Section: Biochemistry

Research

AN INVESTIGATION OF CLINICO NEURORADIOLOGIC CORRELATION IN PATIENTS WITH DEMENTIA

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Abstract

Background: To investigate the relationship between clinical abnormalities in language, attention, and memory in dementia patients and the neuroimaging correlates of the related networks. To investigate the neuroimaging results in thenetworks of attention, language, and memory in dementia patients using MR voxel-based morphometry, MR DTE, and 18-Fluorodeoxyglucose positron emission tomography. To identify neuroimaging correlates of abnormalities in dementia. **Materials and Methods:** In the study, 50 patients with dementia and 25 controls with similar ages and genders were chosen. All of them underwent Addenbrooke's Cognitive Examination III (ACE III), Wechsler's Memory Scale (WMS), Trail Making Test A &B (TMT), and Auditory Verbal Learning Test (AVLT), with scores being tallied in accordance with the results. Control and patients also tested for neuropsychological characteristics. Thereafter neuro-radiological clinical correlation was determined in patients with dementia. **Result:** The protocol's overall reliability was 0.936. Nearly 85% of the cases and 83% of the controls same age range (over 46). ACE-III score of 100, MoCA score of 32. Sample t test's p values under 0.001. Hypometabolism is(75%), (95%), (89%) in temporal association and (91%), (84%) in parital association in high languagefluency scores. Right anterior cingulate is 89.32% with low memory scores and 85.99% with strong memory scores and left anterior cingulate , in 88.06% for low memory scores and 83.60%with strong memory scores. **Conclusion:** Correlation between clinical and neuroradiological parameters was significant for the study of dementia. The current study has a good reliability score of 0.937, suggesting the protocol as a whole. The results showed similarity to the earlier studies and ACE-III and MoCA values were significant for patients tested for dementia. All parameters for neuropsychology and brain diffusion tensor imaging proofed to be significant with each other.

INTRODUCTION

A person with dementia has a deterioration in cognitive performance, which has a major impact on their quality of life and interferes with daily activities. Dementia is becoming more common and is on the rise. This is because longer lifespans have led to larger proportions of elderly people, who have a higher prevalence of dementia. According to the DSM-5 criteria, dementia is defined as a decline from a pre-established baseline in at least one of the following cognitive domains: memory and learning, executive function, language, complex attention, social cognition, and perceptual motor function. It also affects daily activities. These patients' symptoms are not limited to delirium and cannot be attributed to a psychiatric illness.[1,2]

The approach to dementia-related cognitive deficiencies has significantly changed. Instead of being restricted to a single disease-specific anatomic site, cognitive impairments are increasingly localised to domain-specific large-scale networks

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called Connectomes. These connectomes are made up of various grey matter nodes that are linked to one another by white matter tracts that carry processes and information.[2,3] The areas detected by functional investigations during the activity of the particular cognitive domain are classified as contributory components, and studies based on lesions that influence the particular cognitive domain assist identify the essential components.

Cognitive research has existed before the 19th century. However, it was Frank Joseph Gall who first made the distinction between white matter tracts and grey matter cortical areas in the late 19th century. His explanation of the use of additional cranial measurements for calculating cortical dimensions in phrenology has lost favour.[3]

The attention network includes limbic, motor, and perceptual components. The Frontal Eye Field (FEF), Posterior Parietal Gyrus (PPG), and Areas 23 and 24 of the Cingulate Gyrus are all engaged in attention. Between the three areas, there are several reciprocal monosynaptic connections. The superior colliculus, striatum, and pulvinar nucleus of the thalamus are the subcortical regions involved in attention. The subcortical structures are in turn related to the cortical regions. Areas of the limbic and paralimbic systems are involved in memory. The amygdala, hippocampus, and basal forebrain, which includes the septal nuclei and nucleus of basalis of Meynert, are the three primary limbic regions. The orbitofrontal, temporopolar, insula, cingulate, and parahippocampal regions are among the para-limbic areas. The linking white matter fibres in the brain's fornix, mamillothalamic tract, ansa peduncularis, and stria terminalis are implicated in memory. A solid white matter structure called the mamillothalamic tract connects the anterior nucleus of the thalamus and the mammillary body of the hypothalamus. It runs parallel to the fornicial columns. In 1812, Johan Christian Reil discovered nameless white matter fibres near the sylvian fissure. Carl Burdach gave the perisylvian tracts the scientific name fasciculus arcuatus in 1822.[3,4] The motor speech area related to speech production was named by Paul Broca in 1861. Wernicke (1874) identified the speech-related sensory region of the brain that is involved in speech comprehension. Wernicke also talked about the psychic arc that runs between the frontal and temporal regions.

