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Increased frequency of mind wandering in healthy women using oral contraceptives

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ABSTRACT

Oral contraceptive (OC) is the most common type of contraceptive method used in industrialized countries. A recent epidemiological study showed that OC use was associated with the onset of depression in young women. Mind wandering, a cognitive process associated with spontaneous thoughts unrelated to the task at-hand, has previously been associated with depressive thinking. Consequently, mind wandering might be a precursor for cognitive vulnerability in individuals who are at-risk for mood disorders. The purpose of this study was to examine the frequency and nature of mind wandering in women using OC in comparison to two control groups: naturally cycling women and men. We recruited 71 participants (28 women currently using OC, 14 naturally cycling women in the luteal phase of their menstrual cycle and 29 men) aged between 18 and 35 years, and measured the frequency and nature (guilt/fear oriented and positive) of mind wandering using the short version of the Imaginal Process Inventory. In all analyses, we controlled for depressive symptoms to delineate the unique association between OC use and mind wandering. We also measured estradiol, progesterone and testosterone to confirm expected group differences in sex hormones concentrations. Results show that women using OC presented increased frequency of mind wandering when compared to naturally cycling women and men who did not differ between each other. The three groups did not differ in terms of the nature of mind wandering. These results show that OC use is associated with increased frequency of mind wandering and suggest that the association between OC use and dysphoric mood described in previous studies may be partially explained by the impact of OC use on cognitive processes underlying mind wandering.

1. Introduction

Oral contraceptives (OC) are the most common type of contraceptive method used in industrialized countries (Daniels et al., 2015). It is estimated that 26% of women who are of reproductive age currently use OC and 82% of women report using it at some point in their lives (Daniels and Mosher, 2013). Around 10% of OC users report experiencing mood side effects (e.g., depressive symptoms, irritability (Kelly et al., 2010), which are common reasons for OC cessation (Rosenberg and Waugh, 1998; Westhoff et al., 2007). Recent studies also suggest that OC use may be associated with the onset of major depression. In a large prospective cohort study performed in one million Danish women, Skovlund and colleagues reported an increased risk for first depression diagnosis and antidepressant use among users of all types of OC (combined and progestins only) compared to naturally cycling women (Skovlund et al., 2016). Authors of this study reported an adjusted incidence rate ratios of 1.7 for depression diagnosis, and between 1.8 and 2.2 for antidepressant use.

Oral contraceptives typically contain ethinylestradiol and progestin, synthetic forms of the sex steroids estradiol and progesterone. Sex steroids – either endogenous or exogenous – are liposoluble molecules. Consequently, sex steroids cross the blood-brain barrier and bind with specific estrogen and progesterone receptors located in key brain regions involved in emotional and cognitive regulation (Brinton et al., 2008; Wharton et al., 2012) such as the hypothalamus, hippocampus, frontal cortex and amygdala (Osterlund et al., 2000). Effects of

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endogenous estradiol and progesterone on mood have repeatedly been found in naturally cycling women (Balzer et al., 2015; Hammarbäck et al., 1985, 1991; Muse et al., 1984; Payne, 2003; Young et al., 2000). More recently, it was shown that women using OC who previously had experienced emotional side effects in association with OC use presented mood deterioration on a daily basis as well as changes in brain activation in response to emotional stimuli (Gingnell et al., 2013). Altogether, these results suggest that exposure to exogenous forms of sex steroids may be associated with mood changes. One plausible mechanism that could explain this relationship is through the effects of synthetic sex steroids on brain regions involved in mood and cognitive functions in women.

Notwithstanding, millions of women using OC do not develop depression. This suggests that various factors could modulate one's vulnerability to the effects of OC on emotional and/or cognitive processing. In particular, individual variability in cognitive processes may confer vulnerability to depressive disorders (Struijs et al., 2018; Sun et al., 2018). *Mind wandering*, a cognitive process associated with spontaneous thoughts unrelated to the task at-hand, has been associated with depressive cognitive-behaviors. Moreover, recent studies suggest that mind wandering might be a precursor for cognitive vulnerability among individuals who are at higher risk for mood disorders (Marchetti et al., 2016; Murphy et al., 2013).

