NEUROPSYCHIATRIC ASPECTS OF MOVEMENT DISORDERS

INTRODUCTION

- × The term movement disorders refers to a group of diseases of the CNS that primarily involve neurodegeneration of the basal ganglia, cerebellum or both.
- × Psychiatric and cognitive abnormalities are prominent in many patients with movement disorders, resulting in excess morbidity and caregiver burden.
- × In patients with movement disorders, management of psychiatric disorders is potentially complex because treatments of motor symptoms can exacerbate or cause cognitive or psychiatric symptoms.
- × Conversely, psychiatric treatments may result in adverse motor and cognitive side effects.

COMPARATIVE NOSOLOGY

CLASSIFICATION OF PSYCHIATRIC DISTURBANCES ASSOCIATED WITH MOVEMENT DISORDERS

- × According to DSM-5, psychiatric disturbances associated with movement disorders can generally be classified as "due to another medical condition," such as depression due to Huntington disease (HD), psychotic disorder secondary to dementia with Lewy bodies (DLBs) or anxiety disorder secondary to PD.
- × Additional qualifiers designate specific features of the presentation, such as with hallucinations or with major depressive-like episode.

PARKINSON' S DISEASE

- x Parkinson' s disease (PD) is the second most common neurodegenerative disease after Alzheimer' s disease. (Poewe WH et al. 1998)
- × Parkinson's disease is the most common neurodegenerative cause of parkinsonism, a clinical syndrome characterized by lesions in the basal ganglia, predominantly in the substantia nigra.
- × PD generally begins between the ages of 40 and 70 years, with peak age onset in the seventh decade.
- \times PD is estimated to affect 1 to 2% of the population older than 60 years of age.

PARKINSON' S DISEASE

- × The cause of PD is probably multifactorial, with contributions from hereditary predisposition, environmental toxins, and aging. The pathological changes of PD may appear as early as three decades before the appearance of clinical signs. (Davie CA. 2008)
- x PD has been defined by its characteristic motor presentation of tremor at rest, bradykinesia, rigidity, and gait impairment.

PARKINSON' S DISEASE

- × Non-motor signs and symptoms are increasingly recognized as part of PD. Non-motor features of PD include
 - × Cognitive impairment,
 - × Dementia,
 - × Depression,
 - \times Anxiety,
 - × Sleep disturbances,
 - × Apathy,
 - × Psychosis,
 - × Impulse control disorders
- × affect the majority of patients at some time or other during the course of disease.

COGNITIVE IMPAIREMENT

- × Cognitive impairment in PD is heterogeneous in its severity, rate of progression, and affected cognitive domains. (Goldman JG et al. 2014)
- X It varies from subtle cognitive changes or deficits, to mild cognitive impairment (MCI) in which cognitive deficits occur but do not significantly disrupt daily living.
- x MCI in PD increases the risk of conversion to dementia
 (Hoogland J et al. 2017)
- x PD-MCI may not always progress to dementia; on longitudinal assessments, some remain stable as "MCI" and others revert to normal cognition (Broeders M et al. 2013)

DEMENTIA (PDD)

- \times About 25 40% of PD patients develop dementia.
- × Progression to dementia is not inevitable in PD but develops in about 80% of patients with durations, especially longer than 20 years (Hely MA et al. 2008)
- × Risk factors for PDD include advanced age, older age of disease onset, limited cognitive reserve, hallucinations and predominant gait dysfunction (Emre M et al. 2007)
- × Cognitive deficits in PD typically affect executive functions, attention, visuospatial function, and processing speed.
- × The pattern of cognitive impairment varies, however, in not only the extent to which different cognitive domains are affected but also which domains are affected first

DEPRESSION

- x An association between PD and depression is well
 established.
- × Debate continues on whether depression is best seen as an understandable response to a debilitating disease or is part of the disease process itself.
- × Depressive disorders in PD involve more pervasive mood changes and generally resemble idiopathic forms of depression.
- \times Prevalence rates range from 20 90%, with an average reported frequency of 40 50%.
- \times Up to 50% of PD pts. with depression have major depression.

