

IS LIMITING CALORIC INTAKE NECESSARY FOR REAPING THE REWARDS OF DIETARY RESTRICTION – OR IS IT JUST A GUT FEELING?

B. Jones (P), K. Duffy, S. Ramaswamy, R. Anson, P. Pistell, M. Chachick, E. Spangler, R. Spencer, D. Ingram, R. de Cabo

Laboratory of Experimental Gerontology, Gerontology Research Center, National Institute on Aging, 5600 Nathan Shock Drive, Baltimore, MD

Dietary restriction (DR) is the only environmental intervention scientifically proven to increase longevity, decrease the incidence and onset of age-related disease as well as prevent age-related functional declines in various species. However, the mechanism of the DR effect remains unknown. Two popularly studied forms of DR include limited daily feeding, also known as calorie restriction (CR), and every-other-day feeding (EOD). DR studies involve the manipulation of caloric intake, but cannot control or eliminate the induction of hunger. Inability to control for hunger in DR experiments becomes more critical as evidence towards a neuroendocrine hypothesis accumulates as the primary mechanism driving the beneficial effects of DR. Thus, examining the effects of DR under appetite suppression would provide a means for observing the role of hunger in the DR mechanism. With the use of hypothalamic manipulation, by post-natal injection of monosodium glutamate (MSG), the evaluation of hunger suppression on the benefits of DR can be examined. MSG chemically lesions leptin receptors of the arcuate nucleus in the medial hypothalamus, a neural locus involved in appetite control. Loss of leptin receptors results in decreased production of orexogenic neuropeptide-Y (NPY) causing a reduction of appetite displayed by hypophagic behavior. Mice treated with MSG consumed less per unit body mass with the exception of those on CR, however, they exhibited a significant delay in consuming all of their allotted food. The DR related decrease in fasting serum leptin, insulin, and glucose levels as well as the related increase in fasting serum corticosterone was attenuated by appetite suppression. The effects of hunger suppression suggest dietary restriction is mediated by a gut feeling.