CHRONIC LEPTIN INFUSION ADVANCES BUT IMMUNONEUTRALIZATION OF LEPTIN POSTPONES PUBERTY ONSET IN FEMALE RATS

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Postponement of sexual maturation can be due to suboptimal metabolic conditions. As leptin is involved in the regulation of food intake, body weight and reproduction, it is considered as a good candidate to link the nutritional status to the gonadotropic axis and to trigger puberty.
To find out if leptin is the signal triggering the onset of puberty in female rats, we performed a series of studies in which we monitored puberty onset by scoring the moment of vaginal opening (VO). We first compared normal prepubertal rats fed ad libitum with pair-fed food-restricted animals (30% less energy). In the food-restricted group median VO age was higher (35 *vs.* 27 d), but leptin levels at VO were significantly lower than in controls (1.44 ± 0.17 *vs.* 2.79 ± 0.31 ng/ml). In this model of delayed sexual maturation, we centrally (icv) and peripherally (sc) infused leptin (1 µg/day) chronically and continuously for 14 d by means of an osmotic minipump (0.5 µl/h). We observed an advancement of median VO age compared to controls (26 vs. 27 d) but only if leptin was applied centrally. In contrast, both centrally and peripherally infused leptin advanced VO age compared to controls in the food-restricted group (30 *vs*. 35 and 31 *vs.*41 d, respectively). Next, we centrally (icv) administered rat anti-leptin (0.6 µg/day) to prepubertal female rats. Puberty onset was clearly postponed in ad libitum and pair-fed anti-leptin-infused animals compared to control, IgG-infused rats (33 and 31 *vs*. 28 d).
Our data show that the negative effects of food restriction on puberty onset are counteracted or even normalized by the infusion of leptin. In normally fed animals centrally but not peripherally infused leptin advances, whereas immunoneutralization of central leptin postpones puberty onset. We conclude that central leptin might be crucial for initiating puberty in female rats.

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