

NEURODEGENERATIVE PHARMACOLOGY

Dopaminergic nigrostriatal pathway helps to modulate coordination of muscle movement

HUNTINGTONS

MOVEMENT SYMPTOMS

PARKINSONS

Characterized by ↑dopamine

Loss of dopaminergic neurons in SN

Dopamine-depleting

Tetrabenazine

MOA: ↓dopamine levels in SN neurons by inhibiting transport of dopamine into presynaptic vesicles

Target: VMAT transporter

Dopamine Antagonist

Aripiprazole

MOA: competes w/ dopamine for binding at receptor

Tox: same as antipsychotic

Dopamine Precursor

Levodopa

MOA: restores dopamine signaling

can be used in conjunction with:

DOC inhibitor

Carbidopa

COMT inhibitor

Entacapone

Tolcapone

MOA: block the peripheral metabolism of Levodopa, increasing the fraction that reaches the CNS

tox: "wearing off" phenomenon causes dyskinesia as primary tox

interactions: MAOIs

Short term tox:
• N/V
• Orthostatic hypotension
• psychosis

Dopamine agonists

Pramipexol

Ropinirole

MOA: directly substitute for dopamine to restore normal motor control

tox: suppression of prolactin secretion due to ↑DA in tuberoinfundibular pathway.

Sleep attacks, sedation, somnolence. OCD/ICD

MAOB inhibitors

Rasagiline

MOA: block breakdown of dopamine in neurons and increase its release

Dopamine Release Stimulator

Amantadine

MOA: unknown

tox: dizziness, insomnia

Anti-cholinergics

Benztrapine

Trihexiphenidyl

competitive antagonists of ACh

MOA: reestablish balance between ACh and DA signaling in striatum

tox: anti-cholinergic → xerostomia, tachy, constipation, urinary retention

• avoid in older patients

COGNITIVE SYMPTOMS

DEMENTIA w/ LEWY BODIES

Cognitive and neuropsych sx treated with:

Cholinesterase Inhibitors

- Donepezil
- Galantamine
- Rivastigmine

tox: parasympathetic cardiac effects
• various arrhythmias

↓ insomnia, vivid dreams, bradycardia, syncope

ALZHEIMERS

60% of dementia cases

Glutamate Antagonist

Memantine

MOA: inhibits neuronal death caused by extra-synaptic glutamate receptors

• amyloid-beta protein blocks glutamate reuptake → excess spills over causing chronic hyperstimulation