Estrogen Treatment Reduces Brain Functional Connectivity in Post-Menopausal Women

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Introduction

- Loss of estrogen during the postmenopausal period in women can produce measurable and significant impairment of performance on certain cognitive tasks.
- It has been suggested that administration of estradiol may enhance or preserve certain types of cognitive functioning in post-menopausal women.
- We have shown that increased functional connectivity of the frontal cortex and decreased functional connectivity of the medial temporal lobe is associated with higher rates of subjective memory complaints after menopause.
- These data suggest that the etiology of changes in post-menopausal women may be related to changes in brain connectivity.
- Functional Connectivity: the temporal correlation of BOLD signal fluctuations among two or more anatomically distinct regions.
- The coherent low frequency fluctuations during rest are thought to reflect the intrinsic functional architecture of the brain.
- Research Aim: To explore how estrogen treatment in post-menopausal women affects connectivity patterns within specific brain networks.

Participants

Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Estradiol</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55.57 ± 2.9</td>
<td>55.92 ± 3.0</td>
</tr>
<tr>
<td>CI</td>
<td>0.41 ± 0.15</td>
<td>0.21 ± 0.15</td>
</tr>
<tr>
<td>Education</td>
<td>16.7 ± 2.4</td>
<td>15.5 ± 3.0</td>
</tr>
<tr>
<td>Years Since Menopause</td>
<td>5.45 ± 4.3</td>
<td>5.50 ± 3.0</td>
</tr>
<tr>
<td>Prior HRT</td>
<td>Y=2</td>
<td>Y=4</td>
</tr>
<tr>
<td>MPRAGE</td>
<td>21 x 3.0</td>
<td>21 x 3.0</td>
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</tbody>
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This study examined functional connectivity during resting-state fMRI in 23 healthy post-menopausal after 3 months of treatment with 1 mg of oral 17β estradiol or placebo.

Methods

- BOLD T2-FLAIR, and T1 80 x 30, matrix, TE = 2400ms
- 5 mm slice thickness, 90mm gap
- 24 slices
- 256 volumes
- TR = 15000ms
- TE = 35ms

RSFC Preprocessing

- SPM time correlation
- Bandpass filtering
- Smoothing: 6 mm Gaussian kernel

rsFC Analysis

- To identify temporally coincident regional BOLD time courses, rsFC analyses were performed using the Conn toolbox in MATLAB
- A 7-network parcellation of the brain obtained from Yeo et al. (2011) was used as a metric of segmentation and differentiation of distributed brain networks
- The DAN, Frontoparietal, and DMN masks were chosen as networks of interest and each of the 3 individual network ROIs was then entered into the Conn toolbox as a user defined ROI.
- Seed regions were chosen based on prior literature for:
  - Dorsal Attention Network (DAN): bilateral superior parietal lobe (SPL) seeds
  - Frontoparietal Network: bilateral dorsolateral prefrontal cortex (dPFC) seeds
  - Default Mode Network (DMN): posterior cingulate (PCC) seed

Statistical Analyses

- Differences in connectivity between estradiol and placebo treated groups were evaluated using independent samples t-tests.
- Group contrasts for a given seed region were restricted to the appropriate resting-state network mask.

Results

Dorsal Attention Network (DAN)

Greater connectivity was observed in the placebo treated group between bilateral SPL seed regions and regions in DAN (p=0.01, k=38) compared to the estrogen treated group.

Default Mode Network (DMN)

Greater connectivity was observed in the placebo treated group between a PCC seed region and regions in DMN (p=0.01, k=46) compared to the estrogen treated group.

Conclusions

- Results indicate that estrogen treatment in post-menopausal women reduces functional connectivity within DAN and DMN.
- These data add to findings of increased baseline connectivity in post-menopausal women with high levels of subjective cognitive complaints, and suggest that estrogen benefits in cognition is tied to decreased connectivity within DAN and DMN.
- Whether this estrogen effect on connectivity impacts cognitive functioning and subjective cognitive complaints in post-menopausal women will require further work.
- Alteration in brain connectivity may be important for the critical period effects of estrogen on brain functioning that have been noted for cognitive performance in aging.

Support

This research was supported by the following grants: NIA R01 AG021476, NIA K01 AG030380, U1L TR000445, M01-00109, Vanderbilt CTSA grant 1 UL1 RR024975, and the Vanderbilt Brain Institute Clinical Neuroscience Scholars Program (to JNV).

References

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