

USE OF M.R.I. IMAGING & VOLUMETRIC QUANTIFICATION OF BRAIN REGION OF INTEREST ASSOCIATED WITH DEMENTIA

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Abstract : The line of treatment in psychiatry needs revival as clinicians resort to external symptoms, rather than enquiring into the organic cause. The present study is aimed to explore the efficacy of volumetric quantification of the brain through MRI in the diagnosis of Dementia. The study has strong potential to unravel the application of brain volumetric quantification in determining the possibility of detrimental state of the mind in future. We studied volumetric patterns in a variety of psychiatric disorders. The study results confirmed the presence of specific volumetric patterns for multiple Psychiatric disorders. In this study the statistically significant ($p < 0.01$) values have been observed with respect to the region of interest in the brain e.g. level of significance test shows that there is a significant change in the R grey, total greymatter, L/R lat.ventri, L/R thalamus, L/R hippocampus, L/R amygdala, L/R caudate, L/R putamen and L/R accumbence. (L- Left , R- Right) volumetric quantification values exhibit morphological alterations. The present study concludes that Brain Volumetric Quantification has a strong potential for confirmation of Demented brains by the observance of specific volumetric patterns.

Index terms: MRI, mental disorders, imaging, Volumetric quantification.

I. INTRODUCTION

Revolutionary changes have been experienced by the research community in the field of neuro imaging . During last three decades medical imaging has been embarked upon varied level of technological up gradations which not only resulted into the in depth anatomical representation in digital formats but also improved the clarity in clinicians decision making. Extensive use of radio imaging techniques such as CT , MRI, fMRI, and PET has been employed to enquire into the organic deformities leading to brain disorders[1] This research study will emphasise on the efficacy of MRI in prediction of Dementia, a cognitive impairment disorder.[2] The commonest form of the dementia disorder is Alzheimer which is said to be the final stage of dementia [3] where the brain is almost

dysfunctional and resulting into the disoriented behaviours the chief complaints of the patients with dementia are as follows:-

- (1) The subjects experiences difficulty in accomplishing the task, which they use to do it with ease in past.
- (2) Inability to solve the problems
- (3) Mood variations , apathy and withdrawal from social life
- (4) Inability in communicating either verbally or in written.
- (5) Confused state of mind regarding place , episodes and people
- (6) Trouble in identifying the images through visionary senses. [4]

But it is important to note here that not all memory related symptom to be linked with dementia or Alzheimer because cognitive impairment is attributed various conditions such as history of neurological disorders , cardiovascular troubles , head trauma etc [5]As per Alzheimer association of India, there are about 44 million population is affected with dementia or its subtype. And in India the population number affected with dementia amounted to be 4 millions !!! It is therefore mandatory to address this issue seriously. The present psychiatric nosology is limited to the explicit observations and symptoms as noted by the mental health professional and patients relatives, friend etc.[6] But the underpinnings behind this disorder remains an open question !However only CT or MRI scanning will not suffice , but additional computational or machine learning will be essentially helpful in drawing the conclusion based on volumetric differentiations in the brain ROI (Region of Interest) of healthy control and subjects affected with dementia.[7] This will further lead to accurate diagnosis followed by prognosis and line of treatment to be followed with reference to aetiology of the present of the disorder and state of the lesion or atrophy. Therefore role of MRI as a basic diagnostic tool in diagnosis of dementia is very important [8] further to this , the advent of computational psychiatry has opened up the ways to statistically establish the significance of structural asymmetries in the volumes of brain ROI.[9] While focusing on the current methods that can be used for the diagnosis and treatment of a mental illness are psychotherapy, medication, hospitalization, peer support, and support groups. Magnetic resonance imaging (MRI) uses the superconducting magnet to monitor the changes that occur in the protons which are generally caused by pulse sequences. MRI successfully makes differences between the human brains that are suffering from mental illness and those who are not suffering from mental illness as the images of both the brains are entirely different.[10] MRI is highly useful in diagnosing a

disease or injury and plays an important role in monitoring the treatment procedure. MRI of the brain is mainly used for identifying damages in the blood vessel, brain injury, stroke, spinal cord injuries, and others.