Mind wandering is a cognitive state in which the individual's attention is not devoted to the current task or perceptual inputs, but is rather focused on thoughts and images that are irrelevant to the task at hand (Marchetti et al., 2016). Features of mind wandering can be assessed through questionnaires that measure the frequency and/or nature (positive or negative) of self-generated thoughts on a daily basis (Marchetti et al., 2016; Mrazek et al., 2013). State mind wandering (occurring 'here and now') can also be measured through tasks that necessitate sustained attention. In 2010, Killingsworth and Gilbert (Killingsworth and Gilbert, 2010) showed that mind wandering was frequent in a community sample, occurring up to 50% of the time while we are awake. Mind wandering also predicted negative mood later during the day (Killingsworth and Gilbert, 2010).

Mind wandering presents important similarities with cognitive processes associated with depressive thinking. Indeed, both involve a shift of attention away from the task at hand, and lead to the mobilisation of attention towards personally salient information such as worries or anticipation of future events (Smallwood et al., 2007a). It has been suggested that individual differences in the intensity and/or frequency with which one engages in mind wandering could provide a useful marker of cognitive process in dysphoric individuals (Smallwood et al., 2007b). As discussed in a review by Smallwood and colleagues (2007b), past studies have repeatedly reported the presence of a positive association between dysphoria and state mind wandering frequency measures (such as word learning tasks, sustained attention tasks and simple word fragment completion). These studies therefore suggest that this cognitive process represents a risk factor for depressive thinking in healthy adults.

In 2010, Weis and colleagues (Weis et al., 2017) suggested that endogenous sex hormones may be associated with mind wandering in naturally cycling women. Using functional magnetic resonance imaging, they demonstrated that the brain regions involved in mind wandering (i.e., the default brain network (for a review, 23) are differentially activated in women during three different menstrual cycle phases associated with distinct sex hormones patterns (Weis et al., 2017). Their results suggested that endogenous sex hormones could modulate the frequency and/or nature of mind wandering. Whether a similar effect exists for exogenous sex hormones has not yet been verified.

The purpose of this study was to compare the frequency and nature of mind wandering in healthy women using OC in comparison to naturally cycling women and men. Men were included in this study because past studies have shown that the prevalence of depressive symptoms differ greatly as a function of both sex/gender and oral contraceptive use. In general, reproductive women are more vulnerable than men to depression (sex/gender effect (25), and women using OC are more vulnerable than naturally cycling women (Skovlund et al., 2016). Including men in this study is therefore essential for understanding the differential effects of sex/gender and OC use on the frequency and nature of mind wandering. Given 1) previous sex/gender gap ratios reported in depressive symptomatology, 2) past associations reported between OC use and depressive disorders (Skovlund et al., 2016), and 3) previously reported links between mind wandering and depressive symptoms (Smallwood et al., 2007b), we hypothesized that mind wandering would be more frequent and negative in women using OC compared to naturally cycling women, who in turn would have more frequent and negative mind wandering processes than men.

2. Materials and methods

2.1. Participants

Participants were recruited through advertisements posted on local websites as well as in different francophone universities on the island of Montreal. Forty-two women (28 women currently using OC, 14 naturally cycling women who have not been using any forms of exogenous sex hormones in the past year and in the luteal phase of their menstrual cycle) aged between 18 and 35 years (mean = 23.86, SD = 4.11) and 29 men aged between 18 and 35 (mean = 25.31, SD = 4.30) were recruited for the present study. Data were collected between 2012 and 2013 as part of a broader research project on the impact of OC use on physiological stress reactivity. We recruited women in their luteal phase because they present cortisol reactivity similar to that of men, as opposed to women using OC who normally show decreased cortisol reactivity.

The ethics committee of the Research Centre of the Institut universitaire en santé mentale de Montréal approved this study and all participants provided written informed consent to take part in the study. All participants were screened over the phone to make sure that they did not suffer from any physiological or psychological condition that could confound results. Specifically, we ensured that participants did not have any history of neurological, cardiovascular, psychiatric (ex. diagnosed depression, schizophrenia, personality or anxiety disorders), drug use, and general health problems. Participants were free of medication and non-smokers. During screening, women provided information concerning their menstrual cycle (e.g., date of last menses, average cycle days) and OC use. The OC group only included women using combined estrogen–progestin OC. Women in the OC group were required to be using combined OC for a period of at least one year to be included in the study. Women using OC were tested while they were taking active pills.

