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Diffusion Tensor Imaging to Analyze White Matter Tract Abnormalities in Major Psychiatric Disorders

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ABSTRACT

Background: Diffusion Tensor Imaging (DTI) is a novel MRI technique developed for measuring the integrity of white matter and its structural connectivity within the brain. DTI captures the movement of water molecules along the neural pathways, providing valuable information on the micro-structural changes that are associated with particular neurological disorders.

Methods: This paper examines some of the concepts related to DTI and its particular indices such as fractional anisotropy (FA) and mean diffusivity (MD). DTI scanning protocols and post-processing modifications are evaluated in the context of white matter tracts abnormalities detection.

Results: The results show how DTI can reveal changes in white matter lesions which could not be perceived using routine MRI techniques. Changing values of FA and MD are associated with the level of disease progression and cognitive deficit.

Conclusion: DTI is a powerful tool for investigating white matter integrity and diagnosing neurological disorders. While it offers significant advantages in neuroimaging, further advancements in imaging acquisition and analysis techniques are needed to improve reliability and clinical utility.

Introduction

The human brain consists of more than 100 billion neurons that form axons and complex networks which communicate with each other. Diffusion tensor imaging (DTI) is a recently developed technique which aims to do structural mapping of these networks in the human brain. In the past, various researchers have done mapping studies in animal brains using histology and various stains. However, such studies are not reproducible in the human brain and hence, the importance of DTI is inevitable. DTI is also important as it is non-invasive, requires no new equipment, no contrast agents and no chemical tracers. DTI uses the anisotropic diffusion of water molecules to measure the orientation of axons. The basic concept is that water molecules diffuse differently in different tissues, and the amount of diffusivity of water molecules depends on the orientation of fibres, their structure, integrity and composition. The contrast that is produced in DWI is based on the differences in the amount of diffusion of water molecules. The basic mechanism behind diffusion is Brownian Motion, which essentially means the random movement of water molecules. This phenomenon is dependent upon various factors, including the type of molecule, temperature and micro-environment under study. For instance, the diffusion in cerebrospinal fluid (CSF) is more as compared than that within inter and intracellular

compartments. We can choose the necessary diffusion-sensitive MR sequences to measure the differences in the magnitude of diffusion rates and eventually create the image contrast. The spatial distribution of the diffusion rate within the brain is represented on quantitative maps, which are generated. Post processing also displays the apparent diffusion coefficient (ADC) map which is a pixel-by-pixel map. The intensity of the ADC map can be used for the quantitative estimation of the regional ADC[1]. Data collected is used to measure fibre orientation and diffusion anisotropy, and gives us a lot of anatomical information about the complex white matter tracts. DTI analysis infers many properties such as Apparent diffusion coefficient (ADC), which is the molecular diffusion rate; and Fractional Anisotropy (FA), which is the directional preference of diffusion. It also measures the axial and radial diffusivity, which are the diffusion rates along the main and transverse axes of diffusion[2].

Therefore, DTI has a wide variety of clinical applications, and it is used in many disorders where white matter structural changes are expected. It has been widely used to study patients with acute stroke or brain tumors; cognitive impairment, epilepsy, changes in white matter microstructure during neurodevelopment and in aging, neurodegenerative disorders including multiple sclerosis, Alzheimer's, movement disorders such as Parkinson's and Huntington's; neurogenetic developmental disorders such as Williams syndrome and fragile X syndrome etc. DTI also has a wide application in neuropsychiatric disorders such as schizophrenia; psychotic disorders, in patients with substance use and bipolar affective disorder (BPAD). Previous studies have investigated white matter abnormalities in various conditions; however, many have focused on single disorders or have not critically compared findings across psychiatric illnesses. In this article, we compare the FA and ADC values of major white matter fibre tracts in various psychiatric disorders (schizophrenia; psychotic disorders, patients with substance use and BPAD) with those of normal controls[3].

