

## Hormonal contraceptive use predicts decreased perseverance and therefore performance on some simple and challenging cognitive tasks

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### ABSTRACT

A growing body of research suggests that hormonal contraceptive (HC) use may be associated with lower self-control, as well as structural and functional differences in women's brains that could contribute to differences in perseverance on tasks requiring cognitive control. Here, we sought to extend this research by examining the relationship between HC use and college-aged women's perseverance (i.e., time spent) and performance on tasks requiring cognitive control. Across two studies, we find that, compared to naturally-cycling women, women using HCs display less perseverance on both simple (i.e., a spot-the-difference game) and challenging (i.e., Graduate Record Examination quantitative problems) tasks. Moreover, these differences in perseverance were found to predict performance decrements across tasks, with women taking HCs performing worse because they spent less time on the tasks. By demonstrating how HC use may influence perseverance and thereby performance, these results contribute to a growing body of research examining the unintended implications of HC use on cognition, learning, and memory.

If at first you don't succeed, try, try again. The familiar adage may be based on folk wisdom, but it appropriately highlights the incredible power of perseverance in achieving success. For example, research suggests that the ability to persist on difficult tasks is highly predictive of success in several domains of life, including learning and educational attainment (Pintrich et al., 1993; Zimmerman and Pons, 1986), job performance (Littman-Ovadia and Lavy, 2016; Robertson-Kraft and Duckworth, 2014), well-being (Salles et al., 2014), and academic achievement (Muenks et al., 2017). For example, in one study of more than 600 full-time employees, researchers found that perseverance was the trait that was most positively related to effective work performance and most negatively related to counterproductive work behaviors, such as calling in sick for reasons other than illness (Littman-Ovadia and Lavy, 2016). Others have found perseverance to be predictive of success benchmarks as diverse as retention in the United States Military Academy and ranking in the National Spelling Bee (Duckworth et al., 2007). Together, such research suggests that the ability to persevere and work diligently toward goals plays an important role in achieving success in a variety of important life domains.

While much research has investigated the importance of perseverance in success across life domains (Credé et al., 2017), less attention has been given to the role that hormones, generally, or hormonal contraceptives (HC), specifically, play in contributing to observed

variability in perseverance (Warren et al., 2014). However, a growing body of research suggests that HC use may be associated with important structural and functional differences in brain areas important for executive function and the cognitive control of behavior (Hertel et al., 2017; Kirschbaum et al., 1999; Petersen et al., 2014; Petersen et al., 2015; Pletzer et al., 2016). As such, HC use could contribute to observed differences in perseverance and task performance in women. Here, we test this possibility by examining whether HC use in college-aged women is associated with perseverance and performance decrements on tasks requiring the ability to exercise cognitive control of behavior. We hypothesized that women taking HCs (when compared to naturally-cycling women) would exhibit diminished perseverance on both simple and challenging cognitive tasks. We further hypothesized that the predicted differences in perseverance would predict diminished task performance by HC using women. This research will help inform the continued discussion about the potentially far-reaching effects of HCs on women's psychology and behavior.

HCs were first approved for use in pregnancy prevention by the United States Food and Drug Administration in 1960 (Engelman, 2001). Today, nearly 60 years later, approximately 11.2 million women in the United States take HCs, making them the most commonly used method of contraception (Jones, 2011; Kavanaugh and Jerman, 2018). The majority of women taking HCs do so for contraceptive purposes (i.e.,

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avoiding unwanted pregnancy). However, many women use HCs for non-contraceptive benefits, such as reducing pain associated with menstruation, menstrual cycle regulation, and acne reduction (Burkman et al., 2004).

In addition to inhibiting ovulation (the primary mechanism through which HCs prevent pregnancy), HC use is also associated with several additional physiological and psychological effects (see Montoya and Bos, 2017; Pletzer and Kerschbaum, 2014; Welling, 2013 for review). For example, HC use is associated with decreased risk of ovarian cancer (Beral et al., 2008), but increased risk for thrombotic stroke, myocardial infarction (Lidegaard et al., 2012), and breast cancer (Kahlenborn et al., 2006).

Although less frequently discussed, research suggests that HC use may also have effects on women's brain structure and function. Many of these differences are in areas that play an important role in executive function and the cognitive control of behavior. For example, compared to naturally-cycling women, women using HCs exhibit decreased resting state functional connectivity in the brain's executive control network (Petersen et al., 2014; Pletzer et al., 2016), which plays an important role in self-regulatory behaviors such as attention, learning, and memory (Rueda et al., 2004). Others find that HC users have decreased cortical thickness in the lateral orbitofrontal cortex and the posterior cingulate cortex (Petersen et al., 2015), areas which are known to play an important role in self-regulation and executive function (Wagner et al., 2001).

HC users and non-users also exhibit differences in the hippocampus, with HC users having less hippocampal volume than non-users (Hertel et al., 2017). This difference is reasoned to emerge in response to HC users experiencing hypercortisolism. That is, women taking HCs have higher total cortisol levels than do naturally-cycling women (Hertel et al., 2017; Kirschbaum et al., 1999), which can suppress cell proliferation (and may contribute to cell death) in the hippocampus (Gould and Tanapat, 1999; Sapolsky et al., 1985; Woolley et al., 1990). Although this area of the brain is most frequently studied in terms of its direct impact on learning and memory (Axmacher et al., 2007; Meck et al., 1984; Rawlins and Tsaltas, 1983), the hippocampus also plays a role in perception (Lee et al., 2005), as well as motivation and emotion (Frodl et al., 2006; Gray and McNaughton, 1983).