DEPRESSION

- × Lemke et al. (2004) suggests that depression in PD patients is characterised by increased levels of dysphoria and irritability and lower levels of guilt and suicidality.
- \times Lemke et al. (2005) found marked anhedonia in 80% of depressed PD patients.
- × Increased tearfulness has been found to be common in patients with PD, sometimes with 'emotionalism' as indicated by sudden weeping with loss of normal social control (Madeley et al. 1992)

ANXIETY

- × The most common anxiety disorders in PD are generalized anxiety disorder, social phobia, and panic disorder.
- \times Anxiety affects up to 40% of patients with PD (Richard IH. 2005)
- x Anxiety syndromes in PD resemble those in idiopathic conditions and frequently cooccur with depression.
- × There are also anxiety disturbances unique to PD, particularly anxiety associated with fluctuations in levodopa levels and motor function.
- × Some patients describe episodic panic attack-like states that develop at the same time every day and can be associated with motor deficits.

- × Disturbances of sleep are highly prevalent in Parkinson' s disease, affecting up to 96% patients (Garcia-Borreguero D et al. 2003)
- × Sleep problems may be an early sign of Parkinson' s disease, even before motor symptoms have begun.
- × Sleep disturbances can be assessed by validated scales like the Parkinson's disease sleep scale (PDSS).
- × Some of the common sleep problems for Parkinson' s patients
 include:

× Insomnia*

- × Difficulty in sleep initiation, sleep maintenance & awakening too early in the morning occur in patients with PD.
- \times Sleep maintenance difficulties are the most common, affecting up to 74-88% of patients.
- × REM behavior disorder (RBD)*
 - x RBD is a syndrome of abnormal behavior during rapid eye
 movement (REM) sleep.
 - × The response may range from relatively mild restlessness to more severe wild punching and thrashing.
 - × RBD, of varying degrees of severity, occurs in 15-50% of patients with PD.

× Apnea*

- \times Apnea has been found in as many as 50% of patients with PD.
- \times Snoring and apneic episodes also may be up to three times more common in PD (12%) than in the general population.
- x Restless Legs Syndrome (RLS) and Periodic Leg Movements of Sleep (PLMS)*
 - \times RLS and PLMS are common in patients with PD, occurring in up to 15% of patients.
 - × It lead to disrupted sleep and excessive daytime sleepiness.

× Vivid Dreaming*

- × An increase in dreaming is common in PD, with studies suggesting that about 30% of patients develop vivid dreams.
- × Vivid dreams are often a prodrome of daytime hallucinations.
- × Excessive Daytime Sleepiness (EDS)*
 - \times Estimates of the occurrence of EDS range from 15 50%.
 - × The presence of EDS are significantly correlated with more severe disease, more disability, cognitive decline and depression.

× Sleep Attacks*

- x Sleep attacks are abrupt and unavoidable transitions from wakefulness to sleep.
- × These "attacks" are of particular concern as the patient may have little warning that they are about to fall asleep.
- \times The prevalence of sleep attacks in patients with PD varies across studies, from 0 to 30%.

*Menza M, Dobkin RD, Marin H, Bienfait K. Sleep disturbances in Parkinson's disease. Mov Disord. 2010;25 Suppl 1(Suppl 1):S117-22.

APATHY

- \times Apathy occurs in at least 25 % of PD patients and often coexists with depression.
- × It manifests as indifference and a lack of motivation, initiative, perseverance, interest in new things, or concern for one's health.
- × In most cases, apathy is not distressing to the patient, but the absence of spontaneous effort and interest can be frustrating for caregivers, who may perceive the patient as depressed.
- × Neurological signs and symptoms such as akinesia, hypomimia, hypophonia, cognitive dysfunction and bradyphrenia can confound recognition of apathy.

PSYCHOSIS

- × Psychosis affects about 25 40% of patients, with increased prevalence as the disease progresses.
- x In PD, psychotic symptoms include hallucinations and delusions.
- × Atypical symptoms, referred to as minor psychotic phenomena, affect over 66% of patients and include sense of presence, passage hallucinations and illusions.
- x Most common psychotic symptom in PD is visual hallucinations.