II Related Work

The human brain is said to be the controller of human behaviour with the use of various modalities like MRI, fMRI, PET, CT, EEG. We are today able to understand the brain and its functions in the behavioural domain, in-depth.[11] The vast research in the field of neurochemical and neuropsychological processes has been carried out which are associated with different types of behavioural patterns.[12]The complexities of internal activities of the brain are infinite. In order to understand the brain behavioural relationship we have to understand the various structures of the brain and their functions and how variations or asymmetries or damages or lesions can result in the behavioural affect.[13] In this context [14] Godfrey and his team have done research on brain function relationship. However, there have been a series of studies already conducted by many researchers based upon which the conceptual and methodological shift can be observed. It is due to the advent of modern imaging technology,

[15]vivid research in the field of neural network circuitry and advancement in various methods of defining the lesion – deficit causal relationship that is based on such multivariate methods. Godfrey and the team postulated the concept of brain behavioral relationship models which are also known as assumptions model such as (a) Assumptions of Unicity (b) Assumptions of Equivalence (c) Assumptions of Association (d) Assumptions of Summation. [16] These four models enable us to elicit the role of lesions in the cognitive process., It also visualizes the causal association between the normal region of interest (ROI) in the brain and cognitive developments. These four assumptions are said to be the four different models of the brain-behavior relationship. With the help of these models, the location of the particular lesion can be detected and possible treatment can be worked out [17]

III Structural MRI

The researchers have been using the structural MRI modality for visualizing the living human brain anatomy since the 1980's.[18] MRI scanning provides in-depth images of the brain that denotes the hyper or hypo intense structures of regions of interest (ROI) in the brain. This differentiation is possible due to the presence of water and the hydrogen atom, White matter (WM), Grey Matter (GM), Cerebro Spinal Fluid(CSF) in different brain tissues in different proportions. [19]Visual presentation of the brain in MRI

can be done through various planes of view such as Axial view (From bottom to top), Saggital view (From left to right) and Coronal view (From front to back).[20] It can be viewed from an oblique angle to the above-mentioned planes also. It facilitates greater accuracy in alignment of images with internal landmarks which is a mandatory and essential requisite for ensuring the consistency of data from scanning images.

While the MRI of the heart and blood vessels show the condition of the heart and highlight the issues associated with the structure of the heart. It identifies damages caused by a heart attack, recognizes blocked blood vessels and other heart diseases. Likewise, MRI is used for diagnosis or other body parts such as bones, joints, and others and provides useful information about the entire body. While focusing on the importance of MRI by specifically focusing on the mental disorder, it was found that it is used as an essential tool by the neuro markers. It produces images of the brain which are scanned by scientists and experts to indicate the functioning or dysfunction within the brain. It also includes the use of other techniques such as EEG, ERP and PET machines that also help in determining the brain images along with MRI. However, the scientists claim that MRI provides the most précised images of the brain activity that helps the professionals to compare the differences present in the mental state of the individuals. For example, fMRI scans are used by healthcare professionals that provide mind images in the form of time series by capturing images of the brain in every 2 to 3 seconds interval. As a result, it becomes easy for the experts to analyze the movements in the brain and ascertain the functioning of the brain in the case of individuals suffering from mental illness. For this, the professional collects the images and runs them on the computer to mark the significant differences between the images. It helps in identifying the changes occurring in the brain activities over time and determines the health status of the brain. In addition to this, a statistical analysis program is also performed with the help of scanners so that the functioning of the different parts of brains is identified informing which part of the brain is working extensively and which part is least used. All these factors help the neuro markers to frame a chart and identify the characteristics that are associated with normal behaviour and abnormal behaviour of individuals. [21]

The magnetic Resonance Imaging process is highly used by health care professionals in the detection of mental disorders because it works efficiently and provides information about all the sensitive changes that are occurring in the brain. Additionally, the process can be used with a combination of other techniques such as PET, and electromagnetic measurements, magneto encephalography which helps in attaining more

valuable information about the functioning of the brain. It identifies the chemical and neuronal changes with respect to the brain workings and specifies the alterations that are mainly linked with psychiatric illness. Hence, it can be said that MRI is highly useful in analyzing mental disorders among individuals suffering from mental illness.