In addition to being associated with changes in brain structure and function, research finds that HC use may also have an important impact on women's psychology and behavior, particularly in domains related to cognitive control of behavior. For example, in one recent highly-powered, randomized, placebo-controlled study, researchers found evidence of a causal association between HC use and self-control, with women using HCs reporting lower self-control relative to the placebo group (Zethraeus et al., 2017). Others have found that HC use is associated with higher likelihood of academic performance problems in a sample of young female college students (Gregory et al., 2018), suggesting that cognitive control of behavior may be diminished in HC-using women.

Despite these empirical linkages, research examining the relationship between HC use and performance on tasks requiring cognitive control has been largely inconclusive (for review see Warren et al., 2014). Some research finds, for example, that compared to non-users, HC use is associated with impaired performance on mental rotation and verbal fluency tasks, as well as mental math (Griksiene et al., 2018; Griksiene and Ruksenas, 2011; Wuttke et al., 1975). For instance, Griksiene et al. (2018) found that HC users responded more quickly and less accurately than naturally-cycling women on mental rotation tasks, which is consistent with the idea of reduced cognitive control in the context of HC use. However, others find that HC use is associated with better spatial ability (specifically monophasic oral contraceptives; Beltz, Hampson, & Berenbaum, 2015), quicker reaction times, and improvements in working memory (Griksiene and Ruksenas, 2011). Others find no relationship between HC use and performance on tasks requiring cognitive control, including working memory, visuospatial

memory, recognition memory, mental rotation, verbal fluency, visuospatial abilities, and attention (Islam, Sparkes, Roodenrys, & Astheimer, 2008; Mordecai et al., 2008; Wharton, Hirshman, Merrit, Doyle, Paris, & Gleason, 2008; Wright Jr and Badia, 1999).

Importantly, much of the research examining the links between HC use and performance on tasks requiring cognitive control has been conducted using small sample sizes and without examining the relationship between HC use, perseverance, and performance on tasks requiring cognitive control (with exceptions; see e.g., Griksiene et al., 2018). The literature is currently lacking research conducted on large samples that examines the relationship between HC use, perseverance, and performance on tasks requiring cognitive control.

Given this current empirical gap, we designed two studies to examine the relationship between HC use and women's perseverance and performance on simple and challenging cognitive tasks. Others have found that, compared to naturally-cycling women, women taking HCs exhibit diminished performance on a relatively complex mental rotation task (Griksiene et al., 2018; Griksiene and Ruksenas, 2011). In Study 1, we sought to examine whether such differences are also observed using a simple visuospatial task, and whether the predicted decrements in performance are mediated by decreased perseverance. Specifically, we used a timed spot-the-difference task to assess differences in perseverance and performance between naturally-cycling women and those using HCs. This task was chosen because it has been used successfully in past research aimed at assessing attention (Fukuba et al., 2009; Kreplin and Fairclough, 2013) and differences in cognition stemming from structural and functional changes in the brain (Nishiguchi et al., 2015).

In Study 2, we sought to conceptually replicate and extend Study 1, examining whether HC use is also associated with decreased perseverance and performance on more challenging and meaningful tasks. In particular, we examined the relationship between HC use and women's perseverance and performance on complex arithmetic problems (taken from a Graduate Record Examination [GRE] practice book) and both solvable and unsolvable anagrams. The GRE and solvable anagram tasks were chosen because performance on math and language tasks are each associated with the ability to exercise cognitive control of behavior (Cragg and Gilmore, 2014; Cragg et al., 2017; Finn et al., 2014; Gilhooly and Fioratou, 2009; Mendelsohn et al., 1966; Novick and Sherman, 2003). The unsolvable anagram task was chosen based on past research which has demonstrated its utility as a measure of persistence in the face of perceived failure (Eisenberger and Leonard, 1980; Kroll, 1991; Ventura et al., 2013). Given the demonstrated impact of HC use on brain structures related to cognitive control and working memory, we predicted that women using HCs would exhibit decrements in perseverance and performance across both simple and challenging tasks. Further, we predicted that the relationship between HC use and performance would be mediated by changes in perseverance, where women taking HCs perform worse than naturally-cycling women because they spend less time on the tasks.

## 1. Materials and methods

### 1.1. Participants

Participants for both studies were recruited from a private university in the southern U.S. The inclusion criterion for duration of HC use was at least two months. Women who were naturally-cycling were required to have not used HCs for at least three months. All participants received nominal course credit for participation.

The final sample of participants for Study 1 consisted of 149 female undergraduates (73 on hormonal birth control;  $M_{\text{age}} = 20.24$ ,  $SD_{\text{age}} = 2.86$ ). Prior to data analysis, participants were excluded if they: were pregnant or breast feeding ( $n = 1$ ), self-reported having a hormonal disorder ( $n = 14$ ), failed attention filters ( $n = 8$ ), or did not meet recruitment criteria for age or HC duration ( $n = 5$ ).

The final sample of participants for Study 2 consisted of 175 female undergraduates (89 on hormonal birth control;  $M_{\text{age}} = 19.28$ ,  $SD_{\text{age}} = 1.58$ ). Prior to data analysis, participants were excluded if they: indicated they had a hormonal disorder ( $n = 13$ ); failed attention filters ( $n = 19$ ); or did not meeting the recruitment criteria for age or birth control duration ( $n = 3$ ).

