

A 12 months follow-up of morphological and molecular markers in subjects with reverted mild cognitive impairment

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Target audiences

Family physicians, neurologists, psychiatrists, neuroradiologists, public health practitioners and other researchers specialized in dementia, especially in Alzheimer's Disease and patients suffered from the disease.

Background and purpose

Mild cognitive impairment (MCI) is a transitional stage between healthy ageing and Alzheimer's Disease (AD). Normally, MCI gradually progresses to AD with the deterioration of the disease. However, discrete community researches and follow-up population studies reported that MCI patients can revert to normal cognitive status (NCS) with inconsistent percentages ranging from 6 to 53 [1-3]. It seemed that different neuropsychological tests and thresholds used to define MCI were the primary reason for the appearance of MCI reversion [2]. Evidences that the changes of possible biomarkers related to the reversion have not yet found. This study aimed to investigate the changes of selected biomarkers, such as the volume of hippocampus, atrophy rate of the temporal lobe, cerebrospinal fluid T-tau and amyloid beta ($A\beta_{1-42}$) in subjects with MCI reverted to NCS in 12 months based on physicians' diagnoses.

Method and materials

Imaging, biochemical and cognitive data were retrieved from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (<http://adni.loni.ucla.edu>) for subjects with MCI and reverted to NCS (n=17, male/female=13/4, all white, aged 75.2±9.2 years, 15.8±2.3 years of education). Semi-automated hippocampal volumetry from high resolution brain magnetic resonance images (1.5T) was conducted using high dimensional brain mapping tool (Medtronic Surgical Navigation Technologies). For each subject, images at 6 and 12 month were linearly registered to their baseline ones and tensor-based morphometry was used to compute the mean atrophy rate of bilateral temporal lobes. Alterations of the hippocampal volume and MMSE scores were evaluated using repeated measures ANOVA with post hoc of Fisher's least significant difference (LSD). Paired t-test or Wilcoxon sign rank test were used to check the changes in atrophy rate, T-tau and $A\beta_{1-42}$. Pearson correlation was used to test the relations between imaging and biochemical markers. $\alpha=0.05$ was set as the statistical significance level.

Results

MMSE scores increased by 4.7% in 6 months ($P=0.026$, LSD) and 4.9% ($P=0.005$) in 12 month. Mild but insignificant changes were found in the follow-up of the biomarkers ($P>0.05$). On average, the volumes of hippocampus and temporal lobes changed -1.56% and -0.23% between baseline and the 6 month, 1.05% and -0.33% between 7 and 12 month, respectively. T-tau raised 8.83% while $A\beta_{1-42}$ decreased 2.89% over 12 month. Volume of hippocampus significantly correlated with $A\beta_{1-42}$ ($r=-0.703$, $P=0.016$).

Discussion

This pilot study aimed to investigate several possible biomarkers which may be responsible for the occurrence of cognitive improvement in MCI subjects. Significant increase on MMSE scores but insignificant morphological and biochemical changes was found in this study, partially due to the limited statistical power by a small sample size. A small number of included subjects also with a short span of follow-up in this study were attributed to few reverted MCI subjects in ADNI cohort and incomplete follow-up data provided by the ADNI database. Manly et al. [3] previously reported that MCI patients with impairment in memory and multiple cognitive domains (language, memory, executive, attention and visuospatial) [2, 3] were more likely to progress to AD than those with single domain impairment based on a 7 years follow-up study in a multiethnic community with 2364 participants included. Variations in morphological and molecular biomarkers may provide objective evidences in characterizing the reversion of MCI. The dynamics of the biomarkers have the potential for clinical application and disease management, which may provide vital information for possible treatments or delay the progression to the clinical AD stage.

Conclusion

Volumes of hippocampus and temporal lobes, and levels of T-tau and $A\beta_{1-42}$ remained stable in the 12 months follow-up during the cognitive improvement for patients with reverted MCI. Longitudinal study with greater sample size is necessary to better characterize the dynamic of MCI reversion.

References

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