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Literaturempfehlungen

Brain-gut axis in Parkinson's disease: Experimental evidence for a nigro-vagal pathway associated with one of Parkinson's earliest symptoms

Functional gastrointestinal disturbances affect the vast majority of Parkinson's Disease (PD) patients before appearance of the cardinal motor symptoms. As being reviewed recently by Madelyn C. Houser and Malú G. Tansey in "The gut-brain axis: is intestinal inflammation a silent driver of Parkinson's disease pathogenesis?" (Parkinson's Disease 2017 3: 3; doi:10.1038/s41531 -016-0002-0) evidence suggests that the intestines are not only affected in PD. The gastrointestinal tract may be the site where the pathology of PD is initiated decades before the onset of motor symptoms. Until recently, there was no anatomic or physiologic evidence that links the substantia nigra, pars compacta (SNpc) directly to the control of gastric motility and tone.

The team around Professor Alberto Travagli, Department of Neuronal and Behavioral Sciences, Pennsylvania State University is focussing their research on the neurophysiology and neuroanatomy of the brain-gut axis. In an original paper "A Nigro-Vagal Pathway Controls Gastric Motility and Is Affected in a Rat Model of Parkinsonism" (Gastroenterology 2017; 153: 1581–1593), Laura Anselmi and coauthors gave experimental evidence of a monosynaptic nigro-vagal pathway by which the Parkinson-related gastrointestinal dysfunction could be explained. When stimulating the substantia nigra, pars compacta (SNpc) the authors observed an increased gastric tone and motility. Optogenetic studies and immunohistochemistry revealed the activation of dopamine 1 receptors in the dorsal vagal complex (dorsal motor nucleus of the vagus; DMV). In the experimental PD model the nigro-vagal pathway was compromised due to paraquat-injections. The authors concluded that this pathway can serve as a conduit which allows the direct access of ingested neurotoxicants from DMV to SNpc neurons, thus triggering the prodromal GI dysfunction. The identification and characterization of this neurocircuit opens unexpected avenues for the advancement of experimental investigations into both the aetiology of environmentally triggered PD, as well as the prodromal gastric dysmotility that adversely affects the quality of life of most Parkinsonian patients (SNpc) and, later, the cerebral cortex. This pathway might be involved in the prodromal gastric and intestinal (GI) dysfunctions, including gastric dysmotility and delayed emptying, as well as severe constipation. These are prominent non-motor manifestations of PD prodromal to the onset of motor symptoms. The nigro-vagal pathway neurons integrate signals from higher centers, as well as from the adjacent catecholaminergic neurons of the A2 area which provide synaptic modulation via alpha-adrenoceptors. The efferent vagal fibers project to postganglionic myenteric neurons of the enteric nervous system (ENS) that ultimately controls the motility response of the GI tract.

Over the years, the understanding of PD has evolved from identification of an impairment of midbrain neurons to recognition of a multi-system disorder with central and peripheral, motor, non-motor, and pre-motor manifestations. The connections between nervous and immune systems as well as between inflammation and neurodegeneration have become substantial for modern PD research. The involvement of intestinal inflammation in PD presents opportunities for the development and application of novel diagnostics and earlier therapeutic interventions. The discovery of a nigro-vagal pathway may help to link the pathologies of intestinal inflammation and neurodegeneration in PD. As reported, Professor Travagli and his team intend to focus their research around the identification of environmental factors that promote the degeneration of the nigrovagal pathway. A clear aim is the attenuation or prevention of its degeneration altogether.

Impressum
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