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Examining Difference in Social Perceptions between Women Using Hormonal Contraceptives and Naturally Cycling Women

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Johnson, C. B. (2022). Examining Difference in Social Perceptions between Women Using Hormonal Contraceptives and Naturally Cycling Women. *Biological Sciences Undergraduate Honors Theses*
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**Examining Difference in Social Perceptions
between Women Using Hormonal
Contraceptives and Naturally Cycling
Women**

An Honors Thesis submitted in partial fulfillment of
the requirements for Honors Studies in Biology

By

Caroline Johnson

Spring 2022

Biology

J. William Fulbright College of Arts and Sciences
The University of Arkansas

Acknowledgments

I would first like to thank Dr. Anastasia Makhanova for her guidance and leadership as serving as my Honors Thesis Mentor. She invested a lot of her time into my work, allowing me to gain new skills and expertise in topics required for my research. The experience and techniques I have learned through this lab will help me later in my my professional career. I would also like to thank my other committee members Dr. Adam Pare and Professor Kate Walker, and my Honors council representative Mike Plavcan for taking the time to listen and critique my thesis. Finally, I would like to thank the University of Arkansas Honors College for the funding and support of the Spark Lab, allowing me to complete the research needed for my Honors defense.

Table of Contents

Acknowledgments	2
Abstract.....	4
Introduction.....	5
Method	11
Participants	11
Procedure	13
Results	13
Discussion.....	14
References	18

Abstract

The term “stress” refers to a person’s psychological and physiological response to the demands and pressures of the world around them (Farlex, 2021). Past research has shown that stress can have negative side effects on a person’s well-being (Aneshensel et al., 1991; Wunsch et al., 2017; Michie, 2002). Although people experience stress, some people perceive more stress than others. Perceptions are important because the way one understands certain conditions can elicit distinct emotional and physiological responses (Kemeny, 2003). An important factor that has not received a lot of attention is women’s use of hormonal contraceptives. In the United States, 24.4% of women aged 15-49 are currently using hormonal contraceptives and of those women 14% are using oral contraceptives (Centers for Disease Control and Prevention, 2020). Past research has begun to link hormonal contraceptive use to changes in women’s physiological processes unrelated to reproductive function. One particular study examined the differences in the salivary cortisol response to psychosocial stress by comparing women who were using hormonal contraceptives to women who were naturally cycling (Roche et al., 2013). One limitation of this prior research is that it considered all oral contraceptive users as a single group. In my research I broke down oral contraceptive users into four distinct groups based on the type of progestin, also known as generation of progestin, the oral contraceptive contains. This led me to my current research question: Is there a difference in perceived stress levels among women taking one of the four generations of contraceptive pills and naturally cycling women? Women were directed to an online study and completed an informed consent. Then they completed a variety of measures. The specific stress index I used is the Perceived Stress Scale (PSS) which is a 10-item questionnaire that is widely used to assess stress levels in people 12 years and older (Cohen et al., 1983). To test my hypothesis if there is a difference in stress levels between the

women taking one of the four generations of contraceptive pills compared to the naturally cycling women. I used a one-way ANOVA test to look at the differences in the means between the five groups. My one-way ANOVA test did not find differences between the groups, $F(4,600) = 1.22, p = .301$. Although my results were not significant past research has shown that hormonal contraceptives can have mental and physical effects on women.

Introduction

Stress impacts every person's life. The term "stress" refers to a person's psychological and physiological response to the demands and pressures of the world around them (Farlex, 2021). Stress results from interactions with one's environment that are perceived as causing strain or threatening their well-being. A person's perception and stress response depends on their personality, physical strength, and general health (Kemeny, 2003). People can react differently to the same stressor. For example, a healthy young person may not be as stressed during flu season as may an elderly person who has a relatively weaker immune system. People feel different levels of stress for different stressors and not all people experience the same amount of stress for the same stressors. There are many biological factors that play into the role stress has on our bodies, for example hormones. Past research suggests that exposure to gonadal steroid hormones can cause long-lasting organizational effects on the brain. Steroid hormones cause these effects by crossing the blood-brain barrier and influencing processes such as neurogenesis, synapse formation, and cell death. These changes in one's brain can affect a person's sensitivity to stress (Brown et al., 2013). However, much less research has examined an additional, modern source of hormones—synthetic hormones in hormonal contraceptives. The present research examines how different synthetic hormones in hormonal contraceptive pills may affect woman's stress levels.

