Total alpha-synuclein assay in the Cerebro-Spinal-Fluid is of interest in the differential diagnosis between Alzheimer's disease and dementia with Lewy bodies from the prodromal stage

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Abstract

Background: Several studies have investigated the value of alpha-synuclein assay in the cerebrospinal fluid (CSF) of Alzheimer’s disease (AD) and Dementia with Lewy Bodies (DLB) patients in the differential diagnosis of these two pathologies. However, very few studies have focused on this assay in AD and DLB patients at the MCI stage.

Methods: All patients were enrolled under a hospital clinical research protocol from the tertiary Memory Clinic (CM2R) of Alsace by an experienced team of clinicians. A total of 166 patients were included in this study: 21 control subjects (CS), 51 patients with DLB at the prodromal stage (pro-DLB), 16 patients with DLB at the demented stage (DLB-d), 33 AD patients at the prodromal stage (pro-AD) and 32 AD patients at the demented stage (AD-d). CSF levels of total alpha-synuclein were assessed using commercial enzyme-linked immunosorbent assay (ELISA) for alpha-synuclein (AJ Roboscreen). Alzheimer's biomarkers (t-Tau, P-Tau, Aβ42 and Aβ40) were also measured.

Results: The alpha-synuclein assays showed a significant difference between the AD and DLB groups. Total alpha-synuclein levels are significantly higher in AD patients than in DLB patients. Interestingly is that the levels seem to be altered from the prodromal stage in both AD and DLB. Furthermore, by dividing the patients according to the profiles of Alzheimer's biomarkers typically found or not for each of the two pathologies and then classifying the patients according to the level of alpha-synuclein, we find that alpha-synuclein levels are elevated not only for AD patients with typical “Alzheimer” profile (i.e. 2 or 3 pathological biomarkers) but also for AD patients with a non-typical “Alzheimer” profile (i.e. none or one pathological biomarker).

Conclusions: The modification of total alpha-synuclein levels in the CSF of patients occurs early from the prodromal stage. Moreover, alpha-synuclein assay appears to be of particular interest in the differential diagnosis of AD in cases where the Alzheimer biomarkers do not have a typical profile of the disease, i.e. when there is only one or no pathological biomarker.

Trial registration: ClinicalTrials.gov, (AlphaLewyMa, Identifier: NCT01876459)

Full-text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed.

However, the manuscript can be downloaded and accessed as a PDF.

