Amphetamine-induced effects on neuropeptide Y in the rat brain

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Abstract:
Repeated (+)-amphetamine sulfate (AMPH) administration (5 mg/kg sc twice daily for 6 days and once on day 7) markedly and reversibly decreased (until 96 h after the final dose) neuropeptide Y-like immunoreactivity (NPY-LI) in the rat striatum (caudate-putamen) and nucleus accumbens, and had no effect on NPY-LI in the hippocampus. No significant alterations were detected in the hybridization signal of NPY mRNA 4 and 24 h after the end of AMPH treatment. A single dose of AMPH (5 mg/kg sc) administered to rats 4 and 24 h prior to sacrifice had no effect on NPY-LI in the brain structures studied. Moreover, AMPH injected 8 days after the last dose of repeated AMPH administration did not change NPY-LI up to 72 h. The minimal dose of haloperidol, the strong mixed dopaminergic D₂/D₃ receptor antagonist, (0.75 mg/kg injected ip 30 min before each of the multiple AMPH administrations) that was sufficient to completely block stereotypy and hyperlocomotion elicited by multiple AMPH administrations enhanced the AMPH-induced decrease in the striatal and accumbens NPY-LI. Our results suggest that NPY neurons in the striatum, nucleus accumbens and hippocampus are not directly involved in the acute behavioral response to AMPH (stereotypy and hyperlocomotion) as well as in the initiation and expression of AMPH-induced behavioral sensitization.

Key words:
d-amphetamine, behavioral sensitization, striatum, nucleus accumbens, hippocampus, neuropeptide Y-like immunoreactivity, NPY mRNA, rat

Abbreviations: AMPH – (+)-amphetamine, NPY – neuropeptide Y, NPY-LI – neuropeptide Y-like immunoreactivity, 5-HT – 5-hydroxytryptamine

Introduction

Amphetamine (AMPH) is a stimulant with psychotomimetic activity. In animals, single AMPH administration dose-dependently induces hyperlocomotion and stereotypy. A consequence of repeated AMPH administration is an augmentation of its behavioral effect after AMPH re-administration, which reflects the sensitization of the central nervous system [32]. It is thought that this phenomenon plays a role in the development of psychostimulant-induced psychosis in humans [42] and it is considered to be an animal model of the acquisition of addiction [33]. The parallels between behavioral sensitization in rats and clinically recognized behavioral sensitization [37] have