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Correlation Between Diffusion Tensor Imaging Method Results and the SCOPA-COG in Parkinson's Disease

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Abstract: Back ground: Cognitive impairments play an important role in Parkinson's disease (PD). Objective: In this study, the relationship between the Diffusion Tensor Imaging (DTI) method and the SCOPA-Cog clinical test was investigated in different domains of cognitive impairment. Method: This study was performed on 20 patients with clinical diagnosis of idiopathic PD. Fractional anisotropy (FA) and mean diffusivity (MD) parameters were calculated by drawing region of interest (ROI) on 15 distinct areas. Cognitive impairment was evaluated using the SCOPA-Cog standard test. Conclusion: The results of investigation of the relationship between the DTI method and SCOPA-Cog clinical test showed that changes in FA and MD values in the Fornix area were significant compared to SCOPA test results. We found correlations between DTI parameters and executive function score in some regions such as Genu, superior fronto-occipital fasciculus (SFOF), anterior limb of internal capsule (ALIC) and posterior corona radiata (PCR). The results showed that there is a significant relationship between DTI parameters and visuospatial score in parieto-occipital domain. The results indicate that there is a correlation between DTI method and the SCOPA clinical test. This information can be used to measure sensitivity and reliability of SCOPA test in early detection of Parkinson's disease.

Keywords: Cognitive Dysfunction, Parkinson Disease, Diffusion Tensor Imaging, White matter, Magnetic Resonance Imaging, Brain, Fractional Anisotropy, Mean Diffusivity

1. Introduction

Parkinson's disease is a progressive degenerative disease. Parkinson's is the second most commonly reported neurodegenerative disease [1]. This disease is associated with motor symptoms such as muscle stiffness and tremble, imbalance, slow motion, and non-motor symptoms such as cognitive disorder, visual disturbances, sleep disturbances, depression, etc [2]. In this disease, 50 to 70 percent of the dopaminergic neurons are degraded in the substantia nigra. In addition to the dopaminergic neurons other neuronal populations that also include the parts of the locus coeruleus (noradrenergic), raphe nucleus (serotonergic), Meynert nucleus, dorsal motor nucleus of vagus (cholinergic), cingulate cortex, entorinal cortex, olfactory bulb and sympathetic and parasympathetic ganglia of the intestine. This disease is caused by an imbalance between stimulation and inhibition in the basal ganglia due to dopaminergic putamen inhibition [3, 4].

Cognitive deficits related with PD can be influenced by multiple domains, including executive function, memory, Visuospatial skills, attention, and language. Although these cognitive disorders are prevalent, a range of disorders and neural basis of cognitive impairment in PD is not completely clear [5, 6].

One of the clinical tools for diagnosis of cognitive impairment in Parkinson's patients is to use neurocognitive tests such as Scales for Outcomes in Parkinson's Cognition (SCOPA-Cog). In this test, memory, learning, attention, performance, and spatial visibility disorders are evaluated [7].

Neuroimaging examination of cognitive disorders is a matter of a growing interest. Diffusion Tensor Imaging is a non-invasive imaging technique used to detect microstructural damage in Parkinson's disease [8, 9]. This technique is based on the investigation of the movement of water molecules inside the brain white matter's microstructure. In brain white matter due to the presence of myelin sheath, which is like a barrier against water release, the water distribution is anisotropic in the nerve fiber bundles and it is higher in the long axis of the bundles. In a situation where the myelin of the axon structure is damaged, for example by a stroke, brain tumors or neurodegenerative diseases, the anisotropy is reduced and the myelin sheath impermeability is affected by this injury [10]. In these cases it is possible to obtain valuable information from the white matter condition by the data obtained from the distribution of water molecules and the processing of this data. Hence, the DTI technique has been considered a lot in clinic in recent years.

Two commonly used parameters for measuring white matter integrity are FA and MD. FA is a quantitative unit for representing the amount of diffusion anisotropy that is a number between zero and one. Mean diffusivity, which describes magnitude of water diffusion in brain tissue [8]. In this study, using the DTI technique, white matter integration was evaluated in four different cognitive domains in patients. Additionally, cognitive disorder level was calculated using the SCOPA clinical test. Subsequently, by examining the results of these steps, the relationship between the data obtained from DTI and the SCOPA clinical test was evaluated using bioststistical tests.

2. Methods

In this study, 20 patients (17 males and 3 females, mean age of 61 years) who were diagnosed with idiopathic PD from the Parkinson's Clinic of Shohada-e Tajrish (hospital of Shahid Beheshti University of Medical School) were evaluated. All of the patients were evaluated and approved for having an idiopathic PD. Moreover, 10 normal patients were considered as healthy controls. All patients signed consent form before including to the study.

