A new behavioral analysis in rats to understand motor fluctuations in parkinsonian patients treated with L-DOPA

Stefania Sgroi, Alain Kaelin-Lang and Christine Capper-Loup

Department of Neurology and Department of Clinical Research, Movement Disorders Center, Inselspital, Bern University Hospital, and University of Bern, Switzerland

Locomotor disorders like bradykinesia (slowness of movement) or hesitation of gait initiation are a hallmark of Parkinson's disease (PD). In the treatment of PD, Levodopa (L-DOPA) remains the most effective drug. However the majority of parkinsonian patients under L-DOPA therapy develops disabling motor complications like motor fluctuations, characterized by on/off phenomena, and abnormal involuntary movements, called dyskinesia.

The purpose of our study is to establish a behavioral animal model which is close to the locomotor activity performance of parkinsonian patients both during and in the absence of L-DOPA therapy.

Parkinsonian rats with 6-hydroxydopamine (6-OHDA) lesions were treated with chronic intraperitoneal injections of L-DOPA (8 mg/kg) once a day for 21 consecutive days; another group of lesioned rats received chronic injection of NaCl (vehicle) and a third group of naive animals received the standard L-DOPA chronic treatment. The motor activity of all groups was valuated using behavioral analysis software (Ethovision) at 19nd day of L-DOPA and NaCl treatment (ON period) and at 22nd day without L-DOPA and vehicle administration (OFF period), respectively.

Results: Preliminary observations about motor performance in parkinsonian rats demonstrated an higher locomotor activity, expressed as "total distance moved" and "mean velocity", in animals during the L-DOPA ON period than during the L-DOPA OFF period. Furthermore, Levodopa-induced dyskinesia were seen only in the ON-state, similar to what is seen in parkinsonian patients under L-DOPA therapy. On the contrary, no difference in motor activity was found in the parkinsonian rats treated with NaCl during ON/OFF period and naive groups during L-DOPA ON/OFF treatment, respectively.

We conclude that our animal model's behavior is close to motor performances in human suffering from ON/OFF motor fluctuations. This experimental model is better suited for pre-clinical study in order to test the use of new pharmacological drugs, able to reduce the motor complications induced by L-DOPA treatment.