Cognitive effects of hormone-based contraception in young healthy women

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Hormonal contraception is a very popular method to avoid pregnancy, but there are little data about the effects of these medications on cognitive functions in women using it. Our study was aimed to analyse how the use of oral contraceptives might impact cognitive functioning. Women without (NC, n = 15) and on hormonal contraceptives (OC, n = 10) were tested during four phases of menstrual cycle. Simple reaction time, visual short-term memory and sustained attention were measured. Significant between-group (NC vs. OC) differences in favour of the OC group in reaction time to the onset of visual stimulus and in short-term memory task were found. These differences were most pronounced during luteal (mid and late luteal for reaction time and mid luteal for short-term memory) phases of the menstrual cycle. OC women outperformed the NC group in almost all other tasks and during other phases, although differences were less obvious and non-significant. No relationship between estradiol level and cognitive performance for nonusers, as well as no significant changes in cognition across the cycle for either group were found.

Key words: hormonal contraception, cognitive functions, menstrual cycle, reaction time, short-term memory, sustained attention

INTRODUCTION

The first hormonal contraceptive was approved for use in the United States by the Food and Drug Administration in 1960 [1]. At present, the use of oral contraceptives (OC) was confirmed as the most widely used method of contraception for reproductive age women in the European population [2] and in the United States [1]. Typically, combination pills of estrogen (ethinyl estradiol) and progestin (synthetic compound that behaves like progesterone) components are used. Oral contraceptives reduce the overall level and prevent from monthly fluctuations of gonadal steroid hormones [3, 4]. Although, correctly used, combined hormonal contraceptives are almost 100% effective and women using an OC reported a very high level (>90%) of satisfaction [2], this method of contraception affects the other body systems as well.

The importance of female sex steroid hormones, estrogen and progesterone, in cognition has been shown by examining different functions in relation to phases of the menstrual cycle and levels of circulating hormones [5–8], estrogen treatment [9, 10], menopausal symptoms and aging [11–13]. Two studies of Bixo et al. [14–15] have shown that there is a variation in women's brain concentrations of gonadal steroids depending on ovarian steroid production, indicating that the secretion pattern during the menstrual cycle is reflected in the brain.

The basal forebrain cholinergic system and the hippocampus are the two brain systems that appear to be involved in both attentional and memory effects of sex steroids [9]. It has been shown that the density of dendritic spines and excitatory synapses on the hippocampus is dependent on the level of circulating 17β-estradiol and progesterone, that these hormones influence learning in a range of rodent memory tasks, have effects on NMDAR-mediated synaptic activity and long-term potentiation, enhance production of new cells in the dentate gyrus, have neuroprotective, neurotrophic and neuroregenerative actions in the brain [10, 12, 16–22].

Activity of numerous brain neurotransmitters, including serotonin, dopamine, glutamate, GABA and

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acetylcholine as well as various peptides modulating cognitive functions, mood, and certain aspects of locomotor behavior, is modulated by estrogens [23].

Although the general effect of hormonal contraception on women has been investigated rather extensively, just a few reports have examined the effects of this method on the cognitive functions in young healthy females. Hormonal contraception has been shown to have a moderating role in verbal memory [7], simple response times and speed of arithmetic calculations [24], creativity [25], cognitive emotional processes typically associated with stress [3], psychological stress [26], neuroticism [27], implicit motives [8].

The purpose of our study was to compare cognitive parameters such as reaction time, short-term memory and sustained attention in hormonal contraception users and nonusers. Experimental sessions in two groups of young healthy women – naturally cycling women and hormonal contraception users – were performed during different phases of menstrual cycle (follicular, ovulatory, mid luteal and late luteal).

MATERIALS AND METHODS

Subjects

Participants of experiments were Vilnius University female students without (NC, n = 15, age 20.5 years ± 1.0 (S. D.), body mass index (BMI) 21.2 ± 2.5) or on hormonal contraceptives (OC, n = 10, age 21.7 ± 1.8 years, BMI 22.1 ± 3.8). Women were excluded from the study if they suffered from psychological, endocrine disorders, cardiovascular diseases, other severe medical illnesses or signs of viral / bacterial infections. During a structured interview, women gave information concerning characteristics of their menstrual cycles, the use of hormonal contraception and current state of health. Only nonsmoking women with a regular ovarian cycle, 24 (minimum) to 34 (maximum) days in length (natural cycling group) or users of combined hormonal contraception (estrogen–progestin) continuously using it for at least three months were included.

