Sex differences in brains reflect disease risks

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Women's brains are different from men's. That's not news. What is news is that the differences are smaller than most people believe. They are not big enough to say that one sex is smarter or better at math than the other.

What is also news is that the small differences can be significant when it comes to memory, arousal, reasoning, and risk of some diseases. The latter include depression, anxiety, schizophrenia, drug abuse, Alzheimer's, diabetes, and heart disease.

"Brain differences, though small, help us to understand the nature of sex differences in disease, and thus will hopefully aid in devising sex-specific treatments and prevention strategies," notes Jill Goldstein, a professor of psychiatry and medicine at Harvard Medical School (HMS).

Here are some examples. Medical experts advise men to take a baby aspirin a day to help protect them against heart attacks. But Julie Buring, a Harvard professor of medicine who works at the Brigham and Women's Hospital in Boston, found that aspirin does not work the same in women.

More women suffer from Alzheimer's disease than men, and it's not just because they live longer. They also have a much greater risk than men for contracting type 1 diabetes, rheumatoid arthritis, lupus, and other diseases caused by a defective metabolic and immune system. Premenopausal women recover from stroke sooner and with less disability than men of the same age or postmenopausal women.

Why? Goldstein and her many colleagues at the Connors Center for Women's Health and Gender Biology at Brigham and Women's are working on answers. They have found a number of brain regions that are significantly different in size in men and women. This has led many people to think that such variations result in sex differences in function and behavior, such as memory and emotionality.

For example, part of the hippocampus at the center of the brain and other areas at the front of the brain contribute to short-term memory, and are larger in women. Does this mean they have better working memories? Other areas in the brain, believed to be seats of mating and arousal, grow larger in males, leading to conclusions that men are more aggressive. "This is not always the case," Goldstein points out. "Size alone does not drive function."

In tests of short-term memory, Goldstein and her colleagues showed that although brain activity differs between sexes, their short-term memory performance is the same. "Such results show that male and female brains can take different actions to arrive at the same behavioral response," she notes. However, these variations in activity may account for a small advantage that women have over men in verbal fluency and speed of perception.

Stressing research

Research to date leads to the conclusion that more variability exists in the size of brain regions and behavior within each sex than between the sexes. "The great value in exploring this variability is to understand the role that these differences play in certain diseases," Goldstein explains.

Another conclusion is that specific behaviors are not driven solely by one region of the brain, notwithstanding those neat diagrams of how the brain works in popular magazines and Sunday supplements. "No single

brain region controls a particular behavior," is the way Goldstein puts it. "The hippocampus is important in memory but other brain regions are involved. Most functions are regulated by a network of brain regions."

Both hormones and genes drive these subtle but significant sex differences in human brains from the womb to puberty and beyond. Goldstein's team studies normal sex differences in order to better understand what goes wrong in mental disorders. The tools they use include scanning techniques that produce images of activity in various brain regions as men and women engage in various tasks.

In a series of experiments, Goldstein's team investigated sex differences in response to stress. While in a scanner, women watched a series of pictures showing both neutral scenes, like cows grazing in a pasture, and those that stimulate high arousal, like horrible car crashes. The women were tested at the beginning of their menstrual cycles and again at ovulation, after eggs leave the ovaries.

Stress regions showed greater activity during the beginning of the cycle than during ovulation, but, surprisingly, the women felt no change in mood. When the same brain networks were examined in men, their brains looked similar to those in women at the cycle start. Goldstein and her team are now mapping out which hormones, like estrogen and progesterone, are associated with the differences.

"This is only one of many studies to identify the role of hormones and genes in regulating sex differences in response to stress," Goldstein notes. "We hope that these findings help us understand the higher rates of depression and anxiety in women than in men." Such findings could also shed light on the diminished sensitivity to trauma in men with depression and anxiety disorders. This new understanding of normal reactions to stress is the first step in putting together sex-specific treatments for women and men who must deal with these mental

disorders.

As an aside, the natural lessening of anxiety during ovulation may increase a woman's availability, receptivity, and desire to mate during this crucial time. "That idea goes beyond what our data shows us," admits Goldstein, "but it's reasonable to think it may be adaptive for survival of the species."

What's more, the brain's stress response network has been implicated in other mental disorders, such as psychosis in which a person loses contact with reality, and in medical problems that include heart disease and diabetes. Stress and anxiety disorders are co-companions with a host of physical problems that show critical sex differences. Studies are under way by Goldstein and others to understand the connections and, perhaps, find effective ways to treat them.

Source: By William J. Cromie, Harvard Medical School

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