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Hypometabolism as a therapeutic target in Alzheimer's disease

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Alzheimer's disease (AD) is an age-associated, neurodegenerative disease characterized clinically by a progressive decline in memory and language, and pathologically by accumulation of senile plaques and neurofibrillar tangles in the brain. Another prominent feature of AD is regional cerebral glucose hypometabolism. Hypometabolism is most prominent in the posterior cingulate, parietal, temporal, and prefrontal cortices, and occurs very early in the disease. Glucose hypometabolism is particularly problematic for the brain. The brain is one of the most metabolically active organs in the body and uses about 20% of whole body oxygen and 25% of total body glucose. The brain relies almost exclusively on glucose for energy. Hence, early glucose hypometabolism may contribute to both the cognitive decline and the pathology associated with AD. The potential for targeting hypometabolism as a therapeutic approach is a growing area of research and represents an alternative to current drug development pathways. In particular, the use of ketone bodies to address the low metabolic rates of cerebral glucose metabolism in AD represents a new area of intervention. Ketone bodies are particularly well suited as an efficient alternative fuel for neuronal cells that are unable to metabolize glucose. Compounds have been developed to elevate serum ketone levels safely, and have been shown to improve memory and cognition patients with mild-to-moderate AD. Treatment outcomes are influenced by apolipoprotein E genotype status. These data suggest that ketosis may be an effective therapy for cognitive dysfunction by providing an alternative substrate for use by glucose-compromised neurons.

Biography

Dr. Henderson completed his Ph.D at the University of Chicago and postdoctoral studies at the University of Wisconsin, Madison, WI. He is Vice President of Research and Development at Accera Inc. Accera, is a privately held biotechnology company that develops breakthroughs in treating central nervous systems disorders. Through its proprietary scientific platform, Accera is developing therapies that address metabolic deficiencies and provide an alternative energy source for brain cells.

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