INCREASED IMPULSIVITY FOLLOWING PROGRESSIVE NIGRAL DEGENERATION AND CHRONIC PRAMIPEXOLE TREATMENT IN A RAT MODEL OF PARKINSON'S DISEASE

H. Jimenez-Urbieta[1,2], L. Merino-Galan[1,2,3], T. Rodriguez-Chinchilla[1,2], M. Delgado-Alvarado[1,4], A. Quiroga-Varela[1,2], B. Gago[5], M.C. Rodríguez-Oroz[1,2,3,6,7,8,]
[1]. Instituto de Investigación sanitaria Biodonostia. Donostia-San Sebastián, Guipúzcoa, España.
[2]. Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Comunidad de Madrid, España.
[3]. Universidad del País Vasco-Euskal Herriko Unibertsitatea, UPV-EHU, España.
[4]. Facultad de Medicina. Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, España.
[5]. Facultad de Medicina. Universidad de Málaga, UMA, Málaga, España.
[6]. Facultad de Medicina, Hospital Universitario Donostia, Donostia-San Sebastián, Guipúzcoa, España.
[7]. Basque Foundation for Science, IKERBASQUE. País Vasco, España.
[8]. Basque Center on Cognition, Brain and Language (BCBL), San Sebastian, Guipúzcoa, España.

Dopamine agonists (DA) that are widely used to treat motor deficits in patients with Parkinson's disease (PD) are frequently associated with the development of abnormal-impulsive behaviors (AIB). The pathophysiology of AIB is poorly understood and there is a need for reliable animal models. We have analyzed the behavior of parkinsonian (injection of adeno-associated viral vectors (AAV) encoding for A53T mutated hα-syn in the substantia nigra compacta) and control (AAV-GFP expression) rats under chronic treatment with the D2/D3 receptor DA pramipexole (PPX) during 4 weeks, in OFF and ON medication states, using the 5-Choice Serial Reaction Time-Task (5-CSRTT). Before PPX treatment, the dopaminergic lesion increased the premature responses rate (waiting impulsivity) that was further increased with PPX during the 4 weeks of treatment in ON medication state and that was significantly higher than in control rats. A similar pattern of changes was observed in the variables related to attention (reduced accuracy in the responses and increased omissions). Premature response rate before and after treatment (both in ON and OFF medication) were correlated. In turn, premature responses before treatment and in OFF correlated with the striatal dopaminergic depletion (Dopamine transporter (DAT) immunochemistry). No significant changes were observed in OFF medication state in premature responses rate respect to the pretreatment state. The striatal expression of FosB/ΔFosB inversely correlated with the DAT expression and was higher in the lateral region of both striata and in the shell and core of the nucleus accumbens in parkinsonian than in control rats. In conclusion, these results indicate that the dopaminergic lesion is a risk factor to develop abnormal impulsive behaviors in PD under DA treatment and that this model could be a valid tool to investigate the pathophysiology of AIB in PD (DFG11/019, PI11/02109).

Topic: Cognitive and Behavioral Neuroscience; Disorders and nervous system repair.