Wernicke's area in the Temporoparietal junction and Broca's area in the frontal operculum make up the anatomic centre of spoken language. Only the process of speech repetition requires more than the two areas and their linkages.[4,5]

In modern cognitive neuroscience, the inferior frontal gyrus, which houses the motor imagery that comprises images of speech, is the first frontal convolution that he characterised. The rearousal of this imagery will create a sound pattern that is managed by the sensory cortex and controlled by distant cortices. The first temporal gyrus, which processes sensory information, has auditory images that correspond to spoken words. The fibrae propriae, which converge through the insular cortex, connect the sensory and motor centres. Wernicke claimed that the impairment in the sensory area's ability to monitor the broca's area causes paraphasias and that the disruption of this pathway causes aphasia.[5,6]

Broca's aphasia comprises receptive and expressive components, although they are of a different kind than Wernicke's aphasia. The language network is the brain's representation of relative and non-obsolete dichotomies like expression/reception, sensory/motor, and syntax/semantics. Comprehension and production are combined in language, a higher cognitive function.[6,7,8] Both the ventral and dorsal streams make up the language network. Arcuate fasciculus and Superior longitudinal fasciculus make up the dorsal stream of language. The extreme capsule, uncinate fasciculus, middle longitudinal fascicle, inferior longitudinal fascicle, and inferior fronto-occipital fascicle make up the ventral stream of language.[8]

MATERIALS AND METHODS

In the period between December 2007 and February 2010, a random sample of 50 patients and 25 controls with similar ages and genders were chosen from the dementia and cognitive neurosciences clinic at PGIMER, Chndighar. The PGIMER institutional ethical committee gave its approval to the study. After acquiring the individuals' or caregivers' agreement, neuropsychological tests were carried out. Patients were chosen based on their MoCA scores, and cases that met the inclusion and exclusion criteria and had a MoCA score of less than 27 were handled as patients and included in the current study. Each patient underwent the Addenbrooke's Cognitive Examination III (ACE III), Wechsler's Memory Scale (WMS), Trail Making Test A &B (TMT), and Auditory Verbal Learning Test (AVLT), with scores being tallied in accordance with the results. A single licenced clinical psychologist evaluated patients' and controls' neuropsychological characteristics. Within one month of the neuropsychological assessment, radiologists conducted imaging tests such MRIs, DTIs, and FDG-PETs. One month after the cognitive evaluation, neuroimaging was carried out. The study has been conducted with the subject data's privacy and confidentiality intact. Rigorous statistical analyses were carried out based on the observation and the assessments made from the patients as well as the control.

Inclusion Criteria

(a) Cases

- All-cause dementia presenting to Dementia Clinic, Department of Neurology, PGIMER, Chandighar with DSM 5 diagnosis of dementia (Major Neurocognitive Disorder).

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- Age between 30 - 85 years.
- Total number of patients included in the study: 60

(b) Controls

- Age, Sex matched subjects
- Total number of controls: 30

Exclusion Criteria

1. Any neurological disorder with cognitive impairment
2. Any self-reported genetic disorder
3. Any serious psychiatric illness like Schizophrenia, Bipolar Affective Disorder and substance dependence other than tobacco
4. Previous significant Head Injury
5. Current use of Medications that interfere with cognition
6. Structural lesions in the brain
7. Pregnancy

RESULTS

Table 1: Comparisons between Patients and Controls in Demographics

		Group				Mann Whitney U Test	
		Patients		Control			
		n	%	n	%	U Value	P – Value
Age	≤ 45 Years	7	14.00	4	16.00	895.000	.965
	46 - 55	9	18.00	4	16.00		
	56 - 65	14	28.00	7	28.00		
	66 - 75	16	32.00	8	32.00		
	> 75 Years	4	8.00	2	8.00		
Gender	Male	37	74.00	13	52.00	840.000	.526
	Female	13	26.00	12	48.00		
Education	Illiterate	19	38.00	0	.00	369.500	.000
	Primary	4	8.00	1	4.00		
	High School	20	40.00	7	28.00		
	Hr. Sec.	1	2.00	4	16.00		
	Graduate	3	6.00	8	32.00		
	Post Graduate	1	2.00	4	16.00		
	Professional	2	4.00	1	4.00		
Demography	Chennai	39	78.00	22	88.00	827.500	.324
	Other Districts in Tamilnadu	9	18.00	2	8.00		
	Other States	2	4.00	1	4.00		

The test schedule utilised in the current study has a good reliability score of 0.937, suggesting the protocol as a whole.

Table 2: Comparisons between Patients and Controls in NeuroPsychological Aspects

	Group				Independent Samples t-test	
	Patients		Control			
	Mean	SD	Mean	SD	t-Value	P-Value
MOCA (32)	16.25	7.26	28.27	.98	-13.638	<0.001
Addenbrooke's (100)	55.33	25.85	95.23	2.87	-11.809	<0.001
Attention (18)	10.77	5.75	17.75	.88	-9.130	<0.001
Memory(25)	10.80	6.80	24.13	1.38	-14.603	<0.001
Fluency (12)	6.92	3.67	12.33	1.03	-10.629	<0.001
Language (27)	18.47	6.99	25.83	.46	-8.125	<0.001
Visuo-spatial (15)	8.38	5.12	15.23	1.07	-9.944	<0.001
WMS	78.98	21.76	125.27	11.65	-13.137	<0.001
AVLT (15)	3.67	2.42	10.63	2.19	-13.281	<0.001
Digit span (15)	5.22	2.89	10.93	1.70	-11.768	<0.001
Story recall (23)	11.93	7.35	22.92	1.19	-11.279	<0.001
Complex figure (15)	2.52	2.79	9.83	2.60	-11.992	<0.001

