

# COMPARISON OF MEDIAL TEMPORAL LOBE MEASUREMENTS ON MRI AMONG ALZHEIMER'S GERIATRIC PATIENTS: A CROSS-SECTIONAL STUDY

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## ABSTRACT

**BACKGROUND:** Alzheimer's is a syndrome mostly affecting geriatric causing medial temporal lobe atrophy and memory impairment. It is untreatable in geriatrics patients, but lack of using simple and reliable measurements to determine the severity of Alzheimer's disease. This paper collects the severity of Alzheimer's geriatric patients based on the popular visual grading system MTA, linear measurements applied on MRI scan to determine the severity of Alzheimer's disease, and the reliability and repeatability of these measurements. **OBJECTIVES:** The aims of this study are to find the common grade of Alzheimer's disease by using a simple and reliable measurement, find the reliability and repeatability of hippocampal linear measurements. Find the relation of the grade of atrophy with gender, and age. Measure hippocampal height and width to give a reference value of Alzheimer's patient and measure radial temporal horn width and compare between right and left side. Compare between the United States and international Alzheimer's patients. **METHODOLOGY:** A cross-sectional study was conducted on 60 geriatric Alzheimer's subjects from ADNI database which represent 5 % of all Alzheimer's population in the United States. By using a visual grading system which is applied on MRI scan and compare them to each other. Statistical analysis was done by SPSS (V-21) software. The aim of this paper is to find the most common grade and the relation between the grade of Alzheimer's with gender and age. Give reference value of mean volume for both right and left hippocampus. Compare between right and left temporal horn width. **RESULT:** The aim of this paper was to find the most common grade of Alzheimer's disease among ADNI database which was done on 60 patients from ADNI. The most common grade is grade one and Alzheimer is more common in males, but it is more severe in females. MTA grading system must change from visual grading system to a system that depends on measurable values. The new MTA system must include hippocampal width since hippocampal width has a higher association with MTA more than the hippocampal height. RR can be used as criteria to verify the grade of the new MTA. **CONCLUSION:** The suggestions and recommendations for future studies are to focus on transforming the MTA grading system to a system that depends on measurable values. Add the width of the hippocampus to the MTA grading system criteria. Provide simple software's that can measure the hippocampal volume in a simple clinical sitting.

**Keywords:** Alzheimer's, Geriatrics, MRI.

## Introduction

According to the World Health Organization (WHO), dementia "is a syndrome - usually of a chronic or progressive nature - in which there is deterioration

in memory, thinking, behavior and the ability to perform everyday activities affects older people and it is not a normal part of aging".<sup>8</sup> Also, WHO reported in a

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fact sheet published in May 2017 that there are 47 million people with dementia, every year 9.9 million more people are affected by dementia, 5 to 8 out of 100 people above 60 years have dementia, in 2030 the patients with dementia will be 75 million and in 2050 will reach 132 million worldwide.<sup>8</sup> The definition according to Roman (2003) "dementia is clinical syndrome has symptoms including memory difficulty and issues with speaking, thinking and the ability for problem-solving which reflex on social life".<sup>4</sup>

The use of simple and reliable measurements or methods to evaluate or predict Alzheimer's disease (AD) immediately is the modern trend in the neuroscientific community. There are many methods to measure the severity of the AD such as; measuring hippocampal volume, detecting tau protein and amyloid level in cerebrospinal fluid (CSF) by magnetic resonance imaging (MRI), and detecting iron deposition in basal ganglia. All the previous measurements are difficult to do in a short time. Furthermore, these measurements need specialists to do the analysis. The most simple and reliable measurements are Medial Temporal Lobe Atrophy (MTA) grading system, hippocampal linear measurements, and radial temporal horn width (rTHW).

### Statement of the Problem

The purpose of this paper is to find the common grade of AD among patients who are registered with Alzheimer's Disease Neuroimaging Initiative (ADNI) database by simple and reliable indicators of the severity of AD. All published research used advanced methods that are difficult to be applied in a clinical sitting. As well, finding the reliability and repeatability of a simple linear measurements of hippocampus which is very simple measurements.

