AGE-ASSOCIATED ALTERATIONS IN CHOLECYSTOKININ EFFECTS CONCERNING ENERGY BALANCE ARE DISPARATE

Nóra Füredi, Judit Tenk, Alexandra Mikó,
Erika Pétervári, Márta Balaskó

Department of Pathophysiology and Gerontology, Medical School,
University of Pécs, Hungary

IINTRODUCTION

Obesity of the middle-aged is followed by anorexia and cachexia in older age-groups leading to sarcopenia. Complex age- and body composition-related alterations in the regulation of energy homeostasis may be assumed in the background. Maintenance of energy homeostasis involves both the regulation of body weight (BW) and that of core temperature (Tc).

AIMS

Age-related changes of the responsiveness to catabolic brain-gut axis peptide cholecystokinin (CCK) possibly contribute to variations in energy balance during aging.
To test our hypothesis, acute effects of CCK on various parameters of energy balance were analyzed during the course of aging.

METHODS

Male Wistar rats of different age and body composition (2-, 3-, 6- or 12- and 18-24 months corresponding to juvenile, young adult, early or late middle-aged and old, respectively) were injected intraperitoneally (5 µg, to test anorexigenic effects on re-feeding after 48-h food deprivation) or intracerebroventricularly (500 ng, to test thermoregulatory actions) with CCK, controls were treated with purified physiological saline (PFS). Calorie-restricted 12 months old (40% reduction, CR) and high-fat diet-induced obese (60% fat calories, HF) 6-months old groups were also established. Food intake was recorded in an automated FeedScale system, thermoregulatory analysis was performed using thermocouples (recording Tc and tail skin temperature to assess heat loss) in an indirect calorimeter (Oxymax) registering oxygen consumption.

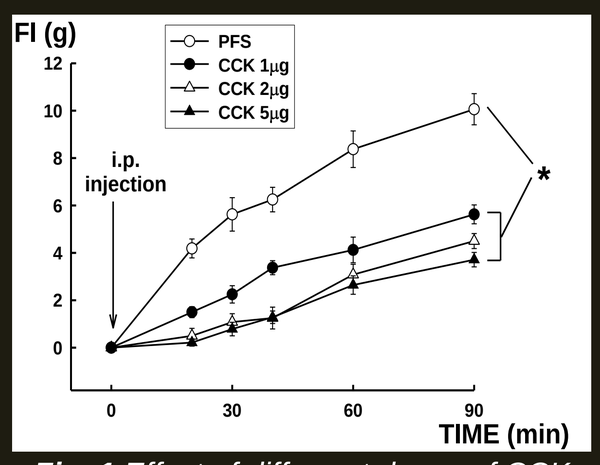

Fig. 1 *Effect of differrent doses of CCK given intraperitoneally (IP) on food intake (FI) in 48-h fasted 3 months old rats.*

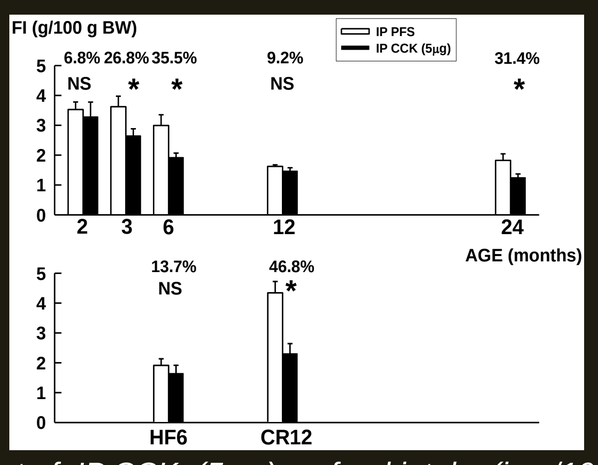

Fig. 2 *Effect of IP CCK (5 µg) on food intake (in g/100 g body weight) in 48-h fasted rats aged 2,3,6,12 and 24 months and in 6 months old high-fat diet –induced obese rats (HF6) and in 12 months old calorie-restricted ones(CR 12).*

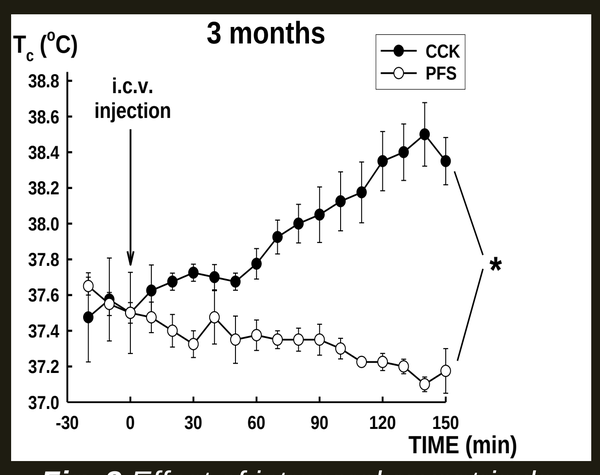

Fig. 3 *Effect of intracerebroventricular (i.c.v.) CCK injection on core temperature (Tc) in 3 months old rats.*

