual cycle starts with the first day of menstruation when both estradiol and progesterone levels are low. Menstruation is part of the follicular phase, which is characterized by low levels of progesterone and by levels of estradiol that continuously increase until reaching a peak level before ovulation. The luteal phase starts after ovulation and shows increasing levels of progesterone and a slight increase in estradiol, followed by a decrease of both hormones towards the end of the menstrual cycle (Abraham et al. 1972).

The use of OC is linked with a noticeable decrease in levels of estradiol and progesterone (Hampson 2020). During the periods of active pill use, the levels of these two hormones are similar to the levels of NC women at the beginning of their menstrual cycle (Elliott-Sale et al. 2013). Moreover, levels of testosterone, a form of androgen, are down by 50 to 60% in women taking OC compared to NC women (Hampson 2020). Combined OC usually contain ethinylestradiol and progestins, which can be androgenic or anti-androgenic. Androgenic progestins are derived from testosterone, while anti-androgenic progestins block androgen receptors (Raudrant and Rabe 2003). The androgenic OC slightly counteract the effects induced by the decreasing levels of testosterone in OC users, but the anti-androgenic OC reinforce them (Zimmerman et al. 2014). Androgenic and anti-androgenic progestins show differences in the brain structures of women taking them compared to NC women (Pletzer et al. 2015). For instance, androgenic progestins masculinize the brain activation patterns in spatial skills (Beltz 2022). Anti-androgenic progestins are often used, not only as a form of contraception, but also to stop

androgenization symptoms such as acne, hirsutism, or alopecia (Schindler 2013).

Considering the differential impact of the various types of OC on women's health, it seems crucial to take this distinction into account while studying women taking OC. First, because of the scale of the phenomenon, based on the data gathered by the United Nations (2019), 16% of women of reproductive age use OC worldwide, which make them the fourth most common contraceptive method, with the highest prevalence in Europe (17.8%). Second, the differential impact of the various types of OC might potentially explain the contradictory results presented in the literature linking anxiety to OC.

The link between hormones and anxiety

The literature is consistent on the fact that anxiety symptoms are related to women's levels of estrogen (Borrow and Handa 2017) and progesterone (Reynolds et al. 2018); however, this relation and its precise mechanism are still understudied. A literature review by Robakis et al. (2019) on the link between OC and mood concluded that OC use does not impact women's mood in a negative manner in the general population. A meta-analysis conducted by Motter (2019) in her thesis showed that OC use can sometimes even enhance mood. However, the literature review conducted by Laird et al. (2019) on the link between OC, mental disorders, and cognitive functions described a lack of consistency in the presented results. This lack of consistency might be due to the following limitations: a lack of distinction between different kinds of OC and a lack of studies on women suffering from anxiety symptoms. According to a review by Beltz (2022), most studies conducted on hormonal contraception also suffer from small sample sizes. This review underlined as well that women taking hormonal contraceptives are similar to women having experienced chronic stress in that they report the same levels of anxiety and their cortisol levels are similar, while they show a blunted acute stress response.

Objective

Taking into account the gap in the literature, i.e., the lack of comparison between the different kinds of OC, the aim of the present study was to test whether the types of OC affect the link between anxiety and its main maintenance factors: worry and perceived stress. In order to do so, we conducted an online cross-sectional study with a large sample. Our hypotheses were that (1) anxiety, worry, and stress are linked together; (2) the levels of anxiety differ between NC women and women taking OC, depending on the types of OC they are using; (3) there is a difference in the levels of worry and perceived stress between NC women and women taking OC, depending on the types of OC they are using.

Methods

Participants

In total, 1289 women participated in the study. 908 of them were included with 499 cycling naturally and 409 taking OC. The OC users were further classified according to the androgenicity of their OC (Mathur et al. 2008; Raudrant and Rabe 2003): 277 participants for the anti-androgenic group and 132 for the androgenic group. The inclusion criteria for participants in the study were as follows: being between 18 and 45 years of age, speaking Polish, taking OC or being NC. The exclusion criteria were as follows: using other forms of hormonal contraception (Pahnke et al. 2019), using a copper intrauterine device, having undergone sterilization, having stopped taking OC in the past 6 months (Hidalgo-Lopez and Pletzer 2017), being pregnant or breastfeeding (Welz et al. 2016). We did not consider the phases of the menstrual cycle or the phases of the OC (active/inactive). In order to determine the sample size for a fixed effects ANOVA, a power analysis was conducted using G*Power (Faul et al. 2007). With a medium effect size of .25, the results of the power analysis showed that a minimum of 252 participants (84 participants per group) would be needed to achieve an appropriate power level for this study.

Materials

We used the GAD-7 Scale (Spitzer et al. 2006), the Penn State Worry Questionnaire (PSWQ; Meyer et al. 1990), and the Perceived Stress Scale (PSS; Cohen et al. 1983). The GAD-7 is a 7-item scale used to screen for GAD by measuring levels of anxiety. The participants reply to the question “Over the last 2 weeks, how often have you been bothered by the following problems?” regarding different symptoms related to GAD such as “Feeling nervous, anxious, or on edge” and using a scale from 0 (“not at all”) to 3 (“nearly every day”). The Cronbach alpha in our study was $\alpha = .91$, which indicated a high internal consistency.

The PSWQ is composed of 16 items measuring trait levels of worry. The instructions for this questionnaire are as follows: “Rate each of the following statements on a scale of 1 (“not at all typical of me”) to 5 (“very typical of me”). An example of an item from the scale is as follows: “Many situations make me worry.” The Cronbach alpha was high ($\alpha = .91$).

The PSS is a 10-item questionnaire and is the most widely used psychological instrument for measuring the perception of stress. The instructions indicate that the questions are referring to the participants’ feelings and

thoughts in the last month and that the participants have to express how often they felt or thought a certain way on a scale from 0 (“never”) to 4 (“very often”). The Cronbach alpha was high ($\alpha = .89$).

Procedure

The participants were recruited via an advertisement posted on social media, which invited them to join a scientific study aiming at examining the link between the menstrual cycle and anxiety in women who take OC and women who cycle naturally. The advertisement presented a description of the study and the necessary criteria to take part in it. The participants who accepted to take part in the study provided informed consent and filled in a battery of questionnaires online. The data were collected between February and November 2022. All the questionnaires were presented in their Polish version. The participants did not receive any compensation for taking part in the study. The study was conducted in compliance with the Helsinki Declaration, and the research protocol was approved by the Ethics Committee of our institution. This study is part of a larger study whose results will be published separately.

Results

Our analyses took on the following structure: first, a one-way ANOVA with group (NC, androgenic-OC, anti-OC) as a between-subjects factor was run for age. There was a significant difference in age between the groups, $F(2,905) = 19.47$, $p < .001$. Post hoc comparisons showed that women taking anti-androgenic OC were significantly younger than the NC women and the women taking androgenic OC. Table 2 presents the descriptive statistics for these comparisons. We then conducted a Pearson’s correlation test to examine the link between the variables. Afterwards, we conducted an ANCOVA in order to check whether there was a difference between groups related to the levels of worry with age and anxiety as covariates and then an ANCOVA with stress and age as covariates. The post hoc comparisons for the ANCOVA were adjusted with the Bonferroni correction. We used bootstrapping with 1000 samples to estimate the post hoc comparisons.

Relationship between anxiety, worry, and stress

We first conducted an examination of the correlations between the variables. As expected, anxiety correlated positively with worry and perceived stress in the general sample and in the three groups: androgenic OC, anti-androgenic OC, and NC. The correlation coefficient

values were transformed into z scores and compared for significance. There were no significant differences in correlation coefficients between groups.

Age correlated negatively with anxiety, worry, and stress in the general sample and in the androgenic OC group. In the anti-androgenic OC group and in the NC group, only worry correlated negatively with age. There was a significant difference in correlation coefficients between the androgenic OC group and the anti-androgenic OC group ($z = -2.12, p = .03$), and between the androgenic OC group and the NC group ($z = -2.60, p = .009$): the correlation was the highest in the androgenic group. The correlations are shown in Table 1.

Differences in levels of anxiety, worry, and stress between groups

In order to check whether there was a difference between groups related to the levels of anxiety, worry, and stress of the participants, we conducted an ANCOVA separately for each variable, and age was added as a covariate in each of the analyses. The analysis did not support any differences between groups in anxiety levels, $F(2, 904) = 1.81, p = .165$, worry, $F(2, 904) = 1.15, p = .318$, or perceived stress, $F(2, 904) = 1.58, p = .207$. Table 2 presents the descriptive statistics for these comparisons.

Differences in worry levels between groups with anxiety, stress, and age as covariates

In order to check whether there was a difference in worry levels between groups related to the levels of anxiety and stress of the participants, we conducted an ANCOVA with anxiety, stress, and age as covariates. After controlling for the levels of anxiety and age, the difference in the levels of worry between groups was not significant, $F(2, 903) = 1.18, p = .307$. However, after controlling for the levels of stress and age, a significant difference in levels of worry between groups emerged, $F(2, 903) = 3.12, p = .045$. Post hoc analysis was conducted using the bootstrapping procedure in order to obtain more accurate results. The post hoc analysis with 1000 bootstrapped samples indicated that women taking anti-androgenic OC had significantly higher levels of worry ($M = 56.62, SD = 13.75$) than NC women ($M = 54.64, SD = 14.01$) ($p = .023$).

Discussion

In this large cross-sectional study, we examined whether women taking different types of OC and NC women differ in their levels of anxiety and its main maintenance factors: worry and perceived stress. We found no differences between groups on all the measures. We did find a significant difference between the groups in age, with the anti-androgenic

Table 1 Pearson’s correlation coefficients

	General sample (<i>n</i> = 908)	Androgenic OC (<i>n</i> = 132)	Anti-androgenic OC (<i>n</i> = 277)	NC (<i>n</i> = 499)
Anxiety				
Worry	.58**	.65**	.55**	.59**
Perceived stress	.68**	.69**	.69**	.67**
Age	-.10**	-.34**	-0.03	-0.08
Worry				
Perceived stress	.70**	.71**	.71**	.69**
Age	-.21**	-.40**	-.19**	-.16**
Perceived stress				
Age	-.09**	-.34**	-0.03	-0.05

Correlation is significant with ** $p < .01$

Table 2 Descriptive statistics

	General sample (<i>N</i> = 908)		Androgenic OC (<i>n</i> = 132)		Anti-androgenic OC (<i>n</i> = 277)		NC (<i>n</i> = 499)	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Age	28.54	6.66	28.89	6.84	26.52	5.92	29.56	6.77
Anxiety	7.06	4.69	6.42	4.61	7.09	4.63	7.21	4.74
Worry	55.06	13.96	53.39	13.97	56.62	13.75	54.64	14.01
Perceived stress	21.47	7.12	20.87	7.84	21.26	7.16	21.75	6.89

OC group being younger than the androgenic OC group and the NC group. After controlling for age and levels of stress, we discovered that women taking anti-androgenic OC had higher levels of worry than women NC women. Nevertheless, a conservative conclusion should be made until the finding is replicated in another independent sample.

According to the literature, hormonal contraceptives in general moderate the association between worry and an enlarged error-related negativity (Louis et al. 2022). The error-related negativity is an electrophysiological marker appearing in the brain after an error in a cognitive task and is strongly related to anxiety, especially in women. Still, according to Louis et al. (2022), the association between worry and the enlarged error-related negativity was strong and only existed in hormonal contraceptive users but not in NC women. Our findings are consistent with Louis et al. (2022) in the sense that hormonal contraception is associated with levels of worry. We know from the literature that women are more likely to be affected by excessive worry than men (Lal et al. 2014). This might explain why anti-androgenic OC, which reduce the levels of male hormones, are linked with higher levels of worry. However, the latest literature review by Hampson (2023) underlines that the association between ethinylestradiol and certain progestins might also have an impact on neurotransmitters such as serotonin or dopamine in rats, which could also explain the difference between the levels of worry in androgenic and anti-androgenic OC users.

Future studies

Our study followed the recommendations of previous literature reviews which underlined the necessity for large sample sizes in studies related to the link between hormonal contraception and anxiety (Beltz 2022), and the need to analyze the results according to the different types of OC (Laird et al. 2019). Both literature reviews noted that the results of previous studies were inconsistent which might have been due to the fact that the different types of OC were not taken into account. In our study, we can see that there is a significant difference in levels of worry between the groups taking anti-androgenic and androgenic OC. Previous studies might have missed these differences in their results if they grouped all the OC users together. Future studies on the link between anxiety and OC should take into account the differences between OC types in order to provide the most accurate results. The review by Hampson (2023) also underlines the need to compare OC types based on their ethinylestradiol levels and to update older findings about the impact of the association between ethinylestradiol and different types of progestins on neurotransmitters.

Moreover, the literature review by Robakis et al. (2019) and the meta-analysis by Motter (2019) showed that OC use is not

linked with a decrease in mood in healthy women but the literature reviews by Laird et al. (2019) and Beltz (2022) concluded that the results are not consistent for women suffering from an anxiety disorder. Future studies should be conducted on women having obtained an actual diagnosis for an anxiety disorder in order to be able to compare them to healthy women. If a link was found between the use of OC, especially anti-androgenic OC, and anxiety disorders, then the prescription of OC should be made according to the individual needs of women and taking into account their risk of developing GAD.

Welz et al. (2016) underlined that studies on the menstrual cycle are often performed with a cross-sectional design and would benefit from using ambulatory assessments to better understand the differences between the phases of the menstrual cycle and the daily changes in women's affect. Indeed, an intensive repeated-measures design would allow a more detailed analysis of the differences between the groups and to control for the different phases of the menstrual cycle in NC women in their daily functioning. Welz et al. (2016) used ecological momentary assessment to perform this kind of study, and more studies with this methodology are warranted.

The review by Laird et al. (2019) underlined the need to conduct more studies that would check the actual levels of hormones at least once in each phase, both in OC users (active/inactive pill phase) and in NC women (menstrual cycle phases), in order to obtain the most accurate results and comparisons between both groups. However, the most accurate results could be obtained when testing the OC users before and after they have started taking OC in order to account for changes directly induced by the treatment, such as in Gingnell et al. (2016).

The limitations of our study were the cross-sectional design which does not allow us to draw any causal conclusions, the use of self-report measures which might not always offer the best accuracy, and the recruitment method (social media) which is linked with a selection bias and does not allow to generalize the results to the whole population. Other limitations present in our study were the lack of the following: participants who had an actual anxiety disorder diagnosis, testing for hormonal levels, verifying whether the participants were taking the OC for contraceptive or gynecological reasons, comparing the different dosages of ethinylestradiol in the OC and analyzing the results depending on the menstrual cycle phase. Our research project includes future studies that will take into account those variables in a daily diary study and a laboratory study.

