Olfactory Identification is Associated with Neuroimaging Biomarkers

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Olfaction in AD

• Multiple studies have shown that patients with MCI and AD show impaired olfactory identification (Doty 1987, Djordjievic 2008, Devanand 2010).

• Studies have also shown an association between olfactory identification impairment and medial temporal lobe neurodegeneration (Growdon 2015, Murphy 2003).

• However, studies have suggested a minimal association with amyloid deposition, which was mostly driven by differences in diagnostic group (Growdon 2015, Bahar-Fuchs 2010).
Goal

With the advent of PET imaging techniques to measure tau deposition \textit{in vivo}, we sought to evaluate the relationship between olfactory identification and cerebral tau deposition on $[^{18}\text{F}]$Flortaucipir PET, as well as medial temporal (MTL) neurodegeneration, in participants at-risk for Alzheimer’s disease.
Methods

- 33 individuals were included in the analysis, including 19 cognitively normal older adults (CN), 7 with subjective cognitive decline (SCD), and 5 with MCI.

<table>
<thead>
<tr>
<th></th>
<th>CN (n=19)</th>
<th>SCD (n=10)</th>
<th>MCI (n=5)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68.5 (6.9)</td>
<td>72.2 (6.4)</td>
<td>75.7 (10.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Education (years)</td>
<td>17.6 (2.0)</td>
<td>17.5 (2.0)</td>
<td>16.0 (4.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Sex (M, F)</td>
<td>4, 15</td>
<td>4, 6</td>
<td>4, 1</td>
<td>0.046</td>
</tr>
<tr>
<td>CDR – Sum of Boxes‡</td>
<td>0.2 (0.3)</td>
<td>0.1 (0.2)</td>
<td>1.2 (1.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>MoCA Total Score‡</td>
<td>26.8 (2.5)</td>
<td>26.1 (2.3)</td>
<td>22.5 (3.8)</td>
<td>0.024</td>
</tr>
<tr>
<td>Craft Story Immediate Recall‡,§</td>
<td>16.4 (3.5)</td>
<td>16.7 (2.1)</td>
<td>12.0 (2.7)</td>
<td>0.016</td>
</tr>
<tr>
<td>Craft Story Delayed Recall‡,§</td>
<td>15.8 (3.5)</td>
<td>17.5 (2.7)</td>
<td>10.1 (4.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>CCI – Self (12 items)‡,¶</td>
<td>16.2 (4.1)</td>
<td>24.0 (4.4)</td>
<td>33.5 (12.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCI – Informant (12 items)‡,#</td>
<td>17.4 (6.6)</td>
<td>15.2 (3.8)</td>
<td>26.1 (2.8)</td>
<td>ns</td>
</tr>
<tr>
<td>UPSIT Total Score**</td>
<td>34.5 (2.3)</td>
<td>35.7 (3.3)</td>
<td>28.7 (7.0)</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Methods

Structural MRI scans were collected and analyzed using Freesurfer version 5.1 to extract medial temporal lobe (MTL) volumes.

28 also underwent [18F]Flortaucipir PET, which was collected and pre-processed using standard techniques to generate SUVR images (normalized to cerebellar crus).

Olfactory identification was assessed with the University of Pennsylvania Smell Identification Test (UPSIT).

The relationship between olfactory identification and neurodegeneration and tau deposition were assessed using a linear regression model, covaried for age, sex, and intracranial volume (MRI only).

http://www.hnoinfo.com/fb/fb0405arnold/tes_top.html
Results

Risacher et al. (2017) *Alz & Dementia: DACM*
Results

Risacher et al. (2017) Alz & Dementia: DACM
Results

Risacher et al. (2017) *Alz & Dementia: DACM*

- UPSIT Total Score vs. Entorhinal Cortex Tau
  - $r = -0.552$
  - $p = 0.009$

- UPSIT Total Score vs. Fusiform Gyri Tau
  - $r = -0.604$
  - $p = 0.004$
Results

A) Association between Tau Deposition and UPSIT Total Score in all participants

B) Association between Tau Deposition and UPSIT Total Score in CN and SCD only

Cluster p<0.05 (FWE)

Risacher et al. (2017) Alz & Dementia: DACM
Conclusions

• Olfactory identification was not associated with amyloid (*data not shown*) but was associated with MTL neurodegeneration.

• Olfactory identification was associated with MTL tau deposition both on regional and voxel-wise analysis.

• Similar results were observed in cognitively normal individuals only (CN/SCD).

• This test may have utility to detect AD neuropathology in early disease stages.
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