Hormones increase frequency of inherited form of migraine in women

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Familial hemiplegic migraine (FHM) is an inherited form of severe migraine that is accompanied by visual disturbances known as aura. As with other types of migraine, it affects women more frequently than men. Most cases of FHM are caused by mutations in the CACNA1A gene, but whether these lead to spreading depression, the event in the brain that suppresses nerve cell activity and that has been linked to nongenetic forms of migraine with aura, has not been determined.

However, Cenk Ayata and colleagues, at Massachusetts General Hospital, have now generated data in mice that address this issue as well as provide insight into the reasons why FHM affects women more frequently than men.

In the study, mice expressing either one of two different CACNA1A mutations that lead to FHM in humans were found to have an increased susceptibility to spreading depression. Interestingly, the mutation linked to more severe FHM caused a greater increase in susceptibility to spreading depression than the mutation linked to a milder form of FHM.

As with humans, female mice were more susceptible to spreading depression than male mice. This difference was reversed if the female mice had their ovaries removed, and then partially restored by replacement of the hormone estrogen. The authors therefore conclude that both genetic and hormonal factors modulate an individual's susceptibility to migraines with aura.

In an accompanying commentary, Takahiro Takano and Maiken Nedergaard, at the University of Rochester, Rochester, explain the importance of these data, highlighting the implications for the serious complications that can accompany FHM.

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