MRI volumetric quantifications in brain regions of mentally ill subjects are performed by using three processes which are manual, semi-automated and fully automated. The technique helps in the quantitative estimation of the atrophy of the brain functions and facilitates the monitoring process for the identification of the disease. In the present condition, all three methods are based on the conventional MRI scanning process and analyze the entire brain or its parts depending on the disease and treatment requirement. In addition to this, the quantifications in brain regions of mentally ill individuals are highly impacted by several factors such as the application of segmentation methods, estimation of the pulse sequence, and the resolution dimensions of the variables selected for the attainment of the diagnosis of the intensity of the disease. The segmentation also depends upon the factors such as the thickness of the tissues and their volumes that creates differences between the cerebral compartments. The determination of the tissue contrasts helps in choosing the volumetric quantification methods. For example, a manual technique is used when the structure of the brain allows taking recording related to brain volumes or conduct estimations. However, it consumes a lot of time. A semi-automated volumetric quantification technique is used to get fast responses in comparison to manual technique. The semi-automated technique performs better than the manual technique because it uses 3D volume segmentation and algorithm process. It provides more intricate learning about brain movements and précised images. It helps in the early identification of the mental illness among the individuals and enables healthcare professionals to initiate the treatment process at earliest. On the other hand, fully automated methods are used just like semi-automated techniques. The only difference between them is that fully automated makes estimations are related to specific regions along with the entire portion while semi-automated is related to the specific body part. It is completely user-based which provides more intercalate information about the size, shape and other aspects of the brain. Moreover, the estimations that are produced with the help of automated technology are more accurate in comparison to the manual technique used for the volumetric quantifications of brain regions of mentally ill subjects.

IV. Materials And Methods

Participants:

The participants were patients who were suffering from Dementia disorder and referred by local physicians. The healthy control sample was free of any disorders, or learning disabilities. Diagnoses were confirmed by experienced staff. Research study procedures were explained in detail and informed consent/assent was obtained.

Research methodology:

In the current study which is related to the efficacy of MRI in the detection of Dementia or possibility of developing dementia in future, the quantitative research approach is to be used with the positivist research paradigm. The study also includes descriptive research design and a deductive research approach so that hypothesis testing and graphical presentation of facts are done effectively. It includes databases from 49 normal individuals and 30 individuals who are suffering from Dementia. All the participants are male and belong to the age category of 40 to 50 years. On the other hand, the MRI database is to be collected by taking 30 individuals in which each individual is affected by disorder who can be male or female belonging to the age group of 18-50 years. Informed consent was obtained from all subjects participated in the research study.

MRI analyses:

All MRI examinations are done based on 3Tesla SIEMENS systems. Axial T1W 3D images were taken for processing and defining the Volumes in Region of Interest (ROI). The control and experimental group depicted the difference in brain ROI volumetry.

micro GL/ VOL brain On line SW for volumetric quantification: MRICRO GL is one of the most widely used software packages for converting the DICOM data to NiFTI. Format was used to convert the Dicom data into Nifti format. After getting Data in .rar / .gs / .nii the **VOLbrain V0.2** open platform on line SW was used to get the volumetric data of Brain for examining neural activity as well as for analyzing the MRI data.

Statistical Analysis:

Brain – Volume measurements were normally distributed. The evaluation of associations between brain Region of Interest (ROI), normal healthy control and brain ROI of Demented group was carried out. The statistics required for the test were constructed for each respective Region of Interest (ROI) in brain anatomy separately and. The statistical observations for each group are as follows:-

- (a) The total sum of Normal Male Group (Control) results in the mean rank of that group.
- (b) The total sum of the Experimental group results in the mean rank of that group.
- (c) The difference in mean rank is observed.
- (d) The **Mann Whitney test** will be decisive in defining the relative difference in mean rank is significant or not
- (e) It is illustrated in the last two columns of each table. The statistical significance is taken into consideration with the U values at $p < 0.001$.