2.2. Measures

2.2.1. Mind wandering

To measure the frequency and nature of mind wandering, participants completed the short version of Imaginal Process Inventory (SIPI; (Huba and Tanaka, 1983). The SIPI is a 45-item Likert scale questionnaire designed to measure the frequency and nature of mind wandering. Items are rated on a five-point scale: 1-Very true or strongly characteristic of me to 5-Definitely untrue or strongly uncharacteristic of me. The SIPI is composed of three subscales: the "Poor attentional control", "Guilt and fear of failure" and "Positive constructive daydreaming" subscales (Singer, 1975). The "Poor attentional control" subscale measures the tendency to show difficulty to concentrate on either the ongoing thought or the external task. Therefore, someone exhibiting an increased score on this subscale would exhibit reduced attentional control, which leads to heightened mind wandering frequency. The other two subscales measure the nature of mind wandering (negative and positive) on a daily basis. The "Guilt and fear of failure"

subscale measures guilty-dysphoric daydreaming, characterized by depressed and guilt oriented thoughts. The "Positive constructive daydreaming" subscale measures wishful imagery, creative and thoughts oriented towards the future. Internal consistencies for the scales are generally good, with mean internal consistency scores approximately α = .81. Test-retest reliabilities are also adequate, with scores ranging from .68 to .86 (MacInnis, 1987).

2.2.2. Salivary sex hormones levels

Two saliva samples (approximately 2 mL) were collected 20 minutes after arrival to the laboratory to assess salivary estradiol, progesterone, and testosterone levels. Collection was performed using the passive drool method guided with sterilized straws. Samples were frozen immediately upon collection at −20 °C and assays were performed within three months of testing to prevent degradation known to influence HPG-axis biomarkers (Granger et al., 2004).

All saliva samples were analysed at the Centre for Studies on Human Stress (www.humanstress.ca). Prior to assaying each sample, frozen samples were brought to room temperature to be centrifuged at 1500xg (3000 rpm) for 15 min. For estradiol determination, or more specifically 17β-estradiol determination, we used a high sensitivity enzyme immune assay kit (Salimetrics®, State College, PA, Catalogue No. 1-3702) where the range of detection is 1–32 pg/ml. For progesterone determination, we used a high sensitivity enzyme immune assay kit (Salimetrics®, State College, PA, Catalogue No. 1-1502) where the lower limit of sensitivity is 5 pg/ml. For testosterone, we used an expanded range enzyme immune assay kit (Salimetrics®, State College, PA, Catalogue No. 1-2402) where the lower limit of sensitivity is 1 pg/ml.Inter-assay and intra-assay coefficients of variance were respectively below 6.6% and 8.32% for estradiol, 9.06% and 7.66% for progesterone and 12% and 4.65% for testosterone. Assays were ran in duplicates and averages were used in statistical analyses.

2.2.3. Potential confounders

2.2.3.1. Beck Depression Inventory-II. Depressive symptoms were assessed with the Beck Depression Inventory (BDI-II; (Beck et al., 1988)), which is a 21 items self-rating scale assessing depressive symptoms that occurred in the past two weeks. Each item is measured on a 4-point Likert scale. The BDI assesses depressive symptoms with statements ranging from 0 to 3 in terms of intensity. A meta-analysis showed that this instrument has a test–retest reliability ranging from r = .60 to .83, and a mean internal consistency at Cronbach's α = .81 for non-psychiatric participants (Beck et al., 1988). In this study, we used the sum score of the BDI for all analyses pertaining to depressive symptoms.

2.2.3.2. Body mass index. Given previous studies showing that body mass index (BMI) is significantly correlated with gonadal hormone levels (Gates et al., 2013; Lokaj-Berisha et al., 2015; Shamim et al., 2015), height and weight were obtained from self-report and BMI was calculated (weight in kg) divided by height (m^2), and entered as a covariate in analyses of sex hormones.

2.3. Procedure

Participants were tested in the afternoon between 1:30pm and 4:30pm to control for circadian variations in cortisol levels. Upon their arrival, participants completed the *Beck Depression Inventory* and the *Imaginal Process Inventory Short Version.* Thereafter, participants provided two saliva samples to measure estradiol, progesterone and testosterone levels. Subsequent tasks were conducted as part of a larger study on the impact of OC on stress hormones levels. One hour prior to the testing session, participants were instructed to avoid major meals, cigarettes, caffeinated/sugary beverages, and dairy products. They were also asked to refrain from oral hygiene and strenuous physical activity two hours before sampling.

