Supplementary information to:

Evidence for Elevated Cerebrospinal Fluid ERK1/2 Levels in Alzheimer's Disease

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1) Age and CSF levels of classical biomarkers tTau, pTau, and Aβ42 in the 4 diagnostic groups

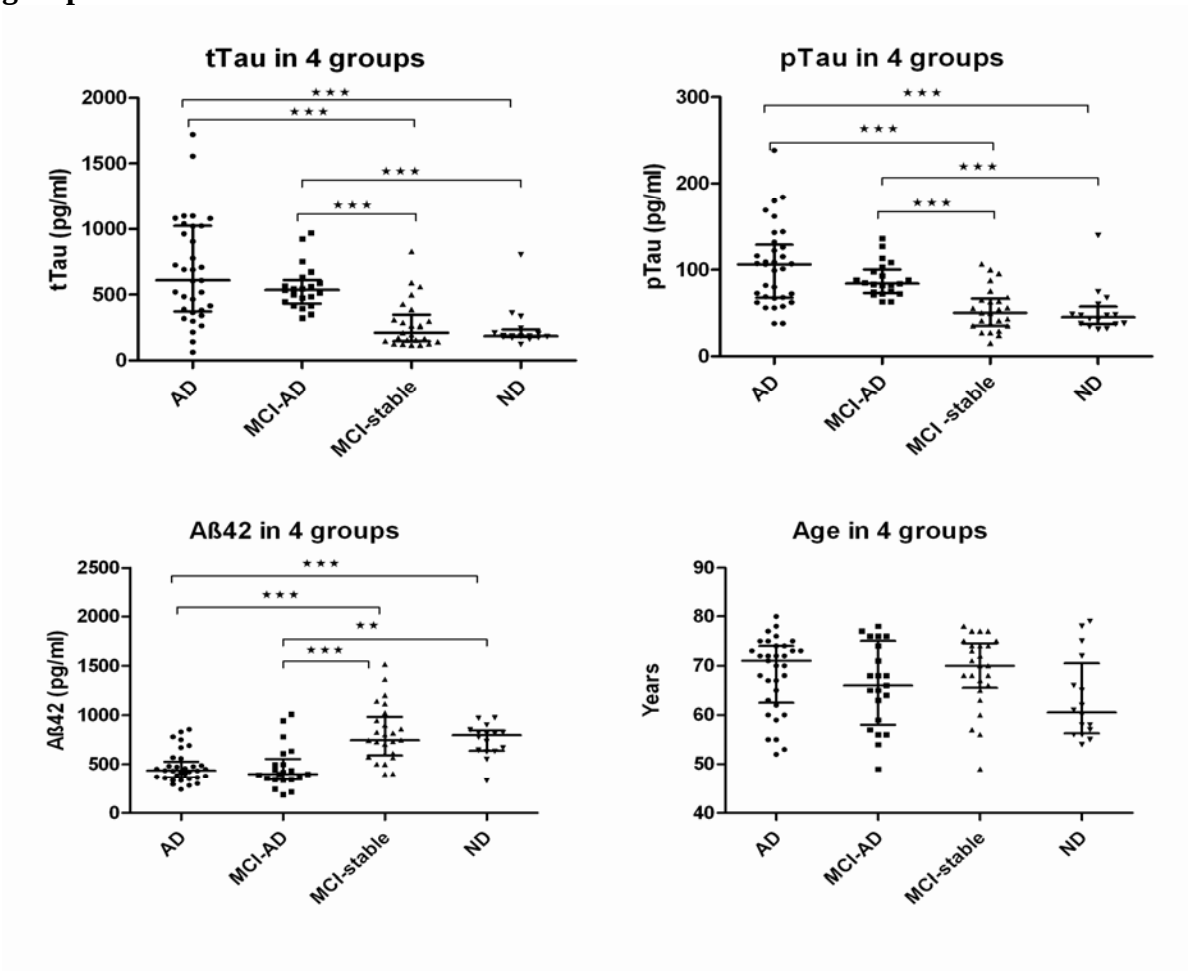

Figure S1: Age distribution and CSF levels of classical biomarkers tTau, pTau, and Aβ42: Non-parametric Kruskal-Wallis test followed by Dunn's multiple comparison test indicated significantly higher tTau and pTau levels (rank sums) in AD- and MCI-AD patients than in the MCI-stable and ND groups. CSF-Aβ42 (rank sums) was significantly lower in the AD and MCI-AD groups than in MCI-stable and ND groups (*: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$). Neither median nor mean ages differed significantly between the 4 groups ($p = 0.1366$ with Kruskal-Wallis test and $p = 0.0999$ with parametric ANOVA test). The bars indicate medians and interquartile ranges. The CSF levels of tTau, pTau and Aβ42 are shown here for comparative purposes. The actual measurements were performed within the context of other studies, and some of the data have been published before [1-4].

2) Table S1: Analysis for correlations between CSF-ERK1/2 and classical biomarkers for each center*.

		tTau	pTau	Aβ42	Age
Perugia all	Spearman r	0.603	0.539	-0.343	0.081
(n=41)	p-value	<0.0001	0.0003	0.028	0.613
Perugia AD	Spearman r	0.359	0.271	-0.45	-0.12
(n=15)	p-value	0.189	0.328	0.092	0.670
Perugia MCI-AD	Spearman r	0.436	-0.319	-0.055	0.083
(n=11)	p-value	0.18	0.339	0.873	0.809
Perugia MCI-stable	Spearman r	0.460	0.460	0.363	0.036
