Antiparkinson drugs

Dopaminergic substances

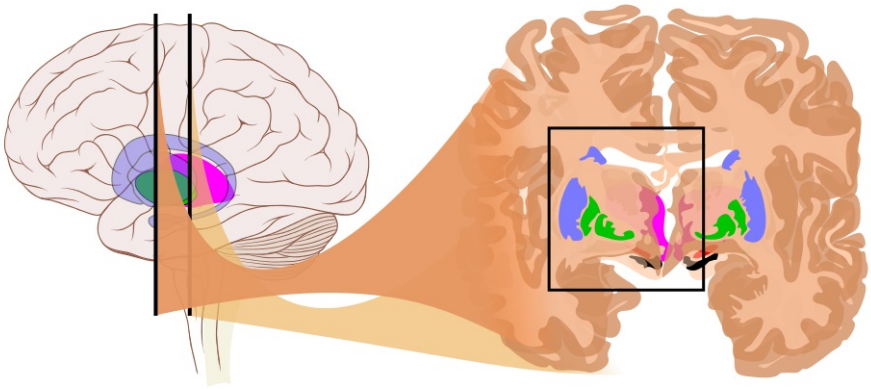
Levodopa (Template:L-DOPA)

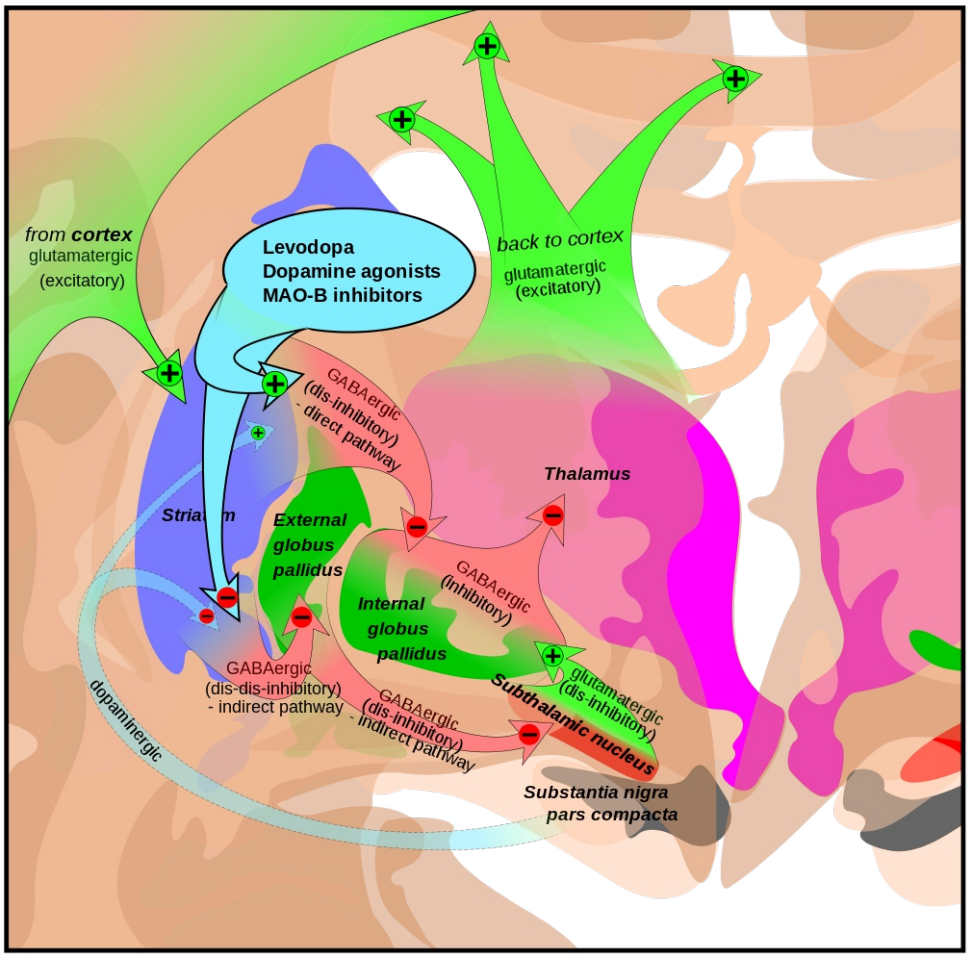
Precursor of dopamine, replenishes dopamine in the basal ganglia. **Dopamine** does not cross the blood-brain barrier and after i.v. administration has no central therapeutic effect.

