DYSFUNCTION OF GABAERGIC SYSTEM IN THE INSULAR CORTEX CONTRIBUTES TO IMPAIRMENTS OF DECISION-MAKING IN METHAMPHETAMINE-DEPENDENT RATS

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Introduction. Patients suffering from neuropsychiatric disorders such as substance-related and addictive disorders have impairments in decision-making, which may be associated with their behavioral abnormalities. However, the neuronal mechanisms underlying such impairments are largely unknown. To address this issue, we developed a gambling test for rodents using an 8-arm radial arm maze, and tested the effect of chronic methamphetamine (METH) treatment on decision-making in rats.

Method. The c-fos staining was applied to determine the brain areas activated by the gambling test. Depolarization-evoked GABA release was measured by in vivo dialysis.

Results. METH-dependent rats choose a high-risk/high-reward option more frequently, and assign higher subjective value to high returns, than control rats, suggesting that decision-making is impaired in the METH-dependent animals. Immunohistochemical analysis of c-fos following the gambling test revealed aberrant activation of the insular cortex (INS) and nucleus accumbens in METH-dependent animals. Pharmacological studies together with in vivo microdialysis showed that GABAergic neurotransmission in INS played a crucial role in decision-making.

Conclusion. Our findings suggest that INS is a critical region involved in decision-making, and that insular GABAergic dysfunction in METH-dependent rats results in risk-taking behaviors associated with poor decision-making.