3-O-E1-4 Oral Sessions

Involvement of Dysfunction of Noradrenergic Neuronal System in the Depression-Like Behaviors in MAGE-D1 KO Mice

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Major depressive disorder (MDD) is a common mental disorder characterized by reduced motivation, diminished interest and pleasure, and anhedonia. We have proposed melanoma-associated antigen D1 (MAGE-D1) knock out (KO) mouse is a MDD model, and which involves the serotonergic hypofunction. However, not only serotonergic but also noradrenergic neuronal malfunctions are involved in depressive behaviors. Here, we investigate the involvement of noradrenergic neuronal system in depression-like behaviors of MAGE-D1 KO mice. MAGE-D1 KO mice showed decreases in locomotor activity, social interaction time and sucrose preference, but increases in immobility time in the forced swimming test (FST), and feeding latency in the novelty suppression feeding test. Noradrenaline (NA) tissue contents in the prefrontal cortex, hippocampus, and amygdala, and potassium-evoked noradrenaline releases in the prefrontal cortex and hippocampus were decreased in MAGE-D1 KO mice. The protein expression of noradrenaline transporter (NAT) was increased in the prefrontal cortex of the MAGE-D1 KO mice. Phosphorylation of NAT at threonine and protein expression of its kinase, protein kinase C (PKC) were decreased, but not changed in ubiquitination or expression of NAT mRNA. Acute administration of NA reuptake inhibitors (desipramine and atomoxetine) attenuated increase in immobility time in the FST and decrease in sucrose preference, but not other behavior changes in MAGE-D1 KO mice. These results suggested that depression-like behaviors in MAGE-D1 KO mice might be associated with hypofunction of noradrenergic neuronal system due to NAT overexpression through decrease in PKC-dependent phosphorylation of NAT.