V. Results

Patient characteristics enumerated in **Table “1”**. A total of 99 Patients underwent MRI scanning. Out of 69 Patients having normal MRI brain scans were chosen as a control group. (32 patients were healthy male control (G1=32) and 37 were Healthy Male + Female control . group (G2=37). And 30 patients being referred by local physicians who have been diagnosed under the category of Dementia (n=30)

Table “2” The automated open platform for evaluation of brain volume was done the quantification was based on each individual T1 W MRI image of the brain. The different ROI (Region of Interest) of both hemispheres (Left (L) & Right (R) of the brain anatomy were considered as variables for measurement of volumes such as Grey Matter, White Matter, White Matter, Lateral Ventricles, Thalamus, Hippocampus, Amygdala, Caudate, Putamen, Global Pallidus, and Nucleus Accumbens area structures were measured volumetrically. The above-said area is associated with, Dementia, All the aforementioned variables were compared between Healthy control group (G1 & G2) & Psychiatric disorder group (Dementia)(**Chart -1**) To analyze the first hypothesis the facts related to efficacy of MRI in detection of mental disorders using volumetric quantification, Mann-Whitney Test was conducted by taking normal male and female group (G2) against normal male group (G1) for 22 Region of Interest (ROI) and it was found that the difference in mean rank of G1 Vs G2 was statistically insignificant. The ascertained values (U) are when the significance of the p-value was less than **.001**. Hence, it can be said that there was no significant difference in G1 vs Normal G2 (Table “ 2”)

We observed alterations in the multivariate model post comparison through statistical inquiry

Normal (Male + Female) Vs. Dementia Group (TABLE “ 3 ”.)

In our sample, 30 participants were evaluated who was diagnosed with Dementia disorder. The MRI scanning followed by volumetric quantification was carried out. The comparative analysis with the volumes of control group (n=37) suggestive of alterations in the Right Grey Matter, Total Grey Matter, Total White Matter, Bilateral Ventricles, L/R - Thalamus, L/R – Amygdala, L/R – Caudate, L/R – Putamen, L/R – Accumbens regions of brain. (Table” B”) The observed difference is statistically significant at $p < 0.001$ for the respective U value. Whereas we observed Insignificant differences in another region of interest (ROI). ($p > 0.001$)

Discussion

As per the above facts, it can be said that mental disorder is a chronic ailment that is impacting a high range of the population. However, it is still difficult to ascertain exact aetiology and path physiological instruments that can evaluate the fundamental stretch of psychiatric disorders. It is because the currently available alternatives are unable to treat the patients suffering from a mental disorder and they are not to settle in the social and professional life. The main reason found behind the cause of the mental disorder changes in the normal functioning of the brain structures. The word dementia is no more in use presently, it is related to gradual impairment of cognitive abilities due to atrophy or de generation of brain cells The disorder comes under the umbrella of NCD (Neuro Cognitive Disorders) related to the loss of neural base of brain and pertaining neurological functions particularly related to the ROI , white matter , or neural tracts , cortical pathways in brain. In Dementia disorder, the areas of brain where maximal age-specific atrophy is observed in posterior Hippocampus, Thalamus and middle cingulated Gyrus [22] The neuropsychology & neuro science which define the correlative aspects of brain lesions or asymmetric volumes or changes in the structure of ROI with memory, perception and thought process that regulates the human behaviour around 60 -70% of the patients affected with Alzheimer are having aetiology of dementia[23] , therefore, it is essential to use modern diagnostic techniques like

Magnetic Resonance Imaging (MRI), so that alterations that are occurring in the brain and volumetric quantification in the posthumous will be ascertained carefully. The T1 and T1 3D Images that are exhibited by the MRI images are not perfect and do not show the symptoms of the illness Hence, there is a need for a more specific diagnosis and treatment process so that the disease such as mental disorder could be identified and treated well. The introduction of new brain mapping techniques will help to attain clear brain images and propose new treatment procedures to cure the patients

limitations

The limitation of the present study is that there is an absence of large sample size due to social taboo and Inability to gather an equal number of patient /control gender-wise. Unavailability of the exact ongoing state of medication by each subject is also included.

