Movement Disorders

Les troubles du mouvement

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Major Movement Disorders - *Les troubles du mouvement majeurs*

To be covered in the next 30 minutes:

- Parkinson’s disease – *la maladie de Parkinson*
- Other parkinsonian disorders – *d’autres maladies parkinsoniennes*
- Essential tremor – *le tremblement essentiel*
- Dystonia disorders – *les dystonies*
- Drug-induced disorders – *les dyskinésies d’origine médicamenteuse*
Parkinson’s disease – la maladie de Parkinson

Outline:

1. The range of clinical manifestations
   - La gamme de manifestations cliniques

2. The diagnosis
   - Le diagnostic

3. Current treatment
   - Le traitement actuel
Core clinical features (i.e., the syndrome of “parkinsonism”):

- Tremor
- Rigidity
- Akinesia
- Postural disturbances
Tremor

Rest tremor (characteristic)
- Occurs in repose
- 3-7 Hz (slow)
- **TIP:** Watch for rest tremor while walking, or during tasks of concentration (e.g., arithmetic, reciting months backward)

Action tremor (less common)
- Occurs with muscle activation
- 6-11 Hz (fast)
Rigidity

- Muscle tone: Increased passive resistance
  - A sign clinicians elicit, not a symptom

- Unlike spasticity, rigidity is uniform (1) in antagonists, (2) throughout a joint range, (3) regardless of speed

- **TIP:** Accentuated by contralateral activity

- “Cogwheeling”: correlated with tremor, not rigidity
Akinesia

- “Akinesia”: *from the Greek for “lack of movement”*
- Impairment of voluntary movement
- Typically causes most of the disability in Parkinson’s disease (PD)
Akinesia

3 components:

Bradykinesia (decreased *speed* of movement)
- e.g. Slow initiation and execution of all movement

Hypokinesia (decreased *amplitude* of movement)
- e.g. Micrographia, decreased arm swing, short stride

Oligokinesia (decreased *quantity* of movement)
- e.g. Reduced blink and facial expression

- *TIP:* Tendency to progressive fatigue with repetition
Micrographia

Drawing loops – *dessiner des boucles*

Right hand

Right-sided parkinsonism

Left hand
Postural Disturbances

2 components:

- Flexion posture, “stooping”
  - Neck, elbows, waist, knees

- Disorder of equilibrium, falls
  - *Exam*: Test for retropulsion
    - Pull backward on shoulders
    - Normal: recover balance in 2 steps
Parkinson’s disease - Range of clinical manifestations

la maladie de Parkinson - la gamme de manifestations cliniques

- Cardinal motor manifestations
  - Tremor, rigidity, akinesia, postural disturbances

- Non-motor manifestations (les manifestations non-motrices)
  - Cognitive (dementia, excess somnolence)
  - Autonomic (constipation, orthostatic hypotension/other cardiovascular instability, incontinence, sexual or sweat dysfunction/failure of temperature regulation)
  - Sensory (restless legs syndrome, loss of smell)
  - Miscellaneous (depression, REM-sleep behavior disorder)
“Premotor” Manifestations – Les manifestations prémotrices

- May precede motor onset by decades
- Strongest evidence established for:
  - Olfactory deficit
  - Constipation
  - REM-sleep behavior disorder
  - Excess daytime somnolence
  - Depression, anxiety

Savica et al. Arch Neurol 2010; 67: 798-801
Lang. Mov Disord 2011; 775-783
Typical Clinical Course of PD

• Starts in one limb
  • Dominant:non-dominant = 3:2

• Progresses slowly over months and years
  • Typically first to the other limb on the same side
  • Eventually becomes bilateral, but remains worse on the side first affected

• Tremor, rigidity and akinesia early; postural instability late (≥ 10 years)
Parkinson’s disease - Diagnosis
la maladie de Parkinson - le diagnostic

Why do patients with PD go to doctors?

1. Involuntary movement
   - Is it a rest tremor?
   - Ask about and look for: Evidence of akinesia, rigidity

2. Trouble with voluntary movement
   - Is it akinesia?
   - Ask about and look for: Tremor, rigidity
Clinical course: did it start unilaterally?

