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Cognitive Pattern in Men and Women Is Influenced by Fluctuations in Sex Hormones

Doreen Kimura and Elizabeth Hampson

Sex hormones (e.g., testosterone and its metabolites, dihydrotestosterone and estradiol) are known to influence the organization of the mammalian brain during critical periods in development, before or just after birth, and can permanently alter an animal's propensity to engage in many sexually dimorphic behaviors. In adulthood, sex hormones continue to activate certain neural circuits and their consequent behaviors. For example, in many species, female sexual activity is facilitated by high levels of ovarian hormones during the fertile phase of the cycle, and male sexual behavior is enhanced by high levels of testosterone. There is evidence that these hormonal influences may also extend to problem-solving abilities.[1] In rodents, for example, the sex difference favoring males on spatial mazes is increased or found only in the breeding season. Variations in complex motor behaviors have been found across the estrous cycle in female rodents. Such findings in other species suggest that there may be variations in cognitive or motor functions in humans as well, as hormone levels fluctuate.

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In fact, there is now substantial evidence that cognitive patterns may vary with phases of the menstrual cycle in normally cycling women and with seasonal variations in androgens in men. We review some of the evidence here.

There is some controversy in the current literature as to the size and extent of sex differences in cognitive abilities.[2] Nevertheless, numerous studies have reported a sex difference in favor of women on tests of verbal fluency, verbal articulation, perceptual speed and accuracy, and fine distal motor movements. A reliable sex difference in favor of men has been reported on tasks involving spatial rotation and manipulation, appreciation of the vertical, and mathematical reasoning.[3] Neutral tasks (those on which there are no sex differences) include general intelligence measures such as vocabulary tests, as well as verbal and nonverbal reasoning tests. Because animal studies show that it is primarily sexually differentiated behaviors that are subject to the effects of gonadal hormones, it was from among these groupings that we selected tests for our studies. Numerous sources of variance, including genetic and experiential factors, contribute to an individual's proficiency within a specific cognitive domain, but in these studies our focus was on the extent to which transient hormonal factors might affect performance.

CHANGES ACROSS THE MENSTRUAL CYCLE

The menstrual cycle provides a convenient natural paradigm for investigating variations in estrogen and progesterone. Studies have shown that well-learned tasks and tasks that require a mixture of different abilities do not vary systematically over the menstrual cycle.[4] Yet certain sexually dimorphic cognitive functions may nevertheless be influenced by the hormonal milieu. The observed pattern of changes does not conform to popular stereotypes: In our studies, we found a reciprocal pattern of changes between spatial ability and a number of skills reported to show a female advantage. Our studies differ from many previous studies of the menstrual cycle in two important respects: We specifically studied cognitive abilities that show reliable sex differences, and we compared phases of the menstrual cycle in which circulating concentrations of estradiol (a potent form of estrogen), or estradiol and progesterone, are maximal or minimal. It may be primarily for these reasons that subtle changes in cognitive performance became apparent in our studies. Although some earlier researchers had reported findings similar to ours, many other prior studies were methodologically flawed and noncontributory.[4]

In our first two studies,[5] young women were tested twice, in counterbalanced fashion, so that the test sessions coincided once with the midluteal phase of each woman's cycle (when estrogen and progesterone levels are high) and once with the late menstrual phase of each woman's cycle (when levels of both hormones are very low). Subjects were unaware of the hypotheses being tested. In the first study, using a within-subjects design comparing the two phases, we found that women performed better on tests of manual dexterity, known to favor females, but more poorly on a perceptual-spatial task (the rod-and-frame test), known to favor males, during the midluteal phase of the cycle. This was the first piece of evidence that high levels of ovarian hormones may facilitate certain skills that show a female advantage, while being detrimental to skills that show a male advantage. The second study employed a broader battery of sexually dimorphic tasks. Tests of verbal and articulatory skills, manual dexterity, and perceptual speed, as well as a broader sampling of visuospatial measures, were included. We chose tests with objective scoring to minimize any possibility of experimenter bias. The statistical analyses focused on composite measures reflecting general performance on each ability, rather than on individual test scores per se. Within-subjects comparisons showed that women performed slightly better on tests of verbal fluency, manual dexterity, speeded articulation, and to some extent perceptual speed when levels of estrogen and progesterone were presumed to be higher than when they were lower. Some problems were encountered with practice effects on the spatial tasks; nevertheless, on first exposure to the tests, women at the menstrual phase outperformed women at the midluteal phase, confirming our earlier results.