## 1.2. Procedure

All sessions were conducted between 8 and 10:30 A.M. Participants arrived at a research laboratory in small groups of 5–12 to participate in a study allegedly examining the relationship between personality and problem solving. All participants were seated at individual computer terminals running Qualtrics experimental software. Participants in Study 2 were provided with pencils, scratch paper, and a basic calculator. After signing an informed consent, participants completed cognitive tasks, which varied by study and are described below. Participants in Study 1 then completed measures related to a separate, unrelated study on mate preferences. Next, all participants provided standard demographic information, as well as information regarding HC use and duration, and completed attention checks. All participants were fully debriefed as to the hypotheses before being dismissed.

### 1.2.1. Hormonal contraceptives

To assess current HC use, participants responded to the following item: “Have you used any form of hormonal contraception within the last 3 months?” If participants answered yes, they were asked to provide information regarding the type (e.g., pill, patch, skin implant, hormonal IUD, etc.) and brand name (e.g., Mirena). Of the 163 women who indicated they were taking HCs across the studies, 138 women provided information about the type of product they were using (see Table 1 for more information). After providing this information, participants indicated how many months they had been taking HCs and whether they were on them currently. Participants were included in the HC condition if they were currently on a HC and had been for at least two months prior to the time of the study (see “participants” section for information about exclusions).

## 1.3. Cognitive tasks

Participants in Study 1 completed a timed spot-the-difference task. In Study 2, participants completed both GRE quantitative problems and anagram problems.

### 1.3.1. Spot-the-difference task

In this task, participants were shown two seemingly identical images side-by-side of the characters from *Frozen*, a popular animated film (see supplemental materials for images). Although seemingly identical, the two images had 10 subtle differences. For example, in the image on the left, one of the characters had a snowflake levitating above her hand, and the snowman had two coal buttons, whereas these details were missing from the image on the right. Participants were instructed to find the differences between the left and the right images by clicking their mouse on the difference points in the right image. They were told that they could go to the next page whenever they wanted and were not told how many differences there were between the two pictures. Total time spent on this page was used as our measure of perseverance. Task performance was measured using the number of differences spotted.

### 1.3.2. GRE quantitative problems

Prior to the GRE quantitative task, participants were informed that they were going to be asked some problem-solving questions. They were instructed to select a single answer choice for each problem and were told to feel free to use the calculator and paper provided when working on these problems. The software then displayed each of the

eight math problems one at a time. An example problem is, “If an integer is divisible by both 8 and 15, then the integer also must be divisible by which of the following?” Each math problem was accompanied by five potential answer options. A total performance score was computed by summing the number of correct responses for each participant. Time spent on each problem was measured via the timing feature in Qualtrics. As a measure of perseverance on the GRE task, a mean composite of time spent was computed by averaging the time spent across each problem.

### 1.3.3. Anagram tasks

Participants were told that the purpose of the task was to examine how they interpret ambiguous word stimuli by unscrambling a series of word jumbles, or anagrams. Two practice items were first given to participants to familiarize them with the task. They were instructed to unscramble the letters presented to create a single word using all of the letters. For example, they were shown “obko,” which was unscrambled to spell “book.” After participants completed each practice problem, they were provided with the correct answer so that they could check their work. Once the practice problems were complete, the software displayed six word scrambles one at a time. The first three anagrams were solvable: “gatmeemna,” “rtnuatoas,” and “smcysagitn.” These can be unscrambled to create the words “management,” “astronaut,” and “gymnastics,” respectively. A performance score was computed by summing the number of correct responses, and perseverance on the solvable anagrams was measured by time spent on each problem. The unsolvable anagrams did not have a correct solution: “Inageatir,” “loimcpris,” and “ircboeyr.” Because they lack a solution, performance on the unsolvable anagrams could not be assessed. They were included to assess perseverance on unsolvable tasks. For each type of word scramble, time spent was recorded via the timing function in Qualtrics. Perseverance measures for each type of word scramble (solvable and unsolvable) were created by averaging time spent across each word scramble within each category.

## 2. Results

### 2.1. Initial data processing

Psychometric analysis performed prior to data analysis revealed positive skew for all of the outcome measures, with the exception of performance and perseverance on the GRE problems. To approximate normal distributions, natural log 10 transformations were applied to the positively skewed outcome measures before conducting analyses testing the hypotheses. Natural log 10 transformations successfully approximated normal distributions for all of the variables except performance and perseverance on the spot-the-difference task (Study 1) and performance on the solvable anagrams task (Study 2). Original and transformed distributions of the dependent variables for each group can be seen in the supplemental materials. Due to this violation, non-parametric Mann-Whitney *U* tests were used to examine the relationship between HC use and the dependent variables of perseverance and performance on the spot-the-difference task and performance on the solvable anagram task. See Table 1 for descriptive statistics. No outliers were found for perseverance (i.e., time spent) on the spot-the-difference task or the GRE quantitative task. Outliers on perseverance were found for both the solvable and unsolvable anagram tasks. However, given that results persisted after outliers were removed from the data set, we report the analyses on the full data set here. Results with outliers removed can be found in the supplemental materials.

