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Clinical Approach to Chorea and Dyskinesia – Beyond HD

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Movement Disorders Neurology

Disclosures

No relevant disclosures

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Learning objectives

- Defining dyskinesias
- Clinical dyskinesia syndromes
- Defining chorea
- Review diagnosis and classification of chorea
- Review differential diagnoses of chorea
- Review management approach to chorea

Defining dyskinesias

- Spectrum of abnormal **excessive** movements that can vary in
  - Amplitude
  - Duration
  - Distribution
  - Rhythmicity
  - Suppressibility
  - Pattern

Spectrum of Dyskinesias:

Faster → Chorea



Slower → Athetosis



Larger → Ballism



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Clinical History

- Onset
  - Age of onset
  - Triggers: infections, medication exposure
- Time course
  - Static, paroxysmal, progressive
- Alleviating/Exacerbating Factors
- Family history
- Medication history
- Toxin exposure

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Primary vs. Secondary Dyskinesias

- Primary Dyskinesias
  - Genetic (e.g., paroxysmal dyskinesias)
- Secondary Dyskinesias
  - Structural lesions
    - Tumors
    - Cerebrovascular disease
    - Demyelinating diseases
  - Hypoxic-ischemic injury
  - Infection
  - Metabolic disorders

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Common Clinical Dyskinesia Syndromes

- Levodopa-induced dyskinesia
- Tardive dyskinesia

Levodopa-Induced Dyskinesia

- Complication of levodopa therapy in Parkinson's disease
  - Types:
    - Peak-dose dyskinesia: most common
    - Diphasic dyskinesia
    - Off-period dyskinesia
  - Risk factors
    - Duration of therapy
    - Younger age of onset of PD
    - Female sex
- Management
  - Medication optimization
  - Amantadine
  - Deep brain stimulation for PD



Can't Eat - Matt, dyskinesia and Parkinson's

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Tardive Syndromes

- Definition: movement disorders that occur after administration of drugs, especially dopamine receptor-blocking agents
  - Usually has delayed onset*
- Risk factors:
  - Age
  - Duration of exposure
  - Medication dose
  - Others: previous brain damage, female sex, affective d/o

Causative agents

Antipsychotics	
• 'Typical'	
Haloperidol	High
Droperidol	High
Loxapine	High
Chlorpromazine	High
Fluphenazine	High
Thioridazine	High
Trifluoperazine	High
Sulpiride	High
Zuclopenthixol	High
Perphenazine	Moderate
Molindone	Moderate
• 'Atypical'	
Quetiapine	Low
Olanzapine	Low
Risperidone	Low
Paliperidone	Low
Clozapine	Very low
Amisulpride	Low
Ziprasidone	Low/Moderate
Aripiprazole	Very low
Lurasidone	Moderate

Antidepressants	
• ***MAOIs***	
○ Phenelzine	Low/Moderate
• ***SSRIs***	
○ Citalopram	Low
○ Escitalopram	Low
○ Fluoxetine	Low
○ Fluvoxamine	Low
• ***SNRIs***	
○ Venlafaxine	Low
○ Duloxetine	Low
• ***Tricyclic antidepressants***	
○ Amitriptyline	Low
○ Imipramine	Low

Annual incidence rate in antipsychotics

First-generation: 7.7%

Second-generation: 2.98%

Antiemetics	
• Metoclopramide	Low/Moderate
• Prochlorperazine	Low/Moderate
Anticholinergics	
• Benzhexol	Low
• Orphenadrine	Low
• Procyclidine	Low
Antiepileptics	
• Carbamazepine	Low
• Phenytoin	Low
• Ethosuximide	Low
Mood stabilisers	
• Lithium	Low/Moderate

Antimalarials	
• Chloroquine	Low
• Amodiaquine	Low
Antihistamines	
• Hydroxyzine	Low
Anxiolytics	
• Alprazolam	Low
Calcium channel blockers	
• Amlodipine	Low
Stimulants	
• Amphetamines	Low
• Methylphenidate	Low
Dopamine depletors	
• Tetrabenazine	Very low

(Mulroy et al, 2020)

Case 1

- 70-year-old woman presented to movement disorder clinic for continuous lips and jaw movements
  - PMH: schizoaffective disorder
    - No other medical history disease including thyroid disease
  - Previously trialed psychiatric medications
    - First-generation antipsychotic drugs: haloperidol, chlorpromazine, thioridazine
  - Current medications
    - Haloperidol 2 mg/day
    - Nortriptyline 100 mg/day

Tardive Dyskinesia

- Choreoathetoid movements
  - Primarily affect lower face: lips, tongue, perioral region
  - ± Low amplitude choreiform movements of distal limbs
  - Unaware of movements
- Management
  - Avoid provoking medications (e.g., benztropine, antipsychotics, antinausea medicines)
  - Wean down/stop provoking medications
  - VMAT2 inhibitors