In both of these studies, estrogen and progesterone varied in parallel (see Fig. 1), so it was not possible to infer which hormone was more closely related to the cognitive fluctuations observed. To help tease this relationship out, we conducted another study.[7] This time, women's menstrual phase performance was compared with their performance a day or two before ovulation, when estradiol levels are extremely high, but progesterone levels are still relatively low. Because this brief phase is difficult to identify accurately from menstrual records alone, serum levels of estradiol, progesterone, and luteinizing hormone were measured for each woman via radioimmunoassay. Once again, we found significantly better performance on tests of manual and articulatory speed and accuracy at higher estrogen levels, and poorer performance on tests of visuospatial ability at this time. This was so despite the fact that on a mood questionnaire administered during the test sessions, women reported enhanced feelings of vigor and positive affect at the preovulatory phase. This study, then, provided further confirmatory evidence for cognitive fluctuations across the menstrual cycle, at least among some sexually differentiated skills, and again revealed reciprocal changes among abilities that show sex differences favoring males versus females. Although the pattern was not identical to that seen in our earlier studies, high levels of estradiol alone did appear to be associated with variation in motor and visuospatial skills.

Other laboratories have begun to confirm our results.[8] For example, Irwin Silverman and his colleagues

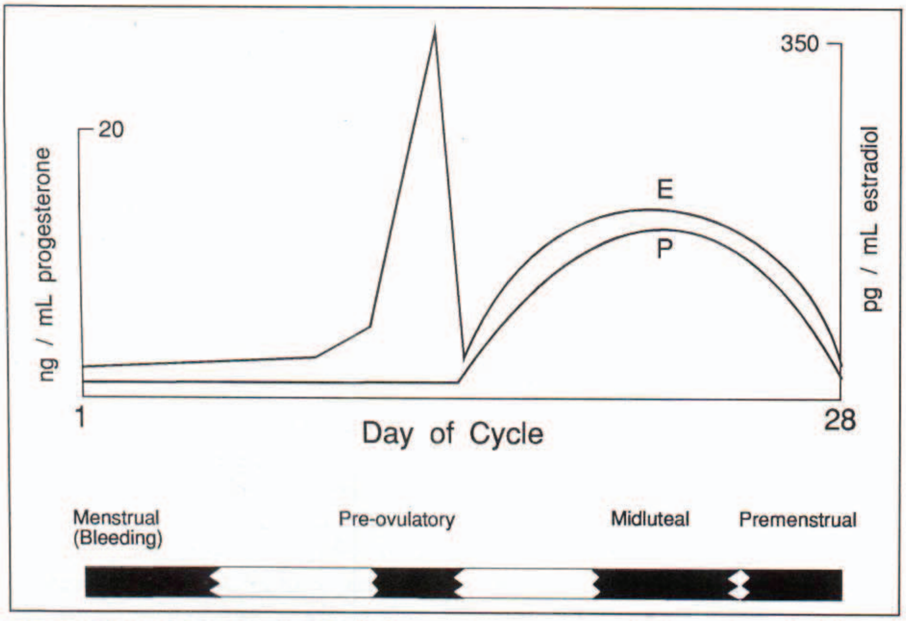

Fig. 1. Schematic representation of changes in serum concentrations of estradiol (E) and progesterone (P) across the menstrual cycle. Tasks on which women excel tend to be enhanced in the high-E and high-E-and-P phases, relative to the low phase; spatial tasks on which men excel show the reverse pattern. Note that E and P concentrations are shown on separate scales. Modified from Ganong.[6]

