Impact of image acquisition systems on Alzheimer's disease-related atrophy detection

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SYNOPSIS (100 words max)

We investigate the potentially confounding effect of image acquisition systems (field strength, manufacturers) on automated Alzheimer's disease detection using standardized Alzheimer's Disease Neuroimaging Initiative (ADNI) data. Disease classifiers based on brain volumetric markers brain volumetric markers computed by FreeSurfer and the MorphoBox prototype were evaluated with and without corrections for acquisition systems. Results show a limited impact of image acquisition systems on Alzheimer's disease detection, however corrections significantly reduced classification errors for mild cognitively impaired patients versus healthy controls or Alzeheimer's patients.

INTRODUCTION

Brain morphometry from T1-weighted images is increasingly used clinically as a quantitative tool to assist diagnosis of brain diseases. It is now well established, for instance, that Alzheimer's disease (AD) related brain atrophy can be detected with some accuracy using conventional morphometry software[1,2]. While there are indications that morphometric measures are affected by image acquisition protocols, our goal here is to investigate to which extent such biases may affect atrophy detection, and whether and how they may be accounted for in practice.

MATERIALS AND METHODS

Experiments were conducted on a standardized Alzheimer's Disease Neuroimaging Initiative (ADNI) analysis set[3] of 1860 screening T1-weighted MR scans from 784 distinct subjects (age range: 54-91 years), including 220 healthy subjects, 386 patients diagnosed with mild cognitive impairement (MCI), and 178 diagnosed with AD. Images were acquired using a common protocol[4] on different sites and different acquisition systems from GE, Philips and Siemens. Each subject was scanned twice without repositioning at 1.5T with a raw voxel size $1.25 \times 1.25 \times 1.2$ mm^3. Scans acquired on GE and Philips systems were subjected to in-plane sinc interpolation (0-filled reconstruction), resulting in 0.9375×0.9375 mm^2 pixel spacing. In addition, 148 subjects (~19%) were also scanned twice at 3T with a voxel size $1 \times 1 \times 1.2$ mm^3 roughly SNR-matched to the 1.5T data. No interpolation was applied to the 3T data.

All scans were processed by both FreeSurfer[6] version 5.3.0 and MorphoBox prototype[7] to estimate the volumes normalized by total intra-cranial volume of ten brain regions known to be affected by AD-related atrophy: total gray matter (GM), left and right temporal GM, left and right hippocampus, total cerebrospinal fluid, lateral, 3rd and 4th ventricles. Volumes were submitted to logistic regression in order to predict clinical diagnostic in three distinct binary classification scenarios (AD vs Normal, MCI vs Normal, AD vs MCI). Three strategies were investigated in each scenario: one in which the logistic regressors were the ten normalized volumes plus age and gender ("basic classification"); one in which field strength, pixel spacing and their interaction were considered as additional regressors ("protocol-corrected classification"); and, finally, one in which additional regressors consisted of offsets specific to the different acquisition systems ("system-corrected classification"). For each morphometry method and classification strategy, accuracy was evaluated using leave-one-subject-out cross-validation, and McNemar's chi square tests were performed to determine whether classifiers were significantly different.

RESULTS AND DISCUSSION

Cross-validated balanced accuracy values in three distinct binary classification scenarios (AD vs. Normal, MCI vs. Normal, MCI vs. AD) are reported in Figures 1 and 2 for MorphoBox and FreeSurfer, respectively. In the case of MorphoBox, both protocol-corrected and system-corrected classifications significantly improved the basic classification by about 2% for both MCI vs. Normal and MCI vs. AD. The effect of correction on AD vs. Normal classification was however insignificant. Also, there were no significant differences between protocol-corrected and system-corrected classifications according to McNemar's tests. FreeSurfer-based classification results showed even smaller differences between classifiers, none of which was found to be statistically significant.

These results suggest a limited impact of image acquisition systems on Alzheimer's disease detection using brain volumetry, hence justifying to some extent training disease classifiers with datasets acquired from different manufacturers as long as they conform to a standard imaging protocol, as is the case in ADNI. The small or negligible reductions in classification errors achieved by correcting for system heterogeneity indicate that the actual effects of Alzheimer's disease on brain morphometry dominate acquisition-related variations. We note, however, that corrections led to small but significant improvements using MorphoBox in both MCI vs. Normal and AD vs. MCI classifications. Therefore, correcting for acquisition system heterogeneity may become more important as the morphometric changes to be detected are smaller.

