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Decrease in Blood Cortisol Corresponds to Weight Gain following Deep Brain Stimulation of the Subthalamic Nucleus in Parkinson's Disease

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It has repeatedly been shown that patients with Parkinson's disease (PD) gain body weight under treatment with deep brain stimulation of the subthalamic nucleus (STN DBS) [1–3]. However, the mechanisms underlying this weight gain (WG) remain unclear. We, therefore, read with great interest the recently published article 'The role of ghrelin, neuropeptide Y and leptin peptides in weight gain after deep brain stimulation for Parkinson's disease' by Markaki et al. [4]. The authors performed body composition measurements and blood sampling before, and 3 and 6 months after STN DBS in 23 PD patients, looking for relations between WG and changes in blood levels of the metabolic hormones ghrelin, neuropeptide Y (NPY) and leptin. A significant WG (3.09 ± 5 kg, mean $\pm$ SD, $p = 0.007$) was observed 3 months after surgery, with no further increase at 6 months. Also the circulating levels of NPY increased significantly ($p = 0.05$) at 3 months, while the increase of ghrelin was significant only at 6

months ($p = 0.001$). WG was associated with changes of ghrelin and leptin levels at 3 and 6 months. The authors concluded that STN DBS may temporarily dysregulate the hypothalamic secretion of NPY and ghrelin, whereas the WG may be related to an increased production of ghrelin and leptin.

These observations bear remarkable similarities to our earlier study, in which we assessed anthropometric and hormonal profiles in 27 PD patients on the day of surgery and at 2, 4, 6 and 12 months on STN DBS [5]. Our patients' weight continuously increased throughout the study, with the mean body weight change with regard to baseline being $+4.16 \pm 3.5$ kg ($p < 0.001$) at 6 months and $+5.18 \pm 5.8$ kg ($p < 0.001$) at 12 months. Furthermore, in both studies, leptin and ghrelin levels correlated with body WG, corresponding to the known roles of the adipocyte-derived leptin and the orexigenic hormone ghrelin.

Curiously enough, Markaki et al. [4] do not pay much attention to their own finding of markedly decreased cortisol levels following STN DBS. Nevertheless, this result is in surprisingly precise agreement with our observation, probably shedding more light on the mechanisms of WG in PD following STN DBS (table 1). At 3 months after STN DBS, Markaki et al. [4] noticed a significant decrease in blood cortisol (-23.8% , $p = 0.027$). In our study, cortisol levels decreased at 2 months, (-23.9% , $p < 0.002$), still remaining significantly reduced compared to baseline at 12 months after DBS implantation (-22.9% , $p = 0.008$) [5]. These results seem to indicate the involvement of hypothalamic-pituitary-adrenal axis in the mechanisms of WG after STN DBS. It can be hypothesized that STN DBS acts on adjacent nerve fibers and structures including hypothalamic nuclei, where it suppresses secretion of corticotropin-releasing factor with a subsequent decrease in the production of cortisol. Since the level of corticotropin-releasing factor is low, its catabolic effect is mitigated; therefore, the homeostatic balance shifts towards predominance in

Table 1. Blood cortisol at different time points and its percent decrease versus baseline

		Baseline	1 month	2 months	3 months	4 months	6 months	12 months
Markaki et al. [4]	Cortisol, $\mu\text{g/dl}$	17.99	NA	NA	13.71	NA	15.81	NA
	Change to baseline, %		NA	NA	-23.8	NA	-12.1	NA
Novakova et al. [5]	Cortisol, nmol/l	688.96	618.78	524.26	NA	521.96	579.74	531.3
	Change to baseline, %		-10.2	-23.9	NA	-24.2	-15.9	-22.9

Bold print indicates significant changes. Conversion factor between conventional units ($\mu\text{g/dl}$) and SI units (nmol/l) for cortisol = 27.59 (source: http://www.globalrph.com/conv_si.htm). NA = Data not available.

anabolic reactions. Interestingly, it has also been previously suggested that increased NPY levels are possibly related to diffusion of the electric current to the hypothalamus causing disruption of the melanocortin system, leading to WG [6].

Our hypothesis is indirectly supported by previous reports showing that cortisol levels were significantly higher in PD patients compared to healthy controls and that cortisol concentrations significantly decreased after levodopa intake, particularly in patients with a more advanced stage of PD [7, 8]. In fact, it has been demonstrated that PD patients lose weight throughout the progression of the disease [9]. The WG following STN DBS might thus mean a compensation of previous loss, rather than an excessive anabolic reaction. Accordingly, we suspect that the observation of a more sustained WG in our group may correspond to a lower initial body mass index than that reported by Markaki et al. (25.8 vs. 28.7), leading to a continued increase in weight in our patients, even if initial values were well above undernutrition in both groups [4, 5].

In conclusion, DBS in PD appears to act not only by exerting its motor effects through the stimulation of the STN, but also by influencing nonmotor functions, namely reversing catabolic processes and inducing WG, by diffusion of the electric current to the adjacent structures including hypothalamus and involving the hypothalamic-pituitary-adrenal axis.

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References

- 1 Barichella M, Marczevska AM, Mariani C, Landi A, Vairo A, Pezzoli G: Body weight gain rate in patients with Parkinson's disease and deep brain stimulation. *Mov Disord* 2003;18:1337–1340.
- 2 Macia F, Perlemonne C, Coman I, Guehl D, Burbaud P, Cuny E, Gin H, Rigalleau V, Tison F: Parkinson's disease patients with bilateral subthalamic deep brain stimulation gain weight. *Mov Disord* 2004;19:206–212.
- 3 Novakova L, Ruzicka E, Jech R, Serranova T, Dusek P, Urgosik D: Increase in body weight is a non-motor side effect of deep brain stimulation of the subthalamic nucleus in Parkinson's disease. *Neuro Endocrinol Lett* 2007;28:21–25.
- 4 Markaki E, Ellul J, Kefalopoulou Z, Trachani E, Theodoropoulou A, Kyriazopoulou V, Constantoyannis C: The role of ghrelin, neuropeptide Y and leptin peptides in weight gain after deep brain stimulation for Parkinson's disease. *Stereotact Funct Neurosurg* 2012;90:104–112.
- 5 Novakova L, Haluzik M, Jech R, Urgosik D, Ruzicka F, Ruzicka E: Hormonal regulators of food intake and weight gain in Parkinson's disease after subthalamic nucleus stimulation. *Neuro Endocrinol Lett* 2011;32:437–441.
- 6 Escamilla-Sevilla F, Pérez-Navarro MJ, Muñoz-Pasadas M, Sáez-Zea C, Jouma-Katati M, Piédrola-Maroto G, Ramírez-Navarro A, Mínguez-Castellanos A: Change of the melanocortin system caused by bilateral subthalamic nucleus stimulation in Parkinson's disease. *Acta Neurol Scand* 2011;124:275–281.
- 7 Charlett A, Dobbs RJ, Purkiss AG, Wright DJ, Peterson DW, Weller C, Dobbs SM: Cortisol is higher in parkinsonism and associated with gait deficit. *Acta Neurol Scand* 1998;97:77–85.
- 8 Müller T, Muhlack S: Acute levodopa intake and associated cortisol decrease in patients with Parkinson disease. *Clin Neuropharmacol* 2007;30:101–106.
- 9 Jaafar AF, Gray WK, Porter B, Turnbull EJ, Walker RW: A cross-sectional study of the nutritional status of community-dwelling people with idiopathic Parkinson's disease. *BMC Neurol* 2010;10:124.