CONTINUUM: Lifelong Learning in Neurology. 25(4):1081-1098, August 2019

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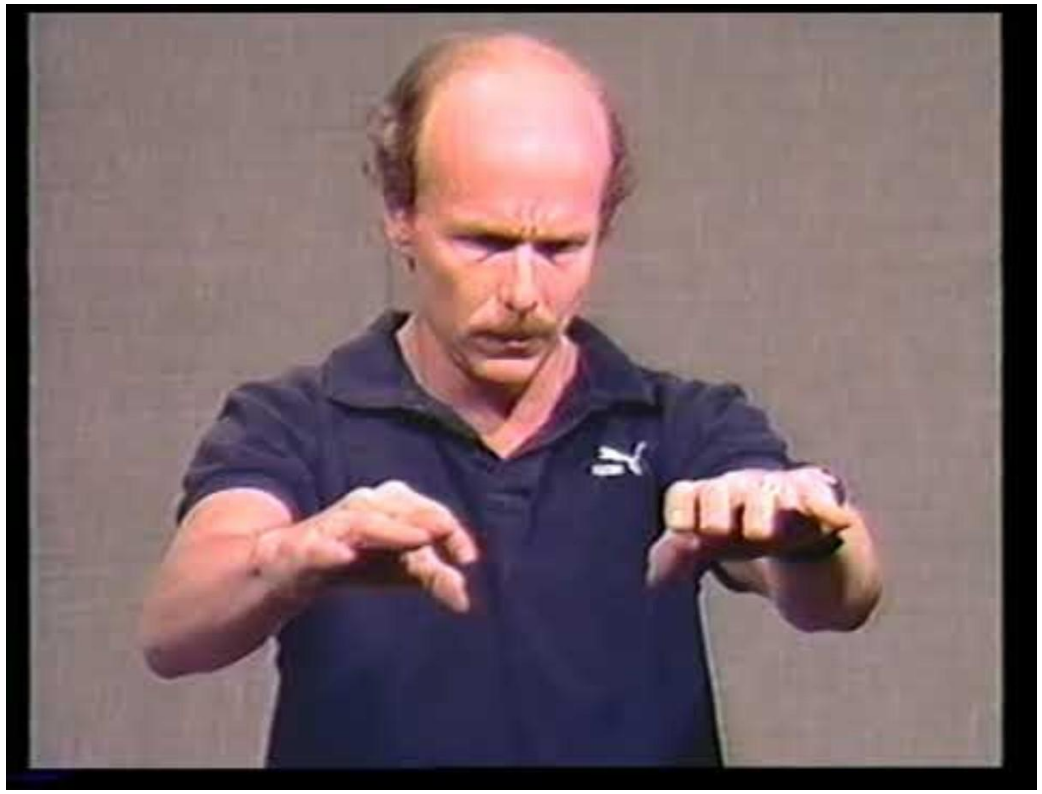
Defining Chorea

- Derived from Greek word χορεια for “dance-like” movements
- Chorea: involuntary, hyperkinetic movement disorder with spontaneous, purposeless, and irregular movements that flow from one body part to the next
  - Subcategory of dyskinesia

(Furr Stimming et. al., 2024)

Phenomenology of Chorea

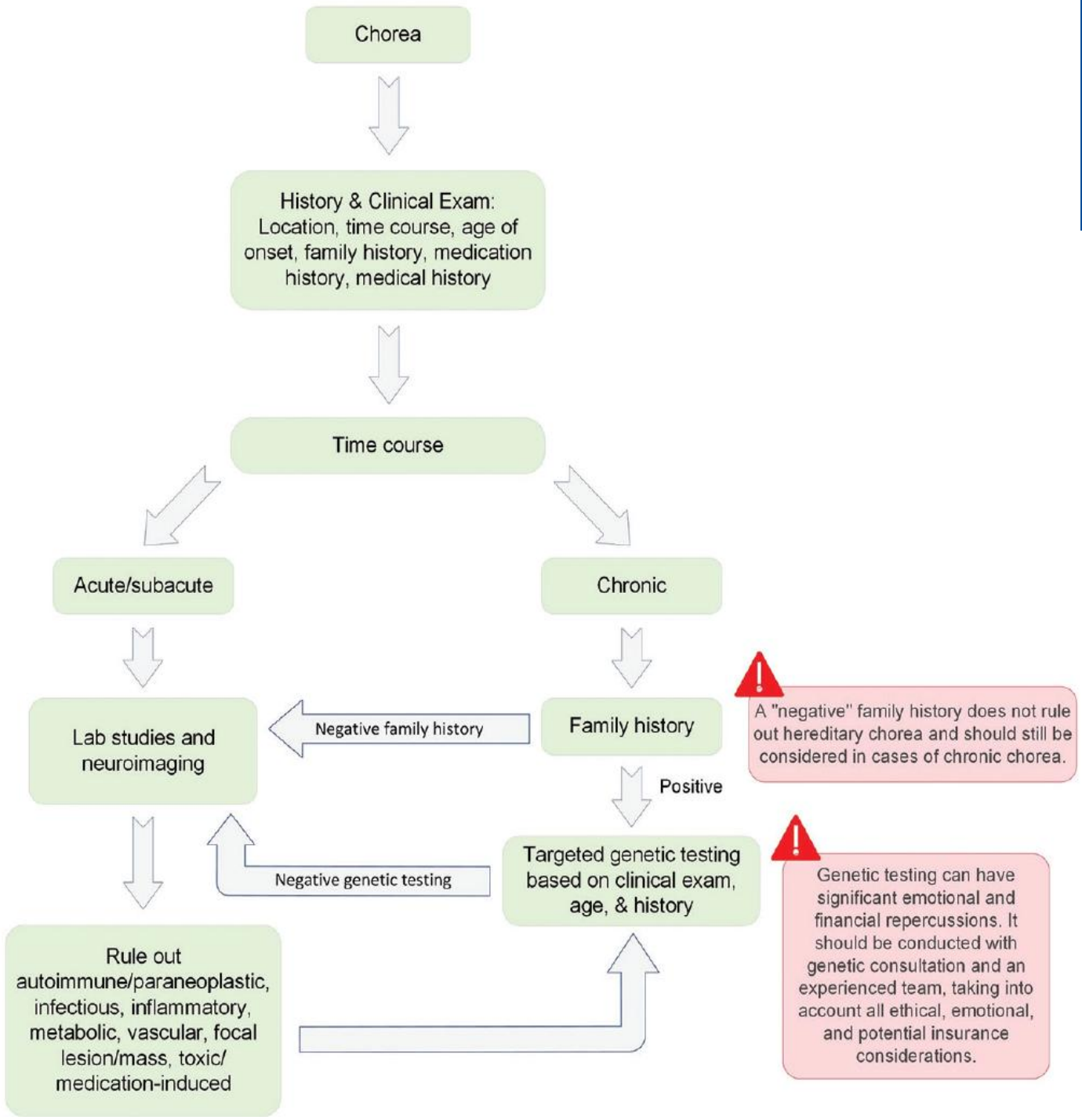
- Non-patterned
- Non-rhythmic
- Motor impersistence (darting tongue, milkmaid's grip)
- Parakinesia
- Pendular and/or hung-up reflexes
- Irregular ("dance like") gait



https://www.youtube.com/watch?v=RxWEilu-Mf4

(Furr Stimming et. al., 2024)
(Cambell, 2020)

