

# Insulin and IGF-1 as Critical Metabolic Regulators

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The role of insulin and IGF 1 in physiological processes has significant implications for diseases seen in humans such as diabetes, alzheimers and cancer. Low IGF-I levels are found in subjects with insulin resistance syndrome and risk for cardiovascular disease. Resistance to insulin and IGF-I in brain accounts for neuronal atrophy and death typical of alzheimer's pathology. Raised IGF-1 levels are associated with risk for prostate, breast and colorectal cancers [1-3].

Insulin and IGF-1 mediates its actions through binding to specific receptors. Insulin can bind to the receptor for IGF-I but with much lower affinity and IGF-I binds weakly to the insulin receptor. IGF-1 is significantly regulated by growth hormone, while insulin regulates IGF-I production from the liver modulating the GH receptor. Most IGF-1 is secreted by the liver and act as an endocrine hormone. IGF-1 take part in cell substrate metabolism besides an important role in regulating cell proliferation and apoptosis.

Insulin regulates cellular energy supply and macronutrient balance and direct anabolic processes of the fed state. Insulin is essential for the intracellular transport of glucose into insulin dependent tissues such as skeletal muscle, adipose tissue and liver. Insulin and IGF-1 promotes protein synthesis in skeletal muscle and several other tissues. On the other hand insulin seems to have an indirect effect on the metabolism in vascular smooth muscle as there are only receptors for IGF 1 in that kind of tissues [4].

Insulin levels are low in the basal state, as during fasting, facilitating mobilization of fatty acids and glycerol from adipose tissue and amino acids from muscle. While insulin levels are typically higher in the fed state, the degree of insulin sensitivity may be influenced by the composition of the diet. Chronic excess energy consumption promotes hyperinsulinaemia and insulin resistance through stimulation of insulin secretion, triglyceride synthesis and fat accumulation with down-regulation of insulin receptors. The effects of fasting on metabolism in vascular smooth muscle seem to be similar to the effects of diabetes on vascular metabolism during the initial phases. High fat diets tend to be associated with insulin resistance, particularly with respect to saturated fat and trans-fatty acids. Fatty acid composition is thought to play a role in the long term development of insulin resistance, via effects on the composition of membrane lipids. Long chain polyunsaturated fatty acids play a physiological role in maintaining cell membrane fluidity and cell signaling; they also influence gene expression and are endogenous ligands for peroxisome proliferator receptors.

High carbohydrate diets are generally associated with improved insulin sensitivity in the short term.

Insulin secretion depends on the type and physical form of the carbohydrates consumed. The GI is lower where digestion, absorption and/or conversion to glucose occur more slowly. The rate of insulin secretion tends to be lower when low GI foods are consumed. Not all carbohydrates are equivalent in their insulin response. For example, fructose tends not to elicit as marked an insulin response as glucose. Chronic overfeeding with sucrose has been reported to increase visceral adipose tissue deposition, which may have long-term implications for insulin resistance.

A lot of evidence supports the role of exercise in improving insulin sensitivity and its beneficial outcomes in insulin resistant states. An important hypothesis is that insulin resistance in skeletal muscle, due to decreased muscle glycogen synthesis, promotes atherogenic dyslipidemia by diverting energy derived from ingested carbohydrate away from muscle glycogen synthesis into increased hepatic lipogenesis.

Epidemiological studies have reported substantial decreases in the relative risk of type 2 diabetes with lifelong regular physical activity. Large controlled clinical trials demonstrate a significant reduction in progression of impaired glucose tolerance to type II diabetes by intensive lifestyle modification which included a minimum of 20–30 minutes of exercise per day.

Insulin resistance is typically seen in the catabolic stress of severe illness with implications for morbidity and mortality. Mechanisms include activation of the hypothalamo-pituitary adrenal (HPA) axis resulting in marked elevation of counter-regulatory hormones, as well as the effects of inflammatory cytokines. The latter impair insulin receptor signalling in skeletal muscle, liver and adipose tissue.

Acute sleep deprivation in healthy young adults has been reported to raise fasting blood glucose concentrations in association with altered diurnal cortisol secretion and reduced heart rate variability. These effects suggest increased counter-regulatory hormone secretion via hyper-arousal with activation of the hypothalamo-pituitary adrenal axis. There is also accumulating evidence that chronic sleep deprivation may impact on insulin and insulin resistance. Epidemiological studies report that reduced sleep duration is associated with increased BMI.

Increased adipose tissue was first associated with diabetes and vascular disease. Insulin resistance increases with increasing body mass index, waist circumference and in particular waist-hip ratio. These reflect increased adiposity especially increased levels of visceral adipose tissue. Visceral adipose tissue refers to intra-abdominal fat around the intestines and correlates with liver fat. Visceral adipose tissue has metabolic characteristics which differ from that of subcutaneous fat. It is more metabolically active with regard to free fatty acid turnover; the increased flux of free fatty acids promotes insulin resistance at a cellular level and increases hepatic VLDL production.

In conclusion, insulin and IGF-1 builds effects in common and that this common effect provides insights into diverse physiological events and the occurrence of major diseases.

## References

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