Disruption of Neuropeptide Y Gene Limits Stress Resistance and Lifespan Extension effects of Calorie Restriction in Mice.

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The beneficial effects of calorie restriction (CR) may be induced by neuroendocrine adaptation to long-term reduction of dietary energy intake. Neuropeptide Y (NPY) expressing neurons in the hypothalamic arcuate nuclei are involved in the neuroendocrine adaptation including suppression of growth and reproduction and activation of stress response. NPY also regulates food intake and its expression was increased in CR mice. Moreover, NPY acts directly in the fat tissue and mediates stress-induced weight gain in ad libitum (AL) fed condition. Therefore, NPY might have crucial roles for the effects of CR. Here we investigated the effects of CR on NPY knock out (KO) mice. Wild type (WT) and NPY KO mice were fed AL or 30% CR diets from 12 weeks of age. Basic metabolic parameters including respiratory quotient were measured. The stress response to oxidative stress induced by 3-nitropropionic acid was enhanced in the WT-CR mice as compared to the WT-AL mice, whereas the response was diminished in the KO-CR mice. The lifespan was significantly extended in the WT-CR mice; however, the effect was abolished in the KO-CR mice. Nonetheless, the CR-mediated neuroendocrine modulations were also observed in the KO-CR mice. These results suggest that NPY's primary roles on CR are not neuroendocrine modulation, however, NPY is indispensable for the beneficial effects of CR.