Diagnostic Approach



(Furr Stimming et. al., 2024)

Clinical History

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- Onset
  - Age of onset
  - Acute and subacute causes: brain lesion, autoimmune, paraneoplastic, infection, toxic/metabolic
  - Chronic (>1 year) causes: genetic causes
- Time course
  - Static, paroxysmal, progressive
- Family history
- Medication history
- Toxin exposure

(Moore, 2025)

Medication hx: Drugs that can induce chorea

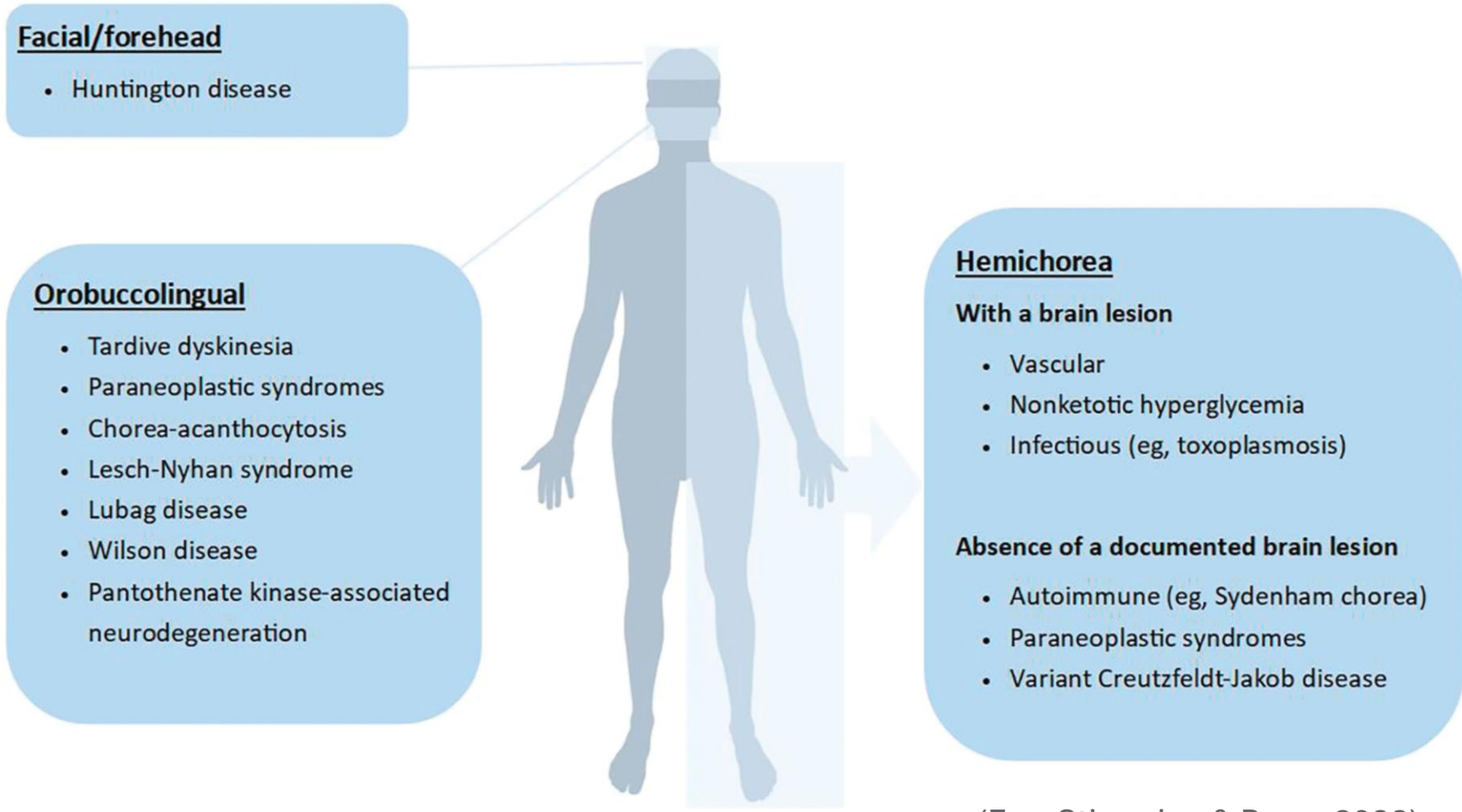
Medication class	Examples	
Antidepressants	• SSRIs • Fluvoxamine	• Paroxetine • Tricyclic antidepressants
Antiseizure medications	• Carbamazepine • Zonisamide • Lamotrigine	• Phenytoin • Gabapentin • Valproic acid
Antihistamines	• Cimetidine • Cyclizine	• Cyproheptadine • diphenhydramine
Antiparkinsonian drugs	• Levodopa • Dopamine agonists	• Anticholinergic drugs (trihexyphenidyl)
Dopamine antagonists	• Dopamine antagonist antiemetics • Phenothiazines	• Butyrophenones • Benzamides
Psychostimulants	• Amphetamines	• Cocaine
Other medications	• Baclofen • Oral contraceptives • Steroids	• Digoxin • Calcium-channel blockers (flunarizine, verapamil)

(Moore, 2025)

Clinical examination

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- Body parts involved:
  - Generalized vs. focal chorea



