Fluctuations in estrogen can trigger atypical functioning in a key brain memory circuit in women with a common version of a gene, NIMH scientists have discovered. Brain scans revealed altered circuit activity linked to changes in the sex hormone in women with the gene variant while they performed a working memory task.

The findings may help to explain individual differences in menstrual cycle and reproductive-related mental disorders linked to fluctuations in the hormone. They may also shed light on mechanisms underlying sex-related differences in onset, severity, and course of mood and anxiety disorders and schizophrenia, which are often marked by working memory deficits. The gene-by-hormone interaction's effect on circuit function was found only with one of two versions of the gene that codes for BDNF (brain-derived neurotrophic factor), a chemical messenger operating in the circuit. This version occurs in about a fourth of white women.

The researchers experimentally manipulated estrogen levels over several months in healthy women with both versions of the gene while monitoring their brain activity as they performed a working memory task. When exposed to estrogen, an area in the brain's memory hub that is typically suppressed during such tasks instead activated in those with the uniquely human gene variant. Both PET (positron emission tomography) and fMRI (functional magnetic resonance imaging) scans showed the same atypical activation. Such gene-hormone interactions may confer risk for mental illnesses, say the researchers.

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