Abstract citation ID: bvac150.1465

Reproductive Endocrinology

RF10 | PMON216

Aromatase Inhibition Fails to Exaggerate Weight Gain and Induce Bone Loss in Ovariectomized Female Marmosets

Molly Willging, BS, Marissa Kraynak, PhD, Alex Kuehlmann, BS, Amita Kapoor, PhD, Matthew Flowers, PhD, Ricki Colman, PhD, Jon Levine, PhD, and David Abbott, PhD

Declining serum estradiol (E2) levels during the menopausal transition are associated with increased central adiposity and heightened risk for metabolic disease. Ovarian estradiol, E2, supports female metabolic function. While ovariectomy (OVX) in rodents enables obesity, OVX in nonhuman primates (NHPs) inconsistently alters weight gain. We therefore hypothesized that in female NHPs, extra-ovarian E2 provides key support for metabolic homeostasis. To test this, we employed aromatase inhibition to eliminate extra-ovarian E2 biosynthesis together with diet-induced obesity (DIO) to enhance weight gain. Thirteen adult female marmoset monkeys were OVX and received: (1) E2-containing capsules and daily oral treatments of vehicle (E2; n=5); empty capsules and daily oral treatments of either vehicle (VEH, 1ml vehicle/kg, n=4), or (3) letrozole (LET, 1 mg/kg in 1ml vehicle/kg, n=4). After 6-7 months, VEH and LET compared to E2 females demonstrated increased % body weight gain ($p=0.01$) and increased caloric intake VEH ($p<0.001$) and LET ($p<0.001$) corrected for fat-free mass. Dual energy x-ray absorptiometry (DXA)-determined body composition at 6 months showed no between female group differences in total fat mass or fat mass in validated body regions of interest. Total body ($p=0.014$), abdominal region ($p=0.002$) and upper leg region ($p=0.025$) DXA-determined fat free mass, however, increased ~5-10% in all female groups. In addition, lumbar spine and total body DXA-determined bone mineral density (BMD) and bone mineral content (BMC) were comparable across all female groups. Relative circulating E2 levels were E2>>>VEH>LET, while those in hypothalamus ranked E2=VEH>LET, confirming aromatase inhibition of local hypothalamic E2 in LET females. Our findings demonstrate ovarian E2 and extra-ovarian E2 depletion induce comparable increases in DIO weight gain without bone loss in female marmoset monkeys and highlight E2 as a key regulator of female metabolic homeostasis in NHPs.

Presentation: Saturday, June 11, 2022 1:48 p.m. - 1:53 p.m., Monday, June 13, 2022 12:30 p.m. - 2:30 p.m.