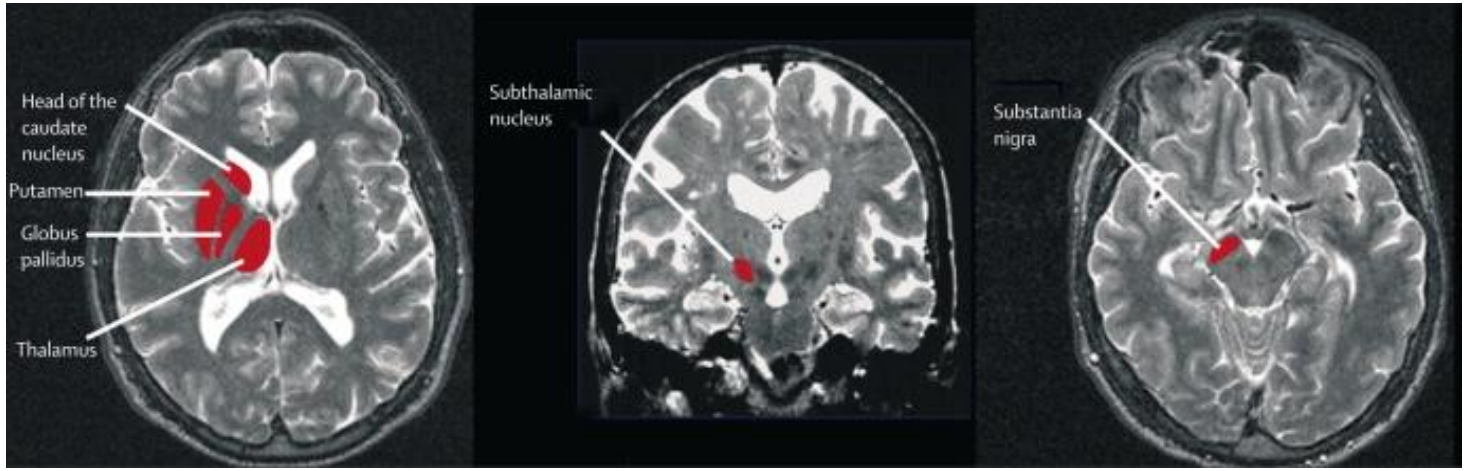
(Furr Stimming & Bega, 2022)

Further Investigations

- Genetic testing
  - Especially for chronic chorea and/or family history
  - Genetic counseling

Further Investigations: Imaging

- Can provide important diagnostic clues to associated diseases:
  - Basal ganglia
  - Cerebellum
  - Brainstem



MRI of important structures implicated in chorea (Cardoso et. al., 2006)

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Classification of chorea

- **Etiology:** sporadic, acquired, or inherited
- **Onset:** childhood vs. adult
- **Location:** facial, orobuccolingual, neck, appendicular, truncal, hemichorea, generalized

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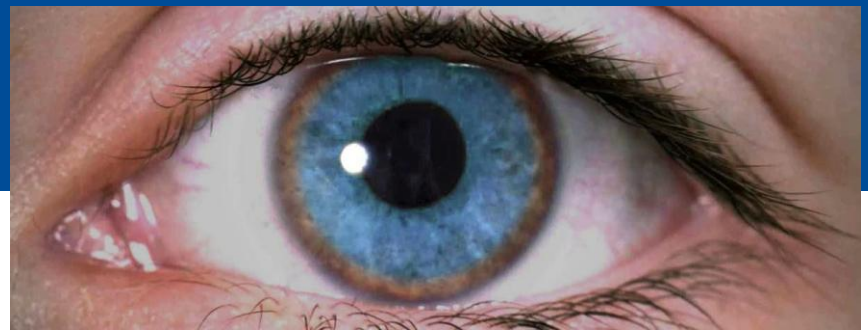
Differential Diagnosis of Chorea

- Hereditary Chorea
  - Huntington disease
  - ***Wilson disease***
  - Neuroacanthocytosis
    - Chorea-acanthocytosis
  - Fahr disease
  - *C9orf72* mutation
  - Friedrich ataxia

- Acquired chorea
  - Structural lesions
  - Autoimmune disorders
  - Paraneoplastic
  - Para-infectious
  - Toxic/metabolic

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Wilson Disease



Kaiser fleischer ring
(https://curiousclinicians.com/2021/01/06/episode-16-why-do-kayser-fleischer-rings-form-in-the-cornea-in-wilson-disease/)

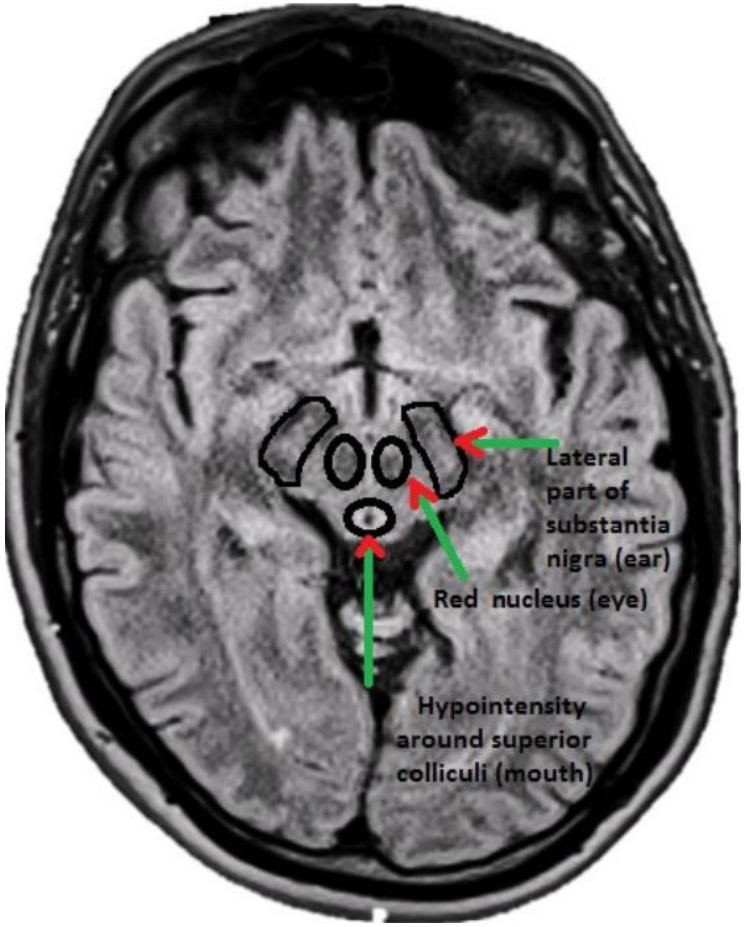
- AR mutation of ATP7B
- Onset: Childhood or early adulthood
- Sx
  - Movement symptoms
  - GI symptoms
  - Neuropsychiatric symptoms
- Dx: low serum ceruloplasmin, high 24h urine copper, and elevated LFTs, genetic testing
- Tx: iron chelation, liver transplant

