EATING LESS TO LIVE LONG: CAN CALORIE RESTRICTION RETARD AGING IN PRIMATES?

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With over 70 years of study, the caloric restriction (CR) paradigm has provided gerontology with a unique intervention. Results of numerous rodent studies have demonstrated that CR can slow aging processes manifested as reduced pathology, retained function, and extended lifespan. Although CR studies had been conducted in many invertebrate and vertebrate species, no experiment had been attempted to determine its relevance to human aging prior to 1987. To this end, the National Institute on Aging initiated that year the first CR study in nonhuman primates. Currently about 200 monkeys, mostly rhesus monkeys (*Macaca mulatta*) with a small number of squirrel monkeys (*Saimiri sciureus),* aged across their respective lifespans at the time of initiation, have been involved in the study. Control groups receive two meals per day sufficient to attain apparent satiety, while the CR group receives 30% less, adjusted for age and body weight. The diet is supplemented with extra micronutrients such that the amount of calories consumed is the only substantive variable manipulated. Results accumulated to date indicate that CR rhesus monkeys are healthier than controls based on the following observations: (1) reduced incidence of various diseases; (2) significantly better indices of predisposition to disease, such as lower insulin levels and greater insulin sensitivity, reduced blood lipids and pressure, decreased arterial stiffness, and elevated HDL; and (3) alterations in candidate biomarkers of aging. Results of recent behavioral studies also indicate enhanced performance in a motor task that shows age-related decline, but we have seen no evidence as yet that the age-related loss in the volume of the neostraitum, which regulates motor performance, has been attenuated by CR. In a related study we have observed that short-term CR in adult rhesus monkeys can provide protection against a neurotoxic insult similar to previous observations made in rodents. CR rhesus monkeys that were juveniles at the onset of the study showed delayed skeletal and sexual maturation, and all CR groups have lower body temperatures than controls. These latter physiological observations are manifestations of a fundamental shift in life history strategy, from growth and reproduction to life maintenance, and appear to reflect adaptations in metabolic and protective gene expression. Although preliminary data suggesting that CR animals exhibit reduced mortality have not yet reached statistical significance, this intervention does appear to exert beneficial effects in primates that suggest a reduced rate of aging. These results, along with others that have emerged from a parallel study in rhesus monkeys being conducted at the University of Wisconsin, offer potential relevance of CR as an anti-aging intervention in humans to support the clinical studies currently underway at several research centers.