Diagnosis can be supported by:
- Non-motor features: REM-SBD, loss of smell
- Imaging of dopaminergic nerve terminals
- Response to medication

Ultimately, we continue to diagnose PD by finding characteristic clinical motor features evolving in a characteristic way.
Parkinson’s disease – Current treatment

- Medications
- Physical activity
- Surgery
Parkinson’s disease – Medications

la maladie de Parkinson – les médicaments

☐ Medications

- 6 categories currently available

- General principles of medications for PD
  - drugs treat only symptoms; the disease progresses
  - all drugs are compatible with each other
  - using small doses of multiple drugs usually produces fewer side effects than large doses of a single drug
  - all side effects are reversible
  - laboratory tests for organ surveillance not required (exception: tolcapone)
Currently Available Medications

Modestly effective
- Anticholinergic drugs
  - diphenhydramine, trihexyphenidyl, benztropine, biperiden, etc.
- Amantadine

Most effective
- Levodopa (plus carbidopa or benserazide)
- Dopamine agonists
  - bromocriptine, pergolide, pramipexole, ropinirole, rotigotine, cabergoline, apomorphine, pirebidil, etc.

Levodopa boosters
- MAO (monoamine oxidase)-B inhibitors
  - selegiline, rasagiline, safinamide, etc.
- COMT (catechol-O-methyl transferase) inhibitors
  - tolcapone, entacapone
Physical activity for PD

- Numerous research studies over the last 15 years have established the value of physical activity
  - Aerobic exercise
  - Resistance exercise
  - Tai chi, yoga
  - Dance
  - Sports

- Every PD patient should be advised to get involved in regular physical activity of some kind
Surgery for PD

- Mainly for patients whose medications fail to control their symptoms consistently, or have intractable tremor

- Surgical options
  - Deep brain stimulation – *la stimulation cérébrale profonde*
  - Jejunal infusion of L-dopa – *infusion intestinale de la L-dopa*
Simplified Differential Diagnosis

- Parkinsonism
  - Drug-Induced
  - Tremor
  - Akinetic-Rigid Syndrome
Akinetic-Rigid Syndromes

- Infectious and postinfectious
- Toxic, metabolic
- Familial
- Young-onset, e.g., Wilson’s
- Diagnosable by imaging studies
- Miscellaneous
- Degenerative
Degenerative Diseases

- Parkinson’s disease
- Progressive supranuclear palsy
- Multiple system atrophy
- Corticobasal degeneration
Progressive supranuclear palsy - *la paralysie supranucléaire progressive*

**Practical Clinical Diagnosis**
- older patient
- vertical ocular motor disorder (slow saccades, restricted range)
- onset with gait disorder and disequilibrium
- no tremor
- rigidity in neck but not in limbs, relatively normal performance of repetitive movements
- little or no response to levodopa
Multiple system atrophy – l’atrophie multisystématisée

Practical Clinical Diagnosis

- younger patient (usually < 60 years old)
- no tremor
- early and prominent autonomic difficulty
- relatively rapid progression of parkinsonism
- poor, unsustained response to levodopa
- may have ataxia greater than parkinsonism
- REM-SBD
Corticobasal degeneration – la dégénérescence corticobasale

Practical Clinical Diagnosis

- patient in 7th decade
- asymmetric presentation
- combination of
  - basal ganglia signs (rigidity, dystonia, akinesia)
  - cerebral cortical dysfunction (apraxia, cortical sensory loss, alien limb)
  - other common features: action and focal reflex myoclonus, nonfluent aphasia
Essential tremor – *le tremblement essentiel*

- If a patient has a tremor, think of essential tremor (ET)
- Causes an action tremor of the hands
  - with sustained posture (“postural tremor”)
  - with movement (“kinetic tremor”)
- More disabling than rest tremor
- Typically interferes with eating, drinking, writing
- Distribution: upper limbs, head (50%), voice (25%)
- Progression is very slow
Essential tremor – le tremblement essentiel

- Frequency: 6-11 Hz (fast)

- Patients are usually neurologically normal, apart from tremor
  - Tremor is the sole source of disability

