Utrecht University

The Effect of the Oral Contraceptive Pill on Emotion Regulation

[Master Thesis]

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Date: 28-11-2023

Make publicly available: Yes

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Abstract

This study looked at the effect of the oral contraceptive pill (OC) on the emotion reactivity and emotion regulation processes, using the neurophysiological component late positive potential (LPP) and additional subjective valence ratings. The hypothesis concerning emotion reactivity was that OC users would have less emotion reactivity than naturally cycling women (NC). The hypothesis for emotion regulation was that OC users would have poorer regulation than NC women. A total of 54 participants were tested. OC users (n = 30) were tested when actively taking the pill and NC women (n = 24) were tested in their luteal phase. The participants filled in several questionnaires (BDI, PANAS, CTQ, Life Events) and performed an emotion regulation task while being monitored by an electroencephalography (EEG). Concerning emotion reactivity, the EEG results showed that OC had less emotion reactivity than NC (in the early time window). No significant differences were observed in the subjective valence ratings. Concerning emotion regulation, neither the LPP measures nor the subjective valence ratings showed significant differences between OC and NC. Nevertheless, in future research the results of this study can be used to further expand on the knowledge of the contraceptive pill and its effects on emotion regulation.

Introduction

In 2022, roughly 150 million women used the contraceptive pill (OC) worldwide (United Nations Department of Economics and Social Affairs, Population Division, 2022). Research on this pill is therefore incredibly relevant on a societal level as these women should know the consequences of taking it. There are many physical side effects from taking the pill, such as headaches, nausea and breakthrough bleeding (Pratt & Bachrach, 1987). The main physical side effect that is researched is a higher risk of vascular diseases (Ory, 1977; Vessey & Mann, 1978; Petitti et al., 1998). Even though emotional side effects such as mood changes are also reported, existing research on mental health side effects remain inconsistent (Pletzer & Kerschbaum, 2014; Cobey & Buunk, 2012). OC use is associated with depression symptoms and a depression diagnosis in later life (Skovlund et al., 2016; Anderl et al., 2020; de Wit et al., 2020) and is associated with increased risk of suicide (Skovlund et al., 2018) and higher antidepressant use (Wiréhn et al., 2010). However, other researchers suggest that OC seems to be associated with improved mood (Toffol et al., 2012; Toffol et al., 2011) and a reduced risk of panic disorder (Cheslack-Postava et al., 2015), anxiety and depression symptoms (Keyes et al., 2013; Doornweerd et al., 2022), premenstrual dysphoric disorder and premenstrual syndrome (Freeman et al., 2012). These conflicting results show that there is no consensus on the effects of OC on emotional well-being, how it works and who is susceptible to it. For instance, many researchers have found that susceptibility to stress, anxiety and depression are common among women who have discontinued treatment with the pill due to the perceived adverse mood effects (Borgström et al., 2008; Hall et al., 2012). However, the data in these studies was gathered according to retrospective reports of adverse mood symptoms, which means there is no confirmation that the mood deterioration is caused by the pill. Therefore, more research is needed regarding the underlying mechanisms of the pill and its possible emotional side effects.

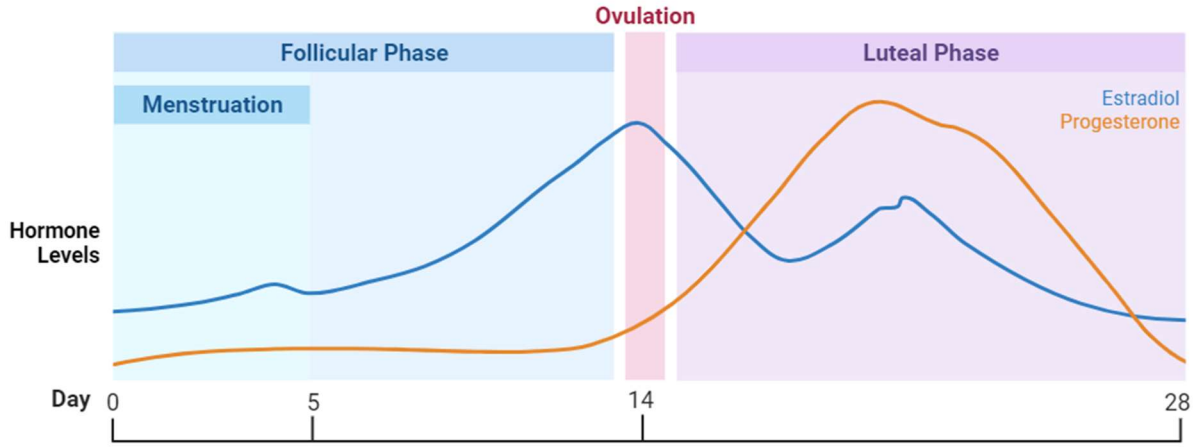
Oral Contraceptive Pill

A regular (natural) menstrual cycle (NC) consists of 28 days, starts at the first day of menstruation and can be roughly divided into two phases (Mihm et al., 2011). The first 14 days are called the follicular phase, after which the ovulation takes place and the next phase of the menstrual cycle called the luteal phase ensues. Estradiol (E) and progesterone (P) fluctuate throughout this cycle through regulation of the hypothalamus-pituitary-gonodal (HPG) axis. During the follicular phase, both E and P are low, then E rises until it reaches a peak at the

ovulation. In the luteal phase E first descends and then peaks along with P. At the end they both descend again and menstruation starts anew (see Figure 1). The OC contains synthetic forms of E and P, which signals through negative feedback to the HPG axis that natural production of these hormones can be haltered, and results in a stable and low level of hormones which prevents pregnancy (Montoya & Bos, 2017).

Figure 1

Estradiol and Progesterone During Natural Cycle



Besides the HPG axis, E and P are known to have receptors located in regions like the amygdala, hypothalamus, hippocampus and cerebral cortex that are responsible for emotion regulatory functions (Jacobs et al., 2015; Boyle et al., 2021). Toffoletto et al. (2014) highlight that E and P exert structural and functional changes in the brain, specifically in those regions. Therefore, fluctuations and alterations of E and P, for instance through the OC, are likely to have an effect on behaviour and brain functions. In line with this, puberty, pregnancy and menopause are marked by major changes in hormonal milieu, and are periods associated with an increase in prevalence of mood disorders in women (Steiner et al., 2003).

Emotion Regulation

Ochsner et al. (2012) state that 'emotion regulation entails the modification of ongoing - or the initiation of new - emotional responses through the active engagement of regulatory processes.' In other words, emotion regulation is the ability to actively change to your emotions. For example, if a student has to move back home to their parents' house and they feel negatively about the move, they could choose to look at the silver lining: they get to spend more time with their family! Emotion regulation is relevant for processing negative emotions and faulty regulation strategies therefore play an important role in depression (Joormann & Gotlib, 2010).

Emotion regulation can be divided in explicit and implicit regulation. Explicit regulation is the conscious effort to monitor and adjust your emotions and implicit regulation happens unconsciously. A form of explicit emotion regulation often used in research is called reappraisal, which involves re-interpretating the event or stimulus you want to regulate in order to change one's emotional response to it (Ochsner et al., 2012). Four control systems have been most strongly implicated in explicit emotion regulation: dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), dorsal anterior cingulate cortex (dACC) and dorsal medial prefrontal cortex (dmPFC) (Diekhof et al., 2011; Ochsner et al., 2012; Buhle et al., 2014). These areas (specifically the ACC and the dlPFC) are tightly connected to the limbic structures, such as the amygdala, in regards to for instance emotional processing (Comte et al., 2016). The limbic system shows high concentrations of receptors that are sensitive to E and P (Catenaccio et al., 2016). These hormones change the structure and activity of the brain through processes such as the menstrual cycle, pregnancy, menopause, and puberty (Rehbein et al., 2021). This may mean that by the hormonal change of E and P, the menstrual cycle could impact emotion regulation processes. However, the pill changes these hormones, which in turn could influence brain activity, specifically on emotion regulation. Therefore, this mechanism could be responsible for hormonal changes that effect emotions during the menstrual cycle and due to hormonal contraceptive use.