Since all of the p values for the independent sample t test are less than 0.001, it is obvious that the mean values of each neuropsychological characteristic are determined to be substantially different between patients and controls. A detailed examination of the mean values reveals that the controls in the MoCA, ACE III (Attention, Memory, Language, Fluency), WMS, AVLT, Digit Span, Story Recall, and Complex Figure tests have higher mean values than the patients.

Table 3: Neuro Psychological Data of All Subjects – Correlations

	Adden brooke's	Attention	Memory	Fluency	Language	Visuo-spatial	WMS	AVLT	Digit span	Story recall	Complex figure
Adden brooke's	1										
Attentio	.954**	1									

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n											
Memory	.957**	.913**	1								
Fluency	.933**	.860**	.880**	1							
Language	.908**	.825**	.793**	.847**	1						
Visuo-spatial	.937**	.880**	.871**	.842**	.805**	1					
WMS	.913**	.879**	.923**	.835**	.765**	.859**	1				
AVLT	.854**	.798**	.880**	.815**	.710**	.787**	.902**	1			
Digit span	.881**	.843**	.850**	.825**	.797**	.821**	.878**	.830**	1		
Story recall	.888**	.863**	.895**	.825**	.747**	.820**	.897**	.827**	.801**	1	
Complex figure	.796**	.717**	.820**	.731**	.661**	.779**	.850**	.839**	.776**	.753**	1

Table 4: Neuro Psychological Data of Patients and Controls – Correlations

Group			**Control**									
		Addenbrooke's	**Attention**	**Memory**	**Fluency**	**Language**	**Visuospatial**	**WMS**	**AVLT**	**Digit span**	**Story recall**	**Complex figure**
Patients	Addenbrooke's	1	.440*	.745**	.570**	.554**	.570**	.369*	.479**	.202	.265	.174
	Attention	.942**	1	.062	-.074	.720**	.041	.483**	.648**	.470**	.535**	.173
	Memory	.940**	.901**	1	.383*	.142	.210	.131	.165	.127	.169	.030
	Fluency	.902**	.811**	.811**	1	.047	.136	.210	.224	-.221	-.017	.074
	Language	.884**	.751**	.721**	.799**	1	.221	.349	.450*	.385*	.358	.264
	Visuo-spatial	.901**	.832**	.811**	.766**	.725**	1	.072	.154	.045	-.052	.101
	WMS	.884**	.876**	.883**	.745**	.699**	.824**	1	.712**	.538*	.285	.270
	AVLT	.818**	.792**	.828**	.761**	.667**	.740**	.784**	1	.525**	.489**	.183
	Digit span	.851**	.806**	.741**	.763**	.734**	.756**	.766**	.642**	1	.483**	.270
	Story recall	.804**	.791**	.824**	.723**	.622**	.715**	.863**	.761**	.660**	1	.090
	Complex figure	.694**	.617**	.678**	.576**	.561**	.728**	.736**	.665**	.547**	.607**	1

Note: *. Correlation is significant at the 0.05 level (2-tailed)**. Correlation is significant at the 0.01 level (2-tailed).

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Table 5: Comparison of Patients and Controls in DTI Metrics on Right and Left hemispheres of Brain

RIGHT SIDE OF BRAIN			**LEFT SIDE OF BRAIN**		
White matter tract	**DTI parameter**	**Patients and Controls**	**White matter tract**	**DTI parameter**	**Patients and Controls**
SLF	NO DIFFERENCE		SLF	RD	P↑
ILF	MD	P ↑	ILF	FA	P↓
	RD	P ↑		RD	P ↑
IFO	FA ADC MD RD	P↓ P↑ P↑ P↑	IFO	FA ADC	P↓ P↑
ARCUATE	ADC AD MD RD	P↑ P↑ P↑ P↑	ARCUATE	ADC AD MD	P↑ P↑ P↑
UNCINATE	MD	P↑	UNCINATE	ADC MD RD	P↑ P↑ P↑
FORNIX	FA ADC MD RD	P↓ P↑ P↑ P↑	FORNIX	FA ADC AD MD	P↓ P↑ P↑ P↑

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				RD	P↑
CINGULUM	ADC MD RD	P↑ P↑ P↑	CINGULUM	NO DIFFERENCE	

Patients were shown to have considerably higher RD in the SLF, lower FA, higher RD in the ILF, higher ADC in the IFO, and higher ADC, AD, and MD in the arcuate fasciculus in the left hemisphere compared to controls. Patients have considerably elevated ADC, MD & RD of the Uncinate fasciculus as well as ADC, MD & RD in the fornix. In comparison to controls, patients had higher ADC, MD & RD in the cingulum fasciculus, higher MD, RD in the ILF, lower FA, higher ADC, MD, RD in the IFO, and higher ADC, AD, MD, RD in the arcuate fasciculus. In addition, it was discovered that patients had 65 cingulate fasciculus, higher ADC, MD, and RD in the fornix compared to controls, and increased MD in the uncinate fasciculus. The mean values of the five DTI parameters in SLF for patients and controls do not significantly differ from one another.

