The impact of pro-inflammatory cytokines on learning and memory in late-life depression and healthy older adults.

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Background
- Learning and memory problems are common in healthy ageing and late-life depression (LLD).
- There is growing evidence that pro-inflammatory cytokines may also affect learning and memory.
- Pro-inflammatory markers are often elevated in ageing, age-related vascular disease and depression.
- The impact of pro-inflammatory cytokines may be exacerbated in LLD versus healthy older adults (HOA).

Hypotheses
- Pro-inflammatory cytokines will be higher in LLD compared to HOA.
- Pro-inflammatory cytokines will be associated with learning and memory, particularly in LLD.

Methods
- Participants: 34 HOA, 24 LLD(aged ≥ 60 years)
- Depression rating: HDRS (LLD, range=15-27; HOA, range=0-6) and GDS.
- Cognitive Assessment: Learning, immediate free recall from CVLT; Logical Memory & Visual Reproduction. Memory, long delay free recall from the above measures.

Table 1: Group demographics, mean (standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>HOA (n=34)</th>
<th>LLD (n=24)</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70.15 (6.07)</td>
<td>67.21 (9.09)</td>
<td>F=2.18, p=.145</td>
</tr>
<tr>
<td>Sex (m,f)</td>
<td>13,21</td>
<td>8,16</td>
<td>X²=.146, p=.786</td>
</tr>
<tr>
<td>Highest Ed.</td>
<td>16.41 (3.01)</td>
<td>15.92 (2.75)</td>
<td>F=.409, p=.525</td>
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<tr>
<td>GDS</td>
<td>2.10 (2.78)</td>
<td>18.86 (5.80)</td>
<td>F=186.50, p&lt;.001</td>
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<tr>
<td>Learning</td>
<td>-.046 (.816)</td>
<td>.065 (.807)</td>
<td>F=.260, p=.612</td>
</tr>
<tr>
<td>Memory</td>
<td>-.096 (.717)</td>
<td>.136 (.882)</td>
<td>F=1.22, p=.274</td>
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</tbody>
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- Pro-inflammatory cytokines: Interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and Interleukin-6 (IL-6) were measured in plasma/serum, ELISA Quantakine kits.
- MRI, acquisition: Philips Achieva 3T. T1-w high resolution 3D MPRAGE; FOV=240mm;134 contiguous axial slices TR/TE=8.4/3.9ms; flip angle=8°; voxel size=1.1X1.1X1.1mm).
- MRI, image analysis: Left and Right hippocampal volumes extracted with Freesurfer image analysis suite.

Results, Group differences

Figure 1: No hippocampal volume by group differences

Figure 2: Association between IL-6 and Memory by group

Table 2: Pro-inflammatory Cytokines by Group

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>HOA (n=34)</th>
<th>LLD (n=24)</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β</td>
<td>1.52 (.699)</td>
<td>2.38 (1.03)</td>
<td>F(1,56)=14.49, p&lt;.001</td>
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<tr>
<td>TNF-α</td>
<td>3.09 (1.40)</td>
<td>4.05 (2.16)</td>
<td>F(1,56)=4.18, p=.046</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.24 (.443)</td>
<td>2.03 (1.22)</td>
<td>F(1,56)=11.73, p&lt;.001</td>
</tr>
</tbody>
</table>

- GDS (across whole sample) correlated significantly with:
  - IL-1β (r=.379, p=.017)
  - IL-6 (r=.390, p=.014)
  - NOT with TNF-α (r=.121, p=.461)

Results, Logistic Regression Analyses

- Learning (41.4%; F=13.05, p<.001) explained by:
  - Education level (21.2%)
  - Right hippocampal volume (20.2%)

- Memory (40.7%; F=9.92, p<.001) explained by:
  - Education level (21.4%),
  - Right hippocampal volume (17.1%),
  - Group x IL-6 interaction term (6.7%)

Conclusion
- IL-1β, TNF-α and IL-6 were higher in LLD versus HOA.
- IL-1β and IL-6 correlated significantly with severity of depression across the whole sample.
- High levels of IL-6 seem to impact Memory in LLD group but not HOA.
- Results suggest that the impact of high pro-inflammatory cytokines may be different in LLD versus HOA.
- Pro-inflammatory cytokines may significantly impact cognition in “at-risk population”, but have a lesser impact in healthy ageing.

Acknowledgments

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