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2. Title
   Pathophysiology of brain acetylcholine nervous system in mouse model of autism

3. Period
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4. Summary

Tuberous sclerosis complex (TSC) is an inherited autosomal dominant disorder caused by mutations in either *TSC1* or *TSC2*. TSC patients display severe neurological symptoms such as autism spectrum disorder (ASD). We previously reported that *Tsc2* heterozygous knockout (*Tsc2(+/-)*) mice exhibited ASD-like social impairment which were improved by mTOR inhibitor administration. We also showed that the expression levels of choline acetyltransferase (*Chat*) and acetylcholine esterase (*Ache*), which are genes encoding key molecules in acetylcholine neurotransmission, were increased in *Tsc2(+/-)* mice and these increases were also suppressed by mTOR inhibitor administration. In the project, we focused on the changes of acetylcholine signal transduction in *Tsc2(+/-)* mouse brain for developing treatment drugs of ASD.

The expression level of *CD68*, *C1qa*, *Cx3cr1*, *Grin1*, *Mbp*, *Slc6a1*, *Slc6a3*, and *Slc17a6* genes was statistically increased in *Tsc2(+/-)* brains. Cell number and distributions of Chat-positive cholinergic neurons in striatum (caudate nucleus and putamen) were not significantly different between *Tsc2(+/-)* mice and wild-type mice. Chat immunostaining also showed a tendency that staining intensity was high in *Tsc2(+/-)* mice rather than wild-type mice.

Regarding for microglial cells and glutamatergic neurons, the expression levels of multiple genes encoding marker molecules were changed in *Tsc2(+/-)* brains, suggesting that number or distribution of microglial cells and glutamatergic neurons would be altered in *Tsc2(+/-)* brains. Increase ratios of gene expression were larger in *Chat* rather than *Ache*. Therefore, acetylcholine neurotransmission would be increased in the *Tsc2(+/-)* mouse brain, and which would be a brain pathology causing behavioral abnormalities in *Tsc2(+/-)* mouse.