2.4. Statistical analysis

Data for the SIPI, BDI and gonadal steroid concentrations were examined for potential outliers via studentized residuals. Residuals ≥ ± 3 would have been considered outliers, although none were found. In a first set of analyses, we tested for a sex effect on mind wandering, comparing men to women on the three subscales of the SIPI. In a second set of analyses, we tested for a OC effect on mind wandering using a univariate MANOVA with Group (Luteal *versus* OC users *versus* men) and subscales of the SIPI (attention *versus* negative *versus* positive MW) as factors. Given the use of two ANOVAs on the same set of data, we used a Bonferronni correction that set our significance level at $p < 0.025$. In analyses pertaining to mind wandering, we controlled for depressive symptoms to delineate the unique association between OC use and mind wandering. In addition, we also ran a supplemental analysis comparing groups on their total scores for the BDI. Finally, MANOVAs with Group (Luteal *versus* OC users *versus* men) and gonadal steroid levels (testosterone, progesterone and estradiol) as factors were used to compare groups on gonadal steroid levels.

3. Results

3.1. Preliminary analysis

Potential confounding effects based on sample demographics were first scrutinized prior to our main analyses. We had missing data for two participants for relationship status and 8 participants on years of education. Preliminary analyses revealed no group differences for age [$F(2,70) = 1.066$; $p = 0.350$] or years of education [$F(2,62) = .280$; $p = 0.757$], although groups differed on BMI [$F(2, 70) = 3.440$; $p = 0.038$], showing that women in their luteal phase presented significantly lower BMI than men ($p = 0.035$). A chi square analysis revealed no group differences in terms of relationship status [X^2 (4, $n = 69) = 5.290$, $p = 0.248$] (Table 1). Given group differences on BMI, this variable was entered as a covariate in subsequent analyses. BDI was also entered as a covariate in every analysis pertaining to the SIPI subscales as justified by the existing literature (Jonathan Smallwood et al., 2003; Murphy et al., 2013; Smallwood et al., 2007b).

3.2. Sex effect on mind wandering

The MANOVA performed on the three subscales of the SIPI revealed a significant sex difference for the frequency of mind wandering as assessed by the Poor attentional control subscale of the SIPI [Wilks' Lambda = .920, $F(1,69) = 8.23$; $p = 0.005$, $\eta_p^2 = 7.7\%$] (Fig. 1**.A**). Group comparisons showed that women scored significantly higher than men on this subscale. No sex difference was observed for the Guilt and Fear of Failure [Wilks' Lambda = .920, $F(1,69) = 1.205$;

Table 1
Descriptive statistics as a function of groups. For age, BMI and years of education, data represent group means (SD) in women under oral contraceptives, naturally cycling women and men. For relationship status, data represent group N (group %). * represents significant differences at $p < .05$.

	Oral contraceptives	Naturally cycling (luteal)	Men	P values
Age	24.07 (3.79)	24.29 (6.04)	25.31 (4.3)	.350
BMI	22.17 (3.23)	21.49 (3.05)	23.17 (5.37)	.038*
Years of education	15.93 (2.38)	15.07 (2.24)	15.97 (3.46)	.757
Relationship status				.248
Single	18 (66.7%)	12 (93.3%)	23 (79.3%)	
In a relationship/ Married	9 (33.3%)	1 (7.7%)	5 (17.2%)	
Separated/ Divorced	0 (0%)	0 (0%)	1 (3.4%)	

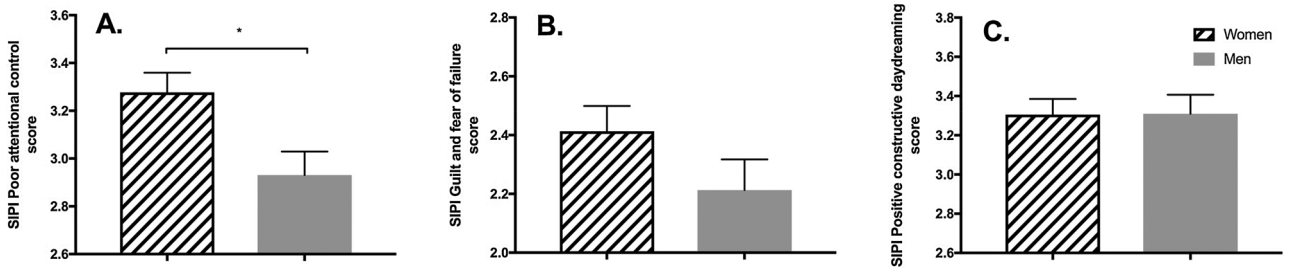

Fig. 1. Scores on the three subscales of the Imaginal Process Inventory (short version; SIPI) in women and men. Fig. 1.**A** Frequency of mind wandering as assessed by the Poor attentional control subscale of the SIPI; Fig. 1.**B** Negative mind wandering nature as assessed by the "Guilt and fear of failure" subscale of the SIPI. Fig. 1.**C** Positive mind wandering nature as assessed by the "Positive constructive daydreaming" subscale of the SIPI. The women group include women in their luteal phase as well as women using OC. Error bars represent standard error. * represents significant differences at $p < .05$.