Acknowledgements

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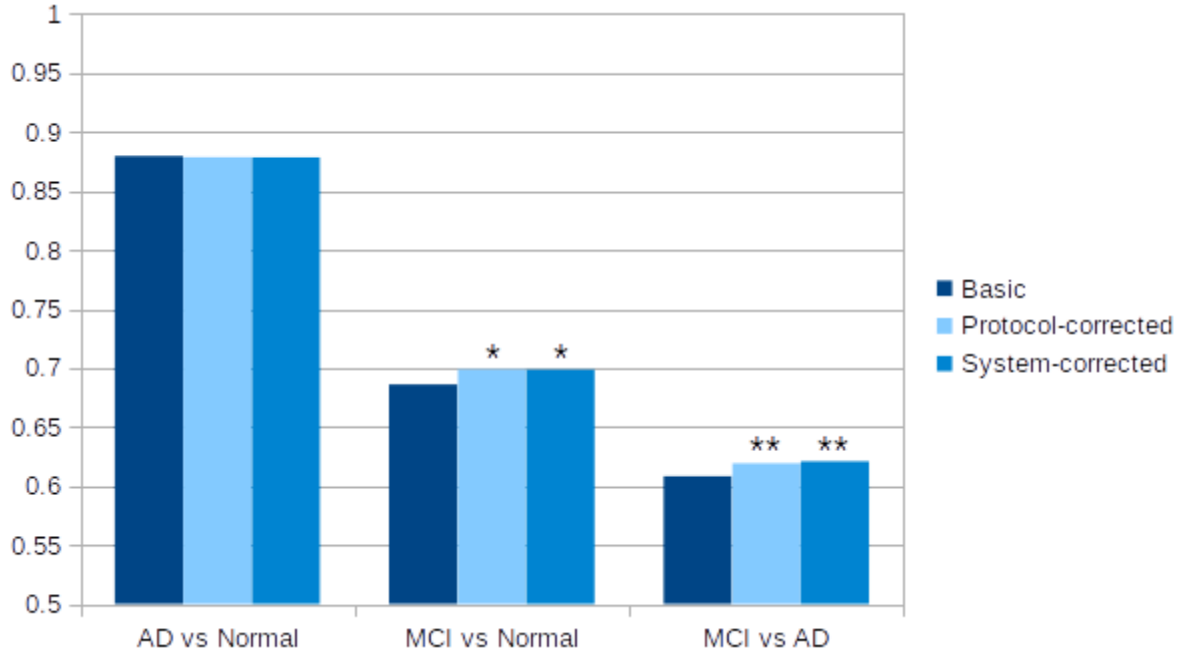

Figure 1 Cross-validated balanced accuracy levels for MorphoBox-based classification. Stars indicate significant differences with the basic classifer (*: p<0.05, **: p<0.01).

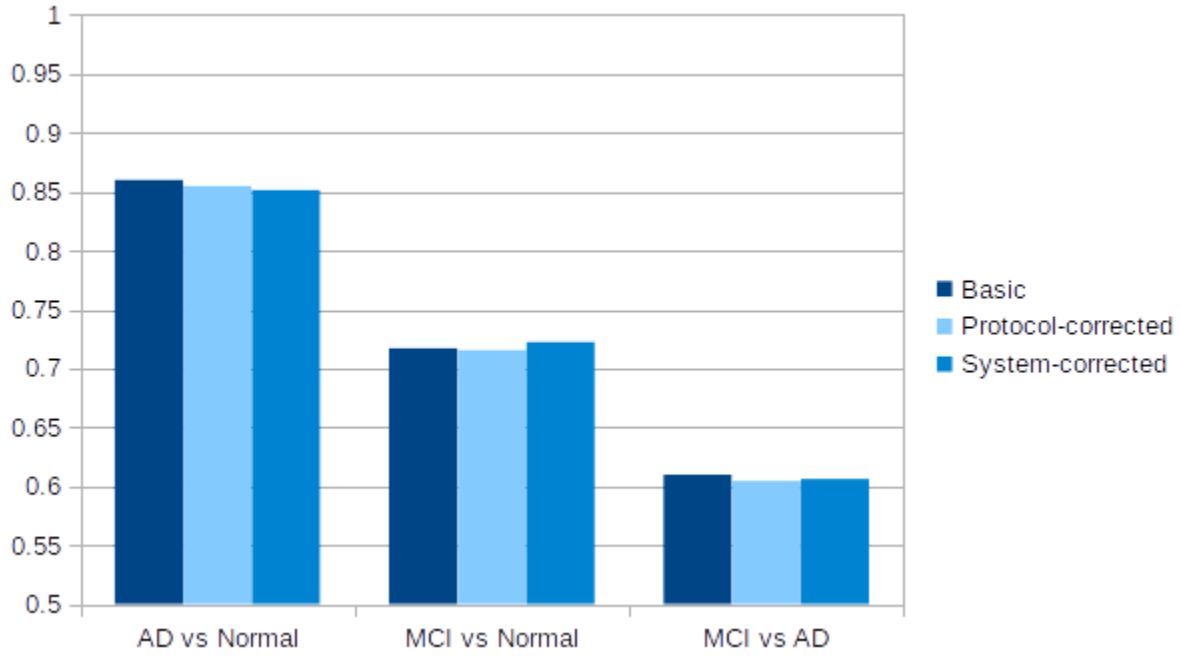

Figure 2 Cross-validated balanced accuracy levels for FreeSurfer-based classification. Effects of protocol/system correction were found non-significant