Conclusion

To conclude, the main contribution of the present large-sample correlational study on women taking OC and NC is twofold. First, we demonstrated that there is a link between

oral contraception and worry levels. Second, by differentiating between OC types, and controlling for anxiety and stress perception, we observed that women taking anti-androgenic OC presented higher levels of worry than NC women. As a result, we suggest that controlling for OC type is a significant factor potentially responsible for the observed inconsistencies in the literature. We also underline that worry is an important risk factor for developing anxiety, and it should be monitored, particularly in women taking anti-androgenic OC.

Author contribution All authors approved the final manuscript. IK, MoK, and MeK conceptualized the study. The funding was acquired by IK and MeK. The materials were prepared by MeK and ZK. The data was collected by MeK and analyzed by all the authors. The first draft was written by MeK and ZK and subsequently reviewed by IK and MoK. IK provided supervision over the whole study.

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Data Availability The data that support the findings of this study are available from the corresponding author, upon request.

Declarations

Ethics approval and consent to participate The study was conducted in compliance with the Helsinki Declaration. All the participants provided informed consent. The research protocol was approved by the Ethics Committee of our institution (decision n°55/2020/2).

Conflict of interest The authors declare no competing interests.

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Melanie Kowalczyk: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, writing – review & editing, visualization, project administration, funding acquisition.

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Anxiety and inhibitory control in women cycling naturally and women taking oral contraceptives

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ABSTRACT

Elevated levels of anxiety are related to longer response times on tasks assessing inhibition, the ability to restrain automatic responses. The literature shows inconsistent results regarding the link between oral contraceptives (OC), anxiety, and inhibition. The present project aimed to compare anxiety levels and inhibitory control towards emotional words, including those eliciting anxiety, in naturally cycling (NC) women and women taking OC containing androgenic progestins or OC containing anti-androgenic progestins. We present two studies: a cross-sectional study with 240 women and a daily diary study with 89 women. There was no difference in anxiety levels between OC users and NC women in both studies. The daily diary study showed a significant difference between groups with anti-androgenic OC users always having the longest response times. Future studies could focus on the link between the different components of OC and inhibitory control as it can be linked to anxiety symptoms in women.

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Introduction



Generalized anxiety disorder (GAD) has a prevalence of 4.5% worldwide (Stein et al., 2021). According to the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; American Psychiatric Association, 2013), GAD is manifested by excessive worry and anxiety about any given topic, a difficulty to control those worries and physical symptoms such as constant tiredness. Anxiety symptoms are linked with cognitive deficits, especially with different biases in memory, interpretation and attention (Eysenck & Holmes, 2020). At the same time, both naturally occurring hormonal fluctuations and hormonal contraception can affect anxiety levels and cognition in women (Beltz, 2022; Russman Block et al., 2023). Women are twice as likely as men to suffer from anxiety (Kessler et al., 2012), which underlines the necessity to study this disorder and its related factors, such as impairments in inhibitory control.


Anxiety and inhibition

According to the Attentional Control Theory by Eysenck and Derakshan (2011), impairments of attentional control are one of the crucial symptoms that lead to the development of anxiety disorders. Attentional control “refers to the ability to control attention voluntarily,

including the abilities to focus and shift attention” (Quigley et al., 2017, p. 742). Impairments in attentional control manifest as increased distractibility, lack of focus, impulsivity, and attentional fatigue (Sarter & Paolone, 2011). A meta-analysis conducted by Shi et al. (2019) confirmed the assumptions of the Attentional Control Theory that deficits in executive functioning in anxious individuals appear in inhibition and switching but not in updating because inhibition and switching involve greater attentional control. Inhibition, switching, and updating are executive functions; a set of top-down cognitive processes that regulate human behaviour (Diamond, 2013; Miyake & Friedman, 2012). According to Miyake and Friedman’s model (2012), inhibition refers to the ability to “deliberately inhibit dominant, automatic or prepotent responses” (p. 57). It is also related to the control of interference: selective attention and cognitive inhibition (Diamond, 2013). Inhibition is the most studied executive function in anxiety disorders, and research has shown that elevated levels of trait or state anxiety are related to slower response times in tasks capturing cognitive inhibition (Shi et al., 2019).

On the one hand, anxiety is linked to deficits in inhibition. Participants show longer response time in tasks measuring attentional control, such as the Emotional Stroop Task, the Go/No-Go task or visual search tasks,

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but without producing errors in accuracy (Shi et al., 2019). On the other hand, anxious individuals show attentional biases toward threatening stimuli. They tend to react faster than control groups to threat-related stimuli, for instance in the dot-probe task (Eysenck et al., 2007). According to the review by Van Bockstaele et al. (2014), “the relation between attentional bias and fear and anxiety is best described as a bidirectional, maintaining, or mutually reinforcing relation” (p. 682). Moreover, the meta-analysis by Hakamata et al. (2010) shows that Attention Bias Modification Treatment (ABMT) is a promising treatment for anxiety.

The Emotional Stroop task

The Emotional Stroop task (Williams et al., 1996) is derived from the classic version of the Stroop task (Stroop, 1935) and uses words that have either an emotional or a neutral valence. This task tests how much interference is produced by the meaning of a word by asking the participants to ignore its meaning and focus only on the colour the word is written in. It tests inhibition deficits towards emotional stimuli and has been used previously to study anxiety disorders (Mogg & Bradley, 2005). Indeed, according to Williams et al. (1996), participants have slower response times when presented with words whose meaning is related to their psychopathology. In Price et al. (2011), the group suffering from GAD needed more time to identify the colour of negative words compared to neutral ones. In studies where GAD-related words were introduced (Becker et al., 2001; Bradley et al., 1995) participants suffering from GAD showed greater interference with GAD-related words.

Anxiety, inhibition and female hormones

Menstrual cycle

Women are twice as likely as men to suffer from GAD, and they are more likely to develop comorbid disorders (Kessler et al., 2012). One of the factors related to both anxiety levels and cognition might be naturally occurring hormonal fluctuations (Russman Block et al., 2023), since women’s levels of estradiol and progesterone vary through the course of the menstrual cycle (Schmalenberger et al., 2021). The menstrual cycle of women who cycle naturally is divided into two parts: a follicular phase and a luteal phase (Fehring et al., 2006). As described by Schmalenberger et al. (2021), the menstrual cycle starts on the first day of menstruation when both estradiol and progesterone levels are low. Menstruation is part of the follicular phase, which is characterised by low levels of progesterone, while levels of estradiol continuously increase until they experience a strong peak

before ovulation. The luteal phase starts after ovulation and shows increasing levels of progesterone and estradiol until the mid-luteal phase during which there is a peak in progesterone and a mild peak in estradiol. Finally, menstruation is triggered by a decline in the levels of estradiol and progesterone.

Menstrual cycle and anxiety

Puberty and the menstrual cycle are considered triggers for the onset, recurrence and increase in symptoms of affective disorders (Altemus et al., 2014). A review conducted by Pinkerton et al. (2009) showed that the luteal phase has been linked with an exacerbation of numerous disorders, including anxiety disorders. The review by Green and Graham (2021) indicates that a decrease in progesterone and estradiol levels could be linked with an increase in anxiety symptoms. Reynolds et al. (2018) found higher levels of anxiety in women who have higher average progesterone levels during their entire cycle. Moreover, even non-anxious women report mental fatigue similar to women suffering from GAD in the mid-luteal phase of the cycle (Li et al., 2020).

Menstrual cycle and inhibition

Graham and Shin (2018) showed that estradiol levels were linked with women’s attentional bias to threat making them more avoidant when estradiol was lower, and more vigilant when estradiol was higher. Hatta and Nagaya (2009) observed that women’s response time in the Stroop task was slower during the luteal phase, when progesterone is higher, than during the menstrual phase, when progesterone is lower. On the other hand, Iriguchi et al. (2019), showed that women had better performances on the Stroop task during the menstrual phase, when both estrogen and progesterone levels are low, than during the ovulation phase when estrogen is at its highest level. Due to these inconsistencies, the link between the phases of the menstrual cycle and the Stroop task needs to be studied further. Associating a cross-sectional study with a repeated measures study permits the observation of day-to-day relationships between hormonal fluctuations, anxiety, and cognition.

Oral contraception

Combined OC usually contain ethinyl estradiol and progestins which can be androgenic or anti-androgenic (Beltz, 2022). Androgenic progestins are derived from testosterone while anti-androgenic progestins block androgen receptors (Raudrant & Rabe, 2003). According to Hampson (2020), the use of OC is linked with a decrease in levels of estradiol and progesterone. Additionally, levels of testosterone, a form of androgen,

are down by 50 to 60% in women taking OC compared to NC women (Hampson, 2020). The androgenic OC slightly counteract the effects induced by the decreasing levels of testosterone in OC users, but the anti-androgenic OC reinforce them (Zimmerman et al., 2014).

Hormonal contraception and anxiety

The literature reviews conducted by Laird et al. (2019), Beltz (2022), and Ciarcia and Huckins (2024) on the link between OC and mental disorders described a lack of consistency in the presented results. Laird et al. (2019), and Ciarcia and Huckins (2024) underlined a lack of studies on the link between GAD and OC use. One of the studies cited found that OC users were less likely to suffer from GAD (Cheslack-Postava et al., 2015). On the other hand, Beltz (2022) described an increase in anxiety symptoms associated with lowering estradiol levels. Since OC users have lower levels of estradiol than NC women (Hampson, 2020), we can hypothesise that OC users might have higher levels of anxiety. The review by Beltz (2022) pointed out that randomized control trials (RCTs) are rare in this field due to ethical concerns, which makes it more difficult to explore the topic as accurately as possible. However, an RCT conducted by Lundin et al. (2017) showed that anti-androgenic OC users experienced an increase in anxiety after starting the treatment, compared to the placebo group, over the span of three months of use. Another RCT conducted by Bengtsdotter et al. (2017) concluded that only women with an ongoing or previous anxiety disorder saw an increase in their symptoms after three months of treatment with an anti-androgenic OC. A study conducted by Kowalczyk et al. (2024) concluded that women taking anti-androgenic OC had significantly higher levels of worry than NC women, but there were no differences between groups in anxiety levels. The study by Kecer et al. (2024) did not find any difference in levels of anxiety between women taking anti-androgenic OC and NC women. In the study conducted by Masama et al. (2022), there was no difference in anxiety symptoms between women taking hormonal contraception and NC women.

Beltz (2022) underlines the necessity to conduct more intensive longitudinal studies to observe individual differences. Both reviews by Laird et al. (2019) and Beltz (2022) stressed the need to consider the different components of OC when conducting studies on anxiety levels and cognition in order to gather more accurate and consistent results.

Hormonal contraception and inhibition

The meta-analysis conducted by Kowalczyk et al. (2023) on the link between the menstrual cycle, OC and

executive functions concluded that there is no difference between OC users and NC women. However, there was a high amount of heterogeneity which indicated a need to homogenise methods when conducting studies comparing executive functions between those two groups. In an RCT conducted by Gingnell et al. (2016), women who performed a response inhibition task (a Go/No-Go task) before and after taking androgenic OC for 21 days showed an improvement in their performance, which was not observed in women from the placebo group. On the other hand, an RCT conducted by Scheuringer et al. (2020) found no difference in the emotional interference of healthy women taking anti-androgenic OC and the placebo group on an Emotional Stroop task with positive words or words related to anxiety. In a study conducted by Cicinelli et al. (2011), the use of anti-androgenic OC was linked with an improved performance on inhibition tasks. On the contrary, a study conducted by Garrett and Elder (1984) showed an impairment in inhibition in OC users compared to NC women. The lack of consensus in the literature on the link between hormonal contraception and inhibition indicates a need to explore this topic further.

Aim of the study

RCTs showed that anti-androgenic OC users might experience an increase in anxiety levels during their treatment (Lundin et al., 2017) and androgenic OC users might see an improvement in their performance in an inhibition task (Gingnell et al., 2016). Considering the gap in the literature, i.e. the lack of comparison between the different components of OC, and the need for more intensive longitudinal studies, the present two studies aimed to compare inhibitory control towards emotional words, including those eliciting anxiety, in NC women, women taking androgenic OC and women taking anti-androgenic OC. The first study is a cross-sectional study meant to assess the link between levels of anxiety and reaction times on an Emotional Stroop task (Smith & Waterman, 2003). The second study is a daily diary study aimed at checking daily levels of anxiety and daily reaction times on an Emotional Stroop task before comparing them between the phases of the menstrual cycle.

Study 1

We hypothesised that there would be differences in anxiety levels and reaction times between women taking OC and NC women, and that the higher the level of anxiety, the longer the reaction times on the Emotional Stroop task.

Material and methods

Participants

240 participants completed a questionnaire and an Emotional Stroop task online. 133 participants were naturally cycling (NC) and 107 were taking OC. The women using OC were further classified according to the androgenicity of their OC (Mathur et al., 2008; Raudrant & Rabe, 2003): 72 in the anti-androgenic group and 35 in the androgenic group. The different OC used by the participants are listed in Supplement 1.

The inclusion criteria for participants in the study were: being between 18 and 45 years of age ($M = 27.09$, $SD = 5.69$), speaking Polish, taking OC or cycling naturally. The exclusion criteria were: using other forms of hormonal contraception (Pahnke et al., 2019), using a copper intrauterine device, having undergone sterilisation, having stopped taking OC in the past 6 months (Hidalgo-Lopez & Pletzer, 2017), being pregnant or breastfeeding (Welz et al., 2016). To determine the sample size for a two-way mixed ANOVA with groups as a between-subjects factor and word categories as a within-subject factor, a power analysis was conducted using G*Power (Faul et al., 2007). We estimated the effect size based on the meta-analysis conducted by Kowalczyk et al. (2023) which compared women taking OC and women cycling naturally on different executive functions. The effect sizes for inhibition tasks ranged from -0.07 to 0.88 with a mean of $M = 0.13$. The results of the power analysis indicated that the required sample size to achieve 95% power for detecting a small effect size of 0.13 , at a significance criterion of $\alpha = .05$, was $N = 138$. Thus, the obtained sample size of $N = 240$ is adequate to test the study hypothesis.

The participants were recruited via an advertisement posted on social media, which invited them to take part in a scientific study aiming at examining the link between the menstrual cycle and anxiety in women who take OC and women who cycle naturally. The advertisement presented a description of the study and the necessary criteria to take part in it. The participants did not receive any compensation. The study was conducted in compliance with the Helsinki Declaration and the research protocol was approved by the Ethics Committee of our institution (decision n°55/2020/2).

Materials

The GAD-7. The GAD-7 (Spitzer et al., 2006) is a 7-item scale used to screen for GAD by measuring levels of anxiety. The participants have to reply to the question "Over the last 2 weeks, how often have you been bothered by the following problems?" regarding different symptoms related to GAD such as "Feeling nervous,

anxious, or on edge" and using a scale from 0 ("not at all") to 3 ("nearly every day"). The Cronbach alpha in our study was $\alpha = .86$, which indicated a high internal consistency. The scores on the scale can be between 0 and 21. The cut-off score indicating the possible presence of GAD is equal or superior to 10. In our sample, the minimum score was $min = 0$, and the maximum score was $max = 21$, with 57 participants (24% of the sample) showing scores equal to or above 10 ($M = 12.77$, $SD = 2.87$). The questionnaire was filled in on the Qualtrics platform (Qualtrics, Provo, UT).

