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## A cross-sectional analysis of verbal memory and executive control across athletes with varying menstrual status and non-athletes

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Data regarding the impact of an athlete's gonadal status on cognitive function are limited. Recent studies in postmenopausal women, girls with Turner syndrome and amenorrheic athletes (AA) have highlighted the role of estrogen deficiency and its replacement on cognition (Baskaran et al., 2017; Ross et al., 2000). Amenorrhea constitutes a major component of female athlete triad and the resultant estrogen deficiency could negatively impact cognition in AA. Conversely, aerobic activity through its cognition-enhancing ability may confer an advantage to an athlete's cognitive performance. The opposing effects of exercise versus estrogen deficiency on cognition are yet to be comprehensively determined. We hypothesized that eumenorrheic athletes (EA) would perform better on tasks involving verbal memory and executive control compared to AA and non-athletes.

Our Institutional Review Board approved this study which was conducted from 2011 to 2015. Well-established cognitive measures used to assess verbal memory and executive control were administered at the baseline visit to normal-weight AA, EA and non-athletes, 14–25 years old, recruited for an ongoing trial (BMI between the 10th and 90th percentiles; mean age  $19.9 \pm 0.3$ ,  $20.3 \pm 0.7$ , and  $20.3 \pm 0.7$  years respectively). We have previously reported an improvement in verbal memory and executive control in a subset of AA following 6 months of estrogen replacement (Baskaran et al., 2017). The current study presents a cross-sectional analysis of verbal memory and executive control in 84 AA compared with 15 EA and 16 non-athletes. The California Verbal Learning Test-II (CVLT-II) assessed verbal memory, while the Delis-Kaplan Executive Function System Color-Word Interference Test (D-KEFS CWIT) assessed executive control. Additionally, Wechsler's Abbreviated Scale of Intelligence (WASI) matrix reasoning and vocabulary tests were administered to determine fluid and crystallized intelligence, respectively, to test general

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cognitive abilities across groups. Athletes included subjects involved in weight-bearing activity of the lower limbs for ≥ 4 h a week, or those running > 20 miles/week for ≥ 6 months in the preceding year. EA were required to have ≥ 9 menstrual cycles in the preceding year, whereas AA were required to have ≥ 3 consecutive months of amenorrhea in the preceding 6 months of oligomenorrhea, defined as a cycle length of ≥ 6 weeks.

The groups did not differ in crystallized and fluid intelligence even after controlling for age. For CVLT-II measures, EA had the highest serial clustering T scores compared with AA and non-athletes for unadjusted analysis, and higher scores than AA after adjusting for age ( $p=0.04$ ). For DKEFS CWIT, Inhibition error analysis score was significantly higher in EA compared to non-athletes after adjusting for age ( $p=0.04$ ). Other CVLT-II and D-KEFS measures did not differ between groups.

The current analyses revealed two key findings. First, compared to AA, EA had higher CVLT-II serial clustering scores indicating a higher ability to remember words serially, which has been linked to better memory performance (Meijs et al., 2013). Kramer et al. showed that women, compared to men, had superior verbal memory and used greater semantic clustering (Kramer et al., 1988), another organizational strategy to enhance learning and memory. Better performance in women suggests that this effect may be mediated via estrogen. Similarly, in our study, serial clustering scores were highest in EA, suggesting that estrogen may exert its effect on memory by facilitating organizational strategy. Second, D-KEFS CWIT inhibition error analysis scores were higher in EA than non-athletes, indicating better executive control over behavioral impulses, consistent with studies reporting improvements in executive control following exercise interventions (Kramer et al., 1999). This difference was observed between EA and non-athletes suggesting that increased executive control in EA is mediated by exercise effects in addition to estrogen status. We thus show that athletes who are eumenorrheic have better organizational strategies that are known to be beneficial for learning and memory, an effect probably mediated by estrogen, and have better executive control, which could represent the combined positive influence of exercise and estrogen status.

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