Abstract only

Role of amylin in the regulation of energy metabolism in health and disease

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Islet β-cells play a central role in the regulation of most cells in the body through secretion of the hormone insulin. These cells are now known to secrete a second hormone-like protein, amylin, which is the major protein present in the islet amyloid which accumulates in almost all patients with non-insulin-dependent diabetes mellitus.

Amylin stimulates the breakdown of glycogen and opposes the actions of insulin in skeletal muscle and liver through alterations it evokes in the activity of key regulatory enzymes such as glycogen phosphorylase and glycogen synthase. It acts as a noncompetitive antagonist of insulin in skeletal muscle, and is able to induce a state of insulin resistance and suppressed insulin secretion when administered to living animals. It has also been shown to potently increase blood concentrations of glucose and lactate, probably through stimulation of the indirect Cori cycle. These actions of amylin are consistent with a view that it is a physiological regulator of carbohydrate metabolism, acting in concert with insulin to promote the redistribution of carbohydrate from muscle glycogen to long term stores in adipose tissue.

It has been postulated that amylin is a newly-recognised endocrine hormone which regulates fuel metabolism in association with other metabolic, endocrine and neural influences. Moreover, excessive pancreatic production leading to elevated blood concentrations of amylin has now been shown to occur in numerous animal models, as well as in humans with impaired glucose tolerance and obesity. This defect has been advanced as a mechanism underlying the insulin resistance which accompanies, and may well cause these conditions.

This presentation will review currently available evidence concerning the role of amylin in the physiological and pathological regulation of fuel metabolism. In it, the author submits that relative hyperfunction of pancreatic islet β-cells, giving rise to hyperamylinaemia as well as hyperinsulinaemia, is a key mechanism underlying the metabolic changes which characterise and define the "thrifty" genotype.

Reference

1. Cooper GJS. Amylin compared with calcitonin gene-related peptide: structure, biology, and relevance to metabolic disease. Endocrine Reviews 1994; 15: 163-201

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