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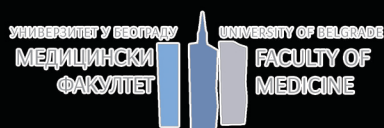


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Chronic mild stress induces sustained-activation of p38 MAPK signaling in the female WKY rats with endogenous depression

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Stress is a major precipitant of depression, the hippocampus (HPC) and prefrontal cortex (PFC) is the main structures affected by depressive disorders. Women are twice more likely to experience depression than men. The WKY rat strain has long been established as a model of depression. Initially bred from the Wistar (WI) rat as the control strain for the spontaneously hypertensive rat, WKY rats demonstrate an exaggerated stress response compared to other strains. WKY strain fails to respond to chronic antidepressant treatment after exposure to chronic mild stress (CMS) and is considered to be nonresponsive to antidepressant drugs. MAPK signaling pathway was most closely related to depression and antidepressant treatment. In the present study, we have examined the effects of CMS on behavior and p38 MAPK signaling in the hippocampus and the medial prefrontal cortex (mPFC) of female WKY rats. We used two very different behavioral tests: forced swim test (FST) and open field test (OFT). WKY unstressed controls exhibited increased immobility duration in the forced swim test and decreased activity in the open-field test compared to unstressed WI rats, while CMS did not further influence behavior. WKY showed increased expression of the p38 only in HPC and further exposure of WKY rats to CMS induces sustained-activation of p38 MAPK in this brain area. The present study demonstrated the brain region-specific protein signatures in the female WKY model with endogenous depression, providing novel insights into the pathogenesis of depression.

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