# DRUGS USED IN MOVEMENT DISOEDERS

► Parkinson disease

- ▶ Other
  - ► Benign essential tremor
  - ► Chorea
  - ► Hemiballism
  - **Tics**
  - ▶ Dystonia

# Go to www.menti.com and use the code 94 13 85

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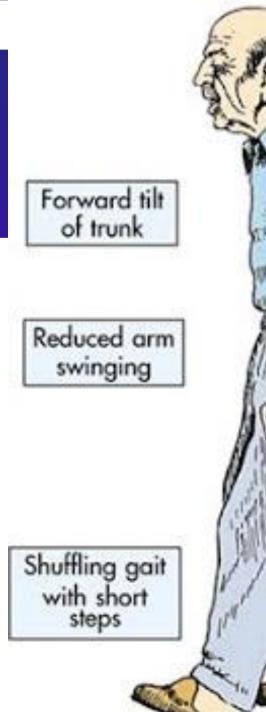
#### Parkinson Disease

Tremor

Rigidity

Akinesia

Postural instability



Rigidity and trembling of head

> Rigidity and trembling of extremities

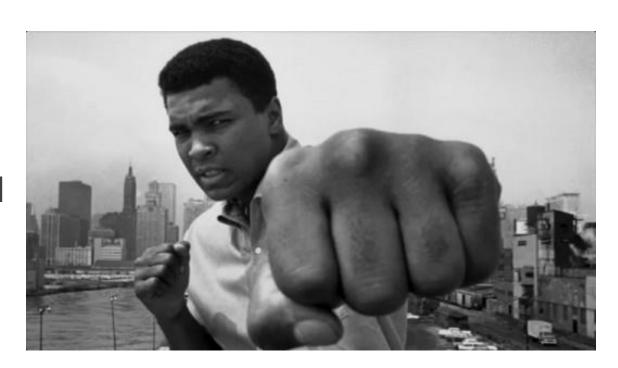
#### Aims of treatment

▶ Control Symptoms ➤ Minimize disability

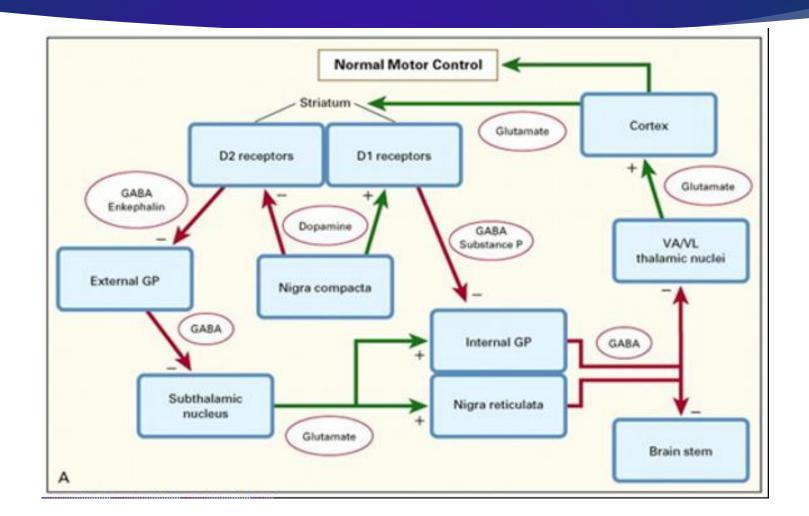
Improve quality of life

Very effective initially

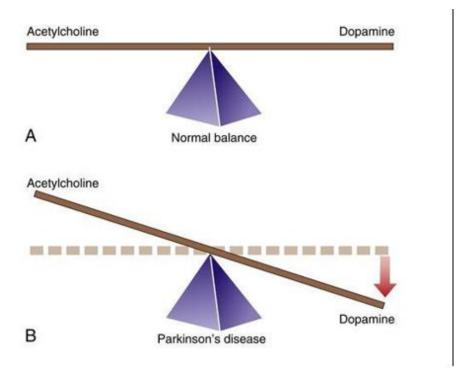
► Long term effectiveness is limited



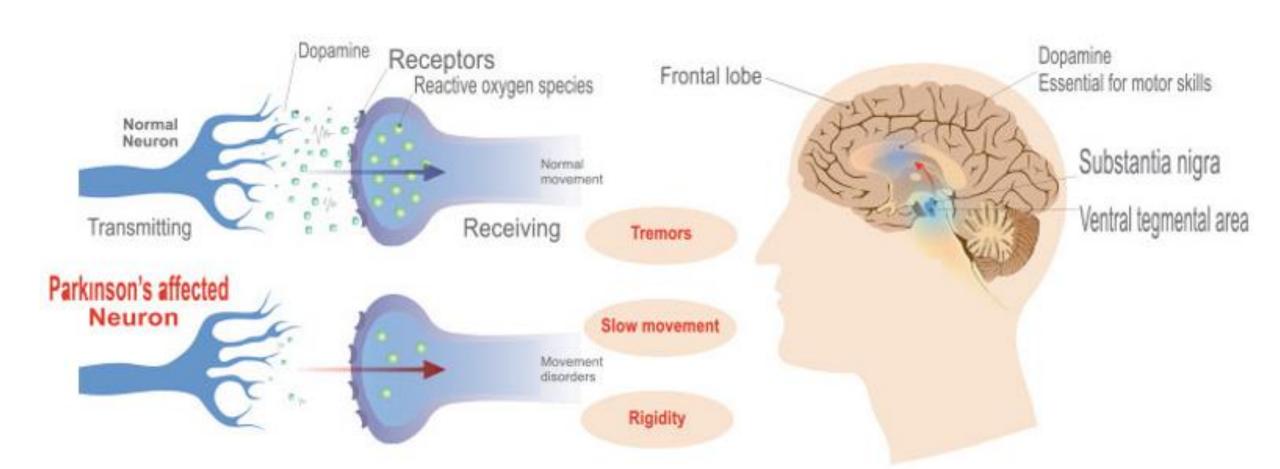
# Pathophysiology



# Pathophysiology



#### Pathophysiology



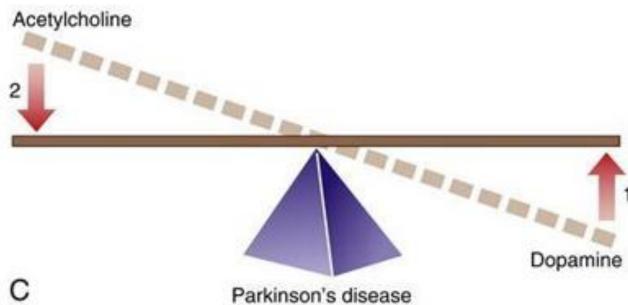
#### Drug induced parkinsonism

#### Dopamine receptor antagonism

Drug frequently causing parkinsonism		Drug infrequently causing parkinsonism	
Typical antipsychotics	Phenothiazine: chlorpromazine, prochlorperazine,	Atypical antipsychotics	Clozapine, quetiapine
