Why women are the stressed sex

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A molecular explanation for why women are twice as vulnerable as men to stress-induced illnesses such as depression and post-traumatic stress disorder is presented in Molecular Psychiatry this week. This study shows a gender-specific difference in the stress signaling response of rats that could cause females to be more highly sensitive to stress hormones and less able to adapt to them than males.
Corticotropin-releasing factor (CRF) is a molecule secreted by the brain that regulates the body’s physiological and behavioral response to stress. Rita Valentino, Debra Bangasser and colleagues injected rats with CRF and found that the brain cells of female rats were excited by doses of CRF that were too low to affect cells in male rats. They determined that this was because the protein that binds CRF signals more effectively in females, which results in a higher sensitivity to stress. In addition, when male rats were exposed to stress, their cells adapted to this stress by internalizing the CRF receptor protein, a process which reduces the number of receptors on the cell membrane available to bind with CRF, and so reduces the effect of CRF. The researchers found that internalization did not happen in females, because they were missing a protein that is necessary for this process. This impaired internalization process explains why females are less able than males to adapt to conditions of high stress.

As most rodent models of stress-related psychopathology use males exclusively, this finding—that the female brain operates differently even at the molecular level—could encourage future studies to take gender into account. This could also influence the development of drug treatments for psychiatric disorders that are more prevalent in females.

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