Supplementary Table 1

Baseline demographic, neuropsychological, biomarker, and genetic characteristics of the MCI due to AD population

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| **Demographic characteristics at time of LP** |
| F/M, n | 23 / 15 |
| Age (y), mean ± SD | 72.3 ± 8.5 |
| Age at disease onset (y), mean ± SD | 69.6 ± 8.9 |
| Disease duration (y), mean ± SD | 2.7 ± 2.5 |
| Amnestic/non-amnestic subtype, n | 35 / 3 |
| **Neuropsychological characteristics at time of LP** |
| MMSE (/30), mean ± SD | 25.0 ± 2.6 (n = 35) |
| Executive disorder, n | 14 (n = 28) |
| Immediate memory disorder, n | 24 (n = 33) |
| Delayed memory disorder, n | 28 (n = 32) |
| Language disorder, n | 11 (n = 34) |
| **Biomarker and genetic characteristics at time of LP** |
| Aβ1-42 (pg/ml), mean ± SD | 473 ± 112 |
| T-tau (pg/ml), mean ± SD | 639 ± 292 |
| P-tau181P (pg/ml), mean ± SD | 90.3 ± 29.0 |
| *APOE* ε4 double carriers, n | 7 (n = 35) |
| *APOE* ε4 single carriers, n | 13 (n = 35) |
| *APOE* ε4 non carriers, n | 15 (n = 35) |
| Executive functioning was measured with the FAB or TMT-B test, where a score ≤14 on the FAB and/or a z-score ≤-1.5 on the TMT-B indicated an executive disorder. Immediate memory was assessed with the HDS – item 8 (registration) (≤7), RBANS or WMS-III or IV immediate memory index scores (z-score ≤1.5). Delayed memory was based on the HDS – item 20 (delayed recall) (≤7), RBANS or WMS-III or IV delayed memory index scores (z-score ≤1.5). Language functioning was measured with the RBANS language index score (z-score ≤1.5), and/or the BNT (≤45).Aβ1-42, amyloid-beta protein of 42 amino acids; APOE, apolipoprotein E; BNT, Boston Naming Test; FAB, Frontal Assessment Battery; HDS, Hierarchic Dementia Scale; MMSE, Mini-Mental State Examination; P-tau181P, tau protein phosphorylated at threonine 181; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; TMT-B, Trail Making Test Part B; T-tau, total tau protein; WMS, Wechsler Memory Scale. |

Supplementary Table 2

Follow-up demographic and clinical characteristics of the MCI due to AD population (‘MCI’)

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| Diagnosis at follow-up | MCI | Probable AD |
| F/M, n (\*) | 9 / 6 | 13 / 9 |
| Follow-up time to latest conversion or last consultation (y), mean ± SD | 2.4 ± 1.1 | 2.3 ± 1.5 |
| Amnestic/non-amnestic MCI subtype at follow-up, n | 13 / 2 | *NA* |
| MMSE at last consultation, mean ± SD (\*\*) | 25.2 ± 3.7 (n = 11) | 16.4 ± 6.6 (n = 21) |

(\*) Out of thirty-eight MCI patients, the total follow-up time of one patient was less than one y, while the other patients (in total n = 37) were followed-up clinically for more than one y, before and/or after LP. Thirty-two of these 37 persons were followed-up for more than one y post-LP (\*\*). However, only 31 patients of these 32 are represented in Fig.5 as thin lines since for one patient, none of the MMSE could be time-linked to the LP (+/- 3 months). Therefore, the linear mixed model analysis also included 36 MCI patients in total.

Follow-up demographic characteristics of the dementia due to AD population (‘AD’) post-LP

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| --- | --- |
| F/M, n (\*) | 19 / 13 |
| Follow-up time to last consultation (y), mean ± SD | 2.3 ± 1.6 |
| MMSE at last consultation, mean ± SD | 14.4 ± 8.8 |

(\*) The total subset of AD patients with MMSE data, included in the linear mixed model analysis, involved 45 persons. Thirty-four of them had more than one MMSE, starting from three months before LP. Three of these 34 had their first MMSE less than three months prior to LP and a second MMSE at LP. These 3 patients are not included in this Supplementary table 2 since there was no follow-up after LP. Of the remaining 11 patients with only one recording, 10 had only an MMSE at LP while one subject had no MMSE at LP but one follow-up MMSE. This latter subject is included in Supplementary Table 2, resulting in 32 AD patients that were followed-up after LP.

Supplementary Fig. 1

To determine the affinity constant (KD) of the mAbs ADxNGCI2 and Ng7, biolayer interferometry was performed using the BLItz-system by fortéBIO. A biotinylated peptide containing the epitope of ADxNGCI2 and Ng7 was therefore loaded onto a sensor pre-coated with streptavidin and following a baseline in Phosphate-buffered Saline (PBS) containing 0.05% Tween-20 and 0.05% ProClin300 (PBST), the sensor was exposed to a range of mAb concentrations: 0.333 – 1.667 – 41.67 or 208.3nM (in PBST). After recording association and dissociation (in PBST), and following subtraction of the background, the BLItz data analysis software performed a global fit on the resulting association (ka) and dissociation (kd) rates of the series of mAb concentrations. The plots shown are the interaction of ADxNGCI2 (upper panel) or Ng7 (lower panel) with the biotinylated peptide. The resulting association and dissociation (depicted in the graphs) of the mAbs are visualized in color. The local fitting for each run is depicted in black and summarized in the tables below the graphs. When performing a global fitting on the multiple datasets, the KD (M) corresponding to Ng7 was 6.168e-10, while the KD (M) of ADxNGCI2 was out of range, i.e., <1e-12.

 

Supplementary Fig. 2

CSF samples (n = 3) were aliquoted at day 0 and stored immediately at -80°C or kept at 21°C (closed circles), 4°C (open squares) as well as -20°C (open triangles) during 1, 8, or 15 day(s) before storage at -80°C pending analysis. Levels of neurogranin trunc P75 in all samples were normalized against the concentration in the aliquot stored at -80°C at day 0.