$p = 0.276$] (Fig. 1.**B**) or the Positive Constructive daydreaming [Wilks' Lambda = .920, $F(1,69) = 0.093$; $p = 0.762$] (Fig. 1.**C**) subscales of the SIPI.

3.3. OC effect on mind wandering

The MANOVA performed on the three subscales of the SIPI revealed a group difference for the Poor attentional control subscale; [Wilks' Lambda = .839, $F(2,69) = 5.878$; $p = 0.004$, $\eta_p^2 = 14.7\%$] (Fig. 2.**A**). Post-hoc analyses revealed that women using OC reported less attentional control compared to women in their luteal phase ($p = 0.019$) and men ($p = 0.006$), who did not differ from each other in terms of attentional control ($p = 0.848$). This result suggests that women using OC showed increased frequency of mind wandering compared to the two other groups. No significant group differences was found on the Guilt and fear of failure [Wilks' Lambda = .839, $F(2,69) = 0.8968$; $p = 0.385$] or on the Positive constructive daydreaming subscale of the SIPI [Wilks' Lambda = .839, $F(2,69) = 0.486$; $p = 0.617$] (Fig. 2.**B and. C**).

3.4. Supplemental analyses

Given that we found both a sex and OC effect on the Poor attentional control subscale, and based on previous studies showing that OC use is associated with depressive symptoms (6), we compared the three groups (women in the luteal phase, women using OC, and men) on depressive scores in secondary analyses to verify whether the group difference observed on the frequency of mind wandering could in fact emerge due to baseline group differences. A univariate ANOVA revealed no group differences on the BDI [$F(2,69) = 2.63$; $p = 0.079$] (Fig. 3). Scores on the BDI across the entire sample of participants correlated significantly with the Poor attentional control subscale ($r = 0.304$; $p = 0.01$, 95% CI [.152, .516]) and the Guilt and fear of failure ($r = 0.325$; $p = 0.006$, 95% CI [.124, .505]) subscales of the SIPI. We found no significant correlation between the BDI and the Positive constructive daydreaming subscale across the sample of participants ($r = -.164$; $p = 0.175$, 95% CI [-3.46, 0.12]).

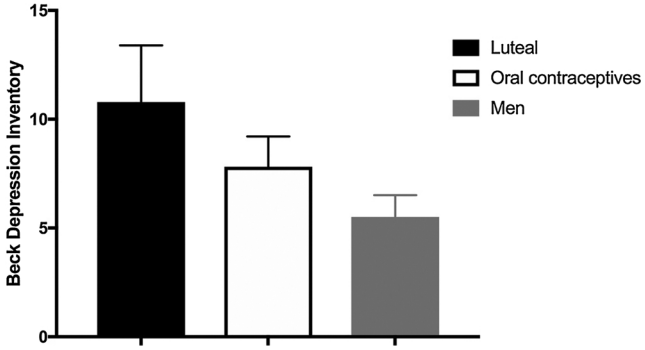

Fig. 3. Scores on the Beck Depression Inventory in women in their luteal phase, women using oral contraceptive and men. Error bars represent standard error.

We verified whether groups (women in their luteal phase, women using OC, and men) differed as a function of salivary gonadal steroid levels using a multivariate ANOVA controlling for BMI. As expected, we found that groups differed on all gonadal steroid levels [estradiol levels [Wilks' Lambda = .225, $F(2,68) = 5.051$; $p = 0.009$, $\eta_p^2 = 14\%$]; progesterone levels [Wilks' Lambda = .225, $F(2,68) = 5.704$; $p = 0.005$, $\eta_p^2 = 16.4\%$]; testosterone levels [Wilks' Lambda = .225, $F(2,68) = 74.443$; $p < 0.0001$, $\eta_p^2 = 67.6\%$]; estradiol/progesterone ratio [Wilks' Lambda = .225, $F(2,68) = 2.464$; $p = 0.042$, $\eta_p^2 = 7.2\%$]. Post-hoc analyses showed that women in their luteal phase had higher estradiol ($p = 0.050$) and progesterone levels compared to both women using OC ($p = 0.017$) and men ($p = 0.003$), with no differences between the two latter groups ($p = 1.00$) (Fig. 4.**A and 4.B**). Men had significantly greater testosterone concentrations when compared to women in their luteal phase ($p < 0.001$) and women using OC ($p < 0.001$), who did not differ between each other ($p = 0.452$) (Fig. 4.**C**).