Subjects from both groups were investigated four times. Naturally cycling women were investigated in four phases of menstrual cycle: the follicular phase (between days 2 and 5 after onset of menstrual bleeding, day 1 was not used to avoid possible confounding effects of physical discomfort on the first day of bleeding), ovulatory phase was determined by ovulation test based on visual detection of urinary luteinizing hormone (LH) (SureScreen Diagnostics Ltd, UK), the luteal phases were determined individually on the basis of the subjects' previous three months' cycle history and ovulation time detected by the LH test. The mid luteal phase was about 6 days after ovulation and the late luteal phase 2–5 days prior to the expected menstrual

onset. The actual onset of the next bleeding was confirmed by a telephone call, and only women tested between 2 and 5 days prior to menses were included in the further analysis. Hormonal contraception users were investigated four times during a 28-day cycle, at days corresponding to the phases of naturally cycling women. Phases of OC women are not real menstrual cycle phases and might be named as pseudo-phases (pseudo-follicular, pseudo-ovulatory, etc.), but for the sake of simplicity we decided to use the same names of phases in both NC and OC groups. The follicular phase in OC group occurred 2–4 days ovulatory – on day 14, mid luteal – on days 19–21, late luteal on days 26–28 after the onset of menstrual bleeding. Phases of naturally cycling women were controlled by measuring the level of 17β-estradiol in saliva. The 17β-estradiol level was not measured in OC users because it is known from the literature that concentration of this hormone is relatively stable and significantly lower in women on oral contraceptives as compared to non-users [4, 7, 8, 25, 26]. All four test sessions extended across one or two menstrual cycles, depending on at which menstrual cycle phase experiments were started. The phase of the menstrual cycle when experiments were started was taken depending on the time more suitable for participants (7 women started at the follicular phase, 13 at ovulatory, 2 at mid luteal and 3 at the late luteal phase).

Twenty-nine women started the experiments; three women from the NC group were discarded because of cycle irregularity and one because the LH test did not show the LH peak.

The design of the study was approved by the Lithuanian Bioethics Committee. All women gave their written informed consent to participate in the study.

Cognitive tests

Reaction time task. Simple reaction time procedures with a single stimulus and single response were performed using modified the Donders [28] reaction time test. Subjects had to react to the onset of a visual or auditory stimulus and the offset of a visual stimulus by pressing a space button on computer keyboard with one finger of the dominant hand. The visual stimulus was a yellow square on a black background, presented at the center of the monitor; the auditory stimulus was a pure tone presented via stereophonic headphones. Intertrial intervals (the time when subjects were waiting for a stimulus) varied from 1.0 to 7.5 s. Each visual and auditory stimulus was presented 12 times. Reaction time was measured from the onset of a test stimulus until response. Ten best responses out of twelve were used for analysis.

Attention task. The Anfimov table [29] was used to evaluate the parameters of sustained attention. This paper-and-pencil test is a modified version of the previously de-

scribed letter cancellation test [30], providing numerically comparable data characterizing the quality and quantity of work performed. Subjects were asked to cross one of four letters – A, X, K or H – in an A4 format page filled with eight different letters (A, B, C, E, H, K, N, X) in random order; 1020 characters were on one page. The test had to be done within a fixed time of 1 min. Characters correctly crossed were calculated, and one parameter – precision of performance – was taken for analysis. Precision of performance was calculated by a simple formula: A (precision of performance) = M (number of characters correctly crossed) / N (number of characters had to be crossed).

Short-term memory task. Short-term memory was evaluated using the computerized visual digit span test based on the concepts described in an early work of J. Jacobs [31]. Sets of digits (seven, eight and nine) were used. Thirty sets were presented during one experiment: ten sets of seven, ten of eight and ten of nine digits. Each set was presented for 1000 ms. Time for response was unlimited. A next set was presented when the answer to the previous task had been readly finished. The task was to remember and immediately type on the computer keyboard digits in correct order. Digits had to be typed forward. The number of correct answers (percentage of correct digits in correct places) was used as a measure of performance.

Saliva sampling and biochemical analysis

Salivary sampling is a non-invasive, simple, stress-free procedure. The salivary level of 17β-estradiol follows a similar pattern to that in the serum; a significant correlation was shown between the salivary and serum levels of 17β-estradiol [32]. Therefore, analysis of salivary 17β-estradiol was established as a feasible method for determining menstrual cycle profiles [33, 34].

Samples of saliva for determination of 17β-estradiol were collected in naturally cycling women at the beginning of each experiment. Participants were asked not to eat, drink, chew gums or brush teeth for 30 min before sampling, but to rinse the mouth with cold water 5 min prior to sample collection. To avoid blood contamination, samples were not collected in cases of oral diseases, inflammation or lesions. Minimum 1 ml of saliva was collected into special tubes (IBL SaliCap). The tubes were stored at −20 °C until assayed. The concentration of 17β-estradiol in saliva was determined by luminescence immunoassay for the *in-vitro* diagnostic quantitative determination of 17β-estradiol in human saliva (IBL-Hamburg, Germany). The analytical sensitivity of the assay was 0.30 pg/ml, the functional sensitivity, being 0.78 pg/ml, precision intraassay 7.0–7.9% and interassay 5.9–13.9%. All samples from the same woman were duplicated in the same assay. Fluoroskan Ascent FL from ThermoLabsystems (Finland) was used for luminescence measurement.

