



Contents lists available at ScienceDirect

Hormones and Behavior

journal homepage: [www.elsevier.com/locate/yhbeh](http://www.elsevier.com/locate/yhbeh)

Review

## Metabolic control of puberty: Roles of leptin and kisspeptins

Miguel A. Sanchez-Garrido, Manuel Tena-Sempere\*

Department of Cell Biology, Physiology and Immunology, University of Córdoba, CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Spain  
Instituto Maimónides de Investigaciones Biomédicas (IMIBIC)/Hospital Universitario Reina Sofía, 14004 Córdoba, Spain

Reproduction is an energy-demanding function. Accordingly, puberty is metabolically gated, as a means to prevent fertility in conditions of energy insufficiency. In addition, obesity has been shown to impact the timing of puberty and may be among the causes for the earlier trends of pubertal age reported in various countries. The metabolic control of puberty in such a spectrum of situations, ranging from energy deficit to extreme overweight, is the result of the concerted action of different peripheral hormones and central transmitters that sense the metabolic state of the organism and transmit this information to the various elements of the reproductive axis, mainly the GnRH neurons. Among the peripheral signals involved, the adipose hormone, leptin, is known to play an essential role in the regulation of puberty, especially in females. Yet, although it is clear that the effects of leptin on puberty onset are predominantly permissive and mainly conducted at central (hypothalamic) levels, the primary sites and mechanisms of action of leptin within the reproductive brain remain unsolved. In this context, neurons expressing kisspeptins, the products of the *Kiss1* gene that have emerged recently as essential upstream regulators of GnRH neurons, operate as key sensors of the metabolic state and funnel of the reproductive effects of leptin. Yet, much debate has arisen recently on whether the putative actions of leptin on the *Kiss1* system are actually indirect and/or may primarily target *Kiss1*-independent pathways, such as those originating from the ventral premmamillary nucleus. Moreover, evidence has been presented for extra-hypothalamic or peripheral actions of leptin, including direct gonadal effects, which may contribute to the metabolic control of reproduction in extreme body weight conditions. In this work, we will critically review the experimental evidence supporting a role of leptin, kisspeptin and putatively related pathways in the concerted control of puberty by energy balance and metabolism.