Title	STUDY OF GLUTAMATERGIC TRANSMISSION IN METHAMPHETAMINE-DEPENDENT RATS
Author	Walailuk Kerdsan
Advisor	Assistant Professor Sutisa Thanoi, Ph.D.
Co-Advisor	Assistant Professor Samur Thanoi, Ph.D.
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ABSTRACT

Methamphetamine (METH) is a psychostimulant drug of abuse that produces long term behavioral changes including behavioral sensitization, tolerance and dependence. It has been reported that METH induces neurotoxic effects in several brain regions via dopaminergic system. Alterations of dopamine function can induce dysfunction of glutamatergic system. Therefore, the purposes of the present study were to examine the effects of METH administration on the expression of glutamate N-methyl-D-aspartate subunit 1 (NMDAR1) and neuronal glutamate transporter (EAAT3) in striatum, frontal cortex and hippocampal formation. Male Sprague-Dawley rats were treated with a single intraperitoneal injection of 8 mg/kg METH in acute group, 4 mg/kg/day for 14 days in chronic group and saline in control group. Expressions of NMDAR1 and EAAT3 were quantified by western blotting analysis.

Results showed that an increase of NMDAR1 immunoreactivity (IR) was observed in striatum in both acute and chronic groups. Moreover, an increase of NMDAR1-IR was found in frontal cortex in chronic group but not in acute group. However, there were no significant differences of NMDAR1-IR in hippocampal formation either acute or chronic groups. These results suggested that the upregulation of NMDAR1 expression may be a response to an elevation of glutamate in the striatum and the frontal cortex. EAAT3 protein expression was found to be increased in hippocampal formation after chronic METH administration, but not in acute group. In striatum, a decrease in EAAT3-IR was observed on both acute and chronic groups. There was no alteration of EAAT3-IR in frontal cortex on both acute and chronic groups. These observations suggested that the upregulation of EAAT3

expression in hippocampal formation may be a compensatory response to an elevation in glutamate in hippocampus whereas a reduction in EAAT3 levels in striatum and prefrontal cortex may be an effect of METH-induced neuronal cell death. As METH has been considered to be a psychostimulant, our findings provide support for a psychostimulant effect on the glutamatergic system. Therefore, it will be worthwhile to further investigate the other components of glutamatergic transmission to understand fully the mechanism underlying the abnormalities of glutamatergic function in METH dependence.