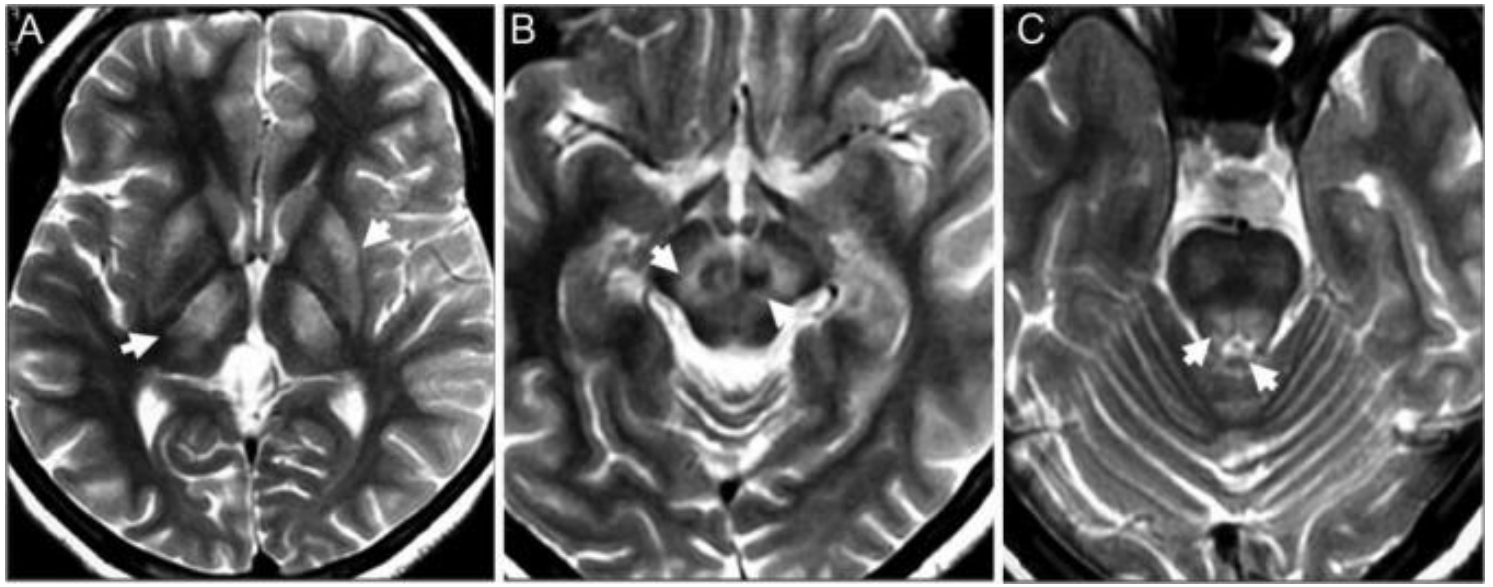


(Furr Stimming & Bega, 2022)

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Further investigation: Imaging





(Furr Stimming et. al., 2024)
(Malek & Newman, 2016)
(Shivakumar & Thomas, 2009)

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Differential Diagnosis of Chorea

- Hereditary Chorea
  - Huntington disease
  - ***Wilson disease***
  - Neuroacanthocytosis
    - Chorea-acanthocytosis
  - Fahr disease
  - *C9orf72* mutation
  - Friedrich ataxia

- Acquired chorea
  - ***Structural lesions***
  - Autoimmune disorders
  - Paraneoplastic
  - ***Para-infectious***
  - ***Toxic/metabolic***

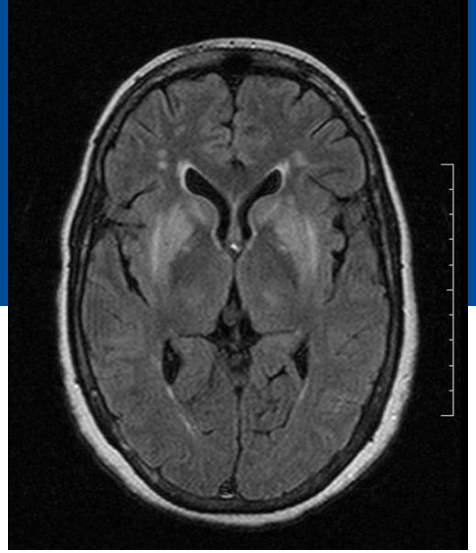
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Structural lesions

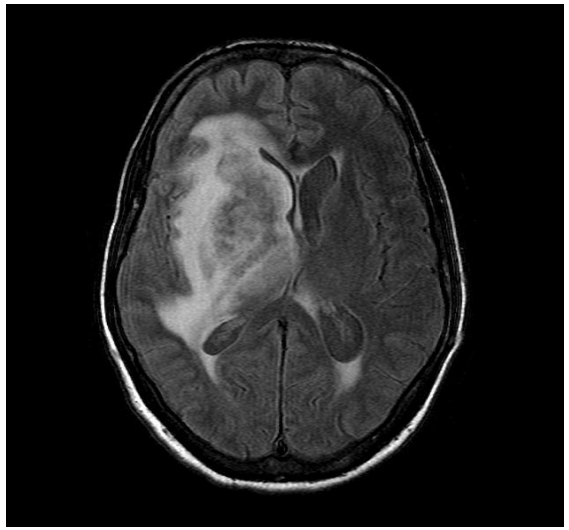
10. Basal ganglia pathologies
    - Iron accumulation
    - Ischemic or hemorrhagic stroke
    - Demyelinating lesions
    - Other space occupying lesions (neoplasm, abscess)
- Presentation:
    - Hemibody or focal chorea
    - ± elevated intracranial pressure



