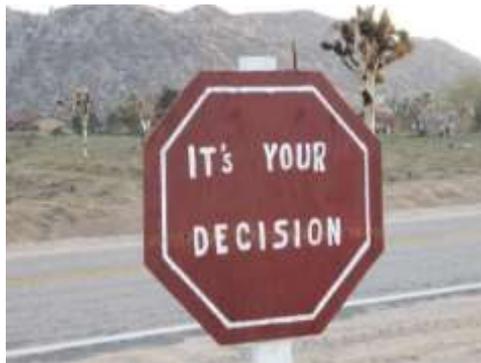


Perceiving Parkinson's

Dopaminergic Oral Medications (Day 42)

In Parkinson's, neuron loss in the substantia nigra results in low levels of dopamine which in turn produces the motor symptoms of tremor, bradykinesia, rigidity, and postural instability. To improve these motor symptoms, neurologists mostly rely on **dopaminergic oral medications** that prolong, mimic, or replace the body's dopamine.

The first decision a person with Parkinson's ought to make is whether they want to start a medication at all. If the motor symptoms are trivial and of little concern, the wisest course of action **may be to wait**. However, if the motor symptoms are bothersome, then there are several options, and the best option usually depends on **the severity of the motor symptoms**. It's your decision; think of the neurologist as an "advisor."



Should you start a medication, and if so, which one? It's your decision.

For **mild** Parkinson's, the following medications can be tried:

(1) **Benzotropine** and **Trihexphenidyl** - The **anticholinergics** were the backbone of treatment in Parkinson's before levodopa was introduced several decades ago. To be honest, anticholinergics are rarely used anymore - they modestly benefit tremor and rigidity, but also have several side-effects including dry mouth, slowed urination, constipation, and memory impairment. If the aim is purely to manage motor symptoms, anticholinergics are **not worth the effort**.

(2) **Propranolol** - This medication belongs to a class called **beta blockers**; propranolol is the one that has been studied the most. Beta blockers may improve the tremor of Parkinson's, although the evidence is not strong. Plus, they can produce fatigue and worsen postural hypotension (when a person's blood pressure falls upon standing). Still, it's fair to say that beta blockers **may be useful for mild, tremor-dominant Parkinson's**.

(3) **Selegiline** and **Rasagiline** - The **monoamine oxidase type B (MAOB) inhibitors** block an enzyme that degrades brain dopamine, allowing brain dopamine levels to stay higher for longer. Randomized controlled trials show that MAOB inhibitors confer a **small but sure improvement** in the motor symptoms of Parkinson's. Usually, one dose per day will suffice. MAOB inhibitors have **minimal side effects** - dizziness, headache, and insomnia rarely occur, and the theoretical risk of a condition called the serotonin syndrome is not supported by the evidence. Arguably, MAOB inhibitors are **the best medications for mild Parkinson's**.

For **moderate** Parkinson's, the following medications can also be tried:

(1) **Ropinirole** and **Pramipexole** - The **dopamine agonists** are basically synthetic dopamine. Dopamine agonists **moderately improve** motor symptoms in Parkinson's, yet they often have **marked side-effects** including nausea, postural hypotension, sleepiness (even "sleep attacks" which can result in car accidents), swelling in the legs or feet, impulse control disorders (obsessive behaviours, such as compulsive gambling), visual hallucinations (seeing things that are not there), and paranoia. That's not to say dopamine agonists aren't useful, but many people suffer from one or more of these side-effects without knowing that it's the fault of the dopamine agonist. Generally, dopamine agonists **are useful in moderate Parkinson's**, but should be used with caution.

(2) **Sinemet** and **Madopar** - These medications contain the amino acid **levodopa**, the precursor to dopamine; sinemet is levodopa plus **carbidopa** whereas madopar is levodopa plus **benserazide**; the carbidopa and benserazide are there to reduce levodopa-associated vomiting. Levodopa **markedly improves** motor symptoms in Parkinson's - it's the best! It has **moderate side-effects** - in the early years these are mainly limited to nausea and postural hypotension, but as the years go by motor fluctuations and dyskinesias may occur. **Motor fluctuations** are alternations between "**on**" periods (when a person has a good response to medication) and "**off**" periods (when the medication benefits have worn off and motor symptoms re-emerge). **Dyskinesias** are involuntary, random writhing movements that may occur if dopamine levels are too high. Crucially, the beneficial effects of levodopa can be **negated if it is taken with any protein** - to avoid this problem take levodopa on an empty stomach, **one hour before or after a meal**, with nothing more than a glass of water. So, while levodopa is **the gold standard medication in Parkinson's**, it must be dosed and timed correctly.



Protein can negate levodopa - take levodopa one hour before or after any meal, with just water.

For **severe** Parkinson's, the following medications can also be tried:

(1) **Entacapone** and **Tolcapone** - The **catechol-O-methyltransferase (COMT) inhibitors** block an enzyme that breaks down blood levodopa, allowing blood levodopa levels to stay higher for longer. These medications must be taken with levodopa. They prolong a person's response to levodopa by **30-60 minutes**; this is not a huge effect, but for people who only get two hours of "on" time from each levodopa dose, it makes a difference. The main COMT inhibitor **side-effects** are that they can worsen dyskinesias, and tolcapone can sometimes produce life-threatening liver toxicity; anyone taking tolcapone must be very careful to have regular liver monitoring. COMT inhibitors are **good for people who experience lots of motor fluctuations throughout the day**.

(2) **Amantadine** - This medication is a **glutamate antagonist** and it is good at lessening dyskinesias; it can also be used in mild Parkinson's, although it is rarely used for that now. Amantadine has several **side-effects** including livedo reticularis (a lace-like discolouration of the skin) and, less commonly, agitation, insomnia, and skin rashes. Amantadine has a unique role in Parkinson's - for some people, it may be **the only way to reduce dyskinesias without reducing levodopa**.

It ought to be clear by now that there are many medications that may be helpful in a person with Parkinson's. Levodopa is the gold standard, but there are **lots of options** and it may not be necessary to go straight to the "big gun" medication. If you have never heard of one of these medications and it intrigues you, ask your neurologist about it. Remember, it's **your decision**; the role of a neurologist is not to issue decrees, but **to advise**.

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References

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(2) Connolly and Lang. 2014. Pharmacological Treatment of Parkinson Disease: A Review. Journal of the American Medical Association 311(16), 1670-1683.