Past research has shown that stress can have negative side effects on a person's well-being (Aneshensel et al., 1991; Wunsch et al., 2017; Michie, 2002). Research using a nonspecific stress model found a positive link between stress and anxiety and substance-use disorder (Aneshensel et al., 1991). Stress can also have negative physical impacts on a person. High amounts of stress can affect one's sleep, causing fatigue and resulting in less physical activity (Wunsch et al., 2017). Stress can be observed by a change in a person's behavior. For example, short term stress causes people to demonstrate increased irritability, fatigue, withdrawal, and aggression. If stress persists it can cause changes in neuroendocrine, cardiovascular, autonomic, and immunological function of a person leading to mental and physical tolls on the body (Michie, 2002). Overall, research has shown that stress can cause have negative effects on people's mental and physical health.

Although people experience stress, some people perceive more stress than others. Perceptions are important because the way one understands certain conditions can elicit distinct emotional and physiological responses (Kemeny, 2003). Past research found that college students with more social support had lower levels of perceived stress (Bovier et al., 2004). This research also found data to support that mastery and self-esteem are important protective factors of mental health. Another study looked into the buffering model of social support which states that effective social support network lessens the adverse psychological consequences of stress. This research found that stress and lack of social support contributes to the creation of depressive symptoms (Aneshensel, 1982). People who perceive high stress in their lives are more likely to have illness episodes than those with low levels of stress (Medalie, 1985). This research also found that social support had an effect on illness and perceived stress; people who have more social support are less likely to perceive high levels of stress (Medalie, 1985). Overall, people's

individual differences and outside factors, like social support, can lead some people to perceive more stress than others.

An important factor that has not received a lot of attention is women's use of hormonal contraceptives. In the United States, 24.4% of women aged 15-49 are currently using hormonal contraceptives and of those women 14% are using oral contraceptives (Centers for Disease Control and Prevention, 2020). Oral contraceptives primary function is the prevention of ovulation. The effects oral contraceptives have on the ovarian functioning is the decrease in pituitary production and secretion of both the follicle-stimulating hormone (FSH) and luteinizing hormone (LH) and prevent the typical midcycle surge of these two hormones (Rivera et al., 1999). There are two types of pills available: the combination pills containing estrogen and progestin, and the progestin only pills. Although there are more side effects associated with estrogen, combination pills are more often prescribed (Dawson, 1979). Most side effects are mild and disappear after continued use or switching to another pill type. These side effects include nausea, weight gain, chloasma, spotting and breakthrough bleeding, pituitary tumors, endometrial cancer, and hepatic effects (Dawson, 1979). Given that hormonal contraceptives impact women's bodies, progestins are most likely having other physiological effects unrelated to suppressing ovulation.

Indeed, past research has begun to link hormonal contraceptive use to changes in women's physiological processes unrelated to reproductive function. Research examined how gender, menstrual cycle phase, and oral contraceptives use effects hypothalamus-pituitary-adrenal (HPA) axis responsiveness to psychosocial stress. This research found that women on hormonal contraceptives had significantly blunted hormone stress responses, as measured by salivary cortisol, to emotionally arousing images compared to naturally cycling women (Nielsen

et al., 2013). Another study was conducted by having participants complete a brief psychosocial stress test and then measured the participants HPA activity by the examining the levels of cortisol in their saliva. The researchers found evidence that taking hormonal contraceptives significantly reduces stress hormone responses to a stressor (Kirschbaum et al., 1999). The findings of this study suggest that oral contraceptives can alter HPA activity in response to a psychosocial stressor. Another study found that hormonal contraception can also alter the reactivity of the sympathetic stress system (Otterstetter et al., 1999). In this study, women completed a maximal exercise task. The study demonstrated that women on hormonal contraception had significantly lower post-exercise concentrations of plasma norepinephrine compared to naturally cycling women (Otterstetter et al., 1999). This past research displays how taking hormonal contraceptives can cause physiological changes that are unrelated to ovulation suppression.

