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Sex Hormones Influence Human Cognitive Pattern

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Abstract The major sex differences in cognitive skills are summarized, and the role of sex hormones in early organization and possible maintenance of these differences is discussed. Using animal models and human hormonal anomalies, a good case can be made that prenatal androgens strongly influence adult cognitive pattern, though the relation between baseline androgens and spatial ability, for example, need not be linear. Moreover, men and women remain sensitive to variation in hormonal state, as evidenced in the fluctuations in cognitive and motor performance across natural diurnal, menstrual and circannual rhythms. Evidence from administration of exogenous hormones in humans is more equivocal, though this field ultimately should yield useful information.

Overview of Cognitive Sex Differences

Sex differences in human problem-solving behaviour have been reliably found across many studies over the past few decades, and in several cultures. The major findings are summarized in Table I. The list is not exhaustive, but men and women clearly display different cognitive strengths, hence different *patterns* of ability. It must be kept in mind that these are *average* differences, and that the overlap between the sexes on many tests is extensive. Predicting an individual's performance level based on sex alone would be highly inaccurate.

Table I. Some abilities favouring men and women, respectively

PROBLEM-SOLVING TASKS FAVOURING MEN	PROBLEM-SOLVING TASKS FAVOURING WOMEN
SPATIAL ORIENTATION – making a correction for a change in orientation of an object, e.g., "mental rotation"	**OBJECT LOCATION MEMORY** – recall of the location of objects in an array
VISUALIZATION – determining how a depicted object will appear when manipulated, e.g. folded	**PERCEPTUAL SPEED** – rapid identification of matching or designated items
LINE ORIENTATION – matching the slope of a line	**VERBAL MEMORY** – recall of a story, paragraph or list of unrelated words
MATHEMATICAL REASONING – solving a novel mathematical problem	**NUMERICAL CALCULATION** – adding, subtracting, etc., of given numbers
THROWING ACCURACY – hitting a distant target	**DEXTERITY** – manual tasks involving precision

REVIEW ARTICLE

Spatial Skills

Spatial skills on which men excel include both simple and complex abilities. Ability to match line orientations would generally be regarded as a simple task, in contrast to the ability to mentally rotate a complex figure [100]. The latter yields the largest currently known sex difference on a paper-and-pencil test. The average difference between men and women across many studies employing the test approaches a full standard deviation, or an "effect size" of approximately 1.0. [59, 67]. Effect size is calculated as the difference between two groups, divided by a measure of the variability within the groups (standard deviation). It is indirectly a measure of overlap between groups – the larger the effect size, the less the overlap. On most other spatial tests that favour males, such as tests of spatial visualization, the effect size is modest, nearer .5.

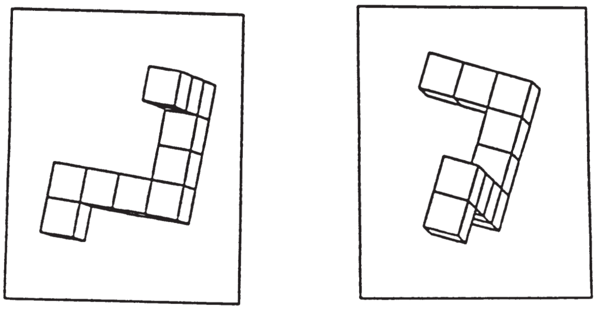

Figure 1. An example of a complex task requiring rotation in "three" dimensions. The subject must decide whether the two figures are the the same figure rotated, or are two different figures.

The Vandenberg Mental Rotations test, based on the Shepard and Metzler designs [91] (Figure 1), depicts complex 3-dimensional figures on a 2-dimensional page. However, the mental rotation of a figure in *three* dimensions is not a prerequisite for producing a large sex difference. Difficult figures requiring imaginal rotation in only two dimensions may yield an equally large effect size [14]. Performance on a mental rotation test has been found to be significantly related to performance on a route-finding task [23] and a computerized labyrinth [78], suggesting that such ability may contribute substantially to navigation.

A quite different spatial task, favouring women, is depicted in Figure 2. The subject is asked to indicate, from memory, which objects have changed locations from the first to the second array [18]. Other studies have confirmed a female advantage in processing the locations of multiple objects in an array [46, 69, 83]. However, when the task emphasizes location *per se*, regardless of object identity, women perform less well than men [43, 83], leading to the suggestion that women may use a common system to process object identity and location, whereas men do not [43, 46]. Such an interpretation would be consistent with findings that females tend more often to employ landmarks in navigating, in contrast to males' employment of geometric cues [105, 109].

