Exploring neurocircuitries of the basal ganglia by intracerebral administration of selective neurotoxins

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The detailed anatomy of the monoamine pathways of the rat, first described by the students of Nils-Åke Hillarp in Sweden, provided the basis for a neurocircuitry targeted pharmacology, leading to important therapeutic breakthroughs. Progress was achieved by the introduction of accurate lesion techniques based on selective neurotoxins. Systematic intracerebral injections of 6-hydroxydopamine let Urban Ungerstedt at the Karolinska Institutet, Stockholm, Sweden, to propose the first stereotaxic mapping of the monoamine pathways in the rat brain; and the 'Rotational Behaviour', as a classical model for screening drugs useful for alleviating Parkinson's disease and other neuropathologies. The direction of the rotational behaviour induced by drugs systematically administrated to unilaterally 6-hydroxydopamine-lesioned rats reveals their mechanism of action at dopamine synapses, as demonstrated when rotational behaviour was combined with microdialysis. The model was useful for proposing a rol