Original Research Paper

Volume - 12 | Issue - 08 | August - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Psychiatry

NEUROPSYCHIATRIC ASPECTS OF MOVEMENT DISORDERS

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ABSTRACT All of the major movement disorders (Parkinson's disease, Huntington's disease, Tourette syndrome) have important associated psychiatric dimensions. These if co-occurring together, cause significant clinical burden and effect patients' quality of life and prognosis gets affected. Similarly, many of the major psychiatric disorders (such as Schizophrenia and Depression), involve abnormalities of movement. Many psychotropic medications are also known to cause movement disorders. A clinician should always assess the psychiatric comorbidities in relation to movement disorders that will help to build a holistic and pragmatic approach to management and consequently, improve the quality of life of the patient.

KEYWORDS : Movement disorders, Neuropsychiatric, Psychiatric comorbidities

INTRODUCTION

Movement disorders refers to a group of diseases of the CNS that primarily involve neurodegeneration of the basal ganglia, cerebellum or both. Movement disorder disrupt motor function by either abnormal , involuntary ,excessive movements (HYPERKINETIC) (1) or curtailing (restricting) the amount of normal free flowing movement (HYPOKINETIC) (2). Diagnosis and treatment of neuropsychiatric conditions in patients with primary movement disorders are challenged by the interplay of motor, cognitive and psychiatric features over the course of the disease. As a result, there are several difficulties which are encountered in the management of the same, that is, treatment of motor symptoms –which may exacerbate or cause psychiatric symptoms. Also, psychiatric treatment may result in adverse motor and cognitive side effects (3).

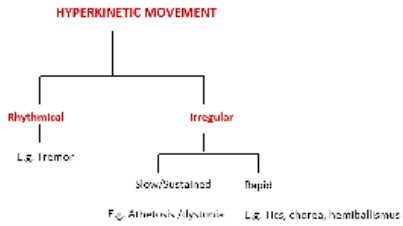
There can be several presentations of movement disorders. Table 1 demonstrates some of the possible symptom complexes pertaining to the disorders.

TABLE 1|Motor symptom complex and associated movement disorders

MOTOR SYMPTOM COMPLEX	MOVEMENT DISORDER
Tremor and akinesia	Parkinson Disease or atypical Parkinsonism
Parkinsonism, ataxia, autonomic dysfunction, spasticity, myoclonus	Multiple system atrophy
Vertical supranuclear gaze palsy and falls, symmetrical parkinsonism	Progressive supranuclear palsy
Akinesia, rigidity, myoclonus, dystonia, apraxia, asymmetrical clinical phenotype	Coticobasal degeneration
Chorea, dystonia and bradykinesia	Huntington disease
Dystonia plus tremor	Primary dystonia
Tremor, dystonia, akinetic-rigid syndrome	Wilson disease

Hyperkinetic movements are unwanted or excess movements that are frequently seen in children with neurologic disorders. They are an important clinical finding with significant implications for diagnosis and treatment. Figure 1 elicits the classification of hyperkinetic movement disorders and the relevant examples in each category.

FIGURE 1 | Classification of Hyperkinetic Movement disorders



PSYCHIATRIC MORBIDITIES OF INDIVIDUAL MOVEMENT DISORDERS

PARKINSONISM

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Although its major manifestation is motor symptoms, resulting from the loss of dopaminergic neurons in the substantia nigra, psychiatric symptoms, such as depression, anxiety, hallucination, delusion, apathy and anhedonia, impulsive and compulsive behaviours, and cognitive dysfunction, may also manifest in most patients with PD.(4)

Key findings done across several studies in this regard are summarised in table 2.

TABLE 2|Psychiatric co-morbidities of Parkinson's disease

Associated psychiatric disorders	Prevalence in PD	Clinical features	Management
1.Depression	30% (Ellwanger et al, 2012)	Reactive depression as a result of chronic illness; pathology in all the brainstem monoaminergic nuclei	First line: SSRI-Sertraline preferred SNRI: Venlafaxine ECT is an effective antidepressant treatment in PD patients
2.Anxiety disorder	20-50% (Pontone et al, 2011)	Generalized anxiety and panic attacks associated with "off" periods are common Social phobia – also common	First line: SSRI Bromazepam, a long-acting benzodiazepine, improved psychological and somatic anxiety symptoms

