The long-lasting impact of postnatal neuropeptide Y

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IT HAS BEEN a long-standing observation that overnutrition during the early lifetime can have a permanent influence on the feeding behavior and body weight gain of the adult individual. The maintenance of energy balance, which is the resultant of energy intake and expenditure, is controlled by a complex network of neurohumoral factors (2, 5, 10). Among those, neuropeptide Y (NPY), a 36-amino acid peptide that is synthesized and released in the hypothalamus, is thought to play a key role in mediating appetite and nutrition uptake (5, 8, 10, 11). Previous studies have shown that alterations in fetal metabolism that may occur in diabetic rats and during intrauterine growth restriction can have profound effects on postnatal hypothalamic NPY release (3, 6).

In this issue of the American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, Dr. Varma and coworkers (9) present a paper in which they tested the hypothesis that high levels of NPY during the critical stages of postnatal development can permanently affect adult appetite, food intake, and body weight. For this purpose, postnatal rats between 2 and 7 days of age received repetitive intracerebroventricular injections of NPY. Compared with the vehicle-treated rats, administration of NPY caused a 32% transient increase in body weight gain and elevated plasma insulin concentrations without significant changes of plasma glucose concentrations. The rise in body weight was fully reversible within 48 h despite continuing daily NPY injections. Notably, a significant decline in body weight gain and food intake was observed in female rats beginning on day 60 of postnatal life. In contrast, no statistical changes in either nutritional behavior or body weight gain pattern were observed in the male animals. Although the hyperinsulinemia persisted after termination of NPY administration until 120 days of age in the female progeny, the plasma insulin concentrations were not significantly different in the NPY- and vehicle-treated male rats. These findings indicate that high levels of intracerebroventricular NPY during early postnatal life can profoundly reduce food intake and body weight gain in female but not in male adult animals. To elucidate the mechanisms that may possibly underlie these effects, the authors measured the hypothalamic NPY content with the use of a sensitive radioimmunoassay. Although hypothalamic NPY was transiently increased in response to exogenous NPY, a threefold decline was found at 120 days of age in female but not in male rats compared with the vehicle-injected animals. Immunohistochemistry revealed that the reduced overall concentration of hypothalamic NPY in the females was due to a reduced content in the paraventricular, dorsomedial, and arcuate nuclear regions. To determine if the NPY responsiveness in the adults was altered due to neonatal injection of NPY, a second intracerebroventricular infusion was performed in female rats at 120 days of age. However, no significant differences in terms of body weight gain and food intake were observed between rats that had previously been treated with NPY and vehicle, respectively. These findings suggest that neonatal infusion did not affect the responsiveness to NPY of adult rats with regard to the control of appetite, feeding behavior, and body weight gain.

The reported observations are remarkable in several aspects. First, they demonstrate convincingly that the levels of NPY in the postnatal hypothalamus can have long-lasting effects on nutrition uptake and body mass in the adult organism. Furthermore, the results indicate gender-specific differences in the NPY-dependent control of energy homeostasis. Although persisting hyperinsulinemia in female rats may contribute to this phenomenon by suppression of hypothalamic NPY content (1, 4, 7), the cause for the gender differences remains to be investigated. In summary, these observations underline the importance of fetal/neonatal metabolism and may set the stage for potential therapeutic interventions before the adult onset of altered eating behavior and obese phenotype.

REFERENCES


