Central Ceramide Signaling Mediates Obesity-Induced Precocious Puberty

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Abstract

Childhood obesity, especially in girls, is frequently bound to earlier puberty, which is linked to higher disease burden later in life. The mechanisms underlying this association remain elusive. Here we show that brain ceramides participate in the control of female puberty and contribute to its alteration in early-onset obesity in rats. Postnatal overweight caused earlier puberty and increased hypothalamic ceramide content, while pharmacological activation of ceramide synthesis mimicked the pubertal advancement caused by obesity, specifically in females. Conversely, central blockade of de novo ceramide synthesis delayed puberty and prevented the effects of the puberty-activating signal, kisspeptin. This phenomenon seemingly involves a circuit encompassing the paraventricular nucleus (PVN) and ovarian sympathetic innervation. Early-onset obesity enhanced PVN expression of SPTLC1, a key enzyme for ceramide synthesis, and advanced the maturation of the ovarian noradrenergic system. In turn, obesity-induced pubertal precocity was reversed by virogenetic suppression of SPTLC1 in the PVN. Our data unveil a pathway, linking kisspeptin, PVN ceramides, and sympathetic ovarian innervation, as key for obesity-induced pubertal precocity.

Palabras clave

KeyWords Plus:HIGH-FAT DIET; HYPOTHALAMIC PARAVENTRICULAR NUCLEUS; POLYCYSTIC-OVARY-SYNDROME; NERVE GROWTH-FACTOR; METABOLIC-CONTROL; CHILDHOOD OBESITY; ESTROUS-CYCLE; HORMONE SECRETION; REPRODUCTIVE AXIS; ARCUATE NUCLEUS

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