Prediction of conversion from amnestic mild cognitive impairment to Alzheimer’s disease using proton magnetic resonance spectroscopy

Toshiyuki Watanabe, M.D., Ph.D. 1) 2)  Akihiko Shino, M.D., Ph.D. 3)  Ichiro Akiyama, M.D., Ph.D. 1) 2)

*Corresponding author: 1) Faculty of Health Science, Kyoto Koka Women’s University  2) Higher Brain Function Research Center, Uji Takeda Hospital.  3) Molecular Neuroscience Research Center, Shiga University of Medical Science

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Background
Amnestic mild cognitive impairment (aMCI) has been considered to be a transitional state between healthy aging and very mild Alzheimer’s disease (AD). Most patients with aMCI convert to AD over time, but some of them remain stable as aMCI.

Objective
To predict the conversion from aMCI to AD using proton magnetic resonance spectroscopy (1H-MRS).

Patients and Method
The subjects were 52 healthy control (HC) subjects and 28 patients with aMCI (Table 1). 1H-MR spectra with single-voxel point-resolved spectroscopy at a short echo time (TE) were acquired from both hippocampi and posterior cingulate cortex (Figure 1).

Results
13 patients converted to AD had significantly lower NAA concentrations in both hippocampi when compared to 15 patients remained stable to be aMCI (Figure 2). The mean NAA concentration of both hippocampi equal to or lower than 7.6 mmol/L predicted conversion to AD at 1.0 sensitivity and 1.0 specificity and the area under receiver operating curve (ROC) was 1.0 (Figure 3, Figure 4).

Conclusion
Absolute quantification of 1H-MRS of hippocampus seems to be a useful marker for predicting conversion to AD from patients with aMCI.

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Table 1 Clinical characteristics of healthy control (HC) subjects, Non-converters and Converters

<table>
<thead>
<tr>
<th></th>
<th>HC</th>
<th>Non-Converters</th>
<th>Converters</th>
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</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>52</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Women/men</td>
<td>18/53</td>
<td>6/9</td>
<td>7/6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>69.4 ± 2.3</td>
<td>73.9 ± 2.2</td>
<td>70.2 ± 7.4</td>
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<tr>
<td>Age range</td>
<td>60 - 81</td>
<td>60 - 84</td>
<td>56 - 80</td>
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<tr>
<td>Education (years)*</td>
<td>10.8 ± 0.6</td>
<td>12.3 ± 2.5</td>
<td>12.2 ± 2.7</td>
</tr>
<tr>
<td>MMSE score*</td>
<td>29 ± 1.3</td>
<td>27.7 ± 1.5A</td>
<td>26.3 ± 1.4A</td>
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*Data are given as the mean ± SD. *p < 0.001 (Shaffe’s test) relative to HC. MMSE: Mini-mental state examination.

Figure 1 Locations of voxels of interest (VOIs) for 1H-MRS. A: bilateral hippocampus, B: posterior cingulate gyrus.

In the posterior cingulate gyrus, the VOI was located in the paramedian position.

Figure 2 Examples of 1H-MR spectra.

Figure 3 The absolute concentrations of N-acetylaspartate (NAA) NAA concentrations of 3 groups from each VOI are shown. MH: mean of bilateral hippocampus; RH: right hippocampus; LH: left hippocampus; PC: posterior cingulate gyrus. HC: healthy controls; NC: non-converters; C: converters

Figure 4 Comparison of the receiver operating characteristic curves for NAA (N-acetylaspartate) concentrations in the right ( — RH) and left ( — LH) hippocampi, posterior cingulate gyrus ( — PC), and for the mean concentration of both hippocampi ( — MH).