PSYCHOSIS

- × Typically, in earlier stages of PD, visual hallucinations include well-delineated animals or people that occur in a clear sensorium. They are not necessarily distressing and insight may be retained.
- × Later in the disease course, some patients experience persistent hallucinations and/or delusions in a clear sensorium but with diminished insight.
- × Aggression, delusional jealousy and other paranoid accusations, delusional fears about eating or medications, inappropriate sexual behaviors and confusion are frequent manifestations that can be difficult to manage and may require hospitalization.

IMPULSE CONTROL DISORDERS

- - × pathological gamoli
 - × hypersexuality,
 - × uncontrolled spending,
 - \times binge eating, are observed in up to 14% of patients with PD.
- \times About 33% of affected patients have more than one ICD.
- × Risk factors for development of ICDs, including younger age of PD onset, unmarried status, family history of problem gambling, cigarette smoking, caffeine use, and a novelty seeking temperament.

PROGRESSIVE SUPRANUCLEAR PALSY (PSP)

- × PSP, an important cause of parkinsonism, was first described in 1964, also known as Steele - Richardson - Olszewski syndrome.
- \times The prevalence is 5 to 6 cases per 100,000.
- \times PSP accounts for 4% of all cases with parkinsonism.
- × Onset of symptoms is usually after age 60 in all races and both genders, but men tend to be affected more often than women.
- × Patients appear "worried" or "astonished" resulting from dystonic contractions of facial muscles between the eyebrows, reduced blinking, lid retraction, and gaze palsy.

PROGRESSIVE SUPRANUCLEAR PALSY (PSP)

- × Cognitively, patients with PSP show features of a subcortical dementia with bradyphrenia, memory deficits, and predominant frontal lobe dysfunction with executive, attentional deficits, memory, visuospatial, and language and social cognitive deficits.
- \times Approx. 10% present with cognitive symptoms and up to 70% develop a dementia over the disease course.
- × Behavioral changes of apathy, irritability, childishness, impulsivity, and disinhibition are the most common psychiatric features.
- × There are also sleep disturbances, depression, pathological laughter and crying and occasionally schizophreniform psychotic symptoms.

CORTICOBASAL DEGENERATION

- × Corticobasal degeneration (CBD) was first described in 1968 as a syndrome of involuntary movements and slowed voluntary movements.
- × The most prominent neuropsychiatric features are lateralized ideomotor and ideational apraxia and the "alien hand syndrome."
- × There are multiple cognitive deficits, including predominant executive, memory, and attentional dysfunction that may be severe enough to amount to dementia.
- × Depression, apathy, disinhibition and delusions are also common in CBD.

FRONTOTEMPORAL DEMENTIA

- x FTD is a clinical syndrome characterized by prominent behavioral or personality changes involving social cognition, language dysfunction, and neuronal loss, spongiosis and gliosis in the frontal and temporal cortices.
- × Onset of FTD is usually after age 50, but ranges from 35 to 75 years. Life expectancy after diagnosis is 3 to 15 years.
- × FTD is neuropathologically, clinically, and genetically heterogenous, with approximately 30 to 50% of cases having a positive family history.

FRONTOTEMPORAL DEMENTIA

- × Symptom onset in FTD is insidious and many patients with FTD are initially misdiagnosed with a primary psychiatric illness.
- × The behavioural variant (bvFTD) involves prominent behavioral and personality changes such as

apathy	overeating and other signs of hyperorality
impulsivity	disinhibition
loss of personal awareness	stereotyped behaviors,
delusions	depression
affective lability	lack of tact or empathy

FRONTOTEMPORAL DEMENTIA

- x A second variant presents with a progressive nonfluent
 aphasia (PNFA)
- × Third variant with a semantic dementia (SD) with receptive language impairments.
- × Cognitive testing reveals profound impairment on tests of executive function but relative preservation of other cognitive domains, including memory.

DEMENTIA WITH LEWY BODIES

- × DLB is a dementia syndrome with Lewy bodies in the cerebral cortex, brainstem, thalamus, and striatum.
- × Second most common form of dementia after Alzheimer disease.
- \times Symptom onset is usually after age 50 and is more common in men.
- \times Average survival is less than 10 years.
- × In the earlier stages, cognitive deficits often involve attentional, visuospatial, or frontal - subcortical skills, and memory impairment may only become apparent with progression.