Mathematical Abilities

School marks on mathematics tests may not show sex differences, or girls may even do better, as they do on most school subjects on average. However, when mathematical *aptitude* tests are given which are not simply variations of previously learned problems, and which therefore emphasize math reasoning, there is a consistent male advantage [60, 66]. On strictly calculation tests, females more often perform better.

The male advantage appears to increase with increasing difficulty or complexity of the problems; and males are over-represented at the high end of most math aptitude tests. In an extensive study in the United States spanning decades that identified mathematically talented youth, males have always outnumbered females [4, 61]. However, the preponderance of males is especially marked at the upper end of this population on the Scholastic Aptitude Test-Mathematics (SAT-M), by more than 10 to one.

On another very demanding mathematical reasoning test available to math-oriented North American undergraduates, the Putnam competition, male and female scores are also very divergent. In 1999, of the top 138 contestants, only five could be unequivocally identified (by name) as female. In a more recent competition in which sex of contestants was identified, there were again four times as many men as women taking the test, but 84% of women and 54% of men failed the test completely, that is, they got no score. 37.4% of men but only 11% of women got passing scores of 10 and higher.

So for many tests of ability, we must look not merely at the average difference, but at the extremes of the scores. Even when the average sex difference on any test is small, the extremes of the distribution may show a sharp divergence. For most professions, it is the upper end which is critical.

Verbal Skills

Although popular opinion holds that women are superior on most verbal tasks, this is not the case. The assumption probably stems from the earlier onset of fluent articulate speech in young girls [see 64 for an early review, 68]. In adults, however, reliable differences to date favouring women are found primarily on tasks of verbal memory [7, 55] and verbal fluency [19], not on vocabulary or verbal reasoning. Verbal fluency tests usually require the generation of words or sentences which have some constraint on the letters they contain, e.g., listing words that begin with a particular letter. Verbal memory taps the recall of material employing words, whether in lists or meaningful paragraphs, and whether the words are abstract or concrete. Verbal memory tests have shown the largest effect sizes so far of tests favouring women, in one study from .58 to .97 on recall of a word list [13].

Perceptual Skills

Women usually obtain better scores on tests which require rapid matching or identification of designated

