

PARKINSON'S DISEASE

Parkinsonism is a progressive neurological disorder of muscle movement, characterized by tremors, muscular rigidity, bradykinesia, and postural and gait abnormalities.

Etiology

SUBSTANTIA NIGRA:

Source of dopaminergic neurons that terminate in neostriatum.

Serves as a tonic, sustaining influence on motor activity rather than participating in specific movements

NEOSTRIATUM

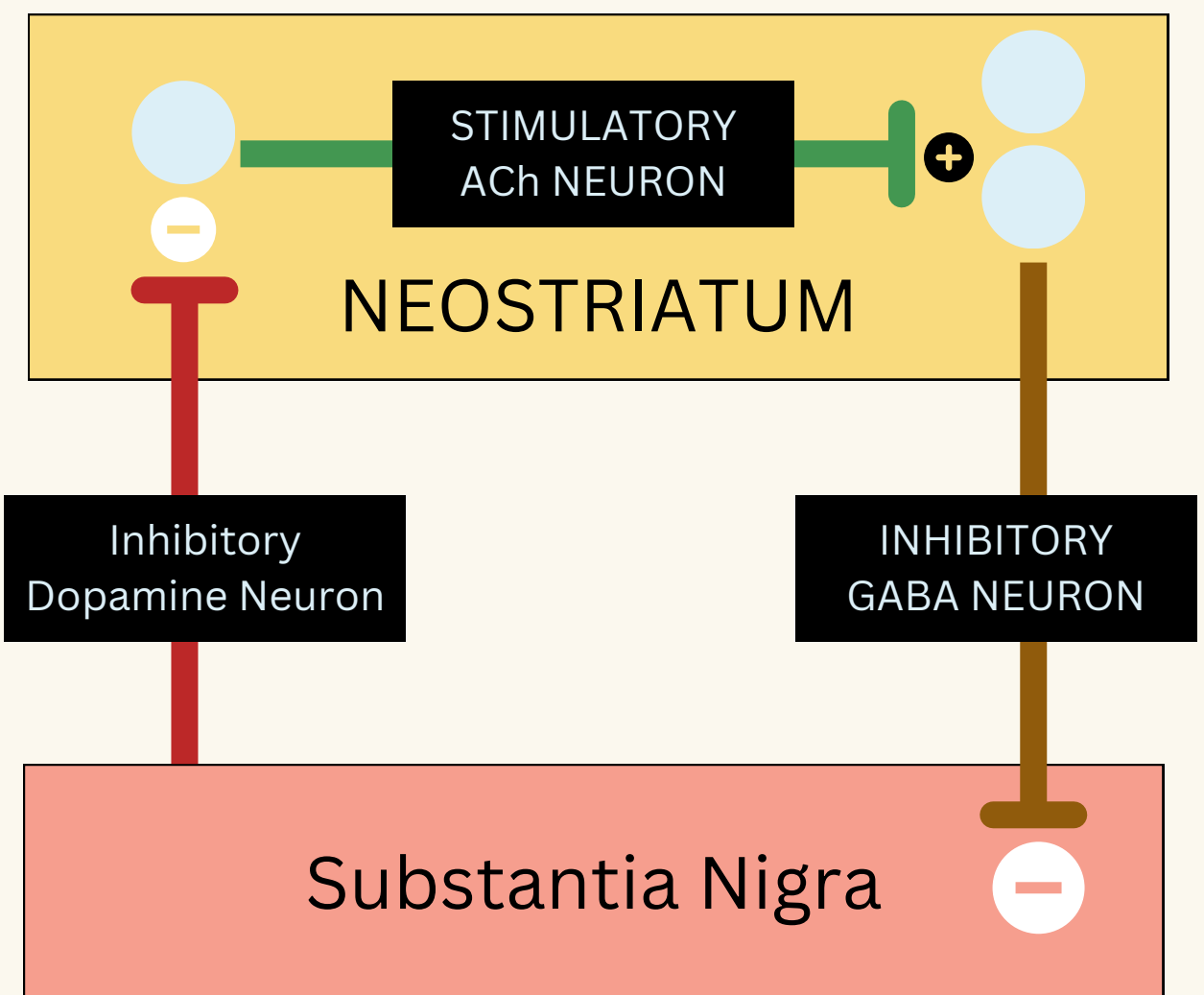
In Parkinson's disease, destruction of cells in the substantia nigra results in the degeneration of the nerve terminals that secrete dopamine in the neostriatum

SECONDARY PARKINSONISM:

Antipsychotic drugs such as the phenothiazines and haloperidol, whose major pharmacologic action is blockade of dopamine receptors in the brain, may produce parkinsonian symptoms (also called pseudoparkinsonism or drug-induced parkinsonism).

