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Estradiol replacement evokes a wide range of transcriptional changes in the frontal cerebral cortex of middle-aged, ovariectomized rats

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Estradiol (E2) plays an important role in the maintenance of cortical functions. Around menopause, the incidence of cognitive disturbances and mood fluctuations increases. The symptoms can be counterbalanced by hormone replacement supporting the idea that estrogens help to maintain the function of the frontal cortex. We used middle-aged, ovariectomized rats and E2 replacement for 4 weeks to dissect the role of the genomic effects of E2 in the maintenance of the function of the frontal cortex. The expression level of 28,000 transcripts was determined by oligonucleotide microarray resulting in the identification of ten E2-regulated functions: neurotransmission (Adora2a, Drd1a, Drd2, Cartpt, Nts, Tac1), signal transduction (Igf2, Igfbp2, Igfbp6), transcription (Etv4, Irf7), transport (Abca1, Hba-a2), extracellular matrix (Col1a2), immunity (C3, CD74), metabolism (Acer2, Osbpl3), miscellaneous and unknown functions. After selection of 39 genes for validation, 74 percent of the changes were confirmed by quantitative real-time PCR. The genomic effects of E2 alter elements of dopaminergic and peptidergic neurotransmission, adenosine and IGF signaling and immune surveillance. These results suggest that the genomic effects of estrogens may play a significant role in the maintenance of cortical functions during hormone replacement in postmenopausal women.

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