2.1. Inclusion Criteria

The patients of both genders who were diagnosed with idiopathic PD were included in this study.

2.2. Exclusion Criteria

The patients with claustrophobia, head surgeries, severe cognitive impairments, Alzheimer disease, dementia and psychiatry disease were excluded from our study.

2.3. Cognitive Assessments

Some cognitive disorders were evaluated by SCOPA-Cog standard test. The SCOPA-Cog subdivided into four main sections: memory and learning, attention, executive functions, and visuospatial functions. This test generally consists of ten questions to assess the cognitive domains. Learning and memory are assessed with verbal memory, indicate cube, delayed recall of a word and digit span backward. The attention subtests are counting backwards and months backwards. Executive deficits are evaluated with Fist-edge-palm, semantic fluency and dice test. Visuospatial ability is measured through completion of unfinished patterns. The total score ranges from 0 to 43, with higher scores indicating better performances.

2.4. Image Acquisition

In this study, MRI was performed on a 1.5 Tesla MRI (GE scanner) using a high-resolution 3D T1-weighted sequence with the following parameters: matrix size = 256 × 256, slice thickness = 1.2mm, flip angle = 12°, a repetition time of 7.77ms, and echo time of 2.79ms. DT imaging was performed by using a single-shot spin echo EPI sequence with the following parameters: matrix size = 112 × 112, TR = 13000ms, TE = 103ms, voxel size = 2.5mm isotropic. Diffusion gradient encoding with b value = 1000sec/mm^2, and an additional measurement without diffusion gradient (b = 0sec/mm^2) were performed.

Eddycurrent correction was used to eliminate distortions and motion artifact in the DTI. Data processing was performed using Explore DTI software. ROI was drawn to calculate the amount of FA and MD in the intended areas. ROIs were plotted based on studies by Zheng and Hermoy et al [15, 16].

2.5. Statistical Analysis

Statistical analysis was performed using SPSS 19 software. The level of significance was set as 0.05 in the calculations. T-test was used to examine the difference between FA and MD values among the groups.

3. Results

The results of this study showed that there was no significant difference between age, disease duration and education duration parameters between groups. The PD group's SCOPA test score was significantly lower than the control group (Table 1).

Table 1. *Demographic and clinical information of indivuduals.*

	HC (n = 10)	PD (n = 20)	P-value
Age, mean (SD)	57 (7.16)	61.49 (3.31)	0.97
Sex, M: F	7:03	17:03	NA
Education duration (yr)	12.5	11.3	0.58
Hoen & Yahr Score (2-3)	NA	2.63	NA
SCOPA (0-43)	32.5	18.5	0.003**
Disease duration Mean (SD)	NA	8.35 (5.47)	NA

HC: healthy control.
PD: parkinson's disease.
**p < 0.01.

In each of the cognitive domains, the corresponding ROIs were drawn. Then each of the FA and MD parameters was

calculated (Figure 1).

