The altered expression of organic cation transporter3 (OCT3) could regulate the effect of psychostimulants

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SLC transporter OCT3 was cloned from the rat placenta by Dr. Ganapathy's group in 1998. In their literature, it was demonstrated that OCT3 is expressed in the brain and can transport monoamines and amphetamines, suggesting its possible involvement in monoamine- and psychostimulant-related psychiatric disorders. In order to prove this hypothesis, we examined the neurobehavioral impact of OCT3 by using antisense against OCT3 (OCT3-AS). The continuous infusion of OCT3-AS into the cerebral ventricle of rats could inhibit the expression of OCT3 at the choroid plexus. In OCT3-AS-treated rats, hyperlocomotion induced by the systemic injection of methamphetamine (MAP) was significantly higher than that in vehicle-treated rats. MAP-induced dopamine release in the nucleus accumbens, an area responsible for locomoter activity, was significantly higher than that in vehicle-treated rats. Moreover, we found that OCT3-AS treatment significantly increased MAP levels in the nucleus accumbens as well as in cerebrospinal fluid without affecting MAP levels in plasma. Taken together, these results suggest that the decreased expression of OCT3 in the choroid plexus might diminish the efflux transport of MAP from the brain, subsequently increasing MAP-induced hyperlocomotion. In addition, we also found that OCT3-AS treatment in mice decreased immobility time in an antidepressant-sensitive forced-swimming test, similar to antidepressants. In conclusion, reagents regulating the function/expression of OCT3 would be novel drugs to treat monoamine- and psychostimulant-related psychiatric disorders such as drug abuse, schizophrenia and depression.