The Emotional Stroop Task. We wanted to test the participants' inhibitory control towards emotional words, including those eliciting anxiety. We based our Stroop task on the Emotional Stroop Task with Keyboard Responses available on the Inquisit Web platform and modified from Smith and Waterman (2003). We prepared our version of the task on the Inquisit 5 software (Millisecond, Seattle, WA, USA). The task is composed of a practice block with 10 words ("one", "two", "three" ...) and five blocks of fear-related words, positive, negative, neutral and colour words. Each experimental block contained 40 words. The order in which the blocks and the words were presented were chosen randomly for each participant. To test for anxiety, we chose 40 words that had the highest mean in the fear category from the Nencki Affective Words List (NAWL; Riegel et al., 2015), the Polish adaptation of the Berlin Affective Word List-Reloaded (BAWL-R; Vö et al., 2009) which is used to study the affective properties of German words. For example, words used in the fear category were: "niebezpieczeństwo" ("danger"), "panika" ("panic") or "horror". Then, based on Ben-Haim et al. (2016), we matched the fear words with positive, negative, and neutral words. The positive words were taken from the happiness category (e.g.: "osiągnięcie" – "achievement", "przyjaciel" – "friend", "spokojny" – "calm"), the negative words from the anger, sadness and disgust categories (e.g.: "niesprawiedliwy" – "unfair", "obrzydzenie" – "disgust", "cmentarz" – "cemetery"), and the neutral words from the neutral word category in the NAWL (e.g.: "lokalizacja" – "localisation", "siadać" – "to sit down", "karafka" – "carafe"). The colour words were chosen randomly. Words were first matched based on their length in characters ($M = 7.61$; $SD = 1.63$), and then on their estimated frequency in the Polish language. If an exact match in frequency was not possible, we tried to balance the bias of frequency between all the words to have a mean of frequency as similar as possible between the fear list and the positive, negative and neutral words list. A one-way ANOVA was conducted to compare the words lists

and verify that they did not differ in frequency between each other. There was no significant difference between groups ($F(3,156) = 0.51, p = 0.68$).

During the task, participants saw a fixation cross appear for 500 milliseconds (ms) in the centre of the screen before each word. They were asked to ignore the meaning of the word and to indicate the colour of the font among four colours: blue, red, yellow and green. They had to press the right response key for each colour (d = red; f = green; j = blue; k = yellow), but the colours were not indicated on the keyboard. A wrong answer in the practice block was indicated by an "X" appearing in the centre of the screen after the word. The strength of the interference created by the meaning of the words was measured by the mean reaction time differences between the categories of words. The number of correct answers was not taken into account in our analysis since most of the participants gave correct answers, and there was a ceiling effect (out of 200 trials the mean of correct answers was $M = 194.50; SD = 13.79$). To identify outliers, Z-scores were calculated for all response times to find the number of standard deviations above and below the means for each value. The cut-off score for outliers is a Z-score under -3.29 or above 3.29 (Tabachnik & Fidell, 2013). As a result, 19 individual mean response times had to be deleted as they were outliers (in the fear category: 6 mean response times, negative: 4, positive: 3, neutral: 3, colour: 3).

Procedure

The participants who agreed to participate in the study provided informed consent and filled in a battery of questionnaires online on the Qualtrics platform, as a part of a larger study the results of which will be published separately. The questionnaires not presented in this article are the Perseverative Thinking Questionnaire (Ehring et al., 2011), the Penn State Worry Questionnaire (Meyer et al., 1990), the Perceived Stress Scale (Cohen et al., 1983) and the Self-Esteem Scale (Rosenberg, 1965). At the end of the questionnaires, the participants were invited to take the Emotional Stroop task on the Inquisit platform. Finally, after completing the Stroop task, they could express their willingness to participate in a future daily diary study.

Results

Relationship between anxiety and mean response times

We first conducted a Pearson's correlation test to examine the link between anxiety levels and mean response times in the Emotional Stroop task for the five blocks of words (anxiety, negative, positive, neutral, and colour words) in each group (NC,

androgenic-OC, anti-OC). Anxiety levels and mean response times in the Emotional Stroop task correlated positively for the words related to anxiety and the neutral ones in the general sample and the group of anti-androgenic OC users with correlations ranging from $r = 0.13$ to $r = 0.29$. We then conducted a Bonferroni correlation correction for multiple comparisons (Curtin & Schulz, 1998). We determined the new p -value by dividing the original one ($\alpha = 0.05$) by the number of comparisons (5). The new p -value necessary for the correlations to be significant was $p < 0.01$. As a result, the correlations were not significant anymore.

Differences in levels of anxiety and mean response times between groups

A one-way ANOVA with group (NC, androgenic-OC, anti-OC) as a between-subjects factor was run for anxiety levels. The analysis did not support any difference between the groups, $F(2, 237) = 0.08, p = 0.92, \eta^2 < 0.001$. A two-way mixed ANOVA with groups as a between-subjects factor and word categories as a within-subject factor was conducted to compare the mean response times for the five blocks of words. There was a significant main effect of words categories, $F(4, 916) = 40.92, p < 0.001, \eta^2 = 0.152$, with the colour words having the strongest interference. There was no significant effect for the groups, $F(2, 229) = 0.53, p = 0.59, \eta^2 = 0.005$, and no interaction, $F(8, 916) = 0.98, p = 0.45, \eta^2 = 0.009$. Table 1 presents the descriptive statistics for these comparisons. Most of the effect sizes were inferior to 0.01 which means they can be considered as small effect sizes (Cohen, 1988).

Study 2

The second study is a daily diary study aimed at checking daily levels of anxiety and reaction times on a daily administered Emotional Stroop task. The participants received financial compensation for participating in this study (around 50€). The study was conducted in compliance with the Helsinki Declaration, and the

Table 1. Descriptive statistics of the cross-sectional study for anxiety and reaction times (ms) in the Emotional Stroop Task.

	General sample ($N = 240$) M (SD)	A. OC ($n = 35$) M (SD)	Anti-a. OC ($n = 72$) M (SD)	NC ($n = 133$) M (SD)
Anxiety	6.83 (4.24)	6.92 (4.38)	6.69 (4.22)	6.92 (4.38)
Fear words	768 (189)	767(176)	776 (210)	767 (176)
Negative words	758 (187)	764 (189)	767 (189)	764 (189)
Positive words	769 (191)	792 (205)	746 (159)	792 (205)
Neutral words	750 (189)	749 (174)	765 (214)	749 (174)
Colour words	866 (224)	877 (229)	866 (223)	877 (229)

Note. A.: androgenic; Anti-a.: anti-androgenic.

research protocol was approved by the Ethics Committee of our institution (decision n°55/2020/2).

Material and methods

Participants

We invited 103 volunteers from the first study to take part in the daily diary study. The sample size was chosen based on Nežlek's (2012) and Welz et al. (2016) recommendations. Nežlek (2012) indicates that for a daily diary study lasting two weeks, the perfect sample size is around 100 participants. Welz noted that, due to the high drop-out rate in daily diary studies, there should be more than 60 participants in total. 14 participants dropped out of the study or had their results withdrawn due to potential unreliability or irregularity in their menstrual cycles. Participants who did not take part in the three phases of the diary were also eliminated. The final sample included 89 women (M age = 26.60, SD = 4.65) with 41 NC women and 48 taking OC. The women using OC were further classified according to the androgenicity of their OC (Mathur et al., 2008; Raudrant & Rabe, 2003): 32 in the anti-androgenic group and 16 in the androgenic group. The different OC taken by the participants are listed in Supplement 2. The groups did not significantly differ in terms of age ($t(71) = 0.70$, $p = 0.71$). The range of values obtained by the participants on the GAD-7 scale (Spitzer et al., 2006) were between $min = 0$ and $max = 21$. 18 participants (17% of the sample) had scores equal or superior to 10, which might indicate the presence of GAD ($M = 13.22$, $SD = 3.21$).

To be selected for the study, the NC participants needed to have regular menstrual cycles. According to Fehring et al. (2006), a regular menstrual cycle is of a duration between 21 and 35 days with less than 7 days of difference between cycles. However, to conduct the diary study, the participants needed to have cycles that lasted at least 28 days so that the phases did not overlap. If the participant indicated a regular menstrual cycle with a variability between 28 and 35 days, then the mean length of their menstrual cycle was calculated.

Materials

The daily diaries. Each participant was provided with her own individual menstrual cycle calendar which was calculated based on the date of her last menstruation onset and the usual length of her menstrual cycle. For the NC participants, the calendar was divided into 3 phases: an early follicular, a late follicular, and a late luteal phase. In each phase, the measures were taken for 5 consecutive days, which amounted to 15 days, as per Nežlek's method (2012). The early follicular phase

started on the first day of menstruation until the 5th day. While Hidalgo-Lopez and Pletzer (2017) started the menstruation phase on the second day of the cycle, we decided to extend it at the beginning to stay within the moment when both estrogen and progesterone are low, and before estrogen starts to rise during the follicular phase. The late follicular phase was calculated based on the expected ovulation which usually happens 14 days before the next menstruation (Fehring et al., 2006). In Hidalgo-Lopez and Pletzer (2017), the pre-ovulatory phase starts 3 days before ovulation, so we calculated the late follicular phase as spanning 5 days before the pre-ovulatory phase. Finally, the late luteal phase is usually stable and lasts 14 days (Fehring et al., 2006). As in Hidalgo-Lopez and Pletzer (2017) this phase was measured over a relatively long span (from 3 days post-ovulation to 3 days before the next menstruation), we based our calculations on Welz et al. (2016), who tested participants on the 6th and 5th day before the next menstruation. The late luteal phase in our study spans from the 9th to the 5th day before the next menstruation. For example, for a menstrual cycle of 28 days, the measured days were as follows: day 1–5 (early follicular), day 7–11 (late follicular), and day 20–25 (late luteal). The participants received commercially available ovulation tests (Horien Medical) which test for the LH surge in urine. These tests were carried out at home by the participants, who received an email at the end of the follicular phase asking them to test for ovulation for 10 days in a row and to provide experimenters with the date on which the test indicated an LH surge. If the ovulation test indicated a mismatch in the cycle phases, the dates of the phases were adjusted, and participants were offered the opportunity to take part in the study again the following month. This offer was repeated for a second month, but if their menstrual cycle presented too much variability in the span of 3 cycles, their results were excluded from the study.

The women taking OC were tested on the same days as the NC participants. The OC users had an average cycle length of 28 days and were tested on the same days as NC participants with a 28-day menstrual cycle. We did not separate the active and inactive pill phases as we chose to match the phases of the OC users to the phases of the NC women, to compare the results of the treatment group (OC) to the non-treatment group (NC), studied in parallel throughout a whole menstrual cycle. The first phase of OC users started the first day of withdrawal bleeding, which takes place in the inactive phase of OC (Rivlin & Davis, 2022). This first phase lasted for 5 days, during which OC users resumed their treatment (active phase). The second

phase was tested during the active phase (day 7–11). OC users in our study had a menstrual cycle of 28 days on average, which means that their withdrawal bleeding started between 4 and 7 days after their last pill intake, depending on whether they were taking 21 or 24-day OC. This indicates that the last phase (day 20–25) represented a mixture of active and inactive phases.

The daily measures were 3 items chosen from the GAD-7 scale used in study 1 (Spitzer et al., 2006) and adapted for daily administration. The main question was “How often today have you been bothered by the following problems?”. The items chosen from the GAD-7 were items 1 (“Feeling nervous, anxious or on edge”), 3 (“Worrying too much about different things”) and 7 (“Feeling afraid as if something awful might happen”). Participants provided answers ranging from 1 (“not at all”) to 7 (“a lot”).

The Emotional Stroop task. The Emotional Stroop task was the same as in the cross-sectional study with a practice block composed of 10 words (“one”, “two”, “three” ...) and five blocks of fear-related words, positive, negative, neutral, and colour words. Each experimental block contained 40 words. The order in which the blocks and the words were presented were chosen randomly for each participant. The task was performed online by the participants once a day for 5 consecutive days in the 3 phases of the menstrual cycle (early follicular, late follicular and, late luteal for the NC women and chronologically equivalent phases for the OC users) following the questions. Z-scores were calculated, and 31 individual mean response times had to be deleted as they were outliers (in the fear category: 14 mean response times, negative: 3, positive: 2, neutral: 1, colour: 11).

Procedure

Participants received a daily email at 8 pm during the 15 days of their individual menstrual cycle calendar. The email included a link to the electronic diary entry on the Qualtrics platform, which then redirected them to the Inquisit platform to perform a daily Emotional Stroop task. The results of participants who completed the diary the next day or later were not taken into account.

Results

The data represents a two-level structure. Level 1 variables (data collected through daily diary measures) were nested in participants (Level 2). The daily measures of anxiety and general mean response times on the Emotional Stroop task were separated into cycle phases (early follicular, late follicular, late luteal). Group

Table 2. Descriptive statistics of the daily diary study.

Daily Variable	Reliability	M(SD)	Level 2 variables (N = 89)	
			Between	Within
Anxiety	0.86	8.72(4.34)	6.50	12.49
Fear words	0.92	598 (150)	11214	11704
Negative words	0.91	597 (162)	12523	14457
Positive words	0.92	600 (161)	13111	13588
Neutral words	0.93	593 (150)	12257	10920
Colour words	0.95	633 (170)	17621	12430

Note. The means of the different categories of words correspond to the reaction times in ms.

types (anti-OC, androgenic OC, NC) were introduced at Level 2. The analyses were carried out in the HLM programme (Raudenbush et al., 2011). The number of measures collected for the 89 participants was $N = 1120$. In the first part of the analysis, we tested the reliability of the daily measures, which is the equivalent of Cronbach’s alpha in multilevel modelling. The reliability estimates for the scales that were used in the analyses are presented in Table 2. Then we ran an unconditional model for each of Level 1 variables with no predictors at Level 1 or Level 2 to estimate sources of variability, whether the variability related to days (Level 1) or participants (Level 2). This analysis allowed us to calculate the means of our daily variables, and the between- and within-person variances estimates. The example of the null model equation for anxiety levels is as follows:

$$\text{Level 1 (within – person): } \text{Anxiety}_{ij} = \beta_{0j} + r_{ij}$$

$$\text{Level 2 (between – person): } \beta_{0j} = \gamma_{00} + u_{0j}$$

Regarding the nomenclature, there were i days nested within j persons, β represents the mean (for j persons), the variance of r_{ij} represents the Level 1 (within-person) variance, γ_{00} represents the grand mean (the mean of β for each person), and the variance of u_{0j} represents the Level 2 (between-person) variance. The descriptive statistics are presented in Table 2. As can be observed, the variance within participants related to the day level is systematically larger than the between participants level, except for the reaction times for neutral and colour words in the Emotional Stroop Task, suggesting a higher variability of score due to differences between days rather than between participants.