### 2.2. Study 1

#### 2.2.1. Spot-the-difference analyses

A Mann-Whitney *U* test indicated that naturally-cycling women spent significantly more time ( $Mdn = 81.51$ ) than women taking HCs

**Table 1**  
Descriptive statistics for perseverance and performance during cognitive tasks as a function of HC use.

	Spot-The-Difference Perseverance		Spot-The-Difference Performance		GRE Perseverance		GRE Performance		Solvable Anagram Perseverance		Solvable Anagram Performance		Unsolvable Anagram Perseverance	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
<b>Study 1</b>														
Naturally-cycling (n = 76)	84.62	41.08	5.57	2.84	97.16	34.92	3.88	1.94	76.10	84.96	0.34	0.68	62.12	59.30
HC (n = 73)	60.06	30.66	4.77	2.79	78.54	28.50	3.21	1.89	44.14	41.24	0.18	0.44	38.55	39.23
<b>Method of HC administration</b>														
Constant dosage (n = 1)	52.43		6											
Hormonal IUDs/skin implants (n = 6)	68.20	18.49	4.67	2.58										
Combination pill (n = 55)	70.94	32.68	4.96	2.87										
Data missing (n = 11)	61.67	26.84	3.73	2.57										
<b>Study 2</b>														
Naturally-cycling (n = 86)					85.05	29.50	3.75	0.96	53.88	26.29	0	0	64.38	60.60
HC (n = 89)					82.09	15.37	2.86	2.19	55.21	45.91	0.29	0.49	61.51	53.89
<b>Method of HC administration</b>														
Constant dosage (n = 4)														
Hormonal IUDs/skin implants (n = 7)														
Nuva ring (n = 2)					83.26	15.10	5.50	3.54	77.42	43.10	0	0	60.36	57.12
Combination pill (n = 63)					75.27	28.10	3.14	1.92	44.35	44.03	0.17	0.46	30.75	30.31
Data missing (n = 13)					89.75	36.15	3.23	1.54	29.05	23.25	0.23	0.44	52.66	52.47

Note. Perseverance represents time spent in seconds. Performance represents number of correct responses.

( $Mdn = 67.42$ ) on the spot the difference task,  $U = 2142.00$ ,  $Z = -2.40$ ,  $p = .02$ ,  $r = 0.20$ . While not statistically significant, results revealed a marginal effect of HC use on numbers of differences spotted, where naturally-cycling women spotted a greater number of differences ( $Mdn = 6$ ) than those who were using HCs ( $Mdn = 5$ ),  $U = 2277.50$ ,  $Z = -1.90$ ,  $p = .058$ ,  $r = 0.16$ . These results suggest that, compared to naturally-cycling women, HC use is associated with less perseverance and marginally worse task performance.<sup>1</sup>

### 2.2.2. Mediation of spot-the-difference performance by perseverance

To examine whether differences in women's performance on the spot-the-difference task could be accounted for by differences in perseverance, a mediation analysis was conducted using the Preacher and Hayes' (2008) macro and bootstrapping procedure. Five thousand bootstrap resamples were performed. The analysis revealed a significant indirect effect of HC use on women's performance on the spot-the-difference task via time spent on the task,  $b = 0.77$ ,  $SE = 0.29$ , 95% CI [0.19, 1.33]. The model, along with statistics measuring the significance of each predictive pathway, can be seen in Fig. 1. Specifically, the results revealed that naturally-cycling women spent significantly more time on the spot-the-difference task than HC women (a path;  $b = 15.56$ ,  $SE = 5.96$ ,  $t = 2.61$ ,  $p = .010$ , 95% CI [3.78, 27.33]), and that increased time spent on the spot-the-difference task predicted increased performance on the task, (b path;  $b = 0.05$ ,  $SE = 0.005$ ,  $t = 10.05$ ,  $p \leq .001$ , 95% CI [0.04, 0.06]). Moreover, the direct effect revealed that the marginal effect of HC use on task performance (c path;  $b = 0.80$ ,  $SE = 0.46$ ,  $t = 1.73$ ,  $p = .086$ , 95% CI [-0.11, 1.71]) disappeared after controlling for the mediating influence of perseverance (c' path;  $b = 0.03$ ,  $SE = 0.36$ ,  $t = 0.08$ ,  $p = .940$ , 95% CI [-0.69, 0.75]). These results are consistent with partial mediation, suggesting that women using HCs exhibited decreased perseverance relative to naturally-cycling women, which led them to perform worse on the task.

### 2.2.3. Additional analyses

To examine whether women in the HC group differed in their performance and persistence on the spot-the-difference task based on the method of HC administration (e.g., constant dosage, skin implant, combination pill), Kruskal-Wallis tests were performed on each dependent variable. No significant differences were revealed ( $ps \geq 0.68$ ), supporting our decision to treat women taking HCs as a unitary group.

