ABSTRACT: Objective: To conduct the first support vector machine (SVM)-based study comparing the diagnostic accuracy of T1-weighted MRI (T1-MRI), FDG-PET and regional cerebral blood flow (rCBF) SPECT in Alzheimer’s disease (AD).

Method: Brain T1-MRI, FDG-PET and rCBF-SPECT were acquired in exactly the same sample of mild AD patients (n=20) and elderly healthy controls (n=18). SVM-based diagnostic accuracy indices were calculated using whole-brain information and leave-one-out cross-validation approach.

Results: Accuracy obtained using PET and SPECT data were similar (PET accuracy was 79~84% and AUC 0.90~0.92; SPECT accuracy was 82~84% and AUC 0.86~0.91), and both had better performance relative to the analysis using T1-MRI data (accuracy of 74%, AUC 0.81). The addition of PET or SPECT to MRI produced higher accuracy indices (79~87%; AUC: 0.85~0.94) than T1-MRI alone but these were not clearly superior to the isolated neurofunctional modalities.

Conclusion: In line with previous evidence, FDG-PET and rCBF-SPECT more accurately identified patients with AD than T1-MRI and the addition of either PET or SPECT to T1-MRI data yielded increased accuracy. The comparable SPECT and PET performances, directly demonstrated for the first time in the present study, support the view that rCBF-SPECT still has a role to play in the diagnosis of AD.13-Nov-201613-Nov-201613-Nov-201613-Nov-2016

Comment: Neuroimaging studies have yielded significant advances in the understanding of the biological mechanisms relevant to the development and course of AD. These advances have not yet increased diagnostic accuracy. This study aims to conduct the first SVM based study comparing the diagnostic accuracy of T1-MRI), FDG-PET and CBF) SPECT in AD. FDG-PET and rCBF-SPECT more accurately identified patients with AD than T1-MRI and the addition of either PET or SPECT to T1-MRI data yielded increased accuracy. This innovative study is methodologically sound and makes an important contribution to this research field. I have a few suggestions and comments that will strengthen the relevance of these findings.

Introduction

-Provide current advantages and disadvantages of each imaging technique.

-Please provide additional information on the use of T1-MRI in the diagnosis of AD

-Please highlight the fact that no single test can show whether someone has AD: briefly mention that blood tests, neurological examination and neuropsychology contribute greatly to the diagnosis of dementia. Cognitive deficits can be detected several years before the clinical diagnosis of dementia. The neuropsychological profile may indicate the underlying neuropathology.

-Briefly explain why cerebellar normalization is important

Methods

-how were participants recruited? Were they inpatients and outpatients?

-please add a short section describing age, gender, onset of cognitive changes, global functioning (e.g. ADL scores) between the two populations. I know you have some of this information in Table but a short description should be addressed. Additional details on premorbid IQ, severity of mood changes, comorbidities (medical, psychiatry)

-did you administer MMSE to HC too? please clarify

-did you evaluate AD using a proper AD neuropsychological assessment? This is routinely done when diagnosing AD (e.g.CERAD) . if not please address this in your conclusions

-could you please provide scores on the CDR for both HC and AD

-please provide names of self-reporting questionnaires evaluating mood and provide scores

-was family history of AD and other medical ailments based on self-reports or medical records. Please clarify.

Results

-Please provide labels and coordinates of primary clusters of voxels that separate HC and AD on the three imaging techniques

-Can you provide a list of the top 10 (or more) ranked features/regions that best separate AD and HC

-Define relevance by associating these voxels with it is currently known about the disease

Conclusions

-Add something about future directions. e.g. predict disease severity, add behavioral data to improve accuracy etc.

-Did you think of creating a probabilistic classifier score determining the likelihood of AD on each imaging technique. E.g. could be compared across techniques by using a score. If not please discuss.

-Did you consider comparing the efficacy of SVM compared to other supervised machine learning models. Please discuss even if briefly

-Please discuss differences between T1 and spectroscopy techniques that may explain the current results (e.g. biological processes start before structural changes)

Details

-Please provide references for your statements on pages 11 and 12 regarding your methodology in terms of SVM.

-A machine learning analysis flow chart would be helpful and should include reference to division of the samples into a training set and a test set, ranking features and selecting the most discriminative voxels,, building the SVM classifier model using the training samples, and evaluating the performance of the SVM model using the test sample.