Design and procedure

To minimize the effects of diurnal variations on hormone levels, all neuropsychological sessions were performed in the afternoon from 2 pm to 7 pm. One test session lasted about 30 min, including the preparation and adaptation period. Experiments started with a rest period of 15 min during which saliva samples were taken and participants were instructed about experimental procedures. Participants were seated in armchairs in a soundproof, light-isolated chamber at a constant temperature (20–22 °C). The order of procedures was the same in all sessions: adaptation, saliva sampling, attention task, short-term memory task, reaction time measurement.

Statistical analysis

Statistical evaluation was based on factorial ANOVA, including the factors of Group (naturally cycling women and oral contraceptive users), Phase (follicular, ovulatory, mid-luteal and late luteal), Experimental session (from the first to the fourth session). Multiple comparisons of means were made by two-tailed Student's t test for paired and unpaired data. Pearson's correlation analysis was used to calculate relationships between different factors. A probability value of less than 0.05 was taken as statistically significant. Statistical analyses were performed with the STATISTICA 7.1 software. Data are presented as the mean ± standard deviation (S. D.).

RESULTS

We examined 15 females without hormonal contraceptives and 10 users of oral contraceptives during the follicular, ovulatory, mid-luteal and late luteal phases of the ovarian cycle. The length of the menstrual cycle of women from the naturally cycling group was 28.1 ± 2.9 days. OC users used seven different kinds of combined hormonal contraceptives: Diane 35 (35 μg etinylestradiol, 2 mg cyproteron) – 2 women, Logest (20 μg etinylestradiol, 75 μg gestoden) – 2, Harmonet (20 μg etinylestradiol, 75 μg gestoden) – 2, Jeanine (30 μg etinylestradiol, 2 mg dienogest) – 1, Yarina (30 μg etinylestradiol, 3 mg drospirenon) – 1, Novynette (20 μg etinylestradiol, 150 μg desogestrel) – 1, Regulon (30 μg etinylestradiol, 150 μg desogestrel) – 1.

Comparison of cognitive functions between NC and OC groups

A factorial ANOVA (group: NC and OC; phase: follicular, ovulatory, mid-luteal and late luteal; experimental session: first to fourth) on the measured parameters revealed a significant effect of the group, but no effects of menstrual cycle phase or the number of experimental session.