Table 6: Comparisons of DTI Metrics between Patients and Controls in All White Matter Tracts DTE with average of both the sides.

White matter tract	DTI parameter	Patients and controls level
CINGULUM	ADC MD	P↑ P↑
ILF	FA MD RD	P↓ P↑ P↑
SLF	NO DIFFERENCE	
IFO	FA ADC MD RD	P↓ P↑ P↑ P↑
ARCUATE	ADC AD MD RD	P↑ P↑ P↑ P↑
UNCINATE	ADC MD RD	P↑ P↑ P↑
FORNIX	FA ADC AD MD RD	P↓ P↑ P↑ P↑ P↑

In comparison to controls, the patients exhibit a considerably higher ADC, MD, and RD of the uncinate fasciculus. In fornix, patients had lower FA and higher levels of AD, RD, MD, and ADC compared to controls.

Table 7: Summary table of Neuro-Psychiatric domains and Diffusion Tensor imaging

Domains	Right side brain			Left Side Brain		
	WMT	DTI	Groups	White Matter Tract	DTI	Groups
Attention	Cingulum	ADC	2 Groups, PL ↑, CON↓, [PH-(PL, CON)]	Cingulum	ADC	Nil
		MD	2 Groups- PH+CON↓, PL↑		MD	Nil
		RD	2 Groups- PH+CON↓, PL↑		RD	2 groups- (PL↑, CON+PH↓)
		FA	Nil		FA	2 groups- PL↓, PH↑, [CON- (PL, PH)]
		AD	Nil		AD	Nil
	ILF	ADC	Nil	ILF	ADC	Nil
		MD	2 groups- PL+PH↑, CON↓		MD	2 groups- PL↑, CON↓, [PH-(PL, CON)]
		RD	2 groups- PL↑+PH, CON↓		RD	2 groups- PL↑, CON↓, [PH-(PL, CON)]
		FA	Nil		FA	2 groups- PL↓, CON↑, [PH-(PL, CON)]
		AD	Nil		AD	Nil
	SLF		Nil	SLF		Nil
Language & Fluency	SLF	FA	Nil	SLF	FA	2 Groups: PL+PH↓, Con↑
	ILF	FA	2 Groups: PL↓ , PH ↑, Con(PL, PH)	ILF	FA	2 Groups: PL↓, Con↑, PH(PL, Con)

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		ADC	2 Groups, Con+PL↓, PH↑		ADC	2 Groups: Con, PH↑, PL↓ (Con, PH)
		RD	2 Groups: Con↓, PL↑, PH (Con, PL)		RD	2 Groups Con, PL↑, PH(PL, Con)
	IFO	FA	2 Groups: PL, Con.↑ PH (PL,Con)	IFO	FA	2 Groups: PL, Con↑,PH(PL, Con)
		ADC	2 Groups, Con, PL↑, PH (Con, PL)		ADC	2 Groups: Con, PL↑, PH (PL, Con)
		MD	2 Groups: Con, PL↑, PH(Con, PL)		MD	2 Groups: Con, PL↑, PH (Con, PL)
		RD	2 Groups:Con, PL↑, PH(Con, PL)		RD	2 Groups Con, PL↑, PH(PL,Con)
Domains	Right side brain			Left Side Brain		
	WMT	DTI	Groups	White Matter Tract	DTI	Groups
	Arcute Fasciculus	FA	Nil	Arcute Fasciculus	FA	Nil
		ADC	2 Groups:Con, PL+PH↑		ADC	2 Groups: Con, PL↑, PH (Con, PL)
		AD	2 Groups: Con, PL+PH↑		AD	2 Groups: Con, PL+PH↑
		MD	2 Groups: Con, PL + PH↑		MD	2 Groups Con, PL↑, PH(PL,Con)
		RD	2 Groups:Con, PL↑, PH(Con, PL)		RD	2 Groups Con, PL↑, PH(PL,Con)
Memory	Uncinate	ADC	Nil	UNCINATE	ADC	2 groups- PL↑, PH↓+CON
		MD	Nil		MD	2 groups- PL↑, PH+CON↓
		RD	2 groups- PL↑,CON↓, [PH-(PL,CON)]		RD	2 groups- PL↑, PH+CON↓
		FA	Nil		FA	2 groups- PL ↓, CON ↑ +PH
		AD	Nil		AD	Nil
	Fornix	ADC	2 groups- PL↑+PH, CON↓	FORNIX	ADC	2 groups- PL↑+PH, CON↓
		MD	2 groups- PL↑,CON↓, [PH-(PL,CON)]		MD	2 groups- PL↑+PH↓, CON↓
		RD	2 groups- PL↑+PH, CON↓		RD	2 groups- PL↑+PH, CON↓
		FA	2 groups- PL↓+PH, CON↑		FA	2 groups- PL↓+PH, CON↑
		AD	Nil		AD	2 groups- PL↑+PH, CON↓
	Cingulum	ADC	2 groups- PL↑, PH+CON↓	CINGULUM	ADC	2 groups- PL↑,PH↓, [CON- (PL,PH)]
		MD	2 groups- PL↑, PH↓+CON		MD	2 groups- PL ↑;CON↓, [PH-(PL,CON)]
		RD	2 groups- PL↑, PH↓+CON		RD	2 groups- PL ↑, PH↓+CON
		FA	Nil		FA	2 groups- PL↓, PH+CON↑
		AD	Nil		AD	Nil

