

DEVELOPMENT OF THERMOREGULATORY COMPETENCE, CIRCADIAN PERIODICITY AND CONTROL OF ENERGY BALANCE IN RAT PUPS: A REVIEW

I. Schmidt, Max-Planck-Institut für physiologische und klinische Forschung, D-61231 Bad Nauheim, FRG.

Despite their neural immaturity suckling-age rats show an endogenous circadian rhythm with torpor-like decreases of metabolic rate (MR) and core temperature (T_c) under cold loads but not at thermoneutrality (TN) (Nuesslein & Schmidt, 1990; Nuesslein-Hildesheim & Schmidt, 1994). This rhythm develops in the first postnatal days and ceases in the 3rd week, i.e. long before the adult rhythm develops (Nuesslein & Schmidt, 1990; Schmidt, 2000). The daily minimum of the juvenile rhythm is associated with a decrease in sympathetically mediated thermoregulatory thermogenesis (TT) in brown adipose tissue and a blunted response to sudden drops of T_a, which are, however, not due to an impairment of TT (Nuesslein-Hildesheim & Schmidt, 1994; Schmidt, 2000). The notion that the juvenile circadian rhythm is a mode of energy saving and not the indication of thermoregulatory incompetence (Nuesslein-Hildesheim & Schmidt, 1994) was confirmed when treatment with recombinant leptin, a hormone produced by adipose tissue and signaling the size of energy stores to the brain, became possible (Stehling *et al.*, 1996). Leptin-treatment under cold load results in a suppression of the daily drop of MR and T_c, as does the destruction of the leptin receptors in the arcuate nucleus, thus causing a higher energy expenditure and a reduced fat storage (Stehling *et al.*, 1996). Treatment of pups at TN causes an improvement in the TT capacity, but no change of basal MR and body fat stores (Stehling *et al.*, 1997). Various lines of evidence suggest that the central sympathetic outflow integrates the afferent commands provided by the thermosensors and by leptin and other signals reflecting the metabolic status of the organism and, thus, forms the common underlying mechanism by which changes in energy balance and in the TT capacity are linked to each other (Schmidt, 2000). Changes in the central sympathetic nervous system might, therefore, also underly the influences of the pre- or early postnatal thermal or nutritional environment which are responsible for the development of normal energy balance regulation or the programming of life-long aberrations, like dispositions for obesity and related metabolic disturbances (Schmidt, 2000; Levin, 2000; Young & Morrison, 1998).

- Levin, B. (2000) The Obesity epidemic: metabolic imprinting on genetically susceptible neural circuits. *Obesity Res.* 8: 342-347.
- Nuesslein, B. & Schmidt, I. (1990) Development of circadian cycle of core temperature in juvenile rats. *Am. J. Physiol.* 260: R270-R276.
- Nuesslein-Hildesheim, B. & Schmidt I. (1994) Is the circadian core temperature rhythm of juvenile rats due to a periodic blockade of thermoregulatory thermogenesis? *Pflügers Arch.* 427: 450-454.
- Schmidt, I. (2000) The role of juvenile thermoregulatory thermogenesis in the development of normal energy balance or obesity. In: *Thermotherapy for Neoplasia, Inflammation, and Pain*, eds. Kosaka, M., T. Sugahara, K. L. Schmidt, E. Simon. Springer, Tokyo, pp. 215-225.
- Stehling, O., Döring, H., Ertl, J., Preibisch, G. & Schmidt, I. (1996) Leptin reduces juvenile fat stores by altering the circadian cycle of energy expenditure. *Am. J. Physiol.* 271: R1770-R1774.
- Stehling, O., H. Döring, B. Nuesslein-Hildesheim, M. Olbort & Schmidt, I. (1997) Leptin does not reduce body fat content but augments cold defense abilities in thermoneutrally reared rat pups. *Pflügers Arch.* 434: 694-697.
- Young, J.B. & Morrison, S.F. (1998) Effects of fetal neonatal environment on sympathetic nervous system development. *Diabetes Care* 21 Suppl. 2, B156-B160.

I.Schmidt@kerckhoff.mpg.de