DEMENTIA WITH LEWY BODIES

- × Cognition is described as fluctuating with variations in attention and alertness.
- x With progression, there are the usual cortical features of dementia (aphasia, apraxia, and agnosia).
- \times The psychiatric symptoms present are
 - × dramatic visual hallucinations,
 - \times depression
 - × paranoid delusions.

MULTIPLE SYSTEM ATROPHY

- \times The term MSA was introduced in 1969.
- × Defined in 1999 to describe a clinically heterogeneous neurodegenerative disorder with variably present parkinsonian, autonomic, cerebellar, and pyramidal manifestations.
- × MSA is now used in place of three older diagnoses,
 - × olivopontocerebellar atrophy (OPCA),
 - \times Shy Drager syndrome, and
 - × striatonigral degeneration,
- x which could not be reliably distinguished from each
 other.

MULTIPLE SYSTEM ATROPHY

\times Two types of MSA are defined:

- x autonomic dysfunction with predominant cerebellar findings
 (MSA-cerebellar, or MSA-C) and
- \times autonomic dysfunction with predominant parkinsonian findings (MSA-P).
- × The disease is rare and affects both sexes equally.
- × It typically begins in late middle-age, with a median survival of about 9 to 10 years after symptom onset.
- x Psychiatric and cognitive manifestations of MSA have received little systematic attention.

MULTIPLE SYSTEM ATROPHY

- × Cognitive impairment is seen in up to to 50% of cases, with a profile of cognitive deficits similar to other parkinsonian disorders.
- \times Dementia is seen in up to 33% of cases.
- × Executive functions are most commonly seen, more in MSA-P, whereas learning and visuospatial impairments are more prominent in MSA-C.
- x Emotional incontinence, depression, anxiety, panic attacks, and suicidal ideation are also reported.

ENCEPHALITIS LETHARGICA

- × Encephalitis lethargica, described by Constantin von Economo, presented as a worldwide epidemic between 1917 and 1929.
- x It is important historically as an early example of the relationship between brain disease and psychopathology.
- × The acute phase was characterized by profound lethargy, hence its name, along with other mental status changes such as psychosis or catatonia and various movement abnormalities, including parkinsonism, choreoathetosis, and myoclonus.
- × The mortality rate was approximately 30% during the acute phase.

ENCEPHALITIS LETHARGICA

- × Psychiatric manifestations included
 - × disinhibition,
 - × mania,
 - \times attentional deficits,
 - × apathy,
 - × narcolepsy,
 - x verbal tic-like behaviors,
 - \times executive dysfunction,
 - × bradyphrenia.
- × Hyperactivity and oppositional behaviors developed in children.

HUNTINGTON DISEASE

- × HD (formerly Huntington chorea) is an autosomal dominant neurodegenerative disorder characterized by
 - \times mid-life onset,
 - \times a relentlessly progressive course,
 - \times a combination of motor, psychiatric, and cognitive symptoms.
- × The disease is caused by a CAG repeat expansion mutation in the huntingtin gene on chromosome 4.
- x The prevalence of HD in the United States is about 5 cases
 per 100,000 individuals.
- × Similar rates found in most European countries.

HUNTINGTON DISEASE

COGNITIVE MANIFESTATIONS

- × Early cognitive changes often affect cognitive flexibility and speed, such that switching from one task to another, or tracking multiple tasks simultaneously, becomes difficult or slow.
- × Work or school performance may suffer to the point that colleagues notice.
- × A four-domain model of cognitive deficits suggests that in early to middle stage HD, visuospatial deficits are the most pronounced deficits, followed by executive dysfunction, and then less prominent memory and verbal deficits.

HUNTINGTON DISEASE

PSYCHIATRIC MANIFESTATIONS

- × 80% of patients with HD develop some form of noncognitive psychiatric disorder within 10 to 15 years of disease onset.
- \times 30 40% of patients with HD develop major depression,
- \times 10 20 % have a nonmajor form of depressive syndromes.
- \times 10% of patients with HD develop mania,
- × Less frequently, patients with HD develop disorders that are clinically indistinguishable from idiopathic obsessive - compulsive disorder, schizophrenia, or delusional disorder.

