Dynamics of whole-body energetics under aninsulæmia

Project type: THEORETICAL
Supervisor: Hugo van den Berg (Systems Biology)  
hugo@maths.warwick.ac.uk +23698

BACKGROUND TO THE PROJECT  With the rise of childhood obesity, the incidence of diabetes mellitus, which already affects millions of people globally, is likely to increase dramatically in the coming decades. Many of these diabetics will die prematurely as a result of diabetes and its complications (e.g. cardiovascular disease). While it has been well established that obesity increases the risk of acquiring diabetes and cardiovascular disease, a clear account of these disease processes is hampered by the fact that compensatory as well as mutually exacerbating interactions occur between the body’s various organ systems (brain, pancreas, liver and adipose tissue). In particular, the direct and indirect effects of obesity per se remain to be clearly distinguished from other metabolic abnormalities that are often found in association with obesity, such as elevated blood glucose, defective insulin action and dyslipidaemia.

From the point of view of underlying physiology, obesity and diabetes result from disregulation of the acquisition and disposition of nutrients. Homeostasis of energy substrates in the blood is regulated by a number of endocrine factors (hormones), which variously control nutrient storage, metabolism, and utilization. By far the most important of these is insulin, which is produced by the β cells of the islets of Langerhans in the pancreas. Insulin stimulates the disposition of glucose as fuel or energy store, the uptake of non-essential amino acids in muscle, as well as the storage of fatty acids in adipose tissue. Other effects of insulin include: anabolic stimulation; suppression of glucose formation in the liver; stimulation of synthesis of triglycerides in the liver, and control of food intake.

The advantage of a mathematical model is that various aspects of disregulation can be studied “in isolation” by disrupting various components separately, and comparing the outcomes of these various perturbations. In the present project, a dynamical model of mammalian body composition and energetics is used to gain more insight in the effects of aninsulæmia (total lack of insulin).

AIMS  The primary objective is to simulate whole-body energetics under total lack of insulin as a profound perturbation of nutrient uptake & disposal, in a dynamical model of mammalian body composition and energetics, to compare these dynamics to the normal (control) situation and to explore the connections with unbalanced diet and obesity. A secondary objective is to investigate how whole-body dynamics relate to the (faster) time scale of nutrient assimilation over the daily activity cycle and its attendant endocrinological regulation.

RESEARCH METHODS  Analysis of non-linear dynamics; numerical solution of initial value problems; review of literature.

REFERENCES  

TIMING OF PROJECT  Both periods are negotiable.

IMPORTANT NOTE  While this project can be pursued in its own right, it is a companion to an experimental project offered by Professor M. Kahn and Dr. S. Pelengaris.