Background:
Individuals with mild cognitive impairment (MCI) have a higher chance of developing Alzheimer’s disease (AD). Amnestic MCI is characterized by impaired delayed recall on verbal and nonverbal memory tests.

California Verbal Learning Test (CVLT) is used to determine an individual’s verbal memory aptitude. Verbal memory is measured with a list of common words that are to be remembered by the subject over several trials. The words are categorized in order to test the subject’s severity in decline. The association between cognitive decline and cortical atrophy can be measured using brain imaging.

Objective:
To identify regional cortical thickness differences associated with verbal memory impairment in a sample of cognitively normal (NC) and MCI subjects.

Methods:
44 NC (mean MMSE 29.3±0.8) and 24 amnestic MCI (mean MMSE 27.9±1.8) subjects from the UCLA ADRC database were scanned with T1-weighted magnetic resonance imaging (SPGR, TR 28 ms, TE 6 ms, FOV 22 cm, matrix 256x192, slice thickness 1.5 mm, no gap).

Mean demographic information is presented in Table 1. We used ANOVA with post-hoc Bonferroni correction and Chi squared tests to examine for demographic and MMSE differences between diagnostic groups. CVLT-II long delay free recall scores were age- and education-corrected. After intensity normalization, the images were aligned to ICBM space. Following 3D hemispheric reconstruction, 38 sulci per hemisphere were traced and averaged across subjects. Cortical thickness defined as the 3D distance from the gray/white matter to the gray matter/cerebrospinal fluid interface was computed at each hemispheric surface point and mapped onto the corresponding hemispheric model in exact spatial correspondence (see Figure 1).

The cortical surfaces were parameterized, flattened and warped, allowing for explicit matching of cortical topography prior to averaging across subjects. Cortical thickness defined as the 3D distance from the gray/white matter to the gray matter/cerebrospinal fluid interface was computed at each hemispheric surface point and mapped onto the corresponding hemispheric model in exact spatial correspondence (see Figure 1).

Linear regression models were applied to investigate the associations between CVLT delayed recall scores and cortical atrophy, while controlling for age and education. Multiple comparisons correction was applied, using the permutation method and a threshold of p<0.01.

Table 1. Demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>NC (N=44)</th>
<th>MCI (N=24)</th>
<th>Statistic</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.1 (7.2)</td>
<td>72.1 (5.7)</td>
<td>F=12.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>26:18</td>
<td>17:7</td>
<td>χ²=0.92</td>
<td>0.337</td>
</tr>
<tr>
<td>Education (years)</td>
<td>17.3 (2.4)</td>
<td>16.7 (2.8)</td>
<td>F=0.82</td>
<td>0.369</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.3 (0.8)</td>
<td>27.9 (1.8)</td>
<td>F=21.49</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results:
CVLT delayed recall showed a significant positive association with cortical thickness in the left hemisphere (p_{corrected}=0.005) and trend-level association in the right hemisphere (p_{corrected}=0.072) (see Figure 2). Regionally, most pronounced associations were seen bilaterally in the entorhinal, parahippocampal, inferior temporal, lateral temporal and posterior cingulate cortical regions. Additional associations were detected in the left superior frontal gyrus, left orbitofrontal, left supplementary motor area and left anterior cingulate cortices.

Conclusions:
The observed associations fit well with our expectations and mapped to cortical areas involved in encoding and recall (entorhinal and parahippocampal areas), retrieval (posterior cingulate cortex), verbal processing (left lateral temporal and parietal cortices) and executive function (frontal association areas). The orbitofrontal cortex is known to play a role in strategizing and resistance to interference during CVLT administration.

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