			Psychological therapy (for example, through a PD specialist nurse) or both, with dramatic improvements in quality of life for all concerned
3. Psychosis	25-40% (Pontone et al, 2011)	Most commonly: complex visual hallucinations Auditory hallucinations occurring in the absence of visual hallucination are rare Accompanying paranoid ideation	Gold standard is clozapine Quetiapine can also be used Other "atypical" neuroleptic agents (olanzapine and risperidone) reduce or eliminate psychosis at low doses, but their effects on striatal D2 receptors are frequently associated with significant motor deterioration Pimavanserin, a selective serotonin 5HT2A inverse agonist
4. Dementia	30%	Visual Hallucination, cognitive disturbance, agitation, visuospatial disturbance	Current treatments for PD dementia are mostly derived from those utilized in Alzheimer's disease; focussing mainly on cholinesterase inhibitors. Memantine, a NMDA receptor antagonist can be used. Rivastigmine, the only Food and Drug Administration approved medication for PD dementia, is a reasonable first choice

Aetiology of Parkinson's Disease

Parkinson's Disease is characterised by progressive loss of dopaminergic neurons in the ventral tier of the SNpc and intraneuronal aggregation of the α-synuclein protein in the form of Lewy bodies. Motor symptoms appear when 60-80% of SNPc neurons degenerate. Transformation of alpha-synuclein protein to fibrillary and oligomeric forms and their aggregation, leads to neurotoxicity and subsequent psychiatric manifestations.(5)

BRAAK HYPOTHESIS

In 2003, Braak et al. postulated the hypothesis that an unknown pathogen (virus or bacterium) in the gut could be responsible for the initiation of sporadic PD, and they presented an associated staging system for PD based on a specific pattern of alpha- synuclein spreading. These publications were followed by the more encompassing dual-hit hypothesis, stating that sporadic PD starts in two places: The neurons of the nasal cavity and the neurons in the gut. This is known as Braak's hypothesis.(6)

It is seen that initial symptoms of PD originate from pathology in the enteric nervous system, medulla, and olfactory bulb, which over the years progresses to Substantia Nigra pars compacta (SNPc). This is supported by evidence, non-motor symptoms such as anosmia, hyposmia, sleep disturbances, constipation, and anxiety and depressive disturbances, often precede onset of motor symptoms by several years.

HUNTINGTON'S DISEASE

It is an Autosomal Dominant Neurodegenerative disorder. Onset is most commonly between 30 to 50 years of age. Late onset of Huntington's Disease is usually after 50 years of age and is associated with more motor symptoms.

Huntington's disease and Psychiatric Disorders

The clinical picture of HD comprises of motor abnormalities (chorea, dystonia, bradykinesia, oculomotor-dysfunction), cognitive impairment, behavioural problems, and psychiatric disorders. The latter are major constituents of the clinical spectrum of HD and have a substantial impact on daily functioning, constituting the most distressing aspect (for both patient and relatives) and often the reason for hospitalization.(7)

The associated psychiatric morbidities and their prevalence is listed in table 3.

TABLE 3 | PSYCHIATRIC MORBIDITIES OF HUNTINGTON'S DISEASE (8)

Irritability	38-73%
Apathy	34-76%
Anxiety	34-61%
Depressed mood	33-69%
Obsessive and compulsive	10-52%
Psychotic	3-11%

Suicide remains a major concern in HD

This is mainly attributable to two reasons: Neuropsychiatric manifestations, with the combination of depression and impulsivity representing a particular risk. Also, most patients know, by virtue of their family history, what their future holds.(9)

Management:

SSRIs are usually helpful in treating depression or OCD (or both). However, they occasionally exacerbate chorea. In this case, low dose Flupenthixol is an alternative. As with PD, atypical neuroleptics allow psychosis to be treated with fewer motor complications.

FAHR'S DISEASE

It is seen as calcium deposition in the basal ganglia areas, as evident on T2 MRI. Psychosis and catatonic symptoms are evident, if onset is between 20-30 years of age. In case of late onset is between 50-60 years, then dementia is the most predominant symptom. (10)

WILSON'S DISEASE

Wilson's disease is an autosomal recessive illness attributed to a defect of the gene ATP7B (on chromosome 13) leading to excessive accumulation of copper in liver, brain, and other tissues. A vast range of psychiatric symptoms has been described in patients with Wilson's disease, so many that the illness has been called "a great masquerader" Associated psychiatric symptoms include Personality disturbances, mood abnormalities and Cognitive dysfunction. Several neurological complications can also be associated with Wilson's disease which include rigidity, dystonia, tremor and dysarthria.(11)

MOVEMENT DISORDERS IN "PRIMARY PSYCHIATRIC DISEASE"