Besides the direct effects of E and P through receptors in the aforementioned brain functions, their effect on emotion processing and behaviour may also occur through effects on the serotonin system, dopamine system (Gasbarri et al., 2012; Shanmugan & Epperson, 2014; Zachry et al., 2021) and through allopregnanolone (THP) (Zheng, 2009). THP is a neurosteroid which is made from P and has GABAergic properties (Schüle et al., 2013). The GABAergic neurotransmission in turn inhibits the amygdala, which plays a central role in emotion regulation (Jie et al., 2018). All three of these systems (serotonin, dopamine and THP) are linked to mood and therefore E and P could have an indirect effect on emotion regulation through these systems as well.

On a behavioural level, Chung et al. (2019) found that higher E levels predict greater dlPFC activity when using cognitive reappraisal of negative emotion. Since OC leads to low levels of E, it is plausible that this could lead to reduced activity during reappraisal. In contrast to the findings of Chung et. al (2019), Rehbein et al. (2022) compared pregnant women (with extremely high levels of E) with NC women and found that high levels of E did not necessarily enhance cognitive reappraisal. Notably, Rehbein et al. (2022) used NC women as the baseline

group with low E levels, while OC users have even lower levels of E. Therefore, while lower levels of E (OC users) might lead to reduced activity during reappraisal, higher levels of E do not necessarily enhance those functions. These contrasting findings highlight the complex and indicative of a non-linear relationship between E levels and emotion regulation.

A neurophysiological way to measure emotion regulatory success is by using an event related potential (ERP) called late positive potential (LPP). The LPP reflects sustained attention toward emotional stimuli and is thought to be a neural correlate for emotional reactivity (Hajcak et al., 2010; Speed et al., 2015). LPP has also been linked to depression and its treatment. Depression has been associated with reduced LPPs (MacNamara et al., 2016; Foti et al., 2010; Kayser et al., 2017) and individuals with larger LPPs for aversive stimuli show a greater response to cognitive behavioural therapy (Stange et al., 2017). Additionally, Meynadasy et al. (2022) found that individuals with depressive symptoms show a blunted LPP regardless of applying reappraisal to affective stimuli. However, other studies suggest that the link between depression and reduced LPPs is absent (McGhie et al., 2021; Nikolin et al., 2020), which means the relationship between LPP amplitude and depression remains inconclusive. LPP has also been linked to sex hormones. Previous research suggests that LPP is sensitive to E, as higher concentrations of E (during follicular phase and ovulation) are associated with more positive LPPs to sexual stimuli (Munk et al., 2018; Krug et al., 2000) and to both negative and positive emotional faces (Zhang et al., 2013).

Regarding the effect of OC on LPP, Monciunskaite et al. (2019) found a lower LPP among OC users (actively on the pill) compared to non-users (in both the follicular and luteal phase) when tested on emotional reactivity to affective stimuli. Although their focus is described as ‘affective processing’, for consistency with the terminology of this research, their findings are referred to as ‘emotion reactivity’. This aligns with previous research, which found that OC is accompanied with decreased emotion-induced reactivity in the left insula, left middle frontal gyrus, bilateral inferior frontal gyri (Gingnell et al., 2013) and in the bilateral amygdala (Petersen & Cahill, 2015). A possible explanation for this finding could be a phenomenon called ‘emotional blunting’, which is a term that signifies reduced emotional reactivity. For instance, Hamstra et al. (2017) found that OC users experienced fewer mood swings than NC, which they attribute to emotional blunting. Possibly, emotional blunting is what causes OC to decrease emotion reactivity. However, there are still mixed results regarding the effect of OC on emotion reactivity. For instance, Spalek et al. (2019) found that OC users subjectively rate negative pictures as more negative and positive pictures as more positive, indicating mixed results in the

relationship between OC use and emotion reactivity (both on a physiological and subjective level). This means more research is needed to clearly distinguish the effect of OC on emotion reactivity. It is also important to not that previous research regarding the effect of OC on LPP (Monciunskaite et al., 2019) has solely looked at emotion reactivity, which means there is still a knowledge gap regarding the effect of OC on the later stages that occur after emotion reactivity such as explicit emotion regulation, on both a physiological and subjective level.

Current Research

The current research will take a look at the effect of the contraceptive pill on the emotion reactivity and emotion regulation process, using the neurophysiological component LPP and additional subjective valence ratings. Therefore, two hypotheses will be made, one for each process. Based on previous research (Monciunskaite et al., 2019), the hypothesis concerning the emotion reactivity process is that OC users will show less emotion reactivity than NC women. This will become apparent through a smaller LPP difference wave and less difference in the subjective valence ratings for the OC group. The hypothesis for the emotion regulation process is that OC users will have poorer regulation than NC women. This will also become evident through a smaller LPP difference wave and less difference in the subjective valence ratings for the OC group. This is based on previous research (Foti & Hajcak, 2008; Krompinger et al., 2008; Moser et al., 2009) which shows that a low LPP (resulting in a larger difference wave) signifies successful emotion regulation. Since more research regarding the oral contraceptive pill and its emotional side effects is greatly needed, this study will contribute to the knowledge gap regarding the pill and its effects on emotion regulation.

Method

Participants

Since OC and NC were compared, the participants needed to either use the contraceptive pill or have a natural cycle. The participants were healthy women aged 20 to 35. Another inclusion criterium was that they had to have a BMI-score between 19 and 30. Exclusion criteria were as follows: the usage of hormonal medication in the last three months; the usage of drugs or psychotropic medication in the last month or as regular as every two weeks; pregnancy or breastfeeding; a hormonal disorder; a diagnosis of a psychiatric or neurological disorder (presently or in the past); a diagnosis of gynaecological disorder/disease (presently or in the

past); an irregular natural cycle of under 25 days or over 32 days; or if they started using hormonal contraceptives less than three months ago.

Originally, 55 participants were tested. However, two participants were excluded from the results, leaving 53 participants divided between OC (n = 30) and NC (n = 23). Three of the naturally cycling participants used a copper spiral, which does not administer any hormones, which is why they were allocated to the NC group. All the participants in the OC group were Dutch. Out of the 23 in the NC group, 12 were Dutch and 10 were of a different nationality. One participant's nationality was not filled in (from the NC group). Participants were recruited through Sona systems, social media platforms and social circles, and mostly fell under convenience sampling. Participants were rewarded either 4.25 test subject hours or 35 euros for participating. The study has been approved by the Ethics Committee (Facultaire Ethische ToetsingsCommissie (FETC)).

Procedure

Before signing up for the study, participants went through an online screening via Qualtrics in which they were screened for the inclusion and exclusion criteria which decided whether they were suitable participants. In the larger study participants were measured twice, for the NC group during the follicular and luteal phase and for the OC group when the pill is inactive and active. However, this study only included measures during the luteal phase for NC and pill active for OC. For the NC group, the measurement during the luteal phase was included, because E and P are at their peak at this time for the NC women and differ most in hormonal profile from the low hormone levels in OC users. Particularly for the NC group, the moment of testing was planned specifically to ensure that they were in the middle of their luteal phase at the moment of testing. This was based on the length of their previous two cycles. If their cycles were short, the middle of the luteal phase would occur at an earlier stage than if their cycles were long. For instance, if the cycle length was 24 days, the lab visit would be planned on day 15 to 19, but if the cycle length was 34 days, it would be planned on day 25 to 29. Upon arrival the participants signed an informed consent form and went through the information letter again. The experiment started with a rinse of the mouth before taking the saliva sample, analysed elsewhere. Afterwards, a fear conditioning task was administered, which was part of the larger study and will be discussed elsewhere. Several questionnaires (BDI, PANAS, CTQ) were filled in after the first task. Subsequently, the electroencephalography (EEG) and electromyography (EMG, which was used for the larger study) apparatus were applied and the emotion regulation

task would start. Afterwards, the EEG and EMG were taken off again and they started the second part of the fear conditioning task. For the larger study, they were tested a second time approximately two weeks later. After the second test moment the participants were handed a debrief of the experiment and they signed a reward form that will be rewarded with participation points or a monetary reward of 35 euros.

