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Verbal and spatial functions across the menstrual cycle in healthy young women

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Abstract

The effects of the menstrual cycle on cognitive functions were investigated using simple verbal and spatial tasks. Eight healthy young women with a regular, established 28-day menstrual cycle and the occurrence of ovulation on day 14 were tested four times during one cycle. Ten women on non-tricyclic birth control pills were also tested weekly during one cycle. Both groups were matched in age, handedness and education. No significant difference in spatial ability was found but improved verbal working memory, as measured by the verbal span score, was associated with periods of high estrogen levels. © 2001 Published © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

With the growing use of Estrogen Replacement Therapy, there has been an increased focus on the effects of estrogen on cognitive functions. During a menstrual cycle, there is natural variation of levels of LH, FSH, estrogen and progesterone.

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During menstruation, estrogen and progesterone are at their lowest levels. Then in the next 2–3 weeks (preovulatory phase), estrogen levels increase steadily and reach a peak. After ovulation, estrogen levels are reduced but progesterone levels increase 10–100 fold (luteal phase). By carefully monitoring the menstrual cycle, it is possible to study cognitive functions in relation to estrogen levels in healthy women.

Estrogen has been linked to improved memory (e.g., Phillips and Sherwin, 1992; Drake et al., 2000), working memory (Shaywitz et al., 1999), articulation (Hampson, 1990), increased verbal fluency (Wolf et al., 1999). In contrast, low estrogen has been associated with better visuospatial abilities (Hampson, 1990). However, conflicting results have also been reported (e.g., Barrett-Conner and Kritz-Silverstein, 1993). For example, Gordon and Lee (1993) found no correlation between hormone levels and visuospatial or verbal abilities and Janowski et al. (2000) reported that estrogen did not improve working memory in women. Overall, effects of estrogen on verbal and spatial functions are not clearly understood. One reason for conflicting results may stem from the fact that much of the past research has focused on post-menopausal women. But when investigating memory performance in the elderly, the aging process must be taken into account in addition to hormonal effects (Sherwin, 1997). These inconsistencies may also be due to the different ways in which estrogen was measured as well as the particular cognitive processes being assessed.

By studying fluctuations in hormones in regularly menstruating healthy women, it may be possible to capture the natural variation in cognitive functions. Since only about 60% of women age 20–24 ovulate each cycle, ovulation must be verified (Metcalf and MacKenzie, 1980). Previous studies have used a wide array of techniques to evaluate the menstrual cycle, ranging from basic methods such as counting forward or backward from the day of menstrual onset, to advanced biochemical methods using radioimmunoassay (e.g., Pierson and Lockhart, 1963; Hampson and Kimura, 1988; Drake et al., 2000; Wolf et al., 1999). Confirmation of ovulation can be demonstrated using basal body temperature (BBT) with the production of a biphasic chart. Following the establishment of ovulation, normal cyclic hormonal levels can be inferred (Kistner, 1979; Sheroff et al., 1994).

Evaluating healthy young women with regular menstrual cycles removes the age confound and therefore, the effects of ovulation and fluctuating hormone levels on cognitive functions can be examined. In this study we assessed the effects of menstrual cycle on verbal and spatial functions in young, healthy women with established regular menstrual cycles.

2. Methods

2.1. Participants

Potential subjects were recruited from a private university by placing advertisements in dormitories and were screened for regular menstrual cycles of approximately 28 days. Informed consent was obtained from all after explaining the protocol. Exclusion criteria were history of any head injury, substance use and DSM-IV Axis 1 disorder. Once they met these criteria, they were asked to monitor the BBT for one cycle. Then only those who had a 28 day cycle with the postovulatory rise in BBT on day 13 or 14 were selected for the "natural" cycle group. The natural cycle group consisted of eight healthy women (mean age=19.4±0.17) who had a consistent and regular menstrual cycle (mean=28.7±0.23 days) with the postovulatory rise in BBT in mid-cycle (mean=13.9±0.03). The subjects in the natural cycle group were not taking any medications. For the "control group", ten women (mean age=19.4±0.17) who had been taking non-tricyclic birth control pills for at least 3 months were recruited. They met the same exclusion criteria outlined above. All subjects were right handed according to the Edinburgh handedness scale, except for two left-handers, one per group. All subjects were paid for their participation.

2.2. Procedure

After having established a 28-day cycle with a postovulatory BBT rise on day 14, participants were then tested four times during their *next* menstrual cycle, on days 0, 7, 14, and 21. Day 0 was defined as the first day of the period. BBT was monitored on the test cycle as well. All natural cycle subjects showed the postovulatory rise in BBT (mean 13.9±0.03 days). Subjects were tested individually in a quiet room. There were two tasks.

2.3. Spatial task

Each trial consisted of a target and 4 test figures adjacent to the target. Subjects were asked to select the test figure that was *not* a rotation of the target. There were 8 trials per day. Subjects were required to complete the task in 45 seconds. There were two versions of the task, equal in difficulty. One was given on days 0 and 14, and the other one on days 7 and 21.

2.4. Verbal task

A verbal working memory task was administered (Gold et al., 1997). Subjects heard a list of letters and numbers. They were then required to recall them stating the numbers first, from the smallest to the largest and then the letters in alphabetical order. The number of items ranged from 2 to 7. There were 24 trials per day.

