Predicting Temporal Progression of Alzheimer's Disease using Hippocampus Surface-based Morphometric Features

Sinchai Tsao[a,b] Niharika Gajawelli[b] Jiayu Zhou[c] Jie Shi[c] Jieping Ye[c] Yalin Wang[c] Natasha Lepore[b]

[a]University of Washington, Seattle, Washington, USA - email: stsao@uw.edu
[b]Children's Hospital Los Angeles & University of Southern California, Los Angeles, California, USA
[c]Arizona State University, Tempe, Arizona, USA

Introduction

Recent work in psychological testing,[3] genetic studies,[4] magnetic resonance (MR) imaging,[5] positron emission tomography (PET) imaging,[6] cerebral spinal fluid (CSF) measurements,[7] cardiovascular status[8] and others have yielded tremendous amounts of diagnostic data for diagnosing and staging dementias, especially Alzheimers disease (AD). Moreover, many of these studies now also include longitudinal information.[3, 9] This has lead to a problem often referred to as the curse of dimensionality, where the size (number of dimensions) of the dataset makes it difficult to do various numerical analysis on the data. This in turn makes it increasingly difficult to draw consistent conclusions from the dataset. Statistical analysis together with clinical disease models have helped with determine how the different sets of diagnostic information interacts with one another but they require a large number of ad hoc assumptions and therefore does not lend itself well to large scale Medical Imaging-based features. These problems become even more important when trying to use machine learning techniques because at some point the predictive power of the model ceases to increase even though we're adding more information or dimensions. The question is then about how to select the "correct" features to maximize predictive power. This paper leverages existing sparsifying machine learning techniques with temporal priors,[1] built specifically for progressive disease models, such as AD, together with multivariate tensor-based morphometric (mTBM) features[10] of the Hippocampus to try and predict AD progression up to 48 months from the baseline MRI measurement. The goal is to evaluate the predictive power of mTBM against those of cortical thickness and other FreeSurfer-based features, demographic information (sex and age) as well as genetic information (ApoE-ε4 Copies).

Methods

AFNI DATA: Data used in the preparation of this article were obtained from the Alzheimers Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu).

- 616 subjects
- M06, 606 M12, 533 for M24, 364 for M36 and 97 for M48. 90% of the data was used for training and 10% used for testing.
- 20 different selection splits of training and testing.
- More information about the demographics and patient selection is available in Zhou et al 2013.[1]

cFSGL (convex Fused Sparse Group Lasso) :

- Prediction of each Time Point can be seen as a Task
- The multi-time point outcomes prediction can be reformulated as a Mult-task learning problem
- Performs much needed Dimension Reduction via the sparsifying Group Lasso penalty
- Simultaneously trains all time points (i.e. performs all tasks simultaenously) to preserve temporal smoothness
- Accomodates missing time points in training data

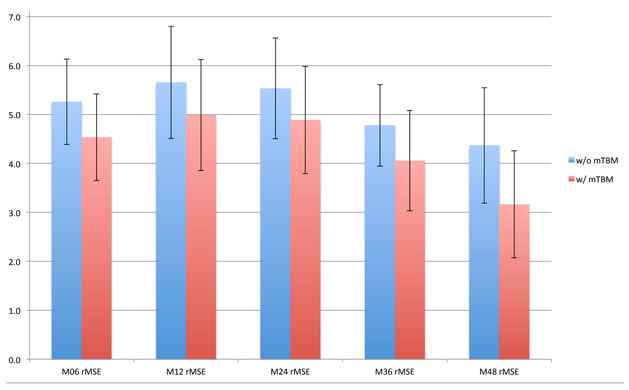

Figure 4:
Bar Chart of the rMSE of predictions with and without mTBM features by time point

Table 1

Comparison of the model performance in predicting ADAS Cognitive Score with and without mTBM features. The base set of features used were MRI volumetric information, Sex, Gender, Age, ApoE and baseline MMSE score.

