Introduction

Alzheimer’s is the most common form (around 50-60%) of all dementia types and is the seventh leading cause of death in all ages in the USA. Although it is estimated that there are over 24 million people worldwide with dementia today [1], this figure is projected to double by 2025 as a result of the rising age population in particular in less developed countries.

Clearly the socio-economic costs are huge, in the USA the average lifetime cost of care for an individual with Alzheimer’s estimated to be $174,000. Moreover, this does not include the additional costs to business for employees who are caregivers.

Although there is currently a lack of treatment options to arrest the disease, early diagnosis and active management strategies can potentially delay the onset of the more debilitating symptoms. Thus, early and accurate detection of AD is therefore critical to improving the quality of life of the patient and caregivers.

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Materials and Methods

Patient cohort

Whole blood was collected prior to diagnosis from 251 individuals in PIGeneTM Blood RNA tubes from memory clinics in Norway. These included 125 patients subsequently diagnosed with AD (based on the NINDS-DS criteria for dementia syndrome). 98 age-matched healthy controls and 28 young healthy controls (see Table 1). In addition 10 MCI patients were included in the study.

Table 1. Demographic information of patient cohort and controls [1].

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
<th>Healthy</th>
<th>AD</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy control (n=98)</td>
<td>78 ± 7</td>
<td>85%</td>
<td>15%</td>
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<tr>
<td>Young controls (n=28)</td>
<td>22 ± 3</td>
<td>67%</td>
<td>33%</td>
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</tbody>
</table>

Gene extraction

The expression analysis was done on the AB 1700 System, which contained an AD-specific gene signature in a custom format. The genes were selected based on the performance characteristics from previous studies using an Applied Biosystems Whole Genome Array [3]. A total of 8995 gene probes were available after data normalization. Selecting variables were selected previously for prototype development. However, AD-grading was not used in the selection process (only AD and control). Subsequently, analysis of the following variables (probe sets) was done with respect to the assigned AD grades: All variables; 1200-set; 184-set; and the 52-set.

Results and Discussion

The data presented show the lack of a definite trend of AD classification with AD grade from 1-4 indicating the complexity in predicting AD-grade solely from the currently available gene expression data (Figure 2). The differences between grade 1, 2, and 3 are subtle, with trained predictors tend to classify samples as grade 2, which is the dominating class in the data set.

The lack of a clear correlation with advancing AD grade is also consistent with other findings. β-amyloid imaging PET in mild AD patients suggests that amyloid deposition reaches an equilibrium or plateau very early in the course of AD [2]. This may reflect a more general principle in the biological progression of the disease and further emphasizes the need for early detection.

Interestingly, the MCI group identified in the current study support an increasing trend from healthy controls to AD grade 1, 2, and 3. This finding further supports the idea that the current gene expression signature could be of value in AD detection in the early stages of the disease.

Conclusions

- The gene expression signature appears to detect AD grades 1-4 with a similar level of accuracy independent of disease severity.
- A linear increasing trend from the healthy controls via the MCI group to AD grade 1 suggests some predictive value.
- Absence of a clear trend with increasing AD grade 1-4 may reflect the biological nature of the disease progression.

Individuals within the MCI group may be associated with a tendency for conversion to AD grade 1.

References