Differences in anxiety levels between groups

To test the differences between the groups on anxiety levels in the different cycle phases, we used the following equation:

Level 1 (within person):

$$\text{Anxiety}_{ij} = \beta_{1j}(\text{Earlyfollicular}) + \beta_{2j}(\text{Latefollicular}) \\ + \beta_{3j}(\text{Lateluteal}) + r_{ij}$$

Level 2 (between person):

$$\beta_{1j} = \gamma_{10}(\text{androgenic}) + \gamma_{20}(\text{anti} - \text{androgenic}) \\ + \gamma_{30}(\text{NC}) + u_{1j}$$

$$\beta_{2j} = \gamma_{11}(\text{androgenic}) + \gamma_{21}(\text{anti} - \text{androgenic}) \\ + \gamma_{31}(\text{NC}) + u_{2j}$$

$$\beta_{3j} = \gamma_{12}(\text{androgenic}) + \gamma_{22}(\text{anti} - \text{androgenic}) \\ + \gamma_{32}(\text{NC}) + u_{3j}$$

The comparisons of anxiety levels in all groups and all menstrual cycle phases are presented in Table 3. Contrast analysis did not reveal any significant differences between groups on daily anxiety levels.

Differences in mean response times between groups

The same equation was used to test the differences between the groups on response times in the Emotional Stroop task in the different cycle phases. Response times from the daily Emotional Stroop Task showed a significant difference between groups for all the categories of words depending on the cycle phase, with anti-androgenic OC users always having the longest response times, while androgenic OC users tended to have the shortest response times, yet this did not reach a conventional statistical significance level. Regarding fear-related words (Figure 1), anti-androgenic OC users had significantly longer response times than androgenic OC users ($X^2(1) = 4.79$) in the second phase and the third phase ($X^2(1) = 9.48$). Anti-androgenic OC users also had significantly longer response times than NC women ($X^2(1) = 6.79$), in their late luteal phase. In the negative words category (Figure 2), anti-androgenic OC users had significantly longer response times than androgenic OC users in their second phase ($X^2(1) = 7.90$), and NC women ($X^2(1) = 8.85$), in their late follicular phase. Anti-androgenic OC users also had significantly longer response times than androgenic OC users in their third phase ($X^2(1) = 4.92$), and NC women ($X^2(1) = 4.11$), in their late luteal phase. Regarding positive words (Figure 3), anti-androgenic OC users had significantly longer response times than androgenic OC users in their third phase ($X^2(1) = 10.56$), and NC women ($X^2(1) = 8.66$) in their late luteal phase. For neutral words (Figure 4), anti-androgenic OC users had significantly longer response times than androgenic OC users in the first phase ($X^2(1) = 6.83$), the second phase ($X^2(1) = 5.74$), and the third phase ($X^2(1) = 8.74$). Anti-androgenic OC users also had longer response times than NC women ($X^2(1) = 6.25$) in their late luteal phase. Finally, in colour words (Figure 5), anti-androgenic OC users had significantly longer response times than androgenic OC users ($X^2(1) = 4.14$), in the second phase. Anti-androgenic OC users also had significantly longer response times than androgenic OC users in the third phase ($X^2(1) = 8.23$), and NC women ($X^2(1) = 7.20$), in their late luteal phase. For descriptive statistics and contrasts comparisons, see Table 3.

Our project aimed to compare anxiety levels and inhibitory control towards emotional words, including those eliciting anxiety, in NC women, and women taking OC

Discussion

Our project aimed to compare anxiety levels and inhibitory control towards emotional words, including those eliciting anxiety, in NC women, and women taking OC

Table 3. Comparison of Level 1 variables based on groups and menstrual cycle phases.

	Early follicular/first phase			Late follicular/second phase			Late luteal/third phase		
	A. OC	Anti-a. OC	NC	A. OC	Anti-a. OC	NC	A. OC	Anti-a. OC	NC
Anxiety									
Coeff.	9.36	8.90	8.22	9.15	8.65	8.58	9.74	8.60	8.60
SE	0.53	0.36	0.33	0.54	0.37	0.33	0.57	0.37	0.33
Fear words									
Coeff.	618	640	629	552*	600*	579	539**	610**	566**
SE	18	12	11	18	12	11	19	12	11
Negative words									
Coeff.	596	632	635	557**	624**	570**	547*	602*	565*
SE	19	13	12	19	13	12	20	13	12
Positive words									
Coeff.	595	636	626	566	597	582	548**	630**	575**
SE	19	13	12	19	13	12	21	13	12
Neutral words									
Coeff.	585**	643**	622	543*	596*	574	541**	609**	567**
SE	18	12	11	18	12	11	19	12	11
Colour words									
Coeff.	655	680	681	579*	630*	604	571**	646**	595**
SE	20	13	12	20	14	12	21	14	12

Note. Bold font indicates a significant difference between groups within each menstrual cycle phase; * $p < 0.05$; ** $p < 0.01$; A.: androgenic; Anti-a.: anti-androgenic; the coefficients are expressed in ms.

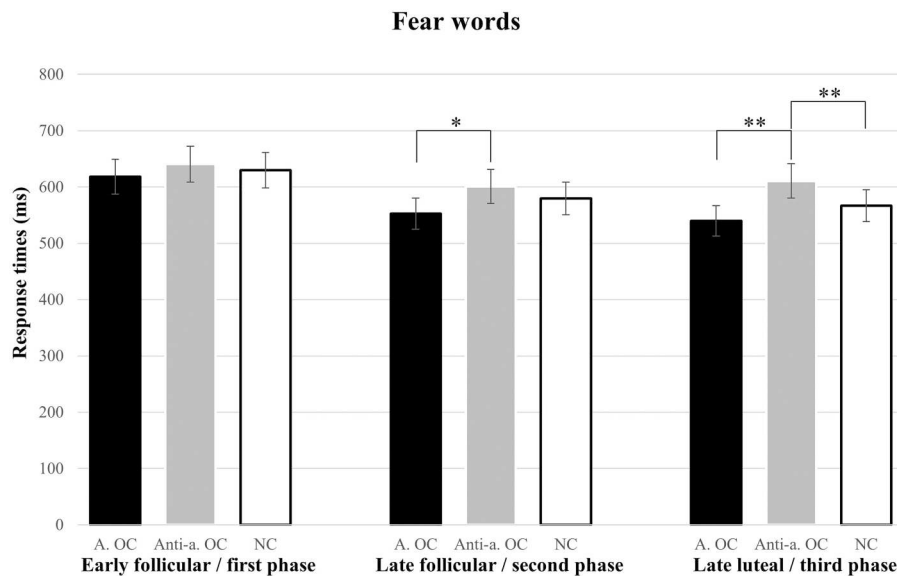


Figure 1. Comparison of response times for fear words based on groups and menstrual cycle phases. $*p < 0.05$; $**p < 0.01$; A.: androgenic; Anti-a: anti-androgenic. OC: oral contraceptives; NC: naturally cycling [To view this figure in colour, please see the online version of this journal].

containing androgenic progestins or OC containing anti-androgenic progestins. We conducted an observational study first (cross-sectional), and then a repeated measures study (daily diaries) enabling us to perform those comparisons in different phases of the menstrual cycle. We used the Emotional Stroop task in both studies to assess inhibitory control.

We did not find any significant difference in anxiety levels between NC women and women taking OC, whether in the cross-sectional study or the daily diary study, no matter the OC used or the menstrual cycle

phase. The RCT by Lundin et al. (2017) showed that women taking anti-androgenic OC saw an increase of anxiety levels during their treatment, compared to the placebo group. Another RCT conducted by Dokras et al. (2016) found that continuous use of androgenic OC resulted in a reduction in anxiety symptoms in women suffering from polycystic ovary syndrome. Our study was only observational and could not explore the direct impact of OC use on anxiety levels. However, our results are in line with previous studies which did not find a difference in anxiety levels

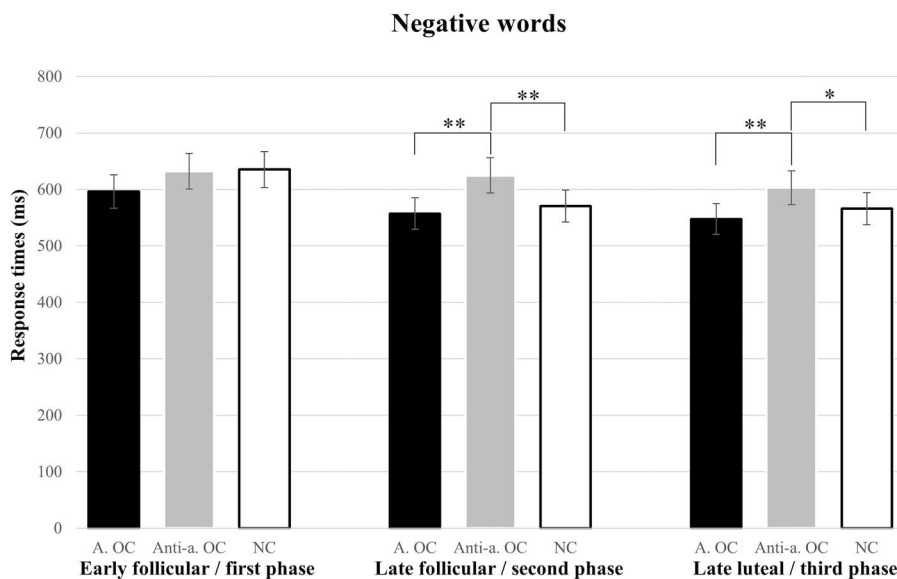


Figure 2. Comparison of response times for negative words based on groups and menstrual cycle phases. $*p < 0.05$; $**p < 0.01$; A.: androgenic; Anti-a: anti-androgenic. OC: oral contraceptives; NC: naturally cycling [To view this figure in colour, please see the online version of this journal].

between hormonal contraceptives users and NC women. Doornweerd et al. (2024) found no difference between NC women and OC users (androgenic and anti-androgenic grouped together) on the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983) and the Screen for Adult Anxiety Related Disorders (SCAARED; Angulo et al., 2017). Kecer et al. (2024) also did not find any differences on the STAI between NC women and anti-androgenic OC users. Kowalczyk et al. (2024) did not report any differences on the GAD-7 scale (Spitzer et al., 2006) between NC women, androgenic OC users and anti-androgenic OC users. Masama et al. (2022) did not find any differences in levels of anxiety tested with the Beck Anxiety Inventory (Beck et al., 1988) between NC women and women using varied forms of hormonal contraception, including OC. Finally, Zelionkaitė et al. (2024) did not report any differences between NC women and users of hormonal intrauterine devices on the GAD-7 scale, as well as between NC women and OC users (androgenic and anti-androgenic) on the same scale (2025).

In the cross-sectional study, there was a link between anxiety levels and mean response times in the Emotional Stroop task for the words related to anxiety and the neutral words, in the general sample, and in the group of anti-androgenic OC users: the higher the anxiety, the longer the mean response times in these categories. However, after conducting a correlation correction for multiple comparisons, the correlations were not significant anymore. According to the meta-analysis by Shi et al. (2019), anxiety is generally linked with longer response times toward non-emotional stimuli. Williams et al. (1996) indicated that slower response times are also observed when participants are tested on words that are related to their psychopathology. Our study's lack of correlation between anxiety levels and fear-related word processing may stem from the non-clinical characteristics of our sample. Although 17% to 23% of participants exhibited anxiety symptoms consistent with GAD, this cohort does not meet the criteria for a clinical population as the participants were not asked whether they had an actual anxiety disorder diagnosis, and they were not recruited in a clinical setting. Previous research indicates that cognitive impairments associated with anxiety may only be discernible in clinical samples (e.g. Adrover-Roig et al., 2023) and executive processes might appear differently in clinical and non-clinical samples (Eysenck & Derakshan, 2011; Majeed et al., 2023). Consequently, the relationship between anxiety severity and cognitive performance might not be apparent in non-clinical contexts, and/or this relationship may be non-linear. It is important to underline that neither the meta-analysis nor the study conducted by Williams

et al. (1996) took into account hormonal contraception. Even though we did not find differences between groups in the cross-sectional study, we found differences while implementing repeated measures over the course of one menstrual cycle in the daily diary study. This demonstrates the need to consider hormonal contraception in studies related to the Emotional Stroop task.

Our daily diary study showed that anti-androgenic OC users had longer response times (lower inhibitory control) than androgenic OC users in all the categories of words, whether neutral or related to emotional stimuli. To our knowledge, no study tested for these differences previously, as the studies conducted on response inhibition and OC use were RCTs where participants received either androgenic OC (Gingnell et al., 2016) or anti-androgenic OC (Scheuringer et al., 2020), but there was no comparison between androgenic and anti-androgenic OC. Moreover, anti-androgenic OC users showed greater interference than NC women in all the categories of words in their late luteal phase, and with negative words in their late follicular phase. The literature has described an increase in negative symptoms in NC women during the luteal phase (Pinkerton et al., 2009), and a literature review by Lopez et al. (2012) underlined that anti-androgenic OC are often prescribed to reduce severe negative symptoms in the luteal phase, but in our study, the group of anti-androgenic OC users had lower inhibitory control than NC women in this phase. The authors of the review suggested that more RCTs should be conducted to explore the link between anti-androgenic OC and negative symptoms in the luteal phase. It is of note that our study did not show any difference between the OC groups and the NC women in mean response times during the early follicular phase. This phase of the menstrual cycle is characterised by low levels of both estradiol and progesterone (Abraham et al., 1972). In OC users, during active pill use, the levels of these two hormones are similar to the levels of NC women in their early follicular phase (Elliott-Sale et al., 2013). In our study, we did not separate between active and inactive pill phases but based on the calendars prepared individually for each participant, we can deduce that most of the days recorded for them were during their active pill phase, which might explain why there is no difference between OC users and NC women in their early follicular phase.