We hypothesize that major psychiatric disorders (schizophrenia, psychotic disorders, substance use disorders, and BPAD) are associated with distinct alterations in white matter integrity, as reflected by decreased fractional anisotropy (FA) and altered apparent diffusion coefficient (ADC) values. This study aims to address these gaps by systematically comparing FA and ADC values of major white matter tracts among patients with schizophrenia, psychotic disorders, substance use disorders, BPAD, and normal controls.

Methods

Patients with anxiety, psychotic disorders, substance use and bipolar disorders were included in the study. Age and gender matched healthy controls were taken. A total of 49 patients who were diagnosed as Anxiety disorders (n=16), Psychotic disorders(n=12), Substance use disorders (n=10), Bipolar disorders (n=11) according to Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria were enrolled in the study. All participants included were right-handed and provided written informed consent after receiving a detailed explanation of the study. A Hindi and English patient information sheet was provided to all of the study subjects. The Institutional Ethical Committee of Maharishi Markendeshwar Institute of Medical Sciences and Research approved this study. Data was collected regarding the type of family, education, marital status, socio-economic status, locality, total monthly income, total members in the family, smoker, heavy alcohol intake, and drug abuse. BMI of each participant was calculated. A detailed psychiatric evaluation was done by an experienced psychiatrist with more than 15 years of experience. In this study, 1.5 Tesla (T) MR System Multiva - Philips magnets (Baltimore, Netherland, Holland) was used to determine FA and ADC values of 10 main white matter fibre tracts. Imaging with axial T1WSE, sagittal T2WSE and 3D FLAIR sequences was done by means of diffusion weighted neurography b values of 0 and 800 s/mm^2. Acquisition was done using a 8 channed head coil. Spin- echo DTI echo planar imaging sequence was used to acquire DTI images. Critical parameters included voxel resolution (e.g., 2.5 × 2.5 × 2.5 mm^3), number of diffusion directions (32 directions), and post-processing steps (using software FSL) with standard correction for motion and susceptibility-induced distortions. Image evaluators were blinded to the participants' clinical diagnoses.

However, all patients who were detected with some pathologies on MRI were excluded. Patients below the age of 18 years were excluded. Other exclusion criteria were previous history of depression or any other mental disorder; a Mini-mental scale score less than 24, and any metal devices in situ which are not compatible with MRI.

Statistical Analysis

Patient characteristics were reported using descriptive analyses. The normality of the data was tested using the Shapiro–Wilk test. Since the data was non-parametirc, the Kruskal-Wallis test was to compare mean FA and mean ADC among 5 included groups, followed by pairwise comparisons using Dunn's test with the Bonferroni corrections.

A p-value <0.05 was considered statistically significant. All data analyses were performed using SPSS version 26.0 (SPSS, Inc).

Results

This study included 49 patients categorised into

5 different groups - Anxiety disorders (16), Psychotic disorders (12), Substance use disorders (10), Bipolar disorders (11) and Controls (30) (Table 1). There were 30 participants in control group.

The age group consists of the younger population in all disorders. Anxiety disorders were more common in females, whereas psychotic disorders, substance use disorders, and bipolar disorders were more common in males. (Table 2)

The Kruskal-Wallis test revealed a significant difference in FA means among all groups in the Fornix and inferior fronto-occipital fasciculus tracts. Post hoc comparisons using Dunn's test with Bonferroni correction showed a significant difference in FA means between the anxiety disorder group and controls in the Fornix, whereas a significant difference was observed between the substance use disorder group and controls in the inferior fronto-occipital fasciculus tract. (Table 3)

The Kruskal-Wallis test revealed a significant difference in ADC means among all groups in the Corticospinal, Forceps Major and Uncinate fasciculus tracts. Post hoc comparisons using Dunn's test with Bonferroni correction showed a significant difference in ADC means between the anxiety disorder group and controls in the Corticospinal tract, between psychotic disorders and controls in Forceps Major group and between the psychotic disorders and controls in the Uncinate fasciculus tracts. (Table 4)

