INTRODUCTION

- Women undergo cognitive changes as a result of menopause and aging (Halbreich et al. 1995).
- Epidemiologic studies suggest that exposure to estrogen (E2) in the early years after menopause is associated with reduced risk of being diagnosed with dementia/Alzheimer’s disease in later life (Shao et al., 2012).
- However, large interventional trials such as the Women’s Health Initiative show that administration of certain estrogen/progestin non-selectively to older postmenopausal women may increase the risk of dementia (Shumaker et al., 2003).
- Estrogen effects on cognitive processes after menopause are mediated partially through salutary effects on brain cholinergic systems (Dumas et al., 2006).
- Subjective cognitive complaints in later life are associated with an increased risk of dementia (Jessen et al., 2014), but the question of whether women who report cognitive problems might benefit from E2 supplementation in the early years after menopause (during the “critical period”) has not been answered.
- We examined the effects of E2 on cognitive functioning in a group of women who report significant cognitive changes shortly after menopause.

RESEARCH QUESTION

**Will estrogen treatment improve cognitive performance in women who do compared to women who do not report changes in cognitive functioning?**

METHODS

**Subjects:** Forty two (42) normal early postmenopausal women who were cognitively and behaviorally screened and classified as cognitive complainers (CC; n = 21, Age: 56.3 ± 2.9) if they endorsed more than 20% of cognitive symptom items in an extensive self-report battery validated in a study of subjective cognitive impairment (Saykin et al., 2006), or non-complainers (NC; n = 21, Age: 55.5 ± 3.1) otherwise.

**Procedures:** Subjects were scanned (structural and fMRI) and performed a baseline cognitive battery that included tests of attention, speed, and memory. Hippocampally-mediated memory tasks included:

1. **Selective Reminding Task:** The SRT is a multi-trial verbal list-learning task allowing the examination of acquisition, encoding and retrieval and offers measures of storage into and retrieval from both short and long term memory (Buschke 1973).

2. **Virtual Morris Water Maze:** The VMWM is a computerized simulation that uses 16 learning trials and one probe trial to assess spatial navigation and memory. Performance depends on intact hippocampal functioning (Astur et al., 2002).

Subjects were then administered 1 mg of oral 17β estradiol (E2) or placebo daily for 3 months. Follow-up scanning and cognitive testing then took place 3 months later, followed by anti-cholinergic drug challenges (reported elsewhere).

**RESULTS**

**Selective Reminding Task: Estradiol treatment improves performance only in Cognitive Complainer (CC) Group**

**Virtual Morris Water Maze (Spatial Navigation): Estradiol Improves Learning and Memory only in CC Group**

**DISCUSSION**

- Relative improvement in both verbal episodic memory and spatial navigation after estradiol treatment were seen in women who noted a change in their cognitive performance after menopause (“cognitive complainers” but not in women who noted no change after menopause, who showed either no change or worsening with estradiol treatment.
- Subjective cognitive decline after menopause may be a risk factor for late-life cognitive dysfunctions and is associated with a higher risk for dementia.
- This study provides evidence that estradiol may enhance hippocampally-mediated cognitive performance in women who note postmenopausal changes in cognition, consistent with alterations in connectivity seen in CC subjects.
- Estradiol may have promise for maintenance/improvement of cognitive functioning during the “critical window” after menopause in a subgroup of potentially higher-risk women.

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**REFERENCES**


