Conversion to MCI in healthy individuals with abnormal CSF Aβ42 levels is associated with specific longitudinal morphological changes of the brain

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Background
Abnormal levels of Aβ42 in the CSF and brain atrophy are key factors for the development of Alzheimer's disease(AD), even though their mutual influence in the subsequent development of dementia still needs to be fully understood. The aim of this work is to provide a dynamic longitudinal model of the association between CSF Aβ42 levels and structural changes of the brain in healthy elderly. This model is used to characterize potential trajectories towards AD in subjects subsequently converted to MCI.

Methods
Baseline to 3-years brain T1 MR images were selected for 49 healthy subjects with normal levels of CSF Aβ42 (Aβ-), and for 37 with abnormal level of Aβ42(Aβ+) of ADNI. The images were processed according to an optimized pipeline for longitudinal data based on non-rigid registration. Group-wise models of the average longitudinal atrophy were estimated from the subject-specific time series, and statistically compared voxel-wise. Subject-specific longitudinal changes were also quantified by 1) the percentage rate of hippocampal atrophy and temporal horn expansion(atrophy score), and 2) a whole brain score of the longitudinal structural changes due to Aβ42(Aβ-induced score).

Results
Healthy Aβ42+ subjects showed an accelerated atrophy pattern associated to increased matter loss in temporal areas and hippocampi, as well as to increased ventricles expansion. The pattern was more pronounced for the Aβ+ who subsequently converted to MCI (9/37), while the subjects Aβ- converted to MCI (6/49) showed negligible atrophy patterns (Figure 1). Aβ+ subjects had higher Aβ-induced and atrophy scores, and the interaction of these two indices was strongly associated to longitudinal worsening of ADAS11 and CDRSB, and to conversion to MCI stage (Table 1).

Conclusions
Abnormal Aβ42 levels in healthy elderly are associated to 1) significant acceleration of longitudinal brain atrophy in the temporal areas, and 2)global specific longitudinal structural changes. In particular, the Aβ+ subjects with higher specific longitudinal brain trajectories and greater atrophy did subsequently convert to MCI, and were characterized by a typical AD-like atrophy pattern. The present results point out that clinical conversion in presence amyloid is likely associated to early AD, and is already identifiable by a specific trajectory of brain changes and by a stereotypical pathological AD pattern.