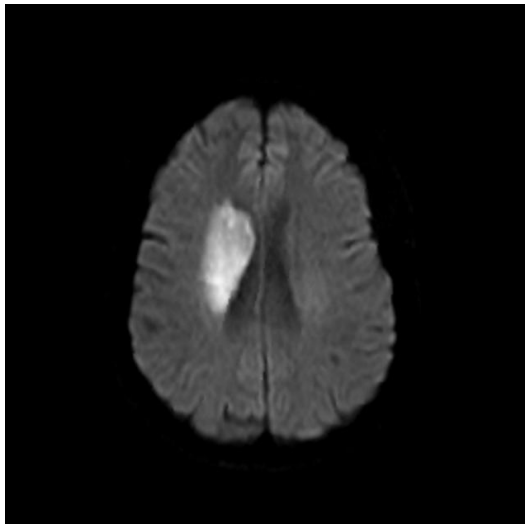
BG Hemorrhage



BG demyelination (FLAIR)



BG necrotizing toxoplasma infection (FLAIR)



BG acute infarction (DWI)

Images courtesy of radiopedia.org

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Para-infectious causes

- Measles, mumps, rubella, varicella-zoster virus, influenza, herpesvirus, Epstein-Barr virus, tick-borne encephalitis, West Nile encephalitis, cytomegalovirus, Japanese encephalitis, human immunodeficiency virus (HIV)
- Chorea often follows course of the infection
    - Can be associated with systemic illness
- Dx: brain imaging, viral panels in serum and CSF

(Furr Stimming & Bega, 2022)

Case 2

- Previously healthy 11-year-old boy presented with involuntary movements that started about a month ago
  - Exacerbating factors: stress
  - Absent during sleep
- He reported having sore throat 4 months prior to presentation
- Workup
  - Throat culture: positive for group A beta-hemolytic streptococcus
  - Anti-streptolysin O: 5x normal limit
  - Mitochondrial antibodies: weakly positive
- Treatment: Penicillin and tiapride



(Wei & Wang, 2013)

Sydenham Chorea

- Acute onset in childhood or early adolescence after streptococcal infection
- Clinical hx: streptococcal infection
  - Can occur later in life as chorea gravidarum
- Sx: tic-like behaviors, irritability, inattention
- Diagnosis: throat cx, antibodies
- Treatment: penicillin

(Furr Stimming & Bega, 2022)

Toxic/Metabolic Causes

- Medication induced (i.e., tardive dyskinesia)
- Toxic causes:
  - Carbon monoxide poisoning
  - Organophosphates
  - Manganese
  - Mercury
- Metabolic causes:
  - ***Nonketotic hyperglycemia***
  - Hyperthyroidism
  - Hypocalcemia
  - Hypo/hypernatremia

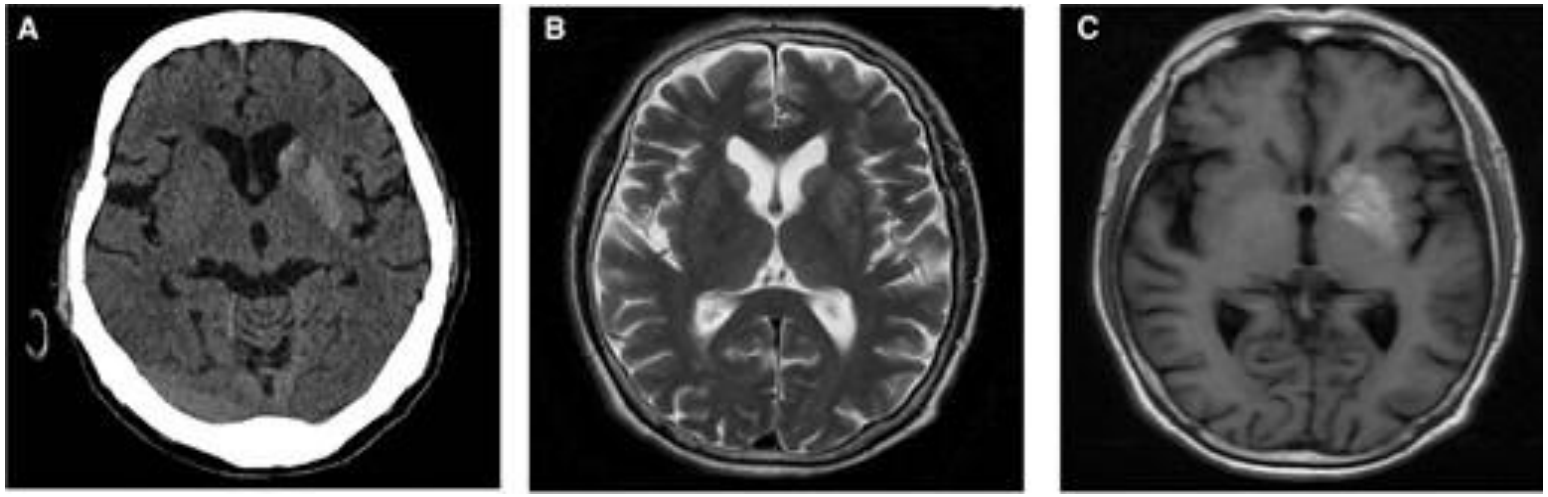
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(Furr Stimming & Bega, 2022)

Case 3

- 75 yo F with subacute onset of involuntary dancing movements of the right arm and leg
- No reported PMH and does not see a PCP
- No pertinent family history
- Exam: nonrhythmic, asynchronous mid to high amplitude writhing movements in right extremities
- Labs:
  - Blood glucose: 385 mg/dL
  - Hemoglobin A1c: 13.7%
  - Negative serum ketones
- Imaging: Signal changes in the left (contralateral) basal ganglia

Case 3 continued



Examples characteristic imaging changes:

A. Computed tomography shows hyperintense signal in the left basal ganglia

B/C. MRI: changes to the left basal ganglia region

B. T2 sequence shows hyperintense signal

C. T1 sequence shows hyperintense signal

Adapted from (Wu et al., 2025)