Role of substantia nigra in Parkinson's disease

Connections to muscle through motor cortex and spinal chord

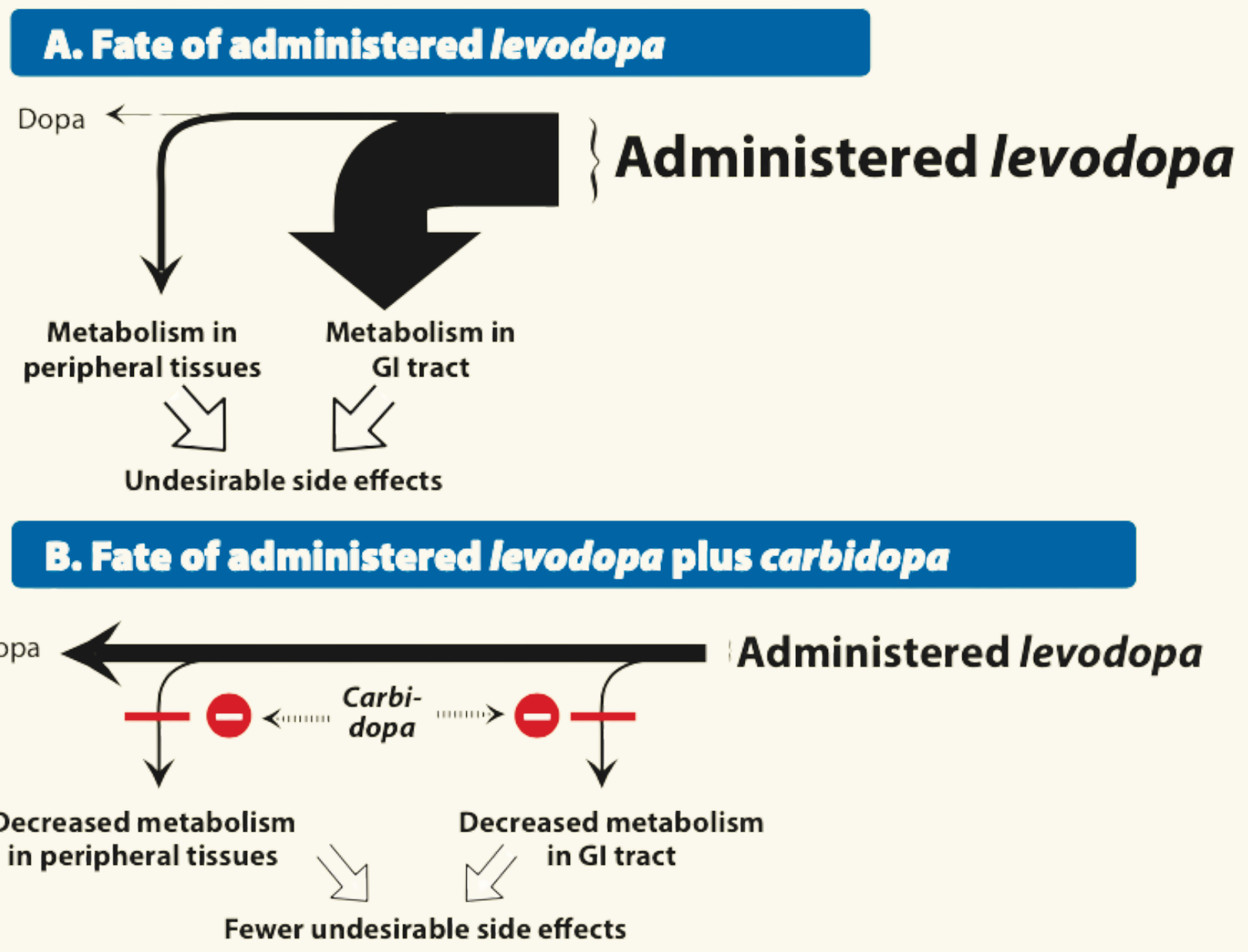
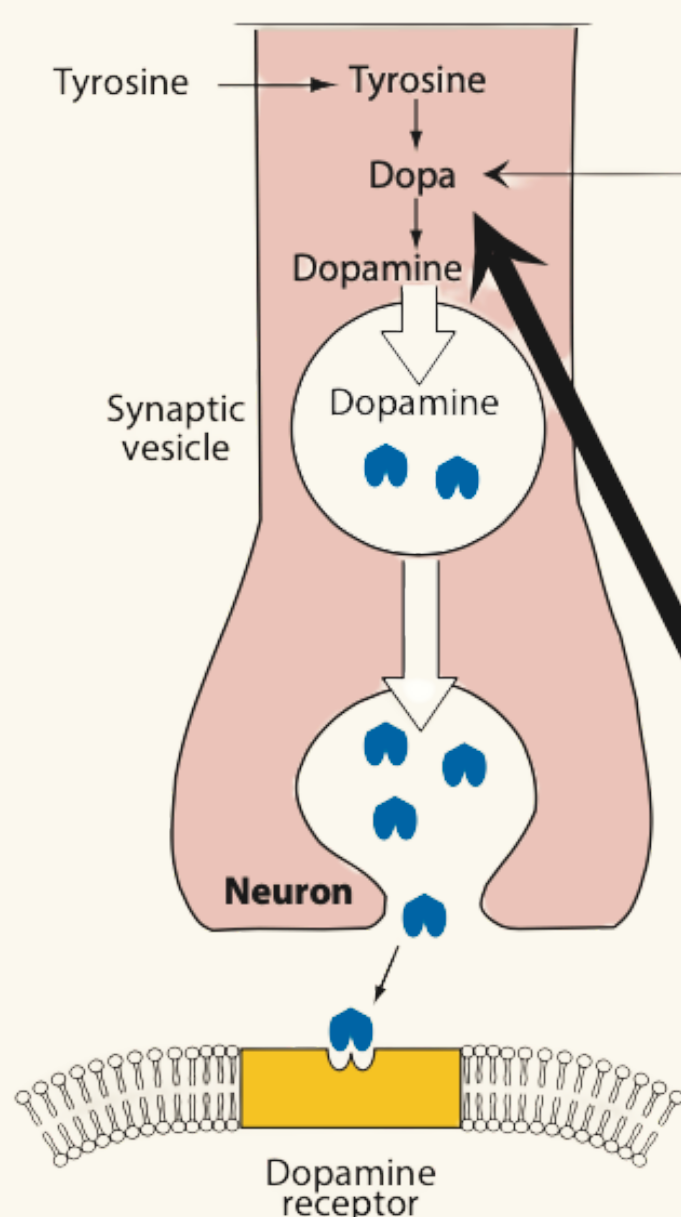


