Loss of function in mouse GAD67 leads to emotional impairments

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Reduced expression of glutamate decarboxylase 67 (GAD67), encoded by *Gad1* gene, is a consistent finding in postmortem brains of patients with schizophrenia, bipolar disorder and major depressive disorder. However, the neurobiological consequences of GAD67 dysfunction in mature brains are not fully understood because the homozygous *Gad1* knockout is lethal in newborn mice. Here, we developed *Gad1*^{TA/STOP-tetO} biallelic knock-in mice using *Gad1*^{STOP-tetO} and *Gad1*^{TA} knock-in mice, and compared them with *Gad1*^{+/+} mice. The expression level of GAD67 protein in brains of *Gad1*^{TA/STOP-tetO} mice treated with doxycycline (Dox) was decreased by approximately 90%. The GABA content was also decreased in the brains of Dox-treated *Gad1*^{TA/STOP-tetO} mice. In the open-field test, Dox-treated *Gad1*^{TA/STOP-tetO} mice exhibited hyper-locomotor activity and decreased duration spent in the center region. In addition, acoustic startle responses were impaired in Dox-treated *Gad1*^{TA/STOP-tetO} mice. These results suggest that global reduction in GAD67 elicits behavioral impairments in mice. These GAD67 knockdown mice will be useful for elucidating the neurobiological mechanisms of emotional abnormalities, such as anxiety symptoms associated with psychiatric disorders.