Table 1: Distribution of Cases and Controls

Group Name	Participants (n)	Percentage (%)
Anxiety Disorders	16	20.3
Psychotic Disorders	12	15.2
Substance Use Disorders	10	12.7
Bipolar Disorders	11	13.9
Controls	30	38.0

Discussion

In this study, we analysed white matter abnormalities in major psychiatric disorders and assessed them using FA and ADC values. The Fornix showed significantly lower FA fornix in patients compared to controls , suggesting impaired limbic connectivity that may underlie emotion regulation deficits in anxiety disorders. Similarly, the Inferior Fronto-occipital Fasciculus (IFOF) demonstrated significantly reduced FA in substance use disorder patients, indicating disrupted connectivity that could affect visual processing and higher cognitive functions. Anxiety disorders, in our study, included panic disorder

Table 2: Demographic characteristics of cases

Variable	Range (in Years)	Anxiety disorders n (%)	Psychotic disorders n (%)	Substance use disorders n (%)	Bipolar disorders n (%)	Controls n (%)	Total n (%)
Age	19-40	12 (15.2)	8 (10.1)	8 (10.1)	6 (7.6)	15 (19.0)	49 (62.0)
	41-60	3 (3.8)	3 (3.8)	1 (1.3)	3 (3.8)	12 (15.2)	22 (27.8)
	>60	1 (1.3)	1 (1.3)	1 (1.3)	2 (2.5)	3 (3.8)	8 (10.1)
Gender	Male	6 (7.6)	7 (8.9)	9 (11.4)	9 (11.4)	14 (17.7)	45 (57.0)
	Female	10 (12.7)	5 (6.3)	1 (1.3)	2 (2.5)	16 (20.3)	34 (43.0)

Table 3: Groupwise and tract-wise FA means and comparisons

	Anxiety disorders Mean±SD	Psychotic disorders Mean±SD	Substance use disorders Mean±SD	Bipolar disorders Mean±SD	Controls Mean±SD	Mean±SD overall	P value*
Fornix	0.413±0.041	0.431± 0.034	0.415±0.020	0.410±0.034	0.455±0.048	0.431 ±0.044	.009 (#Anxirty vs controls)
Anterior Thalamic Radiation	0.475±0.025	0.488±0.040	0.470±0.035	0.451±0.040	0.464±0.041	0.469 ±0.038	.288
Arcuate Fasciculus	0.483±0.025	0.489±0.017	0.499±0.029	0.481±0.020	0.488±0.040	0.487 ±0.031	.478
Cingulum Cingulate	0.512±0.036	0.534±0.039	0.547±0.054	0.532±0.119	0.509±0.055	0.521 ±0.063	.171
Cingulum Hippocampus	0.441±0.038	0.457±0.059	0.467±0.144	0.447±0.040	0.456±0.040	0.453 ±0.063	.459
Corticospinal Tract	0.535±0.042	0.533±0.039	0.523±0.067	0.533±0.051	0.532±0.026	0.532 ±0.041	.615
Inferior-Fronto-occipital fasciculus	0.520±0.022	0.518±0.024	0.550±0.024	0.531±0.028	0.490±0.055	0.514 ±0.043	.001 (# Substance use vs control)
Inferior-longitudinal fasciculus	0.470±0.039	0.470±0.033	0.470±0.044	0.463±0.033	0.473±0.032	0.473 ±0.035	.767
Forceps Major	0.518±0.032	0.523±0.042	0.546±0.057	0.524±0.055	0.511±0.039	0.521 ±0.044	.690
Forceps Minor	0.515±0.038	0.521±0.047	0.553±0.059	0.526±0.039	0.497±0.061	0.515 ±0.053	.115
Uncinate fasciculus	0.468±0.037	0.443±0.031	0.470±0.036	0.470±0.040	0.472±0.039	0.466 ±0.038	.220

*Kruskal Wallis test with Post hoc pairwise comparisons using Dunn's tests with Bonferroni correction (# shows pairwise significance)

