Norepinephrine
– Sympathetic nervous system

Norepinephrine

Sympathetic nervous system

Insulin

Insulin receptor

Hepatic glucose production

LIVER

Glycerol and NEFAs

White adipose tissue

LIPID

HSL

Lipolysis

5' AMP

PDE3B

IRS

cAMP

PKA

ATP

AC

Hepatic glucose production

LIVER

Glycerol and NEFAs

White adipose tissue

LIPID

HSL

Lipolysis

5' AMP

PDE3B

IRS

cAMP

PKA

ATP

AC
Proposed model of the role of brain insulin in regulating adipose tissue metabolism. Recent studies from our lab unveiled a novel role of brain insulin in regulating lipolysis (the process through which fat gets mobilized from adipose tissue) by dampening sympathetic outflow and thereby reducing cAMP signaling in adipose cells. cAMP signaling is a major pro-lipolytic stimulus that results in the release of fatty acids. Fatty acids have multiple functions in our bodies: they are gluconeogenic substrates that are used by the liver to produce more glucose. Increased hepatic glucose production is commonly seen in diabetics and patients with insulin resistance. Fatty acids are also important pro-inflammatory mediators that induce lipotoxicity that then worsen insulin resistance. Thus, unrestrained lipolysis contributes to increased hepatic glucose production and chronic low grade inflammation, both derangements that are commonly seen in diabetics. We have also demonstrated that increased caloric intake impairs the ability of brain insulin to control lipolysis in fat. We speculate that defective hypothalamic insulin action plays an important role in the pathogenesis of diabetes and the metabolic syndrome.