	perphenazine, fluphenazine, promethazine		
	Butyrophenones: haloperidol		
	Diphenylbutylpiperidine: pimozide	Mood stabilizer	Lithium
	Benzamide substitutes: sulpiride		
Atypical antipsychotics	Risperidone, olanzapine,	Antidepressant	SSRI: citalopram, fluoxetine,
	ziprasidone, aripiprazole		praoxetine, sertraline
Dopamine depleters	Reserpine, tetrabenazine	Antiepileptic drugs	Valproic acid, phenytoin
Antiemetics	Metoclopramide, levosulpiride, clebopride	Antiemetics	Domperidone, itopride
Calcium-channel blocker	Flunarizine, cinnarizine		

#### Aims of treatment

Symptomatic control



Cure: C Parkinson's disease stop or slow down neuronal degeneration

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#### Dopaminergic drugs

- Dopamine replacement Levodopa
- Dopamine receptor agonist

Ropinirole

**Bromocriptine** 

Pergolide

Carbegoline

- Inhibition of dopamine metabolism
   MAO inhibitors Selegiline
   COMT inhibitors Entacapone
- Increased synthesis & release of dopamine
   Amantadine

# Cholinergic drugs

- ► Benzhexol
- Benztropine

# Neuroprotective agents

- ► Selegiline?
- ► Ropinirole?
- ► Pergolide ?

