Movement Disorders in Psychiatry
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Learning Objectives:
- To understand and recognize the extra pyramidal phenomena known as movement disorders:
  - Hypokinesia: Parkinsonism
  - Hyperkinesias: chorea, tremor, dystonia, myoclonus
  - Neuroleptic induced movement disorders: akathisia, neuroleptic induced parkinsonism, NMS, tardive neuroleptic induced movement disorders

Overview of Key Points:
- The basal ganglia are important in motor control
- The basal ganglia circuit involves inputs, outputs and internal processing via indirect and direct pathways
- Dopamine plays a key role
- Most movement disorders are associated with basal ganglia dysfunction
Basal Ganglia

- Striatum = Caudate + Putamen
- Globus pallidus (external and internal)
- Subthalamic nucleus
- Substantia nigra

Functions of Basal Ganglia:

- Initiate and maintain desired movements while filtering out undesired movements
- Important in maintenance of posture and balance
- Help in motor learning and habit formation

Information Flow Within The Basal Ganglia

- Direct Pathway uses D1 receptors in striatum (D1 is excitatory)
  Striatum → globus pallidus interna
- Indirect Pathway uses D2 receptors in striatum (D2 is inhibitory)
  Striatum → globus pallidus externa → STN → globus pallidus interna
- GABA is the main neurotransmitter within the striatum and pallidum
Basal Ganglia Connections:
courtesy: absoluteastronomy.com

Connectivity diagram showing excitatory glutamergic pathways as red, inhibitory GABAergic pathways as blue, and modulatory dopaminergic as magenta.

Dopamine in Basal Ganglia Function
- In both direct and indirect pathways, net effect of dopamine is to facilitate movement
- D2 receptor blockers (e.g. AP) block action of dopamine in indirect pathway, causing a reduction in movement.
- This can be therapeutically useful in Tourette's disorder or chorea
- It can be a problem in drug induced parkinsonism

Parkinsonism: Symptoms and Causes
- Sx: Bradykinesia, Tremor, Rigidity, Post. instability
- Causes:
  - Parkinson's disease (idiopathic)
  - Parkinson plus degenerative syndromes (DLB, MSA, PSP)
  - Drug induced parkinsonism
  - Other hereditary disorders (Wilson disease, HD and Dopa responsive dystonia)
  - Structural lesions and infections (e.g. post encephalitic parkinsonism in early 20th century)

Chemical Basis of PD
- Dopamine deficit (deficient in substantia nigra)
- Role of Ach (relative excess of striatal Ach results in imbalance)
  - Anticholinergics may help to some extent
  - Depletion of cortical Ach in later stages affects cognition
- Serotonin deficit
  - Locus ceruleus is also a target
  - Depression and anxiety are common
Epidemiology:
- 1.5 million Americans have PD
- Mean age of onset is 60, 1-2% over 60 have PD
- Diagnosis is clinical
- Exclude treatable causes (e.g. meds, Wilson disease in young people)
- Additional signs may suggest a different dx (ataxia, chorea, spasticity, early dementia, gaze palsy, apraxia or dystonia….)

Parkinson disease: Presentation
- Asymmetric; resting tremor often heralds PD
- Varying degrees of bradykinesia, rigidity, postural instability
- Responds to L-Dopa

Nonmotor symptoms in PD
- REM behavior disorder, daytime sleepiness
- Anosmia
- Autonomic dysfunction (if very severe and early, may suggest MSA)
- Depression and anxiety
- Fatigue
- Slow thinking (bradyphrenia) which is not necessarily dementia

Medical management of Motor symptoms
- L-Dopa (with carbidopa) is most effective and usually best tolerated
- Dopamine agonists (ropinirole, pramipexole)
- Anticholinergics (e.g. trihexiphenidyl, benztropine) can help with tremor and rigidity
- MAO-B inhibitors selegiline and rasagiline
- Amantadine
Neuroleptic Induced Parkinsonism:

- Referred to as pseudoparkinsonism, the symptoms are clinically indistinguishable from PD.
- Symptoms comprise rigidity, bradykinesia, tremor at rest and postural instability and are usually bilateral but may be asymmetrical.
- Face appears masked and there may be drooling of saliva.
- Posture is flexed and speech may become slow and lacking in intonation.
- Initial symptom may be a tremor or muscle stiffness and reduced arm swing and increased muscle tone obvious on examination.
- Sx develop later than dystonia or akathisia although most people develop it in the 1st week of neuroleptic treatment or dose increment.

