SciMedCentral

Journal of Neurological Disorders & Stroke

Mini Review

Neuropsychiatric Symptoms in Parkinson's disease: Beyond Complications

AA Kehagia[1]* and P Shotbolt[2]

[1]Department of Neuroimaging, Institute of Psychiatry, King's College London, UK
[2]Department of Psychological Medicine, King's College Hospital, UK

*Corresponding author
Angie A Kehagia, Department of Neuroimaging, Institute of Psychiatry, King's College London, DeCrespigny Park, PO89, London SE5 8AF, UK, Email: angie.kehagia@gmail.com

Submitted: 22 October 2014

Accepted: 01 December 2014

Published: 02 December 2014

Keywords
- Parkinson's disease
- Symptoms
- Complications
- Nosology
- Neuropsychiatry

Abstract

In this viewpoint, we present the position that many neuropsychiatric phenomena in Parkinson's disease (PD), which are often referred to as complications, mightbe more usefully conceptualised as symptoms, since they stem from the pervasive pattern of neurodegeneration and multiple neurotransmitter system compromise seen in the disease. We discuss psychosis, sleep disturbance, depression, and dementia within this framework, dissociating these from impulse control disorders which appear to stand alone as iatrogenic complications. We conclude that evolving the concept of the disease to encompass neuropsychiatric phenomena as bona fide symptoms will improve their management and ultimately lead to improved quality of life for patients with PD.

INTRODUCTION

Parkinson's disease (PD) extends beyond movement to encompass a range of psychiatric phenomena, such that it is considered the prototypical neuropsychiatric disorder [1]. Neuropsychiatric symptomsare the inexorable consequence of its multi-faceted neuropathology and are recommended by the EFNS/MDS-ES Task force as criteria to aid differential diagnosis [2].While the movement disorder is linked to central dopamine dysfunction, neurodegenerative events in the main noradrenergic, serotoninergic and cholinergic nuclei precede motor symptom onset by a decade or longer[3], and extensive frontal and posterior cortical compromise occurs. Nonetheless, psychiatric phenomena in a movement disorder fall between the remits of neurology and psychiatry. Perhaps as a consequence, these are often demoted to and referred to as complications caused by treatments that target dopamine to alleviate motor symptoms, to the detriment of diagnostic accuracy and effective clinical management. We argue that, ontologically, psychiatric symptoms in PD reflect the interacting contributions of multiple neurotransmitter systems and sometime seven present prodromally. As such we consider that they constitute core clinical features of the condition. We elaborate on this theoretically significant difference in nomenclature below.

PD psychoses, particularly visual hallucinations, have been attributed to dopaminergic overstimulation, despite inconsistent findings regarding their relationship to agonist or levodopa exposure [4,5]. Instead, cognitive impairment and other factors such as the severity and duration of disease reliably increase the risk for PD psychosis. The role of serotonin in these phenomena has been highlighted by arecent trial of the selective 5HT2A inverse agonist pimavanserin [6], which was well tolerated and improved positive symptoms. Unlike atypical antipsychotics, it did not exacerbate motor symptoms, owing to the absence of affinities for other receptor types. Studies such as this contribute to clinical management in PD on the basis of reconceptualising psychoses as a set of symptoms with a potentially additional serotoninergic substrate, rather than a dopaminergic complication.

Other neuropsychiatric symptoms ensue from the non-dopaminergic pathology of PD. REM sleep behaviour disorder (RBD) is another core prodromal symptom of PDimplicating serotonin. It is robustly associated with psychosis [7] and was also improved by pimavanserin [6]. Moreover, prodromal mood disturbanceindicatesearly serotoninergic and noradrenergic pathology and significantly increases the risk of a future PD diagnosis [8]. Itis the second highest quality of life predictor in PD [9], but remains underdiagnosed and undertreated [10], probably because clinicians investigate and patientsreport motor symptoms only. Conversely, dementia, syndromically distinct from the more prevalent pattern of mild cognitive impairment mirroring monoaminergic dysfunction, appears during the disease course and has a clear cholinergic character [11].

The psychiatric phenomena which currently appear to stand alone as treatment complications are impulse control disorders (ICD), collectively referring to gambling, hypersexuality, punding and the compulsive use of anti parkinsonian drugs [12].These alone appear following the administration of DA agonists in vulnerable patients with distinctive dopaminergic

pathophysiology, and are thusaccurately conceptualised as iatrogenic complications.

Collectively, these observations supporta nosological argument for distinguishing bona fide neuropsychiatric symptoms in PD from complications, predicated on acknowledging the pervasive effects of the disease. Certain psychiatric phenomena may precede the PD diagnosis itself, representing identifiable and clinically relevant disease prodromes. Others appear as the disease progresses and may be exacerbated by medication, while ICDs represent an agonist complication. The profound impact of neuropsychiatric dysfunction on quality of life in PD, as well as its under diagnosis, represents the most compelling observation that evolving the concept of the disease beyond dopamine and motor dysfunction is a necessity.

REFERENCES

1. Weintraub D, Burn DJ. Parkinson's disease: the quintessential neuropsychiatric disorder. Mov Disord. 2011; 26: 1022-103.
2. Berardelli A, Wenning GK, Antonini A, Berg D, Bloem BR, Bonifati V, et al. EFNS/MDS-ES/ENS [corrected] recommendations for the diagnosis of Parkinson's disease. Eur J Neurol 2013; 20: 16-34.
3. Hawkes CH, Del Tredici K, Braak H. A timeline for Parkinson's disease. Parkinsonism Relat Disord. 2010; 16: 79-84.
4. Fenelon G, Alves G. Epidemiology of psychosis in Parkinson's disease. J Neurol Sci. 2010; 289: 12-17.
5. Shotbolt P, Samuel M, David A. Quetiapine in the treatment of psychosis in Parkinson's disease. Therapeutic advances in neurological disorders. 2010; 3: 339-350.
6. Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial. Lancet. 2014; 383: 533-540.
7. Pacchetti C, Manni R, Zangaglia R, et al. Relationship between hallucinations, delusions, and rapid eye movement sleep behavior disorder in Parkinson's disease. Mov Disord. 2005; 20: 1439-1448.
8. Shen CC, Tsai SJ, Perng CL, Kuo BIT, Yang AC. Risk of Parkinson disease after depression A nationwide population-based study. Neurology. 2013; 81: 1538-1544.
9. Kuopio AM, Marttila RJ, Helenius H, Toivonen M, Rinne UK. The quality of life in Parkinson's disease. Mov Disord. 2000; 15: 216-223.
10. Chaudhuri KR, Prieto-Jurcynska C, Naidu Y, Mitra T, Frades-Payo B, Tluk S, et al. The nondeclaration of nonmotor symptoms of Parkinson's disease to health care professionals: an international study using the nonmotor symptoms questionnaire. Mov Disord. 2010; 25: 704-709.
11. Kehagia AA, Barker RA, Robbins TW. Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease. Lancet Neurol. 2010; 9: 1200-1213.
12. Weintraub D, Siderowf AD, Potenza MN, Goveas J, Morales KH, Duda JE, et al. Association of dopamine agonist use with impulse control disorders in Parkinson disease. Arch Neurol. 2006; 63: 969-973.

Cite this article

Kehagia AA , Shotbolt P (2014) Neuropsychiatric Symptoms in Parkinson's disease: Beyond Complications. J Neurol Disord Stroke 2(5): 1091.