Classification of mild cognitive impairment based on cerebral white matter fiber tracts

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ABSTRACT

The aim of this study is to research the features of white matter in the brain by Diffusion Tensor Image (DTI) from the patients with mild cognitive impairment (MCI), and using the features to identify MCI and normal control (NC) to explore new methods for MCI diagnosis. In this study, 38 brain DTI images of MCI patients and NC were extracted respectively, and the parameters of cerebral white matter fiber tracts were analyzed. Using automatic fiber tract quantification (AFQ) technology, the index values with significant differences between MCI patients and NC were calculated. Support Vector Machine (SVM) model was built to classify MCI patients from NC. We found significant differences in right cortical spinal tract (CST_R), right uncinate fasciculus (UNC_R), left internal fronto-occipital tract (IFOF_L), and callosum forceps major (FP) in MCI patients and NC. The classification accuracy, sensitivity and specificity of the training set and test set were 94.73%, 92.11% and 97.36%, respectively. This study demonstrates that there are significant differences in certain fiber tracts in MCI patients compared with NC, and using these fiber tract groups can effectively classify the MCI patients and NC, which can provide noval information for MCI white matter decline.

Keywords: Diffusion tensor image (DTI), mild cognitive impairment (MCI), normal control (NC), automatic fiber tract quantification (AFQ)

1. INTRODUCTION

Alzheimer's disease is a common senile central neurodegenerative disease and one of the most usual types of dementia. Clinical features include memory deficits, environmental cognitive loss, and motor dysfunction, along with symptoms of psychosis[1]. Mild cognitive impairment (MCI) is a transitional stage between natural aging and Alzheimer's disease, and research on anomalous changes in the brain's white tracts has important implications for the diagnosis and trerapy of cognitive diseases.

Due to the rapid progress of noninvasive imaging techniques in recent years, it has become possible to visualize the connection of fiber tracts in the brain. Diffusion tensor imaging (DTI) technology is one of them, which can reconstruct the white matter fiber tracts in the brain[2]. It also shows how these fiber tracts are connected in the brain. There are two methods commonly used to quantitatively study the features of fibers in the brain: voxel based analysis (VBA) and region based spatial statistics (TBSS)[3-5]. Since mild cognitive impairment may only cause localized changes in fiber tracts, but not all, the above two methods cannot precisely locate lesions with local abnormalities in fiber tracts. Therefore, this paper takes a deeper look at the measurement of fiber tract indicators within the brain.

The automatic fiber bundle quantification algorithm (AFQ) is an open source software (see https://github.com/jyeatman/AFQ), and the working platform is Python. It can automatically identify up to 18 key white matter tracts within the brain and quantify indicators of diffusion characteristics at multiple locations in the fiber tracts[6].

2. METHODOLOGY

2.1 AFQ fiber tractography

The AFQ method processes can be generalized in four steps:

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- A deterministic tracking imaging algorithm is used to image fibers of each subject's brain, and then all white matter fiber tracts are traced.
- Segmentation of entire brain fibers into bundles using an automated ROI method.
- Before cleaning fibers from the center of the fiber group, the centre of the bundle is defined by representing the fiber group and free fibers are rejected that deviate from the centre of the fiber group[7].
- The value of the diffusion parameter along the trajectories of the fiber group is calculated, and the contribution of each fiber to the parameter value is calculated based on its distance from the center.

We use spline interpolation to calculate four fiber bundle diffusion features, namely: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). We then focus on the FA measure between MCI patients and NC, which is widely used in medical outcome analysis.

2.2 FA indicator analysis

SPSS 21.0 software was used to perform independent sample *t* test on the FA indicator of the extracted 18 groups of fiber bundles, and the fiber bundle groups with significant differences between the MCI and NC groups were selected. All subjects information as shown in Table 1. The statistical results of fibers are as shown in Table 2.

2.3 Support vector machine classification

The above-mentioned fiber bundle groups with significant differences were sent into SVM to obtain a training model, and the ten-fold cross-validation method was used to estimate the classification accuracy, sensitivity and specificity.

3. DATA

3.1 Image data acquisition

The parameters of the NMR data we used are as belows: repetition time (TR) = 3400 ms; echo time (TE) = 100 ms; gap 0 mm; flip angle = 135°; field of view (FOV) = 220× 220 mm2; acquisition matrix = 300×190. Imaging sequence parameters for DTI images are as belows: TR = 6600 ms; TE = 90 ms; number of slices 45; slice thickness 3.0 mm; gap 0 mm; b-value = 1000 s/mm2; = 128×128.

3.2 Subjects

From January 2019 to December 2020, 29 patients with confirmed MCI were recruited by the Brain Hospital Affiliated to Nanjing Medical University, including 22 males and 16 females, aged (71.96±8.23) years. Meanwhile, 38 healthy elderly people matched with the patient group in gender, age and years of education were recruited as healthy control group.