#### Levodopa

- ▶ 1<sup>st</sup> line therapy
- ▶ The most effective drug for symptomatic control
- ► A precursor of dopamine

# Why not dopamine?

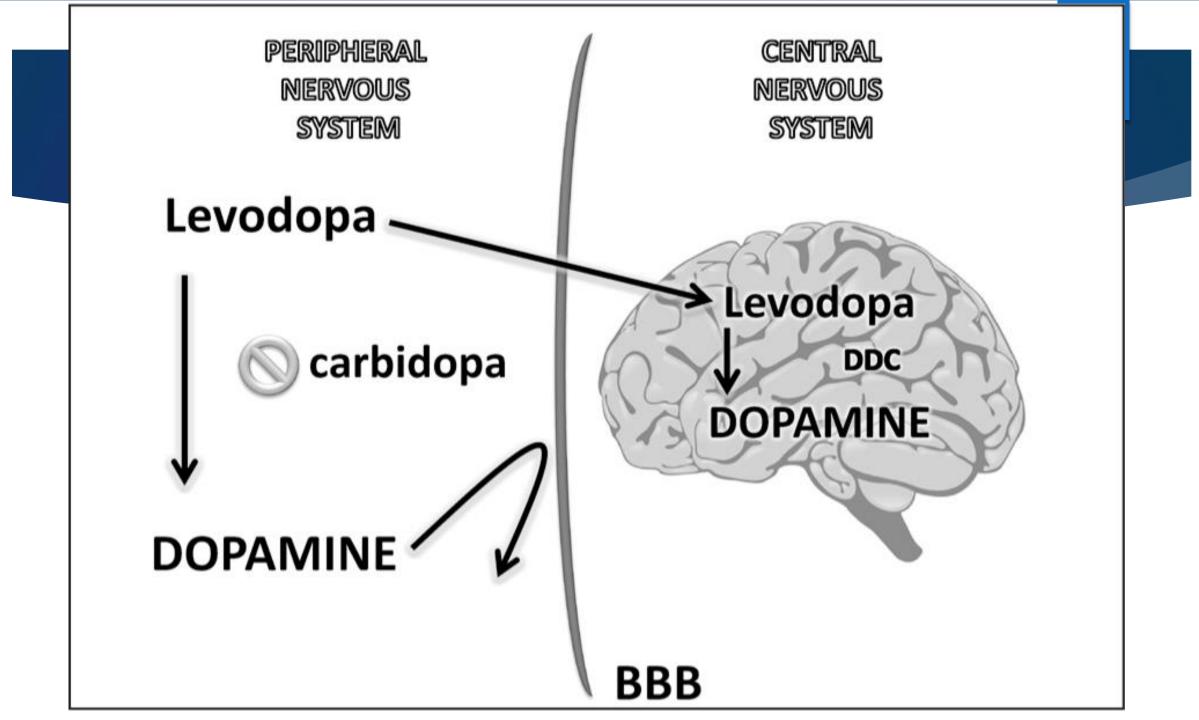
#### Why not dopamine?

Extensively metabolized in gut, liver and blood by COMT and MAO

▶ Not lipid soluble : Poor CNS penetration

#### Dopamine

- ► Brain: Therapeutic effect
- ► Periphery : Adverse effect



- Dopa decarboxylase inhibitors
  - Carbidopa
  - Benserazide

- Carbidopa + Levodopa = Co-careldopa (Sinemet)
- Benserazide + Levodopa = Co-beneldopa (Madopar)

- ▶ Do not cross BBB
- ► Reduce peripheral adverse effects
- ► Allow to use lower doses of L-dopa

# Levodopa - Adverse effects

Central AE	Peripheral AE
Confusion	Altered bowel habits
Hallucinations	Abdominal pain
Delusions	Nausea, Vomiting
Agitation	Arrhythmias
	Postural hypotension
	Polyuria
	Urinary incontinence
	Difficulty in micturition

