Abstract Information

First Name :	Pascal
Last Name :	Fossat
Email :	pascal.fossat@u-bordeaux.fr
Address :	146 rue leo saignat

Participation :	symposium
Title of the Symposium :	An update in the pathophysiology of the non-motor symptoms in Parkinson?s disease
Category :	Academic/Researcher
Thematic Area :	Neurodegeneration, Neuroplasticity, and Repair
Title :	Brainstem serotonin amplifies nociceptive transmission in a mouse model of Parkinson?s disease.

Co-Authors : Zoé Grivet1,2, Franck Aby1,2, Aude Verboven1,2, Rabia Bouali-Benazzouz1,2, Benjamin Sueur1,2, François Maingret1,2, Frédéric Naudet1,2, Thibault Dhellemmes1,2, Philippe De Deurwaerdere3,4, Abdelhamid Benazzouz1,2,# and Pascal Fossat1,2,*# 1. Université de Bordeaux, Institut des Maladies Neurodégénératives, UMR 5293, F-33000 Bordeaux, France. 2. CNRS, Institut des Maladies Neurodégénératives, UMR 5293, F-33000 Bordeaux, France. 3. Université de Bordeaux, Institut des neurosciences cognitives et intégratives d?aquitaine, UMR 5287, F-33000 Bordeaux, France. 4. CNRS, Institut des neurosciences cognitives et intégratives d?aquitaine, UMR 5287, F-33000 Bordeaux, France.

Abstract : Parkinson's disease arises from the degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to motor symptoms such as akinesia, rigidity and tremor at rest. The non-motor component of Parkinson's disease includes increased neuropathic pain, the prevalence of which is 4 to 5 times higher than the general rate. By studying a mouse model of Parkinson's disease induced by 6-hydroxydopamine, we assessed the impact of dopamine depletion on pain modulation. Mice exhibited mechanical hypersensitivity associated with hyperexcitability of neurons in the dorsal horn of the spinal cord (DHSC). Serotonin (5-HT) levels increased in the spinal cord, correlating with reduced tyrosine hydroxylase (TH) immunoreactivity in the nucleus raphe magnus (NRM) and increased excitability of 5-HT neurons. Selective optogenetic inhibition of 5-HT neurons attenuated mechanical hypersensitivity and reduced DHSC hyperexcitability. In addition, blockade of 5-HT2A and 5-HT3 receptors reduced mechanical hypersensitivity. These results reveal, for the first time, that PD-like dopamine depletion triggers spinal-mediated mechanical hypersensitivity, associated with serotonergic hyperactivity in the NRM, opening up new therapeutic avenues for Parkinson's disease-associated pain targeting the serotonergic systems.