DIFFERENT SUSCEPTIBILITY TO PRAMIPEXOLE-INDUCED IMPULSIVITY IN A RAT MODEL OF PARKINSON'S DISEASE

H. Jimenez-Urbieta[1,2], L. Merino-Galan[1,3,4], T. Rodriguez-Chinchilla[1], A. Belloso-Iguerategui[1,4], M. Delgado-Alvarado[1,5], I. Navalpotro-Gómez[1,6], A. Quiroga-Varela[1,4], B. Gago[1,7], M.C. Rodríguez-Oroz[1,4,8,9]

[1] Instituto de Investigación Sanitaria Biodonostia, Donostia-San Sebastián, Guipúzcoa, Spain
[2] Instituto de Investigación Sanitaria Biocruces Bizkaia, Barakaldo, Vizcaya, Spain
[3] Universidad del País Vasco-Euskal Herriko Unibertsitatea (UPV/EHU), Lejona, Vizcaya, Spain
[4] Centro de Investigación Médica Aplicada (CIMA), Pamplona, Navarra, Spain
[5] Hospital de Sierrallana, Torrelavega Cantabria, Spain
[6] Hospital del Mar, Barcelona, Barcelona, Spain
[7] Instituto de Investigación Biomédica de Málaga, Facultad de Medicina, Universidad de Málaga (UMA), Málaga, Málaga, Spain
[8] Basque Foundation for Science, IKERBASQUE. País Vasco, Spain
[9] Basque Center on Cognition, Brain and Language (BCBL), San Sebastian, Guipúzcoa, Spain

Impulse Control Disorders (ICD) in patients with Parkinson's disease (PD) are abnormal impulsive behaviors caused by long-term use of dopamine agonists. The pathophysiological mechanisms are poorly understood. Thus, using parkinsonian rats (adeno-associated viral vectors-mediated overexpression of A53T human α-synuclein in the substantia nigra compacta), we evaluated the impulsive behaviour under acute (0.25 and 3 mg/kg) and chronic (0.25 mg/kg for 4 weeks) administration of the D2/D3 receptors agonist pramipexole (PPX). The Variable Delay-to-Signal (VDS) task was employed to analyse two different impulsivity domains, motor and choice impulsivities. Changes in striatal D1 and D2 receptors expression were analysed to determine its association to impulsive behaviour. Before treatment, the striatal dopaminergic depletion caused a significant increase of both impulsivity domains with respect to basal condition. In lesioned rats, acutely given PPX 0.25 mg/kg dose increased choice impulsivity only with regard to basal values. Meanwhile, 3 mg/kg PPX increased choice impulsivity compared to their own values at different conditions: basal, before treatment and after acute 0.25 mg/kg PPX administration. After chronic administration, two populations of lesioned animals were distinguished, one showing the same behaviour as control animals and other displaying an increased motor/response (first week of treatment) and cognitive/choice impulsivities (third week of treatment) compared to control animals. This impulsive behaviour disappeared when animals were tested in OFF state. Lower D2 expression in both Caudate-Putamen and Nucleus Accubens and lower D1 levels in Nucleus Accumbens in lesioned rats than in control animals were observed. Therefore, our results indicate that the pro-impulsive effect of PPX in this animal model of PD depends on the dose and administration paradigm employed and the individual predisposition, and it is associated to striatal dopamine receptors expression changes, especially in Nucleus Accumbens. Thus, this model could constitute a valid tool to investigate the pathophysiology of ICD (DFG11/019, PI11/02109).

Topic: Disorders and nervous system repair