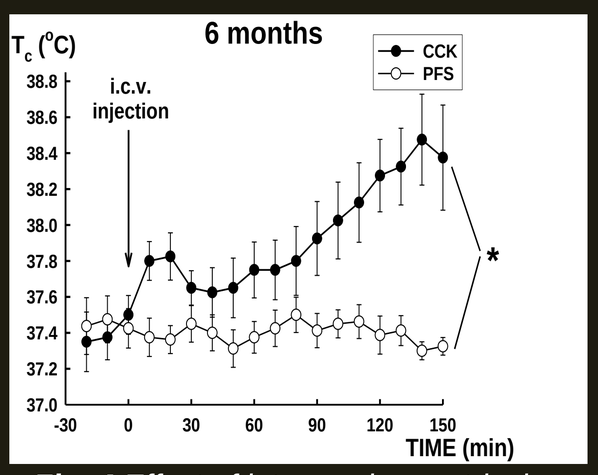

Fig. 4 *Effect of intracerebroventricular (i.c.v.) CCK injection on core temperature (Tc) in 6 months old rats.*

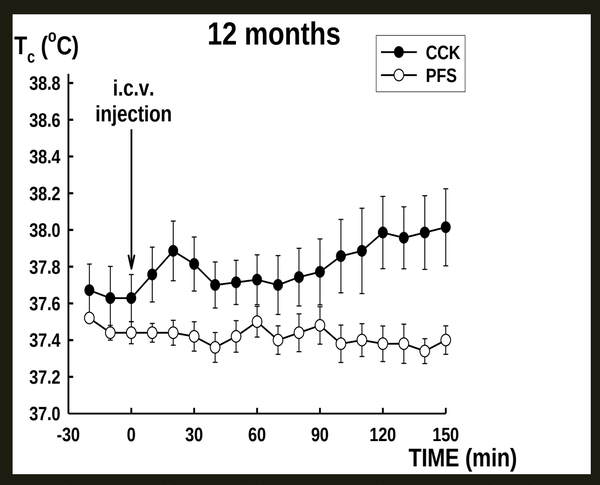

Fig. 5 *Effect of intracerebroventricular (i.c.v.) CCK injection on core temperature (Tc) in 12 months old rats.*

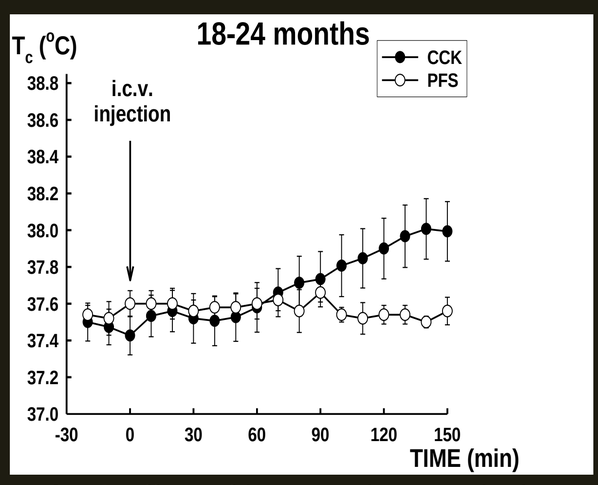

Fig. 6 *Effect of intracerebroventricular (i.c.v.) CCK injection on core temperature (Tc) in 18-24 months old rats.*

REULTS AND DISCUSSION

1. CCK suppressed re-feeding in young adult, early middle-aged and old, but not in juvenile and late middle-aged rats. (Figs. 1,2)
2. Conversely, in the HF early middle-aged rats CCK-induced suppression of re-feeding was diminished. (Fig. 2)
3. Regarding thermoregulatory responsiveness, disparate age-related alterations were found: strong hyperthermic effects in young rats that rather diminish with aging. (Figs. 3,4,5,6).
4. It is concluded that age-related changes in responsiveness to CCK may contribute to the age-related obesity of middle-aged as well as to the anorexia of old animals.
5. CCK-responsiveness is also influenced by body composition: calorie-restriction prevents the development of resistance to CCK, pre-existing obesity enhances it.
6. Age-related alterations in thermoregulatory vs. anorexigenic effects are disparate.

Nemzeti Fejlesztési Ügynökség
www.ujszechenyiterv.gov.hu
06 40 638 638
MAGYARORSZÁG MEGÚJUL
A projekt az Európai Unió támogatásával, az Európai Regionális Fejlesztési Alap társfinanszírozásával valósul meg.

OTKA PD84241, PTE AOK-KA-34039-02/2010, 34039/KA-OTKA/11-01