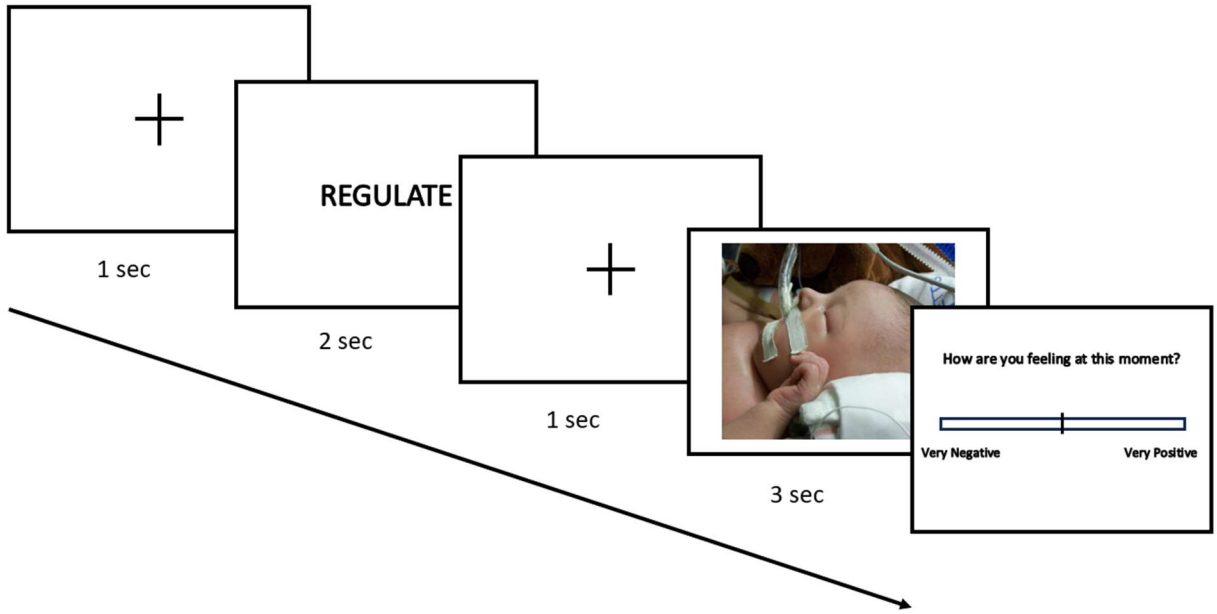
Emotion Regulation Task

The emotion regulation task was based on a paradigm by Ochsner et al. (2002). In this task, pictures with different emotional valences were shown to participants who received different instructions (view, regulate) before each picture. In total, the task contained 120 pictures which were gathered from the International Affective Picture System (Lang et al., 2008), the Nencki Affective Picture System (Marchewka et al., 2014) and the Geneva Affective Picture Database (Dan-Glauser et al., 2011). The pictures were divided into four conditions (positive, neutral, negative view and negative regulate) with 30 pictures per condition. All pictures contained people. The positive pictures mostly consisted of smiling people or children playing. The negative pictures have been selected to elicit mostly empathic responses. For example, a needle in an arm or a woman with half her face burned off. The most gruesome ones were not included to prevent eliciting a disgust response. The neutral pictures do not elicit a big emotional response, and were for instance a person on a bicycle or a person sitting on a chair with a natural face expression. In the positive, neutral and negative 'view' condition the participant received the instruction to simply view the picture and allow any and all emotions that were being brought up by the pictures. For the negative regulate condition, participants were instructed to regulate their emotions (see Figure 2), and were trained in different strategies with the following instructions: 1) Reinterpret the picture by: imagining the people on the picture as actors; convincing yourself that the situation is different from what is suggested on the picture; or convincing yourself that the outcome is different than the picture suggests. 2) Take distance from the situation that is pictured by interpreting it in a different way: remind yourself that you a looking at a picture and that you are safely sitting in this room. After every picture participants were asked: 'My feelings at this moment are:'. They would indicate this on a scale from 1 (very negative) to 100 (very positive). Since there were 120 pictures, there were also 120 trials. One trial went as follows: a fixation cross for 1 second, the instruction to view or regulate for 2 seconds, a fixation cross for 1 second, the picture for 3 seconds, and lastly the question on how they were feeling at that moment with no time limit. The order of the trials

were randomised and two versions of the task were made that were counterbalanced among the groups for the two measurements.

Figure 2

Emotion Regulation Task: Example Negative Regulate Condition



Questionnaires

The Positive And Negative Affect Schedule (PANAS; Watson et al., 1988) measures both positive and negative emotions. It consists of 20 words: 10 positive and 10 negative. For each word the participant indicates how much they feel that emotion at that moment. They do so on a Likert scale from 1 (absolutely not) to 5 (extremely). An example of a positive word is 'interested' and an example of a negative word is 'angry'. The Cronbach's alpha of the positive affect schedule is .89 and the Cronbach's alpha of the negative affect schedule is .85. Therefore, both schedules have a high reliability.

The Beck Depression Inventory (BDI; Beck et al., 1996) measures depressive symptoms based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) with 21 items with 5 subscales: emotional, cognitive, motivational, physical and delusional. An example item is sadness. The participant can choose between 4 options: 'I do not feel sad'; 'I feel sad'; 'I am sad all the time and I can't snap out of it'; and 'I am so sad and unhappy that I can't stand it'. The answer options differ per question,

but number of options is 4 for every question. This item is part of the emotional subscale. The Cronbach's alpha of the BDI is .91, giving it a high reliability.

The Childhood Trauma Questionnaire (CTQ; Bernstein et. al., 2003) measures childhood trauma symptoms with 28 items and 5 subscales: physical abuse, emotional abuse, sexual abuse, physical neglect and emotional neglect. An example of an item is: 'During my childhood I did not have enough to eat'. The participant answers the questions on a Likert scale from 1 (never true) to 5 (very often true). This item is part of the physical neglect subscale, which has a Cronbach's alpha of .61. The other subscales (and their respective Cronbach's alpha) are emotional abuse (.87), physical abuse (.83), sexual abuse (.92) and emotional neglect (.91). These alpha's suggest that the CTQ has a high reliability.

Psychophysiological measures

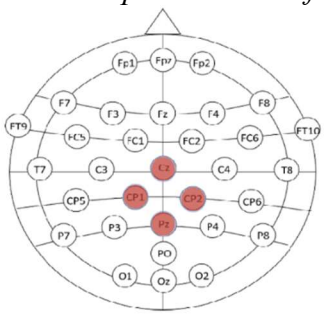
EEG data were collected using a Biosemi ActiveTwo amplifier, recording 32 channels of EEG signals, along with 8 EMG electrodes placed on the face and mastoids. The sampling rate was set at 256 Hz. The data underwent preprocessing using Brain Vision Analyzer 2.0 and Matlab (Version 7.11). The raw EEG data was re-referenced to the average of all electrodes and filtered using a 50 Hz bandpass filter. Initial artifact rejection was applied with an amplitude range of -300 to 300 μV. Due to the complexity of the visual stimuli, a double automatic ocular correction process was employed. First, independent component analysis (ICA) was used to address major vertical and horizontal eye movement artifacts. Then, a Gratton and Coles correction was applied to further remove any residual eye movement artifacts. A second artifact rejection was carried out using an amplitude range of -150 to 150 μV.

The EEG recordings were segmented from -200 to 3000 ms based on stimulus onset and baseline corrected starting from -199.22 milliseconds. The data was then grand-averaged according to conditions (neutral, negative view, negative regulate). Subsequently, difference waves were computed to analyse the variations between conditions (negative view – neutral, negative regulate – negative view).

An ERP waveform analysis was conducted to facilitate a comparison of affective processing between NC and OC women. The LPP is a well-known ERP component localised centroparietally. The electrodes CP1, CP2, Cz and Pz (Figure 3) were selected based on the largest difference wave values (see Figure 4). The time windows for the LPP were divided into early (400-800 ms), middle (800-1400 ms), and late (1400-3000 ms) LPPs.

