



FDG PET imaging and clinical features in Mild Cognitive Impairment: their role in predicting the conversion to Alzheimer's disease



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INTRODUCTION

The combination of CSF and PET/MRI imaging may improve the sensitivity in predicting the conversion from Mild Cognitive Impairment (MCI) to Alzheimer's disease (AD). However, the availability of all biomarkers in each patient is not frequent in everyday clinical practice. FDG PET has been used not only as a diagnostic tool for differential diagnosis of dementia, but also as a predictor of conversion from MCI to AD. Several methods have been applied, such as regions of interest (ROI)¹, statistical parametric mapping (SPM)² and more recently using the PET Score³

Aim of this study is to evaluate the role of clinical features and different FDG PET post processing methods in predicting MCI conversion to AD.

METHODS

56 MCI patients were recruited and followed for 4 years. Age at onset, cognitive impairment (MMSE and neuropsychological tests*) and behavioral symptoms (NPI) were evaluated at baseline and during follow up. Clinical and imaging features of single domain MCI (sd MCI) patients and multiple domain MCI (md MCI) were compared. Each patient underwent a FDG PET and the images were analysed with PMOD and Statistical Parametric Mapping (SPM). PET score was calculated as $PET\text{-score} = \log_2 \{AD\ t\text{-sum}/11.089\} + 1\}$ ³.

Statistical analysis: clinical features were analysed using SPSS software version 13.5. Chi Square Test was used for categorical variables comparison, Pearson Test for continuous variables, Mann Whitney test and Kruskal-Wallis test were used for continuous and categorical variables comparison.

*Digit Span, Rey Auditory Verbal Learning Test, Rey Complex Figure Test, Babcock, Corsi Block Tapping Test, Weigl Test, Visual Search Test, Clock test, Verbal Fluency, Stroop Test, Frontal Assessment Battery, WAIS R, Token Test, Praxies.

RESULTS

At PMOD analysis 39 patients of 56 showed an abnormal AD t-sum while 17 patients showed a normal one. 27 patients with abnormal AD t-sum converted into AD, while 12 remained MCI. All the 17 patients with normal AD t-sum converted into other diseases than AD (fig. 1). The mean time to conversion (TC) was 21.78 ± 2.3 months; 53.63% of sdMCI converted after 25.29 ± 2.5 months while 71.25% mdMCI converted after 15.00 ± 1.8 months.

Clinically, TC was associated to lower baseline MMSE ($p < 0.001$) and to higher NPI agitation/aggression, irritability, disinhibition and appetite and eating changes ($p < 0.05$) (fig. 2)

The PET score was directly associated to conversion ($p < 0.001$) and indirectly to TC ($p < 0.005$).

At SPM analysis, a lower temporo-parietal metabolism was associated to higher conversion rate ($p < 0.001$) and to a shorter TC ($p < 0.001$). Moreover, a more severe frontal hypometabolism (associated to NPI symptoms agitation/aggression, irritability, disinhibition and appetite and eating changes) was inversely related to TC ($p < 0.001$) (fig. 3).

