PD 101

WHAT IS THIS ALL ABOUT ANYWAY?

ISN'T IT JUST TREMORS?

James W. Allen
Ambassador
Davis Phinney Foundation

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What Is Happening Inside Us?

Many diseases have a known set of symptoms, known causes, and known progression patterns.

Parkinson's Disease (PD) presents with an inexhaustible list of possible symptoms, has no known cause, and no regular progression pattern.

What is going on inside us that is so strange?

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The Parkinson's Iceberg

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PD is a "control" problem.

All PD symptoms trace to our brains' increasing inability to control our bodies, for two main reasons.

1. Damage to the dopamine-creating cells in the substantia nigra.
2. Expansion of Lewy Bodies in our nervous system.

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The Substantia Nigra

The SN is not a separate structure, but a "smear" of black neurons along either side of the basal ganglia.

It is very small, with each side being only about 1/5 of an inch deep.

It produces most of the brain's dopamine.

In PWP, these cells are dying.

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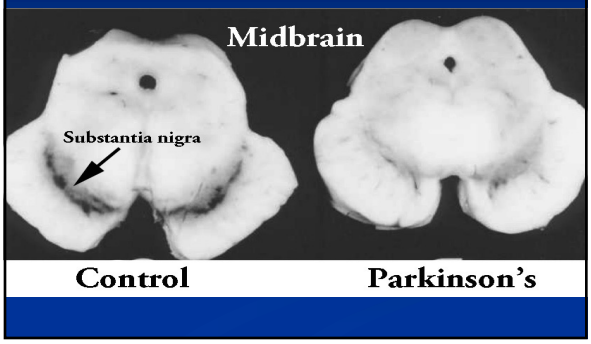
What do we mean by "dying"?



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Why does dopamine matter?

Dopamine is how the brain communicates to accomplish every single thing it does.

Dopamine is the neurotransmitter (sending agent) for messages within the brain.

Dopamine is necessary for everything the brain does, from movement to senses to digestion to body temperature to swallowing to sleeping.

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Why does dopamine matter?

In the "control" system of our brains, the loss of dopamine means the brain cannot function as it normally functions. It cannot command the body as it normally commands.

Autonomic controls are the first to be affected. Body temperature, digestion, blood pressure, heart rate, respiration, are all autonomic.

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How about Replacing Dopamine In the Brain?

Taking dopamine is useless because dopamine cannot cross the blood-brain-barrier (a set of closely packed endothelial cells that block the blood going to the brain).

But we can help our bodies make more dopamine by taking levodopa, which our bodies turn into dopamine, both inside and outside the brain.

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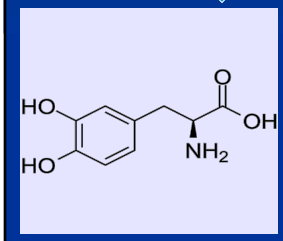
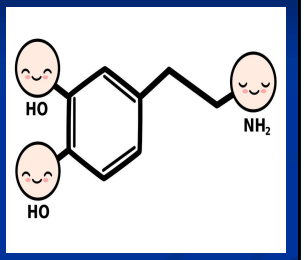
LEVODOPA TO DOPAMINE

Decarboxylase enzymes



Levodopa



Dopamine

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Why do we take Carbidopa?

Levodopa can cause severe nausea when taken orally.

Also, decarboxylase enzymes consume most of the levodopa before it gets to the brain.

Carbidopa is a decarboxylase inhibitor but does not enter the brain. So less is converted in the body, more in the brain.

Carbidopa also eases nausea.

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Lewy Bodies

The key to the Lewy Body issue is the "alpha-synuclein" protein (AS). AS are in nerve cells and are important parts of cell health.

In some people, AS become "folded" and begin to stick together, forming "oligomers" (clumps) and "fibrils"(chains).

AS also moves from cell to cell, infecting more cells.

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How Lewy Bodies Form

These oligomers and fibrils attract other cell bodies, as well as each other, eventually creating "Lewy Bodies."

Lewy Bodies, first found in PWP in the 1920's, are a major pathological sign of PD and are believed by many to be the cause of PD in non-genetic cases.

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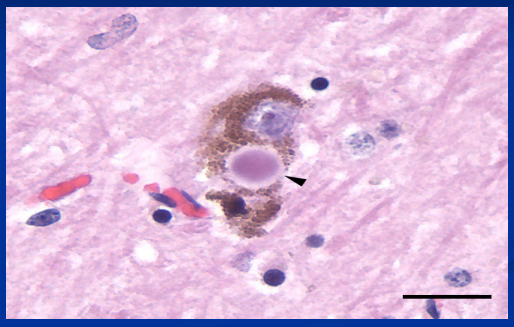
Looking at a Lewy Body



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What is the result?

As misfolded AS moves to other nerve cells, nerve cells die all over the body.

The death of these cells creates barriers in the body's ability to carry messages from the brain.

So, while our brains have trouble sending messages properly (due to SN loss and Lewy Bodies), our bodies cannot hear the messages clearly, due to Lewy Body losses in the body.

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The Parkinson's Biomarker

In 2023, a tool was developed to identify misfolded alpha-synucleins in spinal fluid.

The test is called the A-synuclein Seeding Amplification Assay (sSyn-SAA).

The hope is that they can now learn to use blood tests for the same purpose. A test has been proposed.

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Hopes for Treatment

Research is being done on

1. How to prevent creating toxic AS;
2. How to prevent misfolded AS from moving between cells ("extracellular AS") (monoclonal antibodies).
3. How to reduce the toxic oligomers from becoming fibrils.
4. How to destroy toxic AS.

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WHAT RESEARCH IS BEING DONE?

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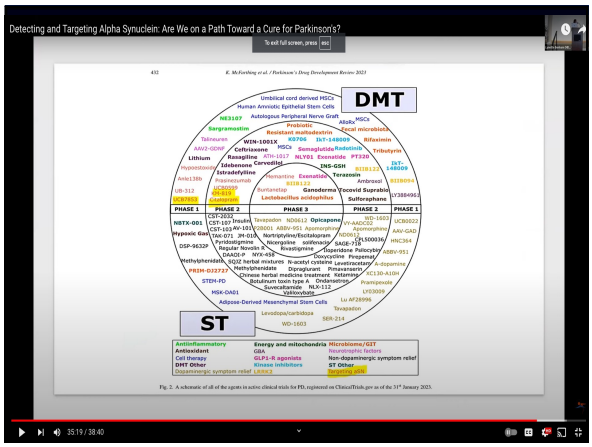

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Medical science has proven time and again that when the resources are provided, great progress in the treatment, cure, and prevention of disease can occur.

-- Michael J. Fox

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