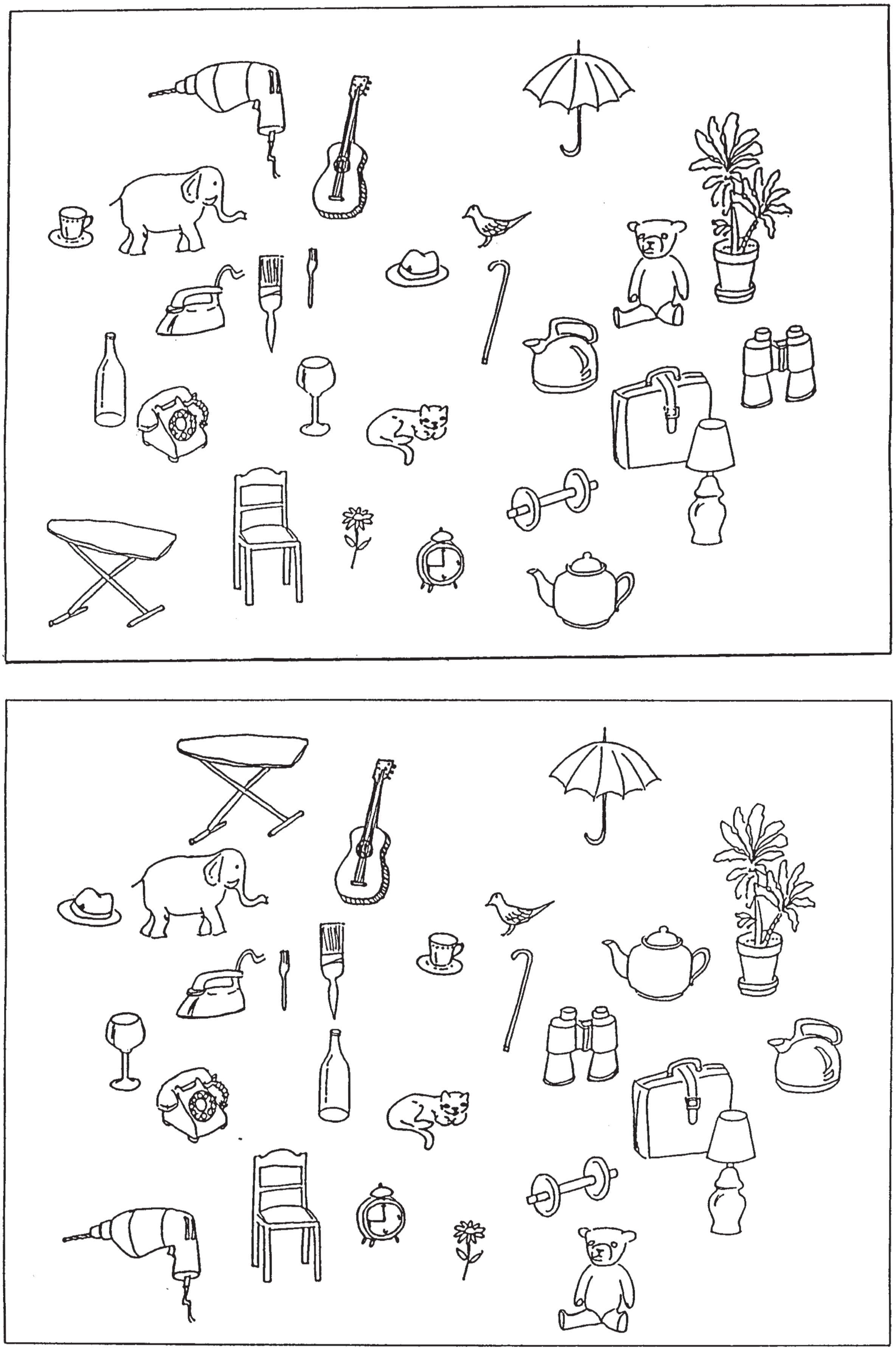

Figure 2. The object location memory task, from Silverman and Eals, 1992. Reproduced by permission of the authors. The top array is shown first and studied for one minute, followed by the bottom array. S indicates which objects have changed location.

Table II. Prepubertal sex differences in cognitive and motor function.

AUTHOR/ YEAR	AGES	FINDINGS
Rosser *et al.*, 1984	4–5	Boys better at spatial rotation
Vederhus & Krekling, 1996	9	Boys better on spatial tasks
Lunn, 1997	3–4	Boys better on targeting
Levine *et al.*, 1999	5–6	Boys better on spatial transformations, mazes
Denckla & Rudel, 1974	5–11	Girls faster at colour naming
Ingram, 1975	3–5	Girls better at copying hand postures
McGuinness *et al.*, 1990	7–10	Girls better memory for words

stimuli, labelled as "perceptual speed". Examples are Identical Pictures, and Finding a's from the ETS battery [19]. The differences between men and women are generally small, less than .5 effect size.

Motor Skills

A very large advantage for men is found on tasks that require hitting a target with a missile, or intercepting a moving target [48, 106, 107]. This advantage does not appear to depend simply on men's greater strength, nor on the their more active sports history. It appears to depend on the accurate co-ordination of spatial targets with large-amplitude aiming movements, but it is not significantly related to scores on paper-and-pencil spatial tasks on which men also excel [107]. The fact that homosexual men, whose physical build, sex of rearing and gender identity is male, throw less accurately on average than heterosexual men [31, 89] suggests that the male advantage is founded on a distinctive cognitive ability, rather than being reducible to somatic characteristics.

In contrast, women do better than men on small-amplitude fine motor skills, such as required on the Purdue Pegboard. Some studies have found this advantage to be related to women's smaller finger size but this is not so in other studies [e.g., 31]. Women also tend to be better at performing manual sequences, relative to their speed on the individual movements [80]; and this advantage is enhanced when performing without vision [12], suggesting that women's motor skills may be more closely related to intrapersonal than to extrapersonal neural systems.

