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Editorial

Appetite Control with Relevance to Mitochondrial Biogenesis and Activation of Post-Prandial Lipid Metabolism in Obesity Linked Diabetes

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Editorial

In various communities in the developing and developed world the understanding of the ingestion of a healthy diet [1] and hepatic fat metabolism has become of critical importance to the treatment of obesity linked Type 2 diabetes that is now linked to various organ diseases [2]. In the developing world transition to healthy diets has become urgent to prevent insulin resistance [3,4] and the obesity pandemic [5-8]. The liver is the major organ for the metabolism of dietary fat and after consumption of a meal in healthy individuals the fat is rapidly metabolized by the liver. In obesity linked Type 2 diabetes the post-prandial metabolism of a fat meal by the liver is defective with fat transport to the adipocyte relevant to adipocyte and brain appetite centre dysfunction [9-11] (Figure 1). In obese and diabetic mice post-prandial lipid metabolism has been shown to be defective with defects in the appetite centre associated with hyperglycemia and hyperphagia. Activation of hepatic fat metabolism with restricted food intake in these rodent studies may be relevant to adipocyte lipid metabolism and adipocyte signals that relate to appetite control [12] are vital to the treatment of obesity linked diabetes [13].

Interests in appetite control with food restriction of ingested fat in chronic diseases has accelerated to reduce plasma chylomicrons and lipoproteins that contain bacterial Lipopolysaccharides (LPS), lipophilic xenobiotics and lipophilic drugs that may be toxic to mitochondrial biogenesis with delayed post-prandial metabolism related to liver and adipose mitochondrial apoptosis. Interest in lipid science and technology has accelerated to reverse mitochondrial apoptosis [14] that is now a major defect in obesity linked diabetes and autonomous organ disease [11]. Appetite control involves nitric oxide consumption [15] and foods that contain excessive nitric oxide should be avoided and food restricted to maintain mitochondrial apoptosis versus mitochondrial biogenesis [16-18].

The treatment of obesity linked diabetes by appetite control now identifies the appetite gene Sirtuin 1 (Sirt 1) as the gene involved in nitric oxide metabolism, defective lipid metabolism in various tissues such as the adipocyte, liver and brain [19] with relevance to improved post-prandial lipid metabolism and relevant to reversal of obesity and Type 3 diabetes [20]. Sirt 1 regulation is critical for insulin therapy and mitochondrial biogenesis with appetite control essential to improve post-prandial metabolism. Nutritional regulation of Sirt 1 in many tissues is linked to mitochondrial biogenesis and inhibitors such as palmitic acid/LPS of nuclear receptor Sirt 1 is associated with appetite dysregulation by interference with neuropeptides (neuropeptide Y, brain derived neurotrophic factor) and endocrine hormones such as thyroid hormone that are linked to mitochondrial biogenesis [21,22].

Appetite control in rodents and man can be measured with relevance to Sirt 1 regulation of Fibroblast Growth Factor 21 (FGF21) that has effects on the central nervous system and injected FGF21 therapy has become important to the treatment of metabolic stress in obesity and diabetes [23-25]. In the aging process the delayed post-prandial lipid metabolism is connected with inactivation of the AMP-Activated Protein Kinase (AMPK)-Sirt 1 pathway that is responsible for mitochondrial biogenesis and nitric oxide homeostasis [26-28] with FGF21 essential for this integrated signaling network [29]. FGF21 therapy has important implications to the treatment of obesity linked diabetes with activation of the adipose tissue cross-talk associated with accelerated hepatic lipid metabolism.

Assessment of gene-environment interactions that regulate mitochondrial biogenesis have become of major research interest to the survival of the species with a single gene such as Sirt 1 defective and involved with nutrigenomic diet treatment in global populations

