Hormone Therapy Use and Risk Factors for Alzheimer’s disease: Data from the Wisconsin Registry for Alzheimer’s Prevention

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BACKGROUND

Until recently, it was widely believed that hormone therapy (HT) could reduce a woman’s risk for dementia by up to 50%. See Reviews [1-2]. In contrast, two Women’s Health Initiative ancillary analyses of the WHIMS Study (WHIMS; [3-6]) and WHI Study of Cognitive Aging (WHSCA; [7,8]) revealed adverse cognitive effects of a widely-used form of oral HT, conjugated equine estrogen (CEE) for women age 65 and older. However, new data, including that from the WHI ([9,10] and WHIMS [11]) suggest that the harm associated with CEE forms of HT may not apply to women younger than age [11,12], or to estradiol forms of HT ([13-15]). Overall, there is an emerging understanding emerging understanding of the relationship between parental history and HT efficacy. Further research is needed to clarify several unanswered questions related to the cognitive and neurobiological effects of HT. For example, it is unclear whether cognitive effects of menopausal HT vary in relation to risk factors for Alzheimer’s disease (AD), such as parental history of AD or presence of Apolipoprotein E (ApoE) ε4 allele. The relationship between ApoE4 genotype and response to HT has been investigated more extensively than the relationship between parental history and HT efficacy. This study sought to examine the cognitive effects of HT in middle-aged women possessing an ApoE4 allele. In contrast, other studies suggest that there is no difference in cognitive response to HT based on the presence of ε4 allele, [18,19] and still others report an enhanced response among ε4+ women [12,20,21].

OBJECTIVES

This study sought to:

1) Clarify whether cognitive profiles differed for women who were HT Users (past or current) or Never Users.
2) Examine the possible interaction in cognitive efficacy between (a) HT-status and APOE4 genotype
(b) HT-status and parental history of AD

METHODS

Participants

Data were obtained from 532 postmenopausal women enrolled in the Wisconsin Registry for Alzheimer’s Prevention (WRAP), a widely-used form of oral HT, conjugated equine estrogen (CEE) for women age 65 and older. However, new data, including that from the WHI ([9,10] and WHIMS [11]) suggest that the harm associated with CEE forms of HT may not apply to women younger than age [11,12], or to estradiol forms of HT ([13-15]). Overall, there is an emerging understanding of the relationship between parental history and HT efficacy. Further research is needed to clarify several unanswered questions related to the cognitive and neurobiological effects of HT. For example, it is unclear whether cognitive effects of menopausal HT vary in relation to risk factors for Alzheimer’s disease (AD), such as parental history of AD or presence of Apolipoprotein E (ApoE) ε4 allele. The relationship between ApoE4 genotype and response to HT has been investigated more extensively than the relationship between parental history and HT efficacy. This study sought to examine the cognitive effects of HT in middle-aged women possessing an ApoE4 allele. In contrast, other studies suggest that there is no difference in cognitive response to HT based on the presence of ε4 allele, [18,19] and still others report an enhanced response among ε4+ women [12,20,21]. This study sought to examine the cognitive effects of menopausal HT in women whose risk for AD due to the presence of the ApoE4 genotype and/or a parental history of AD has been characterized.

RESULTS


table1. characteristics of the analytical sample

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>HT Never (n=158)</th>
<th>P-Value</th>
<th>HT Users (n=374)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>House (Age)</td>
<td>0.08</td>
<td></td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Mean Education (SD)</td>
<td>15.82 (2.7)</td>
<td></td>
<td>15.96 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>67.36 (3.7)</td>
<td></td>
<td>67.42 (3.5)</td>
<td></td>
</tr>
<tr>
<td>Parental History (n=532)</td>
<td>0.95</td>
<td></td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>% positive</td>
<td>0.68</td>
<td></td>
<td>0.68</td>
<td></td>
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<tr>
<td>% positive</td>
<td>0.32</td>
<td></td>
<td>0.32</td>
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</tr>
<tr>
<td>% positive</td>
<td>0.25</td>
<td></td>
<td>0.25</td>
<td></td>
</tr>
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</table>

CONCLUSIONS

1) HT exposure (past or current) is associated with better
   • Verbal ability
   • Visuospatial ability
   • Verbal learning and memory

2) Effects may be more substantial in non-users
3) Interactions with risk factors for AD: Group differences appear primarily related to HT exposure or ApoE4 status with no differential effect based on risk profile.

REFERENCES


Analyses

General linear models were used to compare groups defined by
1) HT use (never users vs. HT exposed), 2) by HT use and ApoE4 status (non-users vs. users), and parental history. Covariates for the models included age, education, and score on a depression scale (CES-D).