

P3.10.

Calorie-restriction reverses leptin resistance in middle-aged rats.

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Adipose tissue-derived leptin, a dominant catabolic mediator acts mainly in the arcuate nucleus. It stimulates the expression of catabolic peptides and inhibits that of anabolic ones. Aging is associated with leptin-resistance, which may contribute to age-related obesity. On the other hand, obesity itself has been shown to promote decreased responsiveness to leptin. In the present study parameters of energy balance [food intake (FI), body weight (BW), core temperature (Tc), heart rate (HR, indicator of metabolic rate)] of normally fed young (2 months old, NF2), normally fed and calorie-restricted middle-aged 12 months old (NF12, CR12, respectively) male Wistar rats were recorded in a biotelemetric system during a 7-day (1 µg/µl/h) intracerebroventricular infusion of leptin. Leptin reduced FI and BW in all NF but not in CR12 rats. During the infusion daytime Tc and HR were elevated in all groups, whereas nighttime values increased only in CR12 animals. On the one hand, NF12 animals showed weaker responses to leptin than NF2 rats. On the other hand, anorexic and metabolic responses to leptin changed in a disparate way in the CR12 group: regarding FI and BW they were resistant to leptin, but showed the most pronounced metabolic responses. In conclusion, calorie-restriction partially restores leptin responsiveness in middle-aged rats. Lack of anorexic response in calorie-restriction is probably due to their high orexigenic tone.

OTKA 49321, OTKA PD-84241