The impact of Amyloid PET as biomarker of Alzheimer's disease in the differential diagnosis of dementia: a multidisciplinary team study

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Introduction

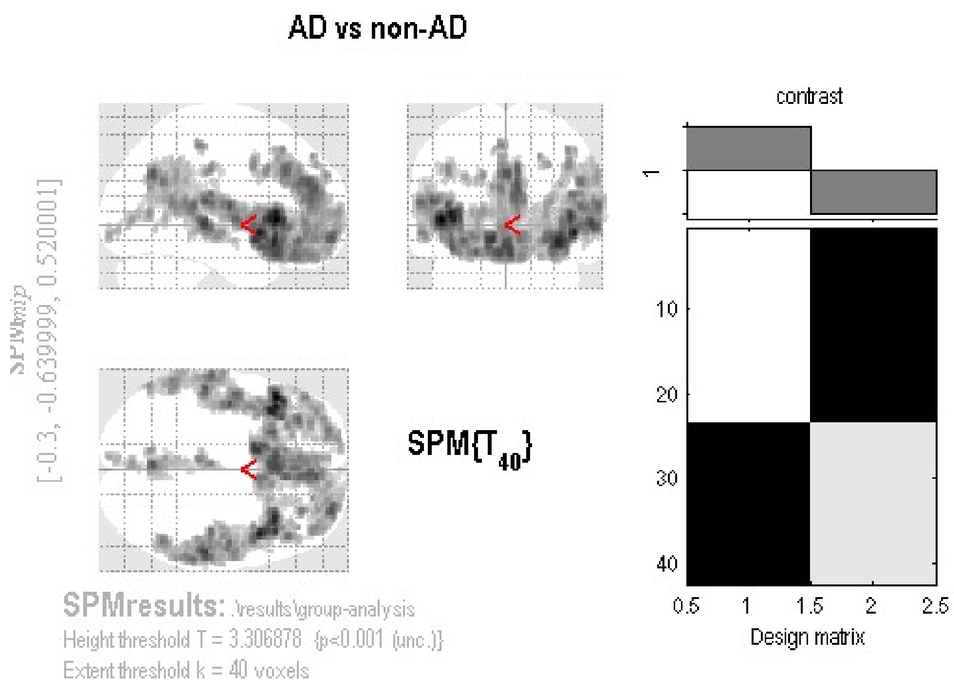
We assessed the relative impact of 18F-Florbetaben Positron Emission Tomography (Amyloid PET) using a new processing imaging algorithm in correlation with clinical data, neuropsychological assessment and cerebrospinal fluid (CSF) analysis (Aβ, tau and phospho-tau (p-tau) proteins levels) to diagnose Alzheimer's disease in the differential diagnosis of dementia.