Figure 3

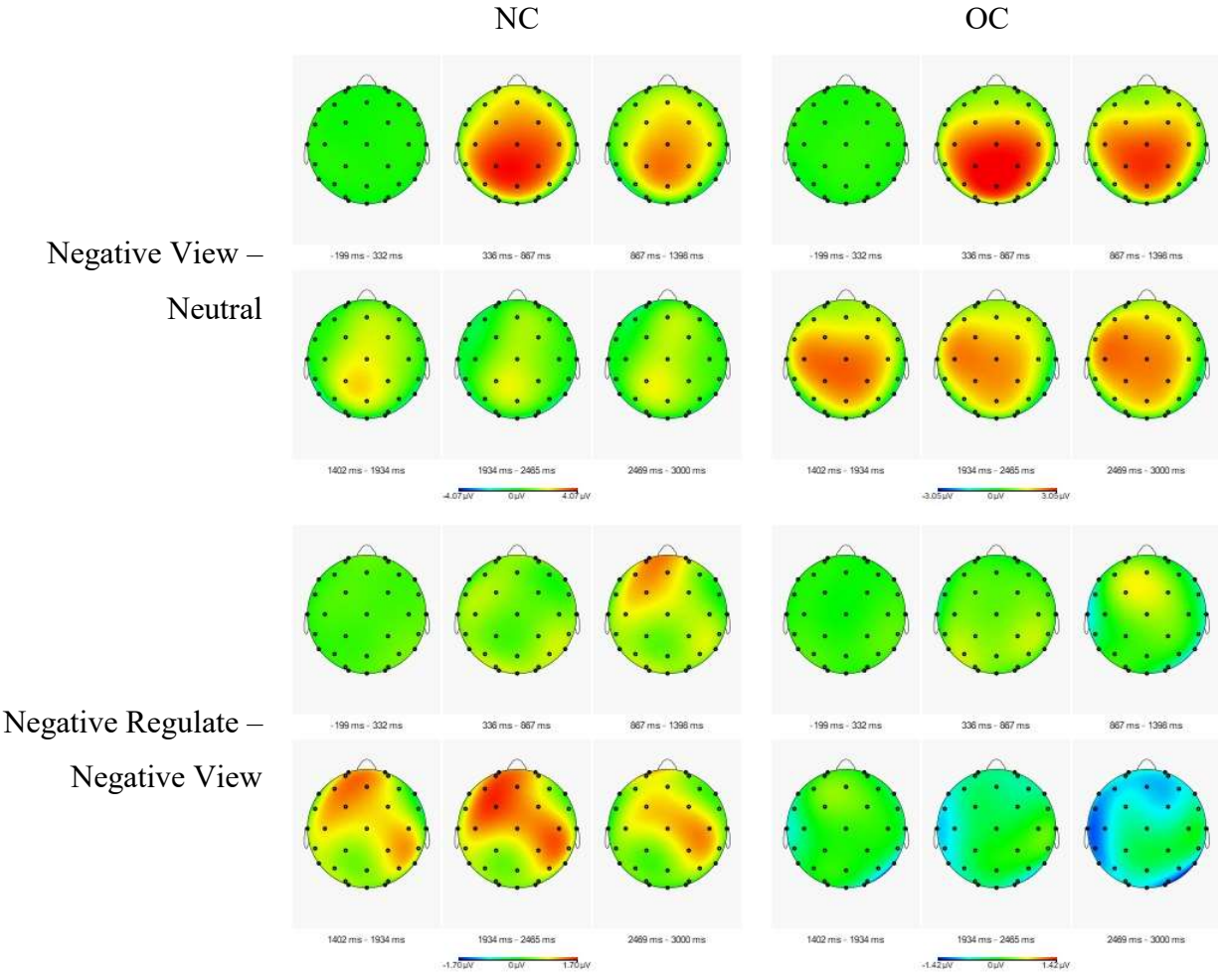
Schematic Representation of the Chosen Electrodes



Note. The original image was made by Haputhanthri et al. (2019).

Figure 4

Topographical Heatmaps per Group per Difference Wave



Note. Regarding emotion reactivity (negative view – neutral), the four electrodes at the back of the head (CP1, CP2, Cz, Pz) distinctly show the largest difference wave for both NC and OC. For emotion regulation (negative regulate – negative view), the results are more ambiguous. Therefore, CP1, CP2, Cz and Pz were chosen for this research.

Statistical Analyses

The group differences in demographic variables including age, education, alcohol use and drug use were analysed using a two-tailed independent t-test. The assumptions of an independent t-test are the assumption of normality, the assumption of equal intervals, the assumption of homogeneity of variance and the assumption of independence. Should the assumption of homogeneity be violated, this was corrected by looking at 'equal variances not assumed'. If any assumptions were violated, a two-tailed non-parametric t-test (Mann-Whitney U test) was performed additionally. Subsequently, the *p* or non-parametric *p* was chosen based on whether the assumptions were violated. Furthermore, the questionnaires: the BDI, the PANAS, the CTQ and the question whether they had been through something traumatic in the last six months (Life Events) were compared between groups using a two-tailed independent t-test.

To examine the subjective valence ratings, the difference waves were calculated to analyse the emotion reactivity and emotion regulation processes. For emotion reactivity, the 'negative view' scores were subtracted from the 'neutral' scores and for emotion regulation, the 'negative view' scores were subtracted from the 'negative regulate' scores. The difference between OC and NC on this difference score were analysed using a two-tailed independent t-test for each effect. The assumptions of this test are the same as previously mentioned. Should the assumption of homogeneity be violated, this was corrected by looking at 'equal variances not assumed'. If any assumptions were violated, a two-tailed non-parametric t-test (Mann-Whitney U test) was performed additionally. The *p* or non-parametric *p* was chosen based on whether the assumptions were violated.

To examine the LPP measures, an average of the difference waves of the chosen electrodes (CP1, CP2, Cz, Pz) was calculated per time window. The effect of the group (OC vs NC) and the time windows (Early, Middle, Late) on both the emotion reactivity and emotion regulation processes (difference waves) were analysed with a mixed ANOVA, since the effect of the group is a between-subject independent variable and the effect of the time windows is a within-subject independent variable. Both the main effects and the interaction effects were looked at and if significant, a post hoc analysis was applied. The assumptions of this test are the assumption of normality, the assumption of homogeneity and the assumption of sphericity. If the assumption of sphericity was violated, the Greenhouse-Geisser correction was looked at and to account for multiple comparisons, a Bonferroni correction was employed.

In addition, the LPP measures were correlated with a couple of variables. A selection of variables was made for this study to manage the risk of false positives. Firstly, only the most significant time window was used for the correlations. Within this time window, the LPP measures were correlated with the subjective valence ratings; with solely the demographic variables that were significant in previous independent t-tests; and with the PANAS and BDI questionnaires. The PANAS was chosen as it directly measures current emotional states, which is directly relevant to the LPP measures. The BDI was chosen as it assesses depressive symptoms, which could also directly impact emotion regulation and therefore the LPP measures. While the CTQ and Life Events remain relevant factors, they measure long term historical factors and experiences, which are not directly aligned to current emotional states at the time of testing. This was done with a (two-tailed) Pearson correlation test per group. The assumptions of the Pearson correlation test are the assumption of level of measurement, the assumption of related pairs, the absence of outliers and the assumption of linearity. To account for multiple comparisons, a Bonferroni correction was employed.

Results

Descriptives and Questionnaires

The participants filled in a menstrual cycle questionnaire (MCQ) about their respective OC or NC use. The frequencies of the MCQ answers per group can be found in Table 1, 2 and 3 in Appendix A.