	w/o mTBM	with mTBM
nMSE	0.345 ± 0.075	0.249 ± 0.039
wR	0.828 ± 0.036	0.873 ± 0.022
M06 rMSE	5.259 ± 0.872	4.534 ± 0.883
M12 rMSE	5.653 ± 1.143	4.989 ± 1.134
M24 rMSE	5.532 ± 1.029	4.885 ± 1.094
M36 rMSE	4.777 ± 0.833	4.055 ± 1.024
M48 rMSE	4.367 ± 1.179	3.164 ± 1.091

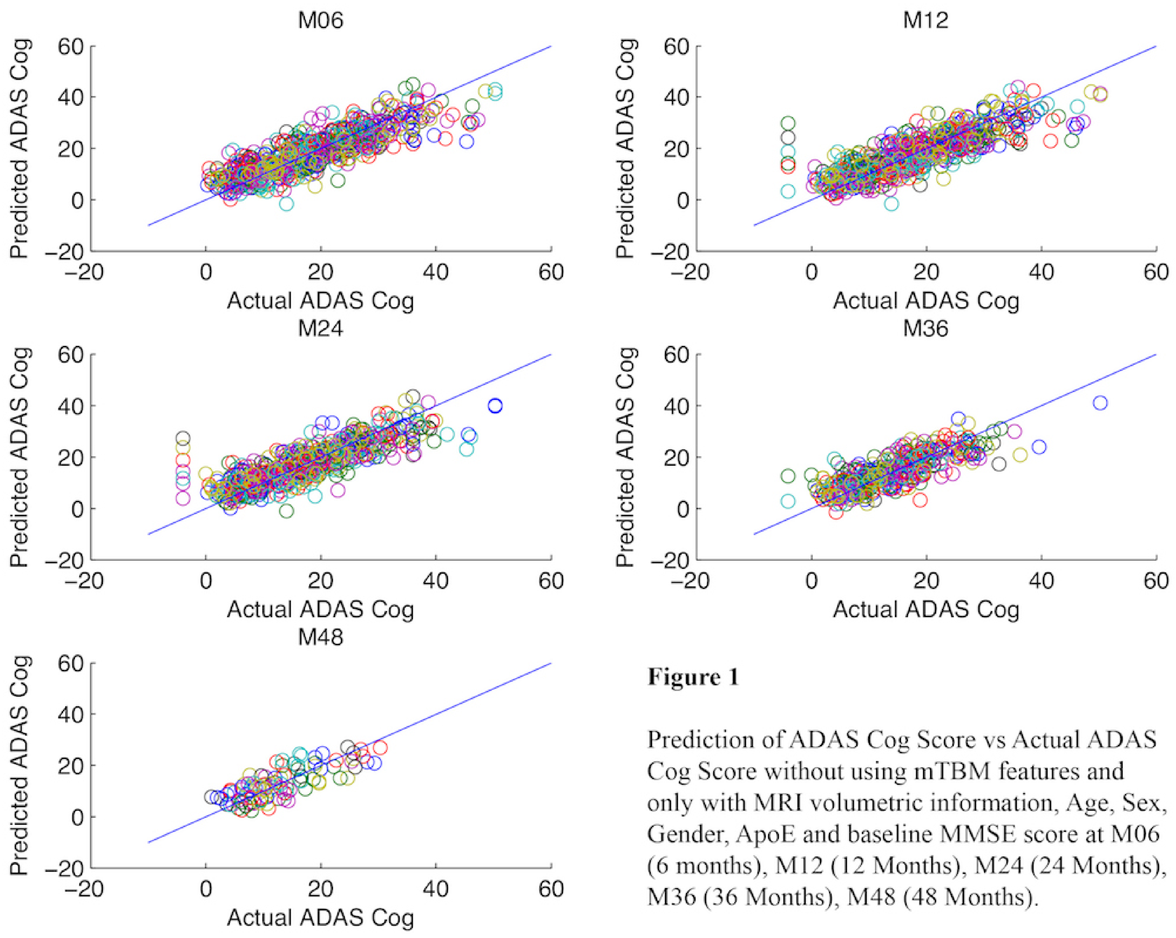

Figure 1

Prediction of ADAS Cog Score vs Actual ADAS Cog Score without using mTBM features and only with MRI volumetric information, Age, Sex, Gender, ApoE and baseline MMSE score at M06 (6 months), M12 (12 Months), M24 (24 Months), M36 (36 Months), M48 (48 Months).

