Scholars International Journal of Anatomy and Physiology
Abbreviated key title: Sch. Int. J. Anat. Physiol.
A Publication by "Scholars Middle East Publishers"
Dubai, United Arab Emirates

ISSN: 2616-8618 (Print)
ISSN: 2617-345X (Online)

Evidence Based Alzheimer's Like Pathology in Normal Aging Brain

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Original Research Article

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Article History
Received: 04.08.2018
Accepted: 20.08.2018
Published: 30.08.2018

Abstract: The evidence-based morphometric study was carried out to ascertain the Alzheimer's like pathology in normal aging brain in Navi Mumbai, India.35 normal human cadaver brain specimens were acquired from MGM Medical College, Navi Mumbai, and (Alzheimer`s disease brains) NIMHANS, Bangalore, after meeting the ethical clearance from MGMIHS. Control group of Alzheimer's disease was considered. A history based on CERAD criteria was used for informent scale. We divided the total brains into five groups; group I (20 to 39 years), group II (40 to 59 years), group III (60 to 79 years), group IV (>80 years) and a control-group V (Alzheimer`s brain specimen). We recorded gross features, cortical thickness and the ventricular dilatation in each brain. The chi - square test was applied for calculating cortical atrophy and ventricular dilatation of various age groups. One way ANOVA test was applied to the relation between different age groups using the SPSS19 software. In our study, the mean reduction in brain weight was evident from the 6th decade of life with minimum weight of 800gm (951.90±101.3gm). A substantial difference in the average weight of the brain in different age group was observed (p<. 001). Cortical atrophy and ventricular dilatation was evident of 20% in group II, 60% in group III and 100% in group IV (*p<. 01*).
Keyword: Alzhimers disease, Aging, Atrophy, Degeneration, Dementia.

INTRODUCTION

The brain, additionally kenned as Encephalon is divided into 3 regions on a substratum of embryonic development into forebrain (prosencephalon), midbrain (mesencephalon) and spinal cord (hind brain). Forebrain further comprises cerebrum and cerebellum. Cerebrum is made of two cerebral hemispheres connected by the corpus callosum. Each hemisphere consists of the convoluted part called the gyri (singular-gyrus) which are dissevered by deep fissures called the sulci. Below the gyri are the white matter which encloses the diencephalon and the basal ganglia. Lateral ventricle is large central cavity in each cerebral hemisphere for CSF [1].

The cerebrum has always been the element of interest till day, researchers all around the world are endeavoring to reveal its kept secrets. The total surface area of the normal human Encephalon is 2200-2500 cm^2 [2] with 100 billion neurons and more of non-neuronal cells [3]. Human cerebral cortical thickness is about 0.3-0.4 cm [4]. The decrement in weight of the forebrain is due to the neuronal loss. But the neuronal loss is not optically discerned simultaneously in all areas with advancing age [5]. 50% loss of minute neurons is documented from the temporal region in layer 2 and 4 [6]. Similarly, 60% loss of sizable voluminous pyramidal cells [5], 48% from visual cortex [7] and 12% from hippocampus [8], are withal recorded with advancing years. Neuronal loss and glial proliferation are visually perceived more in Alzheimer's disease.

Neuronal loss and atrophy of the cortex are accompanied by dilatation of the ventricles. This dilatation is symmetrical and is more marked in Alzheimer's disease [9].

Dementia is broadly classified based on histopathology into the Alzheimer's disease, vascular dementia, dementia with Lewy body and frontotemporal dementia. Alzheimer's disease is the leading cause of dementia (*https://www.cdc.gov/aging/aginginfo/alzheimers.htm*), but it alone does not cause dilatation and cerebral atrophy [10]. In India we have under reported statistical data for Alzheimer`s like changes due to poor understanding and early attention to the disease. Thus we aim to study Alzheimer`s like morphometric changes in the normal aging brain.