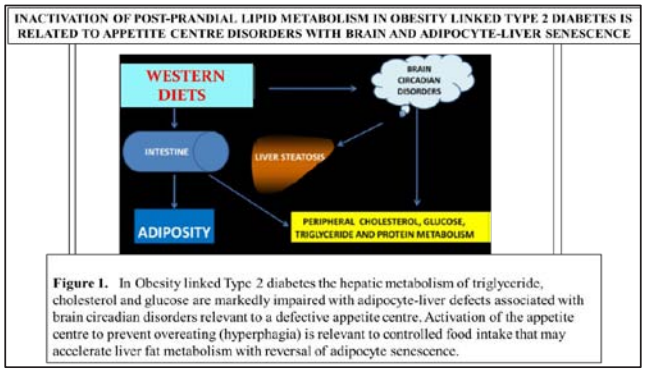

Figure 1. In Obesity linked Type 2 diabetes the hepatic metabolism of triglyceride, cholesterol and glucose are markedly impaired with adipocyte-liver defects associated with brain circadian disorders relevant to a defective appetite centre. Activation of the appetite centre to prevent overeating (hyperphagia) is relevant to controlled food intake that may accelerate liver fat metabolism with reversal of adipocyte senescence.

Figure 1:

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[30]. In the developing world the obesity and diabetes epidemic may indicate that specific activators (magnesium, zinc) of Sirt 1 may be decreased in the plasma of these insulin resistant individuals. Magnesium is an important activator of Sirt 1 with connections to both appetite control and mitochondrial biogenesis [31]. Magnesium therapy is important to maintenance of glucose control and duration and amount of food intake may be relevant to magnesium binding to cell membranes to maintain magnesium/Sirt 1 cellular functions.

In the developing world the gene-environment interactions may have changed with relevance to the global aluminium industry. Aluminium has specific cell membrane lipid binding sites [15] with interactions with phosphatidylinositol and 1-palmitoyl-2-oleolyl-phosphatidylcholine and food levels of aluminium indicate that consumption of aluminium may have reached between 3-12 mg/day [15]. The relevance to magnesium therapy indicate possible competition between aluminium and magnesium for lipid membrane binding sites [15] with increased magnesium consumption required to prevent membrane lipid peroxidation by aluminium [32]. Zinc deficiency in obesity has been reported in global populations with relevance to appetite and mitochondrial biogenesis but excessive zinc replacement should be monitored carefully with relevance to interference with magnesium absorption [33-36]. Foods that are contaminated with LPS should be restricted for consumption with relevance to LPS effects on zinc and magnesium deficiency [1,30,37,38].

In obesity linked diabetes the use of magnesium therapy in mi-RNA stability may be essential for Sirt 1 regulation of hepatic lipid metabolism to prevent liver steatosis and NAFLD [31]. Zinc deficiency is associated with increased expression of mi-RNA 34a in cells [39,40] with mi-RNA 34a involved as a transactivation inhibitor of p53 [41] linked to p53/Sirt 1 [30] expression. Regulation of magnesium and zinc levels has become important in global populations to reduce miR-34a levels and maintain mitochondrial biogenesis and prevent the development of liver steatosis and NAFLD [42]. In the developing world the rising plasma LPS levels associated with antibiotic resistance [43] induce a direct p53 associated mitochondrial dysfunction that interfere with hepatic lipid metabolism and induce NAFLD [30,37,44,45]. Mi-RNA 34a is released by many cells and tissues with elevated mi-RNA 34a associated with cardiac disease [46,47] and blood brain barrier disruption [48] with zinc deficiency and magnesium deficiency involved in brain appetite centre dysregulation.

Conclusion

The development of hyperphagia is associated with accelerated corruption of the adipose tissue-liver crosstalk with delayed post-prandial lipid metabolism associated with mitochondrial apoptosis and liver disease. In the developing world the rising LPS levels delay post-prandial lipid metabolism in individuals with obesity-linked diabetes and food restriction is required to reduce nitric oxide consumption to maintain mitochondrial biogenesis. Healthy diets lower the defective transcriptional activation of nuclear receptors by miR-34a/Sirt 1 interactions and allow effective FGF21 therapy via AMPK-Sirt 1 signaling with relevance to nitric oxide and appetite control that involve neuropeptide and endocrine hormone interactions. In the developed world the nature of the food system (magnesium/zinc/aluminium) and its distribution [49] may be relevant to mitochondrial apoptosis with delayed post-prandial lipid metabolism involved in the induction of global obesity-linked diabetes. Consumption of appropriate magnesium and zinc levels are needed to regulate the appetite centre, prevent hyperphagia and activate the adipose tissue-liver interactions to accelerate the hepatic metabolism of fats.

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