IN PARKINSON'S DISEASE, IS THE AGGREGATION OF A-SYNUCLEIN PROTEIN TO FORM LEWY BODIES A PROTECTIVE OR A PATHOLOGICAL RESPONSE?

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Lewy Bodies, Lewy's "concentric hyaline cytoplasmic inclusions", have been ascribed controversial roles in Parkinson's disease pathology research as to how they interfere with the disease's progression. With theories naming them from protectors to penetrators, LBs serve a role in PD pathology that still remains elusive.

Attempts to relate the burden in LBs and neurotoxicity in PD have failed to give a clear answer since LBs are not restricted to PD patients nor they are present in every PD case; on the other hand α-synuclein bearing LBs have been positively linked to hallucination and dementia symptoms of the disease. Studies linking α-synuclein with familial PD and descriptions of its presence in LBs have given α-synuclein a key role in investigating their participation in PD. Through toxic gain of function and loss of function mechanisms, α-synuclein seems to be implicated in neurotoxicity in PD throughout its aggregation to form LBs, however in a degree not enough to elicit the full pathology of the disease. More inclusive theories like the aggresome theory, suggest that LBs are the outcome of a cytoprotective response, formed in a cellular environment that promotes protein aggregation through disturbances in quality control systems responsible for the protein production-degradation balance.

Protectors or penetrators, LBs are the hallmark of PD pathology and participate in its processes in ways deserving further investigation. A conclusion on the latter could serve as a valuable tool for enhancing our understanding of the disease pathophysiology and thus promoting our use of molecular therapeutic interventions for PD.