Note: PL – Patient with low score, PH – Patient with high score, CO – Control
[ ]– Group that has been split

Table 8: Summary of significant findings noted in either low score patient group or high score patient group in comparison to controls

DOMAIN	WHITE MATTER TRACT	R/L	FA	AD	RD	MD	ADC
Attention	CINGULUM	R L	□		□ □	□	□
	ILF	R L	□		□ □	□ □	
	SLF	R L					
Language and Fluency	IFO	R L	□ □		□ □	□ □	□ □
	ARCUATE	R L		□ □	□ □	□ □	□ □
	ILF	R L	□		□	□	□

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			□		□	□	
	SLF	R L					
Memory	UNCINATE	R L	□		□ □	□	□
	FORNIX	R L	□ □	□	□ □	□ □	□ □
	CINGULUM	R L	□		□ □	□ □	□ □

In the low memory score patient group as compared to the control group, FA was lowered while RD, MD, and ADC were enhanced in the left uncinate fasciculus. In the right fornix, FA was lower and RD, MD, and ADC were higher in the patient group with low memory score compared to the control group. In the left fornix, FA was lower and AD, RD, MD, and ADC were higher in the patient group with low memory scores compared to the control group, pointing to the fornix's critical function in the memory domain. When compared to the control group, the low memory score patient group had higher levels of RD, MD, and ADC in the right cingulum.

Table 9: Percent of Patients having Hypometabolism in various cortical regions studied.

Cortical Area	Hypometabolism (%)
ATTENTION DOMAIN	
Frontal Association - Right	78.63
Frontal Association –Left	87.89
Anterior Cingulate– Right	87.89
Anterior Cingulate–Left	85.32
Posterior Cingulate– Right	71.37
Posterior Cingulate- Left	74.93
Parietal Association – Right	80.48
Parietal Association –Left	91.74
Caudate – Right	91.74
Caudate –Left	90.59
LANGUAGE DOMAIN	
Frontal Association – Right	78.63
Frontal Association –Left	87.89
Temporal Association – Right	76.78
Temporal Association –Left	77.63
Parietal Association – Right	80.48
Parietal Association –Left	92.74
MEMORY DOMAIN	
Anterior Cingulate - Right	87.89
Anterior Cingulate - Left	84.19

In the right and left frontal association areas, right and left anterior cingulate cortex, right and left posterior cingulate cortex, right and left parietal association cortex, right and left caudate, and right and left temporal association cortex, hypometabolism was found in 78.63, 87.89, 87.89, 85.32, 71.37, 74.93, 80.48, 91.74, 91.74, 90.59, 76.78%.

Table 10 (a): Table showing Hypometabolism in low attention score and high attention score patient groups in attention domain

Cortical Areas studied in attention	Low Attention Score Patient Group (% showing Hypometabolism)	High Attention Score Patient Group (% showing Hypometabolism)
Frontal Association Right	86.90	65.66
Frontal Association - Left	94.94	82.89
Anterior cingulate - Right	91.90	84.70
Anterior cingulate - Left	86.86	81.94
Posterior cingulate - Right	71.72	67.67
Posterior cingulate- Left	82.80	64.62
Parietal Association - Right	83.80	77.20
Parietal Association - Left	97.95	81.94
Caudate - Right	85.90	96.30
Caudate - Left	92.91	92.50

In the right association cortex, hypometabolism was present in 83.80% of the low attention score patient group and 77.20% of the high attention parietal score patient group. Patients with poor attention scores displayed hypometabolism in the left parietal association cortex in 97.95% of cases and patients with high attention scores in 81.94% of cases. In the right caudate, hypometabolism was present in 86.30% of patients with poor attention scores and 96.30% of those with high attention scores. Hypometabolism was present in the left caudate in 92.91% of patients with poor attention scores and 92.50% of those with high attention scores.

