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INSIGHTS INTO DEMENTIA: A PROSPECTIVE CLINICO-NEUROLOGICAL STUDY ON DEMENTIA AT JODHPUR, RAJASTHAN

Neurology

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ABSTRACT

Background: Dementia presents a formidable challenge as it involves a gradual deterioration of cognitive abilities and daily functioning. This condition not only impacts individuals directly but also places substantial burdens on caregivers and healthcare systems globally. **Objective**: To get insights into the neuroanatomical and functional alterations associated with dementia. **Methods:** This study conducted at the MDM Hospital of Dr S. N. Medical college, Jodhpur involved a total of 40 dementia patients and 20 age- and gender-matched controls, recorded clinical manifestations of dementia. The study employed advanced neuroimaging methods, identified characteristic pathological hallmarks. **Results:** Results shows that 90% of dementia patients are above 45 years of age, males constitute 70% cases. Alzheimer's disease was the most common cause of dementia followed by fronto-temporal dementia, vascular dementia, Parkinson's dementia. MoCA, ACE-iii both scores are lower in patients then the healthy controls. DTI revealed decreased fractional anisotropy and increased diffusivity in patients with impaired attention, but shows did not show any statistically significant involvement on either side of language domain in our study. **Conclusion:** This paper underscores the importance of an integrated approach to dementia assessment, incorporating clinical, neurological, and biomarker data to optimize patient care and outcomes.

KEYWORDS

Dementia Prevalence, Alzheimer's Disease, Connectomics in Dementia, Neuroimaging, Cognitive Deficits, Diagnostic Accuracy, Dementia Assessment, Structural and Functional Neuroimaging, Cognitive Domains, Clinico-Neurological Correlates.

INTRODUCTION:

The prevalence of dementia is on the rise, attributed to increased longevity leading to a higher proportion of elderly individuals, who are at a greater risk of developing dementia.[1] The DSM-5 criteria define dementia as a decline in at least one cognitive domain, such as memory and learning, executive function, language, complex attention, social cognition, and perceptual motor function, which affects daily living activities. It's noteworthy that these symptoms do not occur exclusively during delirium and are not explainable by a psychiatric disorder.[2]

The global prevalence of dementia was estimated to be above 60 million in 2023, and projections indicate a considerable increase to 75.63 million in 2030 and 135.46 million in 2050. In India, the prevalence of dementia in the elderly is estimated to be between 0.9% to 4.8% in urban areas and 0.6% to 3.5% in rural areas, prevalence increases with age.[3]

The identification of the apolipoprotein E ε4 allele as a genetic risk factor for late- onset AD, along with neuropathology findings, provides support for the amyloid cascade hypothesis as a key contributor to AD pathogenesis (Hardy and Higgins 1992).[4] It is important to note, however, that other intersecting mechanisms likely play significant roles in non-Mendelian forms of AD. [5,6]

The approach to cognitive deficits in dementia has evolved towards the concept of "Connectomics," in which cognitive deficits are attributed to domain-specific large-scale networks called Connectomes, as opposed to being localized to specific disease-specific anatomical loci. These Connectomes consist of gray matter nodes interconnected by white matter tracts, with different components classified as critical or contributory based on lesion studies and functional studies during the activity of particular cognitive domains. [7]

The precise mapping of each connectome is required for accurate knowledge of its function and the deficit that would arise from its lesion. The mapping of the connectome would also play an important role in the intervention during neurosurgery. These newer techniques will also plan and enable the neurosurgeon to decide the approach, trajectory and extent. Individual, regional and racial variability in the connectome are possible as the genes play crucial in the development of these circuits. [8]

The nature of these connectomes in health and disease will also vary depending upon the etiology especially dementia. Hence, this study is aimed at studying the association between clinical deficits in cognitive domains of attention, memory and language in subjects with dementia and the neuroimaging correlates of the corresponding networks. [7]

Evolution of cognitive neurosciences, from the topological approach versus the hodological approach, we know today neural networks related to attention, language, and memory, white matter tracts, gray matter hubs, and neuropsychological tests to evaluate cognitive domains. [9] Aim of study was to find out association between clinical deficits in cognitive domains of attention, memory and language in subjects with dementia and the neuroimaging correlates of the corresponding networks.

MATERIAL & METHODS

The study conducted at the MDM Hospital in Jodhpur involved a total of 40 dementia patients and 20 age- and gender-matched controls.

Inclusion Criteria:

Cases: All-cause dementia presenting to Dementia Clinic, Department of Neurology, with DSM 5 diagnosis of dementia (Major Neurocognitive Disorder). Age between 30 - 85 years. Total number of patients included in the study: 40 Controls: Age, Sex matched subjects Total number of controls: 20

Exclusion Criteria: Any neurological disorder with cognitive impairment, Any self reported genetic disorder, Any serious psychiatric illness like Schizophrenia, Bipolar Affective Disorder and substance dependence other than tobacco, Previous significant Head Injury, Current use of Medications that interfere with cognition, Structural lesions in the brain, and Pregnancy

The patients were assessed using various clinical & neuropsychological tests, including the Montreal Cognitive Assessment (MoCA), Addenbrooke's Cognitive Examination III (ACE III), Wechsler's Memory Scale (WMS), Trail Making Test A & B (TMT), and Auditory Verbal Learning Test (AVLT). These assessments were performed by a trained clinical psychologist.

