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The central effects of corticotropin releasing factor (CRF) on energy homeostasis show disparate shifts in the course of aging.

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Background: Corticotropins [including corticotropin-releasing factor (CRF) and urocortins] form a prominent neuropeptide system with multiple roles in stress-adaptation, anxiety and energy homeostasis. CRF produced in significant quantities in the hypothalamic paraventricular nucleus has been shown to have coordinated catabolic actions including anorexigenic and hypermetabolic components that lead to weight loss. Antipyretic effects of CRF have also been detected.

As age-related alterations in body weight and body composition (i.e. aging obesity in middle-aged and cachexia of aging in old individuals) do not only present population-wide public health challenges, but also appear in mammals, complex age-related regulatory alterations in the anabolic and catabolic peptide systems may be assumed in the background.

Our previous studies have already revealed well-defined age-related shifts in the responsiveness of energy balance to centrally applied melanocortin (MC) agonist alpha-melanocyte-stimulating-hormone. Concerning anorexic effects, these shifts include a decline in middle-aged and a pronounced enhancement in old age-groups that defy prior expectations of monotonous decline in neuropeptide efficacy and contribute to the explanation of middle-aged obesity and aging cachexia. On the other hand, hypermetabolic effects showed a disparate pattern, with strong responsiveness in middle-aged and older rats. The corticotropin system acts downstream of MCs among the catabolic network of neuropeptides of the hypothalamus.

Aims: We hypothesize that similar age-related shifts may be observed concerning the catabolic activity of corticotropins as those of MCs.

In the present study age-related changes in the responsiveness of the corticotropin system was tested regarding parameters of energy balance.

Methods: The effects of a 7-day intracerebroventricular CRF infusion (0.2 µg/µl/h) were measured in various age-groups of male Wistar rats (3 months - young adult, 12 months - middle-aged, 18- and 24 months - aging and old). Core temperature (Tc), heart rate (HR) and spontaneous horizontal activity of freely moving animals were recorded in a biotelemetric system (VitalView, MiniMitter). Food intake and body weight (BW) were measured daily.

Results: The CRF infusion significantly suppressed BW in the young, aging and old rats, but failed to reduce it in the middle-aged group. The anorexigenic response was significant and pronounced only in the oldest rats. Components of hypermetabolic effects (Tc or HR) were detected in all age-groups, they were even maintained in the oldest rats.

Our results show that middle-aged rats exhibit the weakest, the oldest age-group the strongest catabolic responsiveness to CRF. Anorexigenic and hypermetabolic responses to CRF show non-parallel changes with aging. Pronounced CRF-related weight loss in old animals appears as a consequence of greatly enhanced anorexic and maintained hypermetabolic actions. These observations may contribute to the explanation of middle-age obesity and aging anorexia. (OTKA PD84241, PTE AOK-KA-34039-02/2010, 34039/KA-OTKA/11-01)