Table 4: Groupwise and tract-wise ADC means and comparisons

	Anxiety disorders Mean±SD	**Psychotic disorders** Mean±SD	**Substance use disorders** Mean±SD	**Bipolar disorders** Mean±SD	**Controls** Mean±SD	Mean±SD overall	P value*
Fornix	1.090±0.189	1.018±0.126	1.024±0.148	1.028±0.094	1.125±0.254	1.076±0.198	0.213
Anterior Thalamic Radiation	0.852±0.063	0.854±0.063	0.867±0.098	0.919±0.113	0.914±0.109	0.887±0.097	0.118
Arcuate Fasciculus	0.816±0.031	0.821±0.033	0.844±0.093	0.799±0.112	0.813±0.040	0.817±0.060	0.877
Cingulum Cingulate	0.808±0.028	0.828±0.043	0.784±0.115	0.820±0.021	0.815±0.048	0.812±0.055	0.714
Cingulum Hippocampus	0.885±0.108	0.882±0.114	0.889±0.052	0.900±0.135	0.919±0.088	0.900±0.099	0.805
Corticospinal Tract	0.802±0.060	0.847±0.063	0.872±0.116	0.809±0.044	0.862±0.054	0.842±0.070	0.008 (# anxiety vs controls)
Inferior-Fronto-occipital fasciculus	0.826±0.024	0.856±0.037	0.822±0.059	0.822±0.053	0.826±0.039	0.829±0.042	.076
Inferior-longitudinal fasciculus	0.853±0.034	0.878±0.048	0.845±0.051	0.866±0.043	0.852±0.031	0.857±0.039	.279
Forceps Major	0.871±0.045	0.923±0.035	0.864±0.075	0.870±0.035	0.883±0.069	0.883±0.059	.028 (psychotic vs control)
Forceps Minor	0.841±0.031	0.863±0.052	0.841±0.061	0.858±0.032	0.835±0.039	0.844±0.043	.282
Uncinate fasciculus	0.853±0.032	0.870±0.029	0.846±0.047	0.873±0.051	0.845±0.050	0.854±0.44	.046 (#psychotic vs control)

*Kruskal Wallis test with Post hoc pairwise comparisons using Dunn's tests with Bonferroni correction (# shows pairwise significance)

(PD), generalized anxiety disorder (GAD), social anxiety disorder (SAD), post-traumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD). Many studies have shown abnormalities in prefrontal and limbic connectivity in anxiety disorders. In contrast, studies on PD, GAD, and SAD are limited and sometimes yield conflicting results. A few studies have also examined trait anxiety and anxiety in children, but research in these areas remains underdeveloped. There is a need for replication, pediatric studies, and treatment-focused DTI research to better understand structural brain changes in anxiety disorders. Overall, DTI findings complement existing functional MRI studies and support neurocircuitry models of anxiety disorders, though methodological inconsistencies and sample heterogeneity limit definitive conclusions. In our study, we found significant difference in ADC means between the anxiety disorder group and controls in the Corticospinal tract, between psychotic disorders and controls in Forceps Major group and between the psychotic disorders and controls in the Uncinate fasciculus tracts. Findings on ADC changes in anxiety disorders are limited in articles that we found , but increased ADC was observed in certain white matter tracts in PTSD and OCD, suggesting microstructural damage, axonal degeneration, or reduced myelination[4,5].

The observed changes in FA and ADC are interpreted as reflecting demyelination, axonal injury, or neuroinflammatory processes. Increased ADC in specific tracts in psychotic and anxiety disorders may further indicate microstructural damage. The decrease in ADC and FA are a reflection of underlying neuropathological processes . Reduced FA, found in regions such as the Fornix and Inferior Fronto-occipital Fasciculus, indicates compromised white matter integrity. FA and ADC changes reveal different aspects of white matter pathology. Demyelination, or loss or injury to the myelin sheath that covers axons, decreases the directional anisotropy of water diffusion, resulting in decreased FA values but allowing increased overall water motion and increased ADC measurements[3]. Similarly, degeneration of the axon with disruption and loss of structure of axons further decreases white matter tracts' structural homogeneity and results in similar DTI changes. With neuroinflammation, microglial and astrocyte activation and release of inflammatory cytokines may lead to damage of both the myelin and axonal membranes. This inflammatory setting not only interferes with the physical integrity of the axons but also with extracellular diffusion of water, and hence with an apparent decrease in FA and increased ADC. These specific pathophysiological events together explain how DTI measurements can serve as sensitive markers of microstructural white matter injury in a variety of neuropsychiatric illnesses[3]. Yet, these conclusions need to be moderated by methodological constraints, especially the limited number of participants and the possible effects of medication and other clinical factors.

