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Research report

Weight gain after STN-DBS: The role of reward sensitivity and impulsivity

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ABSTRACT

Weight gain has been reported after deep brain stimulation of the subthalamic nucleus (STN-DBS), a widely used treatment for Parkinson's disease (PD). This nucleus has been repeatedly found to be linked both to reward and to inhibitory control, two key aspects in the control of food intake. In this study, we assessed whether weight gain experienced by patients with PD after STN-DBS, might be due to an alteration of reward and inhibitory functions. Eighteen patients with PD were compared to eighteen healthy controls and tested three times: *before surgery*, in ON medication and *after surgery*, respectively five days after the implantation in ON medication/OFF stimulation and at least three months after surgery in ON medication/ON stimulation. All participants were assessed for depression (Beck Depression Inventory), anhedonia (Snaith-Hamilton Pleasure Scale) and impulsiveness (Barratt Impulsiveness Scale). They performed a battery of tests assessing food reward sensitivity (Liking, Wanting and Preference) and a food go/no-go task. Results showed that body weight significantly increased after STN-DBS. A few days after surgery, patients were slower and more impulsive in the go/no-go task, showed a higher preference for high calorie (HC) foods and rated foods as less tasty. Months after subthalamic stimulation, the performance on the go/no-go task improved while no differences were observed in reward sensitivity. Interestingly, weight gain resulted greater in patients with higher levels of attentional impulsiveness pre-surgery, higher wanting for low calorie (LC) foods and impulsivity in the go/no-go task in ON medication/ON stimulation. However, only wanting and attentional impulsivity significantly predicted weight change. Furthermore, weight gain resulted associated with the reduction of L-Dopa after surgery and disease's duration.

Abbreviations: DBS, deep brain stimulation; STN, subthalamic nucleus; C, controls; UPDRS, Unified Parkinson's disease rating scale; BDI, Beck Depression Inventory; SHAPS, Snaith-Hamilton Pleasure Scale; BIS, Barratt Impulsiveness Scale; GPi, globus pallidus internus; FA, false alarms.

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In conclusion, our findings are consistent with the view that weight gain in PD after STN-DBS has a multifactorial nature, which reflects the complex functional organization of the STN.

1. Introduction

Recently much attention has been directed to explain the role of the subthalamic nucleus (STN) in regulating the basal ganglia circuits (Nelson & Kreitzer, 2014). Beyond its motor functions, the STN has also been recognized as playing an important role in non-motor domains such as reward processing and response control (Rossi, Gunduz, & Okun, 2015). As far as reward is concerned, several animal studies have demonstrated that the STN is involved in the motivation for food. In rats, for instance, STN lesions increase motivation for stimuli associated with food in several behavioural tasks and decrease motivation toward artificial rewards (Baunez, Yelnik, & Mallet, 2011). In monkeys, an increase in STN activity has been observed during food reward anticipation and delivery (Darbaky, Baunez, Arecchi, Legallet, & Apicella, 2005; Espinosa-Parrilla, Baunez, & Apicella, 2015). Reports on humans are consistent with these observations, since patients with stroke or tumour of the STN may show hyperphagia and increased appetite (Bartuca, Turgut, Meydan, & Ozsunar, 2003; Etemadifar et al., 2012). Interestingly, weight gain, food craving and binge eating have been reported in patients with Parkinson's disease (PD) after subthalamic nucleus-deep brain stimulation (STN-DBS), a therapeutic option in the treatment of the disease widely used nowadays (Aiello, Eleopra, & Rumiati, 2015; Ardouin et al., 2006; Kistner, Lhommée, & Krack, 2014; Lim et al., 2009; Witjas et al., 2005; Zahodne et al., 2011). Several hypotheses have been put forward to explain this outcome, including changes in energy metabolism (due to motor improvement) or in medication, dysphagia and hypoosmia. However, none of them alone has explained weight gain renforcing the idea that the underlaying mechanism is more likely multifactorial (see Aiello et al., 2015; Kistner et al., 2014, for recent reviews). Despite the evidence linking STN to reward, only a few studies have investigated the association between weight gain and change in motivation toward food. In a first study, 20 STN-DBS patients with PD were tested in both ON and OFF stimulation conditions. Patients rated rewarding (erotica and food), aversive fearful, and neutral pictures according to valence and arousal (Serranová et al., 2011). The authors found that postoperative weight gain correlated with arousal ratings of food pictures only in the STN-DBS ON-condition (Serranová et al., 2011). In a second study, the same authors observed that weight gain correlated with the level of acoustic startle reflex inhibition observed with positive food pictures in the ON-condition (Serranová et al., 2013). Consistently with these studies, Růžička et al. (2012) reported that patients with at least one contact located medially in the STN (defined as its limbic subdivision), experienced significantly greater weight gain than those with both active contacts located laterally. More recently, Saleau et al. (2014) observed significant correlations between weight gain after STN-DBS and brain metabolism in associative and limbic areas and no correlation with metabolism in motor areas. These results confirmed the view that cognitive and emotional mechanisms may be associated with changes in body weight following STB-DBS (Sauleau et al., 2014). Interestingly, more recently these authors (Saleau et al., 2016) documented an inverse pattern of correlation in a sample of patients with PD undergoing GPi-DBS (i.e., significant correlation between weight gain and brain metabolism in motor areas and absence of correlation with brain metabolism in limbic and associative areas), suggesting that weight changes after STN and GPi stimulation may be explained by different mechanisms.

Furthermore, it has been argued that the STN may be a key component of the brain network that mediates behavioural inhibition. Indeed, in rats, lesions or high frequency stimulations of the STN increase premature responses in different reaction time (RT) tasks and impair animal's ability to inhibit responses. Moreover, STN-DBS or subthalamotomy in PD can be associated with behavioural and psychiatric problems that reflect deficits in inhibitory control or with the appearance of impulse control disorders (see Balarajah & Cavanna, 2013; Jahanshahi, Obeso, Baunez, Alegre, & Krack, 2015). For instance, several studies in which go/no-go paradigms were used reported that STN-DBS impairs the ability to withhold responses on no-go trials (Ballanger et al., 2009; Georgiev, Dirnberger, Wilkinson, Limousin, & Jahanshahi, 2016; Hershey et al., 2010, 2004; but see also; van den Wildenberg et al., 2006). To our knowledge, no research until now has examined the role of impulsivity in weight gain after STN-DBS.

It is reasonable to expect, however, that both motivation and control will likely play an important role in determining food intake (Berthoud, 2007; Ziauddeen, Alonso-Alonso, Hill, Kelley, & Khan, 2015). Alterations in reward sensitivity are associated with eating disorders (Berridge, 2009) and, in general, influence appetite and body weight control (Finlayson, King, & Blundell, 2007). In particular, sensitivity to reward includes both the sensory pleasure associated with eating (liking) and the degree to which food elicits the motivation to eat (wanting) (Berridge, 2009). Interestingly, there is evidence pointing to the critical role of dopamine in modulating wanting rather than liking (Robinson, Sandstrom, Denenberg, & Palmiter, 2005). Recent evidence also supports a role of inhibitory processes in the control of palatable food intake (Martin & Davidson, 2014). High levels of impulsivity have been described in binge eaters (Schag, Schönleber, Teufel, Zipfel, & Giel, 2013) and found to be associated with unhealthy eating (Guerrieri, Nederkoorn, Schrooten, Martijn, & Jansen, 2009), unsuccessful dieting (Jansen et al., 2009) and vulnerability to overeating, especially in the presence of a