Origins of Cognitive Sex Differences

Most researchers into cognitive sex differences view them as a product of our long evolutionary history as hunter-gatherers, in which men's and women's roles and hence their problem-solving abilities, became quite distinctive and complementary [18, 25,26, 51, but see 58 for an alternative view]. Men were assumed to be responsible for long-and-short-distance hunting and scavenging, travelling farther from the home base than women. They were also responsible for defence. Women, in contrast, were indispensable for infant and child care, and were active in caring for the home. Their contribution to foraging was generally limited to gathering or gleaning near the home.

These complementary roles are assumed to have put different selection pressures on the abilities of the two sexes. Men would be selected for navigational skills which employed geometric cues such as distance and direction (including the ability to correct for changes in direction), and to evolve motor skills directed more at distant targets. Women might be expected to evolve navigation skills employing local landmarks, and motor and perceptual skills appropriate to domestic activities and child care.

There are some nonhuman parallels to human cognitive sex differences, which bolster evolutionary interpretations. In polygynous vole species, in which the male's territory is larger than in monogamous species, males perform better than females on a maze learning task [24]. Male rats make fewer errors than females in a radial arm maze, and moreover the sexes employ different methods of solution [109]. Male baboons perform better on a mental rotation task [102], consistent with their navigational role in guiding the troop.

Whatever the ultimate determinants for human cognitive sexual differentiation, the evidence suggests that the proximate mechanisms have relied heavily on sex hormones, discussed later.

Sociological Hypotheses

In the past, social scientists have attributed cognitive differences between men and women almost entirely to differences in lifetime experience; and given our prior lack of knowledge of the effects of sex hormones, this may have been a defensible point of view. However, it has since emerged that some of these sex differences appear well before puberty and before large differences in experience (Table II); and they appear across cultures that differ in the activities available to men and women (Table III).

It might be expected, to the extent that sex differences are determined by lifetime experiences, that they should have declined in the last few decades. Such claims have indeed been made [21], but there are difficulties in comparing the heterogenous tests and heterogeneous populations over time. For example, the samples of people taking the tests over time has probably changed [32]. Moreover, some tests have been deliberately altered to dilute sex differences, by removing some items that differentiate the sexes.

We are on firmer ground comparing sex differences over different time periods when we know that the same test has been used throughout, and that the samples we are comparing are equivalent. For example, sex differences on the Vandenberg Mental Rotation test have remained quite stable over the last three decades. We have already noted that this task shows a large sex difference, the effect size hovering around 1.0. Masters and Sanders [67] reviewed 14 studies employing the task between 1975 and 1992, nearly all on college students. Effect sizes varied from .69 to 1.27 across samples, but there was no systematic change across time. The 1975 study showed an effect size of 1.0, and the two most recent papers they cited found effects sizes of 1.27 and 1.14. We can add to that from our own studies – in 1997 we found an effect size of .86 [14], and in 1999, effect sizes of .98 and .90 in two samples [13]. In 2001 Geary and DeSoto found an effect size of approximately 1.06 [27].

Alternative methods of evaluating experiential contributions to sex differences in cognition have employed attempts at relating past activities which were rated as more spatial (e.g., skiing, building model planes), to current scores on a spatial visualization test [79]. A small but significant correlation was found. However, this kind of result does not allow us to determine whether life activities influence spatial ability, or the reverse. A review of studies in which men and women were given intensive practice on a variety of spatial tasks, to see whether women might be differentially advantaged by such practice (as might be expected if lack of past experience were the critical factor), reported negative findings. The sex differences were not erased with short-term intensive practice in adulthood [3].

Of course we would not conclude that life experience plays no role in the appearance of sex differences in cognition. However, it seems inevitable that such experience will manifest itself within the context of nervous systems already differently predisposed at birth.

Early Organizational Effects of Sex Hormones

Sexual Differentiation

Sex differences in cognitive pattern may be interpreted within the general context of mammalian sexual differentiation. The principles of differentiation of male and female structure and behaviour, derived primarily from non-human research, can also be applied, and tested, in the sphere of cognitive or problem-solving behaviours in humans.

The "simple" version of mammalian sexual differentiation [see 30] is that the undifferentiated or default form is the female, and that active processes, largely under control of androgens and their derivatives, are needed to produce a male. The story appears to be very well established for formation of genitalia and general physical type, and for some reproductive behaviours. It has also been convincingly applied to some non-reproductive behaviours, including rough-and-tumble-play and certain problem-solving activities.

