ANALYSING THE CAUSES OF PARKINSON’S DISEASE: AN ENERGY SYSTEMS APPROACH

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Abstract

Neurodegenerative diseases are among the most difficult conditions to study and analyze. For example, the causes of Alzheimer’s Disease and Parkinson’s Disease are unknown; they are hard to study in-vivo, and animal model and in-vitro studies are constrained by the complexity of the conditions and their apparent uniqueness to the human animal. Given these points, we claim that an in-silico systems approach, based upon mathematical modelling and control systems analysis, offers a valuable new framework for studying the complexities of these poorly understood diseases. Taking idiopathic Parkinson’s Disease (iPD) as the example, the talk will illustrate how the concept of a systems approach, originally developed for analysis of complex technological systems, can be used to build a systematic framework for disease study. The framework provides both an objective collection point for knowledge of the disease, and an analysis tool with which we can study the bio-dynamics and interactions that are potentially involved in disease causation.

Our systems approach is based upon the mathematical modelling of the process that allows the mind to function – namely the brain energy metabolism. A properly calibrated brain energy metabolism model is used as a core tool for analysis. This core can be built upon by attaching models of cellular sub-systems thought to involved in iPD causation. The potential role of these subsystems in iPD can then be examined by analysing in-silico the possible results of their failure, or flaws in the energy metabolism that supports them. In this way, the mathematical model provides an in-silico platform for disease study that:

a. complements practical experiments,
b. provides a quantitative, objective repository of biological knowledge, and
c. forms a systems tool for the objective analysis of possible disease mechanisms.

All this is supported by a compelling biological rationale for an energy systems approach to iPD. We do not know the causes of iPD - the only factor common to all iPD victims is their advanced age, and with advanced age comes a deterioration of the energy metabolism. We therefore hypothesize that a weakened or damaged brain energy metabolism may be an enabling factor for iPD, whereby the weakened metabolic processes creates opportunities for a range of pathological mechanisms to operate; mechanisms that would normally be held in check by a healthy metabolism. Thus the energy systems approach offers not only a systematic framework for study of iPD, but also a potential explanation for the diversity of pathological mechanisms that have been proposed, and a reason for the wide variation in Parkinsonian symptoms observed in the predominantly elderly patients.