One of the main limitations of our study is the impossibility of reaching a causal conclusion, as the study is only observational. As mentioned in the review conducted by Beltz (2022), RCTs are difficult to implement in this field but comparing participants before and after they start taking OC might be a way to obtain more accurate results. Another limitation of our study is the use of

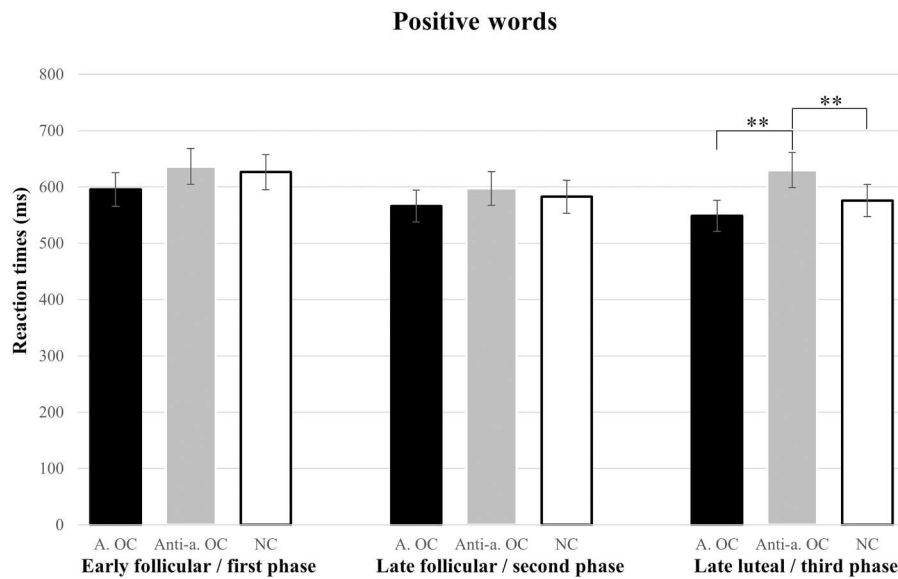


Figure 3. Comparison of response times for positive words based on groups and menstrual cycle phases. $**p < 0.01$; A.: androgenic; Anti-a: anti-androgenic. OC: oral contraceptives; NC: naturally cycling [To view this figure in colour, please see the online version of this journal].

self-report measures to determine anxiety levels which might not always offer the best accuracy. Laird et al. (2019) underlined that there is a lack of studies with participants having received an actual anxiety disorder diagnosis. Future studies could compare healthy participants with diagnosed ones. Our recruitment method (social media) is linked with a selection bias and does not allow us to generalise the results for the whole population. Moreover, the participants in our study were not randomly assigned to groups. Our cross-sectional study

lacked information about the phase of the menstrual cycle the NC participants were in, and both studies lacked testing for actual hormonal levels to confirm the menstrual cycle phases but also to compare the levels of anxiety and performance on the Emotional Stroop task to the levels of hormones. We did not ask our NC participants about perceived symptoms that might have been related to premenstrual syndrome or premenstrual dysphoric disorder during the luteal phase (Pinkerton et al., 2009), which might be asked in future studies. We

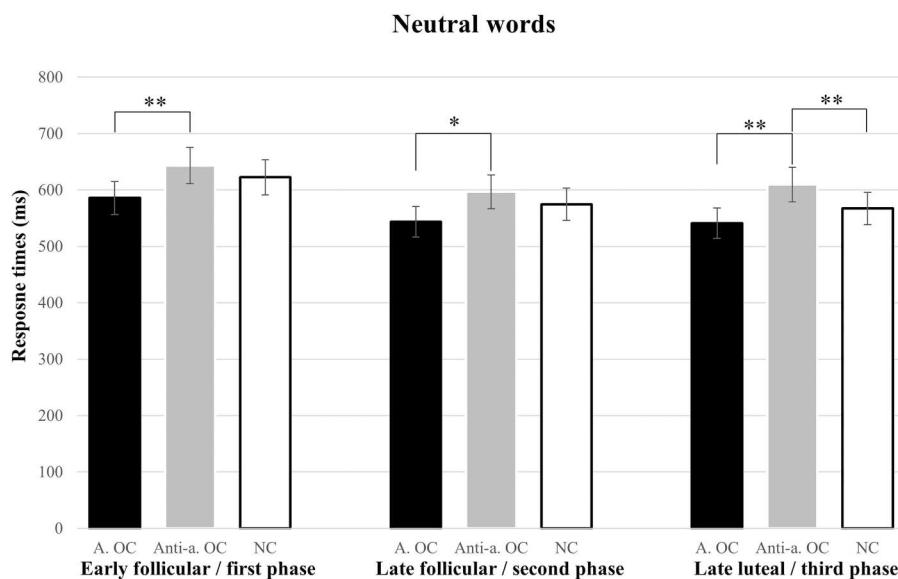


Figure 4. Comparison of response times for neutral words based on groups and menstrual cycle phases. $*p < 0.05$; $**p < 0.01$; A.: androgenic; Anti-a: anti-androgenic. OC: oral contraceptives; NC: naturally cycling [To view this figure in colour, please see the online version of this journal].

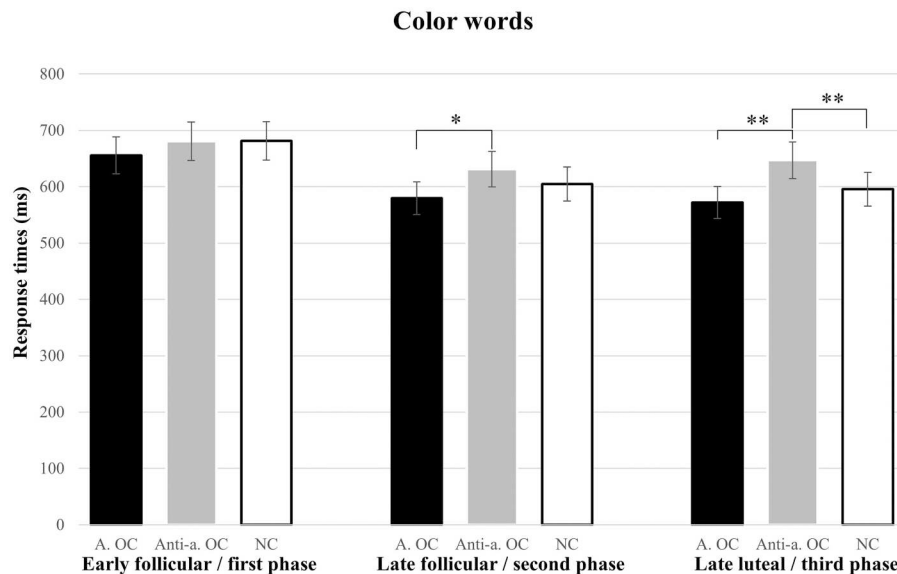


Figure 5. Comparison of response times for colour words based on groups and menstrual cycle phases. * $p < 0.05$; ** $p < 0.01$; A.: androgenic; Anti-a: anti-androgenic. OC: oral contraceptives; NC: naturally cycling [To view this figure in colour, please see the online version of this journal].

did not verify the reasons that motivated the participants to start taking OC, whether those were gynecological or not, and that information might have allowed us to draw more accurate conclusions. We did not compare the different dosages of ethinyl estradiol in the OC, which might be a novel way to classify OC in studies (Beltz, 2022). It might also be worth comparing the active and inactive phases of OC users to verify whether those phases are linked with the participants' anxiety levels and performance on the Emotional Stroop task. We did not ask the participants how long they had been taking OC or if they had an individual or a family history of mood disorders. All these variables can be taken into account in future studies to ensure more accurate results. Finally, while the number of participants was similar in the NC group and the OC group, the number of participants taking androgenic OC was much smaller than the number of participants taking anti-androgenic OC in both studies.

To conclude, our study contributes to the literature by presenting findings on the topic of anxiety, inhibitory control and oral contraceptives in a cross-sectional study with a large sample size, and in a repeated measures study conducted over the span of one menstrual cycle, comparing NC women with women taking both androgenic and anti-androgenic OC. Our study shows no difference in anxiety levels between NC women and OC users. Anti-androgenic OC users have lower inhibitory control compared to androgenic OC users but also compared to NC women in their late luteal phase. Our findings underline differences in

inhibitory control in women, depending on whether they use OC or not, and depending on the components of their OC. Further studies could focus on the link between the different components of OC and inhibitory control which can be linked to anxiety symptoms in women.

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Data availability statement

The data that support the findings of this study are openly available on osf at <http://doi.org/10.17605/OSF.IO/TB3XY>.

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Monika Kornacka: conceptualization, methodology, validation, formal analysis, resources, writing – review & editing, supervision.

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1 **Anxiety, depression and perseverative cognition in women cycling naturally or**
2 **taking oral contraceptives – a diary study**

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10 **Abstract**

11 *Background:* While the literature is inconsistent about the link between anxiety
12 and oral contraceptives (OC), the link between depression and OC is recognized
13 in women who started OC during adolescence. Perseverative cognition is a stress-
14 coping mechanism present both in anxiety and depression. Our study aimed to
15 understand the differences between women taking OC and naturally cycling (NC)
16 women regarding their daily levels of anxiety, depression, related negative factors
17 (perseverative cognition and stress), and protective factors (self-esteem and life
18 satisfaction).

19 *Methods:* The study was conducted on 89 adult women (M age = 26.60, SD =
20 4.65) (48 – OC; 41 – NC) who participated in a 15-day online diary study divided
21 into 3 phases throughout one menstrual cycle. The women using OC were further
22 classified according to the androgenicity of their OC (androgenic and anti-

23 androgenic). The participants were sent an email in the evening with
24 questionnaires they had to complete on the same day. The daily measures were
25 taken from existing trait-level scales and adapted for daily administration. The
26 analyses were conducted using hierarchical linear modeling, with a significance
27 level of $p < 0.05$.

28 *Results:* There were no differences between groups in daily levels of anxiety,
29 perseverative cognition, and stress. However, anti-androgenic OC users had
30 higher levels of daily depression than NC women in the three menstrual cycle
31 phases tested for, while androgenic OC users had higher levels of daily depression
32 than NC women in two phases. Both groups of women taking OC had lower
33 levels of daily self-esteem than NC women in all three phases. Androgenic OC
34 users had higher daily satisfaction with life than anti-androgenic OC users in one
35 testing phase.

36 *Conclusions:* OC users had higher daily levels of depression and lower daily
37 levels of self-esteem than NC women. Future studies could explore the link
38 between depression and the different types of OC in adult women, especially with
39 longitudinal methods.

40

41 *Keywords:* anxiety; depression; menstrual cycle; oral contraceptives; daily diary;
42 perseverative cognition; self-esteem; satisfaction with life

43

44 **1. Background**

45 *1. 1. Menstrual cycle and oral contraceptives*

46 The menstrual cycle of women who cycle naturally is composed of two distinct
47 phases: first, a follicular phase, and then a luteal phase (1). As described by

48 Schmalenberger et al. (2), the beginning of the menstrual cycle corresponds with the
49 onset of menstruation when the levels of estradiol and progesterone are low. In the
50 middle of the follicular phase, estradiol levels increase until they reach a peak just
51 before ovulation. The luteal phase begins after ovulation. Progesterone levels start to
52 rise before reaching their peak during the mid-luteal phase. At the same time, estradiol
53 remains at a moderate level with a slight peak in the middle of the phase. The menstrual
54 cycle ends when a sharp decline in the levels of estradiol and progesterone triggers the
55 next menstruation. The luteal phase (i.e., premenstrual phase) has been linked with an
56 exacerbation of numerous disorders, including anxiety disorders and depression (for a
57 review, see Pinkerton et al. (3). Compared to naturally cycling (NC) women, oral
58 contraceptive (OC) users exhibit significantly lower levels of estradiol and progesterone
59 (4) and a lack of hormonal variability (4). The composition of combined OC is an
60 association between ethinylestradiol and progestins, with the progestins being either
61 androgenic or anti-androgenic (5). Androgenic progestins originate from testosterone,
62 whereas anti-androgenic progestins block androgen receptors (6). The literature reviews
63 conducted by Laird et al. (7) and Beltz (8) on the link between OC, mental disorders,
64 and cognitive functions demonstrated a lack of consistency in the results obtained in
65 previous studies.

66

67 *1. 2. Anxiety, the menstrual cycle, and oral contraceptives*

68 Generalized anxiety disorder (GAD) affects 4.5% of the population worldwide
69 (9), and women are twice as likely as men to suffer from it (10). According to the
70 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (11),
71 some symptoms of GAD are excessive anxiety and worry and an inability to control
72 them, associated with different symptoms such as irritability or muscle aches. Changes

73 in anxiety symptoms are associated with the menstrual cycle, i.e., symptoms increase
74 before menstruation and at the beginning of menstruation (for a systematic review, see
75 Green & Graham (12)). The most consistent findings in the literature are retrospective
76 self-reports of an increase in anxiety symptoms during the premenstrual phase (for a
77 review, see Nillni et al. (13)).

78 The review by Laird et al. (7) pointed to a lack of studies on the link between
79 GAD and OC use, and the only cited research found that OC users were less likely to
80 suffer from GAD (14). A randomized controlled trial (RCT) conducted by Lundin et al.
81 (15) showed that adult women experienced an increase in anxiety after starting OC,
82 compared to the placebo group, over 3 months of use. The lack of studies on the link
83 between OC and anxiety symptoms and the lack of consensus in the literature indicate a
84 need to conduct more studies on this topic.

85

86 *1. 3. Depression, the menstrual cycle, and oral contraceptives*

87 Similar to the higher prevalence of GAD in women, they are also twice as likely
88 as men to suffer from depression (16). The DSM-5 (11) indicates that depression is
89 accompanied by symptoms such as a depressed mood, a loss of interest and pleasure,
90 feelings of worthlessness, or decreased concentration. Women's increased risk of
91 suffering from depression starts with puberty and decreases after menopause (17).
92 Moreover, the premenstrual and menstrual phases are linked with an increase in
93 depression (for a review, see Handy et al. (18)).

94 The only consensus found on the link between the use of OC and depression
95 suggests that starting OC during adolescence is related to a vulnerability to receiving a
96 diagnosis of depression in adulthood (19,20). Regarding the link between depression
97 and the use of OC in adult women, results differ between studies. Some studies have not

98 found any association between combined OC and depression (21), while others have
99 found an increase in depressive symptoms in the first two years after starting OC (22).
100 The established link between OC use during adolescence and the increased risk of
101 developing depression in adulthood indicates a need to delve deeper into the
102 relationship between OC use and depression in adult women.

103

104 *1. 4. Factors related to anxiety and depression*

105 To obtain accurate results, we studied negative variables linked with anxiety and
106 depression, namely perceived stress and perseverative cognition. Higher levels of
107 perceived stress are linked with higher levels of anxiety (23), and stress plays a role in
108 the onset of depression (24). According to the literature, one of the key transdiagnostic
109 factors being a common mechanism to anxiety, depression, and stress, might be
110 perseverative cognition (25). It has been defined as “the repeated or chronic activation
111 of the cognitive representation of one or more psychological stressors” ((26) p. 114).
112 This stress-coping mechanism, present both in anxiety and depression (27,28), has a
113 higher prevalence in women (29). Additionally, the literature shows that it can enclose
114 patients in a vicious circle where perseverative cognition triggers psychopathology
115 symptoms and the symptoms cause more rumination (typical for depression, (30) or
116 worry (typical for anxiety, (31), impairing also instrumental behavior and problem
117 solving (30). Our study explored separately those two types of perseverative cognition,
118 which have rarely been studied when comparing OC users and NC women.