Short-term memory. The results of the short-term memory test were statistically significantly better in the
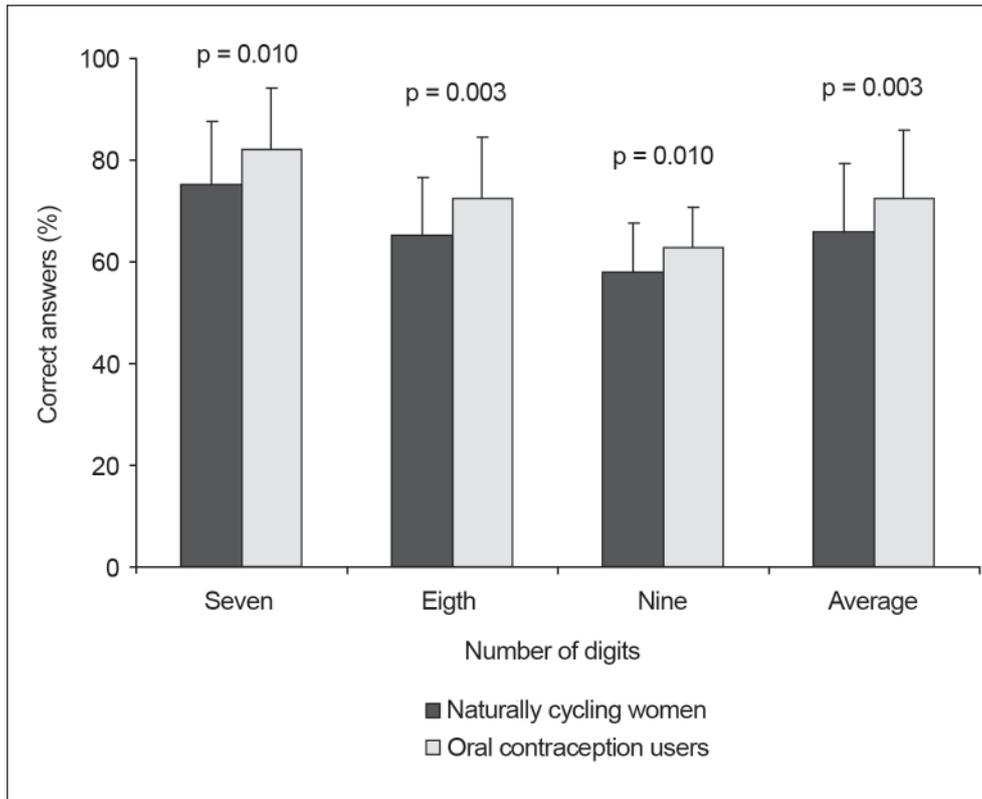
Fig. 1. Visual short-term memory. p-Values above the bars illustrate differences between OC and NC groups, calculated using Student's t test for unpaired data
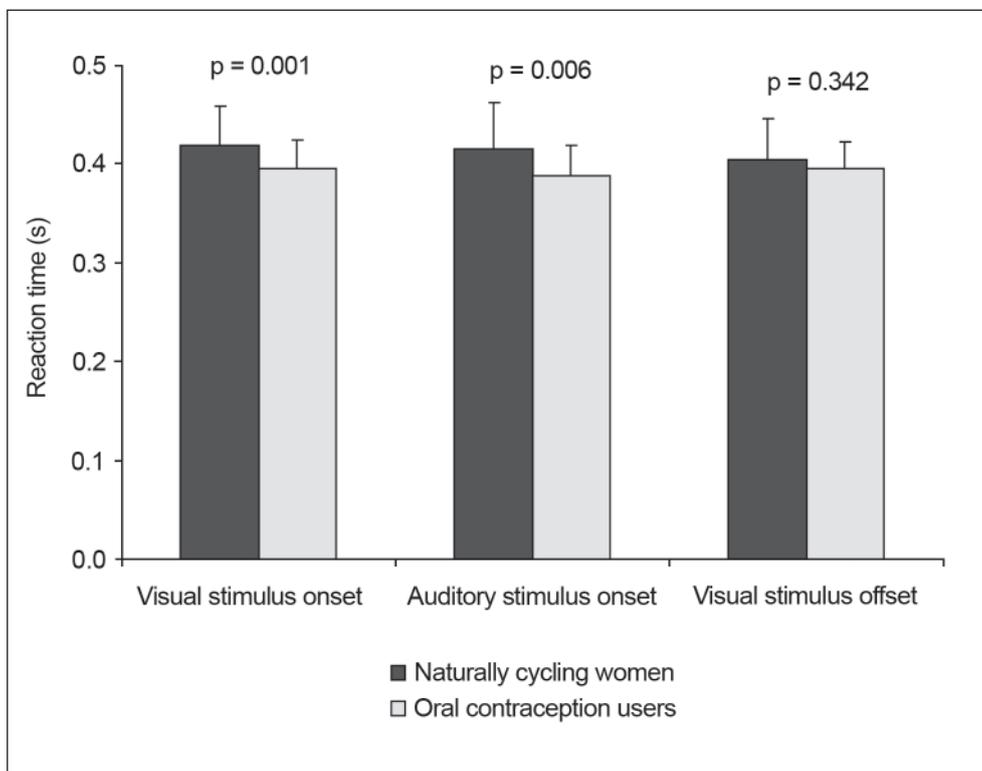

Fig. 2. Reaction time to onset of visual and auditory stimuli and visual stimulus offset. p-Values above the bars illustrate differences between OC and NC groups, calculated using Student's t test for unpaired data

Table. Salivary level of 17β-estradiol (mean ± SD) and cognitive test scores (mean ± SD) across the menstrual cycle of naturally cycling women

Group, phase		Reaction time (s)			Short-term memory (% of correct responses)[a]	Attention (precision of performance)	17β-estradiol in saliva (pg/ml)
		to visual stimulus		to auditory stimulus onset			
		onset	offset				
Naturally cycling		0.42 ± 0.04	0.40 ± 0.04	0.42 ± 0.05	66.0 ± 13.3	0.94 ± 0.06	
OC users		0.39 ± 0.03**	0.40 ± 0.03	0.39 ± 0.03**	72.4 ± 13.4**	0.96 ± 0.04	
Follicular ph.	NC	0.42 ± 0.05	0.40 ± 0.04	0.42 ± 0.04	64.4 ± 7.5	0.95 ± 0.04	3.8 ± 1.8
	OC	0.41 ± 0.04	0.40 ± 0.03	0.38 ± 0.04	73.6 ± 11.3	0.97 ± 0.03	–
Ovulatory ph.	NC	0.42 ± 0.04	0.41 ± 0.04	0.42 ± 0.05	65.3 ± 9.4	0.92 ± 0.09	8.1 ± 4.3
	OC	0.40 ± 0.03	0.41 ± 0.03	0.39 ± 0.03	70.8 ± 7.9	0.97 ± 0.03	–
Mid-luteal ph.	NC	0.42 ± 0.04	0.41 ± 0.05	0.42 ± 0.04	64.8 ± 9.7	0.96 ± 0.05	7.4 ± 3.7
	OC	0.38 ± 0.03*	0.39 ± 0.02	0.40 ± 0.03	74.7 ± 7.4**	0.94 ± 0.06	–
Late luteal ph.	NC	0.42 ± 0.04	0.41 ± 0.05	0.42 ± 0.06	67.6 ± 12.9	0.94 ± 0.05	5.3 ± 2.3
	OC	0.39 ± 0.02*	0.39 ± 0.02	0.38 ± 0.03	70.0 ± 10.0	0.96 ± 0.03	–

Note. * $p < 0.05$, ** $p \leq 0.01$ for differences between OC and NC groups, [a] averaged from sets of 7, 8 and 9 digits.