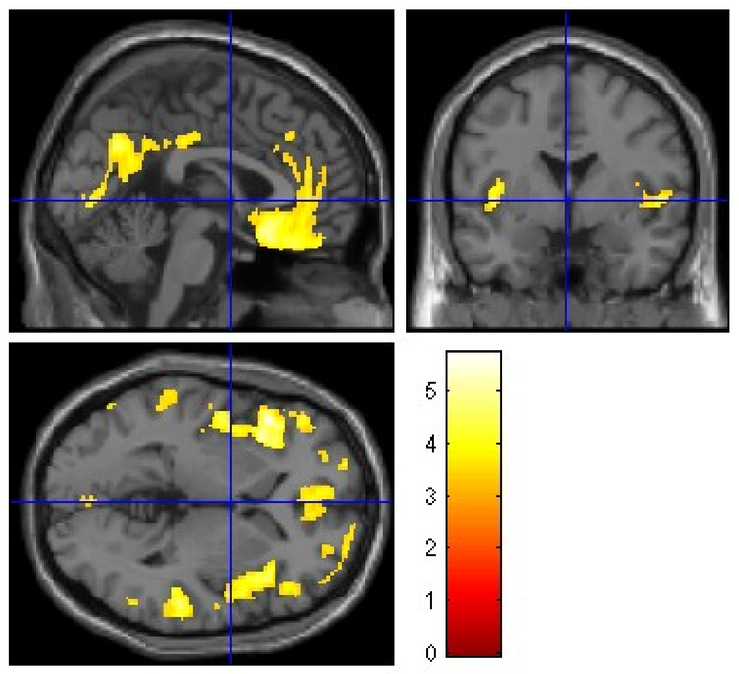
Method

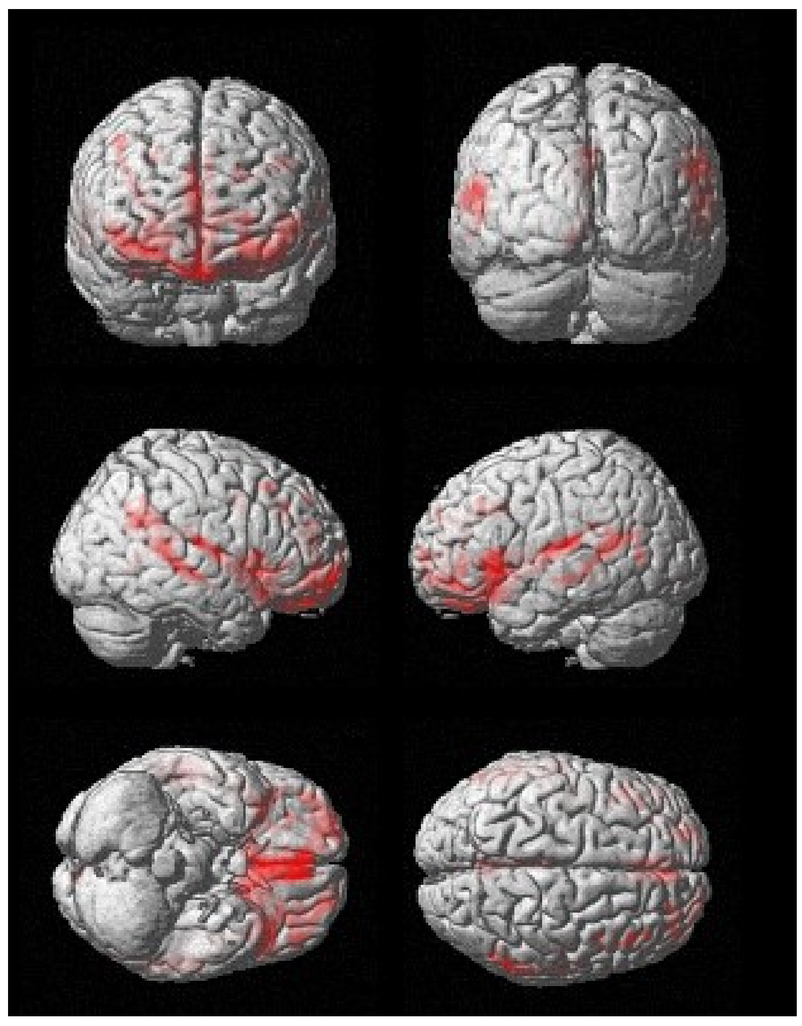
Forty-four patients with clinical evidence of dementia, undergoing diagnostic Amyloid PET (18F-Florbetaben) at the Dementia Clinic of Cefalù (Italy), were retrospectively evaluated by a multidisciplinary team (MDT) including specialists in neurology, nuclear medicine, radiology, neuropsychology and laboratory medicine. Amyloid PET results were correlated with clinical, cognitive status, CSF analysis and other imaging when available. PET images were processed in a statistical parametric mapping (SPM) and converted in standard space (MNI space) by normalizing them with tissue probability map as template. Automated anatomical labeling atlas was used to mask each regional volume of interest (VOI) followed by extraction of standard uptake value ratio (SUVr), normalized on the medial cerebellum region. The regional SUVr and scores from clinical and cognitive tests were used to create Receiver Operating Characteristic (ROC) curves and obtain the best thresholds for the clinical diagnosis. Leave-one-out cross-validation was carried out in order to validate the results.

Results

A total of 26/44 patients showed elevated amyloid burden at Amyloid PET scan. After integration with FDG PET, clinical data and CSF protein levels, 22 of them were classified by MDT as AD, the remaining 4 as vascular or fronto-temporal dementia. Among the variables ordered by area under curve (AUC), Amyloid and FDG PET (qualitative evaluation), CDR value 1, CSF Tau and p-tau levels presented the best true positive and true negative rates (Amyloid PET: AUC= 0.85, sensitivity 0.91, specificity 0.79; FDG PET: AUC= 0.76, sensitivity 0.86, specificity 0.67; CDR 1 AUC 0.72, sensitivity 0.75, specificity 0.67; CSF-Tau: AUC=0.75, sensitivity=0.84, specificity=0.64; CSF p-TAU AUC 0.66, sensitivity 0.72, Specificity 0.65). At semi-quantitative evaluation of Amyloid PET a SUVR value of 1.006 in the inferior frontal cortex and a SUVR of 1.03 in the precuneus region were the best cutoff SUVR value and good correlation for the diagnosis of AD (inferior frontal cortex AUC 0.883; precuneus region AUC 0.826). By using two-tailed Pearson correlation between SUVR values of all brain region and neurophiscological tests, a significant moderate inverse correlation has been found especially for inferior frontal cortex and Attentive-memory test (R=-0.455; p=0.008), Ray Auditory-verbal learning Test (R= -0.459; p=0.006), Corsi-Span Test (R= -0.408;p=0.017), Raven Test (R= -0.405;p=0.022). Similarly, an inverse correlation was found also between precuneus brain region and Raven Test (R=-0.420;p=0.017) and rolandic operculum region and Ray Auditory-verbal learning Test (R= -0.426; p=0.012), Attentive-memory test (R= -0.477;p=0.005) and Corsi-Span Test (R= -0.427;p=0.012).







Conclusion

Amyloid PET, especially when using SPM normalized SUVr analysis, confirms high predictive power for the differential diagnosis of dementia over FDG PET, neuropsychological tests and CSF analysis. When evaluating patients with dementia, however, a multidisciplinary approach is still crucial for the final classification of patients with AD.

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XLVIII CONGRESSO NAZIONALE
14-17 OTTOBRE 2017 – NAPOLI

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