at York University have replicated some of our findings using a different spatial measure, the Vandenberg and Kuse Mental Rotations test (Fig. 2). In Silverman's study, women showed significantly better spatial performance during the menstrual phase of the cycle, compared with their performance during the early luteal phase, a part of the cycle characterized by relatively high estrogen and progesterone levels. More recently, Phillips and Sherwin reported a slight menstrual-phase decrease in women's scores on a test involving memory for designs. This type of visual memory shows a small female advantage, so this finding is consistent with our data. It also serves to emphasize that it is the demand for spatial transformations, not the presence of pictorial material per se, that is the key element behind the observed menstrual-phase enhancement on spatial tasks.

PHASES OF HORMONE REPLACEMENT THERAPY IN POSTMENOPAUSAL WOMEN

Menstrual cycle studies by their very nature are correlational. One must therefore ask whether fluctuations in cognitive function are truly a direct consequence of hormonal variation or, for example, the influence of some independent pacemaker within the central nervous system. Evidence from postmenopausal women undergoing hormone replacement therapy suggests that hormonal variation is sufficient to produce at least part of the changes. Because such therapy is given on a calendar-month basis, it is random with respect to any residual biorhythms that postmenopausal women might have.

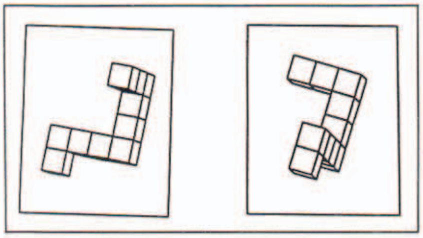

Fig. 2. Example of a spatial rotation task. The subject must determine if the two figures are rotated versions of each other or not. This type of task is performed better by women in the low-estrogen-and-progesterone phase of the menstrual cycle (i.e., during menstruation) than during higher E and P phases. It is performed better by men in spring, when testosterone levels are relatively low, than in fall. On average, men perform better than women, but between-sex effect sizes are larger in spring than in fall.

Our postmenopausal subjects were on a monthly therapy regime whereby they received estrogen for 16 or 25 days at the beginning of the month. A minority of the women had progesterone added from Day 16 through Day 25. All women went off all therapy from Day 26 to the end of the calendar month. They were tested twice, in counterbalanced order, once between Days 10 and 15, in the estrogen-alone phase, and once at least 4 days after going off all therapy.

We found that postmenopausal subjects performed better in the estrogen phase than in the off-therapy phase on a manual sequencing task and on an articulatory task, as well as on one perceptual speed test.[9] There were no effects on either a two-dimensional rotation task or a disembedding task. The latter two tasks are less sensitive to sex differences than other, more demanding spatial tests, which might account for the lack of effect of hormone therapy status. It also appears that hormone therapy results in estrogens being dissipated less rapidly than occurs during the natural menstrual cycle, in that levels of estrogen higher than pretreatment levels can be detected for several weeks after cessation of therapy. This might mean that the difference between phases of therapy was attenuated compared with the difference across phases of the menstrual cycle. Even so, the effect on motor and articulatory abilities was significant, suggesting that such tasks may be more sensitive to fluctuations in estrogen than are spatial tasks, at least in older women.

