Anxiolytic behaviors and the disruption of brain redox signaling in chronic kidney disease model mice

Yuki Kurauchi[1], Hina Kawamoto[1], Hiroshi Watanabe[2], Toru Maruyama[2], Takahiro Seki[1], Hiroshi Katsuki[1]

[1]Dept. Chemico-Pharmacol. Sci., Grad. Sch. Pharm. Sci., Kumamoto Univ., [2]Dept. Biopharmaceutics, Grad. Sch. Pharm. Sci., Kumamoto Univ.

Chronic kidney disease (CKD) is a risk factor for cerebrovascular diseases, and patients with CKD are susceptible to ischemic and hemorrhagic stroke. Many CKD patients complain of anxiety and other psychiatric symptoms; however, involvement in the mechanism of brain disfunction associated with decreased renal function is unknown. In this study, we analyzed psychiatric symptoms and the changes in the brain of 5/6-nephrectomized (CKD) mice, focusing on redox signaling pathways. In the dark/light box test and the elevated plus maze test, anxiety level of CKD mice was higher than sham mice. Compared with sham mice, sociability was lower in CKD mice using sociability test. In addition, the expression levels of Iba1, a marker of microglia, and GFAP, a marker of astrocytes, were increased in the brain of CKD mice. We also found the increase in the protein expression levels of iNOS and eNOS, but not nNOS, in the brain of CKD mice. Notably, in CKD mice, eNOS dimer to monomer ratio was reduced compared with sham mice, indicating the increase in reactive oxygen species (ROS) production. Furthermore, tyrosinated proteins as well as glutathionylated proteins were increased in the brain of CKD mice. These results indicate that disruption of redox signaling in the brain following decreased renal function causes psychiatric symptoms in mice.