**Two minds**

The cognitive differences between men and women

By Bruce Goldman
Illustration by Gérard DuBois

When [Nirao Shah](https://med.stanford.edu/profiles/nirao-shah) decided in 1998 to study sex-based differences in the brain using up-to-the-minute molecular tools, he didn’t have a ton of competition. But he did have a good reason.

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“I wanted to find and explore neural circuits that regulate specific behaviors,” says Shah, then a newly minted Caltech PhD who was beginning a postdoctoral fellowship at Columbia. So, he zeroed in on sex-associated behavioral differences in mating, parenting and aggression.

“These behaviors are essential for survival and propagation,” says Shah, MD, PhD, now a Stanford professor of psychiatry and behavioral sciences and of neurobiology. “They’re innate rather than learned — at least in animals — so the circuitry involved ought to be developmentally hard-wired into the brain. These circuits should differ depending on which sex you’re looking at.”

His plan was to learn what he could about the activity of genes tied to behaviors that differ between the sexes, then use that knowledge to help identify the neuronal circuits — clusters of nerve cells in close communication with one another — underlying those behaviors.

At the time, this was not a universally popular idea. The neuroscience community had largely considered any observed sex-associated differences in cognition and behavior in humans to be due to the effects of cultural influences. Animal researchers, for their part, seldom even bothered to use female rodents in their experiments, figuring that the cyclical variations in their reproductive hormones would introduce confounding variability into the search for fundamental neurological insights.

But over the past 15 years or so, there’s been a sea change as new technologies have generated a growing pile of evidence that there are inherent differences in how men’s and women’s brains are wired and how they work.

Not how well they work, mind you. Our differences don’t mean one sex or the other is better or smarter or more deserving. Some researchers have grappled with charges of “neuro­sexism”: falling prey to stereotypes or being too quick to interpret human sex differences as biological rather than cultural. They counter, however, that data from animal research, cross-​cultural surveys, natural experiments and brain-imaging studies demonstrate real, if not always earthshaking, brain differences, and that these differences may contribute to differences in behavior and cognition.

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Nirao Shah studies how some genes at work in the mouse brain determine sex-specific behaviors, like the female trait of protecting the nest from intruders. He says most of these genes have human analogues but their function is not fully understood.
Photograph by Lenny Gonzalez

**Behavior differences**

In 1991, just a few years before Shah launched his sex-differences research, Diane Halpern, PhD, past president of the American Psychological Association, began writing the first edition of her acclaimed academic text, *Sex Differences in Cognitive Abilities.* She found that the ​animal-​research literature had been steadily accreting reports of sex-associated neuroanatomical and behavioral differences, but those studies were mainly gathering dust in university libraries. Social psychologists and sociologists pooh-poohed the notion of any fundamental cognitive differences between male and female humans, notes Halpern, a professor emerita of psychology at Claremont McKenna College.

In her preface to the first edition, Halpern wrote: “At the time, it seemed clear to me that any between-sex differences in thinking abilities were due to socialization practices, artifacts and mistakes in the research, and bias and prejudice. ... After reviewing a pile of journal articles that stood several feet high and numerous books and book chapters that dwarfed the stack of journal articles … I changed my mind.”

Why? There was too much data pointing to the biological basis of sex-based cognitive differences to ignore, Halpern says. For one thing, the animal-research findings resonated with sex-based differences ascribed to people. These findings continue to accrue. In a study of 34 rhesus monkeys, for example, males strongly preferred toys with wheels over plush toys, whereas females found plush toys likable. It would be tough to argue that the monkeys’ parents bought them sex-typed toys or that simian society encourages its male offspring to play more with trucks. A much more recent study established that boys and girls 9 to 17 months old — an age when children show few if any signs of recognizing either their own or other children’s sex — nonetheless show marked differences in their preference for stereotypically male versus stereotypically female toys.

Halpern and others have cataloged plenty of human behavioral differences. “These findings have all been replicated,” she says. Women excel in several measures of verbal ability — pretty much all of them, except for verbal analogies. Women’s reading comprehension and writing ability consistently exceed that of men, on average. They out­perform men in tests of fine-motor coordination and perceptual speed. They’re more adept at retrieving information from long-term memory.

Men, on average, can more easily juggle items in working memory. They have superior visuospatial skills: They’re better at visualizing what happens when a complicated two- or three-dimensional shape is rotated in space, at correctly determining angles from the horizontal, at tracking moving objects and at aiming projectiles.