The descriptive results show that, on average, the OC group was younger (M = 22.19, SD = 2.16) than the NC group (M = 24.73, SD = 3.53). This difference was significant, $t(31.007) = -2.91$, $p < .01$. The results also show that, on average, the NC group was higher educated (M = 2.68, SD = 1.09) than the OC group (M = 1.90, SD = 1.06). This difference was also significant, $t(50) = -2.60$, $p < .05$. For alcohol and drug use, no significant differences were found between the groups (see Table 4). For the questionnaires, also no significant group differences were found (see Table 5).

Table 4

Demographics: Descriptive Statistics & Significance Levels

	OC (n = 30)	NC (n = 22 [a])	*P*
Age (in years) [b], mean (SD)	22.19 (2.16)	24.73 (3.53)	.006
Education, mean (SD)	1.90 (1.06)	2.68 (1.09)	.013
Alcohol, mean (SD)	2.13 (.57)	1.86 (.77)	.157
Drugs, mean (SD)	1.63 (.81)	1.50 (.74)	.562

Note. Education, Alcohol and Drug use were used a numeric variables to conduct the analyses. This was done in the following order, for education level: 1 = high school, 2 = college/associate degree, 3 = bachelor's degree and 4 = master's degree; for alcohol use: 1 = none, 2 = several days a month and 3 = several days a week; and for drug use: 1 = no drugs, 2 = soft drugs and 3 = hard drugs.

[a] Unanswered by one participant in the NC group (n = 22).

[b] Unanswered by two participants from each group (OC: n = 28; NC: n = 21).

Table 5

Questionnaires: Descriptive Statistics & Significance Levels

	OC (n = 30)	NC (n = 23)	*P*
BDI, mean (SD)	6.70 (5.42)	9.39 (9.07)	.477
PAS, mean (SD)	31.03 (4.54)	28.22 (6.54)	.070
NAS, mean (SD)	14.83 (4.43)	15.00 (4.06)	.718
CTQ, mean (SD)	33.07 (6.32)	34.48 (11.49)	.299
Life Events, mean (SD) [a]	1.47 (.51)	1.43 (.51)	.819

[a] Life Events was used as a numeric variable to conduct the analysis: 1 = Yes and 2 = No.

Subjective Valence Ratings

The results of the subjective valence ratings show that the difference between OC and NC was not significant for neither the emotion reactivity nor the emotion regulation process (see Table 6). The differences of the subjective valence ratings per effect per group can be seen in Figure 5.

Table 6

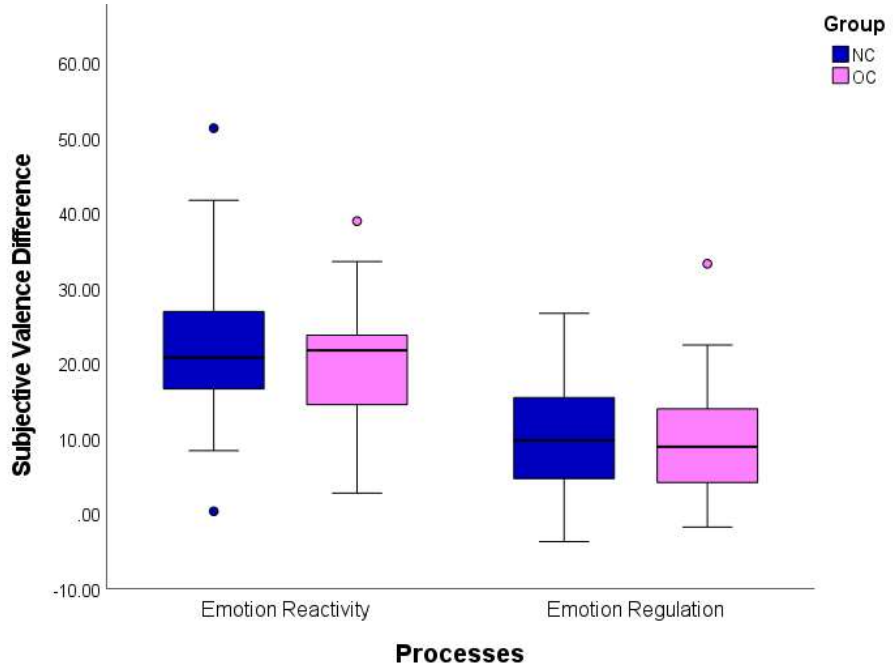
Subjective Valence Ratings: Descriptive Statistics & Significance Levels

	OC (n = 30)	NC (n = 23)	*P*
Emotion Reactivity, mean (SD)	20.03 (8.75)	22.47 (11.68)	.389
Emotion Regulation, mean (SD)	10.08 (8.04)	10.04 (8.40)	.985

Note. These subjective valence differences signify the difference in subjective ratings between certain conditions. For emotion reactivity, 'negative view' was subtracted from the 'neutral' condition. For emotion regulation, 'negative view' was subtracted from the 'negative regulate' condition. This was done per group.

Figure 5

Clustered Boxplot of Subjective Valence Difference per Process per Group



Note. This clustered boxplot is a schematic representation of the subjective valence ratings presented in Table 6.

LPP Measures

As for the LPP measures, the results of the emotion reactivity process show that the main effect of time window, $F(1.67, 85.39) = 21.17$, $p < .001$, and the interaction effect between time window and group, $F(1.67, 85.39) = 7.38$, $p < .01$ was significant (see Table 7). Therefore,

the pairwise comparisons were looked at for those effects (see Table 8, 9 and 10 in Appendix B).

The pairwise comparisons showed that, within the NC group, there was a significant decrease from the early time window to the late time window (2.80 (95% CI, 1.54 to 4.06) LPP difference wave, $p < .001$). Within the NC group, there was also a significant decrease from the middle time window to the late time window (1.96 (95% CI, .99 to 2.92) LPP difference wave, $p < .001$). Moreover, OC scored significantly lower than NC within the early time window (1.10 (95% CI, .07 to 2.14) LPP difference wave, $p < .05$). The mean difference wave through time per 100 ms and per time window can be seen in Figure 6. The means of the difference waves per time window per group can be found in Table 11 in Appendix A.

Table 7

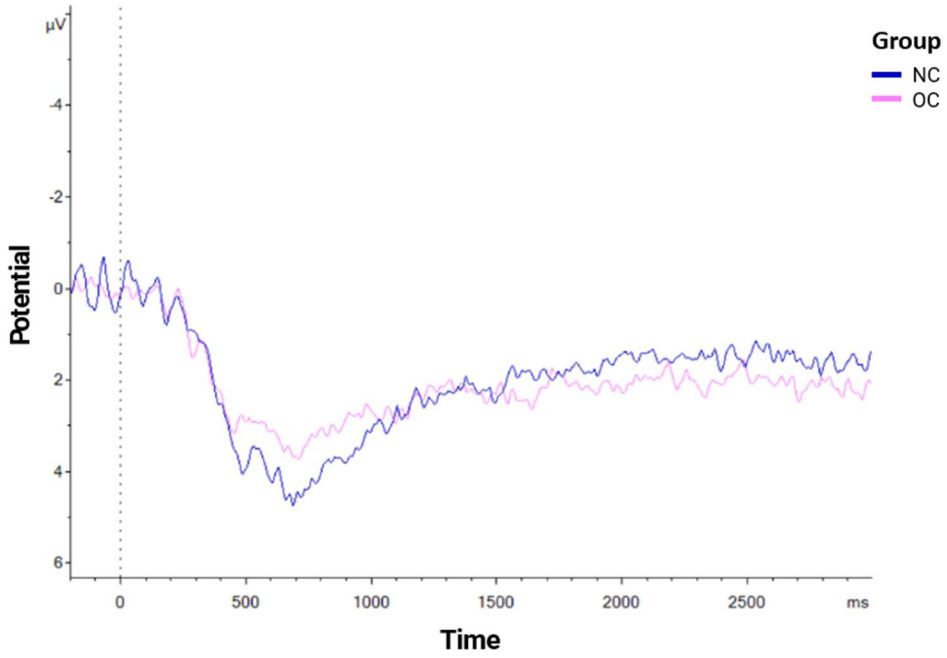
Emotion Reactivity: Significance Levels

Main & Interaction Effects	Report	*P*
Group	$F(1, 51) = .57, p > .05$	.453
Time Window	$F(1.67, 85.39) = 21.17, p < .001$	< .001
Time Window * Group	$F(1.67, 85.39) = 7.38, p < .01$	.002

