MedicalXpress

Gender bias in research ignores estrogen's effect on the brain

April 19 2011

(PhysOrg.com) -- A recent study by UC Berkeley neuroscientists Emily Jacobs and Mark D'Esposito highlights the need to include female animals in research studies, since sex hormones have an impact on how females respond. The research, published April 6, showed that estrogen levels affected how women scored on memory tests.

Few people would argue that the rise and fall of hormone levels, whether the hormone in question is estrogen or testosterone, can have a powerful influence on everything from emotions and mood to energy levels and fluctuations in weight. It's therefore somewhat surprising to learn that scientists do not generally take hormonal differences into consideration when performing animal-based research.

"Biomedical research shows a striking sex bias," says Emily Jacobs, Ph.D., a Robert Wood Johnson Foundation (RWJF) Health & Society Scholar (2010-2012). "The National Institutes of Health have guidelines about the inclusion of women in human studies, but those rules don't extend to animal research. In the biological sciences, animal-based studies rely predominantly on male animals and in the fraction of studies that include females, the data are rarely analyzed by sex," she says.

That's a very important issue, Jacobs explains, because "human models of brain function and neurological disorders are informed by work conducted at the animal level. But when research is carried out exclusively in male animals and then generalized to females, the conclusions are at best, incomplete and at worst, incorrect. Therefore,

it's unjustified to assume that beyond the reproductive system, sex differences don't exist. There is an abundance of data to the contrary."

Jacobs and her collaborator and RWJF mentor, Mark D'Esposito, Ph.D., director of the Henry H. Wheeler Jr., Brain Imaging Center at the University of California, Berkeley, explored the relationship between estrogen and cognition in the study, "Estrogen Shapes Dopamine-Dependent Cognitive Processes: Implications for Women's Health," published in the April 6, 2011 issue of *The Journal of Neuroscience*.

A neuroscientist who recently completed her studies at the University of California, Berkeley, Jacobs' work provides an important example of why studying females yields insights about brain function that would be overlooked in a male-only study. Her research focused on working memory, a cognitive function that underlies problem-solving and reading comprehension. Working memory relies on precise levels of dopamine in the brain's frontal lobe. Both too little and too much of the neurochemical impairs performance; moderate amounts result in optimal performance. Since estrogen has been shown to enhance dopamine, Jacobs theorized that estrogen levels may affect cognition.

Hormones and the Brain

"For our study, we tracked 24 women over a period of five months, monitoring their menstrual cycles and measuring brain activity when estrogen levels were naturally high and low," Jacobs says. "We found that estrogen impacts working memory, but the effect is not the same in all women. Moreover, the direction of estrogen's effect—whether it enhances or impairs performance—was highly dependent on a woman's baseline level of dopamine." Women with naturally low dopamine showed a cognitive boost when estrogen levels were elevated, while women with naturally high dopamine performed better when estrogen levels were low.

This line of research has several implications, and one of the most critical relates to the use of dopaminergic drugs (medications that manipulate dopamine levels), such as Ritalin for ADHD and l-DOPA for Parkinson's disease. "If a boy and a girl present with ADHD and you give them both a drug such as Ritalin, the boy and the girl are going to have very different biological responses to the medication," Jacobs says.

Another recent study, conducted by Annaliese Beery, Ph.D., a former Robert Wood Johnson Health & Society Scholar (2008-2010), indexed all studies conducted in mammals in 2009, in more than 2,000 articles, 40 journals and across ten disciplines. Eight of the ten disciplines reviewed showed a bias toward relying predominantly on male animals. For this reason, "sex bias in basic science, including pharmacology and neuroscience, may limit progress in public health, since results gleaned from males are being used to draw conclusions about everyone's health," Jacobs explains.

"Examining sex differences and, more narrowly, estrogen's action in the frontal lobe, represents a greatly understudied area of research," Jacobs says. "While the Women's Health Initiative, currently the largest study of its kind on women and estrogen, included a measure of global cognition, it was a very general measure and did not have the precision to reveal estrogen's full impact on brain function."

Learning More—New Research

"It's clear that sex differences and hormone effects stretch well beyond the reproductive system. In my upcoming work, I will focus on clarifying the impact estrogen has on brain function with the hope of harnessing that knowledge for improved medical treatment for women," she says. "For both studies though, I credit my RWJF term with giving me the independence to pursue a unique research trajectory, while simultaneously providing a forum for exploring the implications of my

research for society.”

Overall, Jacobs says her goal is “to help change the often unquestioned habit of relying almost exclusively on male animals in basic science, a practice that ultimately ignores the health needs of women.”

Provided by University of California - Berkeley