Article: EPA-0138
Topic: EPW11 - Stress and Sleep Disorders

COMT VAL158MET POLYMORPHISM INTERACTS WITH SEX TO INFLUENCE FEAR CONDITIONING AND EXTINCTION IN HEALTHY HUMANS

K. Kuriyama[1], T. Yoshiike[1], M. Honma[1], H. Ikeda[1], Y. Kim[1]

[1]Department of Adult Mental Health, National Center of Neurology and Psychiatry National Institute of Mental Health, Kodaira, Japan

The acquisition and extinction of conditioned fear underlies the pathophysiology of anxiety disorders, including PTSD. Women have higher lifetime prevalence and greater risk of PTSD than men. Such sex differences may be attributed to a combination of genetic and hormonal factors. The catechol-O-methyltransferase (COMT) gene encodes an enzyme that metabolizes catechol compounds, including dopamine. The COMT Val158Met polymorphism affects the enzymatic activity of dopamine and has been associated with altered fear memory performance. Besides, when estrogen secretion is elevated, women show a greater extinction of conditioned fear than men. Here, we investigated the relationship between the COMT genotype and sex in the acquisition and extinction of conditioned fear. In a 3-day cued fear conditioning experiment, acquisition and extinction performance of 75 healthy men (21.8 years) and 45 healthy women in follicular phase (21.2 years) were examined. Visual cues and electric shocks were used as the conditioned stimulus and unconditioned stimulus, respectively. Subjects with Met/Met homozygotes showed less fear acquisition ($p < .0001$). Female Val carriers showed more extinction ($p = .009$) and less reconsolidation ($p < .0001$) than male Val carriers. Women with Val/Val homozygotes were less affected by a reinforcing stimulus than men with Val/Val homozygotes ($p = .0001$). These findings suggest a clear interaction between the COMT gene and sex in fear memory function, and that women have a greater tolerance for aversive experiences than men. Higher estrogen levels mediate increased dopaminagic activity, potentially optimizing the prefrontal function known to contribute to the fear-related symptomatology of PTSD.

https://doi.org/10.1016/S0924-9338(14)77610-2 Published online by Cambridge University Press