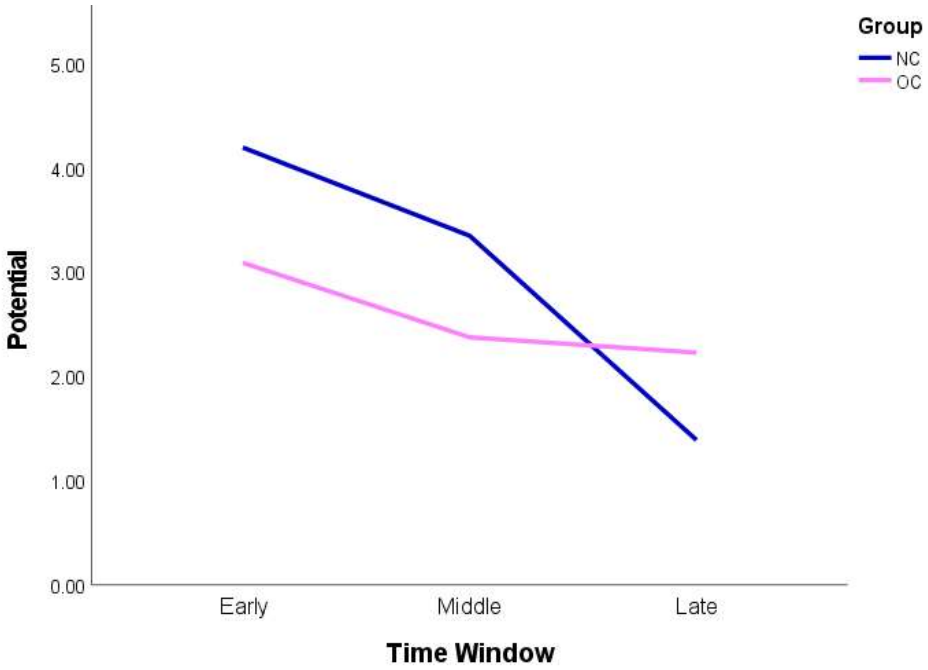
Figure 6

Emotion Reactivity: Averaged Difference Wave per Group A) Through Time and B) per Time Window

A)



B)



Note. The potential signifies the averaged LPP difference waves of the chosen electrodes: CP1, CP2, Cz and Pz. For emotion reactivity, this difference wave is the difference between the 'negative view' and 'neutral' condition (negative view – neutral). Figure A shows the timeline per 100 ms and Figure B shows the same results for each time window.

For the emotion regulation process, the results show that none of the analyses were significant (see Table 12), Therefore, the pairwise comparisons were not looked at. The mean difference wave through time per 100 ms and per time window can be seen in Figure 7. The means of the difference waves per time window per group can be found in Table 11 in Appendix A.

Table 12

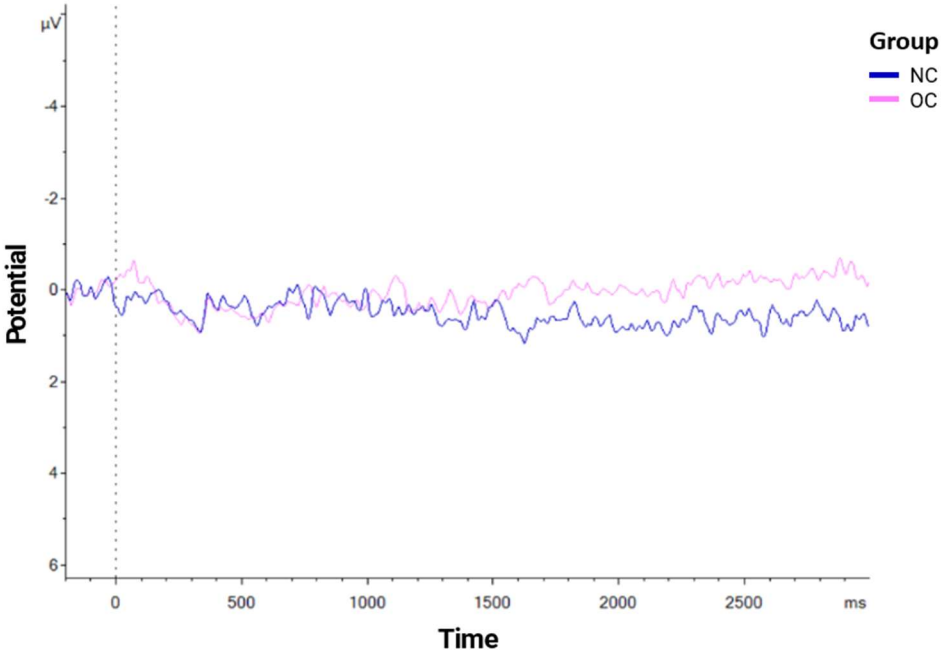
Emotion Regulation: Significance Levels

Main & Interaction Effects	Report	*P*
Group	$F(1, 51) = .01, p > .05$	.928
Time Window	$F(2, 102) = .35, p > .05$	.705
Time Window * Group	$F(2, 102) = 3.01, p > .05$	.054

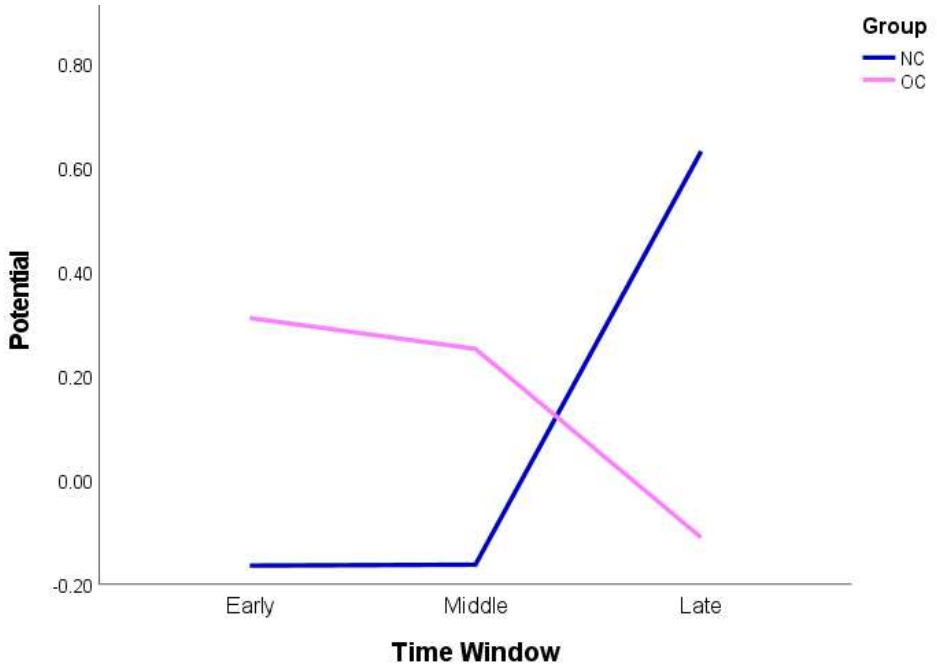
Figure 7

Emotion Regulation: Averaged Difference Wave per Group A) Through Time and B) per Time Window

A)



B)



Note. The potential signifies the averaged LPP difference waves of the chosen electrodes: CP1, CP2, Cz and Pz. For emotion regulation, this difference wave is the difference between the 'negative view' and 'negative regulate' condition (negative regulate – negative view). Figure A shows the timeline per 100 ms and Figure B shows the same results for each time window.

Correlations

Since OC and NC differed significantly on age and education, these descriptive variables were taken into account for the correlation analyses. Moreover, since OC and NC differed significantly in the early time window on the emotion reactivity analysis, this time window was chosen for the correlation analyses. Six correlations were done per group, making the corrected p = .0083 after the Bonferroni correction was applied. The results of the correlations show that none of the variables were significantly correlated (even if p = .05) to the LPP measures for neither emotion reactivity nor emotion regulation. The correlation tables (Table 13 and 14) can be found in Appendix C.