119 Among trait dispositions considered as a protective factor allowing one to better
120 handle anxiety, positive psychology literature points to low self-esteem as a predictor of
121 higher levels of anxiety and depression (32). We also measured daily satisfaction with
122 life, as GAD is associated with a higher likelihood of experiencing lower life

123 satisfaction and lower well-being (33). Lower levels of life satisfaction are also
124 associated with a higher risk of developing depressive symptoms (34).

125

126 *1. 5. Aim of the study*

127 The goal of our study was to examine the differences between daily anxiety and
128 depression levels between OC users and NC women, as well as the protective and
129 negative factors associated with these symptoms, while taking into account the different
130 types of OC (androgenic and anti-androgenic).

131 Hypothesis 1: There is a link between anxiety and depression, between anxiety and
132 perseverative cognition, and between depression and perseverative cognition when
133 measured daily (25,27,28).

134 Hypothesis 2: There are differences between NC women and OC users in daily
135 levels of anxiety (14,15) and depression (22), as well as in the daily levels of the
136 protective (self-esteem and satisfaction with life) and negative factors (perseverative
137 thinking, worry, stress) associated with these symptoms.

138 Hypothesis 3: NC women have higher daily levels of anxiety and depression in their
139 luteal phase (3). The daily levels of perseverative thinking, worry, and stress are higher
140 in this phase, whereas the daily levels of self-esteem and satisfaction with life are lower.

141 Hypothesis 4: Since OC users do not experience fluctuations in their hormonal
142 levels (4), they also do not experience significant fluctuation in their daily levels of
143 anxiety and depression throughout their menstrual cycle. The daily levels of the
144 protective and negative factors associated with these symptoms do not change
145 significantly either.

146

147 **2. Methods**

148 2. 1. *Participants*

149 For this study, 103 women volunteered to participate, but 14 of them dropped
150 out before the end of the study or had their results withdrawn due to potential
151 unreliability or irregularity in their menstrual cycles. Participants who did not take part
152 in the three phases of the diary were also excluded. The final sample included 89
153 women (M age = 26.60, SD = 4.65) with 41 NC women and 48 taking OC. The groups
154 did not significantly differ in terms of age ($t(71) = 0.70, p = 0.71$). The women using
155 OC were further classified according to the androgenicity of their OC (7, 21): 32 in the
156 anti-androgenic group and 16 in the androgenic group.

157 The inclusion criteria for participants in the study were: being between 18 and
158 45 years of age, Polish speakers, taking OC or naturally cycling with a regular
159 menstrual cycle (according to Fehring et al. (1), a regular menstrual cycle is of a
160 duration between 21 and 35 days with less than 7 days of difference between cycles).
161 To conduct the diary study, participants were additionally required to have cycles that
162 lasted at least 28 days, so that the phases did not overlap. If the participants reported a
163 regular menstrual cycle with a variability of 28 to 35 days, the mean length of their
164 menstrual cycle was calculated. The exclusion criteria were based on Kowalczyk et al.
165 (35), namely: “using other forms of hormonal contraception, using a copper intrauterine
166 device, having undergone sterilization, having stopped taking OC in the past 6 months,
167 being pregnant or breastfeeding” (p. 243). The descriptive statistics of participants are
168 reported in Table 1.

169

170

171

172 Table 1. Descriptive statistics for participants.

	General sample (<i>N</i> =89)	A. OC (<i>n</i> =16)	Anti-a. OC (<i>n</i> =32)	NC (<i>n</i> =41)
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)
Age	26.60(4.67)	27.88(3.93)	25.13(4.18)	27.24(5.08)
Cycle length	29.24(1.70)	28.38(0.89)	28.75(1.37)	29.95(1.90)

Note. A.: androgenic; Anti-a.: anti-androgenic

173

174 The sample size was chosen based on Nezlek's (36) and Welz's (37)
 175 recommendations. Nezlek (36) suggests that the ideal sample size for a two-week daily
 176 diary study is approximately 100 participants. Welz noted that, due to the high drop-out
 177 rate in diary studies, there should be more than 60 participants.

178 The participants received a gift voucher of around €50 for participating in this
 179 study. The study was conducted in compliance with the Helsinki Declaration, and the
 180 research protocol was approved by the Ethics Committee of our institution (Decision
 181 No. 55/2020/2).

182

183 2. 2. Materials

184 2. 2. 1. Questionnaires

185 The following questionnaires were used at the beginning of the study: the GAD-
 186 7 Scale (38), the Perseverative Thinking Questionnaire (PTQ, (27), the Penn State
 187 Worry Questionnaire (PSWQ, (39), the Perceived Stress Scale (PSS, (40), and the Self-
 188 Esteem Scale (SES, (41). The descriptive statistics for these responses are reported in
 189 Table 2. The reliability of the scales (Cronbach's alpha) was acceptable. The groups did
 190 not significantly differ on the trait level of the tested variables before the
 191 implementation of the diary procedure (see Table 2).

192

193

194

195 Table 2. Descriptive statistics for pre-test measures by groups.

Measure	Reliability (Cronbach's alpha)	<i>M (SD)</i>			
		NC (<i>n</i> = 41)	OC (<i>n</i> = 48)	A. OC (<i>n</i> = 16)	Anti-a.OC (<i>n</i> = 32)
GAD-7	0.89	6.63(4.76)	6.67(3.94)	6.06(3.36)	6.97(4.22)
PTQ	0.93	32.93(12.76)	34.73(9.44)	36.50(6.63)	33.84(10.55)
PSWQ	0.92	54.29(14.13)	57.90(10.67)	55.25(10.98)	59.22(10.43)
PSS	0.87	20.05(7.44)	20.54(6.83)	21.63(7.45)	20(6.56)
SES	0.82	17.34(5.12)	15.79(5.45)	15.56(5.29)	15.91(5.61)

196 *Note.* A.: androgenic; Anti-a.: anti-androgenic; NC: naturally cycling; OC: oral contraceptives; GAD:
 197 generalized anxiety disorder; PTQ: Perseverative Thinking Questionnaire; PSWQ: Penn State Worry
 198 Questionnaire; PSS: Perceived Stress Scale; SES: Self-Esteem Scale.

199

200 Most of the daily measures were taken from existing trait-level scales and

201 adapted for daily administration. This procedure of item adaptation followed the

202 guidelines discussed in Nezlek (36). All daily items included the word “today” to

203 maximize the likelihood that participants were describing how they felt each day.

204 Participants provided answers ranging from 1 (“not at all”) to 7 (“very much”).

205 *Daily anxiety.* The daily measures for anxiety consisted of three items selected from the

206 GAD-7 scale (38). The main question was “How often today have you been bothered by

207 the following problems?”. The items chosen from the GAD-7 were items 1 (“Feeling

208 nervous, anxious or on edge”), 3 (“Worrying too much about different things”), and 7

209 (“Feeling afraid as if something awful might happen”).

210 *Daily depression.* The daily measures of depression consisted of three items

211 corresponding to the elements of Beck’s cognitive triad (46), adapted by Nezlek &

212 Gable (42). The first item was related to the negative view of self (“Overall, how

213 positively did you feel about yourself today?”), the second item to the negative view of

214 life in general (“Thinking of your life in general, how well did things go today?”) and

215 the third item to the negative view of the future (“How optimistic are you about how

216 your life will be tomorrow?”). These items were then reverse-coded.

217 *Daily perseverative cognition (perseverative thinking and worry)*. The daily measures
218 for perseverative thinking were three items chosen from the Perseverative Thinking
219 Questionnaire (PTQ; (27)). The main question was “How often today have you been
220 bothered by the following problems?”. The items chosen from the PTQ were items 1
221 (“The same thoughts kept going through my mind again and again.”), 4 (“I think about
222 many problems without solving any of them.”) and 10 (“My thoughts prevented me
223 from focusing on other things.”). The questions measuring daily levels of worry were
224 adapted from Thielsch et al. (48) for daily administration: “How much did you worry
225 today?” and “How much were you bothered by worry today?”

226 *Daily stress*. The daily measures to assess stress levels consisted of three items from the
227 Perceived Stress Scale (PSS, (40)). The items chosen were items 2 (“In the last month,
228 how often have you felt that you were unable to control the important things in your
229 life?” which was transformed into “How often today did you feel that you were unable
230 to control the important things in your life?”), 6 (“In the last month, how often have you
231 found that you could not cope with all the things that you had to do?” which was
232 transformed into “How often today did you feel that you could not cope with all the
233 things that you had to do?”) and 10 (“In the last month, how often have you felt
234 difficulties were piling up so high that you could not overcome them?” which was
235 transformed into “How often today did you feel that difficulties were piling up so high
236 that you could not overcome them?”).

237 *Daily self-esteem*. The daily measures for self-esteem were three items chosen from the
238 Self-Esteem Scale (SES, (41)). The main question was “How often today have you felt
239 that:” and the items chosen from the questionnaires were items 1 (“On the whole, I am
240 satisfied with myself” transformed into “How often today have you felt that on the
241 whole, you were satisfied with yourself?”), 2 (“At times, I think I am no good at all”

242 transformed into “How often today have you felt that you were no good at all?”), 3 (“I
243 feel that I have a number of good qualities” transformed into “How often today have
244 you felt that you had a number of good qualities?”). Item 2 was reverse-coded.
245 *Daily satisfaction with life.* To determine daily life satisfaction, three questions were
246 asked. Two were based on Oishi et al. (43), as in Nezlek et al. (44): “How was today?”
247 with answers ranging from 1 (“terrible”) to 7 (“excellent”) and “How satisfied were you
248 with your life today?” with answers from 1 (“very dissatisfied”) to 7 (“very satisfied”).
249 The last question was based on item 4 of the Psychological Well-Being Scale (45): “The
250 demands of everyday life often get me down,” which was transformed into “How much
251 did the demands of everyday life get you down today?”. The third item was rated from 1
252 (“not at all”) to 7 (“very much”) and was then reverse-coded.

253

254 2. 2. 2. *Diaries*

255 Each participant was provided with an individual menstrual cycle calendar,
256 which was calculated based on the date of her last menstruation onset and the usual
257 length of her menstrual cycle. The calendar was divided into three phases, which we
258 defined as the menstrual, follicular, and luteal phases for the NC women. The menstrual
259 phase is part of the follicular phase but corresponds to menstruation in our study. Three
260 parallel phases were chosen for the OC users. In each phase, measures were taken for 5
261 consecutive days, totaling 15 days, as per Nezlek’s method (36). The menstrual phase
262 started on the first day of menstruation until the 5th day. The follicular phase was
263 calculated based on the expected ovulation, which usually happens 14 days before the
264 next menstruation (1). In Hidalgo-Lopez et al. (46), the pre-ovulatory phase begins 3
265 days before ovulation; therefore, we calculated the follicular phase as spanning 5 days
266 before the pre-ovulatory phase. Finally, the luteal phase is usually stable and lasts 14
267 days (1). In Hidalgo-Lopez et al. (46), this phase was measured over a relatively long

268 span (from 3 days post-ovulation to 3 days before the next menstruation); therefore, we
269 based our calculations on Welz et al. (37), who tested participants on the 6th and 5th
270 day before the next menstruation. As a result, the luteal phase in our study spans from
271 the 9th to the 5th day before the next menstruation. For example, for a menstrual cycle
272 of 28 days, the measured days were as follows: day 1-5 (menstrual), day 7-11
273 (follicular), and day 20-25 (luteal). The NC participants received commercially
274 available ovulation tests (Horien Medical), which measure the luteinizing hormone
275 (LH) surge in urine. These tests were conducted at home by the participants, who
276 received an email at the end of the follicular phase, instructing them to test for ovulation
277 for 10 consecutive days and to provide the experimenters with the date on which the test
278 indicated an LH surge. If the ovulation test indicated a mismatch in the cycle phases, the
279 dates of the phases were adjusted, and participants were given the opportunity to take
280 part in the study again the following month. This offer was repeated for a second month,
281 following which, if their menstrual cycle showed too much variability over the span of
282 three cycles, their results were excluded from the study. OC users reported cycles that
283 lasted around 28 days, and the three phases during which they were tested corresponded
284 to the same days NC women were tested when they had menstrual cycles lasting 28
285 days. We did not separate the active and inactive pill phases as the OC users' phases
286 were meant to match the phases of the NC women to observe the results in the treatment
287 group (OC) and the non-treatment group (NC) simultaneously throughout a whole
288 menstrual cycle. The goal was to compare how NC women and OC users feel
289 throughout their menstrual cycle and whether the lack of hormonal variability is linked
290 with a difference in well-being. The first phase of OC users began on the first day of
291 withdrawal bleeding, which happens during the inactive phase of OC (47). OC users
292 resumed their treatment during the 5 days corresponding to the first phase of their study

293 (active phase). The second phase was tested during their active phase (days 7-11). We
 294 did not verify whether the OC users decided to observe a stop week at the end of their
 295 menstrual cycle. If they did not, then their third phase corresponded to the active phase.
 296 If they did, then based on the fact that they had a menstrual cycle of 28 days on average,
 297 their withdrawal bleeding started between 4 and 7 days after their last pill intake,
 298 depending on whether they were taking a 21 or 24-day OC. In this case, their last phase
 299 (days 20-25) represented a mixture of active and inactive phases. Precise information
 300 about the oral contraceptives taken by our participants can be found in Table 3.

301

302 Table 3. Oral contraceptives used by the participants.

Oral contraceptive brands	Active and placebo	Active substance	Concentration $\mu\text{g}/\mu\text{g}$	<i>N</i>	Androgenic or anti-androgenic
Drovelis	24+4	Estetrol/drospirenone	14200/3000	2	anti-androgenic
Zoely	24+4	Estradiol valerate/nomegestrol acetate	1500/2500	2	anti-androgenic
Belara	21	Ethinyl estradiol/chlormadinone acetate	30/2000	3	anti-androgenic
Novynette, Ovulastan	21	Ethinyl estradiol/desogestrel	20/150	2	androgenic
Aidee, Atywia, Jeanine	21	Ethinyl estradiol/dienogest	30/2000	8	anti-androgenic
Atywia Daily	21+7	Ethinyl estradiol/dienogest	30/2000	1	anti-androgenic
Axia Conti, Daylette, Vixpo	24+4	Ethinyl estradiol/drospirenone	20/3000	3	anti-androgenic
Teenia, Yasminelle	21	Ethinyl estradiol/drospirenone	20/3000	2	anti-androgenic
Vibin mini	21+7	Ethinyl estradiol/drospirenone	20/3000	5	anti-androgenic
Drosfemine Forte, Lesine,	21	Ethinyl estradiol/drospirenone	30/3000	2	anti-androgenic
Vibin	21+7	Ethinyl estradiol/drospirenone	30/3000	2	anti-androgenic
Kontracept	21	Ethinyl estradiol/gestodene	20/75	3	androgenic
Sylvie 30	21	Ethinyl estradiol/gestodene	30/75	1	androgenic
Vines	24+4	Ethinyl estradiol/gestodene	15/60	5	androgenic
Orlifique	21+7	Ethinyl estradiol/levonorgestrel	20/100	1	androgenic

Microgynon 21, Rigevidon	21	Ethinyl estradiol/levonorgestrel	30/150	2	androgenic
Elin	21	Ethinyl estradiol/norgestimate	35/250	2	androgenic
Slinda	24+4	Drospirenone	4000	2	anti-androgenic

303

304

2. 3. Procedure

305

The data were collected between February and December 2022. The participants

306

were recruited online. Our institution shared an advertisement on social media.