Figures

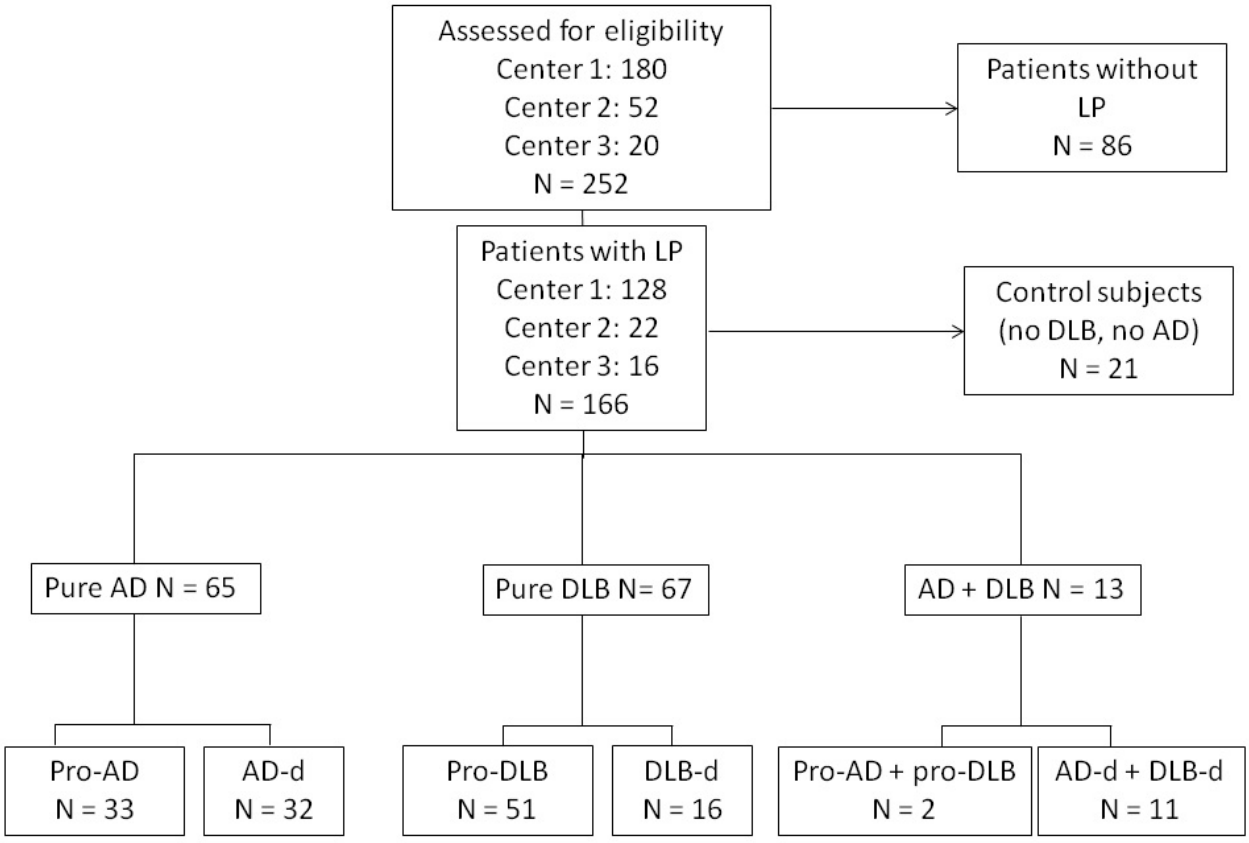

Figure 1

Flowchart of patient selection from AlphaLewyMA study. Center 1: CHU de Hautepierre; Center 2: Hôpital de la Robertsau; Center 3: Hôpitaux Civils de Colmar; AD, Alzheimer's disease; DLB, Dementia with Lewy Bodies; Pro-AD, prodromal-AD; Pro-DLB, prodromal-DLB; AD-d, AD-demented; DLB-d, DLB-demented