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Table 10 (b): Table showing Hypometabolism in low attention score and high attention score patient groups in Language and Fluency domain

Cortical Areas studied in Language and Fluency Domain	Low Language & Fluency Score Group (% showing Hypometabolism)	High Language & Fluency Score Group (% showing Hypometabolism)
Frontal Association - Rt	83.10	62.00
Frontal Association - Lt	92.20	75.00
Temporal Association - Rt	74.00	95.00
Temporal Association - Lt	78.30	89.00
Parietal Association – Rt	80.60	91.00
Parietal Association – Lt	94.20	84.00

When it comes to the language and fluency score group, patients with hypometabolism have left frontal associations of 75%, right temporal associations of 95%, left temporal associations of 89%, right parietal associations of 91%, and left parietal associations of 84%.

Table 10 (c): Table showing Hypometabolism in low attention score and high attention score patient groups in Memory domain

Cortical Areas studied in Memory	Low Memory Score Patient Group (% showing Hypometabolism)	High Language Score Patient Group (% showing Hypometabolism)
Anterior Cingulate – Rt - Grp	89.32	85.99
Anterior Cingulate – Lt - Grp	88.06	83.60

89.32% of patients with low memory scores and 85.99% of patients with high memory scores both had hypometabolism in the right anterior cingulate cortex. Hypometabolism was seen in the left anterior cingulate cortex in 88.06% of individuals with poor memory and 83.60% of patients with good memory.

Table 11: ROI Areas and comparisons between patients and controls on the two sides of hemisphere

ROI	Left/Right	Peak-level (T- Value)	Peak-level (P Uncorr)	MNI Coordinates		
				x	y	z
Brocas Area	Left	9.60	<0.001	-32	24	6
	Right	8.5	<0.001	33	24	6
Cingulate gyrus	Left	8.10	<0.001	-3	-26	42
	Right	7.60	<0.001	2	-51	27
DLPFC	Left	6.95	<0.001	-42	2	30
	Right	4.90	<0.001	8	45	18
Frontal Eye Fields	Left	4.35	<0.001	-5	35	54
	Right	4.30	<0.001	26	21	53
Hippocampus	Left	7.55	<0.001	-33	-14	-12
	Right	7.10	<0.001	20	-33	-2
Inferior Parietal Lobule	Left	6.30	<0.001	-51	-24	14
	Right	6.88	<0.001	56	-47	24
Nucleus Accumbens	Left	7.5	<0.001	-18	6	-15
	Right	7.40	<0.001	15	6	-15
Occipital Eye Fields	Left	6.9	<0.001	-15	-56	0
	Right	5.56	<0.001	14	-56	3
Superior Parietal Lobule	Left	6.70	<0.001	-2	-54	35
	Right	6.40	<0.001	3	-69	30
Uncus	Left	7.47	<0.001	-26	6	-21
	Right	7.92	<0.001	26	8	-21
Wernicke ‘s Area	Left	6.20	<0.001	-53	-30	5
	Right	7.73	<0.001	62	-27	-2

The multiple comparison correction small volume adjustment with a sphere of 10 mm radius was used, and the significance level was set at p 0.001 (uncorrected). The peak discrepancies' MNI co-ordinates were reported and are listed in table.

DISCUSSION

The age range of the study's patients is similar to that of studies on dementia. 85 percent of the patients were older than 46, and dementia rates rose as patients' ages did. Our study had a plurality of male participants, with 70% of them being men. Numerous studies have indicated a range of dementia prevalence rates according on gender. According to the Framingham study, women were more affected by Germany's fall in dementia prevalence than men. On the other hand, according to a study by Matthews FE et al., dementia cases are only declining among men in the UK, although they were more prevalent among Spanish men.[9,10] In the current study, dementia incidence is higher in the population with lower educational status. This is consistent with prior research. In our study, approximately 83% of patients completed high school, compared to almost 90% of controls who

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completed further education. Education acts as a defence against dementia. 15 cohort studies were included in a meta-analysis by Wei Xu et al.[11,12] (2015) to evaluate the connection between education and dementia. In our study, dementia was most frequently caused by Alzheimer's disease. When a cutoff score of 26/27 was utilised as the cut off for the diagnosis of dementia in Parkinson disease, S. Hoops et al. reported a sensitivity of 100% and a specificity of 53%.

Jordi A. Matias-Guiu found that dementia patients' MoCA scores were statistically significantly lower than those of the healthy control group.[12,13] In our study, the dementia population's average scores were much lower than those of the healthy controls. In our study, patients' scores on the ACE III subcategories of attention, memory, fluency, language, and visuo-spatial abilities were lower than those of the control groups. Jordi A. Matias-Guiu found that dementia patients' ACE III values were statistically significantly lower than those of healthy controls.[14,15] In his investigation, he showed that a cut off of less than or equal to 73 had a sensitivity of 95.57% and a specificity of 67.65%. In our study, the dementia population's average scores were much lower than those of the healthy controls. Wechsler's memory scale, animal fluency tests, the RAVLT short delayed verbal recall test, and the WAIS-R digit symbol test were all mentioned by Mary Tierney C et al as being excellent predictors of the development of dementia over the course of five years. Test of trail-making.[15] In our study, the dementia population's average scores were much lower than those of the healthy controls. In their study, Lee Ashendorf et al. found that combining the characteristics of time to completion and number of errors improved the classification of participants into normal and dementia subjects. AVLT In our study, the dementia population's average scores were much lower than those of the healthy controls.[15,16] In their work, Zhao Q et al. demonstrated improved MCI to dementia conversion detection with a balanced sensitivity and specificity.

