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Navigating life with Parkinson's: A perspective from a medical educator

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Approximately 50,000-60,000 new cases of Parkinson's disease are diagnosed each year in the United States, adding to the one million people who currently have Parkinson's. It has been estimated that 7-10 million people worldwide are living with Parkinson's. The good news is that my diagnosis explains all of the health issues I've had for the past three years. The bad news is that I've been diagnosed with Parkinson's. My symptoms are made better when I am not cold, not under undue stress, and have adequate sleep. My simple analogy about Parkinson's and dopamine is like a car with a fuel tank leak. You constantly are low on fuel (dopamine) so you are always adding fuel back (dopamine agonist), yet you never have a full tank. My life now is balancing fuel consumption (use of a dopamine agonist plus remaining dopamine) with factors that accelerate dopamine (fuel) consumption. Everyone with Parkinson's expresses his or her disease differently, it's very unique, but I remain dedicated to slowing the progression. My strategy for treating Parkinson's goes as follows: Dopamine Agonist; Isradipine; Complementary and Alternative Medicine (lots of supplements); Stretching and Exercise; Meditation; Deeptissue massage; LSVT Loud; LSVT Big; and playing Golf. For those of us with Parkinson's, we remain hopeful for new treatments, advances and one day ahead, a cure. But for now, we use courage and determination, mixed with a will to survive, and all held together by glue we call hope. Overall, I'm doing my best navigating life with Parkinson's

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The interplay between synuclein alpha, sphingolipids signaling and sirtuins in molecular mechanism of dopaminergic cells death in Parkinson Disease experimental model

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The pathological hallmarks of Parkinson's disease (PD) include specific degeneration of dopaminergic neurons in the substantia nigra pars compacta and loss of axonal projection into striatum. Moreover, PD is characterized by the formation of Lewy bodies and Lewy neurites that are composed mainly of aggregated biologically inactive alpha synuclein (ASN). However, ASN in oligomeric form exerts cytotoxic effect by activation of oxidative/nitrosative stress, alteration of Ca+ homeostasis and dopaminergic signaling. Additionally extracellular ASN oligomers may play a role in the propagation of neurodegeneration. The recent study demonstrated that also sirtuins, highly conserved deacetylases can influence the progression of neurodegenerative disorders by modulation of transcriptions factors activity and directly by deacetylating of selective proteins. Up till now the exact mechanism of dopaminergic neuronal death is not fully elucidated and the therapy of PD is not satisfied. Our last data indicated significant inhibition of sphingosine kinase 1 (SphK-1) the key enzyme responsible for sphingolipids biostat and for regulation of cells survival /death in PD experimental model induced by 1-methyl-4-phenylpyridinum (MPP+). SphKs synthesize, sphingosine-1-phosphate (S1P) which act as a secondary and primary messenger. It can be secreted from the cells and then may acts through G protein operated receptors (S1P1-S1P5). This bioactive sphingolipid is involve in regulation of transcription, cells proliferation and viability, glutamate release and in secretion of other compounds. We have found that inhibition of SKs(using specific inhibitor (SKI II) significantly enhanced ASN secretion into extracellular space. Exogenous ASN oligomer s(0.5uM) acting extracellulary decrease significantly PC12 cells viability by activation of apoptotic signaling. ASN and its mutated forms in oligomeric state significantly down regulated gene expression and activity of SphK1and 2. Inhibition of SphKs subsequently lead to activation of pro-apoptotic proteins and to cells death at similar extent as inMPP+ PD model. Concomitantly pro-survival molecular processes are activated including enhancement of AKT phosphorylation/ activity, up regulation of gene expression for sirtuins 3,4 in mitochondria and superoxide dysmuthase (SOD) and also other antioxidative proteins. Moreover, ASN evoked enhancement of gene expression for sirtuin 5, protein which could be also involved in mechanism of cells survival. Summarizing our data suggest that alteration of SphKs may play a crucial role in PD pathology. Exogenous S1P (1uM) down regulated pro-apoptotic proteins (Bax, HrK) expression ,suppressed oxidative stress. S1P and S1P1 receptor agonist protected significant pool of cell against death in PD model.

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