SEASONAL FLUCTUATIONS IN COGNITIVE PATTERNS IN MEN

Hormone-related fluctuations in cognitive function are not limited to women: We have found seasonal differences in cognitive performance in men, seemingly related to variation in testosterone levels. Previous research had shown that normal male undergraduate students with testosterone levels below the median performed better on spatial tests than did those with levels above the median.[10] Such studies suggest that there is some optimum level of testosterone for spatial ability, and that this level is above the level of the average female but below the level of the average male. It is also known that, at least in the northern hemisphere, testosterone levels are higher in men in autumn than in spring, presumably an evolutionary remnant related to optimal mating and offspring production times. If lower testosterone levels within the normal range are associated with better spatial ability, one might expect men's scores on spatial tasks to be higher in spring than in fall. This indeed turned out to be the case.[11]

Three examples each of three kinds of tests were administered: (a) The "neutral" tests—those not showing sex differences—were Advanced Vocabulary, Inferences, and a modified Raven's Progressive Matrices; (b) the "masculine" tasks—those on which males typically excel—were Hidden Figures, Paperfolding, and Mental Rotations; (c) the "feminine" tasks—those on which females typically excel—were two perceptual speed tests, Finding A's and Identical Pictures, and a test of divergent thinking, the Thing Categories test.

To facilitate comparison across tests with different maxima, all scores were converted to standard scores, and a composite for each of the three types of tests (neutral, masculine, feminine) was derived. Testosterone levels were measured by salivary radioimmunoassay.

Thirty-six men and 34 women were seen in fall, and 34 men and 34 women were seen in spring. (Only across-subjects data are reported here because within-subjects data collection is in progress.) A multivariate analysis of variance was performed across the three composite scores (neutral, masculine, feminine), two sexes (male, female), and two seasons (spring, fall). The expected sex differences on masculine and feminine tests were found. In addition, there was a significant Sex × Season × Test-Type interaction ($p = .004$). A breakdown of the data showed a significant sex-by-season interaction only for the masculine composite. Further breakdown indicated that the seasonal effect was significant only in males ($p = .047$), not in females ($p = .326$). As Figure 3 shows, men performed better on the masculine composite in spring, as predicted.

This finding, coupled with the data on cognitive function across the menstrual cycle, suggests that a significant amount of the variation in the size of sex differences from study to study may be related to season or menstrual phase. Nevertheless, although seasonal effects alter the size of the sex difference, they do not obliterate that difference. Male superiority on mental rotation, for example, is still evident in fall ($p < .03$), although the effect size is substantially larger in spring (.89) than in fall (.46).

