Volume-based vs. voxel-based brain morphometry in Alzheimer's disease prediction

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Introduction. Voxel-based morphometry from conventional T1-weighted images has proved effective to quantify Alzheimer's disease (AD) related brain atrophy and to enable accurate automated classification of AD patients, mild cognitive impaired (MCI) patients and elderly controls [1,2]. Little is known, however, about the classification power of volume-based morphometry, where features of interest consist of a few brain structure volumes (e.g. hippocampi, lobes, ventricles…) as opposed to about a million voxel-wise gray matter (GM) concentrations. This work aims to experimentally compare voxel-based and volume-based brain morphometry for automated disease classification.

Materials and Methods. Experiments were conducted on a standardized Alzheimer's Disease Neuroimaging Initiative (ADNI) analysis set [3,4] consisting of 818 T1-weighted MR scans from different acquisition systems and vendors (667 screening scans acquired at 1.5T and 151 baseline scans acquired at 3T), all from distinct subjects diagnosed as either normal, MCI, or AD based on careful clinical assessment, yielding a total of 229 scans labeled as normal, 401 MCI, and 188 AD. All scans were processed by SPM8 [5], a voxel-based morphometry package, as well as FreeSurfer 5.1.0 [6] and Siemens prototype MorphoBox [7], two volume-based morphometry packages. Extracted features were Jacobian modulated GM concentration maps in the case of SPM, and a set of 10 regional volumes normalized by total intra-cranial volume in the case of both FreeSurfer and MorphoBox, namely: total GM, left and right temporal GM, left and right hippocampus, total cerebrospinal fluid, lateral, 3rd and 4th ventricles. For each method, features were corrected for the effect of normal aging using linear detrending [8] and fed into a support vector machine (SVM) for automated classification. Balanced classification accuracy (averaged sensitivity and specificity) was evaluated for each classifier using a classical leave-one-out cross-validation procedure, which included the optimization of the SVM cost parameters.

Results and Discussion. Balanced accuracy values are reported in Fig. 1 for the three considered morphometry methods in three distinct classification scenarios: AD vs. normals (NL), MCI vs. NL, and AD vs. MCI. As verified by McNemar tests, all classifiers performed significantly above chance ($p<0.0001$). Despite methodological differences, morphometry packages proved fairly consistent across classification tasks. Higher accuracy was observed in all cases for AD vs. NL (85-89%) than for MCI vs. NL (73-76%) and AD vs. MCI (57-68%), reflecting the increasing inherent difficulties of the respective classification problems. Differences amongst methods were found to be the most significant in MCI vs. AD classification, where the accuracy of SPM-based classification was 10-11% lower than FreeSurfer-based and MorphoBox-based classification. This suggests that volume-based morphometry may be relatively more discriminant as the populations to be compared are statistically more similar. Overall, our results provide evidence that volume-based morphometry is a valuable alternative to voxel-based morphometry to assist the diagnosis of Alzheimer's disease and mild cognitive impairment.

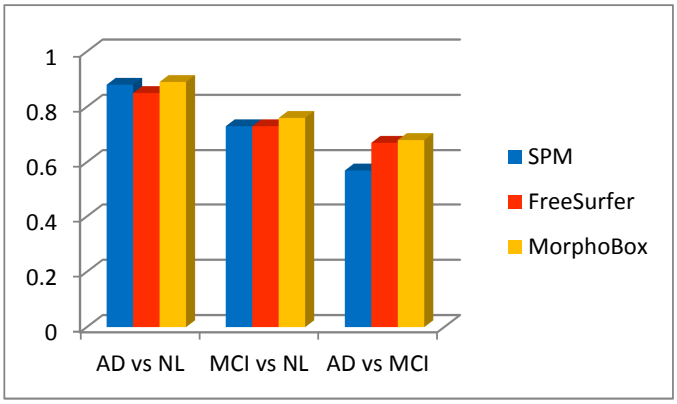

Fig. 1 *Balanced accuracy for multivariate classifiers respectively based on SPM, FreeSurfer and MorphoBox*

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