

Summery

The underlying mechanisms of weight gain and other affective and cognitive changes after initiation of deep brain stimulation in Parkinson's disease are still unclear. Considering the functional organization within the subthalamic nucleus (STN); limbic, associative and sensorimotor regions residing in the medial, central and later STN respectively, we hypothesized that weight gain may be related to medial localization of stimulation, while motor improvement may be related to lateral localization of stimulation within the STN (**study 1**). We further hypothesized that stimulation close to the limbic and associative part of the STN may be associated with negative impact on limbic system leading to enhanced anxiety and changes in the hypothalamic-pituitary-adrenal axis (HPA)(**study 2**). Therefore, the primary aims our study were to assess changes in body weight (**study 1**) and the hypothalamic-pituitary-adrenal axis (HPA) (**study 2**) in relation to the position of the active stimulating contact within the nucleus. The secondary goals were to elucidate whether morning plasma cortisol changes after the initiation of stimulation are related to postoperative anxiety and weight gain. **Study 1.** Regular body-weight measurements were performed in 20 patients with advanced Parkinson's disease within a period of 18 months after implantation. T1-weighted (1.5T) magnetic resonance images were used to determine electrode position within the STN and the Unified Parkinson's disease rating scale (UPDRS-III) was used for motor assessment. We observed weight gain inversely related to the distance of contacts from the wall of the third ventricle, and patients with at least one contact located medially in the STN experienced significantly greater weight gain than those with both active contacts located laterally. On the contrary, motor improvement was related to the lateral part of the STN. **Study 2.** Plasma cortisol measurements were taken on the day of initiation of bilateral STN-DBS and then repeated after 1 and 17 months in twenty patients with advanced Parkinson's disease. After initiation of stimulation, cortisol levels significantly decreased and cortisol changes after 1 and 17 months strongly correlated with the position of active contact in subthalamic area. Patients with at least one contact localized more medially in the STN experienced a significantly greater decrease of cortisol than those with one or both active contacts localized more laterally. Furthermore, lower cortisol levels were strongly associated with higher trait anxiety and weight gain, suggesting a negative impact of STN-DBS on limbic system. Thus, medial position of the active contact is associated with weight gain, cortisol and anxiety changes, corresponding to manifestations of chronic stress and suggesting a regional effect of STN-DBS on adjacent limbic structures.