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Glp-1 Receptor Stimulation Preserves Neuronal Function In Rodent Models Of Stroke

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Recent studies suggest that the incidence of stroke is elevated in individuals with Type 2 diabetes mellitus (T2DM), signifying common mechanisms. Stroke is the second leading cause of death worldwide and is the primary cause of disability in the USA. The pathophysiology of cerebral ischemic injury is complex, and numerous studies have demonstrated that oxidative stress and inflammation are key in the underlying mechanisms. T2DM or pre-T2DM, it is speculated that insulin resistance increases stroke susceptibility. We have developed novel glucagon-like peptide-1 receptor (GLP-1R) agonists to test their efficacy in diabetic stroke mice. We hypothesize that not only would P5 and derivatives have a significant impact on the development and progression of diabetes, but would reduce the influence of stroke pathogenesis. Specifically, P5 and the brain-penetrant derivatives would appreciably attenuate stroke and provide long-term preservation of “outcomes”, resilience and sustainability. Using primary neuronal cultures and cell lines, the impact of P5 and derivatives we tested their protective role in cells treated with various concentrations in ischemia/reperfusion injury. The impact of P5 and derivatives will be tested in a mouse models of T2DM (Leprdb/db mice) and stroke. The db/db with stroke mice will be treated with various doses of P5 and derivatives to determine the impact on the initiation and/or progression of stroke. Our data show that P5 and derivatives have a significant impact on both in vitro and in vivo stroke models by reducing cell death and infarct volume and improves long-term behavioral outcomes. In conclusion, the present data demonstrates the benefit of GLP-1R agonists for primary stroke prevention and the reduction of fatal cerebrovascular outcomes. These studies suggest that studies are warranted to evaluate the benefit of these drugs for secondary stroke prevention.

Biography

Dr. Kindy is currently a Professor of Pharmaceutical Sciences department at the University of South Florida at Tampa. He is also a Senior Research Career Scientist in the VA. He received his Ph.D. in biochemistry at Boston University. He received a B.S. from the University of Massachusetts at Amherst. His research interest includes neuroscience and neurodegenerative diseases. He is the director of the Botanical Medicine Research and Education Consortium at USF. He is the author or coauthor of more than 230 papers in international refereed journals and more than 100 conference contributions. He has given numerous talks at international conferences.

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