OC group as compared to the NC group ($F_{(1.88)} = 9.39$; $p = 0.003$), but no effect of menstrual cycle phases or experimental session was found. On average (across all cycle phases), OC users were about 8.8% better in remembering seven-, eight- and nine-digit numbers (see Table and Fig. 1).

Reaction time to the onset of visual and auditory stimuli and offset of visual stimuli. Analysis of reaction time (RT) showed the group to be a significant factor to affect the time of stimulus onset (visual stimulus onset ($F_{(1.89)} = 10.16$, $p = 0.002$), auditory stimulus onset ($F_{(1.91)} = 9.78$, $p = 0.002$), but not visual stimulus offset ($F_{(1.9)} = 1.17$, $p = 0.28$). Reaction to the onset of visual and auditory stimuli was about 7.1% better (reaction time on average shorter by 30 ms) in the group of OC users (see Table and Fig. 2).

Student's t test for dependent samples was used to compare three types of reaction time. Reaction time to the offset of a visual stimulus (0.40 s ± 0.04) was significantly shorter as compared to the reaction time to the onset of a visual stimulus (0.42 s ± 0.04, $p < 0.001$) and the onset of an auditory stimulus (0.42 s ± 0.05, $p = 0.02$) in naturally cycling women, whereas there were no differences in the OC group (see Table).

Sustained attention. Sustained attention was evaluated as performance precision in the test with the Anfimov table. Although, due to technical failures, attention data of 19 experiments (out of 60) from the NC group were lost and we did not get significant differences between the groups (see Table), OC users were by 2.1% better in this task also ($F_{(1.75)} = 3.16$; $p < 0.08$).

Comparison of cognitive functions in different menstrual cycle phases

The concentration of 17β-estradiol in saliva was compared in different phases (follicular vs. ovulatory, follicular vs. mid luteal, etc.), and a correlation between the level of 17β-estradiol and the parameters of cognitive functions of naturally cycling women was calculated. Performance of cognitive functions was compared in different menstrual cycle phases within each group and between NC and OC groups in analogous phases (follicular in NC vs. follicular in OC, ovulatory in NC vs. ovulatory in OC, etc.).