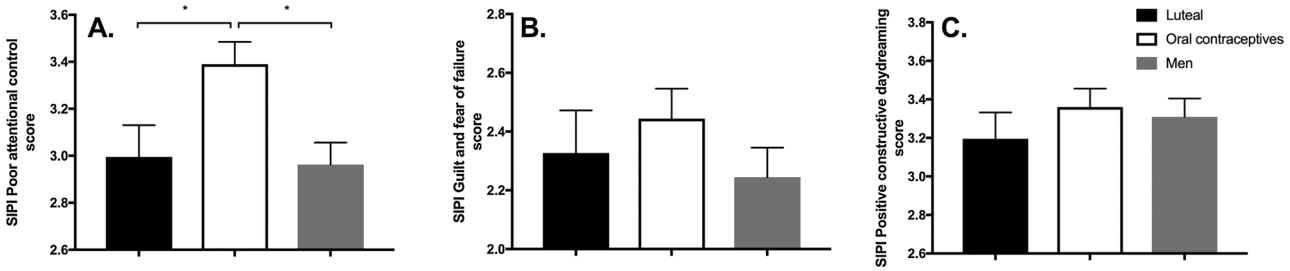

Fig. 2. Scores on the three subscales of the Imaginal Process Inventory (short version; SIPI) in women in their luteal phase, women using oral contraceptive and men. Fig. 2.**A** Frequency of mind wandering as assessed by the Poor attentional control subscale of the SIPI; Fig. 2.**B** Negative mind wandering nature as assessed by the "Guilt and fear of failure" subscale of the SIPI. Fig. 2.**C** Positive mind wandering nature as assessed by the "Positive constructive daydreaming" subscale of the SIPI. Error bars represent standard error. * represents significant differences at $p < .05$.

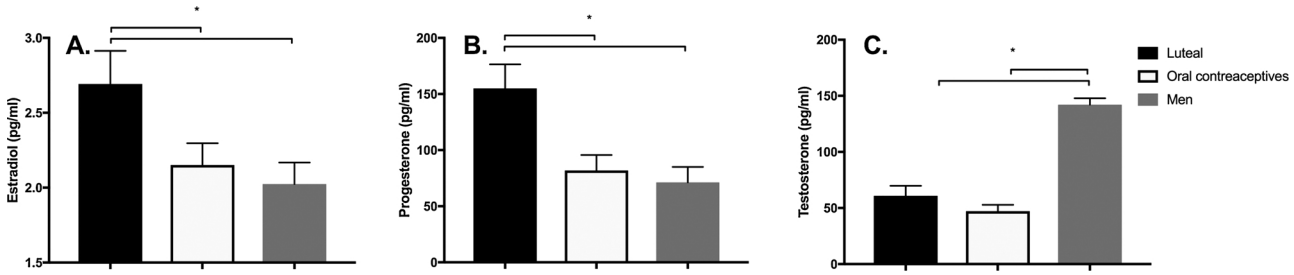

Fig. 4. Salivary gonadal steroids levels in women in their luteal phase, women using oral contraceptive and men. Fig. 4.**A** Salivary estradiol levels; Fig. 4.**B** Salivary progesterone levels; Fig. 4.**C** Salivary testosterone levels. Error bars represent standard error; * represents significant differences ($p < 0.05$).

4. Discussion

The goal of this study was to compare the frequency and nature of mind wandering in women using OC in comparison to naturally cycling women and men. Given 1) previous sex differences in depressive symptomatology (sex/gender effect), 2) past associations reported between OC use and depressive disorders (OC effect), and 3) previously reported links between mind wandering and depressive symptoms, we predicted that mind wandering would be more frequent and negative in women using OC compared with naturally cycling women, which would be more frequent and negative as opposed to men.