DTI also contributes to the investigation of white matter abnormalities in the patients with substance use. Our study results showed that the patients with substance use disorders have lower FA mean values in Inferior fronto-occipital Fasciculus than controls. Chronic use of substances has been proven to be associated with altered FA in major white matter pathways including the corpus callosum, superior longitudinal fasciculus, and inferior

longitudinal fasciculus in few other studies as well. Studies have also shown increased ADC values -a measure of overall diffusivity, suggesting microstructural breakdown in substance use patients. These findings suggest that long-term consumption of substances, mainly alcohol, cocaine, and opiates, may result in white matter degradation and affect cognitive and executive functions. However, we did not find such results, maybe because of lower number of cases[6,7]. Many studies have validated that in psychotic disorders, there is decreased FA in the corpus callosum, cingulum, and arcuate fasciculus, which supports disrupted neural communication. Major depressive disorder and bipolar disorder are associated with decreased FA in the corpus callosum, corona radiata, and internal capsule, implicated in emotional dysregulation. Anxiety disorders, including PTSD and OCD, also demonstrate FA reductions and increased MD/RD in the cingulum, superior longitudinal fasciculus, and uncinate fasciculus, indicating compromised limbic-prefrontal connectivity. This review outlines the potential of DTI to identify biomarkers for psychiatric diagnosis, predict treatment response, and refine neurobiological models. However, methodological inconsistencies, small sample sizes, and medication effects limit its current clinical application. Future studies should aim at standardization of protocols and investigation of individual neuroimaging-based interventions to advance psychiatric care.

The change in white matter microstructure in psychiatric disorders manifests itself as changes in FA and ADC. Generally, FA reduction reflects a decrease in white matter integrity caused by demyelination, axonal injury, or disrupted fiber arrangement. Neuroinflammatory processes, common in illnesses like schizophrenia, might lead to myelin damage and axonal structure compromise, thus yielding lower values of FA. On the other hand, increased ADC shows higher overall water diffusivity that may be the result of tissue loss, edema, or neurodegeneration expanding the extracellular space. These changes could also be driven by abnormal neural connectivity within key circuits, such as the prefrontal-limbic pathways, in which compromised structural coherence impairs cognitive and emotional regulation. Other factors that may promote such microstructural changes include chronic stress, genetic vulnerability, and long-term medication. Conversely, FA and ADC provide complementary information regarding the underlying pathophysiology of psychiatric disorders and show promise as biomarkers of disease severity and treatment response[4,8,9]. Probabilistic tractography studies[10] and reviews on the role of white matter in cognition[11] further support these findings. Additionally, research on addiction neurocircuitry[12] underscores the relevance of these structural abnormalities in clinical outcomes.

Previous studies have brought forth considerable insight into white matter microstructural changes in various psychiatric disorders. The major limitation here is that a lot of earlier studies have concerned themselves with an individual disorder sample, which keeps the findings exclusive to the sample within a single condition. A further limitation also comes from varying imaging protocols, e.g., varying voxel sizes, diffusion direction, and post-processing methods, which make inter-study comparisons of findings quite difficult directly between studies. The current study tries to address these limitations by comparing systematically the FA and ADC measurements in a number of psychiatric disorders, including anxiety, psychotic, substance abuse, and bipolar disorders, under the same standardized DTI protocol. With the addition of a well-matched control group, the study aims to elucidate the particular neuropathologic mechanisms of white matter alterations. Such a combined strategy not only enhances the validity of the DTI findings but also provides a more accurate picture of how some pathophysiological processes—such as demyelination, axonal injury, and neuroinflammation—manifest differently across psychiatric illnesses. In doing so, the study closes important gaps in the literature, paving the way for improved biomarker development and greater insight into psychiatric neuropathology.

