The Trouble with Sex Differences

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Sex differences in the brain are real and clinically important but often grossly distorted in popular discourse. Considering the public's deep fascination with sex difference research and its impact on issues from mental health to education and workplace equity, neuroscientists should pay greater heed to its misappropriation and to studying how gender enculturation shapes neural function.

Neuroscientists are in a difficult bind when it comes to studying and reporting male-female differences. On the one hand, many features of the brain and behavior do vary by sex, and so researchers—whether studying humans or other animals—should include both male and female subjects and analyze their data with sex as a possible covariate. Just as medical research for too long overlooked women's health issues, current research cannot ignore sex differences in behavior or brain anatomy, physiology, and neurochemistry, especially considering the different prevalence of many psychiatric and developmental disorders in males and females (Cosgrove et al., 2007).

On the other hand, research findings about sex differences have been distorted and exploited by nonscientists to an extraordinary degree—perhaps second only to research on weight loss. Beginning with the wildly popular 1992 book *Men Are from Mars, Women Are from Venus*, public discourse has been saturated with faulty factoids about men, women, boys, and girls that have settled deeply into society's collective understanding of gender roles. From education and parenting to corporate leadership and marital harmony, so-called scientific findings about the male and female brain have been used to validate various stereotypical practices that are discriminatory to both sexes.

Consider that over 500 public schools in the U.S. now administer single-sex academic classes, fueled in large measure by claims about sex differences in the brain and neuropsychological function, according to the website of the National Association for Single-Sex Public Education (http://www.singlesexschools.org). For example, a recent application for a public charter school in Palm Beach County, Florida that centered on single-sex instruction for kindergarten through eighth grade (Rogers, 2011) states under its "Guiding Principles" that "the brain develops differently," which is then further explained, "In girls, the language areas of the brain develop before the areas used for spatial relations and for geometry. In boys, it's the other way around." The next heading is titled "The brain is wired differently" and continues, "In girls, emotion is processed in the same area of the brain that processes language. So, it's easy for most girls to talk about their emotions. In boys, the brain regions involved in talking are separate from the regions involved in feeling."

These statements are in reference to the 2005 book *Why Gender Matters* by Leonard Sax, an influential physician who uses claims about brain and sensory differences between boys and girls to lobby for gender segregation in schools. As he further elaborates in an article for teachers (Sax, 2005):

> Researchers at Virginia Tech used sophisticated electrophysiologic imaging of the brain to examine brain development in 508 normal children ranging in age from 2 months to 16 years. These researchers found that while the areas of the brain involved in language and fine-motor skills such as handwriting mature about four years earlier in girls than in boys, the areas of the brain involved in geometry and spatial relations mature about four years earlier in boys than in girls. When it comes to learning geometry, the brain of the average 12-year-old girl resembles the brain of the average 8-year-old boy. When it comes to writing poetry, the brain of the average 12-year-old boy resembles the brain of the average 8-year-old girl.

In fact, the Virginia Tech study, which was a cross-sectional analysis of development of the electroencephalogram (Hanlon et al., 1999), found something quite different: a spiraling pattern of cortical maturation thought to reflect multiple waves of synaptic pruning. The study did reveal a difference between boys and girls, but it was a matter of cyclic phase, not a years-long developmental delay in either sex. The same brain areas showed recurrent developmental spurts in both sexes, making it impossible to say that one area matures earlier than the other in either boys or girls. Nonetheless, the seeming scientific validation of a dramatic sex difference in brain maturation makes a great story, which is why *TIME Magazine* repeated Sax's above misinterpretation almost verbatim in a February 27, 2005 cover story about women's aptitude for math.

Leonard Sax is not alone in misrepresenting the neuroscience of sex differences. Many examples appear in a 2008 book, *Leadership and the Sexes*, by best-selling author and corporate consultant Michael Gurian (Gurian and Annis, 2008). Gurian and coauthor Barbara Annis introduce their book on so-called "neuro-leadership" with the startling claim that:

> Men have approximately six and a half times more gray matter related

> to cognition and intelligence than women have, and women have nearly ten times more white matter related to cognition and intelligence than men have … (pp. 32–33).

