Abstract Information

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Title :	Neuromodulation and an update on the pathophysiology and treatment of Parkinson?s disease

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Abstract :

Parkinson?s disease (PD) is a neurological disease characterized by the manifestation of motor and non-motor symptoms. Over several decades, a considerable amount of research in animal models, particularly rodents and non-human primates, and in patients has contributed to our understanding of the pathophysiology of the motor symptoms of PD and the development of new therapeutic approaches. Numerous studies have demonstrated the key role of the subthalamic nucleus (STN) in the manifestation of these symptoms, and their alleviation by high frequency electrical stimulation of this nucleus. Recently we also discovered that the STN is also involved in the pathophysiology of the non-motor symptoms of PD, including pain which is affecting around 85% of patients and contributing to a deterioration in their quality of life. Using in vivo extracellular electrophysiology we have shown that STN neurons are able to detect nociceptive stimuli, encode their intensity and generate windup-like plasticity. However, these phenomena are impaired in dopamine-depleted animals. Indeed, the intensity response is altered in both STN and wide dynamic range (WDR) neurons of dorsal horn of the spinal cord (DHSC). Moreover, neuromodulation of STN by high frequency electrical stimulation, named also deep brain stimulation, in dopamine-depleted animals showed an improvement in mechanical allodynia and thermal hyperalgesia compared to sham animals. This effect is mediated by descending brainstem projections leading to normalization of nociceptive integration in DHSC neurons. Our study highlights the centrality of the STN in nociceptive circuits, its interaction with the DHSC and its key involvement in pain sensation in Parkinson's disease. Furthermore, our results provide for the first-time evidence that subthalamic DBS produces analgesia by normalizing the responses of spinal WDR neurons

via descending brainstem pathways.