One particular study examined the differences in the salivary cortisol response to psychosocial stress by comparing women who were using hormonal contraceptives to women who were naturally cycling (Roche et al., 2013). The participants consisted of 209 women, 72 using hormonal contraception and 137 naturally cycling, that were in good physical health and were between the ages of 18 and 30. The participants completed two sessions that consisted of either stress or rest protocols. The first session always consisted of the stress protocol and the rest day was the second session. The stress protocol, which consisted of public speaking and arithmetic, was followed by a rest period that was a total of 105 minutes in which the subject provided five saliva. The study found that the stressor increased salivary cortisol levels in naturally cycling women, but not in women using hormonal contraceptives (Roche et al., 2013). Another study looked at whether the use of hormonal contraceptives was positively associated

with the use of antidepressants and a diagnosis of depression (Skovlund et al., 2016). This cohort study combined data from the National Prescription Register and the Psychiatric Central Research Register in Denmark. They had a total of 1,061,997 women ages 15-34 included in their analysis. The researchers concluded that the use of hormonal contraceptives was associated with subsequent use of antidepressants and a first diagnosis of depression. This suggests that depression is a potential adverse effect of hormonal contraceptive use (Skovlund et al., 2016). Overall, the use of hormonal contraceptives appears to disrupt the way that women react to stress.

One limitation of this prior research is that it considered all oral contraceptive users as a single group. In my research I broke down oral contraceptive users into four distinct groups based on the type of progestin, also known as generation of progestin, the oral contraceptive contains. Combined oral contraceptives contain two synthetic hormones, an estrogen and a progestin. Since all estrogens in oral contraceptives are the same, I focused on the differences in progestin. Progestins used in hormonal contraceptives have been developed to mimic endogenous progesterone to inhibit ovulation and pregnancy (Mitchell et al., 2020). There is a total of four generations of progestins in oral contraceptives. The first generation, pill consist of estranes derived from testosterone creating the progestins found in these pills: norethindrone, norethynodrel, norethindrone acetate, and ethynodiol diacetate. The second generation, pill consists of gonanes derived from testosterone creating the progestins found in these pills: levonorgestrel and norgestrel. The third generation, pill consists of gonane (Levonorgestrel) derivates creating the progestins found in these pills: desogestrel, gestodene, norgestimate/norelgestromine, and etonorgestrel. The fourth generation, pill consists of non-ethylated estranes and pregnane creating the progestins found in these pills: dienogest,

drospirenone, nesterone, nomegestrol acetate, and trimegestone (Davtyan, 2012). The progestins vary in different affinity for estrogen, androgen, and progesterone receptors, resulting in various side effects for each progestin. For example, second generation progestins like levonorgestrel with high androgenic activity are more prone to cause acne, weight gain, fatigue, and depression compared to progestins with less androgenic activity (Cari, 2006). There are different side effects for high levels of estrogenic, pregestational, and androgenic activity. High levels of estrogenic activity causes bloating, nausea, breast fullness, breakthrough bleeding, irritability, and hypertension while high levels of pregestational causes headache, break pain, and hypertension. Most first generation progestins are high for all three activity levels, second and third generation progestins are high for pregestational and androgenic activity levels, and fourth generation progestins are pretty low for all three activity levels (Cari, 2006). Although research has some understanding of how these progestins were created and work, how they can affect women's mental health is still largely unknown.