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MATERIALS AND METHODS

36 human cadaveric brain specimens were used during dissection in the Anatomy department at MGM Medical College, Navi Mumbai and Brain bank of NIMHANS (National Institute of Mental Health and Sciences) Bangalore, during the period of Jan 2016-Aug 2017 after obtaining the Ethical clearance from MGMIHS. The control group was taken with a confirmed case of Alzheimer's disease from the NIMHANS brain bank.

A defined protocol with proper clinical history from the next of kin (close relative – the person taking charge of a patient for last 6 months) was taken. The clinical history was designed as per CERAD (Consortium for Establishing a Registry for Alzheimer's disease) scale to rule out any known neurological or psychological problems. Informed written consent was taken for utilizing the brains for research and educational purpose.

We divided the total brains into five groups; Group I-20-39yrs (10 specimens), Group II-40-59yrs (10 specimens), Group III-60-79yrs (10 specimens), Group IV-80yrs and above (5 specimens), and control group (1specimen).We considered,

- *Gross weight of* (10%) *neutral formalin-fixed human cadaveric Cerebrum,*
- *Gross appearance of sulci and gyri of each hemisphere,*
- *Gyri thickness,*
- *Ventricular enlargement in relation to white matter* after taking a coronal section at mammillary body level.

Statistical Method

We calculated mean and standard deviation for weight in different age groups using student t-test. The chi-square test was used for calculating the correlation of different age groups with cortical atrophy and ventricular dilatation. One way ANOVA test was utilized in the relation to different age groups. SPSS19 software was utilized.

OBSERVATIONS AND RESULTS

Table-1: Descriptive Statistics for Age

Age group (yrs)	Specimens	Mean Age	SD	SEM	Age	
					Min.	Max.
20-39	10	29.30	4.57	1.45	20.00	35.00
40-59	10	50.00	6.32	2.00	40.00	59.00
60-79	10	67.70	4.42	1.40	62.00	75.00
80 & above	5	86.60	4.88	2.18	81.00	92.00
Total	35	54.37	20.48	3.46	20.00	92.00

Table-2: Descriptive Statistics for Weight of Brain (GM)

Age group (yrs)	Specimens	Mean weight	SD	SEM	Age	
					Min.	Max.
20-39	10	1178.20	136.66	43.22	950.00	1375.00
40-59	10	1028.20	151.94	48.05	750.00	1206.00
60-79	10	951.90	101.32	32.04	800.00	1116.00
80 & above	5	965.60	27.36	12.23	925.00	993.00
Total	35	1040.31	150.38	25.42	750.00	1375.00

Table-3: ANOVA for Weight of Brain (GM)

	Sum of Squares	df	Mean Square	F	Significance
Between Groups	297674.24	03	99224.75	6.527	0.001
Within Groups	471239.30	31	15201.27		
Total	768913.54	34			

One Way ANOVA test was applied to compare the average weight of the brain in different study groups. The result indicates a significant difference in the weight of the brain (GM) according to the study groups ($p < .001$).

Table-4: Multiple Comparisons for Weight of Brain (GM)

LSD (Least Significant Difference**)**				
Age Group		**Mean Difference (I-J)**	**Std. Error**	**Significance**
20-39	40-59	150.0*	55.13849	.011
	60-79	226.30*	55.13849	.000
	80 & above	212.60*	67.53059	.004
40-59	60-79	76.30	55.13849	.176
	80 & above	62.60	67.53059	.361
60-79	80 & above	-13.70	67.53059	.841

*Significant

The above table shows multiple pairwise comparisons according to the study groups using LSD (Least Significant Difference) Post HOC test. The result of LSD indicates that there is a significant difference in the mean weight of the Brain (GM) in age groups 20-39with the age groups 40-59, 60-79 and 80+.