## 2.3. Study 2

### 2.3.1. GRE analyses

Independent samples *t*-tests were conducted to compare perseverance and performance on the GRE problems in women taking HCs and naturally-cycling women. Levene's test for equality of variances was met for the perseverance ( $p = .05$ ) and performance ( $p = .76$ ) GRE variables. Results revealed that naturally-cycling women ( $M_{\text{seconds}} = 97.16$ ,  $SD_{\text{seconds}} = 34.92$ ) spent more time on GRE problems than women on HCs ( $M_{\text{seconds}} = 78.53$ ,  $SD_{\text{seconds}} = 28.50$ ),  $t(173) = -3.87$ ,  $p \leq .001$ ,  $d = 0.58$ . Further, results revealed that naturally-cycling women ( $M = 3.88$ ,  $SD = 1.94$ ) correctly solved more GRE problems than women taking HCs ( $M = 3.21$ ,  $SD = 1.89$ ),  $t(173) = -2.32$ ,  $p = .02$ ,  $d = 0.35$ . These results indicate that naturally-cycling women not only exhibit more perseverance on GRE math

<sup>1</sup> Follow-up correlational analyses were performed to examine whether duration of HC use was related to performance and perseverance on the spot-the-difference task for women who were taking HCs. No significant relationship between duration of HC use and performance ( $p = .72$ ) or perseverance ( $p = .28$ ) was found. Analyses of covariance (ANCOVA) conducted on the spot-the-difference performance and perseverance variables revealed that, while controlling for duration of HC use, the pattern of results persisted (spot-the-difference performance:  $F(1, 146) = 2.80$ ,  $p = .097$ , partial  $\eta^2 = 0.02$ ; spot-the-difference perseverance:  $F(1, 146) = 7.39$ ,  $p = .007$ , partial  $\eta^2 = 0.05$ ).

problems, they also perform better.<sup>2</sup>

### 2.3.2. Mediation of GRE performance by perseverance

To examine whether perseverance on the GRE math problems mediated performance on this task, a mediation analysis was conducted as was done with the previous task. The analysis revealed a significant indirect effect of HC use on women's performance on GRE questions via perseverance,  $b = 0.40$ ,  $SE = 0.13$ , 95% CI [0.18, 0.67]. The model, along with statistics measuring the significance of each predictive pathway, can be seen in Fig. 2. Naturally-cycling women spent significantly more time on the GRE problems than HC users, (a path;  $b = 18.62$ ,  $SE = 4.81$ ,  $t = 3.87$ ,  $p \leq .001$ , 95% CI [9.12, 28.12]), and increased time spent on the problems significantly predicted increased performance on the GRE questions, (b path;  $b = 0.02$ ,  $SE = 0.004$ ,  $t = 5.00$ ,  $p \leq .001$ , 95% CI [0.01, 0.03]). The effect of HC use on GRE performance (c path;  $b = 0.67$ ,  $SE = 0.29$ ,  $t = 2.32$ ,  $p = .022$ , 95% CI [0.10, 1.24]) disappeared after controlling for the mediating influence of perseverance (c' path;  $b = 0.27$ ,  $SE = 0.28$ ,  $t = 0.96$ ,  $p = .34$ , 95% CI [-0.29, 0.83]), providing evidence that changes in perseverance mediated the relationship between HC use and performance on GRE problems.

### 2.3.3. Word scramble analyses

Independent samples *t*-tests were conducted to compare perseverance on the anagram problems in naturally-cycling women and women taking HCs. Levene's test for equality of variances was met for the solvable ( $p = .77$ ) and unsolvable ( $p = .84$ ) perseverance variables. Results revealed that naturally-cycling women ( $M_{\text{seconds}} = 76.11$ ,  $SD_{\text{seconds}} = 84.95$ ) spent significantly more time on the solvable anagrams than those taking HCs ( $M_{\text{seconds}} = 44.14$ ,  $SD_{\text{seconds}} = 41.24$ ),  $t(173) = -4.13$ ,  $p \leq .001$ ,  $d = 0.48$ . The same pattern of results emerged for the unsolvable anagrams, where naturally-cycling women ( $M_{\text{seconds}} = 62.12$ ,  $SD_{\text{seconds}} = 59.30$ ) spent significantly more time attempting to solve the unsolvable anagrams than women taking HCs ( $M_{\text{seconds}} = 38.55$ ,  $SD_{\text{seconds}} = 39.23$ ),  $t(173) = -2.99$ ,  $p = .003$ ,  $d = 0.47$ . The Mann-Whitney *U* test performed on the task performance variable (solvable word scrambles only) indicated no significant difference between naturally-cycling women ( $Mdn = 0$ ) and women taking HCs ( $Mdn = 0$ ),  $U = 3441.00$ ,  $Z = -1.64$ ,  $p = .10$ ,  $r = 0.12$ .<sup>3</sup>

### 2.3.4. Mediation of solvable word scramble performance by perseverance

Consistent with the previous analyses, a mediation analysis was conducted to examine if perseverance on the solvable anagrams mediated performance. The analysis revealed a significant indirect effect of

<sup>2</sup> ANCOVAs were conducted on the GRE performance and perseverance variables to examine whether the pattern of results would persist while controlling for duration of HC use. Results indicated that the effect of HC use on GRE problem performance and perseverance held while controlling for duration of HC use,  $F(1, 172) = 4.38$ ,  $p = .04$ , partial  $\eta^2 = 0.03$ , and  $F(1, 172) = 6.54$ ,  $p = .01$ , partial  $\eta^2 = 0.04$ , respectively. As in Study 1, follow-up correlational analyses were next conducted to examine whether duration of HC use impacted performance and perseverance on the GRE problems for those taking HCs. Results indicated that there was no significant relationship between duration of HC use and performance or perseverance on the GRE problems ( $ps = 0.65$ ).