Research that has started looking at this distinction suggests that there may be different psychological effects of the different progestin formulations. One study has examined the use of hormonal contraceptives effects on sleep quality (Bezerra et al., 2020). This study consisted of 1,286 women who filled out self-reports of sleep through a web-based cross-sectional survey. They found that women who were using hormonal contraceptives reported more frequent sleep complaints, increased excessive daytime sleepiness, and more insomnia symptoms than naturally cycling women. Women using progestogen-only therapies reported lower sleep duration compared to combined therapy users (Bezerra et al., 2020). Another study found that third generation combined oral contraceptive pills have a better effect on mood in women than the

second generation pills (Shahnazi et al., 2014). Past research has only begun to look at the protentional psychological differences between progestin formulas.

This led me to my current research question: Is there a difference in perceived stress levels among women taking one of the four generations of contraceptive pills and naturally cycling women? I conducted an online survey to examine women's perceptions of recent stress and asked women to report if they were using hormonal contraceptives or not. I then coded the brands of oral contraceptives women reported to categorize women into groups based on the progestin generation. To test my research question, I compared the stress levels of the women on the different types of the oral contraceptive pills and naturally cycling women. I predicted that overall women on oral contraceptives will report higher stress levels compared to naturally cycling women, but I did not have predictions for specific difference in stress levels among the four generations of progestins found in oral hormonal contraceptives pills.

Method

Participants

Women were recruited through flyers around campus of the University of Arkansas and social media apps including GroupMe. A total of 822 women participated in the broader study, which was approved by the University's Institutional Review Board. My thesis looked at 605 of these women who were either naturally cycling or pill users, who have generation progestin data, and answered the Perceived Stress Scale. The generation progestin data was obtained by participants reporting the specific pill brand they were currently taking, and then our researchers looked up the progestins the pills contained. The women were divided up into groups based on the generation of progestin found in their current hormonal contraceptive pill. The ages of the participants were ($M = 20.68$, $SD = 5.11$, range: 18-44). Of the participants, 342 were naturally

cycling women who reported having regular menstrual cycles and 263 women were currently on a hormonal contraceptive for at least one month. I analyzed my data based on the different generation of progestin the women were taking: 102 women were on the first-generation pill, 27 women were on the second-generation pill, 89 women were on the third-generation pill and 45 women were on the fourth-generation pill. We also had women report the number of months they have currently been taking birth control; participants reported being on oral contraceptives for 33 months on average ($M = 33.12$, $SD = 31.28$, range: 1-240). Women reported beginning oral contraceptive use around age 16 ($M = 16.46$, $SD = 2.11$, range: 11-24).

Our participants also filled out demographics including race, political orientation, religiosity, and sexual identity. Over 85% of the participants reported they were White, Caucasian, or European American. We measured political orientation a scale from 1 (extremely liberal) to 10 (extremely conservative); participants reported being around the midpoint of the scale on average ($M = 4.85$, $SD = 2.61$, range: 1-10). We measured religiousness a scale from 1 (not religious at all) to 10 (extremely religious); participants reported being around the midpoint of the scale on average ($M = 6.05$, $SD = 2.89$, range: 1-10). We also asked the participants current relationship status: 49.4% reported being single, 26.9% seriously dating, 9.8% casually dating, 4.3% cohabitating, and 7.4% married. We asked participants if they were able to choose the pill they were currently on. The majority of women (64.6%) answered no and 29.1% answered yes. Finally, we asked participants the reason they were taking hormonal contraceptives. Most women said that their main reasons were to correct menstrual irregularities (51.3%) and to ease menstrual pain (51%).

