What does it mean to have a ketogenic brain; protection against HIV-1 Tat-induced neurotoxicity. Review

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The ketogenic diet is today an accepted therapeutic modality. An unresolved issue is the nature of the many physiologic and biochemical responses of brain function that the diet presumably evokes. Several hypothetical mechanisms have being proposed; (a) A high-fat, low-carbohydrate diet favors production of “ketone bodies,” perhaps acidifying the brain parenchyma and inhibiting neuronal $H^+$-sensitive ion channels. (b) Ketosis may hyperpolarize neuronal membranes through an effect of ketone bodies or long-chain fatty acids on adenosine triphosphate (ATP)-sensitive $K^+$ channels (c) acetone, which quickly enters brain, diminishes seizure threshold and severity; (c) glucose, even in physiologic concentration, may increase neuronal excitability.

HIV-1-associated neurocognitive disorder (HAND) is a syndrome that ranges clinically from subtle neuropsychological impairments to profoundly disabling HIV-associated dementia. Implicated in HAND are soluble factors including HIV-1 viral products/proteins and pro-inflammatory mediators released from infected glia and monocytes. HIV-1 infection induces apoptosis via a cornucopia of mechanisms; Tat causes a rapid dissipation of the mitochondrial transmembrane potential ($\Delta \Psi_m$) as well as cytochrome c release in mitochondria isolated from mouse liver, heart, and brain. Tat inhibits cytochrome c oxidase (COX) activity, induces apoptosis of hippocampal neurons by a mechanism involving caspase activation, calcium overload, and oxidative stress, causes a decrease in Bcl-2 expression and an increase in Bax expression.

Ketogenic strategies have been used clinically for treatment of neurological disorders and now there’s evidence supporting that ketone bodies may protect against HIV-1 Tat-induced neuronal cell death.

Biography

Tintos-Hernandez JA has completed his PhD in human genetics at the age of 29 years from Universidad de Guadalajara in Mexico. Currently he is a postdoctoral student in the Center for Mitochondrial and Epigenomic Medicine (CMEM), Children’s Hospital of Philadelphia Research Institute.

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