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Marzia Pesaresi a, Carlo Lovati b, Pierluigi Bertora b, Enrico Mailland b, Daniela Galimberti c, Elio Scarpini c, Pierluigi Quadri d, Gianluigi Forloni e, Claudio Mariani b

a Department of Neuroscience, Istituto di Ricerche Farmacologiche “Mario Negri”, 20157 Milan, Italy
b Neurology Unit, Ospedale Luigi Sacco, University of Milano, Italy
c Department of Neurological Sciences, IRCCS Ospedale Maggiore Policlinico, Milan, Italy
d ORBV, Mendrisio, Switzerland

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Abstract

We compared plasma levels of beta-amyloid 1–42 (pg/ml) found for 146 sporadic Alzheimer (AD) patients, 89 subjects with mild cognitive impairment (MCI) and 89 age-matched controls (CT). AD patients had significantly lower levels (38, 54, 52; \( p < 0.01 \)), unrelated to severity of the disease as assessed by MMSE score, age, sex or APOE4 status. Twenty cases investigated at two time points 18 months apart did not demonstrate further decreases. Thus, the reduction in beta-amyloid 1–42 may be a marker for AD status, specifically, a transition from normal status or MCI to AD, rather than a marker for neurodegenerative processes occurring in the disease.

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1. Methods

The 324 study subjects were recruited at neurology clinics located in Italy and Switzerland. A diagnosis of probable AD was made by exclusion according to NINCDS-ADRDA criteria [3]. Memory impairment was the only cognitive symptoms for the MCI group. The control group was not demented and had MMSE score \( \geq 28 \). The plasma concentration of beta-amyloid 1–42 was measured by a specific sandwich-type enzyme-linked immunosorbent assay ELISA (Inno-geneics Ltd., Belgium). APOE genotype was determined by PCR-RFLP. Levels found for the tree groups were compared by one-way analysis of variance and Tukey’s post hoc test. Statistical significance was set at \( p = 0.05 \).

2. Results and comments

The AD, MCI and CT groups had similar age, sex and educational attainment, the frequency of APOE4 carriers was expectedly group-specific (AD > MCI > CT) (Table 1). The AD group had lower mean plasma beta-amyloid 1–42: 38, 54, 52 (\( p < 0.01 \)) (Fig. 1). For AD, patients levels was unrelated to age, sex or APOE status. No trend was found in relation to severity of disease as measured by MMSE score (Fig. 2 , also see Supplemental material ) or clinical dementia rating (CDR) (data not shown). For the 20 cases followed for 18 months, the mean levels \( \pm S.D. \) were initially 39.3 \( \pm 22.83 \) and 40.9 \( \pm 20 \) pg/ml after follow-up, demonstrating no decrease over time.

One interpretation of these results is that amyloid is sequestered in senile plaques, as has been suggested for the lower levels of beta-amyloid 1–42 in the CSF of AD patients [4]. In support of this point of view lower levels of CSF are found with greater accumulation of amyloid in autopsy stud-
Table 1
Characteristics of the population in the study, the frequency of ApoE –/4 and mean plasma beta-amyloid 1–42 levels

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>AD</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>89</td>
<td>146</td>
<td>89</td>
</tr>
<tr>
<td>Age (years ± S.D.)</td>
<td>68.23 ± 12.08</td>
<td>73.76 ± 7.62</td>
<td>75.37 ± 8.18</td>
</tr>
<tr>
<td>Range</td>
<td>24–92</td>
<td>47–99</td>
<td>52–90</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>57/32</td>
<td>111/35</td>
<td>56/33</td>
</tr>
<tr>
<td>Education (mean ± S.D.)</td>
<td>10.13 ± 4.08</td>
<td>6.72 ± 3.68</td>
<td>9.19 ± 3.65</td>
</tr>
<tr>
<td>Range</td>
<td>3–19</td>
<td>0–19</td>
<td>3–20</td>
</tr>
<tr>
<td>MMSE (mean ± S.D.)</td>
<td>27.11 ± 2.45</td>
<td>18.05 ± 5.1</td>
<td>24.14 ± 3.45</td>
</tr>
<tr>
<td>Duration of illness (mean ± S.D.)</td>
<td>3 ± 1.0</td>
<td>2 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>ApoE –/4 carriers (%)</td>
<td>5.50</td>
<td>29.09</td>
<td>20.00</td>
</tr>
</tbody>
</table>

CT: elderly, cognitively normal controls; AD: Alzheimer’s disease; MCI: mild cognitive impairment.

Fig. 1. Plasma Aβ (1–42) levels in control, AD and MCI subjects. Larger markers show the mean value for each group. The inset shows the histogram of the same values. CT: elderly, cognitively normal controls; AD: Alzheimer’s disease; MCI: mild cognitive impairment.

Fig. 2. Plasma Aβ (1–42) in relationship to clinical severity of AD assessed by the mini mental state examination (MMSE). MMSE had no correlation with Aβ (1–42) levels.

Figures [1] and mice overexpressing mutated human APP [2]. In transgenic mice, there was an equilibrium between plasma and CSF levels. Our data are consistent with both sequestration and equilibrium. Clinically, the transition in MCI status to AD status might thus be identified by serial samples of measurements made for selected patients. This possibility should be investigated.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neurobiolaging.2006.03.004.

References