17β-estradiol concentration in saliva. The mean saliva concentration of 17β-estradiol for all NC subjects (through all phases) was 6.3 ± 3.6 pg/ml. This value is in a good agreement with data presented by other authors [8, 33–35]. The concentration of 17β-estradiol in saliva was compared using Student's t test for dependent samples (see Fig. 3 and Table). The saliva 17β-estradiol level was significantly lower in the follicular phase (3.8 ± 1.8 pg/ml) as compared to ovulatory (8.1 ± 4.3 pg/ml, $p = 0.02$), mid-luteal (7.4 ± 3.7 pg/ml, $p = 0.01$) and late luteal
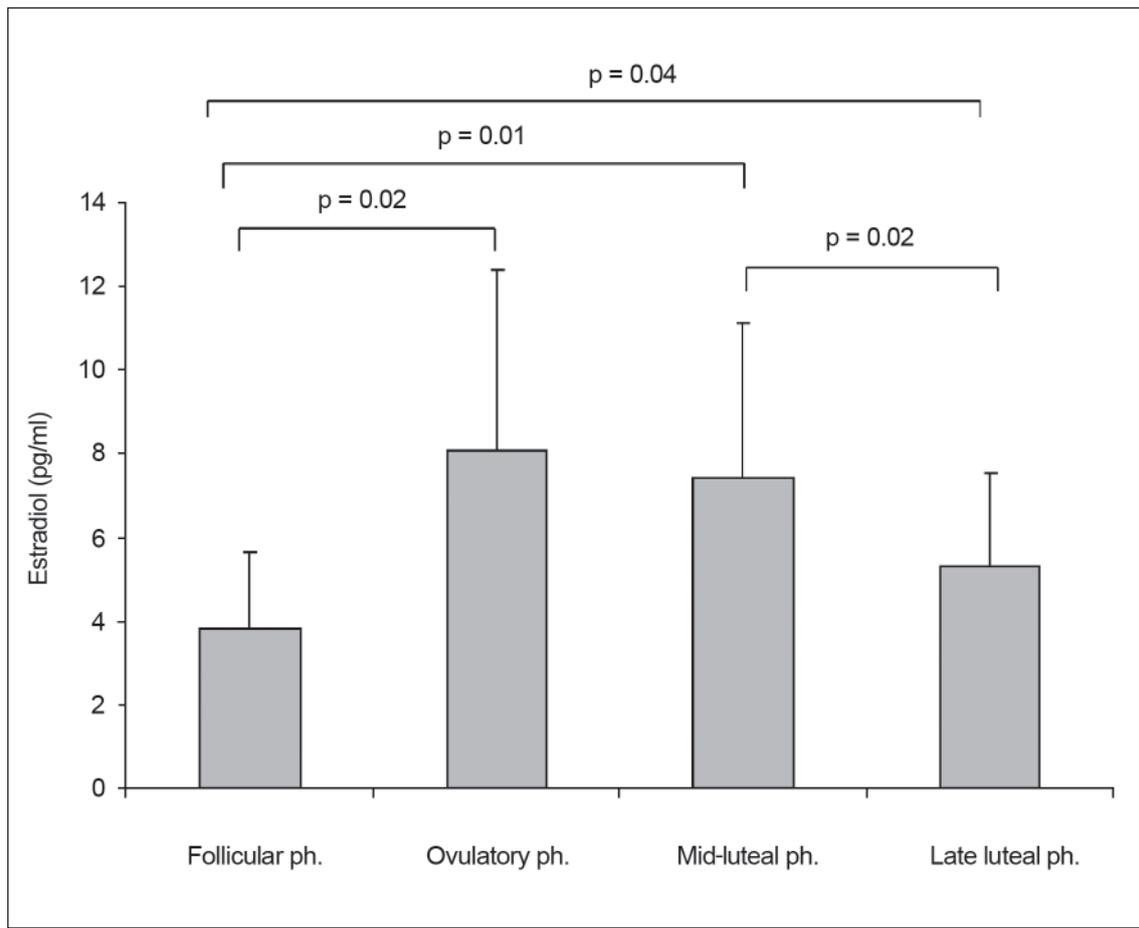
Fig. 3. 17β-estradiol levels (pg/ml) in saliva of naturally cycling women (n = 15) during four phases
of menstrual cycle. p-Values above the bars illustrate differences among phases, calculated using
Student's t test for paired data

(5.3 ± 2.3 pg/ml, p = 0.04) phases. The level of 17β-estradiol in the late luteal phase was significantly lower (p = 0.02) than in the mid-luteal phase.

The highest variability of 17β-estradiol concentration was found in the ovulatory phase. In some subjects, 17β-estradiol concentration in the ovulatory phase was lower as compared to the mid-luteal phase. The reason for this discrepancy could be methodological: we took the LH peak day as a "marker" of ovulation and expected a high 17β-estradiol concentration on the next day, but the peak of 17β-estradiol may have already had occurred on the preceding day.

Pearson's correlation analysis demonstrated that there were no significant correlations (equal to or below 0.1 and p > 0.5) between the level of 17β-estradiol and any of cognitive measures.

Performance of cognitive tests during different phases of menstrual cycle. The parameters of cognitive functions were compared in different phases in naturally cycling women and in hormonal contraception users by Student's t test for dependent samples. The values of all parameters

changed very little across the cycle phases (see Table). There were no statistically significant differences among the phases in NC or OC groups.

Comparison of performance of cognitive tests (Student's t test for independent samples was used) between the NC and OC groups in analogous phases (follicular vs. follicular, ovulatory vs. ovulatory, etc.) showed the mid-luteal and late luteal phases to be most different from the other phases with respect to differences between OC and NC. In the mid-luteal phase, reaction time to visual stimulus onset and short-term memory were statistically significantly better for oral contraception users as compared to naturally cycling women in the same phase (reaction time to visual stimulus onset 0.38 ± 0.03 s vs. 0.42 ± 0.04 s, p = 0.01; short-term memory (presented as a number of correct answers in %, averaged from sets of 7, 8 and 9 digits) 74.7 ± 7.4% vs. 64.8 ± 9.7%, p = 0.04). During the late luteal phase, only reaction to visual stimulus onset was significantly faster in the OC group as compared to the NC group (0.39 ± 0.02 s vs. 0.42 ± 0.04 s, p = 0.04). The other parameters, except performance precision, were also worse for the NC group

in the mid-luteal and late luteal phases, although the differences were less pronounced and non-significant. Reaction time to visual and auditory stimulus onset and short-term memory were also better in OC users (although differences were not statistically significant) in follicular and ovulatory phases, but the reaction to visual stimuli offset did not differ between the groups (see Table) in these phases. Precision of performance in the attention task showed no significant difference (all p > 0.05) between the OC and NC groups in different phases, and the tendency was different from the other parameters: OC users performed on average by 3.2% better during follicular, ovulatory and late luteal phases, but in the mid-luteal phase the NC group was somewhat more (by 2.1%) precise.