Within this framework it has been proposed that there are critical developmental periods, prenatal and immediately postnatal, during which the action of androgens irreversibly masculinizes the brain. Some of these actions depend on the aromatization of testosterone to estrogen; hence the female brain is thought to be protected from such influence by the sequestering of estrogen by a substance called alpha-fetoprotein. Such early developmental influence is called "organizational". In adulthood, sex hormones are again required to activate the hormonally predisposed brain along male or female lines, as appropriate – called an activational influence. Some behaviours organized by androgens, such as rough-and-tumble play, need no further activational influence to appear.

Table III. Cross-cultural studies of sex differences.

AUTHOR/ YEAR	GROUPS COMPARED
Males better at math reasoning:	
Engelhard, 1990	USA & Thailand
Lummis & Stevenson, 1990	USA, China & Japan
Campbell, 1991	USA– Asian & Caucasian
Females better at computation:	
Jensen, 1988	USA – Blacks, Asians and Caucasians
Engelhard, 1990	USA & Thailand
Males better at spatial tasks:	
Chang & Antes, 1987	USA & Taiwan
Mann *et al.*, 1990	USA & Japan
Owen & Lynn, 1993	South Africa – Blacks, Indians & Caucasians
Silverman *et al.*, 1996	Canada & Japan
Geary & DeSoto, 2001	USA & China
Females better at verbal memory:	
Mann *et al.*, 1990	USA & Japan
Owen & Lynn, 1993	South Africa – Blacks, Indians & Caucasians

Since this pioneering schema, the story has inevitably become more complex:

1) The line between organizational and activational influence has become less distinct, with suggestions that these phases overlap in their mechanisms of operation, if not in time [110].
2) Doubts have been raised about assumptions concerning the negligible role of ovarian hormones in organizing female behaviour [see 22 for review].
3) There is clearly variation in the critical hormone-sensitive time period for different behaviours [29], raising the possibility that early individual variation in timing of hormone surges also influences cognitive patterns.
4) It is unclear whether the demonstrated contribution to sexual differentiation by aromatization to estrogen in rodents, is as important in primates [99], including humans [98].
5) In addition to the genomic effects of hormones, acting through the cell nucleus to bind to DNA, and slowly taking effect, there are more immediate non-genomic effects acting on the cell membrane [70].

These considerations may all have a bearing on the interpretation of the role of sex hormones in human cognition. Generalizing from non-humans has provided useful models, but these must ultimately be assessed in humans. Such models can usually only be tested in people by means of naturally-occurring hormonal variation, or in hormonal anomalies, since the opportunity for manipulation of hormones for other than therapeutic purposes is very limited. However, since such anomalies are often the result of a genetic variant, it is sometimes difficult to rule out non-hormonal genetic influences.

Some of the naturally occurring hormonal anomalies studied in the context of cognitive makeup include congenital adrenal hyperplasia (CAH), androgen insensitivity (AI), idiopathic hyogonadotropic hypogonadism (IHH), and Turner's syndrome. Cognitive pattern has also been studied in relation to individual hormone levels across normal men and women, the underlying assumption being that there is a stable base which can vary from person to person.

Evidence for Organizational Hormone Effects on Cognition

The rodent model for organizational effects on problem-solving spatial abilities was presented in a study on rats [109]. Employing a radial maze with 12 arms, open at the top, with food placed consistently in eight of the 12 arms, normal males were found to locate all the food, over many trials, with fewer wrong choices than females. However, males that had been castrated right after birth, and thus had no or little circulating androgens, made more errors as adults than normal males; whereas females that had been injected with estradiol within 10 days of birth performed better than normal females. The authors suggest that the superior performance of males is related to early exposure of the brain to testosterone, presumably by conversion to estrogen. (In later work [108] it was demonstrated that similar hormonal manipulations after day 10 had no such effects.)

If after training the maze was surrounded by a circular curtain, so that the geometry of the room could no longer be used as a cue, the performance of normal males and hormone-treated females, but not of the other two groups, was negatively affected. Conversely, if after training no curtain was used, but the landmarks (pictures on the wall, furniture, etc) around the maze were moved, then the performance of only the normal females and the castrated males was negatively affected. Thus not only the overall performance, but also the cues that were used, were influenced by early hormonal manipulation.

