Acute methamphetamine administration impairs cognitive function in a mouse model of schizophrenia with both of CNV and SNV in ARHGAP10 gene that confer high risk of schizophrenia with severe clinical symptoms.

Jingzhu Liao¹, Taku Nagai¹, Daisuke Mori², Bolati Wulaer¹, Kazuhiro Hada¹, Toshitaka Nabeshima³, Norio Ozaki², Kiyofumi Yamada¹

¹Department of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, ²Department of Psychiatry, Nagoya University Graduate School of Medicine, ³Advanced Diagnostic System Research Laboratory, Fujita Health University Graduate School of Health Sciences, ⁴Aino University

ARHGAP10, a member of Rho GTPase-activating protein (RhoGAP) superfamily which contributes to neuronal development, polarization and function. We developed a mouse model of schizophrenia with both a deletion-type copy-number variation (CNV) and a single-nucleotide variation (SNV) in the RhoGAP domain of ARHGAP10 gene (ARHGAP10 mutant mice). Methamphetamine (METH) is one kind of highly addictive drug which induces cognitive deficit in human and rodents. In this study, we investigated the effect of METH on performance of ARHGAP10 mutant mice and wild-type mice in the touchscreen-based visual discrimination task. Mice were initially trained to discriminate between a pair of stimuli. On the testing day, mice were injected with either saline or METH (0.3 mg/kg, intraperitoneal injection) 30 min before the test. METH-treated ARHGAP10 mutant mice showed a marked reduction of percentage of accuracy compared with METH-treated wild-type mice as well as saline-treated ARHGAP10 mutant mice. We demonstrated by using the translatable visual discrimination task that cognitive function in ARHGAP10 mutant mice are highly vulnerable to acute METH treatment.