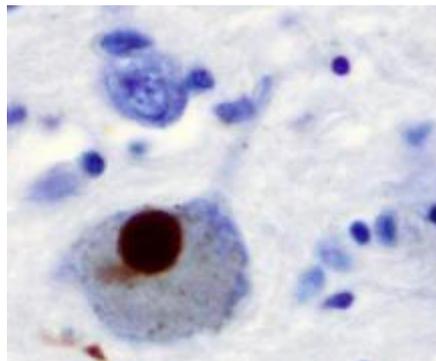


Perceiving Parkinson's

The Lewy Body Enigma (Day 10)

We have seen that Parkinson's is essentially a neuron-killing disease; somehow, it elicits the death and loss of neurons in certain areas of the brain, autonomic nervous system, and enteric nervous system. Since it is the loss of these neurons that produces the myriad clinical symptoms of Parkinson's, neuron loss is the ultimate **pathological marker** of Parkinson's. Interestingly, some researchers believe that there is one other pathological marker of Parkinson's.

In 1912, the German-born neurologist Fritz Heinrich Lewy published his findings on the discovery of what were eventually called **Lewy bodies** - microscopic, spherical collections of biological material that accumulate in certain neurons of a person with Parkinson's. Lewy Bodies contain many different substances, but their major constituent is a protein called **alpha-synuclein**. Normally, alpha-synuclein is **soluble** (it dissolves) and it is found at the tips of neurons where it is thought to help regulate dopamine release. In Parkinson's, much of the alpha-synuclein becomes **insoluble** (it no longer dissolves) and "aggregates" within certain neurons. Nobody knows the reason for this.

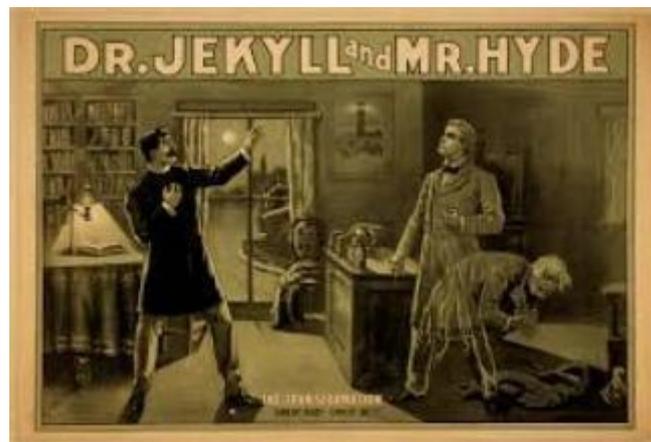


Lewy body (dark spot) inside a neuron.

Like neuron loss, Lewy body formation is a systemic phenomenon that occurs throughout the body, afflicting certain neurons in the brain, autonomic nervous system, and enteric nervous system. Yet unlike neuron loss, which is undeniably a bad thing, there is a high degree of **uncertainty** surrounding the exact role of Lewy bodies in Parkinson's, for a couple of reasons.

First, **Lewy bodies do not always correlate with Parkinson's**. The presence of Lewy bodies does not necessarily mean that the clinical symptoms of Parkinson's are present - there are **many Lewy bodies** in the brains and enteric nervous systems of 15% of elderly people **without Parkinson's**. Conversely, the absence of Lewy bodies does not necessarily mean that the clinical symptoms of Parkinson's are absent - there are **no Lewy bodies** in several regions of the brain in most people **with Parkinson's**, yet these regions still suffer a substantial amount of neuron loss.

Second, **the role of Lewy bodies is not known**. For decades, it was simply assumed that Lewy bodies were "bad guys" contributing to Parkinson's, and many *in vitro* and animal lab experiments seemed to support this assumption. Yet these experiments remain severely weakened by the truism that *in vitro* and animal experiments **do not accurately model the situation in humans**. In fact, a growing number of researchers now consider Lewy bodies to be innocent bystanders or even "good guys" that are part of a protective mechanism against neuron loss in Parkinson's. Supporting this assertion, it has been shown that neurons containing Lewy bodies surprisingly appear **healthier** and **die less frequently** than those lacking Lewy bodies. To use an analogy, the presence of a fire truck (Lewy body) at a fire (neuron loss in Parkinson's) is simply an **association**; it should not be automatically assumed that the fire truck contributes to the fire, yet this is what many researchers have done in years gone by with Lewy bodies and neuron loss in Parkinson's.



The Lewy body – Jekyll, Hyde, or neither?

Thus, it is far better to think of Parkinson's as a neuron-killing disease **marked by neuron loss**, not Lewy body formation; it is neuron loss that produces the myriad symptoms of Parkinson's, not Lewy bodies. The role of Lewy bodies in Parkinson's is not clear - they do not always correlate with Parkinson's, and we have no idea what their role is, if any. We just don't know enough about them and until we do, neuron loss is the best pathological marker of Parkinson's!

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