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Attenuation of mossy fiber long-term potentiation by acute behavioral stress and effects of zinc and theanine

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The hippocampus plays an important role in memory and recognition of novelty, in which glutamatergic neurons are involved. Histochemically reactive zinc exists in the presynaptic vesicles of glutamatergic neurons and is released with glutamate; all giant boutons of mossy fibers contain the zinc in the presynaptic vesicles, while approximately 45% of Schaffer collateral/commissural pathway is zinc-positive. The extracellular concentrations of glutamate and zinc are increased by excitation of zinc-containing glutamatergic neurons. In a novel environment, however, extracellular glutamate is increased in the hippocampus, while extracellular zinc is decreased. The mechanism of the decrease in extracellular zinc and its significance are unknown.

In the present study, the supposition that stress response elicits the decrease in extracellular zinc in the hippocampus was examined by using rats subjected to tail suspension under hippocampal perfusion. Thirty second-tail suspension elicited a persistent decrease in extracellular zinc, which continued for 60 min, in spite of a short increase in extracellular glutamate. These results suggest that zinc uptake into hippocampal cells is facilitated by acute behavioral stress. In hippocampal slices prepared 1 h after the tail suspension, mossy fiber LTP was attenuated. A short perfusion with 100 μM $ZnCl_2$ prior to LTP induction also attenuated mossy fiber LTP. The attenuation of mossy fiber LTP by the tail suspension was completely restored when rats were pretreated with clioquinol (30 mg/kg) to block the action of Zn^{2+}. The present study demonstrates that the facilitated zinc uptake by tail suspension is a possible mechanism to attenuate mossy fiber LTP. On the other hand, LTP at Schaffer collateral/commissural pathway was also attenuated in hippocampal slices prepared 1 h after the tail suspension. Interestingly, this attenuation was not observed in hippocampal slices from rats that were subjected to administration of 0.3% theanine from the birth. Theanine may protect the hippocampus against acute stress.