Each of the above subjects underwent whole-brain MRI scans, physical examinations, and neuropsychological scales such as Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Clinical Dementia Rating Scale (CDR) scores and so on (Table 1).

Table 1. Information of MCI patients and NC.

Index		**Participant Groups**	
		MCI	**NC**
Age (year)		71.96±8.23	70.48±7.58
Sex, n (%)	Female	16(42%)	18(47%)
	Male	22(58%)	20(53%)
Education (years)		10.83±1.68	11.77±2.32
MMSE score		20.58±5.12	28.66±4.22
MoCA score		11.22±4.33	27.87±3.66
CDR score		0.69±0.45	0

Table 2. Comparison of FA between MCI and NC groups.

Fiber	**n1: n2**	**MCI**	**NC**	***t* test**		
		(N = 38)	**(N = 38)**	***F***	**df**	***p***
ATR_R	38:38	0.4212±0.064	0.4193±0.040	10.754	174	0.807
ATR_L	37:37	0.4047±0.0930	0.4168±0.064	5.857	184	0.273
CGC_R	38:37	0.4519±0.1038	0.4696±0.0755	3.904	190	0.158
CGC_L	37:37	0.4774±0.095	0.4742±0.0921	0.027	208	0.808
CST_R	38:37	0.4872±0.1480	0.5240±0.0441	21.596	208	0.016
CST_L	37:37	0.5054±0.1272	0.5118±0.1111	1.025	208	0.247
IFOF_R	38:37	0.4654±0.0780	0.4755±0.04291	2.746	208	0.698
IFOF_L	38:37	0.4703±0.0811	0.4883±0.0463	3.670	208	0.05
ILF_R	38:38	0.4312±0.0646	0.4393±0.0444	3.126	208	0.295
ILF_L	38:38	0.4309±0.0655	0.4385±0.0419	5.243	208	0.323
SLF_R	38:38	0.4200±0.0642	0.4295±0.0560	0.954	208	0.254
SLF_L	38:38	0.4028±0.0615	0.4080±0.0499	1.593	208	0.493
ARC_R	38:37	0.4210±0.0894	0.4434±0.04327	8.073	208	0.435
ARC_L	38:38	0.4624±0.0424	0.4658±0.0388	1.104	208	0.544
UNC_R	38:38	0.3605±0.0659	0.354±0.0613	0.029	208	0.022
UNC_L	38:38	0.3369±0.0716	0.3415±0.0850	1.053	208	0.676
FA	38:37	0.4354±0.0944	0.4590±0.0475	4.586	208	0.253
FP	38:35	0.4754±0.2129	0.5416±0.1254	8.840	153	0.023

4. RESULTS

4.1 Mean diffusion measures of MCI and NC groups

In Table 2, we list the number of subjects in each tract (named n1:n2) that were correctly tracked using FDR correction. The AFQ method does not perform well in some fibers, especially the large tract of corpus callosum in this study. Fiber bundles like CGC_R, CST_L and IFOF_R are missing 1-2 FA values, and the tracking results of other fiber bundles (such as ILF_R, SLF_R and UNC_R) are complete. This may be caused by the threshold setted of the fiber tracking, or it may be due to individual differences or atrophy of the associated fiber bundles. The total number of fiber tracts traced to MCI and NC will be added to future studies to better assess white matter damage in the brain.

We used a $p < 0.05$ threshold to compare the FA feature of each white matter tract between the MCI and NC groups in a statistical analysis and identified tracts with significant differences. Compared with the normal controls, four fiber tracts showed a significant difference, which were bolded: CST_R, IFOF_L, UNC_R and FP.

The magnitude of the FA indicator value was also significantly different between the MCI and NC groups. Figures 1-4 show the FA indicator of some fiber bundles between the two groups. The horizontal axis is the number of subjects (38 cases in total), and the vertical axis is the FA index value. The blue line segment is the NC group, and the orange line is the MCI group.

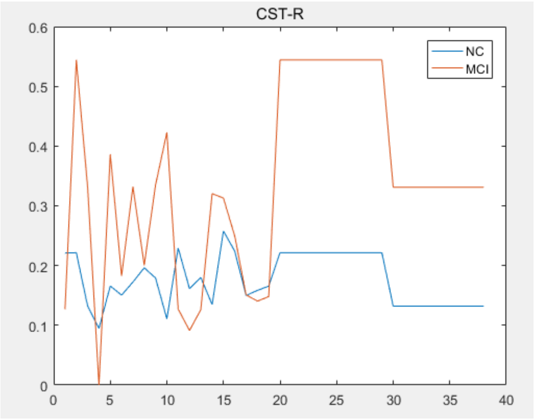

Figure 1. FA indicator of CST_R between the two groups.