In Analysis of Discriminant Function linear discriminant function analysis was conducted to determine which 78 factors from the delivered neuropsychological tests, either alone or in combination, have the greatest ability to distinguish between patients and controls. It became clear that only 5 of the 12 neuropsychological characteristics under consideration were necessary to categorise the subjects as either patients or controls. These include the AVLT, digit span, and complex figure tests, as well as the attention and memory subset of the Addenbrooke Cognitive Examination III (ACE III). With a success rate of 99% overall, 49 out of 50 cases and 25 out of 25 controls were accurately classified into the relevant groups when the discriminant function analysis was applied to our study population. 98.3% of the patient group's classification attempts were successful, compared to 100% for the control group.[17,18] The classification of the controls had a higher success rate than the patient group, according to the study by Bonnie M. et al. Utilizing linear discriminant function analysis shortens the time required to administer neuropsychological tests and eases financial strain in environments with limited resources. However, shrinkage can occur when analysing linear discriminant functions.[19,20]

A DTI image In healthy controls, there were no variations in the diffusion tensor imaging measures between the two sides. This is because, as outlined by Corballis et al., there are functional differences between the hemispheres. Diffusion tensor imaging revealed structural evidence of hemispheric symmetry, which was consistent with Hardyck et al's claim that 79 brain areas engaged in cognitive processes do not differ between the two hemispheres.[18,19] Diffusion tensor imaging in the area of attention: The superior longitudinal fasciculus, inferior longitudinal fasciculus, and cingulum were all studied as part of the diffusion tensor imaging of the attention domain. In our analysis, neither side of the superior longitudinal fasciculus shown any statistically significant participation in our domain. This was in line with the conclusions reached by Kantarci et al., who similarly did not discover any major SLF participation. In our investigation, the inferior longitudinal fasciculus had decreased fractional anisotropy and increased diffusivity on the right side and increased diffusivity on the left side.[19,20] In our investigation, the cingulum showed that the right side had higher diffusivity and the left side had higher diffusivity and lower fractional anisotropy. In our investigation, the right handed fasciculus did not exhibit decreased fractional anisotropy, however the left sided fasciculus did. Similar involvement of the inferior longitudinal fasciculus and cingulum was discovered by Kantarci et al. Grieve et al. have found a similar involvement of the cingulum seen in diffusion tensor imaging with a reduction in fractional anisotropy. In our investigation, as in a few previous studies, the radial diffusivity was consistently implicated in both the inferior longitudinal fasciculus and the cingulum.[21]

Language of Diffusion Tensor Imaging: The superior longitudinal fasciculus and arcuate fasciculus are parts of the dorsal stream that are involved in language. There was no statistically significant difference between the fractional anisotropy and diffusivity of the SLF. In our investigation, their impact on language was minimal. This was congruent with the 80 discovery in the superior longitudinal fasciculus made by Kantarci et al.[21,22] Significantly enhanced diffusivity was seen in the arcuate fasciculus on both the right and left sides. Arcuate fasciculus was more frequently and consistently affected by radial diffusivity. The inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, uncinate fasciculus, extreme capsule, and middle longitudinal

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fasciculus were all located in the ventral stream, which is responsible for language. In our research, diffusion tensor imaging of the inferior longitudinal fasciculus showed reduced fractional anisotropy and higher diffusivity in both the right and left side. There was no inclination to the side. This was consistent with observations in the inferior longitudinal fasciculus made by Kantarci et al. Similar to our investigation, his study found no evidence of a side tendency.[22] In our investigation, the inferior fronto-occipital fasciculus on either side likewise shown decreased anisotropy and increased diffusivity. ILF more frequently and consistently included the radial diffusivity. Memory Diffusion Tensor Imaging Uncinate fasciculus, fornix, and cingulum were studied using diffusion tensor imaging in the memory domain. In patients with attention deficits, the left uncinate fasciculus showed lower fractional anisotropy and increased diffusivity. In this investigation, only the radial diffusivity was found to be elevated in the right uncinate fasciculus. In our investigation, the uncinate fasciculus, fornix, and cingulum, which are related to the medial temporal lobe, revealed notable changes that could be seen on diffusion tensor imaging. Similar alterations in the cingulum and ILF were found by Kantarci et al.[22,23] when the memory domain was compromised. His research found that alterations in fornix were not appreciably different. Among the fasciculi investigated for memory in our investigation, the involvement of the fornix with a decrease in FA and an increase in diffusivity was a reliable conclusion. In the diffusion tensor imaging investigations, the research on the function of the fornix is notably underrepresented. The fornix is the primary efferent from the hippocampus to the mamillary bodies, anterior thalamus, and frontal cortices and plays a large role in the memory network, particularly episodic memory, hence the fact that its role is important is conceivable. Aggleton et alresearch, which stated that forniceal lesions presented with memory deficits, particularly in episodic memory, confirmed the fornix findings. The corollary was investigated by Zahr et al [. in 2009, who discovered an association between memory improvement and higher FA and lower diffusivity. Furthermore, Fletcher et al. (2013) showed the fornix's function as an imaging biomarker, showing that fornix involvement with low fornix volume and greater axial diffusivity was linked to an enhanced conversion to mild cognitive impairment/dementia.[24]

