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NEUROPROTECTION WITH HORMONE THERAPY IN OLDER MENOPAUSAL MONKEYS.

M.L Voytko,

Department of Neurobiology and Anatomy, Wake Forest University School of Medicine, Winston-Salem, NC 21517, USA.

Presenter's Email: mlvoytko@wfubmc.edu

The unexpected findings of the Women's Health Initiative Memory Study produced more questions than answers regarding hormone therapy (HT) and cognitive function in women. Our studies in monkeys are addressing some of the factors that may have contributed to these findings in postmenopausal women and are broadening our understanding of HT effects on cognitive and neurobiological profiles in monkeys. Our current studies focused on the effects of a novel HT regimen in older ovariectomized (OVX) rhesus monkeys. All monkeys were preoperatively trained on a series of cognitive tasks, ovariectomized (mean age of 19.7$\pm$0.5 years at time of OVX), and had HT begun immediately (n=8 untreated controls [PL], n=9 estrogen therapy only [ET], n=8 estrogen plus progesterone [E+P]). We based our novel HT regimen on the monkey menstrual cycle where implants delivered constant low levels of estradiol and a monthly estradiol injection produced an estradiol peak. Monkeys receiving E+P received daily oral doses of progesterone for 12 days at the end of the monthly treatment phase. Cognitive function was retested at 2, 12 and 24 weeks following OVX/HT. Monkeys receiving ET were comparable to those receiving E+P. In comparison to the estrogen-treated groups of monkeys, monkeys with PL performed more poorly in tests of visual memory, executive function, and attention. In addition, imaging studies suggest that dopamine receptors were preserved with HT compared to PL. Our findings suggest that this novel HT regimen may be beneficial for cognition and neurobiology protection in menopausal monkeys. Supported by NIA AG13204.

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