Neuroleptic Induced Parkinsonism continued:

- Dose related and more prevalent with high potency drugs.
- Increasing age and female gender are additional risk factors.
- Drugs with intrinsic anticholinergic property have a lower propensity.
- Reversible with cessation of drug although this may take months especially after the use of depot neuroleptics.
- Emergence of neuroleptic induced parkinsonism is managed best by modification of the AP regimen & if not anticholinergics are used.

Parkinson Video

Chorea:

- Rapid, purposeless, irregular jerky movements that seem to flow randomly from one body part to another.
- Unlike stereotypy, chorea is random.
- Unlike akathisia, chorea lacks inner restlessness.
- Chorea is more flowing and complex than myoclonus.
Chorea: Causes

- Huntington disease
- L-dopa dyskinesias in PD
- Sydenham chorea in children (Group A post streptococcal pharyngitis)
- Stimulants (e.g. cocaine and amphetamines)
- Basal ganglia lesion (hemichorea/hemiballismus in stroke)
- Infection (especially HIV and related infections)
- Wilson disease, hyperthyroidism

Chorea Video

Huntington Disease:

- Most common cause of chronic chorea in adults
- Autosomal dominant triplet repeat expansion disorder
- Higher repeat number means earlier onset and greater severity
- Genetic anticipation
- Caudate atrophy

Huntington Disease continued:

- Psychiatric disorders; suicide risk
- Personality change and dementia
- Chorea may be absent in young patients, who may have more parkinsonism
- Ataxia, falls, dysphagia, motor impersistence
- Ultimately fatal in most persons in 15 years
- Chorea treated with dopamine depleters tetrabenazine. Often quetiapine and olanzapine are also used
Wilson’s disease:
- AR defect in copper transporter, copper builds in brain, liver and other tissues
- Age less than 40 with any of the following: dysarthria, gait change, tremor, dystonia, parkinsonism (suspect in any movement disorder)
- Psychiatric disease and/or dementia are common
- Prognosis good if diagnosed and treated early (low copper diet, penicillamine)
- Can be fatal if untreated
- 24hr urine copper high with low serum ceruloplasmin
- KF ring (Copper deposits around iris)

KF Ring in Wilson’s disease:
- Wikimedia Commons

Tics:
- Tics are sudden stereotyped, repetitive, nonrhythmic movements or utterances; preceded by a sensory urge
- Simple tic examples: throat clear, grunt, blink, eye roll, head toss
- Complex tic examples: coprolalia, self punching, spinning (overlap with compulsion)

Tourettes’s syndrome:
- Multiple motor tics + at least one verbal tic present at some point
- Tics for more than 1 year, with no more than 3 consecutive tic-free months
- Onset <18 years
- Other causes (HD, drugs) excluded
Tourette's syndrome continued:
- Dominant inheritance but gene(s) not clear
- Associated with ADHD, OCD and anxiety disorders in the same or related individuals
- When tics need treatment evidence best supports DRBs (pimozide, haloperidol)
- Lately atypical AP have been used to control tic movements (risperidone 0.5 to 4mg/day, olanzapine 5-30mg/day and ziprasidone 80-200mg/day)
- Clonidine (0.1-0.4mg/day), guanfacine (0.5-2mg/day) and clonazepam (0.5-4mg/day) also used
- Botulinum toxin injections used for focal tics involving small muscle groups

Tremor:
- Rhythmic involuntary oscillation of a body part
- Apart from hands, may affect head, chin, voice, palate or lower extremities
- May be better or worse with certain actions or positions

Upper limb tremor:
- Resting tremor (parkinsonism) is maximal at rest and becomes less prominent with activity.
  - A rest tremor that develops acutely is usually due to toxins (such as exposure to MPTP) or DRB
- Action tremor is postural and or kinetic (essential tremor, Lithium induced, Valproic acid, stimulants, tricyclics) which is maximal while limb posture is actively maintained against gravity, it is lessened by rest and is not markedly enhanced during voluntary movement toward a target.
- Essential tremor:
  - MCC and dominant inheritance
  - More with increasing age, shaky hands, sometimes head and voice too
Upper limb tremor continued:

- **Essential Tremor:**
  Better after an alcoholic drink
  Does not increase mortality
  Rx with propranolol, primidone

- **Intention tremor:** is most prominent during voluntary movement toward a target and is not present during postural maintenance or at rest. It is a sign of cerebellar disease

- **Asterixis:** May superficially resemble a tremor, is an intermittent inhibition of muscle contraction that occurs with metabolic encephalopathy. This leads for example to a momentary and repetitive partial flexion of the wrists during attempted sustained wrist extension.

