Individual Structural Connectivity Networks Enable Automated Prediction of Alzheimer's disease in Subjects at Risk

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INTRODUCTION

Alzheimer's disease (AD) degrades progressively the brain's grey and white matter. White matter changes reflect changes of brain's structural connectivity pattern. The reports of spreading cell loss and white matter deterioration have motivated the hypothesis that the cognitive and behavioral symptoms of AD are the consequence of disconnection between brain regions (Lo et al., 2010; Sorg et al., 2009). We therefore hypothesized that subject-specific patterns of changed white matter connectivity reflect the emergence of observable deficits in behavior and cognition. Here, we asked (i) whether individual structural connectivity networks (ISCNs) based on DWI-tractography are already changed in pre-dementia forms of AD and (ii) whether ISCNs can be used to distinguish individual patients with pre-dementia or mild AD from healthy controls (HC).

MATERIALS AND METHODS

Diffusion-tractography was used to construct ISCNs for 21 healthy controls (HC), 23 patients with mild cognitive impairment and conversion to AD dementia within 3 years (AD-MCI), and 17 patients with mild AD dementia with a fully automated procedure (see Figure 1). For each between-region connection of ISCN, three attributes (fiber density, fractional anisotropy and mean diffusivity) were extracted to represent its pattern. Afterwards, relying on information gain feature selection criteria, most distinctive connections for the discrimination among HC, AD-MCI and mild AD were identified. Finally, three machine learning-based pattern classifiers including Support Vector Machine, Naive Bayes, and *k*-Nearest Neighbor were applied for prediction with 10-fold cross validation and one-leave-out cross validation.

