

Estrogen alters memory circuit function in women with gene variant

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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.

More information: S-M Wei et al, Brain-derived neurotrophic factor Val66Met genotype and ovarian steroids interactively modulate working memory-related hippocampal function in women: a multimodal neuroimaging study, *Molecular Psychiatry* (2017). [DOI: 10.1038/mp.2017.72](https://doi.org/10.1038/mp.2017.72)

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