Coping with Tremor

Intention Tremor Video

Dystonia and its classification:

- Involuntary sustained muscle contraction causing abnormal position or twisting of a body part
- Categorized by age of onset, body part(s) involved, presence of other signs and etiology

**Dystonia Classification:**

- Primary dystonia (only dystonia is present, may be idiopathic or genetic)
- Secondary dystonia (dystonia due to some insult; e.g. medication, brain lesion, stroke, infection)
- Dystonia plus (Dystonia plus other neurologic findings like parkinsonism or myoclonus)
Primary Dystonia

- Idiopathic focal or segmental dystonia. Onset usually in older adults. Include cervical dystonia, writer’s cramp, blepharospasm, oromandibular dystonia, laryngeal dystonia.
- Lower extremity not involved.
- Rx with botox injections
- Generalized dystonia. Onset usually in childhood. Widespread involvement including legs or trunk

Neuroleptic induced acute dystonia:

- Sx varies with common manifestations being torticollis, tongue protrusion, opening or closing of jaw, facial grimacing, limb torsion or rolling the eyes upwards sometimes with deviation to the side (oculogyric crisis)
- Exception is laryngopharyngeal spasm that may compromise respiration and may even cause death
- Incidence is determined by the type of drug used, dosage, route of administration and age of individual
- High potency drugs like haloperidol generally produce acute dystonia in 30-40% of cases.
- Most dystonias occur within 2-3 days of initiation or significant increment in dose of neuroleptic and parenteral administration increases the risk

Neuroleptic induced acute dystonia:

- Children and young adults appear to have greatest risk and males develop it twice as often as females
- Pathophysiology has been poorly understood with the focus having been on dopaminergic mechanisms.
- Arguments have been presented for acute dopamine antagonism (DA function hypothesis) and a compensatory increase in dopamine release leading to mismatch (DA hyperfunction hypothesis)
- In the acute situation the parenteral administration of benztropine, biperiden, procyclidine or other anticholinergic drug or the antihistaminic/antichol. diphenhydramine is usually effective in 15-20 min.
Myoclonus:
- Sudden, brief, shock like involuntary movements
- Important causes:
  - Drugs: SSRI, TCA, Li, Opioids, stimulants
  - Part of serotonin syndrome
  - Seizures
  - Medical illness (renal and liver disease, hyperthyroidism)
  - Other neurological and neurodegenerative disorders (e.g. AD, PD, CJD)
  - Anoxic brain injury

Myoclonus Video

Neuroleptic induced movement disorders:
- Acute dystonic reactions
- Acute akathisia
- Neuroleptic induced parkinsonism
- NMS
- Tardive neuroleptic induced movement disorders

Acute neuroleptic induced akathisia:
- The syndrome of akathisia has come to refer to the development of restlessness seen most commonly as an acute adverse effect of neuroleptics, although other drugs such as SSRI, calcium channel antagonists also may produce it.
- Subjective and objective report needed
- The sensations in the legs are localized deep inside and paresthesias are uncommon
- Recognized as important cause of non-compliance in schizophrenia
- It develops within a few days of the initiation or increment in dose or change to high potency neuroleptic with most cases developing in the first 2 weeks
Acute neuroleptic induced akathisia:

- Risk increases with higher drug doses, rapid increment of dosage and higher potency of the drug.
- Development of parkinsonism also increases the likelihood of akathisia developing.
- Akathisia is difficult to treat and its prevention or modification through appropriate use of neuroleptics is the most important strategy.
- Drugs used to treat akathisia include anticholinergics, B-blockers and benzos.
- Anticholinergics may be more effective in those who have associated parkinsonian symptoms.

Neuroleptic Malignant Syndrome:

- Although uncommon, NMS is the most serious adverse effect of neuroleptics and it is potentially fatal. Most cases involve AP’s but syndrome has been reported with other drugs including lithium, antidepressants of various classes, metoclopramide and sudden withdrawal of dopamine agonists in PD.
- With AP the risk is highest with high potency drugs in particular haloperidol that are rapidly increased in dose.
- However it has been reported with atypical AP including clozapine and quetiapine in monotherapy.
- Condition twice as common in men as women and 80% of cases occur in patients under age of 40 years.