The results of this study partially confirm this prediction since we found both a sex and an OC effect for the frequency of mind wandering. We did not, however, find any group differences for the nature (positive or negative) of mind wandering. In a first set of analyses, we found that women (naturally cycling and OC users combined together) reported significantly greater frequency of mind wandering than men. However, in a second set of analyses testing for an OC effect, we found that this sex effect was driven by women using OC. Indeed, we found that the increased frequency of mind wandering is only present in OC users, and that naturally-cycling women do not differ from men. In fact, on all measures of mind wandering (frequency or nature), we found that naturally cycling women present similar levels of mind wandering as men.

As opposed to an epidemiological study that found increased depression diagnosis and antidepressant intake in women using OC compared to naturally cycling women (Skovlund et al., 2016), in the present study, we did not find group differences in depressive symptoms as assessed by the Beck Depression Inventory (BDI). However, we found that groups differed in terms of the frequency of mind wandering, which itself correlated significantly with BDI scores across the sample. It is possible that we did not find increased depressive symptoms in OC users because women in our sample were younger than those tested in the Skovlund et al. (2016) study, and none of them reported history of clinical depression. Indeed, we did not include women who reported having previously received a psychiatric diagnosis or that had a history of antidepressants intake. The BDI questionnaire might therefore not have been sensitive enough to detect symptoms of pre clinical depression in our sample. It would be interesting in future studies that assess the impact of OC initiation on mind wandering in young healthy women to directly measure its effect on dysphoria or related cognitive processes such as rumination (Broderick, 2005) or emotion regulation (Joormann and Gotlib, 2010). This would allow to measure whether frequency of mind wandering in OC users can serve as an endophenotypic marker of risk for depressive disorder in women.

We also reported that OC users differed significantly from naturally cycling women in their luteal phase in terms of circulating levels of salivary estradiol and progesterone. Here, we showed that OC users had significantly lower levels of salivary estradiol and progesterone when compared to naturally cycling women, and that estradiol and progesterone levels in OC users were not significantly different from men's levels. This concords with a previous study showing that hormonal contraceptives lead to a reduction of endogenous estradiol and progesterone levels (Sahlberg et al., 1987). Given that progesterone has a high affinity for 5α-reductase, an enzyme responsible for the conversion of testosterone into dihydrotestosterone (Rosvall et al., 2013), OC-induced reduction in progesterone levels could lead to more testosterone being converted to dihydrotestosterone. If this is the case, then it is possible that OC may facilitate testosterone actions on the brain, which could explain some of the OC effects on cognitive vulnerability to depression. However, we found in the present study that, although OC users had similar estradiol and progesterone levels than men, they exhibited significantly lower circulating levels of testosterone. It is thus unclear how the present results could be related to circulating levels of peripheral gonadal steroids.

Because we were underpowered in one group of participants ($N = 14$), we could not conduct correlational analyses between sex hormones concentrations and frequency of mind wandering. However, the increased vulnerability of OC users to present greater frequency of mind wandering could be due to basal estradiol and/or progesterone effects on the brain. Sex hormones are liposoluble steroids that rapidly access the brain where they bind to sex steroid receptor-dense regions, particularly the amygdala, and the frontal cortex (Osterlund et al., 2000). A recent study by Petersen and colleagues reported that OC use was associated with significantly lower cortical thickness measurements in the lateral orbitofrontal cortex and the posterior cingulate cortex, two brain regions involved in responding to rewards and evaluating internal states/incoming stimuli. In a previous study from our lab, we found that early menarche is associated with high depressive symptoms in adolescent girls (Trépanier et al., 2013). To explain this result, we proposed a 'brain vulnerability hypothesis' in which exposure of the developing brain to high levels of sex steroids could induce a heterotypic reorganization of synaptic development, programming of neurotrophic factors, and/or changes in gene expression in various brain regions that could modify the developmental trajectories of these girls. Given previous studies showing that cortical brain regions (particularly the frontal lobes) tend to develop until the late 20 s (Mills et al., 2014), and given studies showing that OC use can impact brain function (Petersen et al., 2015), it is quite possible that OC use in young women induces changes in brain functions and/or structures that confer cognitive vulnerability to mind wandering and/or depression. Clearly, future studies assessing the effects of OC use on other cognitive and/or brain functions in adolescent girls are warranted to better understand the effects of OC use on female brain development and whether the observed effects are based on specific estradiol and/or progesterone and/or testosterone effects.