- Two distinctive features:
  - Responds to a low dose of alcohol
  - Positive family history (~75%), consistent with autosomal dominant inheritance
Essential tremor – *le tremblement essentiel*

- **Examination – *l’examen***
  - Hold arms outstretched forward at shoulder level – «*la manoeuvre du serment*»
  - Finger-to-nose testing - *l’épreuve «doigt-nez»*
  - Optional: handwriting, drawing, drinking from a glass
2 main agents used:

1. Primidone: start 25 mg qHS; ↑ by 25 mg as tolerated or needed
   - Side effects: drowsiness, dizziness

2. Propranolol: start 10 mg t.i.d. or 60 mg of long-acting preparation q.d.; titrate upward as needed and tolerated
Essential Tremor – Response to Medication

An 84-year-old man with a 4-year history of essential tremor

Prior to treatment

On primidone 500 mg qHS
Essential Tremor

Medical treatment (others, less established)

1. Methazolamide
2. Gabapentin
3. Mirtazapine
4. Topiramate
5. Clonazepam
A 79-year-old woman with a 40-year history of essential tremor

Prior to treatment

On primidone 150 mg daily

On primidone 250 mg, propranolol 120 mg, and methazolamide 225 mg daily
An 84-year-old man with a 56-year history of essential tremor

Prior to treatment

On methazolamide 50 mg t.i.d. and gabapentin 200 mg t.i.d.
Essential Tremor

Surgical Treatment – *le traitement chirurgical*

- Thalamotomony - *la thalamotomie*
- Deep brain stimulation of the thalamus - *la stimulation cérébrale profonde du noyau VIM du thalamus*
- Gamma knife therapy - *la thalamotomie par gamma knife*
- Focused ultrasound - *la thalamotomie par ultrasons focalisés*
Dystonia – Characteristic Features

- Continuous (tonic) or irregularly repetitive (clonic) muscle contractions, often resulting in sustained abnormal postures

- Two distinctive features:
  - Response to sensory “tricks” – *les gestes antagonistes*
  - Induced or ameliorated by specific actions ("task-specific" induction or suppression)
Dystonia - Classification

By etiology
- Primary: no identifiable pathology
- Secondary: identifiable cause

By distribution
- Focal
- Segmental
- Multifocal
- Generalized
- Hemidystonia
Primary Dystonia

Focal dystonia:
- Almost always sporadic
- Onset in adulthood
- Involves cranial, cervical or upper limb muscles
- Remains focal, rarely generalizes
Common Focal Dystonias

- Blepharospasm
- Oromandibular dystonia
- Spasmodic torticollis (cervical dystonia)
- Laryngeal dystonia (spasmodic dysphonia)
- Writer’s cramp
Secondary Dystonia

Dystonia may be due to a wide variety of causes of brain injury:

- Metabolic disorders (Wilson’s, Leigh’s, etc.)
- Trauma – central or peripheral
- Stroke
- Cerebral palsy
- Drugs
- Degenerative diseases (Parkinson’s, CBGD, Hallevordern-Spatz, etc.)
- Psychogenic
Dystonia - Treatment

☐ Medications
  ▪ Trial of levodopa in children

☐ Botulinum toxin injections
  - *les injections de toxine botulique*

☐ Surgery
Botulinum toxin -

*la toxine botulique*

- “Chemodenervation” of muscle: Botulinum toxin prevents release of acetylcholine at neuromuscular junction
- Onset: within days, up to one week
- Duration: average 3 months
- Side effects: most commonly weakness in or near the region injected
Drug-Induced Disorders - Antidopaminergic Drugs

2 major drug categories involved:

- **Antipsychotic drugs**
  - Drugs used to treat hallucinations/delusions, or for behavioral modification (a.k.a. “neuroleptics”)
  - Haloperidol, risperidone, olanzapine, etc.
  - Typical antipsychotics cause more problems than atypical antipsychotics

- **Antinauseant drugs**
  - Drugs used as primary antiemetics, or as adjuncts for chemotherapy
  - Metoclopramide, prochlorperazine, etc.
Drug-Induced Disorders - Antidopaminergic Drugs

