Age-related neuroendocrine, cognitive, and behavioral co-morbidities are promoted by HIV-1 Tat expression in male mice

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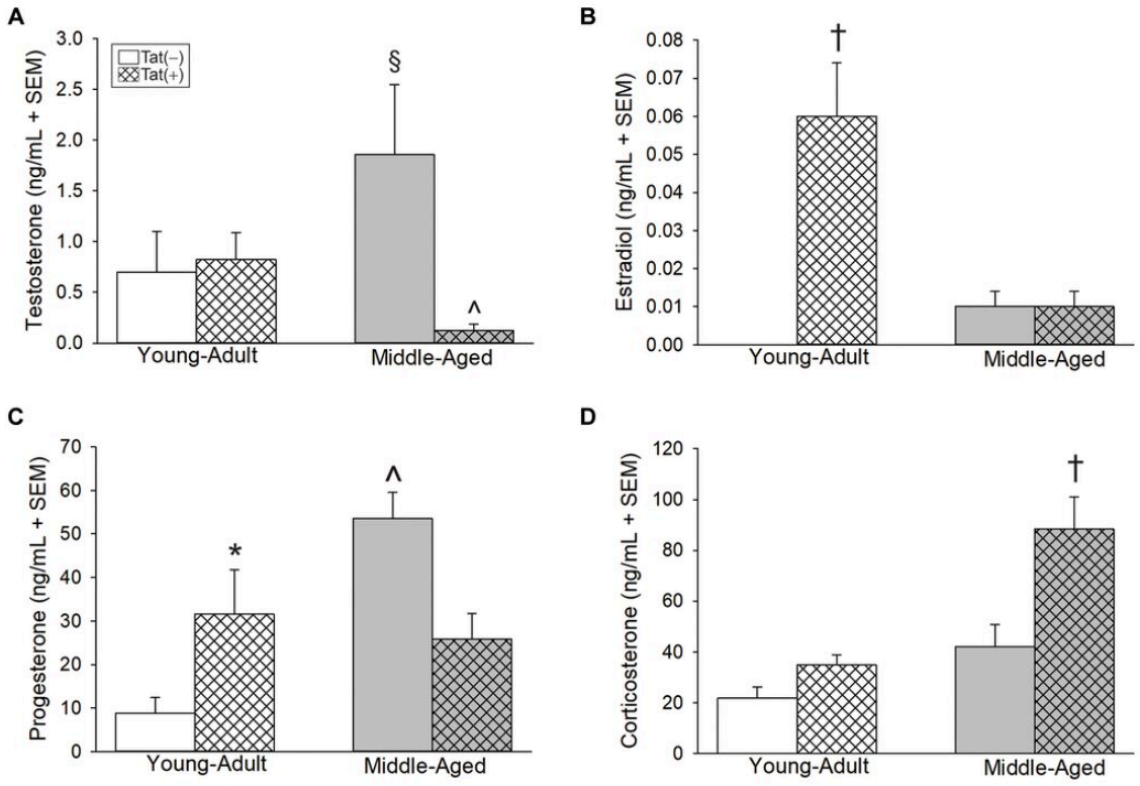

Circulating steroids (ng/mL) among young adult and middle-aged HIV-1 Tat-transgenic male mice [Tat(+)] or their non-Tat-expressing age-matched counterparts [Tat(−)]. Credit: Qrareya et al, *Aging* (2022). DOI: 10.18632/aging.204166

In the United States, approximately 1.2 million people are living with human immunodeficiency virus type-1 (HIV-1), with men accounting for the majority of cases (~75%). About half of HIV-infected individuals are 50 years of age and older. People living with HIV contend with an accelerated onset of age-related diseases and disorders; however, the pathophysiology underlying accelerated aging is poorly understood.

While the mechanisms(s) are unknown, the HIV-1 trans-activator of transcription (Tat) protein disrupts neuroendocrine function in mice partly by dysregulating mitochondria and neurosteroidogenesis.

Researchers Alaa N. Qrareya, Fakhri Mahdi, Marc J. Kaufman, Nicole M. Ashpole, and Jason J. Paris, from the University of Mississippi and Harvard Medical School's McLean Hospital, investigated the combined effects of aging and HIV-1 Tat expression on the development of neuroHIV-like sequelae in young adult (6-8 months) and middle-aged (11-13 months) male mice to determine whether Tat precipitates age-related dysfunction.

"We hypothesized that conditional Tat expression in middle-aged male transgenic mice [Tat(+)] would promote age-related comorbidities compared to age-matched controls [Tat(−)]. We expected Tat to alter steroid hormone milieu consistent with behavioral deficits."

Middle-aged Tat(+) mice had lower circulating testosterone and progesterone than age-matched controls and greater circulating corticosterone and central allopregnanolone than other groups. Young Tat(+) mice had greater circulating progesterone and estradiol-to-testosterone ratios. Older age or Tat exposure increased anxiety-like behavior (open field; elevated plus-maze), increased cognitive errors (radial arm water maze), and reduced grip strength. Young Tat(+), or middle-aged Tat(−), males had higher mechanical nociceptive thresholds

than age-matched counterparts. Steroid levels correlated with behaviors. Thus, Tat may contribute to HIV-accelerated aging.

"In conclusion, our data suggest that older age and Tat expression exert independent and interactive effects to worsen neuroendocrine, affective, cognitive, and neuromuscular comorbidities. Novel steroid replacement therapies may be useful adjunctive therapeutics to cART in the aging HIV+ population."

More information: Alaa N. Qrareya et al, Age-related neuroendocrine, cognitive, and behavioral co-morbidities are promoted by HIV-1 Tat expression in male mice, *Aging* (2022). DOI: 10.18632/aging.204166

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