BRAIN ENERGY METABOLISM: A COMPUTATIONAL INVESTIGATION OF THE ROLE OF ENERGY DEFICITS IN PD RISK FACTORS

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We describe a mathematical model of the brain energy metabolism (BEM) as a flexible computational and analytical framework for the in-silico study of neurodegenerative disorders. Specifically, ATP is a general 'input' requirement for all neuronal functions. Thus a model of the energy generation mechanism with ATP as its 'output' forms a framework to which we can attach computational modules of the relevant cellular functions for a particular target disease. In the case of PD we attach models of neuronal functions such as protein disposal, oxidative stress regulation and calcium homeostasis. For AD, other relevant neuronal functions would be used.

In both AD and PD the long-term deterioration of energy metabolism has been suggested, indicating the intrinsic relevance of an in-silico model of BEM to the study of age-related neurodegeneration. In particular, using a computational model of BEM, suggested physiological effects that take decades to unfold can be simulated in milliseconds in a controlled and repeatable manner. It follows therefore that a mathematical model of the BEM is of significant investigative importance as an efficient test bed for studying long-term energy-related factors. We show the results of such an in-silico study, in which the long-term weaknesses in BEM are studied as potential risk factors in PD. Then, using the modelling framework, we develop the argument that energy deficits are a common denominator linking all risk factors associated with a predisposition to PD.