<sup>3</sup> ANCOVAs were conducted to examine whether the patterns of results would persist while controlling for duration of HC use. The pattern of results persisted for perseverance on the solvable and unsolvable anagrams while controlling for duration of HC use,  $F(1, 172) = 10.17$ ,  $p = .002$ , partial  $\eta^2 = 0.06$ , and  $F(1, 172) = 4.28$ ,  $p = .04$ , partial  $\eta^2 = 0.02$ , respectively. When controlling for duration of HC use, the effect of HCs on unsolvable anagram performance remained nonsignificant,  $F(1, 172) = 2.09$ ,  $p = .15$ . As we did with the GRE items, we conducted follow-up correlational analyses to examine whether duration of HC use impacted performance and perseverance on the anagram problems for those taking HCs revealed that there was no significant relationship between duration of HC use and perseverance or performance on the anagram problems ( $ps \geq 0.65$ ).

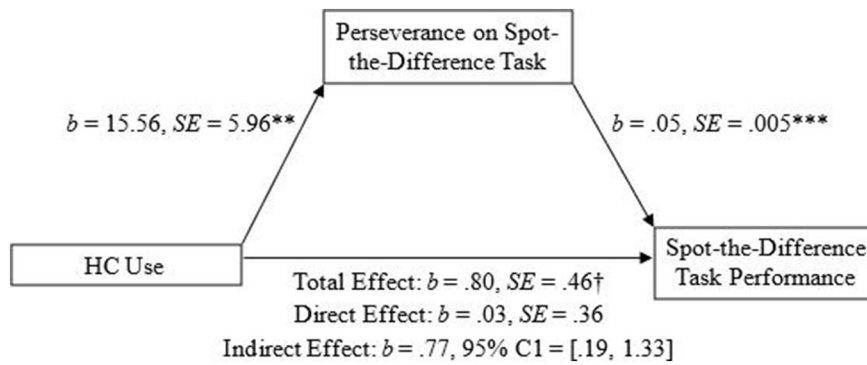


Fig. 1. Study 1 unstandardized regression coefficients for the relationship between HC use and performance on the spot-the-difference task as mediated by perseverance on the task.

Note: † indicates  $p = .09$ , \* indicates  $p < .05$ , \*\* indicates  $p \leq .01$ , and \*\*\* indicates  $p \leq .001$ .

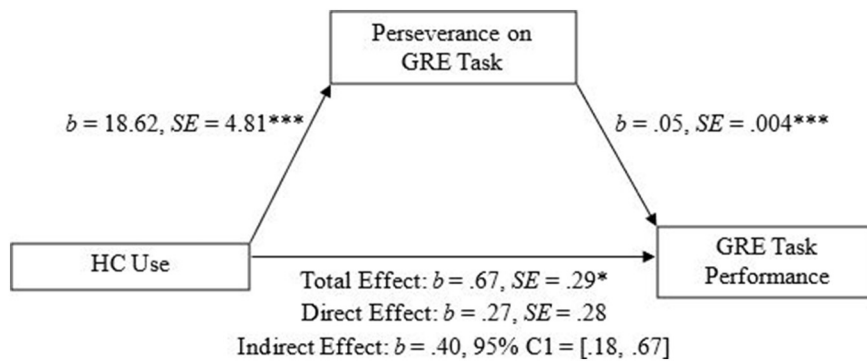


Fig. 2. Study 2 unstandardized regression coefficients for the relationship between HC use and performance on the GRE task as mediated by perseverance on the task.

Note: \* indicates  $p < .05$ , \*\* indicates  $p \leq .01$ , and \*\*\* indicates  $p \leq .001$ .

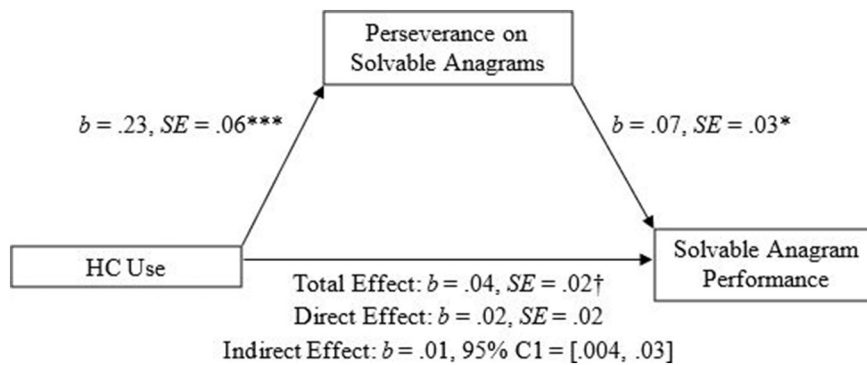


Fig. 3. Study 2 unstandardized regression coefficients for the relationship between HC use and performance on the solvable anagram task as mediated by perseverance on the task.

Note: † indicates  $p = .08$ , \* indicates  $p < .05$ , \*\* indicates  $p \leq .01$ , and \*\*\* indicates  $p \leq .001$ .