Table-5: Association between Age and Atrophy

Age group	**Atrophy**				**Total**	
	Normal		**Abnormal**			
	No	**%**	**No**	**%**	**No**	**%**
20-39	10	45.45%	0	0.0%	10	28.57%
40-59	8	36.36%	2	15.4%	10	28.57%
60-79	4	18.18%	6	46.2%	10	28.57%
80 & above	0	0.00%	5	38.5%	5	14.29%
Total	22	100.00%	13	100.0%	35	100.00%
Chi-square= 17.867, df=3, p <.01, Significant Association						

Table-6: Association between Age and Dilatation

Age group	**Dilatation**				**Total**	
	Normal		**Abnormal**			
	No	**%**	**No**	**%**	**No**	**%**
20-39	10	45.45%	0	0.0%	10	28.57%
40-59	8	36.36%	2	15.4%	10	28.57%
60-79	4	18.18%	6	46.2%	10	28.57%
80 & above	0	0.00%	5	38.5%	5	14.29%
Total	22	100.00%	13	100.0%	35	100.00%
Chi-square= 17.867, df=3, p <.01, Significant Association						

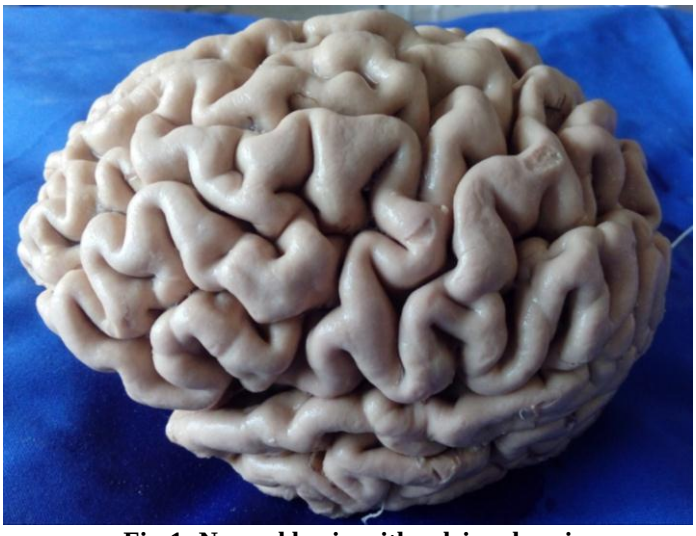

Fig-1: Normal brain with sulci and gyri

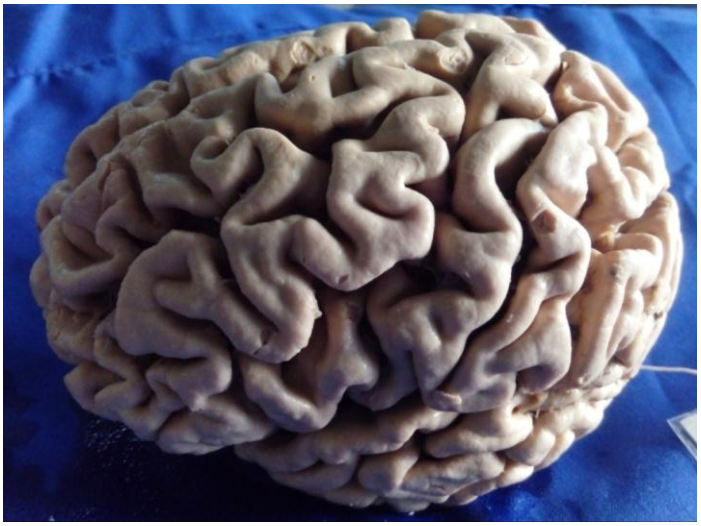

Fig-2: Brain showing atrophy of gyri with widen sulci

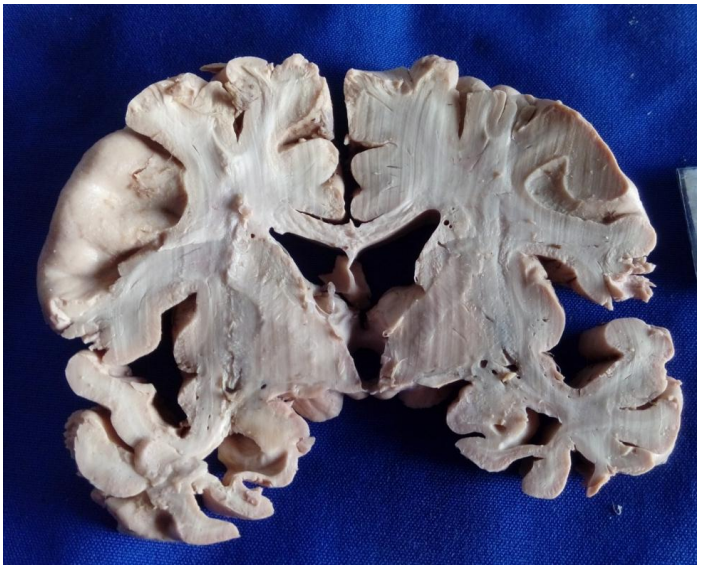

Fig-3: Atrophy of cortex with dilatation of ventricles

DISCUSSION

In our study group I showed no gross morphological changes, group II showed atrophic changes in two specimens (55/F, and 56/M) and in group III atrophy was restricted to 50% of specimens in the frontal and parietal region and it equally affected both the genders. Group IV showed atrophy in almost all the specimens and restricted to frontal, parietal, temporal and was less in the occipital and hippocampal region. The brain weight varies irrespective of the growing age. It ranges from 950 grams to 1350 grams in the seventh decade onwards [11].

Prasanna, from Kerala, Kottayam found a difference of 60 GM in the average weight of the brain in both genders and the mean weight was increased in the first three decades, then decrease till the seventh decade [12]. In our study, the mean difference of brain weight in group I and II was 150 GM, between group II and III was 77.2 GM and least between 6th and 8th decade, of 15 GM. Thus the average difference in brain weight reduced to half from 2nd to 6th decade and then gradually slowed by 7 -8 GM/decade in our study.