Cell death results in less dopamine release in the neostriatum.

Loss of the inhibitory effect of dopamine results in more production of ACh, which triggers a chain of abnormal signaling leading to impaired mobility.

DRUGS AFFECTING DOPAMINERGIC SYSTEM	
Dopamine precursors	<ul style="list-style-type: none"> Levodopa Levodopa (with carbidopa)
Peripheral decarboxylase inhibitors	<ul style="list-style-type: none"> Carbidopa Benserazide
Dopamine agonists	<ul style="list-style-type: none"> Bromocriptine Pramipexole Pergolide Lisuride Ropinirole Rotigotine
MAOB inhibitors	<ul style="list-style-type: none"> Selegiline Rasagiline
COMT inhibitors	<ul style="list-style-type: none"> Entacapone Tolcapone
Dopamine facilitators	<ul style="list-style-type: none"> Amantadine¹ Apomorphine

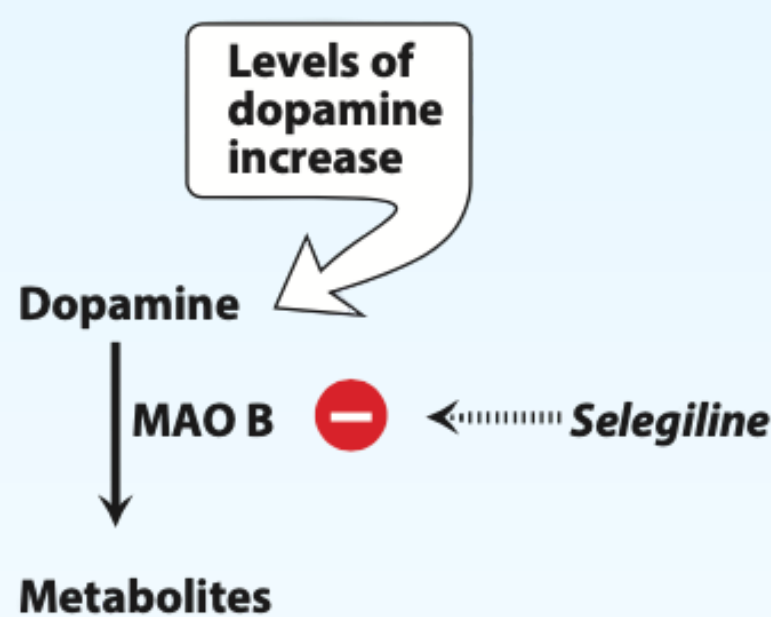
LEVODOPA & CARBIDOPA



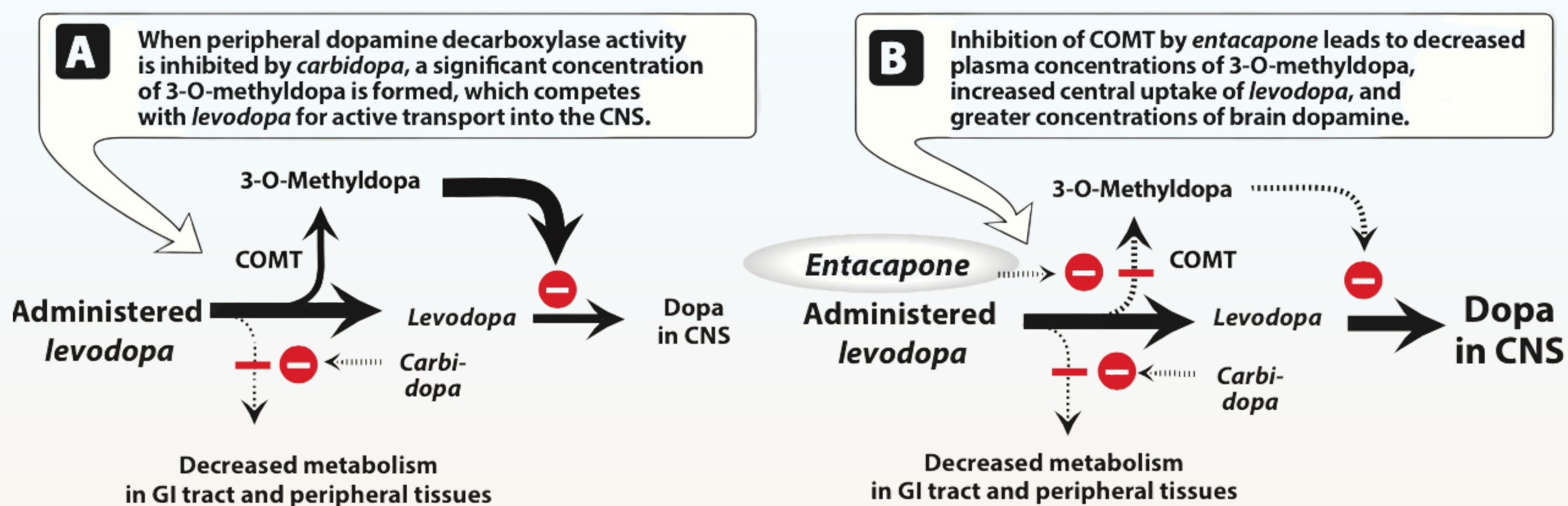
Synthesis of dopamine from levodopa in the absence and presence of carbidopa, an inhibitor of dopamine decarboxylase in the peripheral tissues. GI = gastrointestinal.

MAO-B INHIBITORS

- Selegiline selectively inhibits monoamine oxidase (MAO) type B, an enzyme that metabolises dopamine → increased dopamine
- It does not inhibit MAO type A (metabolises norepinephrine & serotonin)



CATECHOL-O-METHYLTRANSFERASE INHIBITORS



DOPAMINE RECEPTOR AGONISTS

Bromocriptine (Ergot derivative)

- Similar action to levodopa
- More: hallucinations, confusion, nausea, orthostatic hypotension
- Less: dyskinesia

Risks:

- Worsens psychiatric illness
- Vasospasm (caution in MI/peripheral vascular disease)
- Pulmonary & retroperitoneal fibrosis

Non-Ergot Dopamine Agonists

Drug	Route	Special Use
Pramipexole	Oral	Renal excretion (dose adjust in renal impairment)
Ropinirole	Oral	—
Apomorphine	Injectable	Acute “off” episodes in advanced PD
Rotigotine	Transdermal patch	24-hour steady drug levels

