Supplementary Online Content

Buchhave P, Minthon L, Zetterberg H, Wallin ÅK, Blennow K, Hansson O. Cerebrospinal fluid levels of β-amyloid 1-42, but not of tau, are fully changed already 5 to 10 years before the onset of Alzheimer dementia. *Arch Gen Psychiatry*. 2012;69(1):98-106.

eFigure 1. The levels of cerebrospinal fluid (CSF) Aβ42 in the different diagnostic groups stratified by presence of APOE ε4 alleles. The green bars represent subjects with one or two APOE ε4 alleles, while the blue bars represents subjects without any allele. The levels of Aβ42 did not differ significantly between carriers and non-carriers of the APOE ε4 allele in any diagnostic group. Error bars represent standard error of the mean (SEM).

eFigure 2. Mixture model classification for CSF Aβ42/P-tau ratio (panel A) and CSF Aβ42 (panel B), respectively. Both the CSF Aβ42/P-tau ratio and the CSF Aβ42 levels exhibited a clear bimodal distribution. An Aβ42/P-tau ratio <6.16 (panel A) or Aβ42 <505 ng/L (panel B) were regarded as pathological. The figure is similar to figures 3C and 3D, but also includes healthy controls. (Prodromal AD in red; cognitively stable MCI in dark green; MCI cases who developed dementias other than AD in light green; controls in blue).

eTable 1. CSF biomarker levels in different subgroups of patients with mild cognitive impairment

eTable 2. Demographic data for false positive vs true positive subjects and false negative vs true negative subjects

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. CSF biomarker levels in different subgroups of patients with mild cognitive impairment.

	MCI to AD within 5 y	MCI to AD after 5 y	MCI to other dementias within 5 y	MCI to other dementias after 5 y	Stable MCI with total follow-up ≤ 5 y	Stable MCI with total follow-up > 5 y
N	60	12	17	4	7	34
Baseline Aβ42, ng/L	333 (115)	359 (157)	607 (129)	528 (115)	597 (141)	608 (172)
Baseline Tau, ng/L	786 (436) [a]	495 (258)	536 (560)	326 (144)	250 (235)	307 (172)
Baseline P-tau, ng/L	92.6 (30.0) [a]	69.2 (20.8)	61.7 (28.9)	53.7 (10.9)	54.7 (12.3)	62.7 (14.1)
Baseline Aβ42/P-tau ratio	4.0 (2.4) [a]	5.8 (3.3)	11.0 (3.7)	10.1 (2.4)	11.1 (2.3)	10.3 (3.7)

Data are the mean (± standard deviation). In the present table the following comparisons were made: MCI to AD within 5 y *vs* MCI to AD after 5 y; MCI to other dementias within 5 y *vs* MCI to other dementias after 5 y; and Stable MCI with total follow-up ≤ 5 y *vs* Stable MCI with total follow-up > 5 y.

[a] $p<0.05$, MCI to AD within 5 y *vs* MCI to AD after 5 y.

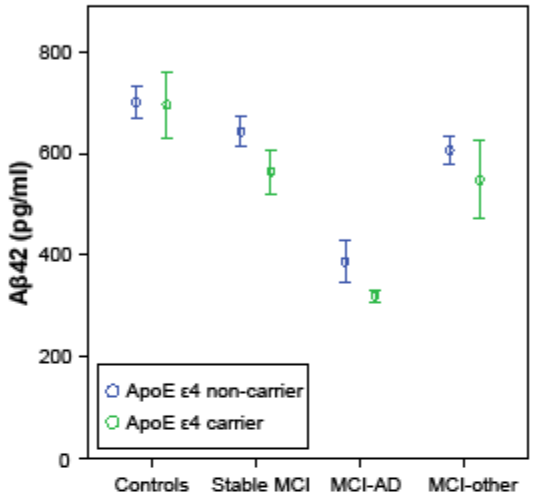
eTable 2. Demographic data for false positive vs true positive subjects and false negative vs true negative subjects.