We did not find increased weight in the brain from 2nd to 6th decade of life as seen by Prasanna *et al*., but the decrease in weight was evident after 6th decade of life. Female showed less in the mean weight as male [12].

In our study atrophy of the cerebral cortex with reduced in cortical thickness and dilated ventricle was evident as early as 55 years of age and was more in female cadaveric specimen. We also found that ventricular dilatation was evident both in old age and confirmed cases of Alzheimer`s disease (AD) brains which was unilateral due to midline shift. We found one specimen from group IV (90/M) with Alzheimer's like

gross pathology showing marked atrophy in frontal, occipital and some atrophy in the polar temporal region. These similar gross changes were seen in confirmed AD brain. Our findings of degenerative distribution, in AD and Alzheimer`s like pathology, matched with Peter *et al.*, [13] study but not with Archana *et al.*, [2] study which showed entire cerebral cortical atrophy with exception in the occipital region.

CONCLUSION

Gross weight and volume of cerebrum decrease with age; we found more reduction in females than males and affecting both sexes equally after the 6th decade of life. Ventricular dilatation with cortical atrophy was also evident after 6^{th} decade, but pronounced after 7^{th} decade affecting more females than males. Degenerative changes may or may not accompany gross morphological changes.Detail examination of brain specimen gives valuable sign of Alzheimer`s like patholgy which can be further evaluated.

ACKNOWLEDGMENT

We would like to thank Anatomy Department of MGM Medical College and Brain Bank, NIMHANS for providing brain specimen.

CONTRIBUTION

Principle investigator – Dr. Pravin planned and designed the research work. Dr. Pravin and Dr. Monali were involved in analyzing and interpretation of the result. All authors did compile of data, framing the manuscript and cross verifying the results. Dr. Aruna Mukherjee gave valuable information of anatomical details.

Conflict of interest: No conflict of interest

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