Discussion

In the current study, the effect of the pill on emotion regulation was examined. OC and NC were compared on both the emotion effect and the regulation effect with LPP measures as well as subjective valence ratings. In addition to the main results, a post hoc power analysis has been performed to make sure enough participants were tested in this study (see Appendix D).

We found a group difference in the LPP measure of emotion reactivity, namely (in the early time window) NC had a larger difference between the 'negative view' and 'neutral' pictures of the task than OC. This supports our hypothesis that OC users would exhibit less emotion reactivity than NC women. This matches findings from Monciunskaite et al. (2019), who also found a larger difference between unpleasant and neutral stimuli in OC users. It also resonates with research by Hamstra et al. (2017), who attributed the reduced emotion reactivity from OC users to emotional blunting. This phenomenon of emotional blunting (due to the OC) might also be responsible for the results of this study.

However, no significant difference in subjective valence ratings was found between the two groups. This does not confirm our hypothesis that OC would have less negative valence ratings for the 'negative view' pictures compared to the 'neutral' pictures, resulting in less subjective emotion reactivity than the NC group. This outcome contrasts with previous research (Monciunskaite et al., 2019; Hamstra et al., 2017; Gingnell et al., 2013; Petersen & Cahill, 2015) that says the OC leads to decreased emotion-induced reactivity, subsequently leading to less negative valence ratings than the NC women. It also contrasts with the findings of Spalek et al. (2019), who reported the opposite effect that OC users would rate negative pictures as more negative. Additionally, since there was an effect found in the LPP measures, but not in the subjective valence ratings, this could indicate a disconnect between the conscious and unconscious perception of the pictures. The absence of a significant difference in subjective valence ratings in this study underlines the notion that there are still mixed results in this subject matter.

We did not find a group difference in the LPP measure or in the subjective valence ratings of emotion regulation. This does not align with our hypothesis that OC users would show less emotion regulation than NC, which would become apparent through a smaller LPP difference wave and less difference in the subjective valence ratings for the OC group. Given that the effect of OC on emotion regulation has hardly been studied so far, there are not many studies to compare the results of this study to. Therefore, the absence of significant differences, both in LPP measures and in subjective valence ratings, is still a result that contributes to this area of research and underlines the importance of future research to be done on the possible effects of OC on emotional regulation.

Moreover, no significant correlations were found, which means age, education, the BDI and the PANAS all did not meaningfully relate to the emotion reactivity and regulation process. The LPP measures also did not significantly correlate with the subjective valence ratings, which

can be expected, given the lack of significant differences from the subjective valence ratings for both processes.

Strengths and Limitations

A limitation of this research is that it was not verified whether the participants were actually regulating enough according to the task instructions. In other words, a manipulation check was not performed. This could also be a possible reason for the lack of emotion regulation that was found (since there was also a negative difference wave) and there being no difference between the two groups. This could be due to the task or due to the way the task was measured. Concerning the task itself, some participants gave the feedback that they started regulating before seeing the picture, even when they were not supposed to, and some found the pictures upsetting while others found them underwhelming. This means the task might not have made the participants regulate the way they were meant to. Concerning the way it was measured, there were some positive difference waves found, which should have been negative, considering the 'negative regulate' pictures should have resulted in a lower LPP than the 'negative view' pictures and 'negative view' was subtracted from 'negative regulate'. Moreover, the heatmaps in Figure 4 do not clearly show activation of the four chosen electrodes (CP1, CP2, Cz and Pz) like with the emotion reactivity process, which means either the participants were not regulating or different electrodes should have been chosen to study the emotion regulation process. Future research could be done with for instance an fMRI to accurately map which regions of the brain are being used at the moment of regulation, such as Moodie et al. (2020) performed when researching emotion regulation. Additionally, Moodie et al. (2020) gave the participants a training before the actual task, which could ensure that the participants actually regulate their emotions during the testing phase.

Another limitation of this research coincides with a limitation that Monciunskaite et al. (2019) identified in their research, which is that the personality profiles of the participants were not assessed. Certain personality profiles could impact how adapt individuals are to using reappraisal as an emotion regulation strategy. Kobylińska et al. (2020) found that reappraisal mediates the link between low neuroticism and life satisfaction and positive affect and John and Gross (2004) found a small negative correlation between neuroticism and reappraisal. They concluded that "individuals low in neuroticism may find it easier to use reappraisal to regulate negative emotion". Furthermore, some research suggests that neuroticism can be influenced by taking the pill. Schallmayer and Hughes (2010) found that OC users have higher neuroticism than non-users. However, there are also studies that contradict this finding (Beltz et al., 2019;

Hamstra et al., 2017). Though even if the pill does not influence personality, it would be beneficial for future research to include personality profiles, as it could still impact the results.

Moreover, a few measures have been taken in the larger study that this study was a part of that have not been included in this research. For instance, a saliva sample was taken from all the participants to accurately portray the exact hormone levels at the time of testing. In addition, in the larger study the participants were tested twice. For the OC group when they were taking the pill and when they were not taking the pill and for the NC group in the luteal phase and in the follicular phase. This study only analysed the 'pill active' measurements from the OC group and the luteal phase measurements from the NC group. Monciunskaite et al. (2019) tested NC women in both phases, but found no significant difference between the two and subsequently analysed their data without dividing them into the two phases. Researching both measurements would provide more information on the effects of OC on both processes, even if the results show no significant difference. However, the scope of this research did not allow for further analysis of the additional data that was gathered in the larger study.

A strength of this research is that it researches the effect of the pill on emotion regulation specifically, which has not been extensively researched yet. That makes this research especially relevant since the pill has become such a common form of anticonception, but the existing research about the pill and its side effects remain ambiguous and insufficient. Therefore, this research is a valuable addition to existing literature on the pill and its effects on emotion processing, such as the findings of Monciunskaite et al. (2019). Another strength of this research is that both subjective valence ratings and LPP measures were analysed, as well as multiple questionnaires. This means that comprehensive research was gathered and an extensive data analysis was performed, from which many initial conclusion can be made about the effects of OC. This thorough dataset allowed for much comparison within this study. This was done with a mixed design (for the LPP measures analysis), combining both a within-, and a between-subject design. Applying a mixed design allows for a more comprehensive understanding of the effects of OC on both the emotion reactivity and regulation process. The large dataset that was gathered in this study can also be used in future research as a means of comparison and as a stepping stone from which to refine the research methods concerning the effects of OC.

Conclusion

In conclusion, for emotion reactivity, the LPP measures showed that only in the early time window NC had a significantly larger emotion reactivity process than OC, and within NC

there was a significantly larger emotion reactivity process in the early and middle time window compared to the late time window. For emotion regulation, no significant differences were found. Concerning the subjective valence ratings, no difference was found between OC and NC for emotion reactivity and for emotion regulation. An implication of this study is that it is a new addition to the existing limited literature, even if it does not add to the existing findings as the results can be used to further expand on the knowledge of the contraceptive pill and its effects on emotion regulation.

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Appendices

Appendix A: Descriptive Statistics

Table 1

MCQ Frequencies

		OC	NC
Mean age first period [a]		12.90	12.36
Have you ever switched contraceptives?	Currently using one and have switched between them	6 (20%)	3 (13.04%)
	Not currently using one but have used one in the past	0 (0%)	6 (26.09%)
	Never used a contraceptive	0 (0%)	13 (56.52%)
	Current contraceptive is the only one I've ever used	24 (80%)	0 (0%)
	unanswered	0 (0%)	1 (4.35%)
How long have you been using your current contraceptive?	(Less than) three months	0 (0%)	0 (0%)
	(Less than) half a year	0 (0%)	1 (4.35%)
	(Less than) a year	2 (6.67%)	0 (0%)
	(Less than) two years	4 (13.33%)	1 (4.35%)
	(More than) three years	24 (80%)	0 (0%)
	N/A	0 (0%)	21 (91.30%)
Mean age first contraceptive		16.77	16.56 [b]
Main reason for starting birth control	As a contraceptive	15 (50%)	2 (8.70%)
	Acne treatment	1 (3.33%)	0 (0%)
	Planning of menstruation	6 (20%)	0 (0%)
	Reducing physical symptoms (e.g. abdominal cramps)	7 (23.33%)	0 (0%)
	Reducing psychological symptoms (e.g. premenstrual mood symptoms)	1 (3.33%)	0 (0%)
	N/A	0 (0%)	21 (91.30%)

[a] Unanswered by one participant in the NC group (n = 22).

