

From Patient Data to Personalised Healthcare in Alzheimer's Disease



Dementia has been recently identified as a health priority both in Europe and in the USA. Efficient solutions for early diagnosis and treatments are highly needed. The PredictAD project has developed several approaches for making the diagnosis more efficient and objective.

Global challenge

Alzheimer's disease, the most common cause of dementia, alone accounts for costs equivalent to about 1% of the gross domestic product (GDP) of the whole world and the number of persons affected will double in the next 20 years. Early diagnostics plays a key role in solving the problem because treatments of this irreversible disease should be started in an early phase to be efficient. Various treatments are currently under extensive development. So far, the lack of systematic and objective ways to identify persons for treatments has been apparent.

Diagnostics based on biomarkers

At present only post mortem pathology reliably indicates that an individual suffered from AD. Novel diagnostic guidelines emphasize the importance of various biomarkers from cerebrospinal fluid (CSF), magnetic resonance imaging (MRI), positron emission tomography (PET) and genetic profiling in addition to neuropsychological examinations. Still, the time from symptoms to diagnosis is on average 20 months in Europe. With regards to prevention, the disease is thought to progress even more than a decade prior to the appearance of the first symptoms.

The main goal of the EU-funded PredictAD research project is to develop novel approaches

- for extracting efficient biomarkers, and
- for combining this biomarker information

to enable objective earlier diagnosis and follow-up of treatment efficacy in AD (Fig. 1).

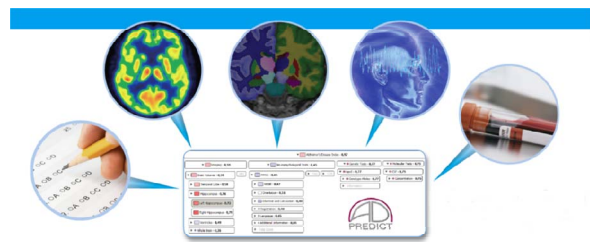


Figure 1: PredictAD combines patient measurements from multiple sources (clinical tests, PET & MRI, electrophysiology and blood).

Improved biomarkers for diagnostics

MRI is an excellent tool for measuring the brain tissue loss, a well-known hallmark of AD. In current clinical practice, images are interpreted mostly only by visual inspection but there is a great need for objective measurements. PredictAD has managed to develop efficient tools for measuring the size of the hippocampus, a key area in AD, and the rate of its tissue loss, and two modern approaches based on comparing patient data with previously diagnosed cases available in large databases. PET is another imaging technology studied in the project. A novel tracer developed recently especially for diagnostics of AD provides promises for very early diagnosis of the disease.

Various biomarkers extracted from CSF are known to be strongly related with the disease. Blood samples would be an excellent source for detecting AD at early phase as blood sampling is not considered an invasive technique. PredictAD has studied the role of metabolomic and protein compounds in AD from blood samples with promising results.

PredictAD has studied the performance of a novel technology, transcranial magnetic stimulation (TMS) combined with electroencephalographic (EEG) measures in detecting the disease. The strength of TMS/EEG is that it allows direct and non-invasive

perturbation of the human cerebral cortex without requiring the subject's collaboration. Our study has shown significant changes in AD patients compared with healthy aging people.

Holistic view of patient

Diagnosis requires a holistic view of the patient combining information from several sources, from biomarkers to interviews. This process involves subjective reasoning and requires strong expertise from the clinicians.

Modern hospitals have huge data reserves containing hidden information about the appearance of different diseases and about the variability of humans in general. This information could be utilised in diagnostics by systematic mathematical modelling leading to more objective and reliable diagnostics.

PredictAD has designed a totally novel approach for measuring objectively the state of the patient. This decision support system, developed in close collaboration with clinicians, compares patient measurements with measurements of other patients in large databases and provides at the end an evidence-based index and graphical representation reflecting the state of the patient (Figure 2).

The project has shown that **clinicians are able to detect persons that convert later to AD more accurately** using the tool than previously. The **clinicians are also much more confident about their clinical decisions**. Both of these factors make possible earlier diagnostics.

Conclusions

Although Alzheimer's disease is one of the biggest health threads during the next decades, even modest improvements achieved in disease progression may have remarkable effects. It has been estimated that delaying the disease by one year would reduce the number of AD cases by 10 % globally. Early diagnostics combined with novel drugs under development and early psychosocial care may delay the institutionalization of patients, reducing suffering and the costs to the society. **PredictAD has taken several steps towards solving the challenge of AD diagnostics by many**

innovations and practical solutions. The exploitation of the PredictAD results has been started. Several patent applications have been filed and the technologies developed have been already licensed.

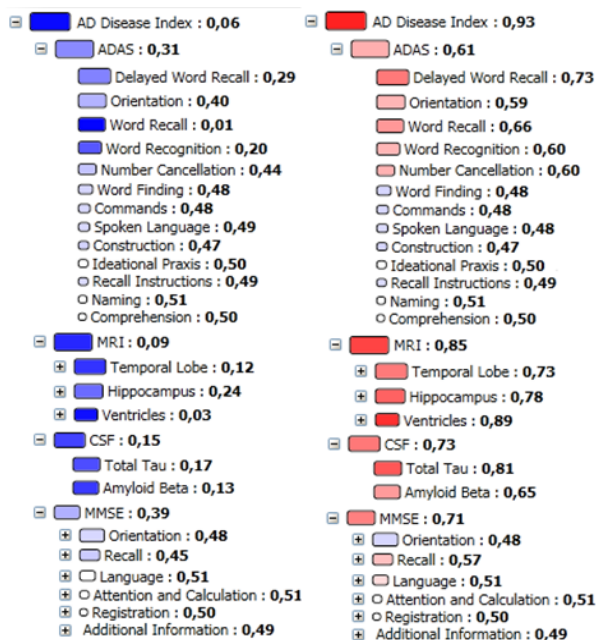


Figure 2: Disease state index (DSI) and its graphical counterpart called disease state fingerprint (DSF), computed for one healthy person (left) and one AD patient (right). The size of the box indicates the relevance of the biomarker (biomarkers not able to separate healthy and AD cases are excluded automatically). Shades of red indicate similarity of the measured data to the AD population, and shades of blue similarity to healthy. The hierarchical representation shows the evidence of the disease for each biomarker, for each measurement system and for all patient data. The disease state index (DSI) is a value between 0 and 1 indicating the disease severity.

Timetable: from 06/2008 – to 11/2011
Total cost: € 3.9 million
EC funding: € 2.9 million
Instrument: ICT-VPH
Project Identifier: ICT-VPH PREDICTAD 224328

Partners

VTT Technical Research Centre of Finland (Finland, co-ordinator), GE Healthcare Ltd. (UK), Nexstim Oy (Finland), University of Eastern Finland (Finland), Imperial College London (UK), University of Milan (Italy), Rigshospitalet (Denmark), and Karolinska Institutet (Sweden).



Important Links:

Project website: <http://www.predictad.eu>

European Commission funded projects: http://ec.europa.eu/information_society/activities/health/research

For further information:

Project Coordinator: Jyrki Lötjönen, VTT Technical Research Centre of Finland: jyrki.lotjonen@vtt.fi
 Tel. +358 20 722 3378