Abstract:

Time-dependent effect of single-doses of acutely administered methamphetamine on regional cerebral blood flow in rats

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Abstract
Methamphetamine (METH) exerts a strong effect on the extracellular release of catecholamines in the brain, particularly in the reward pathway. Neurochemical studies report increases in dopamine typically in the nucleus accumbens shell reaching hundreds of percent of the baseline levels. The aim of this study was to track changes in the regional cerebral blood perfusion (rCBF) assessed by arterial spin labeling (ASL) MRI before and after systemic administration of METH.
Male Sprague-Dawley rats were anesthetized and introduced to the 9.4 T Bruker NMR small animal system and ASL sequence was measured once before and 6 times after intraperitoneal administration of 1, 2, or 5 mg/kg of METH. All rats received all types of treatment in weekly intervals following the Latin square design.
There were no basal rCBF differences among the experimental groups, but there were significant differences between the perfusion of the whole brain compared to specific regions of interest (ROI). The circle of Willis was found to have higher perfusion, while the sensorimotor cortex, piriform cortex, and hippocampus had lower rCBF. The effect of METH was analyzed as relative values obtained as a % of the basal rCBF value of all subsequent measurements in each ROI. METH was found to dose-dependently increase rCBF in the whole brain, sensorimotor and piriform cortices, hippocampus, and thalamus. Only the Circle of Willis was not affected. Furthermore, in the thalamus, a peak of perfusion was found approximately 40 minutes after METH administration.
The study indicates, that METH at a high dose is able to increase rCBF, and this effect peaks 40 minutes after drug dosing, while the absolute amount of blood entering the brain via Circle fo Willis remains unchanged. The time-course of these changes is in accordance with the METH-induced increase of catecholamines in the reward pathway.