Evaluating the Relationship Between Hormone Replacement Therapy and Cognition in the Canadian Longitudinal Study on Aging's Postmenopausal Cohort

Laura Rabin
The Graduate School and University Center of The City University of New York

Maryam Mansuar
The Graduate School and University Center of The City University of New York

Annie Robitaille
The Graduate School and University Center of The City University of New York

Vanessa Taler
The Graduate School and University Center of The City University of New York

Laura Rabin
The Graduate School and University Center of The City University of New York

Abstract

Background: Menopausal declines in endogenous estrogen have been linked to cognitive changes in aging. While longer endogenous estrogen exposure (EEE) may support cognitive health, the cognitive impact of exogenous estrogen via hormone replacement therapy (HRT) remains unclear.

Methods: Data were drawn from 10,978 postmenopausal women in the Comprehensive cohort of the Canadian Longitudinal Study on Aging (CLSA). HRT usage was self-reported at baseline and classified dichotomously (ever/never). Cognitive performance was assessed at baseline and 3-year follow-up using six standardized neuropsychological tests targeting verbal memory and executive functioning. Multiple linear regressions examined whether HRT usage predicted follow-up performance while adjusting for baseline scores, age, age at natural menopause, education, household income, depressive symptoms, health behaviors, and medical comorbidities. A Bonferroni correction was applied ($\alpha = .008$).

Results: HRT usage **did not significantly predict performance** on any cognitive measure at follow-up. In contrast, **later age at natural menopause** predicted better performance in verbal learning and memory (RAVLT immediate recall: $\beta = 0.013$, $p = .006$; delayed recall: $\beta = 0.021$, $p < .001$) and executive functioning (Stroop interference: $\beta = -0.004$, $p = .004$). Older age was associated with lower performance across all tasks, while higher education and income predicted better outcomes.

Conclusions: HRT usage was not associated with cognitive performance over three years, whereas later natural menopause—serving as a proxy for longer endogenous estrogen exposure—was modestly associated with better memory and executive functioning. These findings suggest that **duration of endogenous estrogen exposure may be more relevant to cognitive aging than HRT use alone**. Future research should account for HRT formulation, timing, and duration to evaluate the critical window hypothesis.

Keywords

Hormone replacement therapy, menopause, cognition, estrogen exposure, aging, women's health.