Conclusion

The study examined the facts related to the efficacy of MRI for the detection of mental disorders through Volumetric Quantification. It was found that the MRI in conjunction with volumetric measurement is highly useful in the diagnosis of the symptoms of mental disorder, but it lacks precision and more advanced methods of diagnosis, screening, and imaging is to be discovered so that symptoms of mental disorder could be ascertained at early stages precisely. The study examined that mental disorder is a psychiatric disorder that lowers the individual functioning capabilities and the individual suffering from the illness is not able to perform his/her daily functions properly. Hence

TABLE 1. (PARTICIPANT (N=99) CHARACTERISTICS)

N	Study Group	Male	Female
32	Control – Healthy Male (G1)	32	0
37	Control – Healthy Male+ Female (G2)	23	14
30	Experimental – Dementia (DMN)	15	15

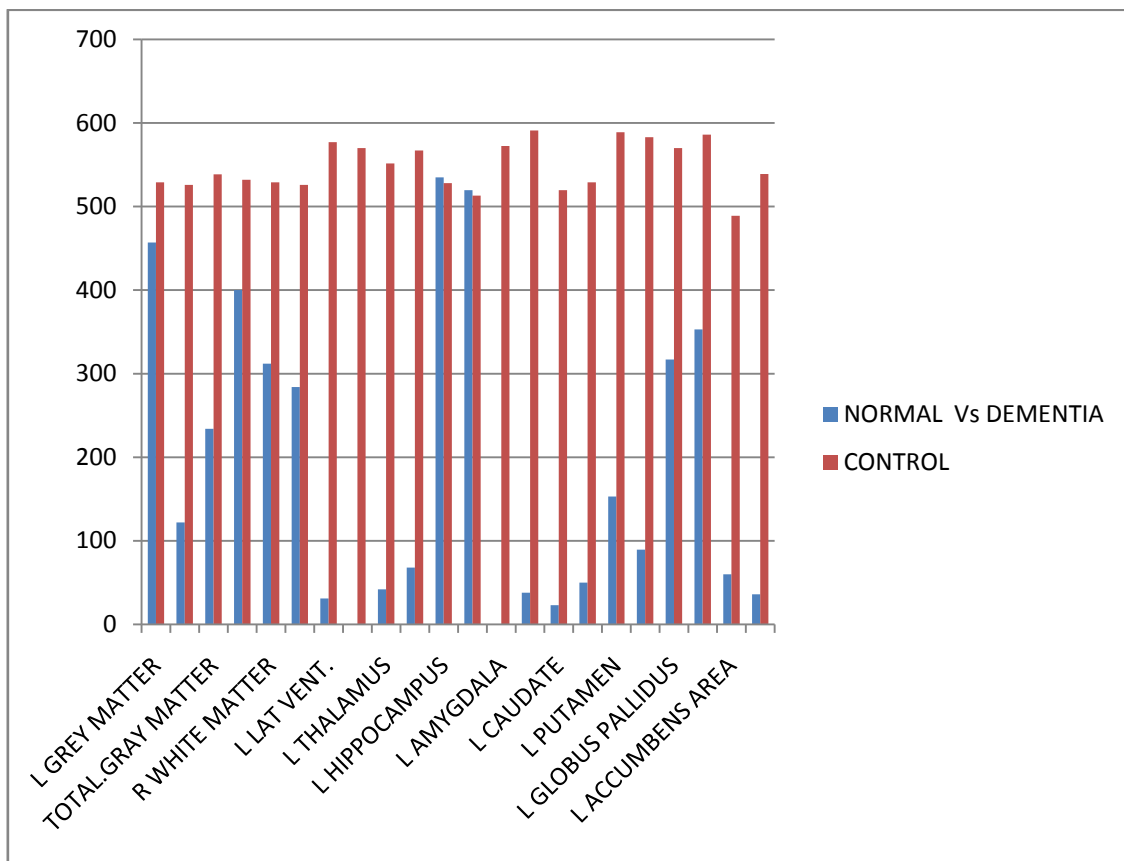
TABLE 2. STATISTICAL DATA (Normal Male Vs Normal Male + Female) POST VOLUMETRIC QUANTIFICATION