NMS continued:

- In its classical form there are 4 elements to NMS:
  - Muscle rigidity: This can be generalized or in milder forms localized to the tongue, facial or masticatory muscles leading to dysarthria or dysphagia.
  - Pyrexia: Mild pyrexia to a temperature above 42°C.
  - Change in conscious level: This can range from mild confusion to coma.
  - Autonomic disturbance: manifest as diaphoresis, tachycardia, labile blood pressure and hypersalivation.
NMS continued:

- Lab findings are nonspecific but useful in supporting the diagnosis.
- Most important is a rise in CK which may vary from greater than 200 to several thousand IU/L. PML is another consistent finding.
- Less common findings are elevated liver enzymes, hypocalcemia, hypomagnesemia, hypothermia, proteinuria and myoglobinuria.
- Pharmacological basis is hypothesized to be a sudden drop in dopamine levels which in the hypothalamus affects thermoregulation and in the striatum leads to rigidity which in turn will cause heat production and contribute to pyrexia.

Management of NMS:

- Stop all AP medication and ideally other prescribed drugs that can cause the syndrome for e.g. lithium and antidepressants.
- Course monitored by regular physical observations and daily serum CPK levels.
- General supportive measures should be instigated including rehydration, cooling and treatment of intercurrent infection.
- BZDs are used for agitation, muscle relaxation and ECT is life saving in severe cases.

Tardive neuroleptic-induced movement disorders:

- Dyskinesias is a generic term that refers to a range of movement abnormalities.
- In case of TD, the movements are choreiform, athetoid, dystonic, stereotypic or a combination of these. Most commonly involve the oro-buccal, lingual, and facial muscles especially in older individuals.
- Lip smacking, puckering, or pouting, chewing, jaw clenching or mouth opening, facial grimacing, blowing, blepharospasm and frowning are also common features.
- Oro-buccal-lingual-facial musculature is involved in three quarters of affected individuals, the limbs in one-half and the trunk in up to one quarter with all three groups being affected in about 10%.

TD Continued:

- Movements of TD typically fluctuate in intensity over time, increase with emotional arousal, decrease with relaxation, and disappear during sleep.
- TD develops after a person has been on neuroleptics for months to years. DSM requires exposure of at least 3 months, but TD may occur as early as one month in elderly individuals.
Tardive Dyskinesia Video

Epidemiology and natural history
- Rates range from 3% to 70% with median rate of about 24% in patients on chronic neuroleptic treatment. (Yassa and Jeste)
- Higher rates in the elderly patients on neuroleptics as well as neuroleptic treated individuals with MR.
- Natural History:
  - For most people, TD does not become progressively worse, and when it does get worse, it generally tends to show a fluctuating course with some spontaneous remissions.
  - From 5-10 years, about 50% of patients demonstrate a reduction in symptoms of atleast 50%. Outcome is more favorable in the young and if drug treatment can be stopped.

Risk Factors:
- Advancing age
- Female gender
- Ethnic differences with higher rates in AA & lower rates in Chinese/Asian populations.
- Affective disorder and in schizophrenic pts, a FH of affective illness
- Brain damage & variables like smoking, DM & alcohol abuse
- Clozapine safest drug

Pathophysiology:
- Not well understood
- Dopamine supersensitivity theory
- Some attention has been given to changes in NE, 5HT, and Ach but changes in GABA are considered to be the most salient for the development of TD.
- Finally the neurodegeneration hypothesis of TD has been presented which postulates free radical and excitatory mechanisms being involved
Management:

- Primary strategy in its management remains preventive
- Dopaminergic Antagonists:
  - Atypical neuroleptics: clozapine, risperidone, olanzapine
  - GABA-ergic drugs
  - Benzodiazepines, valproate, baclofen
  - Antinoradrenergic drugs
  - Propranolol, Clonidine
- Serotonergic drugs
  - L-tryptophan, 5-hydroxy tryptophan, cyproheptadine

Conclusion:

- Movement disorders in psychiatry can be divided in those related to an underlying neurological or other somatic disease and related to a psychiatric syndrome which most commonly is induced by neuroleptics.
- Early recognition of movement disorders is a challenge.
- Some of them can be treated
- Treatment is disappointing and prevention is needed.

Thank you
Questions ????