

## Induction of resilience for depression-like behavior by Shati/Nat8l knockdown in the striatum of mice

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[Background] In pathogenesis of depression, BDNF in the brain play an important role. We found that Shati/Nat8l mRNA is increased in striatum of depression model mice exposed repeated social defeat stress (R-SDS). It is reported that BDNF mRNA levels are increased in any brain regions of Shati/Nat8l KO mice. In this study, we revealed the roles of striatal Shati/Nat8l in depression and mechanism of regulation in BDNF by Shati/Nat8l.

[Methods] C57BL/6J mice were exposed R-SDS using ICR mice, and the acetylated histone levels of BDNF was measured using chromatin immunoprecipitation. We generated striatal Shati/Nat8l conditional knockdown mice (Shati cKD) using Cre-loxP system. Then we assessed depression-like behaviors in Shati cKD with behavioral experiment after R-SDS, and investigated the effect of Shati/Nat8l to the acetylation of histone.

[results] BDNF mRNA levels in the striatum of mice exposed R-SDS is increased, and acetylated histone levels of BDNF is also increased. In the behavioral experiment, Shati cKD showed the resilience for social defeat stress. BDNF mRNA and acetylated histone levels of BDNF in the striatum is suppressed by knockdown of Shati/Nat8l.

[conclusions] Shati/Nat8l in the striatum play an important role in depression. BDNF in the striatum might regulated resilience for social defeat stress mediated histone acetylation by Shati/Nat8l. Our study suggested the new pathways induce depression-like behaviors, and Shati/Nat8l in the striatum might be a new target for medical tools for depression.