EMIF Deliverable 4.2: Screening algorithms tested and defined

Executive summary

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By using biomarkers diagnosis of Alzheimer's disease (AD) can be made earlier and participants recruited into drug trials in an earlier phase even in the preclinical stage before clinical symptoms are evident. Within EMIF WP2 and WP3 several biomarkers were investigated. In addition, algorithms for the diagnosis of AD based on the criteria of the International Working Group (IWG2) and the National Institute of Aging/Alzheimer's Association (NIA-AA) were applied to the North American Alzheimer's Disease Neuroimaging Initiative cohort (ADNI).

The aim of this deliverable is to report validation of algorithms tested and defined in other cohorts. We applied the most recent update of NIA-AA criteria (2018) labelled as a "research framework" intended to be used in observational and interventional research, not routine clinical care. In these criteria AD is defined by its underlying pathologic processes that can be documented by biomarkers – irrespective of clinical symptoms or signs. Biomarkers are grouped into those of β amyloid deposition, pathologic tau, and neurodegeneration on basis of examination of biofluids or brain imaging.

We validated NIA-AA2018 criteria in the LipiDiDiet study cohort that was the first large long-term nutritional intervention study applying IWG1 criteria for recruitment of subjects with predementia AD. As a whole, in applying the 4 different research criteria (IWG1, IWG2, NIA-AA and NIA-AA2018), large overlap was observed. These results are encouraging for studies recruiting prodromal AD subjects for clinical research which may have access to different or limited types of assessment tools.

Another approach was to apply the Erlangen Score (ES) interpretation algorithm, developed and validated before the current project, and successfully applied in some centres for routine diagnostic purposes. We conclude that 1) ES has a high ability to standardize for the high variability of raw CSF biomarker data, which makes it a useful diagnostic tool for comparing neurochemical diagnoses between different labs or methods used, independently of their specific cutoffs, preanalytical handling procedures, and applied analytical methods. 2) This study further demonstrates the utility of the ES algorithm as a as a tool in predicting cognitive and imaging progression in MCI patients.

In addition, we aimed to replicate the finding from WP3 that brain atrophy measures could increase predictive accuracy for β amyloid deposition in addition to age, memory impairment and APOE-e4 carriership in cognitively normal individuals. We found that hippocampal atrophy did not increased predictive accuracy in an independent clinical dataset. This suggests that hippocampal atrophy may be of limited clinical value for the prediction of β amyloid deposition above age, memory function and APOE genotype.

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