

Neurobiologist proposes 'The end of sex as we once knew it'

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(PhysOrg.com) -- Women are not from Venus any more than men are from Mars. But even though both sexes are perfectly terrestrial beings, they are not lacking in other differences. And not only in their reproductive organs and behavior, either, but in such unsexy characteristics as the propensity for drug abuse, fine motor control, reaction to stress, moods and many brain structures.

According to Rockefeller University's Bruce S. McEwen, who has spent over four decades studying how hormones regulate the brain and nervous system, deciphering the substantial but often ignored differences between the sexes is crucial to developing more effective personalized medicine. In an upcoming issue of *Physiology and Behavior*, he emphasizes that none of the findings suggest one sex is stronger or more intelligent, and in many cases, the differences discovered raise more questions than they answer.

In spite of the subject's political sensitivities, McEwen says, it is ignored at our collective peril. "It's amazing how ignorant people are about this," says McEwen, the head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology. "Medicine is clueless as to how males and females really differ from one another. They have a very mechanistic view of disease and they tend to think it always works the same way in both sexes. That can be dangerous."

His article, "The end of sex as we once knew it," is the introduction to a special *Physiology and Behavior* issue devoted to sex differences and

outlines increasing research into the pervasive role of hormones in the brain. Men and women differ in crucial brain structures such as the hippocampus, which is known to be critical to learning and memory, and the corpus callosum, which permits the brain's two hemispheres to talk to one another and integrate. Work by McEwen's lab and colleagues elsewhere has identified receptors for estrogen and other hormones in many parts of the rat brain and has shown that they do not reside in the neurons' nuclei, but rather in the dendrites, synapses and other processes. So the hormones don't act directly on the genes inside the nuclei, but only indirectly through other signaling pathways, recent experiments suggest. In most cases, scientists do not yet know what the behavioral repercussions of this extensive hormone activity in the brain are, but they are likely to be the source of real differences.

Scientists doubted that hormones could even enter the brain until the 1960s, and since then, most have maintained a dogma that they are only involved in reproductive aspects of brain function, McEwen says. On this question, McEwen is a proud heretic. "We know that sex hormones are active in the entire nervous system, both in sexual differentiation and in terms of the activation of neurological, cognitive and emotional processes," McEwen says.

The debate is not just academic, either. Given the manifold roles hormones seem to play in the brain, and the differences in the hormones of men and women, it is likely that drugs and other treatments for some disorders should be tailored differently for the two sexes, says Elizabeth Waters, a postdoctoral associate in McEwen's lab.

"Females aren't males and it's really important to understand the differences," Waters says. "It is important to recognize that the female brain acts differently. It may be abstract now, because it's a basic science question, but once we understand hormones in a healthy brain we can go on to understand what changes when the brain is diseased or needs to be

treated with drugs.”

“I feel like this critical gap in knowledge is hindering our moving forward and developing better drugs for the clinic,” she says. “We do a disservice to everyone by not being able to treat women, as well as men, as effectively as possible.”

More information: *Physiology and Behavior* online: December 13, 2008 - [dx.doi.org/10.1016/j.physbeh.2008.12.002](https://doi.org/10.1016/j.physbeh.2008.12.002)

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