## Aims and Objectives

### AIMS

To determine the common grade of AD among patients

### OBJECTIVES

To determine the following measurements on MRI scan Determine AD grade of atrophy in relation with gender and age. Compare between right and left medial temporal lobe in each patient. Measure hippocampal

dimensions to give reference value. Measure radial temporal horn width for both sides. Compare between AD geriatrics patients in United States and international. Determine the reliability and repeatability of hippocampal linear measurements.

### Hypotheses of the Study

This paper will determine the severity of AD in the United States. The hypotheses is the severe stage or 4 on MTA score system may be a common variety and mostly severe in females.

### The significance of the Study

The ability to find the common grade, test the reliability and repeatability of the linear measurements, and find the average radiological measurements of the hippocampus in Alzheimer's patients who have enrolled in ADNI database in the United States. It will improve all databases and provide knowledge related to this problem.

### Research Design

A cross-sectional study.

### Sampling Method / Randomization method

Retrograde sample.

### Sample

Alzheimer's Patients who have enrolled and registered with Alzheimer's Disease Neuroimaging Initiative (ADNI) in the United States.

### Subjects

Geriatric patients with AD in the United States.

### Sample size

The sample size required = 60.

The sample size was calculated by using the following formula:

$$n = \frac{z^2 * P (1 - P)}{d^2}$$

Where  $n$  = sample size.

$z$  = level of confidence (2-sided 95% confidence interval = 1.96).

$P$  = Prevalence of Alzheimer's.

$d$  = precision (5%).

### **Inclusion Criteria**

Geriatrics (above 60 years).  
Alzheimer's patient.  
Any gender.

### **Exclusion Criteria**

Younger patient (↓ 60 Year).  
Treatable diseases such as subdural hematomas, tumors, hydrocephalus, strategic infarction of posterior cerebral artery, presenile AD, Vascular dementia, frontotemporal lobe degeneration, dementia with lewy bodies, MCI, Korsakoff's psychosis, recent neurosurgery, epilepsy, post-traumatic stress disorder, schizophrenia, any disease that can affect the hippocampal volume and is not AD, or any psychiatric disorder.

### **Duration of the study**

1 year from 01<sup>st</sup> November 2017 to 01<sup>st</sup> November 2018.

### **Place of the study**

The data is provided by ADNI database which were collected by ADNI organization in the United States after obtaining a personal approval for public access on consent forms from the patients in the United States. This initiative was evaluated and obtained ethical clearance. After applying and showing the research proposal, an access was obtained from ADNI to access their data. The research proposal and ADNI access was provided to the ethical committee, College of Medicine, King Saud University. This study is done under supervision of the Anatomy Department, College of Medicine, King Saud University.

### **Primary researcher**

The primary researcher is student who is pursuing his Master's degree in Anatomy.

### **Materials required**

Digital files of MRI scans on ADNI database.  
Data entry sheet.

### **Outcome measures - primary and secondary**

#### **Primary outcome measures**

Determine the common grade of AD among the patients.

#### **Secondary outcome**

Measure the reliability and repeatability of the linear

hippocampal measurements, determine AD grade of atrophy in relation with gender and age, compare between right and left medial temporal lobe in each patient, measure hippocampal dimensions to give reference value, measure radial temporal horn width for both sides and compare between them, and compare between AD geriatrics patients in the United States and international.

### **Procedure and Data Analysis**

After obtaining an access from ADNI and ethical approval from the ethical committee, College of Medicine, King Saud University. The data was collected and written in the data entry sheet and ethical clearance from the ethical committee. The data was collected, analyzed, and the result is provided.

SPSS (v/21) was used for data analysis of the collected data. The evaluation has been done on MRI coronal plan, T1 weighted images. The slice level was taken at the corpus of hippocampus and at the frontal part of pons. This grading system is a visual rating of the height of the hippocampal formation, choroid fissure width, and temporal horn width.