307

Interested candidates were presented with a description of the study and the required

308

criteria to participate. They provided informed consent before taking part in the

309

recruitment process. At the beginning of the study, before they began the diary,

310

participants completed a set of individual difference measures on the Qualtrics platform

311

(48), the results of which have been published previously (35). Based on the diary study

312

by Sztachańska et al. (49) and Nezlek's method (36), all participants were sent an email

313

at 8 pm during the 15 days of their menstrual cycle calendar with a link to the diary.

314

They were asked to complete the daily questionnaire on that same day, and we accepted

315

results that had been sent before 5 AM the next day. The results of participants who

316

completed the diary later were not included.

317

318

2. 4. Statistical analysis

319

We conducted an exploratory diary study comparing NC women in three

320

phases of their menstrual cycle (menses, follicular, and luteal) to women taking

321

OC who were also tested three times, in parallel to the phases of the NC

322

women. Our goal was to study parallel and dynamic changes in the participants'

323

daily levels of anxiety and depression. We wanted to explore whether the lack of

324

hormonal fluctuation in OC users would be linked with higher or lower levels of

325 these symptoms. Of particular importance was the comparison between the luteal
 326 phase of NC women and the phase leading up to menstruation in OC users, since
 327 NC women tend to experience an increase in negative symptoms before
 328 menstruation (12).

329 The analyses were conducted using hierarchical linear modeling. The data
 330 represents a two-level nested structure. Level 1 variables (data collected through diary
 331 measures) were nested in participants (Level 2). The number of diary entries collected
 332 for the 89 participants was $N = 1178$. The daily measures were separated into cycle
 333 phases (menstrual, follicular, luteal). Although OC users do not experience these phases
 334 in their menstrual cycle, we retained the same names for their phases to facilitate
 335 comparison with the phases of the NC group. Group types (anti-androgenic OC,
 336 androgenic OC, NC) were introduced at Level 2. The analyses followed the instructions
 337 provided by Nezlek (36) and were conducted using the HLM program (50).
 338 Additionally, size effects were calculated using WebPower (51), and confidence
 339 intervals (CI) were calculated through *f*-square Effect Size Confidence Interval
 340 Calculator (52). In the first part of the analysis, we ran an unconditional model for each
 341 of the Level 1 variables with no predictors at Level 1 or Level 2 to estimate sources of
 342 variability, whether the variability related to days (Level 1) or participants (Level 2):

343 Equation 1:

344 Level 1 (within-person): $Anxiety_{ij} = \beta_{0j} + r_{ij}$

345 Level 2 (between-person): $\beta_{0j} = \gamma_{00} + u_{0j}$

346 To test the link between daily anxiety and daily depression (hypothesis 1), we used the
 347 following equation:

348 Equation 2:

349 Level 1 (within-person): $Anxiety_{ij} = \beta_{1j}(depression) + r_{ij}$

350 Level 2 (between person): $\beta_{1j} = \gamma_{10}$

351 Similar equations were used to test the link between daily levels of anxiety and

352 perseverative cognition, as well as daily levels of depression and perseverative

353 cognition.

354 To test the differences between the groups on anxiety levels in the different cycle

355 phases (hypothesis 2), we used the following equation:

356 Equation 3:

357 Level 1 (within-person): $\text{Anxiety}_{ij} = \beta_{1j}(\text{Menstrual}) + \beta_{2j}(\text{Follicular}) + \beta_{3j}(\text{Luteal}) + r_{ij}$

358 Level 2 (between person):

359 $\beta_{1j} = \gamma_{10}(\text{androgenic}) + \gamma_{20}(\text{anti-androgenic}) + \gamma_{30}(\text{NC}) + u_{1j}$

360 $\beta_{2j} = \gamma_{11}(\text{androgenic}) + \gamma_{21}(\text{anti-androgenic}) + \gamma_{31}(\text{NC}) + u_{2j}$

361 $\beta_{3j} = \gamma_{12}(\text{androgenic}) + \gamma_{22}(\text{anti-androgenic}) + \gamma_{32}(\text{NC}) + u_{3j}$

362 The same equations were used for the other dependent variables.

363 To test whether there are between-phases differences in anxiety levels for the NC

364 women (hypothesis 3), we used the following equation:

365 Equation 4:

366 Level 1 (within-person): $\text{Anxiety}_{ij} = \beta_{1j}(\text{Menstrual}) + \beta_{2j}(\text{Follicular}) + \beta_{3j}(\text{Luteal}) + r_{ij}$

367 Level 2 (between person):

368 $\beta_{1j} = \gamma_{10}(\text{NC})$

369 $\beta_{2j} = \gamma_{11}(\text{NC})$

370 $\beta_{3j} = \gamma_{12}(\text{NC})$

371 An analogous equation was used to test for between-phase differences in all the

372 variables. These equations were repeated for the two other groups, androgenic OC users

373 and anti-androgenic OC users (at Level 2) (hypothesis 4).

374

375 **3. Results**

376 To obtain the descriptive statistics of the diaries, we ran Equation 1. They are
 377 presented in Table 4 with the reliability of the scales.

378 Table 4. Descriptive statistics of the diary study.

Daily Variable	Reliability	Level 2 variables ($N = 89$)		
		M	Variances	
			Between	Within
Anxiety	0.87	8.73	6.68	12.49
Depression	0.91	10.60	5.75	7.03
Perseverative thinking	0.90	7.85	7.73	10.90
Worry	0.87	5.98	3.63	6.88
Stress	0.91	8.90	10.21	13.65
Self-esteem	0.94	13.57	8.87	8
Satisfaction with life	0.79	12.97	2.45	8.32

379
 380 To test the link between daily anxiety and daily depression within the sample, we
 381 ran Equation 2. A significant link was found between these two variables ($\beta =$
 382 0.81 , $SE = 0.01$, $p < 0.001$). A similar equation was used to test the link between
 383 daily anxiety and daily perseverative cognition, as well as the link between daily
 384 depression and daily perseverative cognition. There was a significant link between
 385 daily levels of anxiety and perseverative thinking ($\beta = 1.04$, $SE = 0.01$, $p < 0.001$),
 386 and between daily levels of anxiety and worry ($\beta = 1.40$, $SE = 0.01$, $p < 0.001$).
 387 There was also a significant link between daily levels of depression and
 388 perseverative thinking ($\beta = 1.14$, $SE = 0.01$, $p < 0.001$), and between daily levels
 389 of depression and worry ($\beta = 1.52$, $SE = 0.02$, $p < 0.001$).

390

391 *3. 1. Differences between groups in daily measures within each phase*

392 To test the differences between the groups on all the variables in the different cycle
 393 phases, we used Equation 3. Contrast analyses did not reveal any significant differences
 394 between groups in daily levels of anxiety (p -values ranged from 0.221 to > 0.500),
 395 perseverative thinking (p -values ranged from 0.107 to > 0.500), worry (p -values ranged

396 from 0.089 to > 0.500), and stress (p -values ranged from 0.150 to > 0.500). Significant
397 differences between groups were found in daily levels of depression, self-esteem, and
398 satisfaction with life. Anti-androgenic OC users had higher levels of daily depression (β
399 = 10.66, $SE = 0.29$; $\beta = 11.63$, $SE = 0.29$; $\beta = 11.28$, $SE = 0.29$) than NC women ($\beta =$
400 9.64, $SE = 0.26$; $\beta = 10.19$, $SE = 0.27$; $\beta = 10.12$, $SE = 0.27$) in the menstrual phase ($p =$
401 0.008, $f = 0.39$, 95% CI [0.01, 0.35]), the follicular phase ($p < 0.001$, $f = 0.55$, 95% CI
402 [0.09, 0.61]) and the luteal phase ($p = 0.004$, $f = 0.44$, 95% CI [0.03, 0.42]),
403 respectively. Androgenic OC users also had higher levels of daily depression ($\beta =$
404 10.67, $SE = 0.41$; $\beta = 11.35$, $SE = 0.43$) than NC women ($\beta = 9.64$, $SE = 0.26$; $\beta =$
405 10.19, $SE = 0.27$) in the menstrual phase ($p = 0.031$, $f = 0.39$, 95% CI [0.01, 0.35]) and
406 the follicular phase ($p = 0.021$, $f = 0.44$, 95% CI [0.03, 0.42]), respectively. Both anti-
407 androgenic OC users ($\beta = 13.37$, $SE = 0.33$, $\beta = 12.77$, $SE = 0.33$, $\beta = 13.03$, $SE = 0.33$)
408 and androgenic OC users ($\beta = 12.77$, $SE = 0.47$, $\beta = 12.20$, $SE = 0.50$, $\beta = 12.77$, $SE =$
409 0.48) had lower levels of daily self-esteem than NC women ($\beta = 14.51$, $SE = 0.30$, $\beta =$
410 14.25, $SE = 0.30$, $\beta = 14.38$, $SE = 0.31$) in the menstrual phase ($p = 0.010$, $f = 0.40$, 95%
411 CI [0.01, 0.36]; $p = 0.002$, $f = 0.62$, 95% CI [0.14, 0.75]), the follicular phase ($p =$
412 0.001, $f = 0.52$, 95% CI [0.07, 0.56]; $p < 0.001$, $f = 0.73$, 95% CI [0.24, 1.01]) and the
413 luteal phase ($p = 0.003$, $f = 0.48$, 95% CI [0.05, 0.49]; $p = 0.005$, $f = 0.57$, 95% CI [0.11,
414 0.65]), respectively. Androgenic OC users had higher daily satisfaction with life ($\beta =$
415 13.59, $SE = 0.39$) than anti-androgenic OC users ($\beta = 12.46$, $SE = 0.27$) when they were
416 tested in the third phase ($p = 0.016$, $f = 0.39$, 95% CI [0.01, 0.35]). The comparisons of
417 the variables in all groups and all menstrual cycle phases are presented in Table 5.

418 Table 5. Comparison of daily variables (Level 1) based on groups and menstrual cycle phases.

Daily measures	Menstrual			Follicular			Luteal		
	A. OC	Anti-a. OC	NC	A. OC	Anti-a. OC	NC	A. OC	Anti-a. OC	NC
Anxiety									
<i>Coeff.</i>	9.23	8.78	8.50	9.06	8.73	8.61	9.21	8.74	8.52
<i>SE</i>	0.51	0.36	0.32	0.54	0.36	0.33	0.52	0.36	0.33
Depression									
<i>Coeff.</i>	10.67*	10.66**	9.64	11.35*	11.64***	10.19	10.94	11.28**	10.12
<i>SE</i>	0.41	0.29	0.26	0.43	0.29	0.27	0.42	0.29	0.27
Perseverative thinking									
<i>Coeff.</i>	8.40	8.16	7.45	8.24	8.06	8.04	7.53	7.81	7.41
<i>SE</i>	0.50	0.35	0.32	0.53	0.36	0.33	0.51	0.36	0.33
Worry									
<i>Coeff.</i>	6.41	6.12	5.66	6.35	6.03	6.05	5.94	6.02	5.78
<i>SE</i>	0.38	0.27	0.24	0.40	0.27	0.24	0.39	0.27	0.25
Stress									
<i>Coeff.</i>	9.71	8.72	8.77	9.09	8.56	9.09	8.69	9.05	8.86
<i>SE</i>	0.57	0.40	0.36	0.60	0.40	0.37	0.58	0.41	0.37
Self-esteem									
<i>Coeff.</i>	12.77**	13.37*	14.51	12.20***	12.77***	14.25	12.77**	13.03**	14.38
<i>SE</i>	0.47	0.33	0.30	0.50	0.33	0.30	0.48	0.33	0.31
Satisfaction with life									
<i>Coeff.</i>	13.74	12.77	13.47	12.97	12.57	12.63	13.59	12.46*	13.16
<i>SE</i>	0.38	0.27	0.24	0.40	0.27	0.25	0.39	0.27	0.25

419 *Note.* Bold font indicates a significant difference between three groups within each menstrual cycle
420 phase; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. A.: androgenic; Anti-a.: anti-androgenic; NC: naturally
421 cycling; OC: oral contraceptives.
422

423 3. 2. Differences between phases for daily measures in each group

424 To clarify whether there is a group effect between phases, we used Equation 4.

425 There was no significant difference in daily levels for any of the variables tested in the
426 study between the three phases of the menstrual cycle in NC women, with all p -values
427 greater than 0.500. There was also no significant difference in daily levels for any of the
428 variables between the three times during which the anti-androgenic OC users and the
429 androgenic OC users were tested, with all p -values greater than 0.500.

430

431 4. Discussion

432 Our study had the advantage of using an intensive repeated measures

433 method and taking into account androgenic and anti-androgenic OC users,

434 following the recommendations of Laird et al. (7) and Beltz (8), who stressed the

435 need to consider different kinds of OC when conducting studies on mental health
436 disorders to gather accurate and consistent results and the need for more intensive
437 longitudinal studies as a means to observe individual differences.

438 Our first hypothesis was supported, as in our diary study, there was a
439 significant link between anxiety and depression levels within the sample. There
440 was also a significant link between anxiety and perseverative cognition, as well as
441 depression and perseverative cognition. These links have been previously
442 established in the literature (25,27,28) and confirmed in our study.

443 Our second hypothesis was partly supported as there were no differences
444 between groups in daily levels of anxiety, worry, perseverative thinking, and perceived
445 stress. However, there were differences between groups in daily levels of depression,
446 self-esteem, and satisfaction with life. Anxiety and depressive disorders tend to be
447 highly comorbid (53), so worsening symptoms of one disorder could be linked with
448 worsening symptoms of the other one. As a result, we could have expected that
449 significantly higher levels of depression in the OC user groups compared to the NC
450 women would be linked with significantly higher levels of anxiety, but it is not the case
451 in our sample. Anti-androgenic OC users had higher daily levels of depression than NC
452 women in all the phases of their menstrual cycle. In comparison, androgenic OC users
453 had higher daily levels of depression than NC women who were in their menstrual and
454 follicular phases. Both groups of women taking OC had lower daily levels of self-
455 esteem than NC women in all phases of the menstrual cycle. Androgenic OC users had
456 higher levels of daily satisfaction with life than anti-androgenic OC users in two out of
457 the three time points tested.