Navigation studies in both humans and rats show that females of both species tend to rely on landmarks, while males more typically rely on “dead reckoning”: calculating one’s position by estimating the direction and distance traveled rather than using landmarks.

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Many of these cognitive differences appear quite early in life. “You see sex differences in spatial-visualization ability in 2- and 3-month-old infants,” Halpern says. Infant girls respond more readily to faces and begin talking earlier. Boys react earlier in infancy to experimentally induced perceptual discrepancies in their visual environment. In adulthood, women remain more oriented to faces, men to things.

All these measured differences are averages derived from pooling widely varying individual results. While statistically significant, the differences tend not to be gigantic. They are most noticeable at the extremes of a bell curve, rather than in the middle, where most people cluster. Some argue that we may safely ignore them.

But the long list of behavioral tendencies in which male-female ratios are unbalanced extends to cognitive and neuro­psychiatric disorders. Women are twice as likely as men to experience clinical depression in their lifetimes; likewise for post-traumatic stress disorder. Men are twice as likely to become alcoholic or drug-dependent, and 40 percent more likely to develop schizophrenia. Boys’ dyslexia rate is perhaps 10 times that of girls, and they’re four or five times as likely to get a diagnosis of autism spectrum disorder.

Could underlying biological differences — subtle though they may be for most of us — help explain these gaping
between-​sex imbalances in the prevalence of mental disorders and account for the cognitive and behavioral differences observed between men and women?

**How our brains differ**

The neuroscience literature shows that the human brain is a sex-typed organ with distinct anatomical differences in neural structures and accompanying physiological differences in function, says UC-Irvine professor of neurobiology and behavior Larry Cahill, PhD. Cahill edited the 70-article January/February 2017 issue of the *Journal of Neuroscience Research* — the first-ever issue of any neuroscience journal devoted entirely to the influence of sex differences on nervous-system function.

Brain-imaging studies indicate that these differences extend well beyond the strictly reproductive domain, Cahill says. Adjusted for total brain size (men’s are bigger), a woman’s hippo­campus, critical to learning and memorization, is larger than a man’s and works differently. Conversely, a man’s amygdala, associated with the experiencing of emotions and the recollection of such experiences, is bigger than a woman’s. It, too, works differently, as Cahill’s research has demonstrated.

In 2000, Cahill scanned the brains of men and women viewing either highly aversive films or emotionally neutral ones. The aversive films were expected to trip off strong negative emotions and concomitant imprinting in the amygdala, an almond-shaped structure found in each brain hemisphere. Activity in the amygdala during the viewing experience, as expected, predicted subjects’ later ability to recall the viewed clips. But in women, this relationship was observed only in the left amygdala. In men, it was only in the right amygdala. Cahill and others have since confirmed these results.

Discoveries like this one should ring researchers’ alarm buzzers. Women, it’s known, retain stronger, more vivid memories of emotional events than men do. They recall emotional memories more quickly, and the ones they recall are richer and more intense. If, as is likely, the amygdala figures into depression or anxiety, any failure to separately analyze men’s and women’s brains to understand their different susceptibilities to either syndrome would be as self-defeating as not knowing left from right.

The two hemispheres of a woman’s brain talk to each other more than a man’s do. In a 2014 study, University of Pennsylvania researchers imaged the brains of 428 male and 521 female youths — an uncharacteristically huge sample — and found that the females’ brains consistently showed more strongly coordinated activity between hemispheres, while the males’ brain activity was more tightly coordinated within local brain regions. This finding, a confirmation of results in smaller studies published earlier, tracks closely with others’ observations that the corpus callosum-— the white-matter cable that crosses and connects the hemispheres — is bigger in women than in men and that women’s brains tend to be more bilaterally symmetrical than men’s.

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“To some appreciable degree, these brain differences have to translate to behavioral differences,” says Cahill. Numerous studies show that they do, sometimes with medically meaningful implications.

A 2017 study in*JAMA Psychiatry* imaged the brains of 98 individuals ages 8 to 22 with autism spectrum disorder and 98 control subjects. Both groups contained roughly equal numbers of male and female subjects. The study confirmed earlier research showing that the pattern of variation in the thickness of the brain’s cortex differed between males and females. But the great majority of female subjects with ASD, the researchers found, had cortical-thickness variation profiles similar to those of typical non-ASD males.