The notion of a 10-fold sex difference in white matter or a 4-year gap in brain maturation would be laughable, if it were not taken seriously by school principals and corporate CEOs. Gurian and Annis continue, "The gray/white difference is one reason men … like to focus on one task and one task only: 'Just the facts, please' … whereas women … [are] wired for … relationship-friendly work." Virtually the same interpretation—and 10-fold, 6.5-fold claims—were repeated in a medical segment on television's CBS Early Show, broadcast on September 22, 2010 and still available on the Web. This is the familiar "men are rational, women are emotional" stereotype, dressed up in the authority of neuroscience, much to the detriment of workplace and classroom equality.

Space will not allow me to expose every claim about male and female brains distorted in popular discourse (but for more on educational misuses, see Eliot, 2011). The good news is that a few scientists have begun publicly checking some of the more outrageous assertions. Writing in his Language Log website (http://languagelog.ldc.upenn.edu), linguist Mark Liberman has deconstructed several of Leonard Sax's claims about sex differences in hearing and vision. Liberman has also taken on the neurononsense of psychiatrist Louann Brizendine, author of the highly popular book, *The Female Brain*, which opens with the bold confabulation (Brizendine, 2006):

> The female brain has tremendous unique aptitudes—outstanding verbal agility, the ability to connect deeply in friendship, a nearly psychic capacity to read faces and tone of voice for emotions and states of mind, and the ability to defuse conflict. All of this is hard-wired into the brains of women. These are the talents women are born with that many men, frankly, are not. (p. 8).

In short, popular portrayals of sex differences in the brain are riddled with claims that are highly extrapolated, misinterpreted, or just made up but are nonetheless used to justify the differential treatment of boys and girls in school or men and women in the workplace. If educators or corporate consultants extolled similar stories about neural differences between blacks and whites, scientists would be quick to expose their flaws. Somehow, exaggerated claims about sex differences are more culturally acceptable, but the misuse of research to validate stereotypes of any sort is dangerous, so neuroscientists need to exert more care in presenting the true magnitude and multiple causes of sex differences in the brain and behavior.

Sex Differences in the Human Brain Are Still Poorly Defined

Facile myths about male-female brain differences are especially disturbing considering the large amount of data now available on the topic. A recent PubMed search for the terms "brain" and "human" and "sex difference" turned up over 5,600 papers. Still, it is surprising how little consensus has emerged from this research. A few structural differences between male and female brains have been clearly demonstrated (Cosgrove et al., 2007): males' brains are about 11% larger than females' and have a slightly higher proportion of white matter, whereas female brains have a correspondingly larger proportion of gray matter in most cortical areas (contrary to what CBS News has to say!). The difference in brain mass or volume reflects the overall sexual dimorphism between males and females. Adult men are 18% heavier and 9% taller than women, according to the National Center for Health Statistics. Boys are also heavier and taller at birth and through most of development, except between 7 and 11 years, when girls hit their prepubertal growth spurt ahead of boys—the same age range when girls' gray matter stops expanding ahead of boys'. Other organs, like the liver, heart, and kidney, show similar-magnitude differences between the sexes, though they are much less studied than the brain.

Beyond these global differences, sex differences in specific brain structures have been more difficult to verify. One widely publicized notion is that the corpus callosum is proportionally larger in female brains. It began with a tiny postmortem study (DeLacoste-Utamsing and Holloway, 1982) showing a statistically marginal effect, which was nonetheless published in *Science* and made famous by *TIME Magazine*, *Newsweek*, and other popular media. Though thoroughly challenged by a meta-analysis of 49 studies, which collectively showed no significant sex difference in corpus callosum volume or splenial shape (Bishop and Wahlsten, 1997), the claim lives on among sex difference entrepreneurs like Michael Gurian (see also http://www.girlslearndifferently.com), often as an explanation for females' mythically superior "multitasking" abilities. Similarly, the planum temporale, a structure involved in receptive language, is often claimed to be more symmetrical between left and right sides of the brain in females as compared to males, when in fact, meta-analysis of 13 studies found no significant sex difference in its symmetry (Sommer et al., 2008).