WILSON DISEASE

- × WD, also named hepatolenticular degeneration.
- × It is an autosomal recessive disorder in which mutations in the copper-transporting gene ATP7B result in abnormal copper accumulation in the liver, brain, and other tissues, with consequent hepatic cirrhosis and neuronal degeneration.
- × Psychiatric and movement abnormalities are common, and patients may present to a psychiatrist first.
- \times WD is found worldwide, with a frequency estimated at about 1/30,000.

WILSON DISEASE

- \times 20% pts. have psychiatric abnormalities.
- \times The most common symptoms are
 - x personality changes (often described as irritability, aggressiveness, and emotional lability)
 - x Depression (ranging from subsyndromal mood changes to major depression, at times with suicidality)
- × Anxiety disorders, psychotic disorders and catatonia are more common than in the general population.

CEREBELLAR DISORDERS

- × The cerebellum has long been considered a modulator of motor function.
- × Cerebellum also modulates cognition and affect, and that damage to the cerebellum from many different causes can result in cognitive deficits and psychiatric syndromes.
- \times 50% of patients who have alcohol dependence syndromes have cerebellar pathology.
- × This is the single most common cause of cerebellar damage worldwide.
- × The cerebellum is affected in 1.5 to 8% of all strokes, making it the second most common cause of cerebellar damage.

CEREBELLAR DISORDERS

- × The cerebellum is involved in a variety of cognitive tasks including procedural learning, executive function, language processing, visual - spatial orientation, sensory processing, timing, and attention.
- × Within 10 to 15 years of disease onset, about 20% of patients with cerebellar degeneration meet criteria for cognitive decline or dementia.
- × Executive functions impaired in cerebellar degeneration include attention, sequencing, and timing.
- × Executive, visuospatial, verbal and visual memory, and language deficits also frequent.

CEREBELLAR DISORDERS

- × In degenerative disorders predominately limited to the cerebellum, about 75% of patients develop one or more psychiatric syndromes within 10 to 15 years of disease onset.
- \times 33% have MDD & another 33% have other forms of depression.
- \times About 25% develop persistent personality changes.
- x Mania, anxiety syndromes, and psychotic syndromes are also seen.

DYSTONIAS

- × Dystonia is characterized by involuntary, sustained muscle contractions that result in twisting, torsional, repetitive movements of one or more body parts and frequently appear as abnormal and sometimes painful or awkward positions and postures.
- x It is the third most common movement disorder after PD and ET.
- × Pts with focal dystonia have over twice the rate of major depression and anxiety disorders, particularly social phobia (71% in cervical dystonia) and panic disorder.

- × Tourette's syndrome is a neurological disorder characterized by repetitive, stereotyped, involuntary movements and vocalizations called tics.
- x Multiple tics are accompanied by forced involuntary vocalisations that can sometimes take the form of obscene words or phrases (coprolalia)
- \times Age of onset: 3-9 yrs.
- × Prevalence: 0.7 1.85%
- × Male: Female: 3:1
- × The syndrome is more common in children with autistic spectrum disorder (Baron-Cohen *et al.* 1999)

- × Channon et al. (1992) found impairement in sustaining attention and in focusing and shifting sets between salient stimuli.
- × Such deficits were not explicable in terms of depression, anxiety or obsessionality.
- × A high prevalence of self-injurious behaviour (14-60%) has occasionally been reported, including head banging, lip biting and pummelling of the head and chest (Robertson 1992)
- x More serious but rare instances include eye damage and touching hot objects.

ADHD

- × ADHD occurred in 31 91% (Freeman et al. 2000) pts. With Tourette's Syndrome.
- × Occurrence of ADHD is not associated with severity of the tic disorder, although ADHD symptoms are common in severe disease (Robertson & Stern 1998)
- x Knell and Comings (1993) found that ADHD was more common in the siblings of children with Tourette's syndrome.
- × The additional burden of ADHD symptoms impacts substantially on the psychosocial difficulties of Tourette's patients (Bawden et al. 1998; Carter et al. 2000; Subbodelaluy et al. 2002)

- × Sleep disturbances including nightmares, somnambulism and night terrors have occurred in up to 33% pts..
- × Depression and anxiety are more common in adults with the disorder than in the normal population (Robertson et al. 1988, 1993).
- \times Freeman et al. (2000) reported that 20% had depression and 18% anxiety.
- × Several studies reports of patients with bipolar affective disorder or schizophrenia.