Attention domain FDG-PET The parietal association, frontal association, anterior cingulate, posterior cingulate, and caudate regions were examined in the attention domain of the FDG PET imaging. Hypometabolism was detected in the parietal association cortex, frontal association cortex, caudate, anterior cingulate, and posterior cingulate in patients with low attention scores, in the descending order of hypometabolism predominance. The attention hubs including the parietal association, frontal association, caudate, and posterior cingulate cortex were more frequently on the left side. The anterior cingulate showed a right-sided prevalence. Salmon E. et al. showed a similar finding of hypometabolism in the posterior cingulate cortex in their research. In his research, he also discovered a correlation between dementia severity and posterior cingulate hypometabolism. FDG-PET in the domain of language and fluency Parietal association, frontal association, and temporal association cortex were examined in the language and fluency domain of the FDG PET imaging. Hypometabolism was observed in the frontal association cortex, parietal association cortex, and temporal association cortex in patients with low language and fluency scores, in the descending order of hypometabolism predominance in our study. The language and fluency hubs involving the frontal association, parietal association, and temporal association cortex were more frequently on the left side. Similar to our work, Rabinovici et al. found that patients with fronto-temporal dementia have hypometabolism in the left temporal and temporal association cortex. The Memory Domain of FDG-PET The anterior cingulate cortex was examined using FDG PET imaging in the memory domain.[24,25] In our investigation, hypometabolism in the anterior cingulate cortex was detected in patients with poor memory scores. The anterior cingulate cortex's memory hubs were more frequently on the right side. Schroeter ML et al. found hypometabolism in the precuneus, retrosplenial cortex, and hippocampus in AD patients who also had problems with long-term memory. In patients with memory impairment, Salmon E. et al. found hypometabolism in the posterior cingulate cortex. According to research by Frisch et al, medial parietal cortex hypometabolism in AD is connected with memory loss. He also showed that memory loss in FTD was associated with hypometabolism in the frontal cortex. Voxel Based Morphometry, Paying Attention to Voxel Based Morphometry our study, considerable atrophy was found in the patient group compared to healthy controls in the dorsolateral prefrontal cortex, frontal eye field, occipital eye field, cingulum, and superior parietal lobule, which are all involved in the attention domain.[24,25] Contrary to our research, Kantarci et al. failed to find any volumetric alterations in the cortical regions associated with attention deficit. He did, however, see white matter tract involvement, anterior, posterior, and inferior longitudinal fasciculus in these patients, and the results were consistent with our investigation.

Voxel-based language morphometry The ROI of the cortical regions Broca's area, Wernicke's area, and Geschwind area (inferior parietal lobe) in both hemispheres, involved with the language domain, indicated considerable shrinkage in the patient group compared to the control group in our investigation. In their study, Kantarci et al. showed that patients with language impairment had cortical

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involvement in the left temporal pole, posterior inferior temporal gyrus, amygdala, and fusiform gyrus. Voxel-based morphometry in Memory: The cortical regions of the hippocampus, uncus, and nucleus accumbens that have been examined for memory.[25] In our investigation, considerable atrophy was found in the patient group compared to the control group in the ROI of the cortical regions concerned with the memory domain, including the hippocampus, uncinate, and nucleus accumbens in both hemispheres. Similar findings were also made by Kantarci et al, who showed a correlation between substantial memory problems and medial temporal lobe atrophy as seen in volumetric study of the temporal lobes.

CONCLUSION

Our study's distribution of patient diagnoses is comparable to dementia research conducted in other parts of South India. This is consistent with the prevalence of dementia documented in other research conducted in India and across the globe. Fronto-temporal dementia, vascular dementia, Parkinson's dementia, mixed dementia, and CBGD are among the additional causes of dementia in our study. In our study, the dementia population's average scores were significantly lower than those of the healthy controls. Additionally, our research indicates that fornix might develop into an imaging biomarker for the memory connectome. We discovered involvement of both grey matter and white matter, he also observed that white matter tracts anterior cingulum, posterior cingulum, and inferior longitudinal fasciculus were implicated in addition to the cortical involvement. In their study, Patric Meyer et al. discussed the relationship between the integrity of the medial temporal lobar cortex and mnemonic tests for memory. This result does not match what we found in our research.

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