

Neuroimaging / Optimal neuroimaging measures for tracking disease progression

Multivariate prediction of rate of decline in memory functioning over six years using imaging biomarkers

John L. Woodard^{1,2} | Youssef Bellaali³ | Laurence Dricot² | Renaud Lhommel⁴ |
Vincent Malotau⁵ | Lisa Quenon² | Bernard Hanseeuw^{4,6} | Adrian Ivanoiu²

¹ Wayne State University, Detroit, MI, USA

² Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

³ Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

⁴ Saint Luc University Hospital, Université Catholique de Louvain, Brussels, Belgium

⁵ Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

⁶ Gordon Center for Medical Imaging, Radiology Department, Massachusetts General Hospital, Boston, MA, USA

Correspondence

John L. Woodard, Wayne State University, Detroit, MI, USA.

Email: john.woodard@wayne.edu

Abstract

Background: A number of biomarkers have shown utility for predicting cognitive decline and conversion from mild cognitive impairment (MCI) to dementia. However, few studies have investigated the effectiveness of biomarkers combinations and their individual contributions for predicting rate of memory decline. This study evaluated the utility of several imaging biomarkers for predicting annual rate of decline in memory performance, as indexed by the Buschke Free and Cued Selective Reminding Test (FCSRT) Free Recall (FR), Cued Recall (CR), and Delayed Recall (DR).

Method: At baseline, 153 individuals (31 controls, 87 persons with MCI, and 35 persons with subjective cognitive impairment (SCI)) underwent neuropsychological evaluation (including the FCSRT), fluorodeoxyglucose (FDG) positron emission tomography (PET), amyloid PET and MRI measurement of bilateral hippocampal volume (HV) and bilateral entorhinal cortical thickness (EC). Follow-up neuropsychological evaluations were performed after a mean of 2.05, 4.1, and 6.4 years. Individual intercepts and slopes (annualized rates of decline) for FCSRT indexes were computed for each participant using latent growth curve modeling. Bayesian linear regression identified the optimal models for predicting annual rate of change for each memory index. After adjusting for age, sex, and sociocultural level, baseline amyloid and FDG PET, bilateral HV, and bilateral EC were entered as predictors. Bayes Factors (BF_{10}) grade the intensity of support in favor of the alternate hypothesis over the null hypothesis.

Result: Using Bayesian ANOVA, all groups differed significantly in rate of decline for each of the three memory indexes (Figure 1). Amyloid PET, FDG PET, and EC were the best predictors of FR decline ($BF_{10}=3.26e+12$, $R^2=0.45$), Amyloid PET and EC were the best predictors of CR decline ($BF_{10}=3.31e+13$, $R^2=0.39$), and the combination of all four biomarkers was the best set of predictors of DR decline ($BF_{10}=1.95e+12$, $R^2=0.43$).

Conclusion: Different combinations of baseline imaging biomarkers were highly sensitive to rate of decline in specific aspects of memory functioning. Amyloid PET and entorhinal cortex thickness were among the significant predictors for all three memory indexes, implicating their particular sensitivity to all FCSRT memory indexes. The

predictive power of entorhinal cortex thickness may be due to early accumulation of tau in this region.

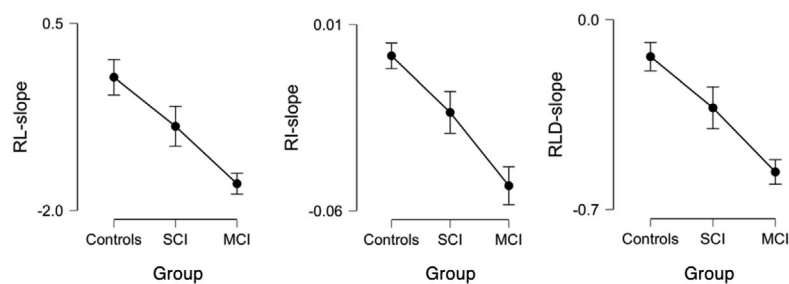


Figure 1. Average annual rate of change over 6.4 years for Free Recall (RL), Cued Recall (RI), and Delayed Free Recall (RLD) on Free and Cued Selective Reminding Test for Controls and Subjective Cognitive Impairment (SCI) and Mild Cognitive Impairment (MCI) patients

FIGURE 1