The precursor of dopamine, **levodopa**, enters the brain and is decarboxylated to dopamine, which has a therapeutic effect.

Levodopa is administered orally, biological half-life is short, around 2 hours. This leads to fluctuating levels, so the daily dose is usually divided into 3-4 and sometimes more parts. Unfortunately, only 1-3% of administered levodopa enters the brain unchanged, while the rest is metabolized extracerebrally, mainly by decarboxylation to dopamine.

If we administer levodopa with peripheral ``dopa decarboxylase inhibitors *(DD), which do not penetrate the blood-brain barrier, its metabolism in the periphery is reduced and a larger proportion of the administered substance is available for transfer to the brain. Simultaneous administration of a peripheral DD inhibitor reduces the daily need for levodopa to 1/4. Decreased production of dopamine in the periphery, adverse effects in the GIT and cardiovascular system. Levodopa is therefore more often than alone administered with these peripheral DD inhibitors, i.e.* ***carbidopa*** *or* ***benserazide*****.**





Levodopa can improve the clinical manifestations of parkinsonism, but is particularly effective in alleviating *bradykinesia* and the resulting difficulties in daily life. The effect on tremor is less pronounced. Levodopa significantly improves the quality of life of patients and also reduces mortality from PN. At the beginning of treatment, around 80% of patients respond favorably to the administration of levodopa, after 3-4 years of treatment, a gradual decrease in the effect is often observed.

Adverse effects – early

- ***GIT:*** If levodopa is given initially without DD inhibitors, it causes nausea and vomiting in about 80%.
- ***KVS:*** Arrhythmias, these are not very common, they are attributed to increased production of catecholamines in the periphery. Combination with DD inhibitors reduces their occurrence.
- ***Effect on the psyche:*** Levodopa can rarely induce a schizophrenia-like syndrome with delusions and hallucinationsmi. Dopa is therefore contraindicated in psychotics.

Adverse Effects – Late

- ***Dyskinesias:*** occur in up to 80% of patients with long-term treatment. The most common are involuntary jerks and twisting movements in the face and on the extremities.
- ***Fluctuations in treatment response (fluctuation):*** Fluctuations in clinical response become more frequent as treatment progresses. It is sometimes related to fluctuations in serum concentrations, and the effect is then reduced towards the end of the dosing interval (*wear-off reaction*). Often, however, there is no time connection with the administration of doses, we speak of the "on-off phenomenon". Off periods with significant akinesia alternate here with on periods when momentum is significantly better. The transition between the on-off phases can be sudden, so that the patient stops walking and can't take his foot off the ground, or can't get up from a chair he sat in without difficulty.

Dopamine agonists

- Semi-synthetic derivatives of ergot alkaloids.

Bromocriptine

Bromocriptine is a potent agonist of dopamine "D2 receptors". It has similar effects to levodopa, also similar side effects, with the fact that dyskinesias and the on-off phenomenon are less frequent. It has a longer effect than levodopa, but is more expensive. It can be combined with other antiparkinson drugs. Its main importance lies in the combination with levodopa.

MAO-B inhibitors

Selegiline (Template:L-deprenyl)

"MAO-B" is involved in the metabolism of dopamine and tyramine. It is abundantly represented in the basal ganglia. Selegiline, an irreversible MAO-B inhibitor, therefore increases and prolongs the antiparkinsonian effects of levodopa.

Central anticholinergic

They can improve ``tremor *and* ``*rigidity* but have little effect on bradykinesia. They alleviate extrapyramidal symptoms caused by neuroleptics.

Side effects

- ***Central:*** drowsiness, bradypsychia, confusion, even delusions and hallucinations.
- ***Peripheral:*** dry mouth, blurred vision, mydriasis, urinary retention, constipation, tachycardia, arrhythmia, increased intraocular pressure.

Medicines are used that penetrate well into the CNS and, compared to atropine, have smaller parasymolytic effects in the periphery:

- **Biperiden, orphenadrine; benzatropin**; **procyclidine**'; **diethazine**.

Links

Related Articles

- Parkinson's disease/PGS
- Parkinson's syndrome
- Extrapyramidal syndromes
- Dopamine

References

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