Reproductive hormones and cognitive function among community-dwelling older men: The Concord Health and Ageing in Men Project

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Are you a man over the age of 70?

Join our world leading study of men’s health

CHAMP

Concord Health and Ageing in Men Project

If you are a man aged 70 or older who lives in the Burwood, Canada Bay or Strathfield areas, Concord Hospital doctors invite you to join CHAMP.

To find out more, call Melisa Litchfield on 1800 174 287.

CHAMP is funded by the National Health & Medical Research Council to improve health of older men.
Introduction

• Age-related changes in male hormones

Age-Related Decline in Blood Testosterone

- MMAS (N=2726)
- BLSA (N=1002)
- Rancho Bernardo (N=856)
- Brazil (N=965)
- Vermeulen (N=250)
- Morley (N=336)

New England Research Institute
Introduction

• Studies have reported conflicting results of associations between testosterone and estradiol levels and cognitive function
• Validity and methodology of these studies remain questionable
• Lack of longitudinal study on this relationship
Methods - Selection

• Baseline cross-sectional (n=1502): diagnosed dementia

• Longitudinal (n=733): change in MMSE; excluded diagnosed dementia, non-english speaker
Methods - Hormones

• Study Hormones: testosterone (TT), dihydrotestosterone (DHT), estradiol (E2), estrone (E1), sex hormone-binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and free testosterone (cFT)

• Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) – GOLD STANDARD for steroid assays
Methods - Cognition

• Cognitive Function: Specialist dementia diagnoses at baseline with MMSE and IQCode screening
• Mini Mental State Examination (MMSE) at both Baseline and 2-Year Follow-up
• Change in MMSE: Reliable Change Index (RCI)
Methods - RCI

- RCI = \((X_2 - X_1) - (M_2 - M_1)\) / SED
- RCI < -1.96 was defined as reliable deterioration (95% CI)

- Eg. \(X_1 = 28.0\) \(X_2 = 24.0\)
  \(M_1 = 28.5\) \(M_2 = 28.4\)
  SED=1.81

- RCI = \(((24.0 - 28.0) - (28.4 - 28.5)) / 1.81 = -2.27\)
Baseline characteristic of the study participants according to diagnosed dementia (n=1502)

<table>
<thead>
<tr>
<th>Diagnosed Dementia</th>
<th>Yes  (n=204)</th>
<th>No   (n=1298)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (ng/ml)</td>
<td>4.30</td>
<td>4.24</td>
<td>0.70</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>54.3</td>
<td>51.3</td>
<td>0.12</td>
</tr>
<tr>
<td>DHT (ng/ml)</td>
<td>0.39</td>
<td>0.37</td>
<td>0.22</td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>10.4</td>
<td>9.26</td>
<td>0.10</td>
</tr>
<tr>
<td>FSH (IU/L)</td>
<td>16.2</td>
<td>14.2</td>
<td>0.12</td>
</tr>
<tr>
<td>E2 (pg/ml)</td>
<td>26.7</td>
<td>25.1</td>
<td>0.36</td>
</tr>
<tr>
<td>E1 (pg/ml)</td>
<td>40.2</td>
<td>40.3</td>
<td>0.96</td>
</tr>
<tr>
<td>cFT</td>
<td>59.1</td>
<td>59.7</td>
<td>0.69</td>
</tr>
</tbody>
</table>
Results

ORs of Cognitive Decline over 2-year Follow-up

- Total Testosterone
- Estradiol
- Estrone
- Free Testosterone
Results

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>+ Age</th>
<th>+Education, BMI, Smoking, Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E2 n=733</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>3.44 (1.10-10.76) *</td>
<td>3.96 (1.23-12.69) *</td>
<td>3.53 (1.07-11.63) *</td>
</tr>
<tr>
<td>3rd</td>
<td>1.84 (0.53-6.41)</td>
<td>2.04 (0.57-7.23)</td>
<td>1.97 (0.55-7.10)</td>
</tr>
<tr>
<td>2nd</td>
<td>0.98 (0.24-3.97)</td>
<td>1.15 (0.28-4.79)</td>
<td>1.08 (0.26-4.52)</td>
</tr>
<tr>
<td>Lowest</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*L*inear Trend p<0.05
Discussion

- Our findings suggest a possible direction of High E2 to cognitive decline in aging men
- Honolulu-Asia Aging Study (n=2974) presented similar results
- Estrogen have no or deleterious effect on cognition in post-menopausal women
Strengths and Limitations

Strengths

• High sensitivity in measuring E2 by LC-MS/MS - new possible risk factor and prevention for cognitive function
• Cross-sectional vs Longitudinal
• Well representative community based sample

Limitations

• Lack of follow-up dementia diagnoses
Conclusion

• Testosterone - null association in cognitive function
• High Estradiol (E2) is associated with cognitive decline
• Biological mechanism of the cause or effect needs to be determined
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Thank You