458 The lack of differences between OC users and NC women on daily levels of
459 anxiety is in line with certain studies conducted previously (35,54,55), which used the

460 GAD-7 scale (38) and the State-Trait Anxiety Inventory questionnaires (STAI-I, STAI-
461 II) (56) to compare NC women with women taking androgenic and anti-androgenic OC.
462 However, the RCT conducted by Lundin (15) showed that women who started taking an
463 anti-androgenic OC experienced an increase in anxiety levels in the 3 months of
464 treatment during which they were monitored. Our study was only observational and
465 could not draw causal conclusions. Cheslak-Postava et al. (14) analyzed data drawn
466 from the 1999-2004 American National Health and Nutrition Examination Survey and
467 found contrary results. They compared NC women with OC users, without specifying
468 the kind of progestins present in the OC and discovered that women taking OC had
469 lower levels of anxiety than NC women. It is challenging to make a direct comparison
470 between our results and those of Cheslak-Postava et al. (14) due to the lack of
471 information on progestin properties. However, we know that anti-androgenic OC have
472 been developed and prescribed more since 2010, in place of the androgenic OC that
473 used to be prescribed previously (57). We can hypothesize, based on the time when the
474 data were collected, that the women surveyed in the study by Cheslak-Postava et al.
475 (14) were taking androgenic rather than anti-androgenic OC. This means that the use of
476 androgenic OC might be linked with lower levels of anxiety. However, there is still a
477 lack of studies conducted on the link between anxiety and OC (7). It is also possible that
478 these studies exist, but they lead to non-significant results (no difference between NC
479 women and OC users) and are therefore not published. The lack of studies on this topic
480 and the mixed results present in the current literature do not allow us to have enough
481 data to draw firm conclusions on the link between anxiety levels and OC use. As the
482 review by Beltz (8) underscores, conducting RCTs in the field of OC is challenging;
483 however, it would be beneficial to conduct more studies evaluating the levels of anxiety
484 before and after treatment initiation, particularly in the long term.

485 Even though we did not find differences in daily anxiety levels, we observed
486 differences in daily levels of depression, with OC users having higher daily levels of
487 depression than NC women in all their menstrual cycle phases. The only exception was
488 the lack of difference between androgenic OC users and NC women in their luteal
489 phase. Our results are in line with the population-based cohort studies conducted by
490 Johansson et al. (22) and Skovlund et al. (20), which showed higher levels of depression
491 in adult OC users, both in androgenic and anti-androgenic ones. However, the higher
492 levels of depression in OC users in these studies were only observed at the beginning of
493 the treatment. We did not ask our participants how long they had been taking OC, which
494 does not allow us to know whether their higher levels of depression could have been
495 due to being at the beginning of their treatment. Nevertheless, the literature remains
496 contradictory regarding the link between OC use and depression levels in adult women.
497 On the one hand, the systematic review and network meta-analysis of randomized
498 clinical trials conducted by de Wit et al. (58) does not indicate a link between the use of
499 OC in adult women and an increase in depressive symptoms. Some studies even show
500 reduced levels of depression in OC users compared to NC women (59,60). These
501 studies used the Center for Epidemiologic Studies Depression Scale (CES-D, (61) and
502 the Beck Depression Inventory-13 (BDI-13, (62) to assess depression, but did not
503 control for the androgenicity of the OC. Nevertheless, one of these studies (59)
504 underlines that women with a history of depression are less likely to choose hormonal
505 contraception as a form of contraception in the first place. In contrast to the studies
506 showing no difference between OC users and NC women, or lower levels of depression
507 in OC users, a meta-analysis conducted by Pérez-López et al. (63) showed a link
508 between hormonal contraceptive use and consumed suicides, without indicating the
509 androgenicity of the OC. This information is important to take into account when

510 studying the link between OC and depression, as the review by Sundström Poromaa and
511 Segebladh (64) indicated that anti-androgenic OC are more efficient at lessening mood
512 symptoms than androgenic OC. However, in our study, anti-androgenic OC users had
513 higher levels of daily depression than NC women during the three phases, whereas
514 androgenic OC users only had higher levels of daily depression than NC women in two
515 phases (menstrual and follicular), but not in the luteal phase. This could be explained by
516 the fact that androgenic OC users have lower levels of testosterone than NC women
517 (65), but their levels of testosterone are not as low as those of anti-androgenic OC users
518 (6), while NC women see a decrease in testosterone levels in the luteal phase (66). Since
519 testosterone has an antidepressant effect on men and women alike (67), it is possible
520 that the depression levels of androgenic OC users do not differ from those of NC
521 women in their luteal phase because their testosterone levels are more similar than those
522 of anti-androgenic OC users and NC women.

523 We did not find any difference in the daily negative factors associated with
524 anxiety and depression, namely worry, perseverative thinking, and perceived stress,
525 between the NC women and the OC group. Few studies have compared these variables
526 in NC women and OC users, let alone using repeated measures. As a result, there is a
527 lack of studies on these topics, and the results are contradictory. A study conducted by
528 Kowalczyk et al. (35) concluded that women taking anti-androgenic OC had
529 significantly higher levels of worry than NC women. In contrast, the study by Louis et
530 al. (68) did not find any differences in worry levels between NC women and hormonal
531 contraceptive users. OC users have also been shown to experience higher levels of
532 neutral mind wandering, which is related to depressive symptoms (69). Regarding stress
533 levels, studies have shown that OC users have higher levels of cortisol (70) and a
534 blunted cortisol response to stress (71) compared to NC women, which might indicate a

535 state of chronic stress in OC users. However, our study did not find any difference
536 between groups. The absence of a difference in daily stress levels between the OC
537 group and the NC group allows us to conclude that the everyday life stress the
538 participants might have encountered throughout the study could not have affected
539 possible group effects. However, these results should be considered with some
540 precautions, particularly that all variables were measured on a daily basis. Future
541 studies may also explore within-day fluctuations (e.g., (72)).

542 We found lower daily levels of self-esteem in both groups of OC users
543 compared to NC women, suggesting, in line with the previous studies, that self-esteem
544 is a protective factor against depression (32). Another protective factor against
545 depression is satisfaction with life, as lower levels of life satisfaction are associated with
546 a higher risk of developing depressive symptoms (34). We found that androgenic OC
547 users had higher levels of daily satisfaction with life than anti-androgenic OC users, but
548 this result should be approached with caution, as it only appeared in one of the testing
549 phases. To the best of our knowledge, no studies have investigated daily self-esteem or
550 daily satisfaction with life in OC users before this. However, studies on the link
551 between OC and general well-being have shown strongly heterogeneous results:
552 hormonal contraceptive users showed lower levels of well-being than NC women in one
553 study (73), androgenic OC users enrolled in an RCT had lower levels of well-being than
554 NC women (74), another study concluded that anti-androgenic OC use was associated
555 with a higher level of psychological well-being (75), while an RCT comparing
556 androgenic and anti-androgenic OC use found an increase in emotional well-being in
557 both groups during the treatment (76). The heterogeneity of the results reported in the
558 literature indicates an important need to conduct more studies on the link between OC
559 use, well-being, self-esteem, and satisfaction in life, as these variables represent

560 protective factors lowering the risk of developing an anxiety disorder or depression.

561 The third hypothesis was not supported, as no differences were observed in daily
562 levels for any of the variables tested during the study between the different phases of the
563 menstrual cycle in NC women. The literature indicates that there is an exacerbation of
564 anxiety (3,12,13) and depression (3,18) symptoms in the luteal phase of NC women,
565 which is not the case in our sample. The lack of exacerbation of symptoms during the
566 luteal phase in our study might be explained by the fact that our sample was not from a
567 clinical population, as we did not know whether our participants had received an official
568 diagnosis of GAD or depression. Moreover, the review by Kuehner and Nayman (77)
569 concluded that around 60% of women suffering from depression experience an increase
570 in their symptoms during the premenstrual phase, but that these conclusions are limited
571 by retrospective assessments, no control of the presence of hormonal contraceptives and
572 psychotropic drug use, and no reliable validation of ovulation. Our study was not
573 retrospective; we verified oral contraceptive use and ovulation date, which might
574 explain why we found different results. Our fourth hypothesis, however, was supported,
575 as neither androgenic OC users nor anti-androgenic OC users showed any differences in
576 any of the variables across the three time points. This finding is consistent with the
577 literature, which has demonstrated that OC users tend to experience less variability in
578 affect during their menstrual cycle compared to NC women (78–80).

579

580 4. 1. *Limitations*

581 While the present study addressed certain limitations from previous studies, such
582 as separating androgenic and anti-androgenic OC or using intensive repeated measures,
583 it is not free from its own limitations. For instance, we calculated the cycle phases based
584 on the date of the participants' last menstruation onset and the usual length of their

585 menstrual cycle, and we also asked them to test for the date of their ovulation. However,
586 we did not conduct any hormonal levels testing to confirm the reliability of the cycle
587 phases. Our study was observational, and we cannot draw causal conclusions from it.
588 We did not ask participants about previous use of OC and the reason for their treatment.
589 For example, women with polycystic ovary syndrome show higher levels of
590 androgenicity and are often prescribed anti-androgenic OC for their symptoms (81).
591 This could have contributed to a possible selection bias confound related to the groups.
592 We did not compare the active and inactive phases of the OC users, and we did not ask
593 the participants whether they were stopping their treatment during the last phase of the
594 study, to experience withdrawal bleeding. We also did not compare the dose of
595 ethinylestradiol present in the OC, as suggested by Beltz (8). The perimenopausal status
596 of the participants was not verified, and we also did not verify at what age the OC users
597 had started their treatment. We did not ask whether the participants were taking any
598 psychotropic medication or whether they had any comorbidities. Finally, while the
599 number of participants was similar in the NC group and the OC group, the number of
600 participants taking androgenic OC ($n = 16$) was much smaller than the number of
601 participants taking anti-androgenic OC ($n = 32$).

602

603 *4. 2. Future studies*

604 The lack of consistency in the literature related to the link between OC use and
605 anxiety and depression indicates a necessity to conduct more studies on these topics.
606 Future studies might also take into account the link between testosterone and mental
607 health issues in NC women and OC users, since it has been demonstrated that higher
608 levels of testosterone are linked with lower levels of anxiety and depression (67).
609 Moreover, the differences between androgenic and anti-androgenic OC users in our

610 study underline the need to control the kind of OC women are using. The review by
611 Beltz (8) provides numerous indications on how to conduct future studies more reliably
612 by taking into account various variables, such as assessing the exact phases of the
613 menstrual cycle using hormonal measures, comparing the active and inactive phases of
614 OC, or considering the composition of OC. Other limitations described in the review are
615 a lack of longitudinal studies, especially those comparing women before and after they
616 started taking OC, and small sample sizes. The present study has shown that protective
617 variables related to handling anxiety and depression better (such as self-esteem or
618 satisfaction with life) should be considered when studying those topics. It might also be
619 important to control for other variables that could help refine the results, such as genetic
620 predisposition (anxiety: (82); depression: (83)), lifestyle factors (84), body mass index
621 (85), menarche age (86,87), or socioeconomic level (88). It could be interesting to
622 examine whether positive psychology interventions, which are efficient in alleviating
623 symptoms of depression (meta-analysis: (89)), could help women who are taking OC
624 and experiencing elevated levels of depressive symptoms.

625

626 **5. Conclusions**

627 We believe that our study has contributed to the literature by conducting an
628 intensive repeated measures assessment of anxiety and depression on a daily level and
629 comparing NC women and OC users during multiple phases of the menstrual cycle
630 while taking into account the differences between androgenic and anti-androgenic OC.
631 We have demonstrated that OC use is linked with a higher level of daily depression and
632 a lower level of daily self-esteem compared to natural cycling conditions.

633

634

635 **List of abbreviations**

636 A. – androgenic

637 Anti-a. – anti-androgenic

638 GAD – generalized anxiety disorder

639 LH – luteinizing hormone

640 OC – oral contraceptives

641 NC – naturally cycling

642 RCT – randomized controlled trial

643

644 **Declarations**

645 Ethics approval and consent to participate: The study was conducted in compliance with
646 the Helsinki Declaration and the research protocol was approved by the Ethics
647 Committee of the SWPS University in Warsaw, Poland (decision n°55/2020/2). The
648 participants provided informed consent before taking part in the recruitment process.

649 Consent for publication: Not applicable.

650 Availability of data and materials: The datasets analyzed during the current study are
651 available from the corresponding author upon reasonable request.

652 Competing interests: The authors declare that they have no competing interests.

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RESEARCH

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Anxiety, depression and perseverative cognition in women cycling naturally or taking oral contraceptives – a diary study

Melanie Kowalczyk^{1*}, Monika Kornacka² and Izabela Krejtz¹

Abstract

Background While the literature is inconsistent about the link between anxiety and oral contraceptives (OC), the link between depression and OC is recognized in women who started OC during adolescence. Perseverative cognition is a stress-coping mechanism present both in anxiety and depression. Our study aimed to understand the differences between women taking OC and naturally cycling (NC) women regarding their daily levels of anxiety, depression, related negative factors (perseverative cognition and stress), and protective factors (self-esteem and life satisfaction).

Methods The study was conducted on 89 adult women (M age = 26.60, SD = 4.65) (48 – OC; 41 – NC) who participated in a 15-day online diary study divided into 3 phases throughout one menstrual cycle. The women using OC were further classified according to the androgenicity of their OC (androgenic and anti-androgenic). The participants were sent an email in the evening with questionnaires they had to complete on the same day. The daily measures were taken from existing trait-level scales and adapted for daily administration. The analyses were conducted using hierarchical linear modeling, with a significance level of $p < 0.05$.

Results There were no differences between groups in daily levels of anxiety, perseverative cognition, and stress. However, anti-androgenic OC users had higher levels of daily depression than NC women in the three menstrual cycle phases tested for, while androgenic OC users had higher levels of daily depression than NC women in two phases. Both groups of women taking OC had lower levels of daily self-esteem than NC women in all three phases. Androgenic OC users had higher daily satisfaction with life than anti-androgenic OC users in one testing phase.

Conclusions OC users had higher daily levels of depression and lower daily levels of self-esteem than NC women. Future studies could explore the link between depression and the different types of OC in adult women, especially with longitudinal methods.

Keywords Anxiety, Depression, Menstrual cycle, Oral contraceptives, Daily diary, Perseverative cognition, Self-esteem, Satisfaction with life

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Melanie Kowalczyk: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, writing – review & editing, visualization, project administration, funding acquisition.

Monika Kornacka: conceptualization, methodology, validation, formal analysis, resources, writing – review & editing, supervision.

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I declare that the authors' contribution to the manuscript, according to the CRediT classification, comprised the following:

Melanie Kowalczyk: conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, writing – review & editing, visualization, project administration, funding acquisition.

Monika Kornacka: conceptualization, methodology, validation, formal analysis, resources, writing – review & editing, supervision.

Izabela Krejtz: conceptualization, methodology, validation, formal analysis, resources, writing – review & editing, supervision, funding acquisition.

I also declare that Melanie Kowalczyk's estimated quantitative contribution to this article was 80%.



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