Procedure

Women were directed to an online study and completed an informed consent. Then they completed a variety of measures. The specific stress index I used is the Perceived Stress Scale (PSS) which is a 10-item questionnaire that is widely used to assess stress levels in people 12 years and older (Cohen et al., 1983). The scale is rated on a 5-point Likert scale 1 being (never) to 5 being (very often). An example question from the PSS is “In the last month, how often have you been upset because of something that happened unexpectedly?”. This scale evaluates the degree to which an individual has perceived life as unpredictable, uncontrollable and overloading over the previous month. The reliability of the PSS scale in my sample was good (Cronbach’s $\alpha = .85$). Participants were divided into groups depending on how they answered the question if they are currently using hormonal contraceptives. Women who answered no were assigned to the group of naturally cycling women and those who answered yes were in the group of current users of hormonal contraceptives. I then broke the group of hormonal contraceptive users down even more by the answer they put for what type of pill they are using. This question divides the hormonal contraceptive women up into the four different generations of progestins they are taking. I used the participants answers from this scale to assess the stress levels of the women on the four different forms of the hormonal contraceptive pills and the women that are naturally cycling.

Results

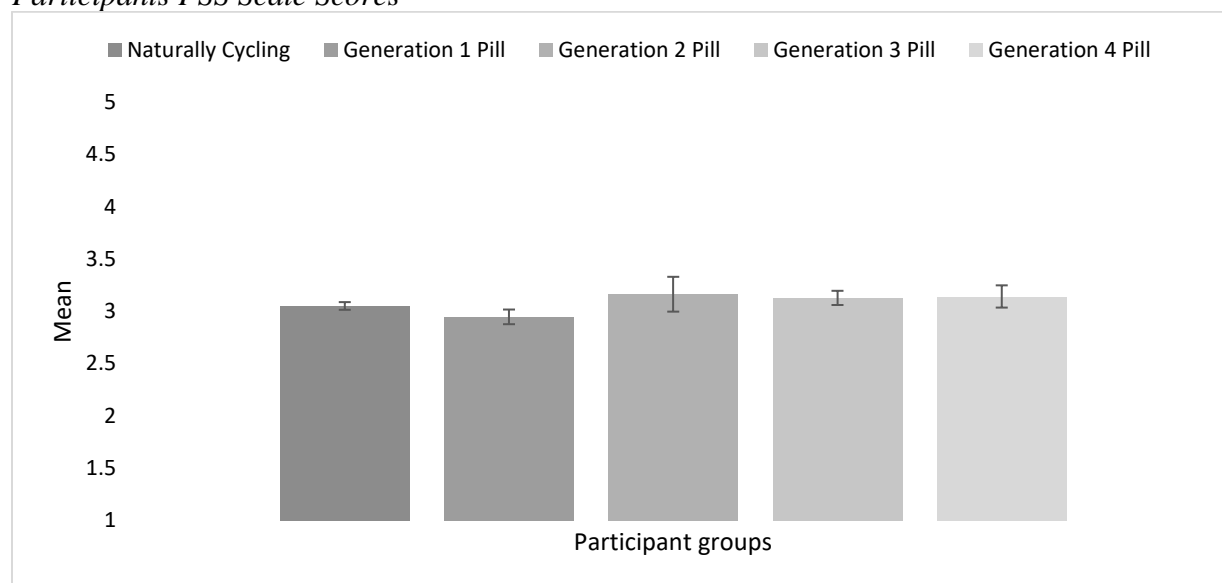
To test my hypothesis if there is a difference in stress levels between the women taking one of the four generations of contraceptive pills compared to the naturally cycling women. I used a one-way ANOVA test to look at the differences in the means between the five groups. My

one-way ANOVA test did not find differences between the groups, $F(4,600) = 1.22, p = .301$.

See Figure 1.

Figure 1

Participants PSS Scale Scores



Discussion

This research was conducted using an online survey consisting of women who were either naturally cycling or using hormonal contraceptives. I analyzed a specific measure of this survey, the Perceived Stress Scale, to test my hypothesis of differences in stress levels between the women taking hormonal contraceptives containing one of the four generations of progestins compared to the naturally cycling women. I did not find any statistically significant differences between the groups, so I cannot say that the hormonal contraceptive pill has an effect on women's stress levels.