DISCUSSION

The present study was designed to compare the basic cognitive functions – simple reaction time, sustained attention and visual short-term memory in naturally cycling women and in hormonal contraception users during four phases of menstrual cycle. Twenty five women (15 naturally cycling and 10 hormonal contraception users) similar in age, education level and other sociodemographic parameters (students, similar BMI, no smoking) were tested during four menstrual cycle phases. The results of this study show that oral contraceptive users statistically significantly better perform on reaction time (to the onset of visual and auditory stimuli) and short-term memory tests when groups are compared without respect to menstrual cycle phases. Comparison of these parameters among analogous phases of NC and OC have revealed that statistically significant differences mainly are determined by luteal phases (mid-luteal for short-term memory; mid- and late luteal for reaction time). The parameters of attention were better in the OC group, although the difference was not statistically significant. Reaction time to the offset of visual stimulus did not differ between the groups. Both naturally cycling women and hormonal contraception users did not display any significant variations in cognitive functions across the menstrual cycle. No relationship was found between the level of 17β-estradiol and cognitive performance in the NC group.

The results of our study partially support and supplement data on the effect of hormonal contraception recently demonstrated by Rosen and Lopez [35]. These authors found that contraceptive users made fewer errors in the attention task than naturally cycling women. Gordon and Lee [4] did not find statistically significant differences in verbosequential or visuospatial neuropsychological tests among naturally cycling women and hormonal contraception users, but the results presented in the paper showed a nice tendency – all parameters of the OC group were bet-

ter as compared to NC, and this tendency is consistent with our findings. Mordecai et al. [7] presented results showing that OC users better performed in verbal memory tests in active pill versus inactive pill phases, which correspond to our mid-luteal and follicular phases, respectively. In our study, results of the OC group on visual short-term memory and reaction time to visual stimulus onset and offset in the mid-luteal phase are also better as compared to other three phases, although the difference is not statistically significant. There are no differences between performance in different phases in the NC group neither in Mordecai et al. [7] nor in our study. In contrast to our study, Becker et al. [36] found a significant effect of cycle phases on some cognitive parameters (including short-term memory) in the NC group, no cycle effect in the OC group and almost no differences between NC and OC. Silber et al. [37] did not find significant differences in performance in the psychometric tests (including simple reaction time to visual stimulus and visual memory) in women tested in their luteal phase before and after four weeks of OC treatment. Grinspoon et al. [38] did not find significant differences in cognitive tests (including Wechsler Memory Scale-Revised and Digit Cancellation test) performance between OC or placebo users for three consecutive 28-d cycles. OC users in these studies were treated with oral contraceptive preparations for a short period (one month in the first two studies and three months in the third) which could be too short to cause a measurable effect. Unfortunately, we did not ask our subjects how long they had been using hormonal contraception; only know that this period was not shorter and in most cases could be longer than three months. Subjects in the Garret and Elder [39] study were similar to ours, but simple reaction time results are opposite: they found that the OC group was much slower than NC throughout all menstrual phases. A few possible reasons for so diverse results could be proposed: different cognitive functions evaluated by tests differing in sensitivity, different amount of ethinyl estradiol and various progestins composing oral contraceptives as well as varying periods of their use.

The psychophysiological mechanisms responsible for the different performance of cognitive tests in NC and OC groups are not clear. We might speculate that hormonal contraception users could perform better because they are less stressed and feel more comfortable due to reduced premenstrual and menstruation-associated symptoms as compared to naturally cycling women [40, 41]. Also, OC women are secured from the fear to become pregnant, because combined hormonal contraception is a highly effective method to prevent pregnancy in almost 100%. Based on the above facts and on the results of studies demonstrating that combined hormonal contraception has a beneficial effect on the general psychological well-being

[42, 43] and on a higher level of a positive effect during the cycle [44], it could be suggested that a combination of a higher physical and psychological comfort in OC users contributes to the better values of the cognitive parameters. However, this assumption contradicts the results presented by Brown et al. [45] who found that women using hormonal contraception reported more negative well-being than women with a natural profile. However, the cause of negative well-being in OC users is not clear, either. Segebladh et al. [46] have shown that psychiatric disorders such as depression and anxiety are common in women who report adverse mood effects from the current or previous use of combined hormonal contraception. No information about current or previous psychiatric health was presented by Brown et al. [45].

Our finding that there are no cycle-dependent differences in reaction time, short-term memory and precision of performance in naturally cycling women corresponds to the report of Phillips and Sherwin [47] in which most of the analyzed parameters of memory, learning and attention did not differ among the phases. But our data do not support results of Hampson and Kimura [48] and Heister et al. [49] that in the middle of the natural cycle reactions were faster and fewer errors were made. The reason could be the difference in cognitive tasks, which in our study were no gender-specific and possibly less sensitive to short-term hormonal fluctuations.