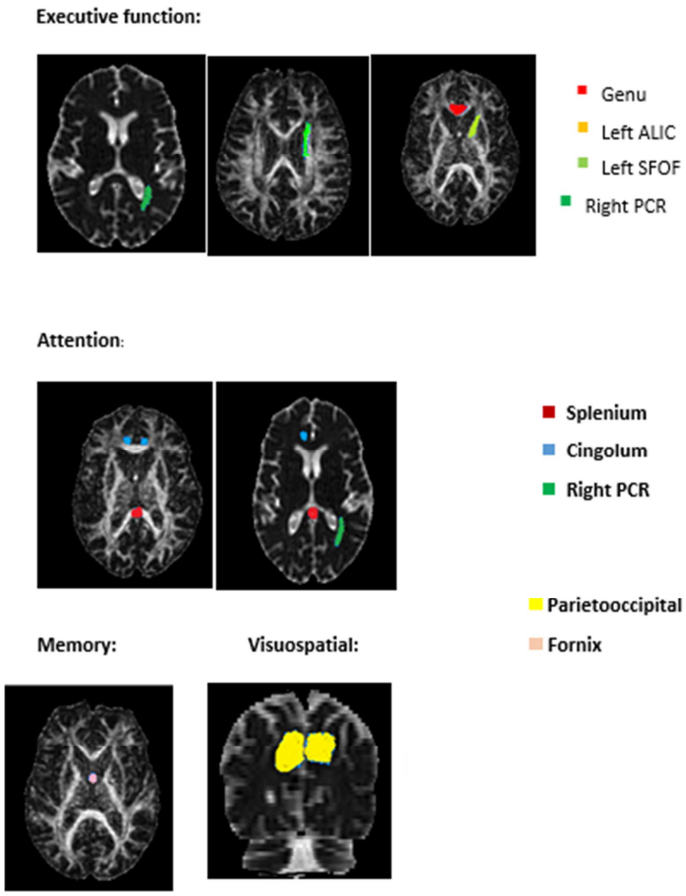

Figure 1. *Presents some ROIs that were drawn in each cognitive domain. The images of executive function, attention and memory are presented in the axial view and the visuospatial image is illustrated in the coronal view.*

The results of the comparison of changes in DTI parameters between the group of patients with Parkinson's disease and the healthy control group in the specified regions showed that the amount of FA parameter in the fornix, Left PCR, Right and left SFOF and splenium (SPL) in Parkinson's patients significantly decreased compared to healthy subjects. MD parameter changes were also significant in the Genu, Fornix, Right and left SFOF, Right and left cingulum (CIN), Right and left superior corona radiata (SCR), Right and left ALIC regions between two groups (Table 2).

Table 2. *Comparison of changes in DTI parameters between the group of patients with Parkinson's disease and the healthy control group.*

Region	FA			MD		
	HC (Mean ± SD)	PD (Mean ± SD)	P-valu	HC (Mean ± SD)	PD (Mean ± SD)	P-value
Genu	0.72 (0.01)	0.68 (0.01)	0.16	0.0007 (0.0000)	0.0013 (0.0003)	0.001***
Fornix	0.49 (0.02)	0.37 (0.00)	0.002**	0.0013 (0.0001)	0.0017 (0.0000)	0.009**
R. PCR	0.56 (0.00)	0.53 (0.07)	0.16	0.0008 (0.0000)	0.0009 (0.0001)	0.09
L. PCR	0.56 (0.00)	0.49 (0.08)	0.004**	0.0008 (0.0000)	0.0089 (0.0000)	0.11
R. SFOF	0.50 (0.03)	0.35 (0.07)	0.003**	0.0007 (0.0000)	0.0009 (0.0001)	0.000***
L. SFOF	0.57 (0.02)	0.35 (0.08)	0.000***	0.0006 (0.0000)	0.0009 (0.0000)	0.000***
R. CIN	0.44 (0.04)	0.38 (0.01)	0.32	0.0007 (0.0000)	0.0008 (0.0000)	0.01**
L. CIN	0.37 (0.03)	0.39 (0.01)	0.72	0.0007 (0.0000)	0.0008 (0.0000)	0.004**
R. SCR	0.51 (0.04)	0.47 (0.00)	0.45	0.0007 (0.0000)	0.0008 (0.0000)	0.000***
L. SCR	0.51 (0.04)	0.45 (0.06)	0.25	0.0006 (0.0000)	0.0008 (0.0000)	0.000***
R. PO	0.21 (0.01)	0.19 (0.00)	0.28	0.0010 (0.0001)	0.0012 (0.000)	0.11
L. PO	0.22 (0.02)	0.17 (0.05)	0.08	0.0011 (0.0002)	0.0016 (0.0001)	0.32
R. ALIC	0.53 (0.02)	0.50 (0.07)	0.36	0.0006 (0.0000)	0.0008 (0.0000)	0.000***
L. ALIC	0.48 (0.03)	0.49 (0.01)	0.96	0.0006 (0.0000)	0.0008 (0.0000)	0.000***
SPL	0.78 (0.01)	0.71 (0.00)	0.009**	0.0003 (0.0000)	0.0009 (0.0000)	0.06

*P < 0.05.
**P < 0.01.
***P < 0.001.

The results of the correlation between the DTI parameters and Scopa test scores in each domain showed that there was a direct correlation between the FA parameter and Scopa test results and there was an inverse relationship between the MD parameter and the clinical test in some domains. The areas where there is a significant relationship between the DTI and the scopa test parameters are shown in Figure 2.