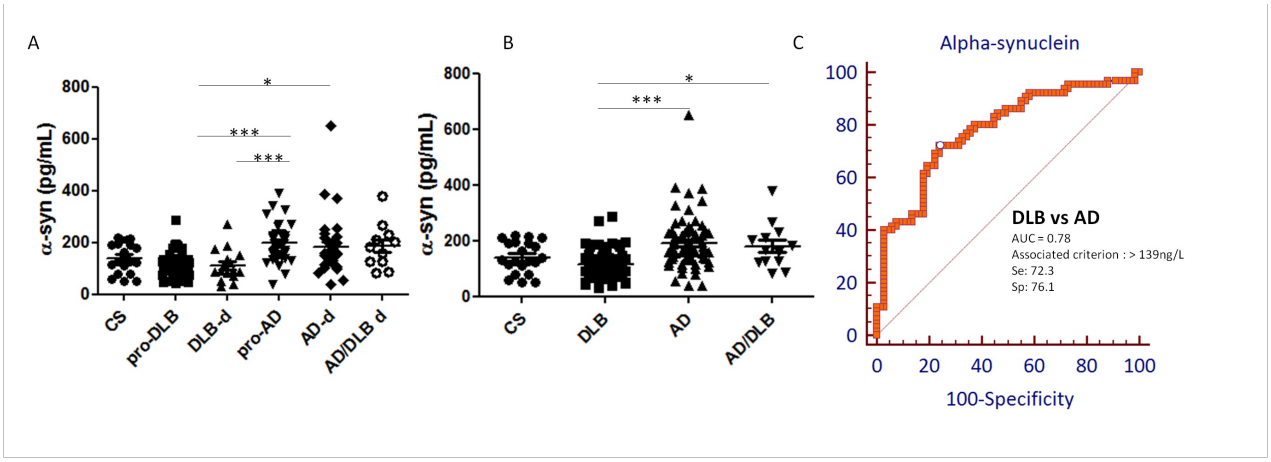

Figure 2

Total alpha-synuclein assay discriminate between AD and DLB (A) and (B) Scatterplots of CSF alpha-synuclein. (A) CSF concentrations of total alpha-synuclein in each patient group (the number of patients per group is: CS n = 21, pro-DLB n = 51, DLB-d n = 16, pro-AD n = 33, AD-d n = 32, AD/DLB-d n = 11) and (B) CSF concentration of alpha-synuclein in CS, DLB (pro-DLB + DLB-d), AD (pro-AD + AD-d) and in AD/DLB (mixed pathologies: pro-AD/DLB + AD/DLB-d). ***p < 0.001; *p < 0,05. p values were calculated using Kruskal-Wallis test with Dunn's multiple comparison test. (C) Alpha-synuclein ROC curve between DLB and AD groups. Prodromal and demented patients were pooled in each group. Number of patients per group: DLB n = 67, AD n = 65. Se: sensitivity; Sp: specificity

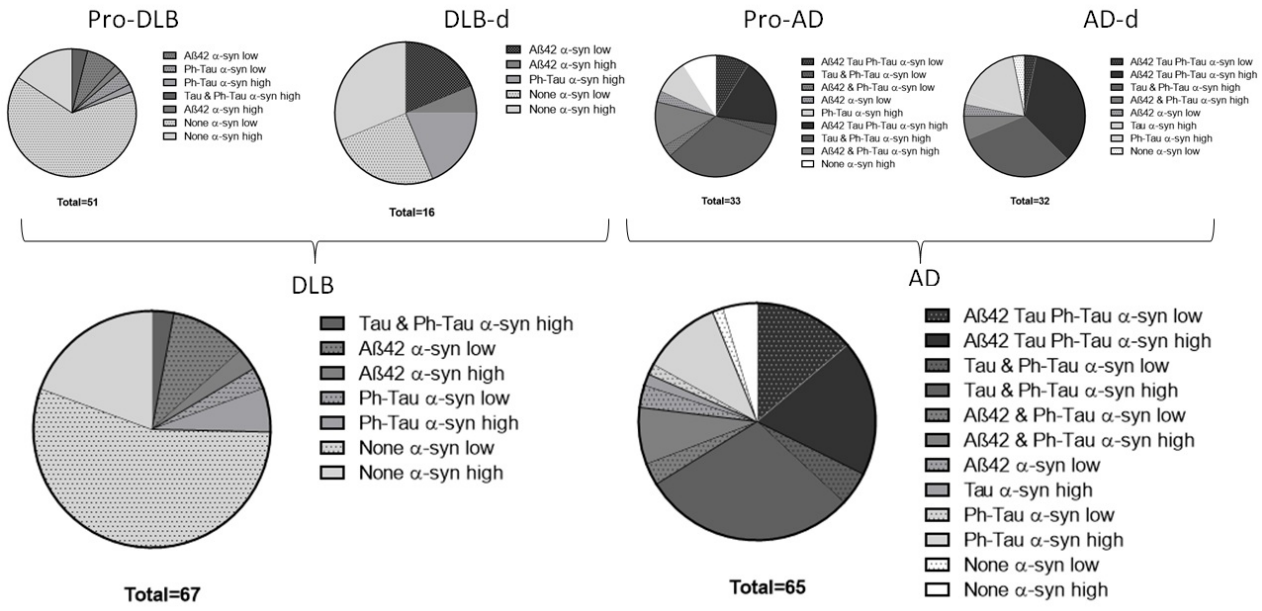

Figure 3

Distribution of the combination of Alzheimer's biomarkers with alpha-synuclein levels for each group. The diagrams show the proportion of patients with pathological Alzheimer's biomarkers, either 3 pathological biomarkers (indicated by Aβ42, Tau and Ph-Tau), or 2 pathological biomarkers (indicated by either Aβ42 and Tau, or Aβ42 and Ph-Tau, or Tau and Ph-Tau), or 1 pathological biomarker (Aβ42, Tau, Ph-Tau), or no pathological biomarker, each with alpha-synuclein level (α-syn low or high using the associated criterion 139ng/L). Note that the pathological “Aβ42” groups include both pathological Aβ42 and/or pathological Aβ42/Aβ40 ratios.