	True Positive (n=63)	False Positive (n=6)	True Negative (n=56)	False Negative (n=9)
Men/Women	21/42	3/3	34/22	2/7[b]
Age, years	73.6 (5.8)	69.2 (7.1)	64.5 (9.9)	75.7 (5.9) [b]
Carrier of any *APOE ε4* allele	78%	67%	36%	44%
MMSE score at baseline, 0–30 p	26.9 (1.5)	27.0 (1.9)	27.2 (1.8)	26.8 (1.1)
Mean annual change in MMSE, points/year	-3.1 (2.2)	-0.5 (1.6)[a]	-0.7 (1.7)	-1.2 (0.7) [b]
Time under risk for AD, years	3.0 (1.7)	6.8 (3.5)[a]	6.7 (3.4)	4.8 (2.4)
Baseline T-tau, ng/L	795 (420)	787 (846)	319 (206)	332 (132)
Baseline P-tau, ng/L	94 (29)	99 (32)	57 (11)	54 (10)
Baseline Aβ42, ng/L	309 (90)	340 (128)	630 (127)	532 (144)
Baseline Aβ42/P-tau ratio	3.5 (1.2)	3.6 (1.5)	11.3 (2.6)	9.9 (2.9)

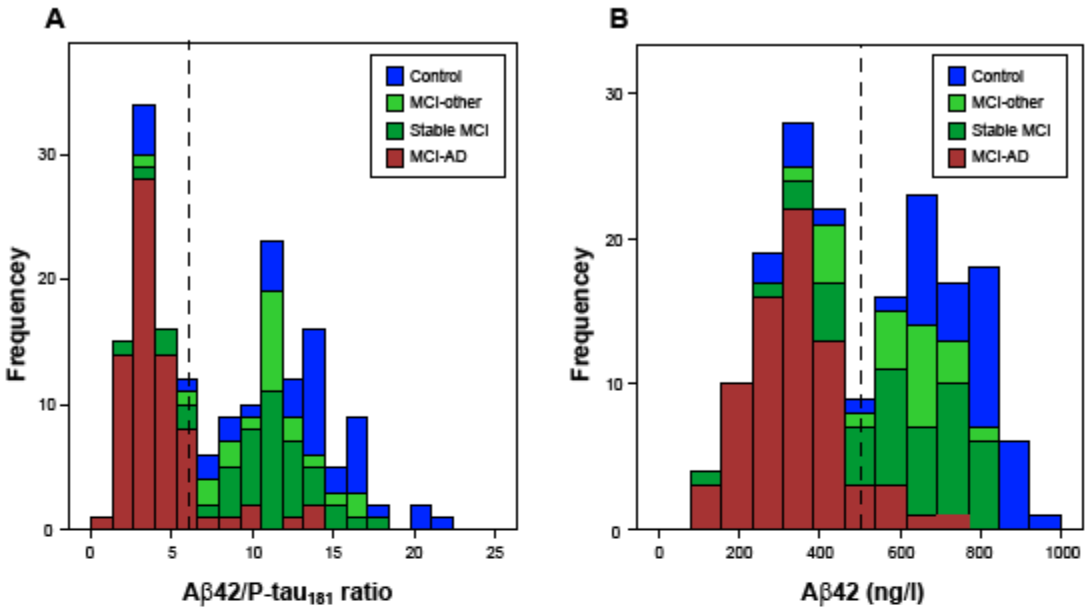
Data are the mean (± standard deviation) or number (%). Only *P*-values <0.008 are considered significant, because of correction for multiple comparisons. Differences between positive and negative subjects are not noted in the table.

[a] p<0.01; True Positive vs False Positive; [b] p<0.05 True Negative vs False Negative.

In eTable 2 we show data on subjects with MCI at baseline with a pathological Aβ42/P-tau ratio (<6.16), who subsequently developed AD (i.e. true positive subjects) and subjects with a pathological Aβ42/P-tau ratio, who did *not* develop AD during follow-up (i.e. false positive subjects). Moreover, we show data on MCI subjects with a normal Aβ42/P-tau ratio (>6.16), who did not developed AD (true negative) and subjects with a normal Aβ42/P-tau ratio, who actually did develop AD (false negative). It is interesting to note that the "true positive subjects" (i.e. MCI-AD cases with a pathological Aβ42/P-tau ratio) exhibited a faster disease progression rate (i.e. they lost more MMSE points per year and exhibited a shorter time period until conversion to AD dementia) than "false negative subjects" (i.e. MCI-AD cases with a normal Aβ42/P-tau ratio) (p<0.05).



eFigure 1
The levels of cerebrospinal fluid (CSF) Aβ42 in the different diagnostic groups stratified by presence of APOE ε4 alleles. The green bars represent subjects with one or two APOE ε4 alleles, while the blue bars represents subjects without any allele. The levels of Aβ42 did not differ significantly between carriers and non-carriers of the APOE ε4 allele in any diagnostic group. Error bars represent standard error of the mean (SEM).



eFigure 2
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