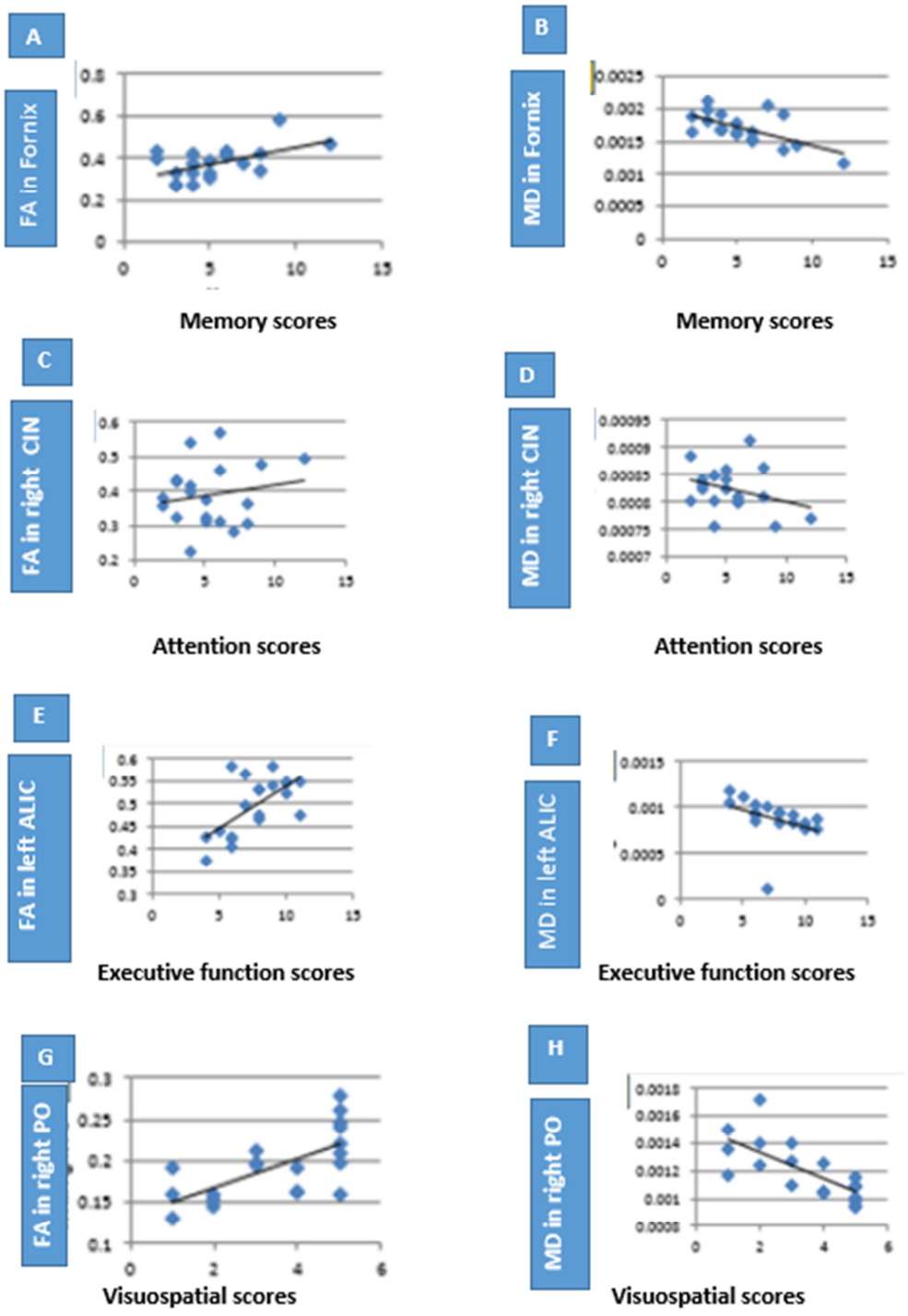

Figure 2. *Regression analyses correlation between DTI parameters (FA and MD) and scopa test score in each domain. Representative regions of the significant correlations from each domain are graphed.*

The results showed that there is a significant direct correlation between FA parameter and memory impairment score in SCOPA test in Fornix area. There is also a significant inverse correlation between the MD parameter and the clinical test in this area.

In attention domain FA value had significant correlation in right cingulate gyrus with attention score directly and in this region there was inversely correlation between MD and

attention score in SCOPA test significantly. Also attention score directly correlated with FA within left cingulate gyrus, right SCR and splenium. Inversely correlation was found between MD and attention score in left PCR and splenium.

Executive function score had directly correlation with FA within left ALIC and also genu of corpus colosum. MD value and executive function score had negative correlation in regions of left SFOF and right PCR.

In Visuospatial performance was found an inversely correlation in right and left parieto occipital gyrus between MD value and related scores in SCOPA test. FA value and visuospatial had positive correlation in right parieto occipital gyrus.