MTA classify the subjects by system into grades from 0 = normal, 1 = minimal atrophy, 2 = mild atrophy, 3 = moderate atrophy, to 4 = severe atrophy (Scheltens, 1995).<sup>5</sup> A manual hippocampal measurements has been used after alignment of the image to give the best visualization of hippocampus. Both hippocampi of each single Alzheimer's patient was measured at the level of the corpus on MRI T1 weighted images with oblique orientation perpendicular to the axis of the hippocampus at level of anterior pons without previous knowledge of the AD severity in the sample. The height was taken at 90 degrees and the alveus was included in measuring hippocampus height because it cannot be distinguished as a separate structure. Slice thickness is 1.2 mm and selection was made to pick the last scan available for the patients because there are many scans for every patient.

The height of hippocampus was measured from alveus to gray matter of subiculum. The width was measured from hippocampal sulcus medially to temporal horn of lateral ventricle laterally as described by (Adachi M et al, 2007).<sup>1</sup> To measure the repeatability and reliability is required to obtain the mean of both sides which calculated by this formula mean of right and left hippocampal height/mean of right and left hippocampal

width as described by (Rana AK et al, 2017).<sup>3</sup> The radial temporal horn width was measured on MRI axial T1 weighted images at the level of orbitomeatal line. Normal temporal horn appears as slit-like and it is normal width range from 3 to 5 mm at the level of choroid fissure origin. It considered extremely enlarged, if the diameter is more than 5.3 mm.

## Result

The sample was randomly collected from ADNI database. The male patients are 32, while the female patients are 28, and the total number of patients is 60. The average age for the male patients is 75.96 and for the female patients is 79.28 years. The distribution of age start from 60 to 96 years and the average age is 70.58 years. The patients  $\geq 75$  years are 29, and patients  $< 75$  years are 31 see (Tab. 7).

The most common grade is grade one in 19 patients see (Tab.1). AD is more common in males than females. Eleven patients of the first grade patients in the sample are males, where only 8 are females see (Tab. 2). The grade zero was never found in any patient in this sample. The average age in grade one is 71, grade two is 77, grade three is 80, and grade four is 76 years see (Tab. 3).

MTA grade					
		Frequency	Percent	Valid Percent	Computed Percent
Valid	1	19	31.7	31.7	31.7
	2	18	30.0	30.0	61.7
	3	12	20.0	20.0	81.7
	4	11	18.3	18.3	100.0
	Total	60	100.0	100.0	

Table 1: The common grade of AD among the sample.

Gender * MTA grade						
Count						
		MTA grade				Total
		1	2	3	4	
Gender	Male	11	11	5	5	32
	Female	8	7	7	6	28
Total		19	18	12	11	60

Table 2: The relation of the common grade to gender.

Average age per grade			
MTA grade	Average age	N	Std. Deviation
1	71.11	19	8.286
2	77.17	18	6.214
3	80.17	12	9.114
4	76.09	11	7.993
Total	75.65	60	8.362

Table 3: The relation between MTA grade and average age in each grade.

The severity of AD is directly proportional with aging. If the patient is old, the severity of AD will be high as well see (Fig. 1). Older patients showed a small hippocampal height, large temporal horn width, and high MTA score.

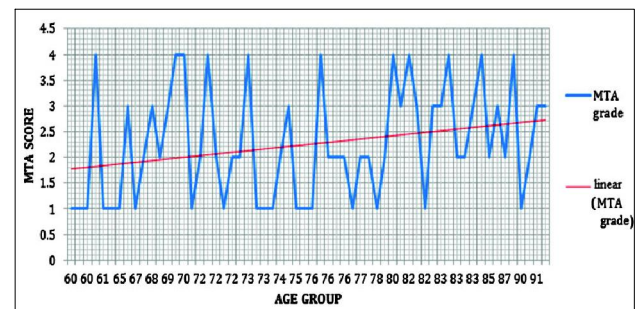


Figure 1: The relation between AD and age.

