論文の内容の要旨

論文題目　Behavioral pharmacological research on the autism-like behavior in mouse models of tuberous sclerosis complex.
（結節性硬化症モデルマウスの自閉症様行動に関する行動薬理学的研究）

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Impairment of reciprocal social interaction is a core symptom of autism spectrum disorder (ASD). Genetic disorders frequently accompany ASD, such as tuberous sclerosis complex (TSC) caused by haploinsufficiency of the *TSC1* and *TSC2* genes. Accumulating evidence implicates a relationship between ASD and signal transduction that involves TSC1, TSC2, and mammalian target of rapamycin (mTOR). Here behavioral abnormalities relevant to ASD and their recovery by the mTOR inhibitor rapamycin are shown in mouse models of TSC. In *Tsc2*$^{+/-}$ mice, enhanced transcription of multiple genes involved in mTOR signaling is found, which is dependent on activated mTOR signaling with a minimal influence of Akt. The findings indicate a crucial role of mTOR signaling in deficient social behavior in mouse models of TSC, supporting the notion that mTOR inhibitors may be useful for the pharmacological treatment of ASD associated with TSC and other conditions that result from dysregulated mTOR signaling.