In other words, having a typical male brain structure, whether you’re a boy or a girl, is a substantial risk factor for ASD. By definition, more boys’ than girls’ brains have this profile, possibly helping explain ASD’s four- to fivefold preponderance among boys compared with girls.

**Why our brains differ**

But why are men’s and women’s brains different? One big reason is that, for much of their lifetimes, women and men have different fuel additives running through their tanks: the sex-steroid hormones. In female mammals, the primary additives are a few members of the set of molecules called estrogens, along with another molecule called progesterone; and in males, testosterone and a few look-alikes collectively deemed androgens. Importantly, males developing normally in utero get hit with a big mid-gestation surge of testosterone, permanently shaping not only their body parts and proportions but also their brains. (Genetic defects disrupting testosterone’s influence on a developing male human’s cells induce a shift to a feminine body plan, our “default” condition.)

In general, brain regions that differ in size between men and women (such as the amygdala and the hippocampus) tend to contain especially high concentrations of receptors for sex hormones.

Another key variable in the composition of men versus women stems from the sex chromosomes, which form one of the 23 pairs of human chromosomes in each cell. Generally, females have two X chromosomes in their pair, while males have one X and one Y chromosome. A gene on the Y chromosome is responsible for the cascade of developmental events that cause bodies and brains to take on male characteristics. Some other genes on the Y chromosome may be involved in brain physiology and cognition.

Scientists routinely acknowledge that the presence or absence of a single DNA base pair can make a medically important difference. What about an entire chromosome? While the genes hosted on the X chromosome and the Y chromosome (about 1,500 on the X, 27 on the Y) may once have had counterparts on the other, that’s now the case for only a few of them. Every cell in a man’s body (including his brain) has a slightly different set of functioning ​sex-​chromosome genes from those operating in a woman’s.

Sex-based differences in brain structure and physiology reflect the alchemy of these hormone/receptor interactions, their effects within the cells, and the intermediating influence of genetic variables — particularly the possession of an XX versus an XY genotype, says Cahill.

**Zeroing in on neural circuits**

Shah’s experiments in animals employ technologies enabling scientists to boost or suppress the activity of individual nerve cells — or even of single genes within those nerve cells — in a conscious, active animal’s brain. These experiments have pinpointed genes whose activity levels differ strongly at specific sites in male versus female mice’s brains.

What would happen, Shah’s team wondered, if you knocked out of commission one or another of these genes whose activity level differed between male and female brains? They tried it with one of their candidate genes, turning off one that was normally more active in females.

Doing this, they found, totally shredded mouse moms’ willingness to defend their nests from intruders and to retrieve pups who had wandered away — maternal mandates that normal female mice unfailingly observe — yet had no observable effect on their sexual behavior. Torpedoing a different gene radically reduced a female mouse’s mating mood, but males in which the gene has been trashed appear completely normal.

All this points to a picture of at least parts of the brain as consisting of modules. Each module consists of a neural or genetic pathway in charge of one piece of a complicated behavior, and responds to genetic and hormonal signals. These modules — or at least some of them — are masculinized or feminized, respectively, by the early testosterone rush or its absence. The mammalian brain features myriad modules of this sort, giving rise to complex combinations of behavioral traits.

Which is not to say every man’s or woman’s brain looks the same. Our multitudinous genetic variations interact with some of our genes’ differential responsiveness to estrogens versus androgens. This complicated pinball game affects goings-on in at least some of the brain’s neural circuits and in whatever little piece of behavior each of these neural circuits manages.

“We think gender-specific behavior is a composite of all these modules, which, added up, give you your overall degree of maleness and femaleness,” says Shah.

Consider the genes Shah has isolated whose activity levels differ significantly in the brains of male and female mice. “Almost all of these genes have human analogues,” he says. “We still don’t completely understand their function in human social behavior. But when we looked at publicly available databases to find out what we do know about them, we found a surprising number that in humans have been linked with autism, alcoholism and other conditions.”

Bigger imaging studies and imaginative animal research now in the works promise to reveal much more about humanity’s inherent — although by no means uniform, and often not substantial — sex-associated cognitive differences and vulnerability to diseases.

Trying to assign exact percentages to the relative contributions of “culture” versus “biology” to the behavior of free-living human individuals in a complex social environment is tough at best. Halpern offers a succinct assessment: “The role of culture is not zero. The role of biology is not zero.”