Case 3 continued

- Diagnosis: nonketotic hyperglycemic hemichorea
- Management:
  - Insulin then oral hypoglycemic medications were started with improvement of movements

Management of chorea

- Considerations
  - Impact on patient's well-being and function
  - Specific therapies for underlying cause
  - Symptomatic treatment options

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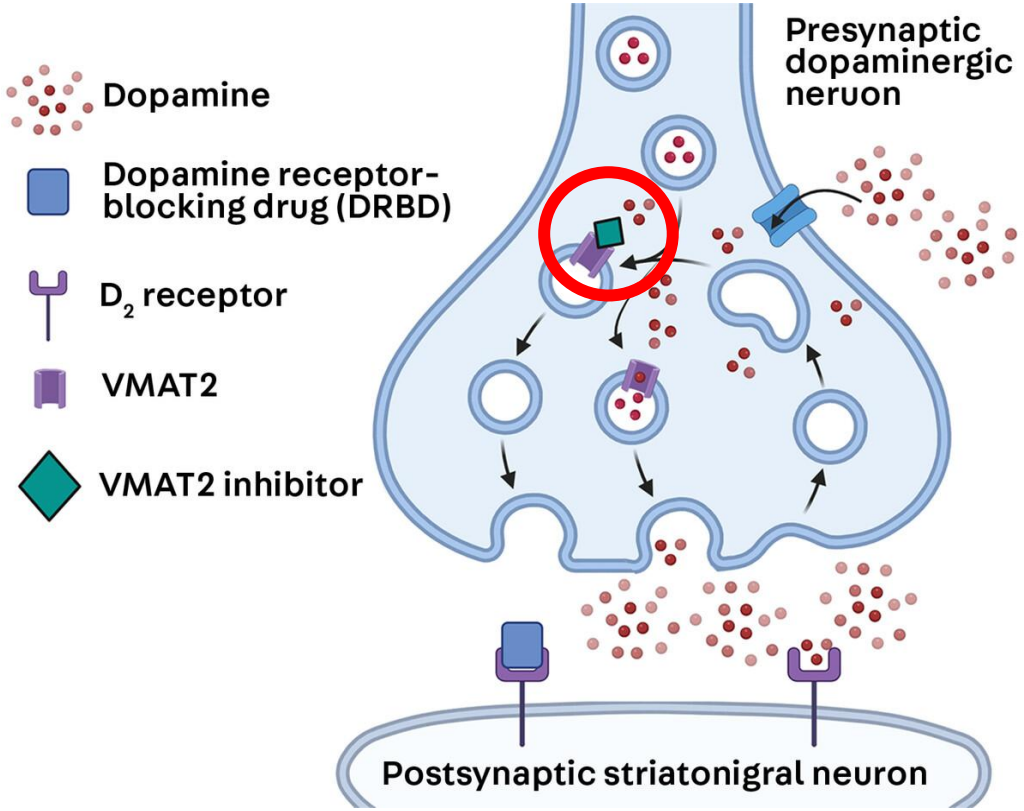
(Bashir & Jankovic, 2018)

Pharmacologic options

- VMAT2 inhibitors
- Neuroleptics
- NMDA receptor antagonist
- Antiseizure medications
- Botulinum toxin

VMAT2 inhibitors

- Mechanism of action:
  - Decrease extracellular release of dopamine by reversible inhibition of VMAT2
- Options:
  - Tetrabenazine
  - Deutetrabenazine
  - Valbenazine
- Shared major side effects
  - Somnolence and sedation
  - Depression
    - Suicidality when used for HD chorea*
  - Parkinsonism
  - QT prolongation
  - Neuroleptic malignant syndrome



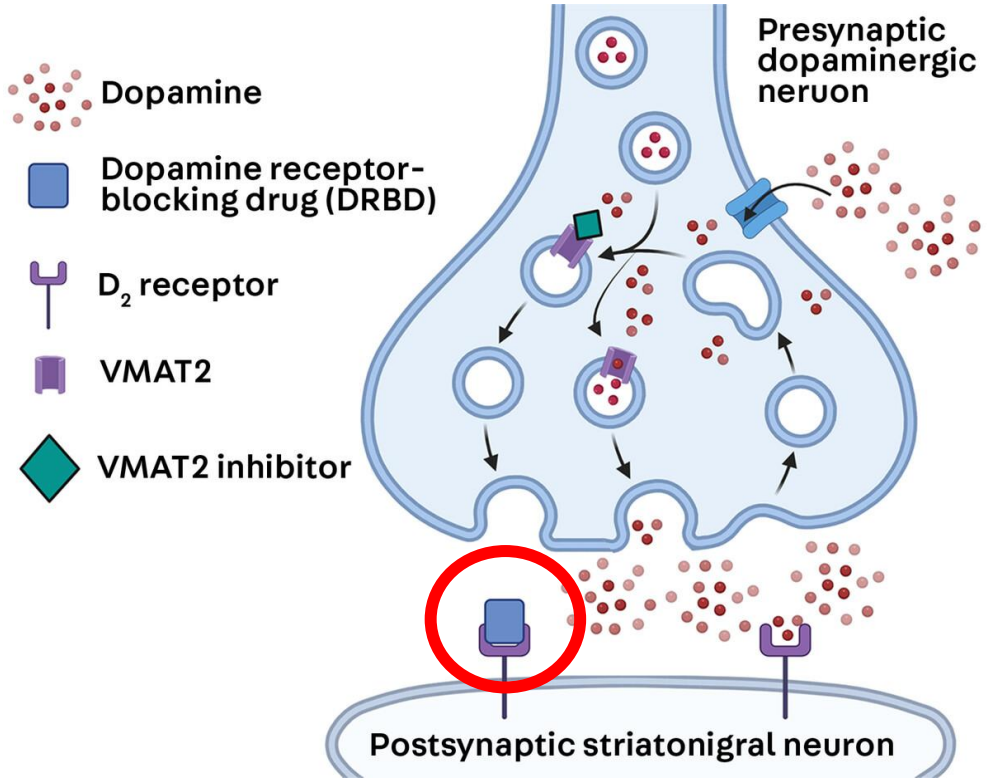
Mechanisms of action of VMAT2 inhibitors and Dopamine receptor blockers. (Moore, 2025)