Moving on to more reliable differences, sexual dimorphism in the third interstitial nucleus of the anterior hypothalamus (INAH3) has now been confirmed by four different laboratories (Garcia-Falgueras and Swaab, 2008), although the function of this tiny (0.1 mm^3) structure, visible only in postmortem tissue, remains unclear. Much more data are available for structures clearly visible by MRI, but surprisingly few findings have been convincingly replicated thus far. Structures that do seem to exhibit reliable volumetric sex differences (at least during certain developmental ages) include the amygdala, caudate, and portions of the orbitofrontal cortex, although a full review of these complex findings is beyond the scope of this article.

Data acquired by fMRI are equally voluminous, but very few sex differences in brain function or connectivity have been confirmed through systematic review. An early claim—that in processing language, men are left lateralized whereas women exhibit more symmetrical activation of left and right hemispheres—has been largely refuted through meta-analysis (Sommer et al., 2008). However, because the early finding received high-profile coverage in *The New York Times*, *Newsweek*, and other media, the claim continues to percolate in popular writings, such as a website promoting all-girls boarding schools that states, "Men tend to use only one brain hemisphere at a time, but women employ 'whole brain' thinking" (http://www.girlslearndifferently.com). Although the issue is far from resolved—some evidence suggests that a sex difference in degree of lateralization may pertain to more specific types of language tasks—any difference in language or other functional lateralization between males and females is clearly much subtler than these popular portrayals.

Indeed, one reason for the difficulty in identifying reliable brain sex differences is probably because behavioral sex differences themselves are mostly modest in magnitude (Hyde, 2005). For example, verbal abilities differ between females and males by just 0.1 standard deviation, so it is not surprising that sporadic findings of sex differences in language-related neural activation have failed to hold up to replication. Even for one of the largest sex differences in cognition, visuospatial ability, it has been challenging to identify consistent differences in fMRI activation patterns between males and females (Clements-Stephens et al., 2009).

Of course, sex differences are also found at cellular and molecular levels of the central nervous system (Cosgrove et al., 2007). But whether it involves gene expression, neuronal signaling, gross structure, or regional blood flow, every brain-related sex difference is not necessarily behaviorally relevant. As Geert De Vries (2004) has shown, sex differences in neural circuitry or neurochemistry often reflect compensation for genetic and hormonal differences and actually end up making male and female behavior more similar than different. McCarthy and Arnold (2011) reinforce this point in a recent review on the complexity of brain sexual differentiation, in which they importantly note that neuroscientists have yet to identify distinct "male" and "female" neural circuits underlying any sexually differentiated behavior, in spite of widespread belief in such circuits.

Role of Cultural Learning in Brain Sexual Differentiation

Unfortunately, this message is not getting through to the public. Beyond the errors and extrapolations in popular accounts of brain sex differences lies an even deeper misperception, typified in the book *A Gendered Choice*, by single-sex school advocate David Chadwell. As rationale for sex-segregated teaching methods, Chadwell (2010) asks teachers to consider "biological brain differences, otherwise referred to as hard wiring" (p. 8). The notion that sex differences in the brain, because they are biological, are necessarily innate or fixed is perhaps the most insidious of the many public misunderstandings on this topic. Neuroscientists know that, in the absence of proof of genetic or hormonal influence, any sex difference in adult neural structure or function could be shaped through experience, practice, and neural plasticity. But even some neuroscientists overlook such possibilities, limiting the Discussion sections of their papers to speculation about evolution and gonadal hormones and neglecting to mention the lifetime of gender-differentiated experience that may shape male-female differences in brain function or microstructure. This bias is likely fueled by the predominance of animal research, in which genetic and hormonal mechanisms can be elegantly analyzed. However, even in nonhuman primates, there is evidence for cultural variation in gender-typical play and the suggestion that young females learn gender-typical behavior by imitating their mothers more than young males do (Kahlenberg and Wrangham, 2010).