SL	Brain Region Of Interest (ROI)	Normal Male Mean Rank (n= 32) – G1	Normal Male+ Female Mean Rank (n=37) – G2	Mann- Whitney U	Significance (At p<.001) for given U values
1	L GREY MATTER	36.97	33.3	529	Insig., p>.001
2	R GREY MATTER	37.06	33.22	526	Insig., p>.001
3	TOTAL.GRAY MATTER	36.67	33.55	538.5	Insig., p>.001
4	L WHITE MATTER	36.88	33.38	532	Insig., p>.001
5	R WHITE MATTER	36.97	33.3	529	Insig., p>.001
6	TOTAL WHITE MATTER	37.06	33.22	526	Insig., p>.001
7	L LAT VENT.	35.47	34.59	577	Insig., p>.001
8	R LAT VENT.	35.69	34.41	570	Insig., p>.001
9	L THALAMUS	36.27	33.91	551.5	Insig., p>.001
10	R THALAMUS	35.78	34.32	567	Insig., p>.001
11	L HIPPOCAMPUS	37	33.27	528	Insig., p>.001
12	R HIPPOCAMPUS	37.47	32.86	513	Insig., p>.001
13	L AMYGDALA	35.61	34.47	572.5	Insig., p>.001
14	R AMYGDALA	34.97	35.03	591	Insig., p>.001
15	L CAUDATE	37.27	33.04	519.5	Insig., p>.001
16	R CAUDATE	36.97	33.3	529	Insig., p>.001
17	L PUTAMEN	35.09	34.92	589	Insig., p>.001
18	R PUTAMEN	35.28	34.76	583	Insig., p>.001
19	L GLOBUS PALLIDUS	35.69	34.41	570	Insig., p>.001
20	R GLOBUS PALLIDUS	34.81	35.16	586	Insig., p>.001
21	L ACCUMBENS AREA	38.22	32.22	489	Insig., p>.001
22	R ACCUMBENS AREA	36.66	33.57	539	Insig., p>.001

TABLE” 3”. Normal (Male + Female) Vs. Dementia Group

SL	Brain Region Of Interest (ROI)	Dementia Group Mean Rank (n= 30)	Normal Male+ Female Mean Rank (n=37)	Mann- Whitney Test Results			Significance (At p<.001) for given U values		
				U	W	Z	Asym. Signi. 2 Tailed (p)	Significance(p <.001)	Insignificance (p>.001)
1	L GREY MATTER	36.65	30.73	457	922	-1.236	0.217	0	1
2	R GREY MATTER	45.7	19.57	122	587	-5.46	0	1	0
3	TOTAL GRAY MATTER	42.68	23.3	234	699	-4.047	0	1	0
4	L WHITE MATTER	29.81	39.17	400	1103	-1.954	0.051	0	1
5	R WHITE MATTER	27.43	42.1	312	1015	-3.064	0.002	0	1
6	TOTAL WHITE MATTER	26.68	43.03	284	987	-3.417	0.001	1	0
7	L LAT VENT.	19.84	51.47	31	734	-6.607	0	1	0
8	R LAT VENT.	19	52.5	0	703	-6.998	0	1	0
9	L THALAMUS	20.14	51.1	42	745	-6.469	0	1	0
10	R THALAMUS	20.84	50.23	68	771	-6.141	0	1	0
11	L HIPPOCAMPUS	34.54	33.33	535	1000	-0.252	0.801	0	1
12	R HIPPOCAMPUS	34.96	32.82	519.5	984.5	-0.448	0.654	0	1
13	L AMYGDALA	19	52.5	0	703	-6.999	0	1	0
14	R AMYGDALA	20.03	51.23	38	741	-6.52	0	1	0
15	L CAUDATE	19.62	51.73	23	726	-6.708	0	1	0
16	R CAUDATE	20.35	50.83	50	753	-6.368	0	1	0
17	L PUTAMEN	23.14	47.4	153	856	-5.069	0	1	0
18	R PUTAMEN	21.42	49.52	89.5	792.5	-5.87	0	1	0
19	L GLOBUS PALLIDUS	27.57	41.93	317	1020	-3.001	0.003	0	1
20	R GLOBUS PALLIDUS	28.54	40.73	353	1056	-2.574	0.011	0	1
21	L ACCUMBENS AREA	20.62	50.5	60	763	-6.243	0	1	0
22	R ACCUMBENS AREA	19.97	51.3	36	739	-6.548	-6.548	1	0

(ROI : Region of Interest; U/W/Z : Mann - Whitney - Wilcoxon test results, L/R : Left / Right; p: Significance Yes= 1, No = 0)

CHART 1 – VOLUMETRIC ANALYSIS :-

(Chart 1.: Volumetric Analysis - Mann Whitney “U” value comparison between Brain ROI(Region of Interest) of Normal(M)+(F) Control Group & Dementia group)

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