HC use on women's performance on the solvable anagram questions via perseverance,  $b = 0.01, SE = 0.01, 95\% CI [0.004, 0.03]$ . The model, along with statistics measuring the significance of each predictive pathway, can be seen in Fig. 3. Naturally-cycling women spent significantly more time on the solvable word scrambles ( $a$  path;  $b = 0.23, SE = 0.06, t = 4.13, p \leq .001, 95\% CI [0.12, 0.34]$ ), and time spent on the problems predicted slightly better performance, ( $b$  path;  $b = 0.07, SE = 0.03, t = 2.22, p = .03, 95\% CI [0.01, 0.12]$ ). While not statistically significant, results revealed a marginal total effect of HC use on solvable anagram performance ( $c$  path;  $b = 0.04, SE = 0.02, t = 1.76, p = .080, 95\% CI [-0.005, 0.08]$ ). The direct effect revealed that the marginal effect of HC use on solvable anagram performance disappeared after controlling for the mediating influence of perseverance ( $c'$  path;  $b = 0.02, SE = 0.02, t = 1.04, p = .30, 95\% CI [-0.02,$

$0.07]$ ). These results provide evidence of partial mediation, consistent with the hypothesis that HC use predicts worse task performance through its mediating influence on perseverance.

### 2.3.5. Additional analyses

To examine whether women in the HC group differed in their performance and persistence on the GRE and word scramble tasks based on the method of HC administration (e.g., constant dosage, skin implant, combination pill), Kruskal-Wallis tests were performed on each dependent variable. No significant differences were revealed ( $ps \geq 0.19$ ), supporting our decision to treat women taking HCs as a unitary group.

### 3. Summary of results

The results of Study 1 found that naturally-cycling women exhibited more perseverance, which lead to better performance on a simple visuospatial task when compared to women taking HCs. These results were conceptually replicated and extended in Study 2, with results revealing that naturally-cycling women spent more time, which lead to better performance on GRE quantitative problems and solvable anagrams than women taking HCs. Further, naturally-cycling women also persisted longer on unsolvable anagrams than did women taking HCs.

### 4. Discussion

Across two studies, we tested whether HC use is associated with decrements in perseverance and performance on both simple and challenging cognitive tasks. We found that women taking HCs (vs. naturally-cycling women) spent less time on both simple (Study 1) and challenging (Study 2) cognitive tasks. While women taking HCs performed worse than naturally-cycling women only on the GRE problems (Study 2), HC-associated differences in perseverance predicted performance decrements across all tasks in both studies. That is, women taking HCs performed worse than naturally-cycling women because they spent less time on the tasks. These results suggest that HC use may affect women's perseverance on simple and challenging tasks, which in turn impacts task performance.

Together, these results are consistent with recent research demonstrating that women taking HCs respond more quickly than naturally-cycling women during mental-rotation tasks, which contributed to their diminished performance on the tasks (Griksiene et al., 2018). Further, the results of the current study also support the brain imaging research suggesting that HC use is associated with structural and functional differences in brain regions that play a key role in executive function and the cognitive control of behavior (Hertel et al., 2017; Lisofsky et al., 2016; Petersen et al., 2014; Petersen et al., 2015; Pletzer et al., 2016; Rueda et al., 2004; Wagner et al., 2001). While the current studies were not designed to uncover the mechanism driving the relationship between HC use and decreased perseverance and/or performance on cognitive tasks, it is possible that decreased resting state functional connectivity in the brain's executive control network and decreased cortical thickness in the lateral orbitofrontal cortex and the posterior cingulate cortex, both of which are found in HC users, could be driving these results. Additionally, estrogen levels, which are generally lower for HC users than for women who are naturally-cycling (for most of their ovulatory cycle), are found to play a key role in hippocampal function. Spencer et al. (2008) find that estrogen influences cell morphology, synapse formation, signaling, and excitability in the hippocampus. Other researchers find that estrogen enhances synaptic plasticity and improves performance on hippocampal-dependent cognitive tasks (e.g. Brann et al., 2007; Li et al., 2004; Luine et al., 2003). While the majority of the work investigating the effects of estrogen on hippocampal function has been done in rodents, it could be that decreases in estrogen levels exhibited by women using HCs may impact the hippocampus in such a way that impairs perseverance and performance on cognitive tasks. While additional research in humans is needed to evaluate these possible mechanisms, the current results provide compelling evidence that differences in perseverance during cognitive tasks exist between women who take HCs and those that are naturally-cycling, which can lead to decrements in performance, and that these differences warrant further investigation.

The current research contributes to a growing body of work examining the implications of HC use on cognition, learning, and memory (Egan and Gleason, 2012; Griksiene et al., 2018; Griksiene and Ruksenas, 2011; Mordecai et al., 2008; Wright Jr and Badia, 1999). Our results suggest that HC use may be associated with decreases in women's ability to exercise cognitive control during problem solving. More specifically, our results find that women taking HCs exhibited less

perseverance on GRE math problems than did naturally-cycling women, and that these differences led to worse performance. Given that many women who use HCs are in their late teens and twenties (which is when most people take standardized tests such as the SAT, GRE, and LSAT), HCs could possibly make it more challenging for women to meet their higher education goals. Moreover, given that HC use is increasing among adolescents (Rashed et al., 2015), young girls taking HCs in middle school and high school may also struggle with cognitive control of learning and persisting through cognitive tasks, which could possibly impact their later career options. This interpretation is consistent with recent research implicating HC use as a predictor of academic problems in younger users (Gregory et al., 2018). Further research is needed to investigate whether taking HCs at a young age corresponds to greater morphological changes in the brain regions involved in executive function and cognitive control of learning than is seen in young adult women taking HCs. It is, however, important to note that HC use can also aid in women's educational attainment by allowing them to prevent unintended pregnancies, which can be an insurmountable barrier for those who wish to further their education. Highlighting this, women with a college degree report fewer unintended pregnancies than those without an advanced degree, and the highest rates of unintended pregnancies are found in women without a high school degree (Finer and Zolna, 2014). Further research examining the unintended consequences of HC use is vital to ensure that women are informed about the potential costs and benefits of using HCs at different points in their lives.