Such studies can be performed in rodents because the brain continues to be susceptible to hormone influences in the first few days after birth, even though the genitals are already formed. No precisely analagous preparations, in whom hormonal disruption is limited to a period right after birth, exist in humans. Several human hormonal anomalies have resulted in prenatal, but due to surgical or therapeutic intervention, minimal anomalous postnatal influence of sex hormones (CAH, cloacal exstrophy, DES exposure). Others have had anomalies throughout their lives (IHH, AI). The former would of course be more informative about any early organizing effects on cognition.

The most compelling evidence for prenatal androgenic influences on cognition in humans comes from CAH cases, in whom high levels of androgens are produced by the adrenals before birth. The androgen overproduction is stopped by cortisol therapy after birth and any virilization of the genitals in females is repaired by surgery. The latter are raised as girls, and most of them are heterosexually oriented and marry men, though their interest in infants is lower than is the case in unaffected women [see 5 for review].

Of interest for cognitive processes is the fact that spatial ability has often been reported to be better in CAH girls than unaffected girls [6, 36, 86]. This advantage appears selective, that is, so far, other abilities are not enhanced. In fact, Hampson *et al*. [36] report that perceptual speed, an ability favouring women, is reduced in CAH girls. Boys may also suffer from CAH and the consequent overproduction of androgens; but their spatial skills are reduced relative to unaffected boys [36]. The reasonable inference, that the optimal level of androgens for the expression of spatial ability is in the low normal male range, is consistent also with studies on normal young adults described below. No cognitive effects of prenatal exposure to diethylstilbestrol (DES), which has some behavioural effects that mimic androgens, have so far been found in humans [41, 42].

Boys born with cloacal exstrophy may have normal prenatal levels of androgens but because they are born without a penis they have in the past usually been castrated within days of birth and raised as girls. An astonishingly high number of them opt to live as males when they reach adolescence [85], in which case one might speculate that their gender identity was determined prenatally. We do not yet have information on their cognitive patterns.

Hypogonadal men who have lower than normal levels of testosterone throughout their lives, with syndromes like Kallmann's, Klinefelter's, and Idiopathic Hypogonadotropic Hypogonadism (IHH), have poorer spatial ability than normal males even though their Vocabulary scores may not differ from normal [1, 40]. Another study found poorer performance not only on a visuo-constructional task, but also on several verbal tasks [81]. In order to rule out current hormonal environment as the causative factor in these studies, we would need to know the cognitive profile of men who had only recently experienced androgen deficiency. Hier and Crowley [40] provide data on five such men and report that their spatial scores are normal, but more data are needed.

Androgen insensitivity (AI) is a syndrome in which genetic males have testes (hidden in the body cavity), and produce testosterone, but the body's cells do not have androgen receptors. Hence, the androgens are ineffective, the external genitalia are female, and the "girls" are raised as such without any indication of their male genetic makeup until they fail to menstruate. Information on cognitive pattern is incomplete, studies to date employing standard intelligence tests, which generally yield no or small sex differences. Even if AI individuals resembled females, as claimed [44], it would be difficult to evaluate the relative contribution of hormonal influences and of being reared as girls.

Testosterone Levels Across Individuals

Variations in testosterone (T) across seasons, time of day, etc., presumably occur on an underlying stable baseline. We do not yet have information on the relation between T levels early and late in life in the same individuals, but correlations between individuals' T levels across a year, calculated from Smals at al. data [97], are highly significant. There is also evidence from a twin study that a large proportion of the variation in T from person to person is genetically based [74]. These facts suggest that some part of the relationship of T to cognitive function reflects a lifelong or "organizational" effect, particularly when chronological factors are controlled.

It is generally found that levels of testosterone are non-linearly related to cognitive function, in particular to spatial abilities of the kind favouring men [28, 76, 92]. Normal young men with lower levels of T perform better than young men with higher levels; but young women with higher levels perform better than those with lower levels. Such findings are consistent with the idea that spatial ability is enhanced in the low normal male range, at least in the 20–30 age group.

One study found a similar trend for math reasoning, for low–T men to have better scores than high–T men [28]. This result has not yet been confirmed.

Fluctuations in Sex Hormones and Cognitive Function

Sex hormones vary naturally across the monthly cycle in women, and across season of the year and time of day in men. In addition, some cognitive functions have been studied in persons undergoing hormone therapy, as in post-menopausal women, older men, and people undergoing a sex change.