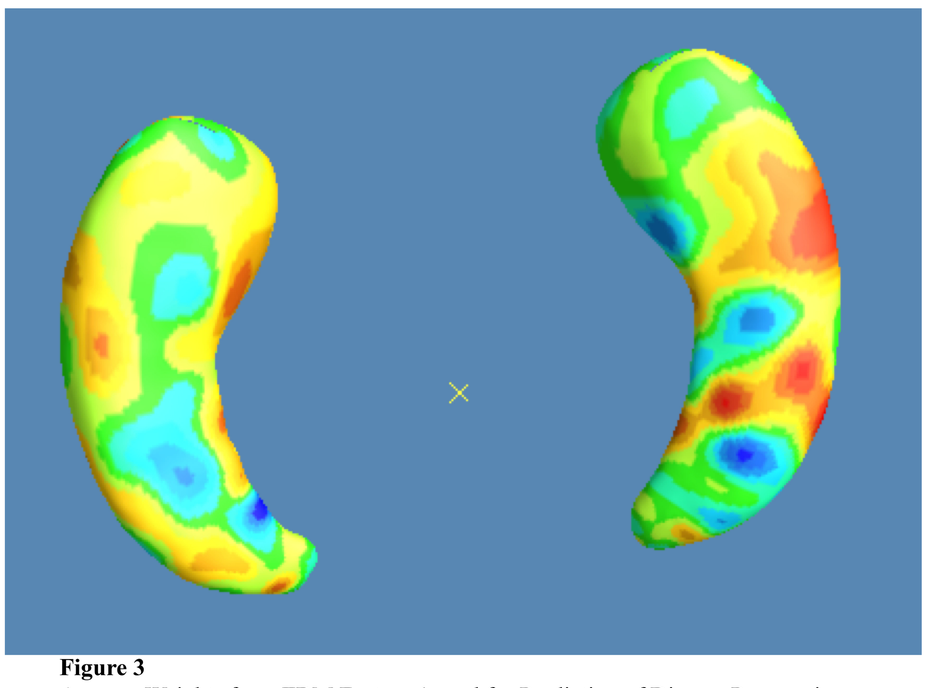

Figure 3
Average Weights for mTBM Feature 1 used for Prediction of Disease Progression