Neurologic Complications:
- Acute dystonic reaction
- Akathisia
- Parkinsonism
- Tardive dyskinesia and other tardive syndromes
- Neuroleptic malignant syndrome
Acute Dystonic Reaction:

- Onset
  - Immediate (often after first dose) up to 72 hours

- Manifestations
  - Severe dystonia of face and/or neck muscles
  - *Oculogyric crisis*: forced gaze deviation
  - Importance: severe discomfort can be alleviated promptly

- Treatment
  - Withdraw the offending agent; resolves within days
  - I.V. or I.M. antihistamine (e.g. diphenhydramine 25 mg)
    - relief within 15 minutes
    - 72-hour prescription for pills to prevent recurrence
Drug-Induced Disorders - Antidopaminergic Drugs

Akathisia:

- **Onset**
  - Days to weeks after first dose

- **Manifestations**
  - Severe restlessness, agitation, intense discomfort
  - Unable to sit still, pacing, rubbing, repetitive behaviors
  - Importance: most common cause of neuroleptic noncompliance

- **Treatment**
  - Withdraw the offending agent; resolves within weeks
  - If needed, symptomatic Rx with propranolol, lorazepam
Drug-Induced Disorders – Antidopaminergic Drugs

Parkinsonism:

- **Onset**
  - Weeks to months after first dose

- **Manifestations**
  - Similar to Parkinson’s disease
  - Less tremor, more symmetric
  - Importance: can be misdiagnosed and treated as Parkinson’s

- **Treatment**
  - Withdraw the offending agent; resolves in up to 18 months
  - If needed, symptomatic Rx with amantadine, anticholinergics
Drug-Induced Disorders - Antidopaminergic Drugs

Tardive Dyskinesia:

- **Onset**
  - Usually a year or more after first dose ("tardive" = late)

- **Manifestations**
  - Orolingual dyskinesias: chewing, licking, lip-smacking movements; head, trunk and limbs variably affected
  - Respiratory dyskinesias, pelvic thrusting: unusual but characteristic
  - Importance: may be irreversible

- **Treatment**
  - Withdraw offending agent (may worsen temporarily)
  - 50% chance of spontaneous remission
Tardive Dyskinesia

Other points:

- Traditional neuroleptics more liable than atypical neuroleptics to cause it
- Occurs in 20% of patients on chronic therapy
- Older women form the most vulnerable population
Other Tardive Syndromes

- **Tardive dystonia**
  - Consists mainly of cranial and cervical dystonia
  - Tends to occur in younger males
  - May not require as prolonged exposure; some cases occur within weeks of initiation of drug
  - Very low chance of spontaneous remission
Other Tardive Syndromes

- Tardive akathisia,
- Tardive myoclonus, and
- Tardive tremor have also been described;

Recognized by “tardive” pharmacologic features:
1. Onset after prolonged exposure
2. Worsening after withdrawal of causative medication
3. Suppression of symptoms by increased dose
Tardive Dyskinesia/Dystonia

Management:

- Prevention: avoid offending agents
- Use/switch to atypical antipsychotics
  - Best is clozapine
- Symptomatic therapy with presynaptic dopamine antagonists (reserpine, tetrabenazine)
- For dystonia: anticholinergics, botulinum toxin
- Alternatives: propranolol, clonidine, benzodiazepines
Drug-Induced Disorders - Antidopaminergic Drugs

Neuroleptic Malignant Syndrome:

- **Onset**
  - Any time during treatment, especially after ↑ dose

- **Manifestations**
  - Extreme rigidity, elevated CPK
  - Fever, dysautonomia
  - Impaired mental status
  - Importance: life-threatening

- **Treatment**
  - Withdraw offending agent
  - For rigidity: dopamine agonist, dantrolene
Final Words

- This is just a sample of the most important and treatable movement disorders
  - We did not even touch on chorea, tics, myoclonus, ballism, or athetosis

- Most movement disorders do not require any technology for diagnosis

- Using your ears and eyes (and occasionally your hands, and a pen and paper), you can be an excellent movement disorders neurologist