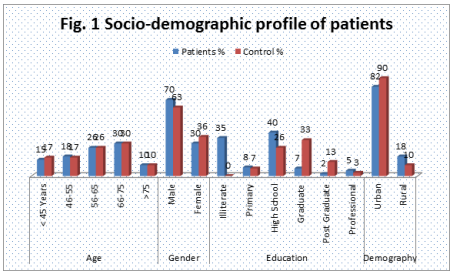
In addition, imaging studies, including MRI Voxel Based Morphometry, MR Diffusion Tensor Imaging, and FDG-PET (for cases alone), were conducted by radiologists within one month of the neuropsychological assessments. The MRI Voxel Based Morphometry involved analyses of regions of interest related to attention, language, and memory networks, while the MR Diffusion Tensor Imaging measured various white matter tracts. The FDG-PET imaging focused on cortical areas related to attention, language, and memory domains.

Diffusion Tensor Imaging (DTI): The DTI Metrics such as Fractional Anisotropy (FA), Apparent Diffusion Coefficient (ADC), Axial Diffusivity (AD), Mean Diffusivity (MD), Radial Diffusivity (RD) values were obtained , the images analysed through the software Neuro 3D for the white matter tracts.

The statistical analysis involved the use of tests such as Chi-square, Mann Whitney test, Proportions test, Independent sample t test, Paired sample t test, One way Analysis of Variance, Correlation analysis, Regression analysis, and discriminant analysis. The data collected from patients and controls were coded, entered into a personal computer, and analyzed using the IBM Statistical Package for Social Sciences (Version 22.)

RESULTS:

Left hemispherical Analysis: Shows patients have significantly increased RD in the SLF, decreased FA, increased RD in ILF, increased ADC in IFO and increased ADC, AD, MD in arcuate fasciculus compared to the controls. Patients have significantly increased ADC, AD, MD, RD in the fornix and significantly increased ADC, MD & RD of the Uncinate fasciculus.



Mann Whitney U test shows a good reliability score of 0.93. The prevalence of dementia increases with increasing age, 70% of subjects being males.

Right Hemispherical Analysis : Patients have increased ADC, MD & RD in cingulum fasciculus, increased MD, RD in ILF, decreased FA and increased ADC, MD, RD in IFO, increased ADC, AD, MD, RD in arcuate fasciculus in comparison to controls. Patients were also found to have increased MD in uncinate fasciculus, increased ADC, MD, RD in fornix and cingulate fasciculus in comparison to controls. There is no significant difference between the mean values of patient s and controls in all the five DTI parameters in SLF.

Attention Domain: The white matter tracts superior longitudinal fasciculus, inferior longitudinal fasciculus and cingulate fasciculus were analysed in both right and left hemisphere. In the right cingulate fasciculus, there was significant increase in RD, MD, ADC in low attention score patient group in comparison with control group. In the left cingulate fasciculus, the FA was decreased and RD was increased significantly in low attention score patient group compared to high attention score patient group. In the right inferior longitudinal fasciculus, RD and MD was significantly increased in low attention score patient group compared to control group.

Alzheimer's disease was the most common cause of dementia in our study. Similar to prevalence of dementia reported in other studies in India and in Global scenario. The other causes of dementia in our study include fronto-temporal dementia, vascular dementia, Parkinson's dementia, mixed dementia and CBGD.

Table: 1 Neuro-Psychological Aspects between Patients and Controls

Group	Patients		Control		Independent Samples t-test	P value
	mean	SD	mean	SD		
Addenbrooke's(100)	55	27	96	2.5	116.6	0.0001
MoCA (30)	15.4	7	28	1	49	0.0001
Attention (18)	11	6	17	.9	44	0.0001
Memory (26)	11	7	24	1	45	0.0001
Fluency (14)	7	4	12	1	11	0.0001
Visual (16)	8	5.2	15	1	11.5	0.0001
Complex figure (14)	2.5	2.8	10	2.5	13.2	0.0001

Table Shows neuropsychological aspects are significantly different between patients and controls since the p values of independent sample t test are all less than 0.001. A close scrutiny of the mean values indicates that the controls have higher levels of mean values compared to the patients in MoCA, ACE III (Attention, Memory, Language, Fluency) and complex figure.

FDG-PET in Attention Domain was analysed for parietal association, frontal association, anterior cingulate, posterior cingulate and caudate. In subjects with low attention scores, hypometabolism was noted in the parietal association cortex, frontal association cortex, caudate, anterior cingulate and posterior cingulate in the descending order of prevalence of hypometabolism in our study. The left side was more commonly involved in the attention hubs involving the parietal association, frontal association, caudate and posterior cingulate cortex. The right sided preponderance was noted for anterior cingulate.