Table 1
Mean accuracy (S.E.) of verbal working memory and spatial rotation tasks during one menstrual cycle

% correct	Day 0	Day 7	Day 14	Day 21
Natural verbal	72.9 (0.039)	77.6 (0.039)	77.6 (0.049)	77.1 (0.046)
Natural spatial	76.2 (0.105)	76.3 (0.093)	78.1 (0.118)	79.1 (0.089)
Pill verbal	77.9 (0.022)	81.2 (0.036)	82.9 (0.027)	82.9 (0.026)
Pill spatial	68.8 (0.062)	81.2 (0.080)	82.5 (0.065)	78.8 (0.053)

3. Results

3.1. scoring

For the spatial task, % correct (out of 8) was calculated. For the verbal task there were two measures: % correct (out of 24), as well as verbal span were calculated. Verbal span was defined as the longest sequence that the subject could recall in the correct order (maximum=7).

3.2. % correct score

A repeated measures group-by-task ANOVA was conducted for the % correct scores. There was no main effect of the group ($F(1,16)=0.237$, $p>0.63$). There was

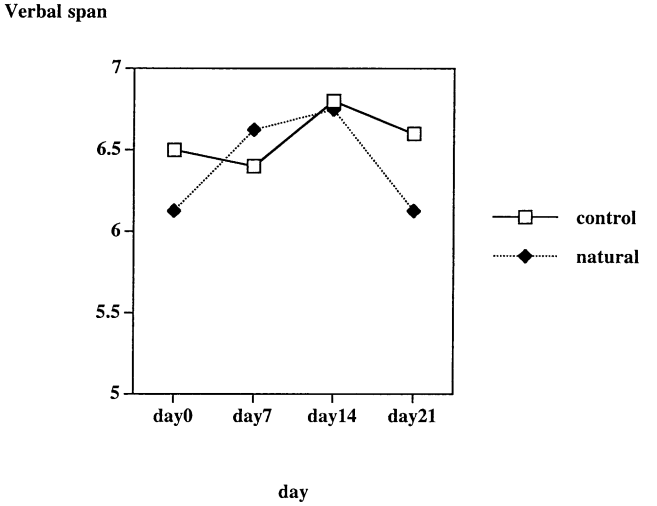

Fig. 1. Verbal working memory span across one menstrual cycle.

no main effect of the task ($F(1,16)=0.039$, $p>0.84$) but there was a main effect of the cycle ($F(3,48)=3.463$, $p<0.024$). The mean scores are presented in Table 1.

3.3. Verbal span score

There was no main effect of the group on the verbal span ($F(1,16)=0.300$, $p>0.59$) but there was a main effect of the cycle ($F(3,48)=4.155$, $p<0.011$) and a trend towards a group-by-cycle interaction ($F(3,48)=2.145$, $p<0.054$, 1-tailed). Figure 1 illustrates the interaction.

In order to examine the cycle effect on the verbal span more closely, contrast analyses (see Rosenthal and Rosnow, 1985) were performed for each group. For the birth control pill group, there was no significant effect of the cycle, as evaluated by a linear ($F=1.038$, $p>0.31$), quadratic ($F=0.106$, $p>0.74$) and cubic ($F=2.562$, $p>0.12$) contrast analyses. For the natural cycle group, there was a significant effect for the quadratic contrast ($F=12.805$, $p=0.0018$) but not for the linear ($F=0.102$, $p>0.75$) or for the cubic contrasts ($F=0.922$, $p>0.34$). These patterns suggest that for the natural cycle group, their verbal span is increased in the middle of the cycle compared with the beginning and the end of the cycle as can be seen in Fig. 1.

4. Discussion

These results suggest that menstrual cycle influences verbal working memory, as indicated by the verbal span score. Unlike the birth control group, who maintain steady estrogen and progesterone levels, the verbal span scores of those undergoing a natural menstrual cycle approximates a bell shape: first improving than decreasing. This pattern, supported by contrast analyses, parallels the body's estrogen levels (see Hampson and Kimura, 1993).

The verbal working memory span during the follicular and luteal phase of the natural cycle group were different, whereas those of the birth control group remained constant. The birth control group maintains a steady estrogen level throughout the cycle whereas women with natural cycles have higher estrogen levels during the middle than at the end of the cycle. This finding supports the hypothesis that increased estrogen levels are associated with improved verbal working memory span. The two groups showed no difference on the spatial rotation task. This finding suggests that increased estrogen may improve verbal working memory but has no discernable effect on the spatial task.

Despite the significant finding of this study, there are caveats. Our sample size was small and restricted to the college population. Also we did not perform hormone assays to verify the actual hormone levels and hence we cannot definitively conclude that verbal working memory span is associated with estrogen levels. Another question concerns the difference between spatial and verbal performance. Although the two tasks do not seem differentially difficult as indicated by the % correct scores, they nevertheless tap different neurocognitive functions. Verbal working memory task is associated with frontal lobe functions (Gold et al., 1997) whereas the spatial rotation task did not tap working memory and is associated with more posterior functions. Therefore we do not know whether the cycle effect we observed is confined to frontal lobe functions. Estrogen increases the density of 5HT-2a receptors in anterior frontal, cingulate and olfactory cortices in the rat (Fink et al., 1996). It also stimulates a significant increase in D2 receptors in the striatum (Fink et al., 1996). However, we do not know the specific role of estrogen in facilitating working memory function in relation to its interaction with serotonergic and dopaminergic systems yet. Future studies with a much larger sample and a more comprehensive neurocognitive tool should be conducted to examine the effects of estrogen on cognitive functions.

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