The fact that there is no relationship between the concentration of 17β-estradiol and the performance of cognitive tests supports results presented in literature [4, 50, 51] and urges a search for the other factors influencing cognitive functions. The estradiol / progesterone ratio may be of interest when measuring cognitive performance. The non-reproductive functions of progesterone have been shown in the central nervous system (for review, see [52]). Another interesting factor could be the male steroid hormone testosterone; according to the literature [7, 8, 35, 53], its concentration is lower in hormonal contraception users. A lot of studies could be found about the effect of testosterone on the cognition of young and elderly men, but there are very few studies of testosterone effect on the brain and cognition in women. The effect of this hormone was demonstrated on women's spatial abilities [54] and delayed verbal memory [7, 47].

Methods used in our study could influence the obtained results as well. We see an advantage in taking four phases of menstrual cycle instead of two or three used in most studies. The ovulation phase is desirable to investigate because the level of 17β-estradiol in this phase is most elevated; moreover, the level of progesterone is still low, therefore we can search for the effect of 17β-estradiol without any influence of progesterone. A weak point here is determination of the phase with the highest level of 17β-estradiol. In our experi-ments, ovulation was determined using the urinal LH test. According to the test instructions, ovulation should happen 24–48 hours after a positive LH test. Exactly this period was taken for measurements, expecting to get the highest level of 17β-estradiol. However, the results have shown that this period is too long if the aim is to find a high concentration of 17β-estradiol.

The cognitive tests we used could also be evaluated differently. The aim was to measure the simple and basic functions representing different levels of cognition at the same time: the fastest level – reaction time, medium – attention, and the slowest one – short-term memory. Hormonal contraception users performed better at all three levels, and this fact allows us to suppose that the effect of hormonal contraception involves different levels of information processing – from the shortest (a simple reaction) to more complex such as precision of performance in the attention test and information storage in the short-term memory. However, it is possible that using more specific and sensitive tests we could get more pronounced differences.

To summarize, hormonal contraception, so broadly used by women in reproductive age, plays not only its direct role, i. e. prevents pregnancy and helps to avoid discomfort associated with menstruations. Although our results should be considered as preliminary since the sample size (especially in the OC group) was small, we found clear tendencies in OC users outperforming NC, with statistically significant differences in some tasks. That is why we suppose that the basic cognitive functions (reaction time, visual short-term memory and sustained attention) are affected by these medications. Therefore, attention should be paid to the usage of hormonal contraception by women taking part in psychophysical experiments because this could be an important factor influencing the results.

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HORMONINĖS KONTRACEPCIJOS POVEIKIS JAUNŲ SVEIKŲ MOTERŲ KOGNITYVINĖMS FUNKCIJOMS

Santrauka

Hormoninė kontracepcija šiuo metu labai populiari apsaugos nuo nėštumo priemonė, tačiau jos poveikis moterų kognityvinėms funkcijoms dar mažai ištirtas. Tyrimo tikslas – ištirti hormoninės kontracepcijos vartojimo poveikį jaunų sveikų moterų kognityvinėms funkcijoms. Natūralų ciklą turinčios (NC, n = 15) ir hormoninę kontracepciją vartojančios (OC, n = 10) moterys buvo tirtos keturių menstruacijų ciklo fazių metu. Matuotas paprastos reakcijos laikas, trumpalaikė regimoji atmintis ir ilgalaikis dėmesys. Nustatyta, kad tiriamųjų grupė (OC ir NC) yra statistiškai patiki-mai reikšmingas veiksnys nustatant reakcijos laiką ir trumpalaikę atmintį. Hormoninę kontracepciją vartojančios moterys statistiškai reikšmingai greičiau reagavo į regimąjį bei girdimąjį stimulą ir geriau atliko trumpalaikės regimosios atminties testus. Šiuos skirtumus geriausiai išreiškia geltonkūnio (reakcijos laikas ir trumpalaikė atmintis) ir vėlyvojo geltonkūnio (reakcijos laikas) fazės. Nors daugumą kitų tirtų užduočių OC grupės tiriamosios taip pat atliko geriau nei NC, gauti skirtumai yra silpniau išreikšti ir statistiškai nereikšmingi. Nenustatyta priklausomybė tarp 17β-estradiolio lygio ir tirtų kognityvinių funkcijų rezultatų NC grupėje, taip pat kognityvinių funkcijų priklausomybė nuo menstruacijų ciklo fazių abiejose grupėse.

Raktažodžiai: hormoninė kontracepcija, kognityvinės funkcijos, menstruacijų ciklas, reakcijos laikas, trumpalaikė atmintis