Natural Fluctuations in Estrogen

The earliest demonstrations of cognitive pattern affected by natural fluctuations in sex hormones came from the study of women across the menstrual cycle [9, 54]. The level of estrogen peaks briefly in mid-cycle, and, along with progesterone, rises again for several days prior to the next menstruation, beginning about 10 days before. Earlier studies suffered from inadequate estimations of the appropriate phase for testing, lack of hormonal assays for verification, or a conceptualization of cognitive function which did not take sufficient account of major sex differences in cognition. Later studies that satisified all these requirements found that women were negatively affected during high estrogen levels (compared to low) primarily on male-favouring spatial tasks, while female-favouring tasks such as fluency and fine motor skill were positively affected [33, 34, 35].

Thus, variations in estrogen appear to *selectively* affect cognitive pattern. Such effects have been confirmed by others [37, 88, 94]. Further evidence for the specificity of the effects of estrogen in the motor sphere comes from a report that in the high-estrogen midluteal phase, performance on a manual sequencing task was predictably enhanced, whereas on a male-favouring throwing accuracy task, there was no overall effect on performance [90]. Several studies measuring behavioural asymmetry have also suggested that right-hemisphere cerebral function is depressed, relative to left, in high-estrogen phases [72, 73, 88, 90].

Natural Fluctuations in Androgens

Testosterone levels vary systematically within men depending on season and time of day [15, 52, 76, 77, 97]. Levels in men, at least in the northern hemisphere, are higher in autumn than in spring. Autumnal peaks in T levels have corresponded to increases in sexual activity [84], which would increase the likelihood of late autumn conception. Conceivably, this could be a hold-over from our evolutionary past, when infants born in winter months might have been disadvantaged. T levels are also higher in early morning than later in the day [2, 15, 76].

Since we know from across-subject studies that men with T levels in the low normal range perform best on certain spatial tasks, it might be expected that we would see both seasonal and diurnal fluctuations in spatial ability. We found, as expected, that men performed better on a composite spatial measure in spring, when T levels were lower, than in fall [52]. Similarly, Moffat and Hampson [76] found performance on either a mental rotations task or a composite spatial measure to be worst in men in early morning, when T levels are highest. Note that not all "masculine" tests need be similarly affected. In our seasonal study, neither math reasoning nor throwing accuracy were substantially influenced by the season. This does not of course preclude early organizing effects on these skills.

Obviously, the size of the sex difference would also be expected to vary with time of day or season of the year, with sex differences smaller in the high–T phases. What little data we have suggests that this might be so. In the one study comparing time of day, scores on a mental rotation task did not differ between the sexes early in the day, but was significant later in the day [76]. These effects were not accounted for by changes in cortisol levels. In our data on seasonal changes on a spatial composite score, although the sex difference was significant in autumn, it was smaller than in spring [52]. Were seasonal and diurnal changes in men, combined with menstrual changes in women, studied *systematically*, there might be other extreme situations where sex differences are diminished or even disappear. However, this would not be expected to happen on a random basis.

Effects of Hormonal Manipulations

Studies on natural fluctuations in hormones, insofar as they yield correlational data, are subject to some reservations concerning attribution of causality, which manipulations are not. However, because hormone manipulations are nearly always carried out for therapeutic purposes, generalizing to non-clinical samples must be done cautiously. Also, hormone therapies are typically carried out in subjects older than those in whom natural fluctuations are studied. Most studies in which exogenous sex hormones are administered do not have measures of the resultant levels of hormones. Nonetheless, such data may be useful in confirming or raising questions about the inferences made from looking at natural fluctuations.

Estrogens

Postmenopausal women experience a sharp decline in production of ovarian hormones, chief of which is estrogen. In the last three decades it has been common for such women to undergo hormone replacement therapy, consisting of estrogens and usually progesterone, to combat hot flashes and dryness of skin. Many physicians also advise therapy to prevent osteoporosis. Hormone replacement therapy has been reported to reduce the probability of dementia after menopause [38], but later reports are equivocal [39, 111]. Many studies evaluating the effects of hormone therapy have emphasized memory function, but Duff and Hampson [17] argue that it is *working memory*, not simply short-term memory of any kind, which may benefit from estrogen. Working memory requires some manipulation of the information in short-term store.