While our findings focused on the Poor attentional subscale of the SIPI, it is important to note that other mind wandering measures may add information to this emerging field of research. Indeed, one critique that was made in accordance with the SIPI is that rather than measuring task-unrelated thoughts (ex. "I do things without paying full attention"), it tends to measure stimulus-independent thoughts (ex. "When I have time on my hands, I daydream") (Mrazek et al., 2013). The SIPI therefore measures reduced attentional control, which eventually leads

to increased frequency of mind wandering, making it a rather indirect measure of this cognitive process. Another critique of the Poor attentional subscale is that it also measures constructs such as distractibility, boredom and rumination, therefore integrating maladaptive and adaptive processes. Although at the time of data collection for the current study the SIPI was one of the main tools used to investigate frequency of mind wandering through daydreaming habits, more recent tools have since been validated. Future studies interested in the association between mind wandering frequency and OC should also include newer subjective measures such as the Mind Wandering Questionnaire (Mrazek et al., 2013). Some strengths that the Mind Wandering Questionnaire when compared to the SIPI is that it assesses task-unrelated thoughts, while excluding cognitive processes such as rumination, making it a more direct and valid measure of frequency of mind wandering. Use of this questionnaire would permit to delineate the maladaptive and adaptive processes that may be heightened by OC. Future studies could also include objective measures of mind wandering such as reaction time tasks (Leszczynski et al., 2017) or physiological measures such as eye movements tracking (Uzzaman and Joordens, 2011). These newer methodologies would allow for a better understanding of the association between exogenous sex hormones intake and mind wandering.

While we may conclude that mind wandering is maladaptive because of its association with depressive symptoms (current study) and dysphoria (Jonathan Smallwood et al., 2003; Murphy et al., 2013, 2013; Smallwood et al., 2007b), it is important to keep in mind that studies have also revealed positive and adaptive aspects of this cognitive process (Watkins, 2008). For example, Singer showed in his early work that daydreaming (which was the broader term initially used in reference to what we now refer as mind wandering) reinforces social skills, relieves from boredom and provides opportunities for constructive planning (for a review, see (McMillan et al., 2013)). Adaptive values of mind wandering have also been shown. For example, Baird and colleagues demonstrated that engaging in activities that promote mind wandering (such as undemanding tasks) increases creative inspiration. The brain default network along with mind wandering were also shown to be associated with offline memory reprocessing (the process through which the brain links relevant older memories to new ones (Wang et al., 2009)), encouraging problem solving. Although in the current study we did not find that women under OC differed in terms of the positive nature of mind wandering, it is possible that they present increased cognitive abilities associated with mind wandering that we did not assess.

Although this study provides novel results on the effects of OC use on mind wandering in young women, some limitations should be noted. First, naturally cycling women included in this study were all in the luteal phase of their menstrual cycle. Although the purpose of our study was not to compare mind wandering across the different phases of the menstrual cycle, inclusion of women in the follicular as well as the luteal stages would have allowed to further understand the impact of endogenous *versus* exogenous sex hormones on mind wandering. Future studies should repeatedly measure menstrual cycle effects to better understand the mechanisms underlying the effects of exogenous sex hormones on mind wandering.

Another limitation of this study is that we did not assess whether or not naturally cycling women have ever used OC in the past, and if they did, for what duration. Although we made sure that participants did not use OC in the past 12 months, we cannot delineate any developmental effects that OC could have had on brain development or neuronal plasticity had they been using OC in the past. In the same line of thought, we did not assess the duration of OC use in our OC group, preventing us from analyzing any developmental effects of the age at exposure to exogenous sex hormones. Those important variables should be taken into account in future studies. Finally, in the context of our study protocol, we cannot assume that OC *causes* an increase in mind wandering because the women using OC were self-selected users. Our significant results could therefore be due to individual differences that pertain to our groups and not to exogenous hormonal use. Therefore, our findings could underestimate any cognitive differences between naturally cycling women and OC users that could explain the results obtained in this study. Future studies could assess the impact of OC on mind wandering in previously naturally cycling women before and after starting OC while comparing the results to a control group who are not exposed to OC. This would help determine whether OC use is a significant predictor of the development of mind wandering.

In conclusion, the results of our study suggest that OC use in adulthood is associated with increased frequency of mind wandering, a cognitive process associated with depressive thinking. Given the young age at which some girls start to use OC, the results of our study could help understand the factors that may render girls more vulnerable to environmental stressors and therefore represents a critical period to intervene to promote mental health.

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