Pulsatile GH secreting profiles in positive energy balance in mice

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Growth hormone (GH) modulates lipogenesis and lipolysis throughout periods of positive and negative energy balances. It is thought that impaired GH secretion in response to dietary induced weight gain contributes to sensitised insulin responsiveness and stimulated lipogenesis, subsequently maintaining normal plasma non-esterified free fatty acid (NEFA) levels. To assess this notion, we investigated the relationship between pulsatile GH secretion and body weight, fat mass, circulating levels of insulin, and non-esterified free fatty acids (NEFAs) in male mice in response to dietary induced weight gain. Data were collected from wild type (WT) mice following 8 weeks of dietary intervention, and throughout progressive weight gain in hyperphagic melanocortin 4 receptor knock out (MC4R KO) mice. Observations demonstrate an inverse association between pulsatile GH secretion and circulating levels of insulin. This relationship occurred alongside an increase in body weight and adiposity, and the maintenance of circulating levels of NEFAs. We confirm a healthy GH pulsatile pattern in MC4R KO mice prior to the development of hyper-phagia-associated hyper-insulineamia or in paired feeding MC4R KO and WT mice. GH secretion in MC4R KO mice decline rapidly alongside an significant increase in feeding, body weight and length, and an elevation in circulating measures of insulin. Collectively, data confirm an inverse relationship between circulating levels of GH and insulin, and the corresponding maintenance of circulating levels of NEFAs. Moreover, observations from MC4R KO mice highlight the potential role for insulin in sustaining low levels of GH following progressive weight gain, and in obesity. We propose that suppressed GH secretion in obesity does not occur in response to endocrine dysfunction, rather the suppression of GH throughout progressive weight gain is a physiological adaptation to maintain normal NEFA levels under unhealthy positive energy balance. We are now addressing the mechanisms that may account for this interaction between GH and insulin.

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