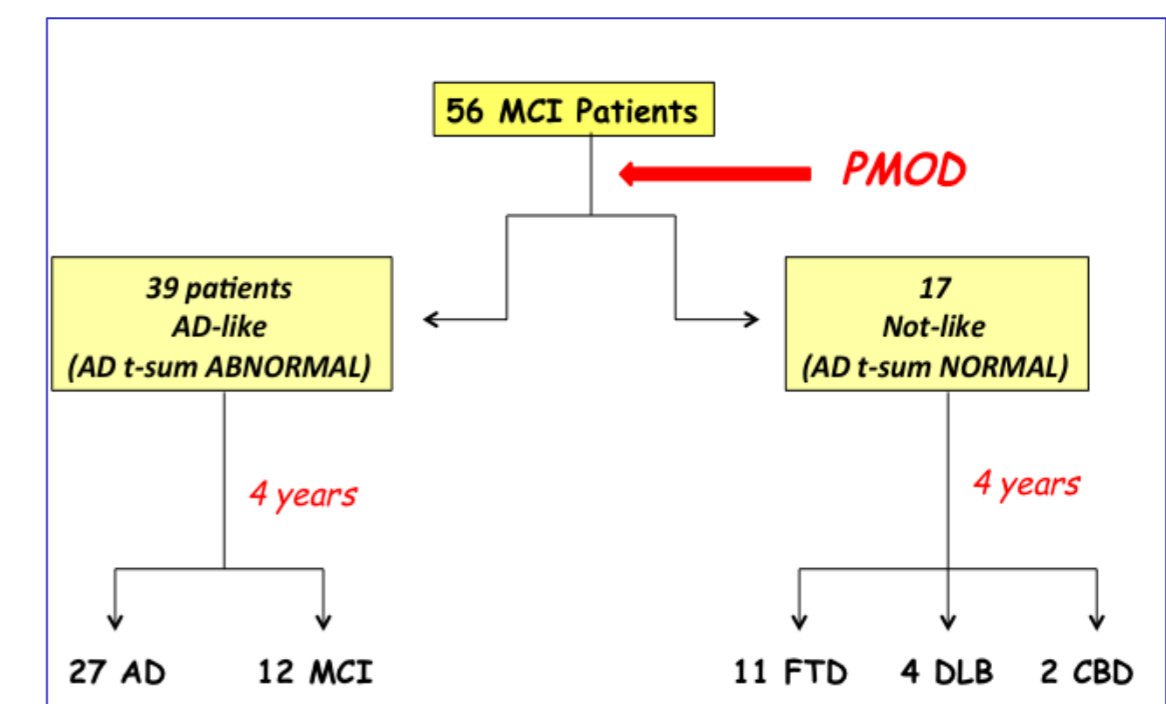


Fig 1: PMOD discrimination power in MCI patients

MMSE TO	$p < 0.001$	Multiple domain aMCI	$p < 0.005$
Rey Complex figure Test	$p < 0.05$	NPI score (agitation/aggression irritability, appetite and eating change, disinhibition)	$p < 0.05$
Trail Making Test A	$p < 0.05$		
PET-score	$p < 0.001$	PET-score	$p < 0.005$