Although my results were not significant past research has shown that hormonal contraceptives can have mental and physical effects on women. According to Skovlund's cohort study in Denmark there is an association between subsequent use of antidepressants and first diagnosis of depression (Skovlund et al., 2016). This study consisted of data from over a million

women presenting a link between hormonal contraceptives and a mental disorder. Two other studies looked at salivary cortisol levels, to measure stress responses, between women who were on hormonal contraceptives and naturally cycling. In Nielsen's study they found that women who were taking hormonal contraceptives had significantly blunted hormone stress responses to emotionally arousing images compared to naturally cycling women (Nielsen et al., 2013). In Kirshbaum's study they found evidence that taking hormonal contraceptives significantly reduces stress hormone responses to a stressor (Kirshbaum et al., 1999). Both of these studies had significant results displaying that hormonal contraceptives play a role in stress responses. This displays that even though my research may not have been significant other studies have begun to find a link between hormonal contraceptives and the mental effects it has on women.

There are various reasons to why my results might have not been significant. First, the sample was small and unrepresentative. My research only consisted of a total of 605 women. These women were then broken down into 5 smaller groups. The second-generation progestin group only consisted of 27 women. This sample size is too small to get reliable and valid results. The demographic of our participants were mostly Caucasian college students. Some participants completed the survey in order to receive psychology class credit. This might have skewed the results based on how much effort they put into the survey. Participants that chose to do this survey voluntarily because they were interested in the study most likely thought through their answer more carefully. Overall, our sample of majority Caucasian, college women is not an accurate representation of the women who are currently on hormonal contraceptives around the world. This study should be replicated with a larger and more representative sample and it might yield significant results.

I also only examined a specific stress index, the PSS. This is a short 10-item scale compared to other stress scales available. I used this stress index since my data was obtained from a survey intended for a larger study. If I was to replicate this study, I would use a much more in-depth scale to measure stress. The PSS asks how you have felt in the past month which is much too broad. I would create a study that measured all aspects of stress and was completed over several days. This survey was filled out in one day which could have also impacted my results. A participant could have been feeling extra happy or depressed while filling out the survey giving an inaccurate result. I think it is important to measure stress more in depth over several days, because one short 10-item scale most likely will not pick up on the differences in such a small sample size.

Another limitation of my research is the time the survey took place. My data was collected September – December 2021. Everyone is still adjusting to changes due to the global pandemic. Participants are adjusting to returning to in person classes after being online for so long. This could cause stress to many people since everyone is being forced back into the world out of the comfort of their home. The added stress of what is going on in the world could have impacted my results. This time may also be stressful due to increase of responsibilities one has. People are able to go back to work, go to classes in person, and do extracurricular activities that were once taken away leaving everyone with more free time. They might have a lot more commitments now and outside factors that are affecting their mood and how they answered the PSS. The past years have been nowhere near normal conditions and I think it would be a good idea to do this study again, not right after a global pandemic.

Research should continue examining the effects hormonal contraceptives have on women's mental and physical health. Future research could examine hormonal contraceptives

effects on sexual desire. This is not a well-researched topic and would be interesting to see if there is an impact. Past research has begun to look at hormonal contraceptives effect mood. It would be neat to look at how this change in mood effects a person's sexual desire. Since birth control is supposed to prevent pregnancy physically it would be fascinating to see if it is somewhat preventing it mentally. There are many potential mental impacts of hormonal contraceptives to be researched.

Another route future research could take is to look at the effects hormonal contraceptives have on sleep patterns and eating habits, which could also be a sign of stress. Weight gain is a side effect of some hormonal contraceptives. It would be interesting to see if this extra weight is caused by overeating or how the hormones are biologically changing a person's metabolism. So little is known about the effects that hormonal contraceptives have on women. It should continue being researched since so many women around the world are on various forms and no one knows the true impact.

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