4. Discussion

There are many standard diagnostic clinical tests for Parkinson's disease. The advantages of these tests include low cost, repeatability, non-invasive nature and time efficiency. Of course, these tests also have disadvantages. For example, the results of this test may produce false positive response in individuals with low educations. Another disadvantage is the low sensitivity of these tests. One of the most important drawbacks of neurocognitive tests is the measurement of executive functions [11]. Given that this disorder is present in various diseases such as Parkinson's disease, dementia, stroke, alcoholism, etc. the results of these tests will not be reliable in assessing the performance of the executive functions.

The disadvantages mentioned in the clinical tests of Parkinson's disease show the need for other modern methods to diagnose this disease. Previous extensive studies have shown that there is a correlation between changes in the white matter structure and the occurrence of motor and cognitive impairment in Parkinson's disease [12, 13]. The development of advanced imaging techniques has made it possible to study the molecular and structural changes in the brain.

In this study, changes in non-invasive DTI parameters in patients with Parkinson's disease were addressed and compared with healthy control group. In addition, the relationship between FA and MD parameters was evaluated by the SCOPA clinical test. Previous studies have shown that most PD patients represent an attentional-executive dysfunction with possible progression to impairments in language, memory and visuospatial. Present study assessed four cognitive disorders include: memory & learning, executive function, attention and Visuospatial in SCOPA test.

Memory impairment had correlation with fornix. Fornix is a set of white mater tract that lie in aspect of two hemisphere in the brain. Fornix has crucial role in the formation and consolidation of declarative memories. Previous studies confirms relationship between fornix and memory [14, 15]. As shown in Figure 2, with the increase of FA values in the Fornix area, memory scores also increased in the SCOPA test. On the other hand, the memory scores are reduced by increasing the MD values. This finding is consistent with the findings of Zheng et al [16].

We assessed left PCR, right SCR, Splenium, right & left Cingulum for attention impairment. There were a significant correlation between FA parameter and attention scores in SCOPA test in right Cingulum region. Also a significant correlation was found about MD parameter and attention scores. In left Cingulum region a direct relation between FA and attention scores was seen. Previous studies have been reported DTI parameters changes in PD in Cingulum region. Some studies have been shown that DTI Parameters associated with attention domain on the cognitive tests [17].

Also we found direct correlation between FA and attention scores in Splenium region and there were relation between MD parameter and attention scores inversely. This is consistent with the results of the findings of Zhang et al [13]. Previous studies have shown that there is a relationship between attention disorders and parietal lobes. In this regard, our founding shown that an inverse correlation between MD parameter and attentional scores in SCOPA test in left posterior corona radiate and also a direct correlation between FA value and attentional scores in right superior corona radiate.

Executive dysfunction is the most common defects in PD patients [18]. These skills are usually controlled by the frontal lobe of the brain. We found correlations between DTI parameters and executive function score in some regions of frontal lobe such as Genu, SFOF and ALIC. Direct correlations were about FA and executive function score in left Genu and ALIC. This correlation was stronger in Genu than left ALIC .There were invers relation about MD and executive function score in left SFOF and also right PCR.

Our results indicated that both frontal and parietal lobe is associated with executive functions. This result is consistent with previous studies [19].

Visual spatial cognition is composed of a collection of multi-faceted functions. Right-hemisphere network of brain regions, including parietal lobe, lateral prefrontal cortex, medial temporal lobe, the temporal inferior cortex, occipital cortex, basal ganglia, and white matter are related to this cognitive domain [20]. We evaluated right and left parieto-occipital cortex. Our result revealed a direct correlation between visual spatial scores and FA value in right parieto-occipital domain. Also there were an inverse correlation between MD value and visual spatial score in both right and left parieto-occipital cortex. We found stronger correlation in right parieto –occipital. To our knowledge this is first study that has assessed this relation in this regions.

5. Conclusions

Based on the findings of this study in Parkinson's disease, FA values in some areas of the brain are significantly lower than normal subjects. The MD parameter also shows significant changes in some areas in these patients. DTI revealed diffusion changes in these areas in patients with PD compared with control subjects. These results suggest that

neurodegenerative changes may occur outside the Substantia Nigra in PD.

Our study results showed that FA values had direct correlation with SCOPA scores in specific ROIs and there were inverse correlation between MD values and SCOPA scores in identified ROIs. Therefore, along with conventional clinical tests, non-invasive DTI can also play a significant role in an early diagnosis of neurodegenerative diseases such as PD.

Also PD is associated with a widespread neurodengerative process affecting a range of cognitive functions with underlying microstructural damage that was mostly region specific to the function assessed.

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