Fig 2: Clinical predictors of AD converters

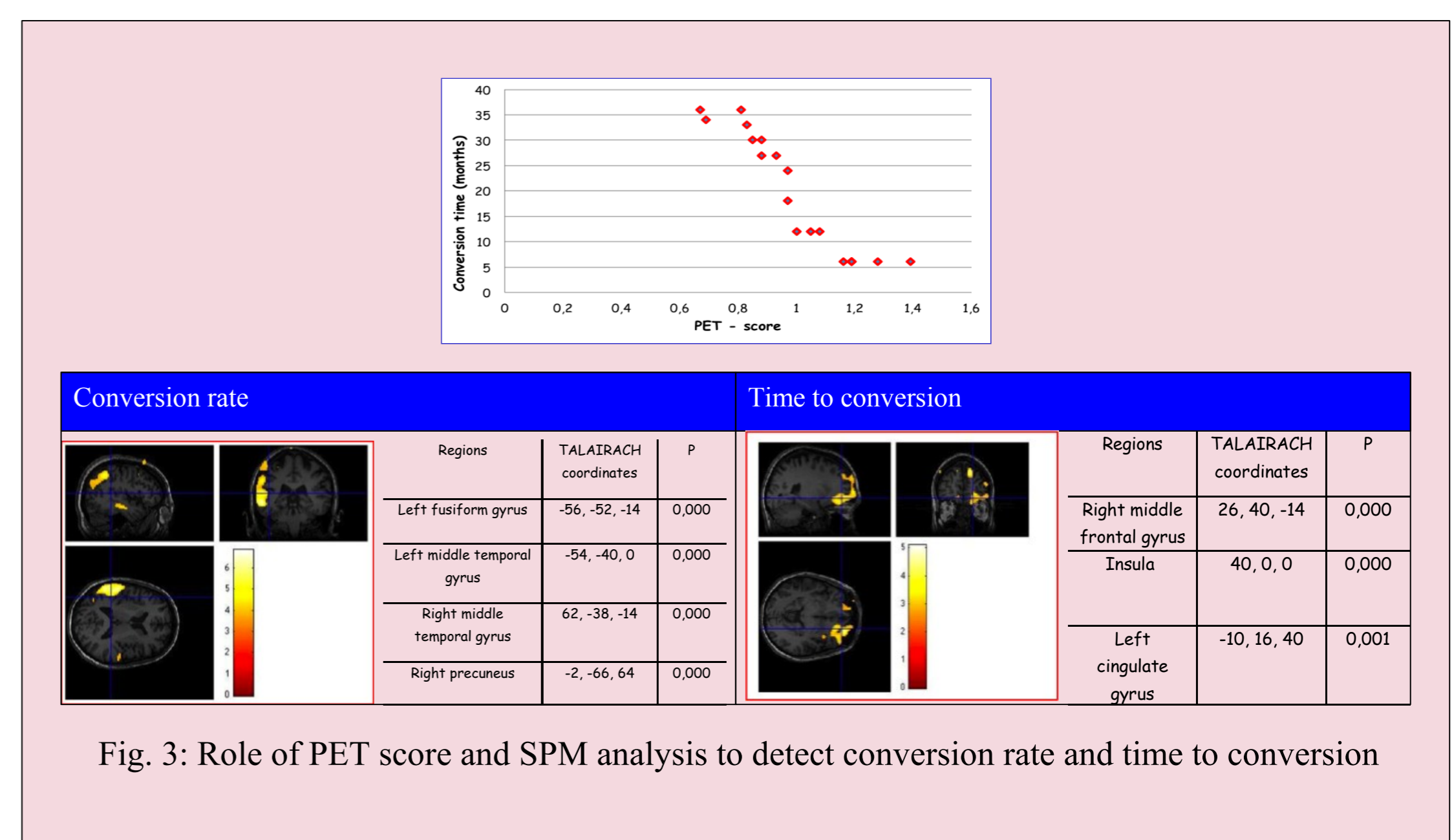


Fig. 3: Role of PET score and SPM analysis to detect conversion rate and time to conversion

CONCLUSIONS

- FDG PET analysis is a helpful tool to discriminate MCI in AD or not AD converters.
- FDG PET may predict the conversion rate and the TC with a high sensitivity.
- Clinically, baseline clinical features and frontal hypometabolism may predict a shorter TC in patients with abnormal AD t-sum.
- FDG PET analysis and clinical features are sensitive tools to predict conversion to AD. It would be helpful to find a standardized index (AD Clinical and Functional Conversion Score *ADCFC score*) based on clinical and PET features to predict the conversion rate and time to conversion towards AD.

References:

1. Choo IH, Ni R, Schöll M, Wall A, Almkvist O, Nordberg A. Combination of 18F-FDG PET and cerebrospinal fluid biomarkers as a better predictor of the progression to Alzheimer's disease in mild cognitive impairment patients. *J Alzheimers Dis.* 2013;33(4):929-39.
2. Drzezga A1, Lautenschlager N, Siebner H et al. Cerebral metabolic changes accompanying conversion of mild cognitive impairment into Alzheimer's disease: a PET follow-up study. *Eur J Nucl Med Mol Imaging.* 2003; 30:1104-13.
3. Herholz K, Haense C, Dunn G. Evaluation of calibrated 18 F FDG PET score as a biomarker for progression in Alzheimer Disease and Mild Cognitive Impairment. *Journal of Nuclear Medicine* 2011; 52; 349-366.