#### Levodopa - Motor complications

- Abnormal involuntary movements
  - Choreoathetoid dyskinesia, dystonia
- End of dose deterioration
  - Predictable weaning off of the effect towards the end of a dosage interval
- On-off fluctuation
  - Unpredictable switching between over treatment with dyskinesia (on phase) and under treatment with freezing (off phase)

#### Levodopa - Motor complications

► Motor complications related to

- Duration of the treatment
- ▶ Dosage of the drug
- ▶ Disease severity

#### Management of motor complications

- More frequent dosing
- Modified release L-dopa
- Adjuvant therapy
  - ► Dopamine agonists
  - ▶ Apomorphine
  - ► COMT inhibitors
  - ► MAO inhibitors

#### Levodopa...

#### Contraindications

➤ Closed angle glaucoma

#### Caution

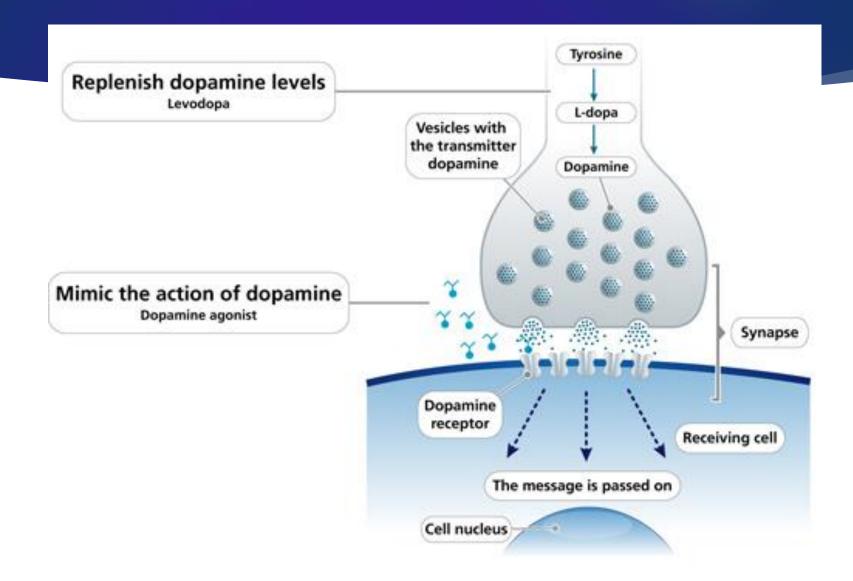
- ► Psychiatric illness
- ► Hx of arrhythmia & IHD

#### Interactions

- ► Increased effect with MAO inhibitors
- Decreased effect with neuroleptics

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# Dopamine agonists



#### Dopamine agonists

- ► Effectiveness: less than L-dopa
- Adverse effects: Less dyskinesia

: More central AE

Uses

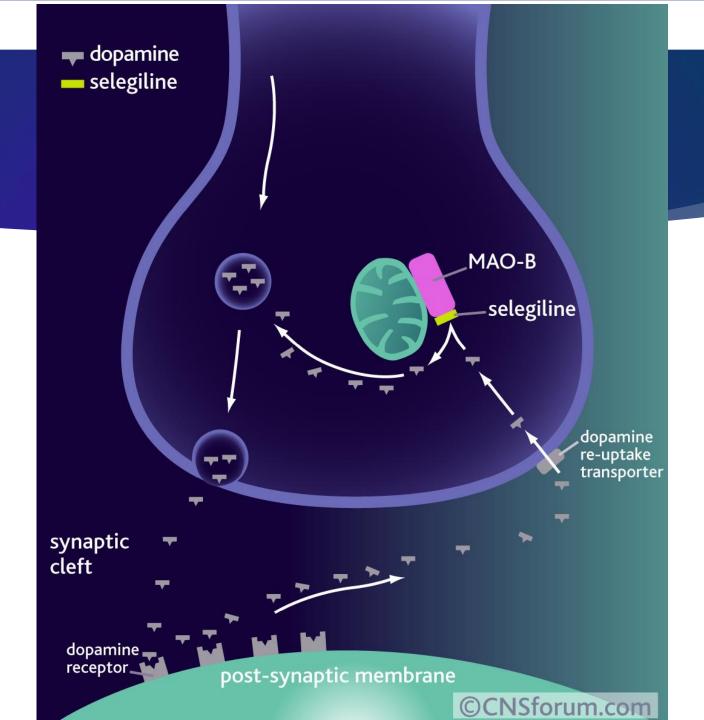
As adjuvant therapy with levodopa

As monotherapy (Ropinirole, carbergoline)

