

MR Spectroscopy in Obesity and its Complications: Diabetes and Insulin Resistance

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Type 2 diabetes is the most common metabolic disease in the world. In the United States it is the leading cause of blindness, end-stage renal disease and non traumatic loss of limb with associated health care costs estimated to exceed \$130 billion per year. Of even greater concern, type 2 diabetes is rapidly becoming a global pandemic and is projected to afflict more than 300 million individuals worldwide by the year 2025, with most of the increase occurring in India and Asia. While the primary cause of this disease is unknown, insulin resistance plays a major role in its development. Evidence for this comes from cross-sectional studies demonstrating the presence of insulin resistance in virtually all patients with type 2 diabetes as well as prospective studies demonstrating the presence of insulin resistance one to two decades prior to the onset of the disease. In addition insulin resistance in the offspring of parents with type 2 diabetes has been shown to be the best predictor for the later development of the disease. Despite much work little is known about the factors responsible for insulin resistance in these individuals. In this regard recent studies measuring muscle triglyceride content by biopsy or intramyocellular lipid content by ¹H magnetic resonance spectroscopy have shown a strong relationship between intramuscular lipid content and insulin resistance in skeletal muscle. Recent studies have also demonstrated increases in intramyocellular lipid content in insulin resistant offspring of parents with type 2 diabetes suggesting that dysregulation of fatty acid metabolism may be responsible for mediating the insulin resistance in these individuals. Increases in the intramyocellular concentration of fatty acid metabolites in turn have been postulated to activate a serine kinase cascade leading to decreased insulin stimulated insulin receptor substrate-1 associated phosphatidylinositol 3-kinase activity resulting in reduced glucose transport activity and glycogen synthesis. This presentation will focus on recent studies using noninvasive ¹³C, ³¹P and ¹H magnetic resonance spectroscopy techniques in humans to examine the mechanism of fatty acid induced hepatic and muscle insulin resistance and more recent studies that have implicated functional defects in mitochondrial activity in the pathogenesis of insulin resistance.

References

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