DEPRESSION

Depression is often accompanied by a phenomenon termed psychomotor retardation by psychiatrists. This retardation is a core feature of major depressive disorder, indicating a more severe disorder with a poorer prognosis. To a neurologist retardation is the same phenomenon as bradykinesia. This view is reinforced by studies of psychomotor function and reaction times showing no difference between depressed patients and PD patients in these measures.(12)

OBSESSIVE-COMPULSIVE DISORDER AND TOURETTE'S SYNDROME

OCD is often associated with disorders of movement. The condition that best illustrates the overlap between neurological and psychiatric manifestations, is Gilles de la Tourette's syndrome (TS). TS is defined on the basis of its movement disorder, with multiple motor and vocal tics, but the accompanying OCD is often the principal source of disability. The phenomenology of OCD in TS is very similar to that of isolated OCD. Checking compulsions more common; repetitive hand washing less common. First degree relatives of TS patients may have isolated OCD without a movement disorder. Conversely, patients with

apparently isolated OCD have an increased frequency of mild tics.(13)

MOTOR SYMPTOMS IN SCHIZOPHRENIA

Most clinicians relate parkinsonism and dyskinesia directly to acute and tardive drug-induced movement disorders. However, parkinsonism and dyskinesia are also present in antipsychotic-naïve patients with psychotic disorders.

At least one motor sign has been reported to be prevalent in 66% of first-episode, never-medicated patients, in 59% of patients on admission, and in 80% of chronically medicated patients.(14)

These include abnormal, involuntary movements such as tardive dyskinesias (TD) which are abnormal, involuntary, repetitive movements of the orofacial, limb, trunk, and respiratory musculature, catatonic symptoms, Parkinsonism, psychomotor slowing and neurological signs(NSS).

PSYCHOGENIC MOVEMENT DISORDERS

Psychogenic movement disorder (PMD) is a clinical syndrome of abnormal movements that is not explained by a medical disorder. It is known to occur in 2%-3% of movement disorder clinic patients.(15) Psychological factors are a supportive criterion in determining the degree of certainty of the diagnosis of PMD, but their presence is not a requirement for diagnosis. The associated motor symptoms include tremor, dystonia, chorea, tics and gait disorders and conversion paralysis. (16)

MOVEMENT DISORDERS AS SIDE EFFECTS OF PSYCHIATRIC MEDICATION

Drug-induced movement disorders (DIMD) are a group of neurological motor disturbances associated with the use of neuroleptic agents.

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) lists eight categories of medication-induced movement disorders. 1)Neuroleptic-induced; 2) NMS; 3) Medication-induced acute dystonia; 4) Medication-induced acute akathisia; 5) Tardive dyskinesia;
6) Medication-induced postural tremor; 7) Other medication-induced movement disorder; 8) Antidepressant discontinuation syndrome; 9) Other adverse effects of medication.

The associated risk factors for EPS are as follows: increasing age being the most important risk factor. Others include, female gender, affective disorder, presence of acute EPS, previous brain injury, poor treatment response to antipsychotic drugs, greater total drug exposure, longer duration, higher cumulative drug doses, polypharmacy (typical more than atypical antipsychotics), diabetes, alcohol or drug dependence.

The most common antipsychotic associated with EPSE is Haloperidol. Others include: Perphenazine, Thiothixene, Fluphenazine, Trifluoperazine, Risperidone, Other antidopaminergic drugs like the antiemetic such as metoclopramide or the tricyclic antidepressant, Selective Serotonergic Reuptake Inhibitors.(17)

Table 4 and 5 describe DIMD in detail

	Dystonia	Pseudo-Parkinsonism	Akathisia	Tardive Dyskinesia
SIGNS AND SYMPTOMS	Muscle spasm in any part of the body, e.g.: eyes rolling upwards (oculogyric crisis) head and neck twisted to the side (torticollis)	Tremor and/or rigidity; Bradykinesia (decreased facial expression, flat monotone voice, slow body movements, inability to initiate movement) Bradyphrenia (slowed thinking) Salivation	A subjectively unpleasant state of inner restlessness where there is a strong desire or compulsion to move e.g. foot stamping when seated constantly crossing/uncrossing legs; rocking from foot to foot constantly pacing up and down	A wide variety of movements can occur such as: lip smacking or chewing, tongue protrusion (fly catching) choreiform hand movements (pill rolling or piano playing) pelvic thrusting

TABLE 4| DIMD CLINICAL FEATURES (18)

TABLE 5| DIMD MANAGEMENT (19)