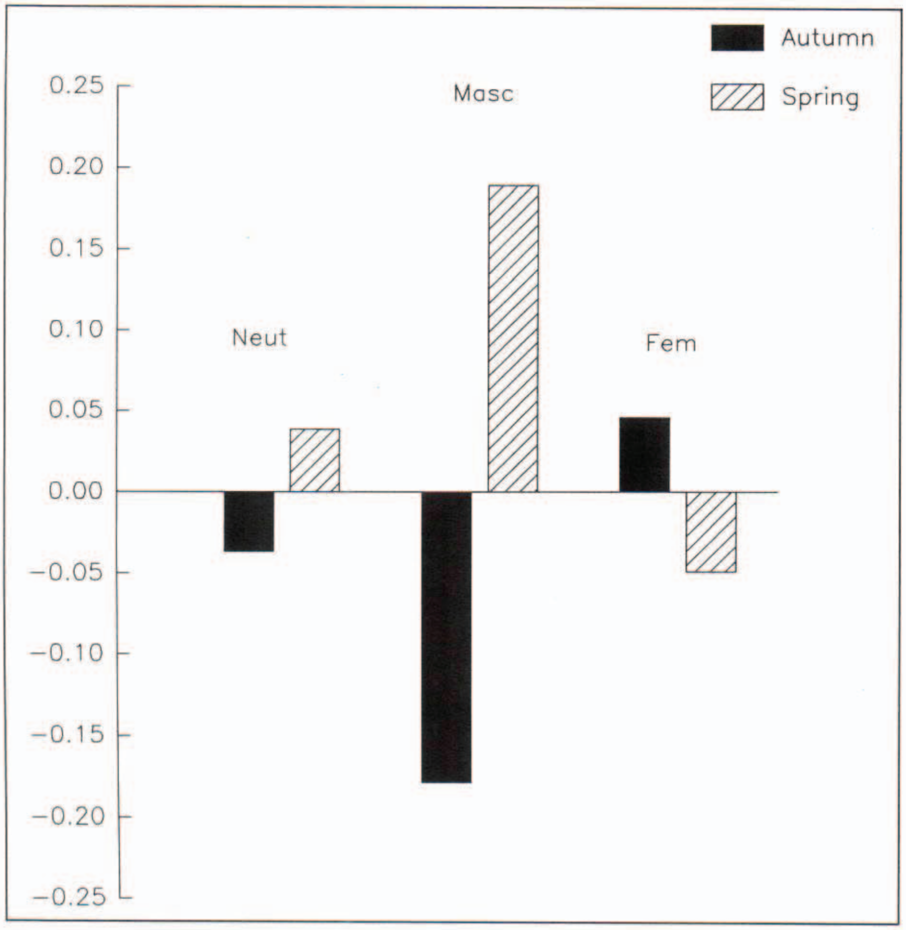

Fig. 3. Standard composite scores in men on neutral, feminine, and masculine tests in spring and fall. Performance on masculine (spatial) tests varies significantly with the season in young men.

Again, one might ask whether it is actually the hormonal changes, confirmed by radioimmunoassay in our study, that are the basis for variation in cognitive function. A general change in intellect or mood is unlikely to be the basis for these seasonal differences in men because the effects are restricted to spatial tasks. Only scores on masculine tests have so far been related to levels of testosterone across individuals,[10] further making it probable that changes in testosterone levels are indeed the critical factor. A recent study by Janowsky and co-workers[12] strengthens this interpretation. Administration of testosterone to older men (whose endogenous testosterone levels would be below those of the young males we studied, and thus below the hypothetical optimum) enhanced performance on a spatial-constructional task, but not on verbal or motor tasks.

CONCLUDING COMMENTS

Cognitive pattern fluctuates with variations in sex steroid levels in both men and women, whether the levels vary spontaneously or by means of exogenous therapy. In our studies, variations in estrogen in women relate to performance on both masculine and feminine tests, but variations in testosterone in men appear to relate only to masculine tests. We do not, however, know what concomitant changes in other steroid hormones may be occurring when testosterone varies because, for example, assays of estrogen have not typically been done in the same subjects.

Our findings of hormone-sensitive fluctuations in cognition, combined with data from other researchers suggesting early organizational effects of sex steroids on the mammalian brain,[13] imply that the group differences between men and women in some specific cognitive abilities are to a significant degree a product not only of current but also of early hormonal environments. This hypothesis is consistent with animal work showing that sexually dimorphic behaviors that are subject to early organizational influences often continue to be sensitive to the effects of sex hormones in adulthood.

Whether fluctuations in cognitive pattern are merely epiphenomena or serve some adaptive function is unclear. Conceivably, it may have been useful for men's spatial ability to be enhanced in spring in nomadic hunter-gatherer societies, when the home camp might be relocated, or hunting might be more intensive; but it is unclear what advantage could accrue from changes in cognitive skills across the menstrual cycle. Nevertheless, the existence of seasonal and monthly fluctuations in cognitive function suggests that these are potentially significant variables in determining the size of sex differences seen across various research studies.

It is also unknown at this point what the precise neural mechanisms producing the changes in cognitive function might be. There appear to be alterations in some aspects of functional hemispheric asymmetry across the menstrual cycle, as indicated by enhanced right-ear superiorities on a dichotic listening test in the high-estrogen phases.[7] It is unlikely, however, that relative hemispheric activation is the only or the fundamental mechanism for cognitive changes. Animal studies suggest that fluctuations in steroid hormones can have a variety of effects on neurochemistry, modulating neurotransmitters in widespread areas of the brain and even inducing transient structural changes, such as changes in synapse density in some regions. Hormonal and cognitive studies in humans need to be combined with measures of neural activity to address this issue.

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