Recent epigenetic studies suggest further ways in which experience may shape persistent sex differences in the brain and behavior. Rat dams treat their male pups to a greater amount of anogenital grooming than their female pups, and such differential maternal nurturing has been found to affect methylation of the estrogen receptor α gene in both the preoptic hypothalamus and the amygdala, potentially influencing behaviors like social recognition and juvenile play fighting (Edelmann and Auger, 2011). Variations in such grooming also are known to influence development of the hypothalamic-pituitary-adrenal axis, stress responses, and later learning via altered methylation of promoter sequences in the glucocorticoid receptor gene (Fish et al., 2004), although such effects have not been systematically compared between male and female pups.

Does differential nurturing and socialization impact brain sexual differentiation in human children? Little research has addressed this issue thus far, even though cultural factors undoubtedly exert a stronger influence over human development than in other species. The fact that, in certain clinical situations, children can be raised to accept a gender identity opposite to their chromosomal sex or prenatal hormone exposure reveals substantial plasticity in psychological gender and its neural underpinnings. In a different vein, research on stereotype threat illustrates the potency of gender enculturation on cognitive and neural function. Developmental psychologists have long appreciated the influence of parent and peer socialization in intensifying behavioral sex differences, but neuroscientists have yet to investigate how such experiential differences impact the developing brain. This gap is especially striking considering the explosion of research in social neuroscience and the growing appreciation of how other cultural components (e.g., religious or ethnic practices) impact neurobehavioral function.

Future Directions

Sex difference in the brain is an important and complex topic, but little of this complexity has penetrated the public discourse. Neuroscientists cannot ignore sex as a possible covariate in most types of studies, from the molecular to the behavioral level. But we must also be careful about communicating the true magnitude and deep intricacy of brain sexual differentiation to stem the widespread and potentially harmful misuse of research in this area.

Whether studying animals or humans, behavior or molecules, neuroscientists should include subjects of both sexes and report their findings, different or not. Too many studies exclude one or the other sex, often with no scientific justification. Even among studies that do include both sexes, too many fail to report data by sex, leading to a file-drawer problem. Such omissions are possibly more common when there is no significant difference between sexes, because scientists and editors are generally uninterested in negative findings. But such omissions distort the published literature and lead to biased reviews and meta-analyses. Although it is difficult to publish a negative result, researchers need not dedicate an entire paper to it; a single sentence or brief paragraph in the Results section of their primary study can suffice to make quantitative data about sex differences or similarities publicly available.

With regard to human research in particular, new insight may come from studies that are beginning to analyze participants by psychological gender role identity, as opposed to just biological sex. For example, Bourne and Maxwell (2010) found that for both males and females, participants' self-assessed "masculinity" added considerable predictive power to the relationship between emotion perception and functional brain lateralization. A handful of other behavioral and imaging studies have similarly found that a continuous variable akin to "gender"—that is, relative masculinity or femininity assessed using the Bem Sex Role Inventory—maps more closely to brain and psychological function than the dichotomous variable "sex." Because gender role identity is likely more influenced by life experience than biological sex, such findings may help identify particular types of education, practice, and training that contribute to average male-female differences in both the brain and behavior.

Despite the complexity, neuroscientists can and must persevere in studying sex differences, especially considering males' and females' different vulnerabilities to many developmental and psychiatric disorders. Done correctly, research on sex difference provides a fascinating window into the nature-nurture interaction that fuels all of brain and behavioral development. Done incorrectly—that is, without consideration of both social and genetic/hormonal influences and without attention to the careless extrapolations in public discourse—this science can reinforce some of the worst biological essentialism.

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