Dystonia	Pseudo-Parkinsonism	Akathisia	Tardive Dyskinesia
Acute dystonia resolves when the offending drug is discontinued or the dose is reduced or switching to an antipsychotic with a low propensity for extrapyramidal symptoms (EPS). In severe cases dystonia can be effectively relieved with a short course of a potent antimuscarinic agent such as benztropine, Diphenhydramine, and Trihexyphenidyl, administered orally, intramuscularly, or intravenously.	Pseudo-Parkinsonism remits slowly after drug withdrawal or reducing the dose, but some patients may develop persistent symptoms. Other options include change to another drug with lower propensity. Second generation neuroleptics are associated with lower risk than first generation antipsychotics. Anticholinergic agents, such as benztropine, amantadine (especially in elderly or in patients already having early signs of Parkinson's disease), or diphenhydramine are prescribed if symptoms persist.	Anticholinergic drugs(benztropine), catecholamine-depleting drugs such as Reserpine, Tetrabenazine, and Oxypertine. Other drugs such as benzodiazepines and opiates with limited utility have been used.	Prevention is the best strategy which includes identifying the risk factors, early diagnosis, and use of antipsychotic medications only when clearly indicated, that too in the lowest effective doses. Once it is recognised, withdrawal of any anticholinergic drugs and a reduction in the dose of antipsychotic drugs has been recommended as initial steps. Alternatively, the clinician may switch the patient to clozapine or change to an antipsychotic with lower propensity for Tardive Dyskinesia. Most frequently prescribed additional drugs for treatment of TD is propranolol, Clonazepam, Tetrabenazine, Vitamin E, Levodopa and Botulinum toxin.

SOME RECENT ADVANCES

Functional neuroimaging in psychogenic dystonia

On fMRI, anatomically distinct patterns of cerebral blood flow in psychogenic and organic dystonia: In organic dystonia - greater regional blood flow in the primary motor cortex and thalamus compared to controls, with a reduction in the cerebellum. In contrast, psychogenic dystonia was associated with greater blood flow in the cerebellum and basal ganglia, with decrease in the primary motor cortex. The prefrontal cortex was implicated in both types of dystonia.(20)

Social cognition in Huntington disease

Social cognition encompasses several subdomains, including the ability to recognize emotions from facial expressions, voice, or body posture, as well as "theory of mind" (ToM). Both patients manifesting disease as well as the premanifest gene carriers have difficulties in decoding facial expressions. Disproportionate impairments in

recognizing angry facial expressions and disgust -neuroimaging studies correlated with damage to the ventral putamen and atrophy of the anterior insula.(21)

Treatment of Tourette syndrome

Tics that prove refractory to conventional pharmacologic treatment and behavioural therapies, several studies over the last decade have suggested that such tics can be improved by deep brain stimulation (DBS). DBS can also help to ameliorate psychiatric comorbidities such as OCD, aggression, impulsivity, depression, and anxiety.(22)

Treatment of Psychosis in Parkinson disease

Pimavanserin, a selective serotonin 5-HT2A inverse agonist is found useful in treatment of Psychosis in PD. In a 6-week double-blind study, it was seen that Pimavanserin had clinically significant improvements on PD-adapted scale for positive symptoms, which is a 9-item scale rating symptoms like delusions and hallucinations.(23)

CONCLUSION

Movement disorders have an important psychiatric dimension that warrants careful enquiry clinically. Despite their high prevalence, there is still a lack of efficacious, well-tolerated therapies to treat psychiatric manifestations of movement disorders. In addition, several psychotropic medications have movement disorders as side effects, both in the short and long-term durations, which requires careful consideration when prescribing. A detail and in-depth knowledge is required for the interface of neurological causes of movement disorders and psychiatric associated comorbidities to improve the overall quality of life of the patient and for better prognosis, thereby, reducing clinical dilemmas and other consultation Liaison matters.

