enhancing properties; however, most of these studies were conducted in naïve animals.

Chronic mild stress (CMS) has been reported to induce an anhedonic-like state in rodents that resembles some of the symptoms of human depression. In the present study we use the CMS model to investigate molecular correlates of possible anti-anhedonic and cognitive enhancing effects of vortioxetine. Adult male Long Evans rats were exposed to 9 weeks of CMS, and treated with vortioxetine (administered in the diet) during the last 4 weeks of the stress period. Sucrose consumption tests were performed weekly during the stress and treatment periods to evaluate the anhedonic state. Cognitive functions were assessed by the social interaction and Barnes maze tests.

Our preliminary data show that the CMS paradigm reduced the sucrose consumption in a subset of the rats, indicating anhedonic-like behavior, while another subgroup of rats were resilient to the CMS. The anhedonic-like state was reversed in 70 percent of the animals in response to chronic vortioxetine treatment, while the remaining animals were resistant (non-responder rats).

To improve our understanding of the molecular mechanisms associated with the anti-anhedonic effect of vortioxetine, we are currently investigating synaptosomes prepared from the hippocampus and prefrontal cortex for synaptic alterations in proteins involved in neuroplasticity with particular focus on proteins regulating dendritic spine function and morphology.

CONCLUSION: At clinically relevant levels of SERT occupancy fluoxetine produce a reduction of the neurotoxic QUIN, whereas ketamine had no effects using an intermittent dosing regimen.

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PS112
Changes of serotonergic functions are mediated via metabolic control of serotonin transporter in stressed mice
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Abstract
Objective: Many kinds of antidepressants, such as tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) have been developed, whereas approximately 30 % of patients with major depressive disorder are “treatment-resistant depression”, which is resistant to existing antidepressants. SSRIs are the first-line antidepressants in the treatment of major depressive disorder, and directly bind to the serotonin transporter (SERT). SERT activity is attenuated by PKC, which induced SERT phosphorylation and surface expression, thereby SERT is a key regulator of SERT-serotonergic functions. The present study was investigated whether PKC is related to depressive behaviors in the forced swimming-stressed mice, and further they are mediated via SERT function in stressed mice.

Method: Mice were forced to swim (the 1st swimming: stressed mice) to get the immobility time stable at the 2nd swimming. On the next day, they were forced to swim again (the 2nd swimming: tested mice), and 20 min later, they were performed the social interaction test. The effects of phorbol 12-myristate 13-acetate (PMA: a PKC activator), imipramine or sertraline (an antidepressant), and chelerythrine (a PKC inhibitor) on the performance of behavioral tests were examined, and PKC activity and SERT expression were analyzed.

Result: The expression levels of phosphorylated SERT protein were decreased in tested mice. PMA as well as antidepressants attenuated the immobility and deficits of social behaviors in tested mice. It also increased in the expression levels of phosphorylated PKC and SERT proteins. Chelerythrine exacerbated both behavioral abnormalities in tested mice and decreased the expression levels of phosphorylated PKC protein.

Conclusion: These results suggest that the PKC activator attenuates some depressive behaviors in stressed mice to promote metabolism of SERT via phosphorylation PKC, and it might be a novel antidepressant.

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Neuroendocrine and behavioural changes in adult offspring of dams treated with venlafaxine during gravidity and lactation
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