Central serotonin2B receptors, dopamine mesocorticolimbic system and drug addiction.

Keywords: cocaine, dopamine, serotonin, microdialysis, rat

Abstract

Subject: The mesocorticolimbic dopaminergic (DA) system is known to play a key role in drug addiction. It is well established that the serotonergic (5-HT) system modulates DA network activity, and 5-HT receptors are currently considered as useful pharmacological targets for improved treatments of drug addiction. In this context, the central 5-HT2B receptor appears to be a promising candidate. Indeed, 5-HT2B receptors have been recently shown to exert a tonic excitatory control on the mesoaccumbal DA pathway, and to participate in the control of the neurochemical and behavioral effects of various drugs of abuse such as amphetamine and MDMA. Although cocaine is one of the most abused drugs worldwide, the influence of 5-HT2B receptors on its effects remains largely unexplored. Also, despite the importance of the medial prefrontal cortex (mPFC) in the regulation of DA mesoaccumbens pathway and its involvement in drug addiction, the role of 5-HT2B receptors in the modulation of mesocortical DA pathway remains unknown. This project aims at assessing the role of 5-HT2B receptors in the biochemical and behavioral effects of cocaine, with a particular attention at identifying the relative contribution of the different DA regions involved in this interaction (mPFC, nucleus accumbens, ventral tegmental area).

Methods: This project will be performed in rats, using a multidisciplinary approach encompassing behavioral (drug self-administration, locomotion), neurochemical (monitoring DA release with microdialysis), and molecular (measurement of Fos expression and DARPP-32 phosphorylation) methodologies. The role of 5-HT2B receptors will be studied using selective 5-HT2B agents (agonists, antagonists) administered systemically and/or locally into the above mentioned brain region.

Qualification required

Basic neurosciences including neuroparmacology; basic experience in behavioral pharmacology molecular pharmacology and/or neurochemistry.