#### Selegiline

- ► A selective MAO inhibitor (Type B)
- Inhibits breakdown of dopamine in corpus striatum

### Selegiline



#### Selegiline

- ► A selective MAO inhibitor (Type B)
- ▶ Inhibits breakdown of dopamine in corpus striatum
- ► Effectiveness: less than L-dopa
- ► Adjuvant to L-dopa in end of dose deterioration
- ▶ Adverse effects : More central AE

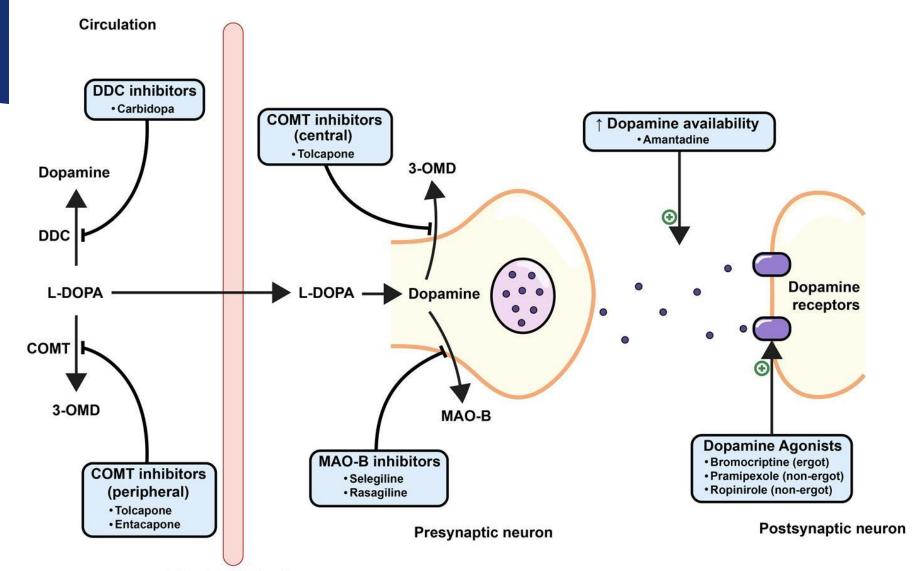
#### Amantadine

- An antiviral
- Increase synthesis and release of dopamine
- ► Effectiveness less than L-dopa
  - more than anti cholinergic

#### Adverse effects

- CNS disturbances
- Postural hypotension
- Ankle oedema

#### Parkinson Disease Drugs



#### Anti cholinergic drugs

- ▶ Idiopathic Parkinson disease
  - ► To control tremors
  - ► Minimal effect on other symptoms
- Rx of choice for drug induced parkinsonism

(dopamine receptors are already blocked)

#### Anti cholinergic drugs

- Adverse effects
  - Central AE's (confusion, hallucinations)
  - Dry mouth, constipation, urine retention
  - ► Blurred vision
  - Can precipitate closed angle glaucoma

# Dyskinesias

#### Dystonias

- Acute drug induced dystonia
- Caused by dopamine antagonist
  - ► Metochlopramide, Domperidone
  - ► Antipsychotics eg: haloperidol, chlophromazine
- Treatment

Benzhexol / Benztropine

#### Benign essential tremor

- ▶ Non selective beta blockers eg: propranolol
- Primidone (an anti epileptic)
- clonazepam

Spasmodic torticollis, hemifacial spasms, blepharospasms Botulinium toxin

Chorea

Phenothiazines, Tetrabenzine

► Hemibalism:

Tetrabenzine

**Tics** 

Haloperidol

Spasticty

Baclofen(GABA agonist), Diazepam

# THANK YOU

# Go to <a href="https://kahoot.it">https://kahoot.it</a>

https://play.kahoot.it/#/?quizld=247bfb82-8299-4eab-a887-54c0361f13b8