While the results of the current research contribute to the literature on how HCs influence women's performance on cognitive tasks, it is not without limitations. One important limitation arises from the cross-sectional nature of the current investigation. Because women were not randomly assigned to testing conditions (HC users versus natural cyclers), it is possible that the results of the current research may have emerged due to pre-existing differences between women based on their HC use. For instance, naturally-cycling women may be more conscientious than HC users, as they may feel a greater need to be careful, given their higher conception probability. Given that conscientiousness is closely related to self-control (MacCann et al., 2009; Roberts et al., 2005) and self-regulation (Ivcevic and Brackett, 2014; Sansone et al., 1999), it is possible that such pre-existing differences could account for the current results. Although recent research suggests that there are no differences in personality characteristics of users versus non-users (Beltz et al., 2019), which detracts from this alternative explanation, experimental work is needed before a conclusive cause and effect relationship between HC use and perseverance on simple and difficult cognitive tasks can be established.

Another limitation is that the current research investigated the differences between women who were naturally-cycling and women taking HCs without considering the different types of progestins in the HCs used by the women in the study. These differences may have important implications for women's cognition and behavior. For instance, first and second generation HCs are more androgenic than third generation HCs, while fourth generation HCs are anti-androgenic (Davtyan, 2012). As such, it is possible that the hormonal profiles of HCs may differentially impact the structural and functional changes observed in the brain, changing their effect on women's cognition and behavior. For instance, third generation HC users are found to spend more time on mental-rotation tasks than naturally-cycling women (Griksiene and Ruksenas, 2011), while fourth generation HC users are found to spend less time (Griksiene et al., 2018). Additionally, we did not collect information about naturally-cycling women's history of HC use beyond the last three months. History of HC use across the lifespan may be an important factor to consider in future research. Moreover, the current research did not include any measurement of sex hormones, which would have allowed us to ask more specific mechanistic questions (e.g., what is the hormonal mechanism driving the relationship between HCs and perseverance). Accordingly, future studies should explore the

possibility that the differing hormonal profiles of HCs may impact women's cognitive performance and perseverance in disparate ways. Further, it is possible that the differences reported here may have been greater between HC and naturally-cycling women in a certain phase of the cycle, but, unfortunately, this possibility could not be addressed in the current research.

A third limitation to consider is the limited number of cognitive tasks utilized in the current research. By only assessing perseverance and performance on one task in Study 1 (one spot-the-difference picture), and two tasks in Study 2 (three solvable word scrambles and eight GRE quantitative problems), we are unable to identify if specific types of tasks are more likely to elicit differences in perseverance and performance than others. Moreover, only the GRE quantitative problems task revealed a statistically significant difference in performance between naturally-cycling women and women taking HCs. This may be because a greater number of stimuli/items were used in this task than were used in the others, producing more variability. It could be that significant differences in performance on the spot-the-difference and the solvable word scramble tasks would have been revealed if a greater number of stimuli/items were included. This possibility should be considered in future research. Although there was no significant direct association between HC use and performance on the spot-the-difference task (Study 1) and the solvable word scramble task (Study 2), we found that differences in perseverance served as a mediator for the relationship between HC use and performance on all tasks. This is most likely due to the relationship between perseverance and performance on tasks (i.e., time spent on tasks predicts better performance; Galla et al., 2014). This result could further suggest that the relationship between perseverance and task performance is likely driven by a number of precipitating factors, including – but not limited to – HC use.

Additionally, the data for two of the three tasks were non-normally distributed. Again, this is likely due to the small number of stimuli/items included in the current research, and future research would benefit from utilizing additional tasks consisting of a larger number of stimuli per task. Finally, although we did not conduct a priori power analyses to determine appropriate sample size, post hoc power analyses conducted using the effect size from the perseverance dependent variable in the current research revealed that power for Study 1 was at 0.74, and power for Study 2 was at 0.87. As such, our studies were adequately powered to detect the predicted effects.

Despite these limitations, the current research poses as an important contribution to the growing body of literature examining how HC use influences women's cognitive performance. While other researchers have targeted performance on cognitive tasks as their primary outcome, the current research was designed to uncover differences in perseverance on cognitive tasks, which was found, as predicted, to lead to differences in performance. These results add to a growing body of literature demonstrating the far-reaching, and often unanticipated, effects of taking HCs (see e.g., Gregory et al., 2018; Hertel et al., 2017; Rohleder et al., 2003; Welling, 2013; Zethraeus et al., 2017). Such information is critical for women hoping to make informed decisions about HC use and for scientists seeking to better understand the psychological impact of HCs.

## 5. Conclusion

While HCs have allowed women to take control of their fertility, it is nevertheless important to consider the unintended outcomes associated with HC use. For instance, a growing body of research suggests that women who take HCs may experience important structural and functional changes in brain areas that regulate learning and task performance. Here, we demonstrate that, compared to naturally-cycling women, women taking HCs display less perseverance on both simple and cognitively taxing tasks. Given that perseverance is highly predictive of success across many areas of life, including learning, educational attainment, work performance, and career success in a variety of

fields – from medicine to military to education – further research examining the role of HC use in perseverance are crucial to understanding how HC use may impact women's education, careers, and wellbeing.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yhbeh.2019.104652>.

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