EVIDENCE FOR THE EXISTENCE OF HOMOLATERAL AND CONTRALATERAL PROJECTIONS FROM THE SUBSTANTIA NIGRA TO THE SUBTHALAMIC NUCLEUS IN THE RAT

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Introduction: Hemichorea/ballism is a rare neurological disorder but the crucial involvement of the subthalamic nucleus (STN) in its pathophysiology is appreciated since decades. The idiopathic Parkinson's disease is a common neurodegenerative disorder but the key role of the STN in the pathophysiological origin of the parkinsonian state became only recently evident. The STN was believed to exert an inhibitory, probably – GABA-mediated, effect on its projection nuclei, and this belief is one of the major reasons to overlook the involvement of the STN in the parkinsonian pathophysiology. It is now firmly established that the STN projection neurons are glutamatergic, excitatory, and heavily innervate by widely branching axons of the substantia nigra (SN), the internal pallidal segment (GPI), followed by the external pallidal segment (GPE) and the pedunculopontine tegmental nucleus (PPN). The most prominent afferent connections of the STN arise in the GPE. The STN is also innervated by glutamatergic corticosubthalamic axons. A substantial, bilateral cholinergic/glutamatergic projection arises in the PPN, while the thalamic centromedian-parafascicular complex also innervates the STN. Finally, serotoninergic fibers from the raphe nuclei terminate profusely within the STN. The nigrosubthalamic connection was demonstrated by axonal transport techniques, and transmitter immunocytochemistry, that offered a firm evidence for the existence of this pathway. The nigrosubthalamic connection arises from the dopaminergic (DA) neurons of the SN pars compacta (SNc). In addition, a moderate projection was described from the parvalbumin immunoreactive, presumably GABAergic neurons of the SN pars reticulata (SNr) to the STN. The nigrosubthalamic connection has always been described as ipsilateral.

Materials and methods: Twenty-five female Wistar Albino Glaxo rats weighing 200-240 g were anesthetized and injected unilaterally with biotynilated dextran amine (BDA) into the SN (survival time 8-13 days). The rats were reanesthetized and perfused transcardially. Serial freeze sections were cut at a thickness of 40 µm. A commercial avidin-biotin-HRP complex (ABC) kit was used to visualize the BDA and counterstaining ocurred with Cresyl violet.

Results: The largest injection sites of the tracer involved the lateral SNr and SNc. The axons destined to the brain stem, and some nigrothalamic axons course dorsally towards the tegmentum, and the ascending axons to the forebrain take initially a medial course towards the prerubral area. Most of them run immediately dorsal to SN, and some axons travers lateromedially of the SNc. Few axons curve ventromedially and travel along the border between SNr and the cerebral peduncle. Reaching the caudal pole of the STN the labeled axons enter the nucleus through its lateral wedge, but also its ventral border, and from the medially running bundle, dorsal to the STN. Within the STN, especially in the lateral half of the nucleus, along with passing fibers oriented mediolaterally, there is a large number of terminal labeling. In the medial part of the STN there are mainly discrete bursts of terminal labeling. Interestingly, although the subthalamonigral projection is a substantial one, only few retrogradely labeled STN neurons are present. The SN axons cross the midline at several places. The most substantial component of crossed axons runs in the mesencephalic tegmentum ventral to the periaqueductal gray. Such bundles are present through the entire rostrocaudal extent of the mesencephalon, and some fibers in the rostral mesencephalon apparently enter the STN through its dorsal border. A second component crosses the midline in the commissure of the superior colliculus and in the posterior commissure. Rostral to the SN, the efferent SN axons cross the midline (crossed nigrothalamic axons), and the last component of crossing axons runs in the supraoptic decussation, immediately above the optic tract. Some of these axons take a dorsomedial course towards the contralateral STN. In the contralateral STN a lower number of labeled axons are seen. However, they form very distinct

mediolaterally extended patches. Most of these discrete fields of terminal labeling are in the central and lateral portions of the STN, but also medially some terminal “whorls” are seen. Selective injections of SNr and SNc will be discussed further in this poster.