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MOLECULAR IMAGING FOR THE EVALUATION OF DRUG-RECEPTOR INTERACTIONS IN PSYCOACTIVE SUBSTANCES OF ABUSE

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BACKGROUND-AIM

The objective of this work is to apply molecular imaging techniques, based on the administration of radioactive tracers in small animal models as a method to investigate the mechanisms of receptor interactions of drugs of abuse. A further objective of the study was to establish, in collaboration with the pharmacology unit of the University of Ferrara, a "pre-clinical research network" able to rapidly investigate the neurobiological mechanisms and the pharmacological effects induced by acute and chronic administration of Novel Psychoactive Substances (NPS) seized by law enforcement agencies.

METHODS

^{123}I-Ioflupane (DaTscan) was supplied by the Nuclear Medicine of S. Anna Hospital of Ferrara. Animal experiments were carried out in compliance with the relevant national laws relating to the conduct of animal experimentation and EU Directive 2010/63/EU. SPECT studies have been performed using a YAP(S)PET scanner. CD-1 mice (male, 35-40 g), divided into three different group, were anesthetized with an intramuscular injection of a mixture of ketamine (100mg/kg) and xilazine (20mg/kg) and submitted to a pretreatment by intraperitoneal injection of vehicle (saline 0.9%), cocaine (20mg/kg) or amphetamine (10mg/kg). Thirty minutes after drug or vehicle administration, mice were submitted to a retrobulbar injection with a solution of 123I-DaTscan (450-500 □Ci). Imaging analysis (128 views/360°) of the head of the animal were performed 2 and 3 h after the administration of ^{123}I-DaTscan and lasted 60 minutes each one. Images were reconstructed by using the iterative EM-ML algorithm including the collimator response. CT images have been acquired using the digital X-ray imaging system integrated into the YAP(S)PET scanner. To evaluate the brain distribution of ^{123}I-DaTscan were selected ROI on SPECT images and the total activities, normalized to the injected ones, have been calculated.

RESULTS

The results showed that the binding of ^{123}I-DaTscan at DAT transporters was decreased in the striatum of mice submitted to a pretreatment with cocaine or amphetamine in comparison with the vehicle-injected animals. In particular, a significantly decreased in the binding of ^{123}I-Ioflupane was observed in animals pretreated with cocaine.

CONCLUSION

As expected cocaine and amphetamine bind and block the dopamine transporter (DAT) in the mouse brain with particular respect to the striatum. This study confirms and strengthens the possibility of employing the technique of SPECT analysis in small rodents to provide quickly information about the structure/activity of Novel Psychoactive Substances. This research has been funded by the Drug Policies Department, Presidency of the Council of Ministers, Italy (project NS-Drugs to M Marti).