

Name of Disorder:
Parkinson's disease

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Essay Title: **Dopamine deregulation and abnormal reward seeking behaviours in Parkinson's disease**

Parkinson's disease (PD) is a degenerative disorder of the central nervous system which typically occurs after age 50 and lead to death. The typical motor symptoms of this clinical condition are the result of the necrosis of the neurons that synthesize and release dopamine.

At the onset of the disease, the most evident symptoms are related to the movement and include tremors, rigidity, slowness of movement and difficulty walking. Later, cognitive and behavioral problems may arise. The diagnosis in typical cases is mainly based on symptoms, with neuroimaging confirmation. The modern treatments are effective to manage the symptoms of the disease early engines, thanks to the use of dopamine agonists and levodopa. As the disease progresses, dopaminergic neurons continue to decrease in number and these drugs become ineffective in the treatment of the symptoms and, at the same time, produce complications such as dyskinesia, which is characterized by involuntary movements.

From a clinical point of view it is very interesting to dwell on the conduct changes typically associated with PD.

Recent studies have identified a subpopulation of PD patients who exhibit impulsive and compulsive behaviours, such as pathological gambling, hypersexuality, compulsive shopping, and binge eating (Wolters et al., 2008). Interestingly,



hypersexuality and pathological gambling have been associated with males, while females may be inherently thought to be more likely to participate in compulsive shopping and binge-eating behaviours.

Pathologic gambling is a failure to resist the urge to gamble, with persistent and recurrent maladaptive gambling behaviour despite deleterious consequences on familial, occupational, and social functioning. Hypersexuality is characterized by a preoccupation with sexual thoughts, frequent demands and desires, and Internet pornography use or contact with sex

Figure. *The Cardsharps*. Caravaggio, 1594

workers (Voon and Fox, 2007). Compulsive shopping is characterized by maladaptive preoccupation of buying or shopping, whether impulses or behaviours

that are experienced as irresistible, intrusive, and/or senseless, resulting in frequent buying of more than can be afforded (Pontone et al., 2006). Compulsive eating refers to an uncontrollable consumption of a larger amount of food than normal in excess of that necessary to alleviate hunger (Nirenberg and Waters, 2006).

All these deranged behaviors are united by shared neurophysiological mechanisms, which refer to the brain circuits involved in the encoding of rewarding outcomes.

These behaviours seem also associated to predisposing and concomitant factors such as higher novelty seeking, impulsivity, and alcohol abuse disorders, thus emphasizing a common underlying susceptibility (Voon et al., 2007).

The degeneration of the dopaminergic neurons as well as the treatment with promoters of dopamine synthesis and/or inhibitors of dopamine antagonists seem to have a direct impact on this reward seeking behaviors, given the direct involvement of this neuromodulator on reward processing. For example, disordered gambling can spontaneously occur in a significant number of PD, but more commonly with the assumption of dopamine (DA) agonists (Voon et al., 2007).

Several hypotheses have been proposed to underlie these behavioural abnormalities.

One possibility is that the dopaminergic therapy may stimulate mesolimbic circuitry related to engagement in motivated behaviours. In PD, dopaminergic treatment treated to alleviate motor dorsal striatal deficiencies may result in an “over-dosing” in ventral cortico-striatal cognitive and limbic pathways. Indeed, hyper-dopaminergic levels induced by overstimulation of relatively preserved mesocorticolimbic dopamine pathway could result in impulse control disorders, in patients with individual predisposition (Cilia et al., 2008).

DA agonists are also known to enhance learning from rewarding outcomes and reinforce impulse choice. Impulse control disorders could be the result of dysfunction of an inhibitor pathway concerning the assessment of negative consequences of an action (Von et al., 2010). Thus, it has been hypothesized that impulsive decisions associated with a distorted estimation of the consequences of actions (positive bias) could lead to abnormal reward seeking behaviours with disastrous repercussions for everyday life (Bonnet et al., 2012).

References: Bonnet A, et al. *Parkinsons Dis.* 2012; 198316: 15; Frank MJ, et al. *Science.* 2004; 306:1940–1943. Lawrence AD, et al. *Front Psychol.* 2013; 4:90; Cilia R, et al. *Archives of Neurology.* 2008; 65: 1604–1611; Nirenberg MJ, Waters C. *Movement Disorders.* 2006; 21:524–529; Pontone G, et al., *Neurology.* 2006; 67:1258–1261; Schott BH, et al. *Brain.* 2007; 130:2412–2424; Shohamy D, et al. *Behav Brain Res.* 2005; 156:191–199; Voon V, Fox SH. *Arch Neurol.* 2007; 64(8):1089–1096; Voon V, et al. *Neuron.* 2010; 65(1):135–142; Wolters E, et al. *J Neurol.* 2008; 255:48–56.