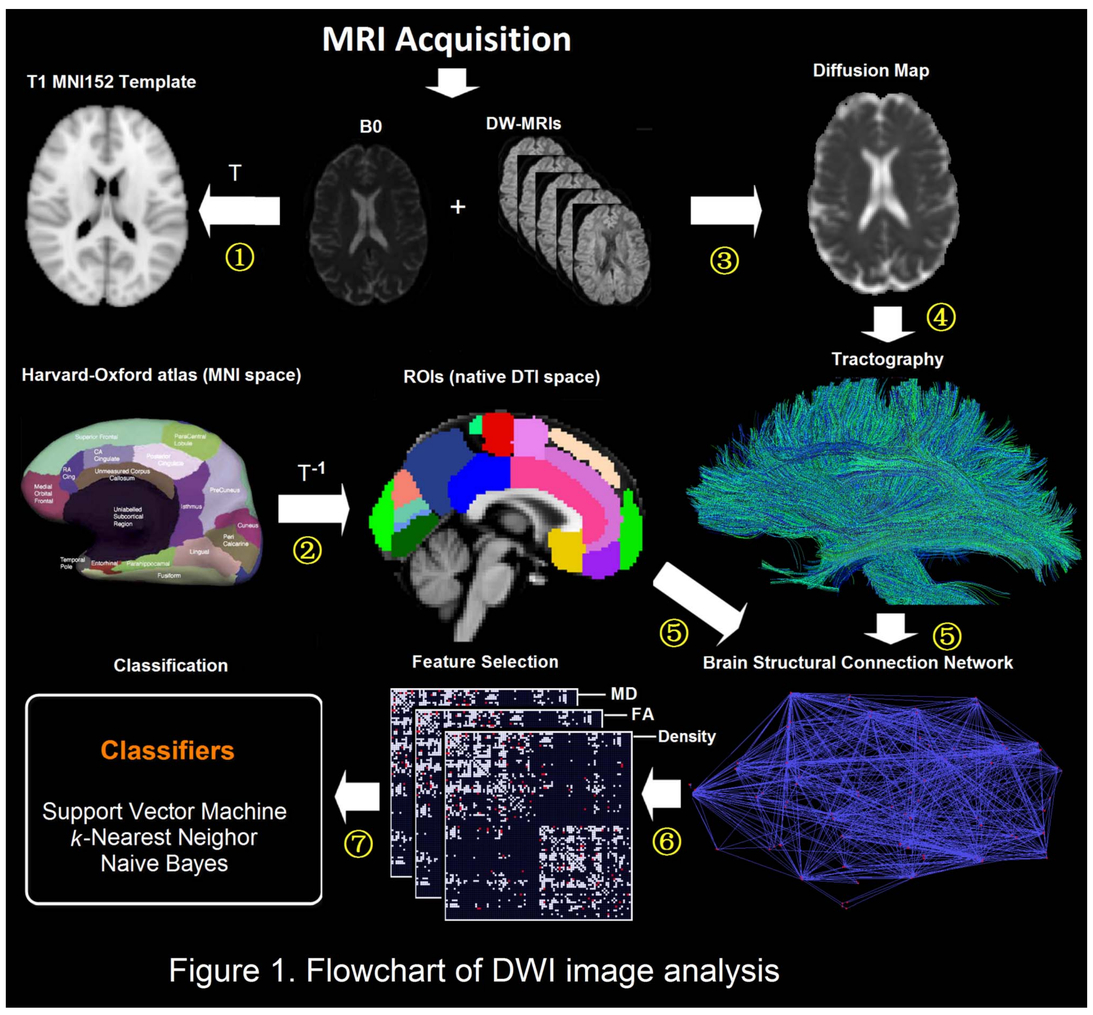

Figure 1. Flowchart of DWI image analysis

RESULTS

Patients with AD and AD-MCI were separated from HC with accuracies above 95% and 90%, irrespective of the prediction approach and the specific fiber measure (Table 1). Most informative connections involved medial prefrontal, posterior parietal, and insular cortex (Figure 2). Patients with mild AD were separated from those with AD-MCI with accuracy of about 85%.

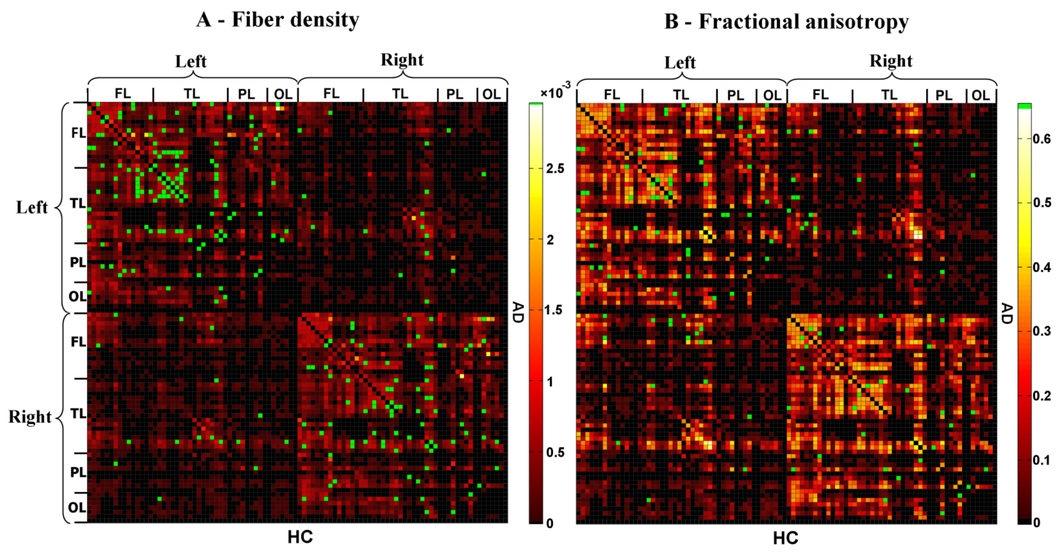

Fig. 2. Selected connections in ISCNs for the comparison between patients with mild AD and HC using information gain.

Table 1. Classification accuracy for individual structural connectivity networks using 10-fold cross-validation.

	SVM	*k*-NN	Naive Bayes
Mild AD vs HC			
Fiber density	100.0%	94.74%	100.0%
FA	92.11%	94.74%	100.0%
MD	100.0%	94.74%	89.47%
Mild AD vs. AD-MCI			
Fiber density	85.00%	85.00%	95.00%
FA	82.50%	75.00%	85.00%
MD	85.00%	82.50%	90.00%
AD-MCI vs. HC			
Fiber density	97.73%	81.82%	95.45%
FA	84.09%	88.64%	97.73%
MD	93.18%	86.36%	100.0%

CONCLUSION

Our finding provides evidence that individual cortico-cortical structural connectivity networks are changed in earliest forms of AD. Cortico-cortical ISCNs may be useful as a white matter-based imaging biomarker to distinguish healthy aging from AD.

Reference

Lo, C.Y., Wang, P.N., Chou, K.H., Wang, J., He, Y., Lin, C.P., 2010. Diffusion tensor tractography reveals abnormal topological organization in structural cortical networks in Alzheimer's disease. J. Neurosci. 30, 16876-16885.

Sorg, C., Riedl, V., Perneczky, R., Kurz, A., Wohlschlager, A., 2009. Impact of Alzheimer's disease on the functional connectivity of spontaneous brain activity. Curr. Alzheimer Res. 6, 541-553.