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Neuropsychologia 40 (2002) 518–529

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

# Implicit memory varies across the menstrual cycle: estrogen effects in young women

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Received 25 November 2000; received in revised form 17 May 2001; accepted 31 May 2001

**Abstract**

Evidence that ovarian steroid hormones such as estrogen and progesterone affect cognition comes from studies of memory in older women receiving estrogen replacement therapy and studies of sexually dimorphic skills in young women across the menstrual cycle. Sixteen women (ages 18–28) completed tests of memory (implicit category exemplar generation, category-cued recall, implicit fragmented object identification) and sexually dimorphic skills (fine motor coordination, verbal fluency, mental rotations) at the early follicular (low estrogen and progesterone) and midluteal (high estrogen and progesterone) phases of the menstrual cycle. Performance on category exemplar generation, a test of conceptual implicit memory, was better at the midluteal than the follicular phase. In contrast, performance on a test of explicit memory, category-cued recall, did not vary across the menstrual cycle. At Session 1, women in the follicular phase performed better on the fragmented object identification task than did those in the midluteal phase. This unexpected finding suggests that high levels of ovarian hormones might inhibit perceptual object priming. Results confirmed previous reports of decreased mental rotations and improved motor skills and fluency in the midluteal phase. Estradiol levels correlated positively with verbal fluency and negatively with mental rotations and perceptual priming, which suggest that estrogen, and not progesterone, was responsible for the observed changes in cognition. Mood did not vary across the cycle phases. Overall, the findings suggest that estrogen may facilitate the automatic activation of verbal representations in memory. 

*Keywords:* Estrogen; Menstrual cycle; Cognition; Memory; Mood

## 1. Introduction

There is increasing interest in the role of sex steroid hormones on neuropsychological functioning, particularly with regard to the possibility that estrogen may enhance memory. Much of this interest stems from recent reports that estrogen replacement therapy (ERT) may lower the risk of Alzheimer's disease and may lessen normal, age-related memory decline. (For reviews, see [21,45]). Although studies of the cognitive effects of estrogen in postmenopausal women have focused mostly on memory and other abilities that decline with age, studies in younger women have focused primarily on sexually dimorphic abilities. Males generally show an advantage in visuospatial abilities and certain mathematical abilities compared with females, whereas females generally show a comparative advantage in verbal abilities, perceptual speed and accuracy, and fine motor skills. (For reviews, see [16,27].) In young women, naturally occurring increases in estrogen are associated with improvements on tasks that favor females and with declines on tasks that favor males [20]. The present study bridges these two domains of research by examining sexually dimorphic abilities and different types of memory (i.e. explicit and implicit) in young women across the menstrual cycle. Our goals were to broaden the investigation of hormonally mediated cognitive abilities and to increase our understanding of the neurobiological substrates of different types of memory.

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0028-3932/01/$ - see front matter 
PII: S0028-3932(01)00126-9

Natural fluctuations in ovarian hormones across the menstrual cycle allow for noninvasive studies of the effects of estrogen on cognition in young women. For women with 28- to 29-day cycle lengths, the menstrual cycle may be divided into two general phases, the follicular and luteal phases [55]. The follicular or proliferative phase extends from Day 1 (the first day of menstruation) to Day 14. Low serum concentrations of both 17-β-estradiol, the most abundant form of estrogen, and progesterone characterize the early follicular phase. Estradiol peaks in the preovulatory surge just prior to ovulation, though progesterone levels remain low. The follicular phase ends at the time of ovulation. The luteal or secretory phase generally extends from Days 14 to 28 and is characterized by high concentrations of both estrogen and progesterone. Cycle phase can be estimated by counting backward to the first day of menstruation. Although this counting method has been used legitimately in some previous research, the approach has been associated with an error rate of 15 [34] to 50% [13]. Confirmation of expected hormone concentrations by radioimmunoassay (RIA) is critical for validating menstrual phase, because accuracy in determining menstrual phase is likely a major factor contributing to incongruent results across previous studies.

Studies indicate that fluctuations in estradiol underlie a reliable pattern of cognitive change across the menstrual cycle. In one study, 45 women completed a battery of cognitive tests during the early follicular and midluteal phases of the menstrual cycle [18]. The battery included 'female' tests of verbal fluency, articulation, manual coordination, and perceptual speed, as well as 'male' tests of deductive reasoning and spatial ability. As predicted, during the midluteal (high estrogen and progesterone) phase, deductive reasoning and spatial ability decreased and verbal articulation improved. Hormonal effects were also evident in an asymmetrical carryover effect, wherein women who first performed spatial tests when hormone levels were low (and therefore conducive to performance) maintained a high level of performance on a second test session when hormone levels were high (and normally detrimental to spatial performance). In a second study, Hampson [17] tested women during both the preovulatory estradiol surge and the follicular phase to control for the potential effects of progesterone on performance. Results paralleled those in the previous study, and hormonal assays revealed a curvilinear relationship between estradiol and spatial ability, with optimal performance associated with intermediate levels. Together, the results suggested that estradiol rather than progesterone was responsible for the observed cognitive effects.

Studies indicating a reliable advantage for women on verbal recall tasks [27] led to speculation that estrogen may enhance verbal memory. Phillips and Sherwin [34] conducted the only published study on memory performance across RIA-validated phases of the menstrual cycle. They reported poorer delayed figural memory during the follicular compared with the luteal phase, but no difference in immediate or delayed paragraph recall. This pattern of results was surprising given their previous findings of enhanced verbal but not figural memory with ERT in surgically menopausal women [46]. A number of subsequent studies corroborated findings of better verbal memory among ERT users compared to nonusers [22,25,31,44] (but see also [1]), and one indicated improvements in figural memory as well [39]. Together, these data suggest that estrogen may improve memory in younger and older women, though the particular domains of memory affected require additional investigation.

The precise mechanism by which estrogen influences memory is not known definitively, but there is reason to believe that the hippocampus and the inferior parietal lobule may mediate the effect. First, animal studies show enhanced survival and growth of neurons in the hippocampus with estradiol. (For a review, see [33]). Moreover, cross-sectional [38] and longitudinal [29] neuroimaging studies in postmenopausal women show hormone-associated differences in patterns of blood flow in the hippocampal formation during performance of figural and verbal delayed memory tasks. Based on findings from a randomized crossover trial of ERT in postmenopausal women, Shaywitz and colleagues speculated that estrogen might improve verbal memory by enhancing short-term storage of phonological stimuli [43]. Compared to placebo, the ERT-treated group in that study showed increased activation of the inferior parietal lobule during storage of nonsense words. That same brain region shows activation associated with the storage and retrieval of phonological material during a working memory task [24] and structural sex differences in regional brain volume [11]. Together, these studies suggest several mechanisms by which estrogen may enhance verbal memory.

To date, studies of hormonal effects on memory have focused on recall and recognition tests. These are termed explicit memory tests because they make explicit reference to a previous event and require deliberate recollection [14]. In contrast, instructions for implicit tests do not call for deliberate recollection, but prior exposure to certain items nevertheless influences (i.e. primes) later processing of those items. For example, in the category exemplar generation (CEG) test, participants study uncommon category exemplars (e.g. plum) and subsequently receive instructions to generate members of a particular category, such as fruit [12]. Priming is evident when participants generate studied exemplars at above-chance levels. The CEG test is considered a test of conceptual implicit memory because it draws on the meaning or semantic associates of studied items.