Animal models for cognitive impairment in schizophrenia

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Clinical features of schizophrenia consist of positive and negative symptoms as well as cognitive dysfunction. Little is known about the neurobiology of cognitive dysfunction in schizophrenia, and no drugs exist that effectively enhance cognition in patients with schizophrenia although some studies indicate that atypical antipsychotics may be more effective than conventional antipsychotic medications at enhancing cognition. In this symposium, we show that repeated methamphetamine (METH) treatment in rats impairs spatial working memory in a delayed spatial win-shift task of a radial arm maze, which is associated with dysfunction of the extracellular signal-regulated kinase 1/2 in the hippocampus. METH-induced impairment of working memory is ameliorated by repeated treatment with clozapine, but not haloperidol. Furthermore, we discuss the mechanism by which acute and repeated METH treatment in mice impairs prepulse inhibition (PPI) of the startle response, a measure of the inhibitory function and time-linked information processing. The METH-induced impairment of PPI is accompanied by attenuation of the prepulse-induced activation of the pallidotegmental GABAergic neurons, which plays a crucial role in the regulation of PPI. Pharmacologic research with animal models would be useful in identifying potential molecular targets for treating cognitive dysfunction in schizophrenia.