[b] n = 3.

Table 2

MCQ Questions only for OC group

MCQ Contraceptive Questions	Answer Options	Frequency (n = 30)
To what extent have you suffered from physical side effects (e.g. painful breasts, nausea, weight gain etc.) due to current hormonal contraceptive?	Not at all	11 (36.67%)
	Mild	11 (36.67%)
	Mediocre	8 (26.67%)
	Seriously	0 (0%)
To what extent have you been affected by mood changes due to current hormonal contraceptive?	Not at all	7 (23.33%)
	Mild	11 (36.67%)
	Mediocre	10 (33.33%)
	Seriously	2 (6.67%)
To what extent have you been affected by changes in libido/sex drive due to current hormonal contraceptive?	Not at all	14 (46.67%)
	Mild	10 (33.33%)
	Mediocre	3 (10%)
	Seriously	3 (10%)

Table 3

MCQ Questions only for NC group

MCQ Cycle Questions	Answer Options	Frequency (n = 23)
Do you generally get your period once a month?	Yes	18 (78.26%)
	No	1 (4.35%)
	N/A	4 (17.39%)
Mean days of cycle [a]		28.94

[a] Unanswered by six participants (n = 17).

Table 11

LPP Measures: Descriptive Statistics

	Time Window	OC (n = 30)	NC (n = 23)
Emotion Reactivity	Early	3.09 (1.74)	4.19 (2.00)
Difference Wave, mean (SD)	Middle	2.37 (1.77)	3.35 (2.51)
	Late	2.23 (2.63)	1.39 (3.02)
Emotion Regulation	Early	.31 (1.97)	-.16 (2.06)
Difference Wave, mean (SD)	Middle	.25 (2.28)	-.16 (2.05)
	Late	-.11 (2.87)	.63 (2.24)

Note. The difference waves signify the difference in the LPP measures between certain conditions. For emotion reactivity: negative view – neutral. For emotion regulation: negative regulate – negative view. This was done per group for each time window.

Appendix B: Pairwise Comparisons Tables (Emotion Reactivity)

Table 8

Pairwise Comparisons of Each Time Window

(I) Time Window	(J) Time Window	Mean Difference (I-J)	Std. Error	Sig. [a]	95% Confidence Interval for Difference [a]	
					Lower Bound	Upper Bound
Early	Middle	.780*	.240	.006	.185	1.374
	Late	1.831*	.338	<.001	.993	2.669
Middle	Late	1.052*	.259	<.001	-1.693	-.410

Note. Based on estimated marginal means. Comparisons significant at the .05 level (two-tailed) are marked with *.

[a] Adjustment for multiple comparisons: Bonferroni.

Table 9

Pairwise Comparisons of Each Group per Time Window

Time Window	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig. [a]	95% Confidence Interval for Difference [a]	
						Lower Bound	Upper Bound
Early	OC	NC	-1.104*	.515	.037	-2.137	-.071
Middle	OC	NC	-.973	.587	.104	-2.152	.207
Late	OC	NC	.838	.777	.286	-.723	2.398

Note. Based on estimated marginal means. Comparisons significant at the .05 level (two-tailed) are marked with *.

[a] Adjustment for multiple comparisons: Bonferroni.

Table 10

Pairwise Comparisons of Each Group per Time Window

Group	(I) Time Window	(J) Time Window	Mean Difference (I-J)	Std. Error	Sig. [a]	95% Confidence Interval for Difference [a]	
						Lower Bound	Upper Bound
NC	Early	Middle	.845	.361	.070	-.049	1.740
		Late	2.802*	.509	<.001	1.541	4.063
	Middle	Late	1.957*	.390	<.001	.992	2.922
OC	Early	Middle	.714	.316	.085	-.069	1.497
		Late	.860	.446	.178	-.244	1.964
	Middle	Late	.147	.341	1.000	-.699	.992

Note. Based on estimated marginal means. Comparisons significant at the .05 level (two-tailed) are marked with *.

[a] Adjustment for multiple comparisons: Bonferroni.

Appendix C: Correlation Tables

Table 13

Correlations Between EEG Date (Early Time Window) and Variables in Emotion Reactivity

Group	Variable	Correlation Coefficient	*P*
OC	Age	-.15	.433
	Education	-.02	.931
	Subjective Valence	.13	.485
	Positive Affect Scale (PAS)	-.24	.208
	Negative Affect Scale (NAS)	-.02	.912
	Beck Depression Inventory (BDI)	.06	.764
NC	Age	-.34	.127
	Education	.05	.834
	Subjective Valence	.40	.061
	Positive Affect Scale (PAS)	-.04	.850
	Negative Affect Scale (NAS)	-.34	.109
	Beck Depression Inventory (BDI)	-.33	.126

Note. n varies for each variable and group. For OC, n = 30; for NC, n varies from 21 to 23. Correlations significant at the .05 level (two-tailed) are marked with *.

Table 14

Correlations Between EEG Date (Early Time Window) and Variables in Emotion Reactivity

Group	Variable	Correlation Coefficient	*P*
OC	Age	-.03	.872
	Education	.05	.800
	Subjective Valence	.04	.835
	Positive Affect Schedule (PAS)	.33	.076
	Negative Affect Schedule (NAS)	-.30	.101
	Beck Depression Inventory (BDI)	-.01	.950
NC	Age	.03	.885
	Education	-.31	.165
	Subjective Valence	-.02	.919
	Positive Affect Schedule (PAS)	.09	.700
	Negative Affect Schedule (NAS)	.07	.761
	Beck Depression Inventory (BDI)	.33	.126

Note. n varies for each variable and group. For OC, n = 30; for NC, n varies from 21 to 23. Correlations significant at the .05 level (two-tailed) are marked with *.

Appendix D: Post Hoc Power Analysis

A post hoc power analysis has been performed for both the subjective valence ratings and the LPP measures. For the subjective valence ratings, an analysis was done with a two-tailed t-test with a sample size of 23 for one group and 30 for the other and an alpha level of .05. With a small effect size of .2, the power would be approximately .11. With a medium effect size of .5, the power would be approximately .42. With a large effect size of .8, the power would be approximately .81.

For the LPP measures an analysis was done with a few scenarios in mind. The analysis was done with a repeated measures analysis with a within and between interaction. A total sample size of 53 was used with two groups and three measurements (three time windows) The worst case scenario would be where there is a very low correlation among the repeated measures (r=.1) and the nonsphericity correction of .5 (which implies a correction of the degrees of freedom due to violation of the assumption). The best case scenario would be a correlation among the repeated measures of .9 and a nonsphericity correction of 1 (as this corresponds to the assumption of sphericity not being violated and no correction on the degrees of freedom). The correlation among the repeated measures was tested with .1, .5 and .9. For all three of those, the nonsphericity correction was tested with .5 and 1. For all six analyses, an effect size of .25, an alpha level of .05 were used. The worst case scenario of these six scenarios had the lowest power, which was a power of .64. This is not considered a large power. However, the other five scenarios have a power of at least .84. Therefore, except for the worst case scenario, this indicates a large chance of detecting a true effect for this analysis.

Thus, for our within-between subject analysis of the LPP measures we would have insufficient power (.64) in the worst case scenario, but in the other scenarios we would have sufficient power (> .80) to detect an effect size of .25 (medium effect size). For our subjective valence ratings analysis we have sufficient power (> .80) to detect an effect size of .8 (large effect size), but insufficient power to detect small to moderate effects.