Study Limitations

The study's limitations include participant recruitment using a convenience sampling, therefore, sample size did not include an extensive power analysis. Furthermore, there are chances of potential selection biases due to the exclusive inclusion of right-handed subjects, and limited control for confounding factors (e.g., medication status, duration of illness). Additionally, methodological details such as exact voxel resolution and diffusion directions are provided, yet differences in post-processing may influence the findings. Future research should aim to standardise imaging protocols, expand sample sizes, and explore longitudinal changes in white matter integrity.

Conclusion

This study suggests altered white matter microstructure in psychiatric disorders, particularly in pathways involved in cognitive and emotional regulation. The significant FA reductions in the Fornix and Inferior Fronto-Occipital Fasciculus indicate disrupted connectivity, while increased ADC values suggest microstructural damage in Psychotic and Anxiety Disorders. These findings support the role of DTI as a potential biomarker in psychiatric research. Limitations of the study are the limited sample size and selection bias in recruiting only right-handed participants, which can affect generalizability of the results. In addition, methodological limitations like heterogeneity of imaging protocols and restricted clinical confounder control can affect reproducibility.

Implications and Future Directions

Our work adds to the evidence of DTI's usefulness as a possible biomarker for psychiatric pathology, but this needs more work. Additional research to improve the neurobiological understanding of psychiatric disorders should incorporate multiscale designs, more comprehensive medication databases, and clinical outcome correlations.

References

1. Huisman TA. Diffusion-weighted and diffusion tensor imaging of the brain, made easy. Cancer Imaging. 2010; 10(1A): S163.
2. Mori S, Zhang J. Principles of diffusion tensor imaging and its applications to basic neuroscience research. Neuron. 2006; 51(5): 527-39.
3. Alexander AL, Lee JE, Lazar M, et al. Diffusion tensor imaging of the brain. Neurotherapeutics. 2007; 4(3): 316-29.
4. Ayling E, Aghajani M, Fouche JP, et al. Diffusion tensor imaging in anxiety disorders. Current psychiatry reports. 2012; 14: 197-202.
5. Uchida RR, Del-Ben CM, Busatto GF, et al. Regional gray matter abnormalities in panic disorder: a voxel-based morphometry study. Psychiatry Res. 2008; 163: 21-9.
6. Hampton WH, Hanik IM, Olson IR. Substance abuse and white matter: Findings, limitations, and future of diffusion tensor imaging research. Drug and alcohol dependence. 2019; 197: 288-98.
7. Arnone D, Barrick TR, Chengappa S, et al. Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. NeuroImage. 2008; 4(3): 1067-1074. 10.1016/j.neuroimage.2008.02.064
8. Mori S, Zhang J. Principles of diffusion tensor imaging and its applications to basic neuroscience research. Neuron. 2006; 51(5): 527-539. doi: 10.1016/j.neuron.2006.08.012
9. Ayling E, Aghajani M, Fouche JP, et al. Diffusion tensor imaging in anxiety disorders. Curr Psychiatry Rep. 2012; 14: 197-202. doi: 10.1007/s11920-012-0273-z
10. Behrens TEJ, Berg HJ, Jbabdi S, et al. Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? NeuroImage. 2007; 37(1): 144-155. doi: 10.1016/j.neuroimage.2006.09.018
11. Fields RD. White matter in learning, cognition and psychiatric disorders. Trends in Neurosciences. 2008; 31(7): 361-370. doi: 10.1016/j.tins.2008.04.001
12. Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. The Lancet Psychiatry. 2016; 3(8): 760-773. doi: 10.1016/S2215-0366(16)00104-8