

# Could hormones explain gender differences in neurological disease?

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Neurological diseases including Parkinson's, Tourette's, attention deficit hyperactivity disorder (ADHD), Alzheimer's, and schizophrenia are all associated with alterations in dopamine-driven function involving the dopamine transporter (DAT). Research published today in the open access journal *BMC Neuroscience* suggests that a number of estrogens acting through their receptors affect the DAT, which may explain trends in timing of women's susceptibility to these diseases.

Rebecca Alyea and Cheryl Watson from the University of Texas Medical Branch investigated how physiological estrogen levels might influence neurochemical pathways including [dopamine](#) signalling. The authors tested the rapid nongenomic effects of several physiological estrogens (estradiol, estrone, and estriol) on dopamine efflux via the DAT in a non-transfected rat [neuronal cell](#) culture model that expresses the three membrane estrogen receptors  $ER\alpha$ ,  $ER\beta$ , and GPR30.

The authors found that estradiol-mediated dopamine efflux is DAT-specific and not dependent on extracellular  $Ca^{2+}$ -mediated vesicular release of dopamine. Using kinase inhibitors they also showed that estradiol-mediated dopamine efflux is dependent on specific signaling kinases (protein kinase C and MEK, but not on PI3K or protein kinase A). While inhibiting dopamine efflux, estrone and estriol caused DAT to leave the plasma membrane.

Previous work by Alyea and Watson indicated that the suppression of efflux occurs mainly via  $ER\alpha$ , and in this new study they show a physical

association of ER $\alpha$  and ER $\beta$  with DAT before and during estrogen action, and trafficking of all three estrogen receptors in and out of the plasma membrane during dopamine efflux.

"The significance of estrogen-coupled regulation of the DAT by both direct and indirect (kinase-mediated) interactions between estrogen receptors and the DAT should provide insights into how [neurological diseases](#) which involve the DAT are related to developmental, gender, and life stage issues," says Watson. "Such regulation may suggest new ideas about treatment and prevention of diseases associated with extreme hormonal fluctuations such as in postpartum depression."

Women experience significant estrogen level changes at various life stages such as adolescence, menopause and as a result of monthly cycles. Women are also most likely to experience the onset or exacerbations of some neurological diseases at these times.

Source: BioMed Central ([news](#) : [web](#))

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