Basal Ganglia pathophysiology and the etiopathogenesis of Parkinson's disease

Jose A. Obeso
Centro Integral de Neurociencias AC (CINAC),
Fundación HM-Hospitales de Madrid , and CEU- San Pablo University, Madrid, Spain
jobeso.hmcinac@hmhospitales.com

Humans can combine automatic habitual and voluntary goal-directed tasks simultaneously with consummate ease. Normally, in daily life, switching between these two modes of behavioural control occurs with consummate easy, as task components encountered are predictable or uncertain. The dopaminergic neurons of the substantia nigra *pars compacta* (SNpc) that innervate the sensorimotor striatum are essential for the acquisition of automatized skills and habits, and are activated when automatic habitual control is deployed.

The origin of neuronal loss in Parkinson's disease (PD) is not well understood and many etiopathogenic factors appear to participate in the neurodegeneration process, implicitly recognizing complex biological interactions in how different mechanisms interact to produce the clinically recognized disorder. The predominant cell loss in PD occurs first and predominantly in the ventro-lateral tier of the substantia nigra *pars compacta* (SNpc) leading to dopamine depletion in the sensorimotor putamen(dorso-lateral striatum in rodents=DLS) which is fundamentally engaged in the acquisition and execution of automatic behaviours (habits). We put forward the idea that the nigro-striatal projection associated with habitual and goal-directed behaviours differs significantly in terms of their anatomo-physiological features. Accordingly, we shall explore the notion that reliance and continuous use of routine behaviour while engaged in other goal-directed activities may represent a functional overload for dopaminergic SNpc neurons in the ventro-lateral tier. This contrasts with the usual concept that SNpc cells are monotonically active firing at a low 4 Hz rate and scarcely responsive to movement and external stimuli. However, recent electrophysiological studies suggest otherwise supporting the idea of functional overloading and stressing of the nigro-striatal system, which becomes more vulnerable with aging.