(n=13)	p-value	0.114	0.114	0.223	0.907
Perugia ND		n too small	n too small	n too small	n too small
(n=2)					
Kuopio all	Spearman r	0.245	0.244	-0.520	-0.178
(n=45)	p-value	0.105	0.107	0.0002	0.242
Kuopio AD	Spearman r	0.123	0.100	-0.544	0.058
(n=17)	p-value	0.639	0.701	0.024	0.825
Kuopio MCI-AD	Spearman r	0.067	0.250	-0.150	0.159
(n=9)	p-value	0.880	0.521	0.708	0.678
Kuopio MCI-stable	Spearman r	0.357	0.357	-0.071	-0.487
(n=7)	p-value	0.444	0.444	0.906	0.267
Kuopio ND	Spearman r	-0.196	-0.357	0.098	-0.158
(n=12)	p-value	0.542	0.255	0.762	0.625

* Spearman correlation coefficients (r) and p-values (two-tailed) are indicated.
ERK1/2 measurements below LLOD (n = 9) were excluded from the correlation analysis.

References cited in the supplementary information:

[1] Herukka SK, Helisalmi S, Hallikainen M, Tervo S, Soininen H, Pirttila T (2007) CSF Abeta42, Tau and phosphorylated Tau, APOE epsilon4 allele and MCI type in progressive MCI. *Neurobiol Aging* **28**, 507-514.

[2] Lanari A, Parnetti L (2009) Cerebrospinal fluid biomarkers and prediction of conversion in patients with mild cognitive impairment: 4-year follow-up in a routine clinical setting. *ScientificWorldJournal* **9**, 961-966.

[3] Parnetti L, Lanari A, Silvestrelli G, Saggese E, Reboldi P (2006) Diagnosing prodromal Alzheimer's disease: role of CSF biochemical markers. *Mech Ageing Dev* **127**, 129-132.
[4] Tapiola T, Alafuzoff I, Herukka SK, Parkkinen L, Hartikainen P, Soininen H, Pirttila T (2009) Cerebrospinal fluid {beta}-amyloid 42 and tau proteins as biomarkers of Alzheimer-type pathologic changes in the brain. *Arch Neurol* **66**, 382-389.