

Why Women Get More Migraines Than Men

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For every man with a migraine, three women are struck by the severe headaches that often come with nausea, sensitivity to light and sound, and aura. That means a staggering 18 to 25 percent of women suffer from migraines, making it one of the most common disabling conditions faced by women around the globe.

This 3-to-1 ratio raises the obvious question: Why? The reason, suggest researchers at UCLA, is that women may have a faster trigger than men for activating the waves of brain activity thought to underlie migraines. If the theory is correct, this triggering mechanism may be a new target for migraine treatment.

Reporting in the Annals of Neurology, currently online, Dr. Andrew Charles, director of the Headache Research and Treatment Program in the UCLA Department of Neurology; Dr. Kevin C. Brennan, a clinical and research fellow in Charles' lab; and colleagues used a mouse model to discover a big difference between males and females with regard to a phenomenon called cortical spreading depression (CSD), which is thought to be a chief culprit in causing migraines. In a separate study, to be published in the September issue of the Journal of Headache and Pain, the researchers report preliminary success in preventing migraines using memantine, a drug that blocks CSD waves.

Migraines were once thought to be caused primarily by constriction and dilation of blood vessels, Charles said. Now, thanks to various neuroimaging techniques, it has been shown that migraines may begin as a problem of brain excitability. Patients with migraines show cortical



spreading depression, which is characterized by dramatic waves of activity that spread across the surface of the brain. CSD may in turn trigger not only the pain of migraine but the visual symptoms, nausea, dizziness and difficulty concentrating so common in migraine patients.

Brennan, working in Charles' lab, used imaging techniques to visualize the initiation and spread of CSD in anesthetized male and female mice. Female mice showed a significantly lower threshold for CSD when compared with males. In other words, it was much easier to evoke the waves of brain activity believed to underlie migraine in females than it was in males.

"The results were very clear," said Charles. "The strength of the stimulus required to trigger CSD in males was up to two or three times higher than that required to trigger the response in females."

A variety of factors may reduce the CSD threshold in both sexes, making them more susceptible to migraines — these include genes, hormones and environmental triggers such as stress, diet, changes in sleep patterns and a host of others. While it is known that migraines in females fluctuate with the menstrual cycle and are more frequent during the menstrual period, the study results appear to be independent of a specific phase of the cycle, according to Charles.

"We didn't monitor the estrous cycle in the female mice, so it's likely we sampled from different estrous phases in different animals," Charles said. "Yet we still found a consistent difference in the CSD threshold between males and females. Our results suggest that the female brain has an intrinsic excitability that predisposes them to migraine that may not be simply linked to a specific phase of the menstrual cycle."

These results are exciting, Charles said, because they may represent a model for understanding the mechanisms underlying the increased



prevalence of migraine in women. In addition, they add to growing evidence that CSD is a key target for the development of new migraine treatments.

In a separate study, the researchers identified what they hope will eventually be a new treatment option for migraine. They found that a medication called memantine (brand name Namenda), which is currently approved for the treatment of Alzheimer's disease, inhibits CSD and appears to be a highly effective treatment for some patients with frequent migraine. In the retrospective study, 54 patients who were treated with memantine for at least two months were asked to fill out a survey describing their experience with the medication. The majority, 36, reported a substantial reduction in estimated headache frequency. These were all patients who had previously tried other treatments without success.

While Charles cautioned that these results need to be confirmed with a larger study, the encouraging results are an example of how new insights into the basic mechanisms of migraine are leading to novel approaches for therapy for the hundreds of millions of individuals worldwide who suffer from this disabling condition.

The full text of the journal article can be found at www3.interscience.wiley.com/cgibin/fulltext/114230925/HTMLSTART

Source: UCLA

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