Dynamics of metabolic and functional rat brain connectivity during MDMA stimulation assessed by simultaneous PET/MR

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Background: MDMA affects the brain by changing the neurotransmitter systems of serotonin and thereby also functional connectivity processes. In this study a PET/MR system was used to research the influence of 3,4-Methylenedioxymethamphetamine (MDMA) on the brain, investigating both, metabolic connectivity (Cometomics) using PET with the Tracers: [11C]DASB (marker for serotonin transporters) and [18F]FDG (marker for glucose metabolism) and functional connectivity using blood oxygen level dependent (BOLD) fMRI.

Methods: Lewis rats (n=4, male, 295g ± 16 g) were measured two times using a simultaneous PET/MR system, designed for small animals (7 T MR; 1.5% isoflurane anesthesia). BOLD-fMRI was measured over 100 min to investigate BOLD-Signal and functional connectivity during resting state (EPI, TR=2000ms, TE=18ms). Simultaneously PET acquisitions were performed with bolus and constant infusion of [11C]DASB. Two days later another PET/MR scan was performed with a constant infusion of [18F]FDG and fMRI. MDMA (3.2mg/kg) was i.v. injected after 40 min. PET and MR data were preprocessed, using SPM 12. For statistical analyses independent component analysis (ICA) were performed as well as Pearson’s correlation coefficient between areas that are involved in prominent resting state networks (RSNs).

Results: In the whole brain there was a significantly increased [18F]FDG uptake. Time activity curves of [18F]FDG revealed an increased trend after MDMA stimulation. The binding potential (BPND) of [11C]DASB was significantly decreased in the whole brain (0.34±0.27 at baseline compared to 0.19±0.10 after MDMA injection, p=0.046). A large significant decrease of BPND (p<0.05) was observed amongst others in the thalamus (0.80±0.54 at baseline, 0.40±0.18 in the late phase), the hypothalamus (0.76±0.43, 0.35±0.17) and the superior colliculus (0.90±0.23, 0.43±0.07). Correlation matrices for resting state networks (e.g. default mode) revealed a disruption in brain connectivity immediately after MDMA administration but also remapping processes.

Conclusions: MDMA administration during the resting state period showed an increased brain glucose consumption, a decreased [11C]DASB binding due to the competitive effect of MDMA in the serotonergic system, and changes of functional and metabolic connectivity in the rat brain. Our simultaneous PET/MR study points out that a complex interplay of functional and metabolic network changes occurs during drug administration. These insights could be of high importance for future research in drug addiction but also in related fields of a variety of pharmacological challenges.