Prediction of Conversion from MCI to AD: Integration and Relative Values of Brain Atrophy Patterns, Clinical Scores, CSF Biomarkers and APOE Genotype

Xiao Da, Jon B. Toledo, Jarcy Zee, David A. Wolk, Sharon X. Xie, Yangming Ou, Amanda Shacklett, Paraskevi Parmpi, Leslie Shaw, John Trojanowski and Christos Davatzikos.

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Prediction of Conversion from MCI to AD: Integration and Relative Values of Brain Atrophy Patterns, Clinical Scores, CSF Biomarkers, and APOE Genotype

X Da, Philadelphia, PA; J B Toledo, MD; J Zee; D A Wolk, MD; S X Xie; Y Ou, PhD; et al. (Xiao.Da@uphs.upenn.edu)

PURPOSE

We evaluate the individual, as well as relative and joint values of indices obtained from MRI patterns of atrophy, cerebrospinal fluid (CSF) biomarkers, APOE genotype, and cognitive performance for prediction of clinical progression of MCI patients, on an individual person basis.

METHOD AND MATERIALS

The SPARE-AD index, a previously characterized imaging biomarker capturing spatial patterns of brain atrophy, was first tested for sensitivity and specificity as a biomarker of Alzheimer’s disease (AD), in a training set of 411 participants. SPARE-AD, and a related mild cognitive impairment (MCI)-specific index called SPARE-MCI, were then evaluated at baseline in 212 MCI patients who either converted to AD within 18 months or remained stable for at least 3 years. Baseline predictive value of SPARE-AD, SPARE-MCI, CSF biomarkers (total and phosphorylated tau and Aβ), MMSE, ADAS-Cog, and APOE genotype were then evaluated using a support vector machine classifier.

RESULTS

SPARE-AD offered excellent diagnostic accuracy of AD (AUC between 0.96-0.98). Excluding CSF biomarkers, MRI-derived SPARE scores offered the highest predictive power for MCI conversion to AD (AUC=0.76); followed by ADAS-Cog (AUC=0.74). Their combination offered the best accuracy (AUC=0.76). Other cognitive and APOE4 markers did not add any predictive power beyond them. In a subset (112 MCI patients) who also had CSF biomarkers, SPARE had the best predictive power (AUC=0.73), being enhanced by CSF biomarkers (AUC=0.76), which by themselves were relatively poorer predictors (AUC=0.68). In amyloid-negative MCI patients, SPARE-AD had high predictive power.

CONCLUSION

MRI patterns of atrophy, quantified via advanced pattern analysis methods, offer the highest predictive power of conversion from MCI to AD, but are slightly better than ADAS-Cog. Combination of MRI and CSF biomarkers improves predictive power. High predictive value of
SPARE in negative amyloid MCI is not expected under the amyloid hypothesis and merits further investigation.

**CLINICAL RELEVANCE/APPLICATION**

A highly sensitive and specific imaging biomarker of AD is evaluated as an earlier predictor of clinical progression from MCI to AD, which can become an AD-specific marker for diagnosis and treatment.
Gray Matter Frequency Map
MCI-SC and MCI-LS Classification