The role of the brain FKBP5 in depression

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Major depression is a life threatening psychiatric disorder. Hyperactivity of HPA axis is one of the pathophysiological changes of depression, and HPA axis is known to be under the neural control of mPFC, hippocampus and amygdala. Besides, FKBP5 is an inhibitory factor of glucocorticoid receptor (GR), and single nucleotide polymorphisms (SNPs) of FKBP5 is reported to be significantly correlated with depression. Here we investigated the effect of single and repeated restraint stress (RS) (3 hr/day) on depression- and anxiety-like behaviors using forced swimming test (FST) and elevated plus maze test (EPM) in rats. Moreover, we assessed the effect of repeated RS on the serum corticosterone by EIA, and on the GR and FKBP5 in the mPFC, hippocampus and amygdala by Western blotting. We performed above these assessments 2 weeks after repeated stress. Seven times RS increased depression-like behavior (immobility in FST) (**P<0.017), and it was antagonized by previous 14 days repeated administration of escitalopram (10 mg/kg), a SSRI (*P<0.0083). Locomotor activity and anxiety assessed by EPM were no change. Serum corticosterone was increased by seven times RS (**P<0.017). Protein level of GR was not changed, but that of FKBP5 was increased in the amygdala by seven times RS (**P<0.05). Hyperactivity of HPA axis and increased FKBP5 in the amygdala may be related to RS-induced depression-like behavior.