CONFLICTS OF INTEREST

Nil

REFERENCES

1. Sanger TD, Chen D, Fehlings DL, Hallett M, Lang AE, Mink JW, et al. Definition and classification of hyperkinetic movements in childhood. Mov Disord. 2010 Aug 15;25(11):1538–49.
2. Roffman JL, Eisenberg T, Stern TA. Neuropsychiatric Phenomena Associated With Movement Disorders: (Rounds in the General Hospital). Prim Care Companion J Clin Psychiatry. 2006 Feb 15;08(01):39–42.
3. Lohr JB, May T, Caligiuri MP. Quantitative assessment of motor abnormalities in untreated patients with major depressive disorder. J Affect Disord. 2013 Mar;146(1):84–90.
4. Han JW, Ahn YD, Kim W-S, Shin CM, Jeong SJ, Song YS, et al. Psychiatric Manifestation in Patients with Parkinson's Disease. J Korean Med Sci. 2018;33(47):e300.
5. Stoker TB, Greenland JC, John Van Geest. Parkinson's Disease: Pathogenesis and Clinical Aspects [Internet]. Codon Publications; 2018.
6. Rietdijk CD, Perez-Pardo P, Garssen J, van Wezel RJA, Kraneveld AD. Exploring Braak's Hypothesis of Parkinson's Disease. Front Neurol. 2017 Feb 13;8.
7. Paoli R, Botturi A, Ciammola A, Silani V, Prunas C, Lucchiari C, et al. Neuropsychiatric Burden in Huntington's Disease. Brain Sci. 2017 Jun 16;7(12):67.
8. Novak MJU, Warren JD, Henley SMD, Draganski B, Frackowiak RS, Tabrizi SJ. Altered brain mechanisms of emotion processing in pre-manifest Huntington's disease. Brain. 2012 Apr;135(4):1165–79.
9. van Duijn E, Kingma EM, van der Mast RC. Psychopathology in Verified Huntington's Disease Gene Carriers. J Neuropsychiatry Clin Neurosci. 2007 Oct;19(4):441–8.
10. Pourshahid S, Salloum MN, Elfishawi M, Barakat M, Basith M. Fahr's Disease: A Differential to Be Considered for Various Neuropsychiatric Presentations. 2018 Mar 11
11. Zimbrean PC, Schilsky ML. The Spectrum of Psychiatric Symptoms in Wilson's Disease: Treatment and Prognostic Considerations. Am J Psychiatry. 2015 Nov;172(11):1068–72.
12. Caligiuri MP, Ellwanger J. Motor and cognitive aspects of motor retardation in depression. J Affect Disord. 2000 Jan;57(1–3):83–93.
13. Worbe Y, Mallet L, Golmard J-L, Béhar C, Durif F, Jalenques I, et al. Repetitive Behaviours in Patients with Gilles de la Tourette Syndrome: Tics, Compulsions, or Both? Sirigu A, editor. PLoS ONE. 2010 Sep 24;5(9): 12959.
14. Walther S, Strik W. Motor Symptoms and Schizophrenia. Neuropsychobiology. 2012;66(2):77–92.
15. Kranick S, Ekanayake V, Martinez V, Ameli R, Hallett M, Voon V. Psychopathology and psychogenic movement disorders. Mov Disord. 2011 Aug 15;26(10):1844–50.
16. Voon V, Brezing C, Gallea C, Ameli R, Roelofs K, LaFrance WC, et al. Emotional stimuli and motor conversion disorder. Brain. 2010 May 1;133(5):1526–36.
17. Pringsheim T, Doja A, Belanger S, Patten S, The Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children (CAMESA) guideline group. Treatment recommendations for extrapyramidal side effects associated with second-generation antipsychotic use in children and youth. Paediatr Child Health. 2011 Nov 1;16(9):590–8.
18. Taylor D, Barnes TRE, Young AH. The Maudsley prescribing guidelines in psychiatry. 13th edition. Hoboken, NJ: Wiley; 2019.
19. Alam SA, Baruah A, Agarwal G, Mohite N. Management of drug-induced movement disorders in psychiatry: an update. Open J Psychiatry Allied Sci. 2016;7(2):111.
20. Schrag AE, Mehta AR, Bhatia KP, Brown RJ, Frackowiak RSJ, Trimble MR, et al. The functional neuroimaging correlates of psychogenic versus organic dystonia. Brain. 2013 Mar;136(3):770–81.
21. Unti E, Mazzucchi S, Frosini D, Pagni C, Tognoni G, Palego L, et al. Social Cognition and Oxytocin in Huntington's Disease: New Insights. Brain Sci. 2018 Aug 26;8(9):161.
22. Savica R, Stead M, Mack KJ, Lee KH, Klassen BT. Deep Brain Stimulation in Tourette Syndrome: A Description of 3 Patients With Excellent Outcome. Mayo Clin Proc. 2012 Jan;87(1):59–62.
23. Tampi RR, Tampi DJ, Young JJ, Balachandran S, Hoq RA, Manikkara G. Evidence for using pimavanserin for the treatment of Parkinson's disease psychosis. World J Psychiatry. 2019 Jun 10;9(3):47–54.