Women on hormone replacement therapy usually have been taking it for prolonged periods, so it is not clear whether any beneficial effects are due to the immediate or long-term influence. In one study comparing medicated women during on-therapy and off-therapy phases, it was found that women performed better in the on-therapy phase on tests of manual sequencing and perceptual speed (both of which normally favour women), but not on two spatial tasks [53]. Yet the same women showed a more generalized cognitive advantage when compared with women not on therapy [50], suggesting that the immediate and long-term effects of estrogen therapy may be somewhat different.

Estrogen therapy, combined with anti-androgen therapy, is common in cases of transsexuals seeking sex re-assignment from *male to female*. This research is in its early stages, and further controls are needed, but there is some indication that male-favouring spatial ability may not be impaired by the treatment combination [75, 96], suggesting that in men such ability may be largely determined early in life. Neither were female-favouring tasks such as verbal fluency or perceptual speed enhanced. However, Miles *et al*. [75] report that scores on a verbal memory task (Paired Associate Learning) were better in the hormone-treated group than in a similar transsexual group who had not yet undergone hormone therapy.

Androgens

The interpretation of the effects of testosterone administration in men is complicated by the fact of differences in T levels across ages, with gradual declines from the 20's to the 70's [104]; and by the fact that the relation of T to spatial test scores is not linear, normal young men with lower levels performing better than those with higher levels (see above). One study reported that testosterone treatment in healthy men over 60 selectively improved performance, relative to a placebo group, on a visuo-constructional task (Block Design) in which blocks must be assembled to match a specified pattern [47]. Almost certainly, these men before treatment had T levels well below the mean of younger men, and thus below the "optimal" level.

In contrast, administration of T to a younger group of men, perhaps raising them to above-optimum levels, *depressed* scores on Block Design relative to a placebo group, at least in the initial weeks of treatment [81]. Verbal fluency and manual dexterity, however, usually better in women, were both improved. The interpretation of another study showing apparent improvement on a mental rotation task after T administration [1] is complicated by the fact that the T levels of the treated group appear lower initially than the comparison group. Since different studies use different assay methods and cite different measures, the elusive "optimal level" is usually difficult to determine.

Androgen treatment is also given to *female-to-male* transsexuals. Investigations into cognitive function so far have not used control groups who did not undergo therapy. Some studies [96, 101] report that F–M transsexuals showed improved scores on male-favouring mental rotation tasks, but female-favouring verbal fluency in one study was unchanged, and in the other got worse.

It would of course be of interest to demonstrate even short-lived cognitive effects of T administration in genetic females, since this might indicate an extension of the role of androgens in cognition into adulthood. However, apart from the lack of control subjects, we should also be cautious about the generalizability of such findings to the non-transgendered population. One study reported that the level of androgens was higher in F–M transsexuals than in control females [8], before any hormone treatment. It is reasonable to assume that individuals of either sex who wish to have their sex re-assigned have a somewhat different brain from those who do not. Some recent anatomical evidence to this effect also exists [56]. Thus, F–M individuals may have brains more susceptible to androgenic influences. Nevertheless, the transsexual population is potentially a rich source of information on the effects of sex hormones on cognition in adults.

Conclusions

There are consistent differences between men's and women's cognitive skills, indicating, whatever the source, that their nervous systems also differ. Cognitive sex differences appear well before puberty, are present across cultures, and to some extent parallel differences seen in nonhuman mammals. Nonetheless, we must keep in mind that in the larger comparative context, the similarities beween men's and women's brains far outweigh the differences.

There is substantial evidence in humans that androgens present before birth influence human cognitive abilities into adulthood, at least for certain spatial abilities of the kind at which men excel. Prenatal androgens may also depress certain functions on which women typically excel, but this is not well established. Across young adults, current levels of both androgens and estrogens are systematically related to cognitive pattern, apparently due in part to a stable individual baseline of these hormones. As well, fluctuations in sex hormones across daily, monthly and yearly cycles are accompanied by changes in several cognitive tests, especially those that are sexually differentiated – suggesting a continuing sensitivity of the nervous system to hormonal changes in the adult. The administration of exogenous hormones, usually for therapeutic purposes, at present provides modest support for such a proposition, but this is still a rich field of information to be tapped.

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(For more detailed discussion of sex differences in cognition, and their putative brain mechanisms, see Kimura D. Sex and Cognition 2000; MIT Press)

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