PHYSIOPATHOLOGY OF BASAL GANGLIA IN PARKINSON'S DISEASE

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Basal ganglia (BG) are unique in brain in terms of abundance of circuits that place all nuclei in reciprocal communication. Through actions exerted by stimulatory D_1 receptors and inhibitory D_2/D_3 receptors, dopamine released in the striatum facilitates normal coordinated and fine movements. Conversely, progressive degeneration of dopamine neurons and consequent loss of dopaminergic tone at different BG levels produces the bradykinesia, rigidity and tremor that characterise the disordered movement of Parkinson's disease. Adaptive changes in striatal peptides (enkephalin and dynorphin) in GAD-67 or *zif-268* mRNA expression as well as modification in GAD-67 or *zif-268* in globus pallidus or substantia nigra have been correlated to Parkinson's disease motor deficits as well as appearance of dyskinetic movements after chronic L-DOPA. These studies have consistently shown that an unbalanced activity of the direct striatonigral and indirect striato-pallidal-subthalamic-nigral pathways in unilaterally 6-hydroxydopamine-lesioned rats, are causally related to dysfunction in execution of movements. In contrast, recent results with the low dyskinetic D_2/D_3 dopamine receptor agonist ropinirole have shown a decreased but balanced response of both direct and indirect pathways, providing the basis for the different dyskinetogenic properties of this drug. These results may represent useful markers to differentiate low dyskinetic from highly dyskinetic treatments. Moreover, modifications of GAD67 and *zif-268* mRNA in the globus pallidus and substantia nigra pars-reticulata neurons, might correlate with the dyskinetic potential of L-DOPA and ropinirole after subchronic treatment. Organisation of basal ganglia is far more complex than assumed in the current model of direct and indirect striatonigral pathway. Axon collateralisations interconnect BG circuitry and areas connecting, but not belonging to basal ganglia, as the excitatory centromedian-parafascicular thalamic complex which actively influence basal ganglia functions. All these parameters should be taken into account in order to develop an integrated view of BG functioning.