Psychiatric-disorder-related behavioral phenotypes and cortical hyperactivity in a mouse model of 3q29 deletion syndrome

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The 3q29 microdeletion is a rare recurrent copy number variant (CNV) leading to an increased risk for neurodevelopmental disorders, such as intellectual disability and autism spectrum disorder (ASD), and a >40-fold increased risk for schizophrenia. However, the neurobiological basis for 3q29 deletion syndrome is currently unknown. In order to investigate the biological changes induced by the microdeletion, we generated a mouse model of human 3q29 deletion syndrome by deleting the orthologous region. 3q29 deletion (Df/+) mice showed reduced body and brain weight. Importantly, Df/+ mice showed deficits in social interaction and prepulse inhibition, which are reminiscent of the phenotypes in patients with 3q29 deletion syndrome. By unbiasedly analyzing the whole-brain neural activity, we found that neuronal activity was abnormally activated in a restricted region of the cortex of Df/+ mice. Furthermore, we found that the expression levels of immediate early genes were increased and that the number of parvalbumin positive neurons was decreased in the cortex of Df/+ mice. Our results suggest that Df/+ mice may provide important clues for understanding the disease-causative molecular and cellular pathology of psychiatric disorders.