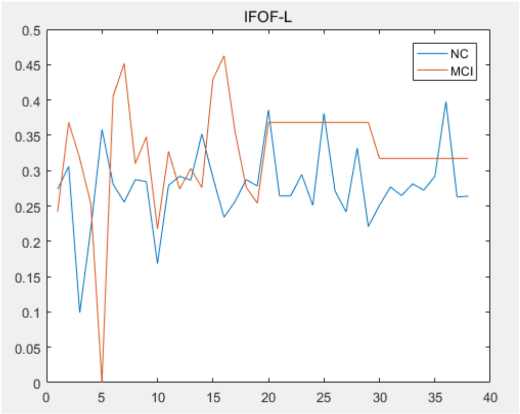

Figure 2. FA indicator of IFOF_L between the two groups.

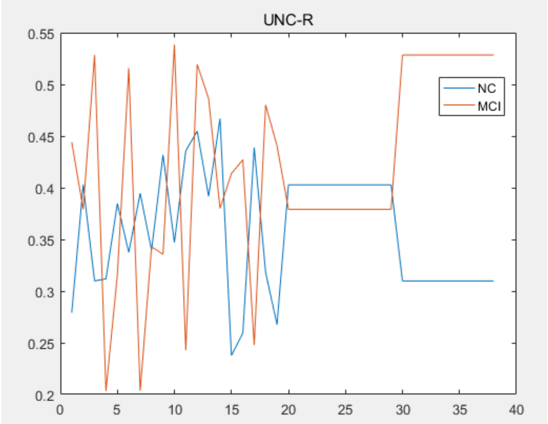

Figure 3. FA indicator of UNC_R between the two groups.

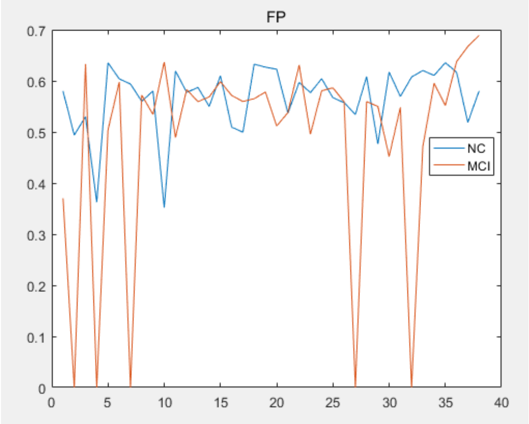

Figure 4. FA indicator of FP between the two groups.

4.2 SVM based classification

Figure 5 is the classification result, where 1 is a predicted positive sample, 0 is a negative sample. An error value of 0 indicates that the classification is correct, 1 is a correct sample that is judged to be an incorrect sample, -1 is an incorrect sample that is judged to be a correct sample, and the overall value is subtracted 5, which is -5, -4 and -6 to avoid confusion.

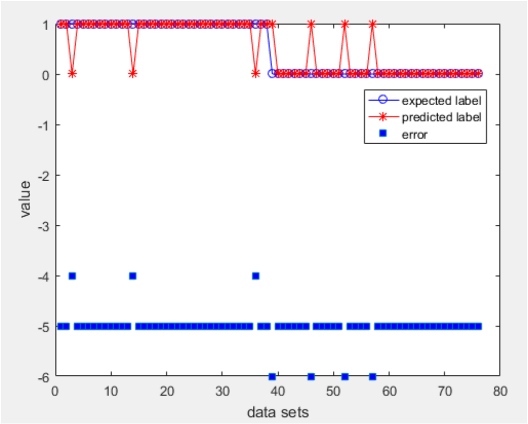

Figure 5. Classification result.

The true negative (TN), true positive (TP), false positive (FP) and false negative (FN) results are 35, 34, 3 and 4 seperately, so the accuracy, sensitivity and specificity are 90.78% (69/76), 89.47% (34/38) and 92.11% (35/38)[8-10].

5. CONCLUSION

Based on the AFQ method, this paper proposes a classification and recognition algorithm for MCI and NC groups, and the final recognition rate is good, which shows that this method is feasible and effective. At the same time, judging from the results of significant differences between MCI and NC groups of fibers, there is a statistically significant difference in the distribution of commissural fibers, commissural fibers and projection fibers in the brain, and further research is needed to explain this in the future.

Different from studies using MR image texture features, hippocampal volume features, etc., this paper innovatively uses fiber bundle groups with significant differences to train the SVM model, and obtains high accuracy, sensitivity and specificity, which illustrates the method in this paper. It is effective. Future work will consider including the gender, age, etc. of the subjects into the features, and consider combining multimodal data to construct feature vectors to increase the accuracy of the classification method.

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