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(Furr Stimming & Bega, 2022)

Neuroleptics

- MOA: D_2 receptor blockade
- Examples: quetiapine, olanzapine, and risperidone.
- Adjunct for behavioral, psychiatric, and movement symptoms in degenerative chorea



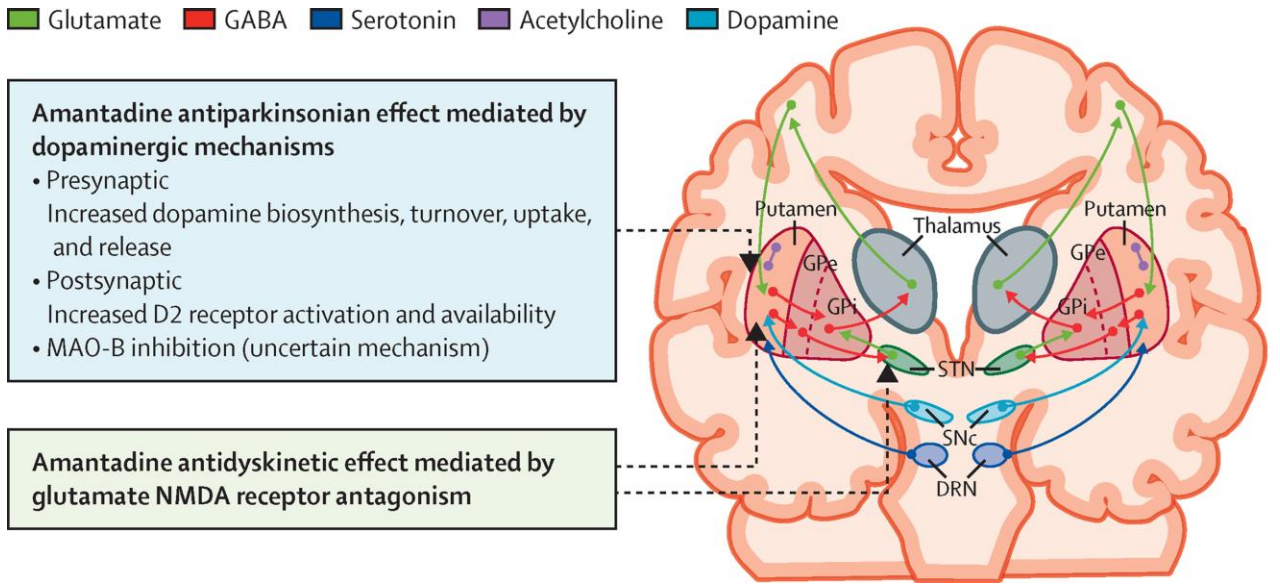
Mechanisms of action of VMAT2 inhibitors and Dopamine receptor blockers. (Moore, 2025)

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(Furr Stimming & Bega, 2022)

Amantadine

- MOA: N-methyl-D-aspartate (NMDA) receptor antagonist
- Uses
  - Adjunct for PD treatment
  - Levodopa-induced dyskinesia
  - Off-label for chorea (HD, tardive dyskinesia)



Potential mechanism of action of amantadine in central nervous system (Rascol, et al., 2021)

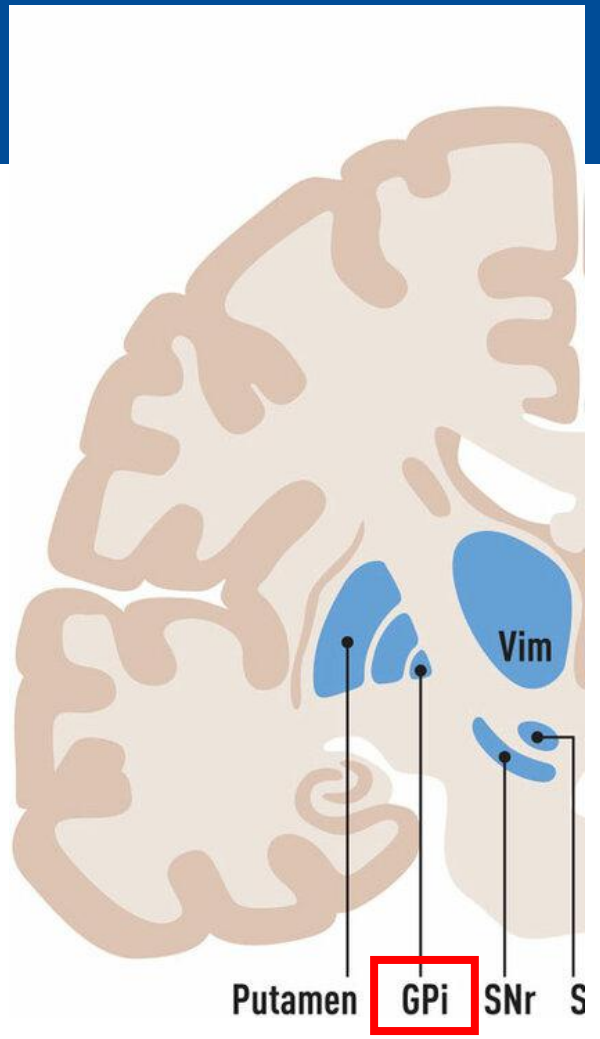
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(Furr Stimming & Bega, 2022)

Other medications

- Antiseizure medications
  - Multiple sites of actions
  - Can be used in patients with co-existing seizures
  - Rarely used in neurodegenerative chorea

Nonpharmacologic options

- Deep brain stimulation
  - Medication refractory cases
  - Target: GPi
- Speech, occupation, and physical therapies
- Genetic counseling
- Nutrition consult



DBS targets (Hariz & Blomstedt, 2022)

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Thank you

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