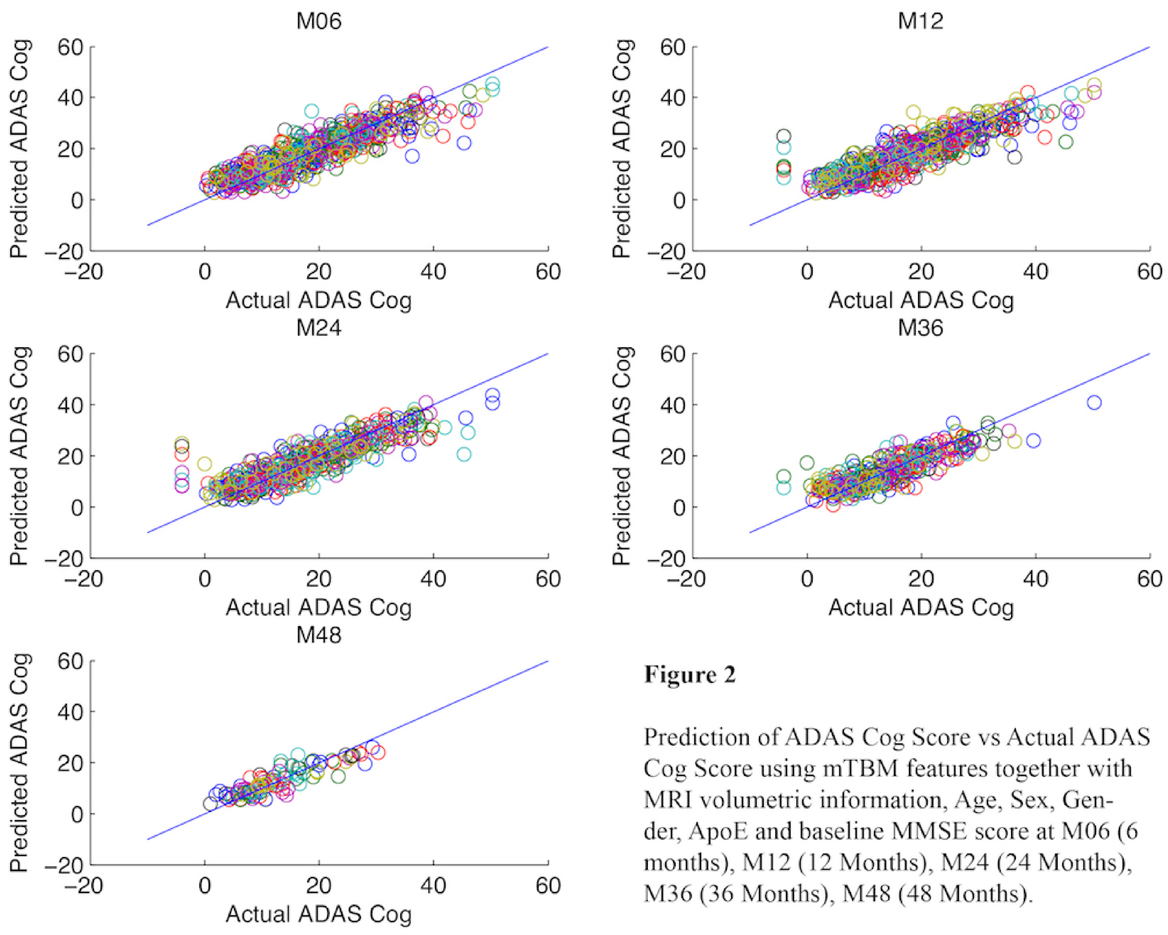

Figure 2

Prediction of ADAS Cog Score vs Actual ADAS Cog Score using mTBM features together with MRI volumetric information, Age, Sex, Gender, ApoE and baseline MMSE score at M06 (6 months), M12 (12 Months), M24 (24 Months), M36 (36 Months), M48 (48 Months).

Multivariate Tensor-based Morphometry (mTBM) features of the Hippocampal Surface:

- Hippocampus Segmentation via FSL[11]
- Parametric Meshes to Model Hippocampal Shapes
- Novel inverse consistent surface fluid registration[2]
- mTBM and radial distance computed via surface deformation analysis[2]

Results

- Predictions using mTBM significantly outperform prediction without using mTBM (Fig. 1 and 2)
- Improved prediction accuracy as shown via nMSE, wR and rMSE in Table 1 and Fig. 4.
- Average weights for one of the mTBM surface features across the 20 trials is shown in Fig. 3.

Discussions and Conclusions

- Improved performance by merging fused mult-task learning with temporal smoothing and Novel AD sensitive surface mTBM maps
- Achieved some of the highest performing predictions based on baseline data only and is consistent with our survey of other comparable studies.1
- Need to investigate more about how to meaningfully incorporate mTBM map weights into the machine learning algorithm, to encode for neighborhood connectivity. (Currently, we use one continuous vector for all features)
- Serves as an illustration of how machine learning methods can be used to perform dimension reduction and how spatial data can be used directly. Possible applications in fMRI, fcMRI and other population studies
- Need more methods in analyzing the resultant weights, currently exploring stability selection.
- Weights analysis can also be used to optimize algorithm by providing a more reasonable starting point during training.

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