FDG-PET in Language and Fluency Domain was analysed for parietal association, frontal association and temporal association cortex. In subjects with low language and fluency scores, hypometabolism was noted in the frontal association cortex, parietal association cortex and temporal association cortex in the descending order of prevalence of hypometabolism in our study. The left side was more commonly involved in the language and fluency hubs involving the frontal association, parietal association, and temporal association cortex. FDG-PET in Memory Domain: The FDG PET imaging in memory domain was analysed for anterior cingulate cortex. In subjects with low memory scores, hypometabolism was noted in the anterior cingulate cortex in our study. The right side was more commonly involved in the memory hubs involving the anterior cingulate cortex.

DISCUSSION:

Significant differences between patients and controls are seen in educational levels, and place from where the subjects come from. In all the 12 neuro psychological aspects such as MoCA, Adenbrook's Cognitive Score (comprising attention, language, fluency, memory and visuo-spatial, WMS, AVLT, Digit Span, Story recall and complex figure, patients have significantly lower levels compare to controls.

Correlation analysis of the Neuro-psychological aspects of all subjects (both patients and controls together) indicates that all the 12 neuro-psychologial aspects are highly significantly correlated with one another. Dementia patients' ACE III values were statistically significantly lower than those of healthy controls.

CONCLUSIONS

Analysis of Diffusion Tensor Imaging indicates that the white matter tract, Superior Longitudinal Fasciculus does not play any major role in attention and language domain. In contrast, Fornix has a major role to play in the memory domain. All the metrics of DTI show significant difference between patients and controls in the white matter tract Fornix on either side of the brain. As far as the DTI metrics are concerned, all the metrics have the same levels on both sides of brain of patients and controls.

In most of the white matter tracts, the metrics, RD, MD, and AD are found to be high among patients compared to controls. FA is found to be low among patients in white matter tracts like IFO and Fornix. The analysis of diffusion metrics suggests the varying involvement of the white matter fasciculi of the respective domains.

REFERENCES:

1. George-Carey R, Adeloye D, Chan KY, Paul A, Kolčić I, Campbell H et al. An estimate of the prevalence of dementia in Africa: A systematic analysis. J Glob Health. 2012 Dec;2(2):020401. doi: 10.7189/jogh.02.020401. Erratum in: J Glob Health. 2012;2(2):020401corr. PMID: 23289076; PMCID: PMC3529309.
2. Emmady PD, Schoo C, Tadi P. Major Neurocognitive Disorder (Dementia). 2022 Nov 19. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32491376.
3. Lee J, Meijer E, Langa KM, Ganguli M, Varghese M, Banerjee J et al. Prevalence of dementia in India: National and state estimates from a nationwide study. Alzheimers Dement. 2023 Jul;19(7):2898-2912. doi: 10.1002/alz.12928. Epub 2023 Jan 13. PMID: 36637034; PMCID: PMC10338640.
4. 2022 Alzheimer's disease facts and figures. Alzheimers Dement. 2022 Apr;18(4):700-789. doi: 10.1002/alz.12638. Epub 2022 Mar 14. PMID: 35289055.
5. Saunders AM, Strittmatter WJ, Schmechel D, George-Hyslop PH, Pericak-Vance MA, Joo SH et al. Association of apolipoprotein E allele epsilon 4 with late-onset familial and sporadic Alzheimer's disease. Neurology. 1993 Aug;43(8):1467-72. doi: 10.1212/wnl.43.8.1467. PMID: 8350998.
6. Karch CM, Goate AM. Alzheimer's disease risk genes and mechanisms of disease

pathogenesis. Biol Psychiatry. 2015 Jan 1;77(1):43-51. doi: 10.1016/ j.biopsych. 2014.05.006. Epub 2014 May 17. PMID: 24951455; PMCID: PMC4234692.
7. Yu M, Sporns O, Saykin AJ. The human connectome in Alzheimer disease - relationship to biomarkers and genetics. Nat Rev Neurol. 2021 Sep;17(9):545-563. doi: 10.1038/s41582-021-00529-1. Epub 2021 Jul 20. Erratum in: Nat Rev Neurol. 2021 Aug 11;: PMID: 34285392; PMCID: PMC8403643.
8. Toga AW, Clark KA, Thompson PM, Shattuck DW, Van Horn JD. Mapping the human connectome. Neurosurgery. 2012 Jul;71(1):1-5. doi: 10.1227/NEU.0b013e318258e9ff. PMID: 22705717; PMCID: PMC3555558.
9. Filley, Christopher M., 'The Neurologic Background', The Behavioral Neurology of White Matter, 2 edn (2012; online edn, Oxford Academic, 1 Apr. 2013), https://doi.org/10.1093/med/9780199743261.003.001, accessed 13 Mar. 2024.