Parkinson Disease (PD) with lysosome dysfunction and PD associated with mitochondrial dysfunction are different diseases.

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There is evidence for neuronal cell organelle failure, as causing PD. This is not new however, as early work on the understanding of this complex disorder was that of dopamine producing nigral cell dysfunction. Since its original description, evidence has accrued supporting mitochondria and/or lysosomes as contributors for apoptosis. There is evidence linking PD as a consequence of autophagy-lysosomes pathways (ALP) and ubiquitin-proteasome system (UPS) failure. Alpha-synuclein is widely distributed in brain tissue and the accumulation and clumping of such protein has been found widely distributed in PD, Lewy body disease, Alzheimer's disease and others. Hence, ALP failure results in accumulation of unwanted toxic-synuclein containing proteins, furthering inhibition of ALP function by binding tightly to the receptor on the lysosomal membrane, enhancing neuronal cell degradation. This complex and toxic intra-neuronal cell environment affects mitochondrial function with activation of the instrumental mitochondrial dependent apoptosis. Current evidence suggest many different morphological types of cell death co-existing in the PD brain, some induced by mitochondria programmed dependent cell death and other independent processes resulting in necrosis. Linking the consequences of these two organelle failure is of utmost importance for furthering the understanding of neuro-degeneration via mitochondrial oxidative stress, accumulation of oxidized dopamine species, reduced glucocerebrosidase enzymatic activity, lysosomal dysfunction and alpha-synuclein accumulation. It has been suggested dopamine abnormal oxidation links mitochondrial and lysosomal dysfunction in PD. Today we will ask ourselves if there is a unifying theory or if PD differs when due to lysosomal dysfunction versus mitochondrial dysfunction.