FDG-PET studies of the effect of MDMA in rat brain

Maria L. Soto-Montenegro , Juan J Vaquero , Antonio Molins , Santiago Reig , Manuel Desco
Medicina y Cirugía Experimental. Hospital General Gregorio Marañón. Madrid. SPAIN

INTRODUCTION

Alterations of the human brain due to MDMA use are a focus of ongoing research. MDMA abuse produces both short and long-term effects on brain; MDMA-induced functional alterations of the serotonergic system are reported to alter local energy metabolism of cortical and subcortical structures. Presently, there are no FDG-PET experimental studies reported in animals. The aim of this study is to assess these brain glucose metabolism changes after a single dose of MDMA in rats by using FDG-PET.

MATERIAL AND METHODS

Adult female Dark Agouti rats, weighting 138-185g, were housed in individual cages at a constant temperature (24±0.5ªC) with a 12 h light/dark circle and given free access to food and water. Racemic MDMA obtained from NIDA (Research Triangle Park, NC, USA) was dissolved in saline (0.9% NaCl) and administrated i.p. Rectal temperature was recorded over the following hour. Rats received a single dose of 15-40 mg/kg of MDMA or saline (N=3). Two study groups: A) PET scan performed 1 hour after MDMA-treatment (N=5) and B) PET scan performed 7 days after MDMA-treatment (N=6). Rats were intravenously injected with [18F]-FDG (1.66±0.44 mCi) and imaged with a dedicated small animal PET after an uptake period of 30 min. Blood glucose was controlled after MDMA and FDG administration. Data sets were reconstructed using a 3D-OSEM algorithm (1.8 mm FWHM).

RESULTS

Following MDMA administration, body temperature increased with respect to that of the saline injected animals, reaching a peak incremen 60 min post-injection ranging from 2.2 ± 0.1ºC for 40 mg/kg to 1.9±0.1ºC for 15 mg/kg. Blood glucose decreased after MDMA administration (2280 mg/dl) and after FDG administration (2455 mg/dl). 2 rats died due to severe hypoglycemia (<11 mg/dl). Preliminary results of PET study show that after 1 hour, MDMA-treated rats presented high FDG-uptake in frontal cortex, motor and somatosensory cortex, auditory and visual cortex, striatum, anterior-limbic-area, hypothalamus and cerebellum with respect to saline-treated rats. Images obtained at day 7 showed a decrease on global brain glucose metabolism, with an important activation on amygdala.

DISCUSSION & CONCLUSIONS

MDMA administration to rats induces changes including hyperthermia, hypoglycemia and hyperlocomotor response. Increase in FDG-uptake in group-A agrees with the acute physiological effects during the peak period after MDMA administration (45-90 min). We found a relation between MDMA dose and brain glucose metabolism, being FDG-uptake higher in those rats receiving the higher doses (40 mg/kg). On the contrary, we found decreases in FDG-uptake in group-B. It has been reported that a single dose of 20-40 mg/kg of MDMA produces an important decrease in 5-HT and 5-HIAA in the cortex, hippocampus and striatum seven days later. This decrease in cerebral serotonin content could correlate with the glucose metabolism changes we have observed. Unexpectedly, a metabolic increase was found in amygdala in group-B that may be related to startle reactions during aversive or stressing experiences (temperature-probe, PET device sound).

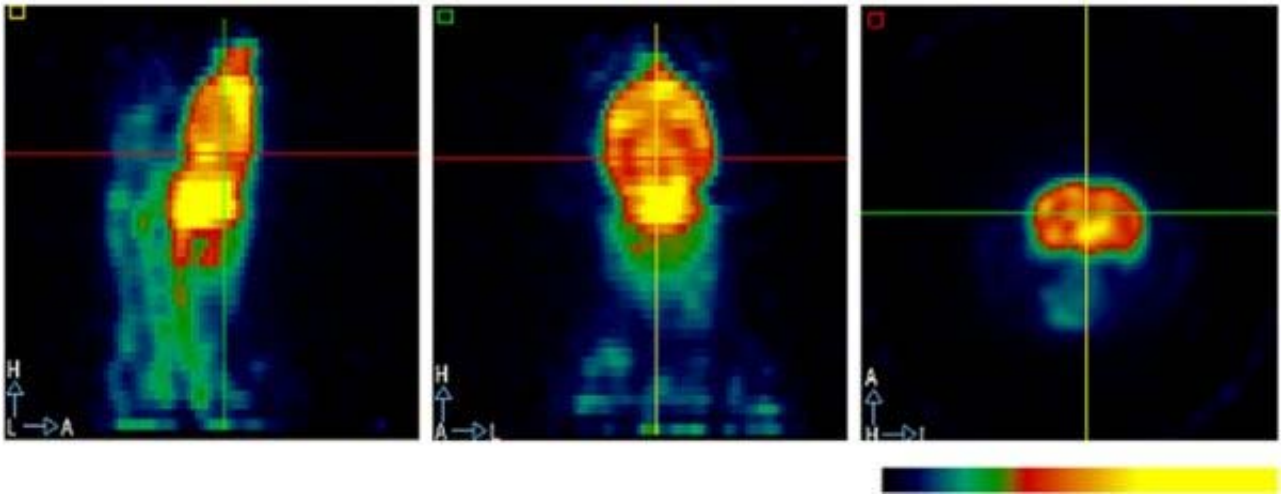

Figure 1 shows the sagittal, coronal and axial sections of the PET scan of the brain of an MDMA-treated rat that was performed 1 hour after MDMA administration. The images show several brain regions with high FDG-uptake: frontal cortex, striatum, anterior-limbic-area, hypothalamus and cerebellum. The Photographic Atlas of the Rat Brain of Kruguer at et (1995) allowed us to localize different structures on the PET images.

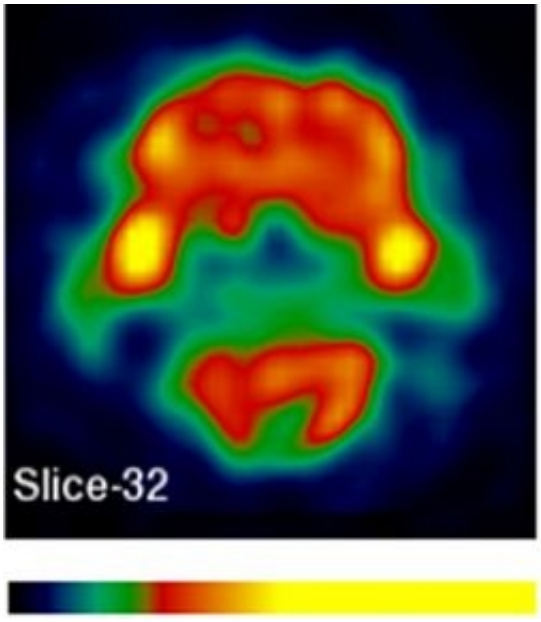

Figure 2 shows an axial section of PET scan of the brain of an MDMA-treated rat that was performed 7 days after MDMA administration. Image shows a high FDG-uptake on amygdala.