OCD

- × In addition to ritualistic behaviours and compulsions to touch objects, a high proportion of patients report obsessional thoughts and activities.
- × Frankel et al. (1986) found that half of their patients had signific cantly elevated scores on a questionnaire for obsessional - compulsive symptoms, many scoring as highly as patients with obsessive - compulsive illness.
- × Obsessional features were observed in 66% of the patients reported by Nee et al. (1982) and Montgomery et al. (1982).

OCD

- x 50% of the children in their epidemiological survey had obsessional ideas, often with associated ritualistic motor behaviour (Caine *et al.* 1988)
- × The commonest included 'evening up', whereby a series of rituals ensured that the body was symmetrical and balanced, also counting games and touching rituals to ward off bad omens.
- × Coffey et al. (1998) and Cath et al. (2000) also report on the need for symmetry and 'doing things right'.

- × Dystonia, akathisia, parkinsonism and choreiform dyskinesia are common side effects of antipsychotic medications.
- × Previously only associated with classical antipsychotic agents such as chlorpromazine or haloperidol.
- × Present studies shows association with a wide range of other psychotropic drugs, including all the atypical neuroleptics, antidepressants (both tricyclic and SSRI,) and anticonvulsants such as sodium valproate.

- × Acute dystonias, usually of the face or neck, can occur within 72 hours of starting a new medication.
- × They are particularly common with haloperidol, occurring in up to 10% of cases, but can occur with other antipsychotics.
- × Tardive dyskinesia is a disorder that results in involuntary, repetitive body movements.
- × The most common is orofacial dyskinesia, provoked by long term neuroleptic treatment and persisting (or worsening) after this is withdrawn.
- × It usually manifests as choreoathetoid movements of the tongue and lower face, although any body area can be involved, including pharyngeal and intercostal muscles.

- x It is particularly common in elderly patients, more in women.
- × Seen in long term treatment (more than 10 years) at higher doses, occurring in up to 50% of patients (Fenton WS et al. 1994)
- × Recent studies shows that tardive dyskinesia can also occur as a result of the schizophrenic illness itself, being seen in up to 15% of drug naïve pts.
- × The standard approach to treatment is to reduce and stop the antipsychotic treatment if possible, substituting with clozapine if necessary.
- \times Clozapine is the only drug that has been shown to improve

- × Akathisia is a common and distressing form of motor restlessness, occurring in 25% of patients with chronic schizophrenia (Halstead SM et al. 1994)
- × It is particularly associated with high potency antipsychotics.
- x If it occurs early in treatment, reducing or stopping the medication responsible, results in improvement.
- × If it occurs more chronically it is often resistant to these measures.

- x Drug induced parkinsonism is a common side effect of antipsychotic medication.
- × It is sometimes clinically indistinguishable from PD.
- × Drug induced parkinsonism is especially common in elderly female patients (1.6:1) and in those on high dose dopamine blocking medication (H.-I. MA et al. 2017)
- \times PET studies of D2 receptor blockade show that parkinsonism develops when D2 occupancy exceeds 80%.
- × A 70% occupancy being sufficient for an antipsychotic effect.

NEUROLEPTIC MALIGNANT SYNDROME

- × Neuroleptic malignant syndrome is a potentially life threatening reaction to antipsychotic medication.
- x It is characterised by altered consciousness, muscle rigidity, fever, and autonomic instability.
- \times Muscle rigidity may cause dyspnoea and dysphagia.
- x Prevalence among pts. in psychiatric hospitals on neuroleptics about 15 per 100,000 (Berman, BD 2011)
- × It has also been described following administration of a wide variety of drugs, but particularly those with potent D2 blockade.

CONCLUSIONS

- × Movement disorders have an important psychiatric dimension that warrants careful enquiry, and can lead to difficulties in treatment.
- × Psychiatric disorders have associated disorders of movement, which require specific treatment strategies.
- × Psychoactive medications have movement disorders as side effects, both in the short and longer term, which require consideration when prescribing.



- × Lishman' s Organic Psychiatry.
- × Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 10th ed.
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THANK YOU