

EFFECTS OF LONG-TERM CALORIE RESTRICTION ON OVARIAN FUNCTION IN RHESUS MONKEYS

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Moderate calorie restriction (CR) is the only proven non-genetic experimental paradigm of life extension. Furthermore, it may delay reproductive senescence in female rodents. This study evaluated the dynamics of ovarian hormone production with age, as well as assessed ovarian cyclicity in rhesus monkeys maintained on long-term CR. Female rhesus monkeys were maintained on control diet (CON) or calorie restricted at 30% CON (CR) for 11-12 years. Monkeys were young (Y; 13-15 years): YCON (n=5), YCR (n=7); or old (O; 18-25 years): OCON (n=6) and OCR (n=5). Estradiol (E2), progesterone (P4), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and inhibin B (INHB) were assayed in serum daily during the follicular phase and every third day during the luteal phase for 3 consecutive spontaneous cycles or approximately 90 days. All Y were regular cyclers (mid-cycle E2, FSH and LH peaks followed by luteal phase levels of P4 for >2/3 expected cycles). O were divided into regular (OR) and irregular (OI) cyclers. No differences were observed between diets in the proportions of old animals exhibiting regular or irregular cycles: OR-CON (n=3); OI-CON (n=3); OR-CR (n=1); OI-CR (n=4). Hormones (LH, FSH, E2, P4 and INHB) in regular cyclers were analyzed relative to the LH peak and similar hormone patterns and levels were found regardless of age or diet. FSH, E2 and INHB were normalized relative to the onset of menses or to troughs (<50pg/mL) in E2 patterns (necessary for OI). No diet effects were found, however age effects were observed. E2 was similar between groups, however, OI had higher ($p<0.05$) FSH and lower ($p<0.05$) INHB than OR or Y monkeys. Thus, despite maintenance on long-term CR, monkeys continue to cycle and demonstrate expected age-related hormone changes. Whether CR prolongs the peri-menopausal interval and/or delays the age at which actual menopause occurs, remains to be determined.