AD severity found to be related to gender. The hippocampal height and width are higher on left side more than right side. The average height of the right hippocampus is 10.29 mm, height of the left hippocampus is 10.58 mm, width of the right hippocampus is 12.03 mm, and width of the left hippocampus is 12.44 mm see (Tab. 11). The hippocampal width has higher significance more than the height see (Tab. 12). As well, the MTA score and severity of AD in females is higher than males see (Tab. 4 and 5). Both right and left, height and width of hippocampus, and radial temporal horn width are larger in males compare to females. The mean in both gender for rTHW are 8.33 mm in left rTHW, 7.34 mm in right rTHW, which mean

Report			
Gender	MTA Average Grade	N	Std. Deviation
Male	2.13	32	1.070
Female	2.39	28	1.133
Total	2.25	60	1.099

Table 4: MTA severity in relation to gender

the left temporal horn is larger than the right side see (Tab. 10).

Difference in AD with gender				
Gender		Rt. rTHW	Lt. rTHW	Diff
Male	Mean	7.6188	8.8094	-1.1906
	N	32	32	32
	Std. Deviation	1.81169	2.13487	1.95206
Female	Mean	7.0357	7.7929	-.7571
	N	28	28	28
	Std. Deviation	1.81602	2.28359	1.64529
Total	Mean	7.3467	8.3350	-.9883
	N	60	60	60
	Std. Deviation	1.82204	2.24559	1.81342

Table 5: The relation among AD, rTHW, and gender.

According to the age criteria of MTA grading system, there are 26 patients were in the normal or early stage of AD who follow the MTA rule see (Tab. 6). The normality or early stage of AD according to the previous criteria are 26 patients, while the abnormal are 34 patients. Normal grade for patients with age  $\geq 75$  years are 20 and abnormal are 9 patients. The normal grade for patients with age  $< 75$  years are 6 patients and abnormal are 14 patients. The total number of the normal are 37 patients of all ages from 60 to 96 years. The abnormal are 24 patients of all ages from 60 to 96 years see (Tab. 6).

Comparison of Age Group with MTA Grade							
			MTA Grade				Total
			1	2	3	4	
Age Group	$\geq 75$ Years	Count	13	7	4	5	29
		% within Age_N	44.8%	24.1%	13.8%	17.2%	100.0%
		% within MTA_Grade	68.4%	38.9%	33.3%	45.5%	48.3%
		% of Total	21.7%	11.7%	6.7%	8.3%	48.3%
	$< 75$ Years	Count	6	11	8	6	31
		% within Age_N	19.4%	35.5%	25.8%	19.4%	100.0%
		% within MTA_Grade	31.6%	61.1%	66.7%	54.5%	51.7%
		% of Total	10.0%	18.3%	13.3%	10.0%	51.7%
	Total	Count	19	18	12	11	60
		% within Age_N	31.7%	30.0%	20.0%	18.3%	100.0%
		% within MTA_Grade	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	31.7%	30.0%	20.0%	18.3%	100.0%

Table 6: Comparison of age with MTA.

MTA Normality Analysis				
	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	26	43.4%	43.4%	43.4%
Abnormal	34	56.6%	56.6%	100.0
Total	60	100.0	100.0	

Table 7: MTA age criteria and normality.

According to the age criteria of MTA grading system, there are 16 patients were in the normal or early stage of AD who follow the MTA rule see (Tab. 7). The normality or early stage of AD according to the previous criteria is 16 patients, while the extreme abnormal are 14 patients. Normal grade for patients with age  $\geq 75$  years are 21 and abnormal are 9 patients. The normal grade for patients with age  $< 75$  years are 16 and abnormal are 14 patients. The total number of the normal are 37 patients of all ages from 60 to 96 years. The abnormal are 23 patients of all ages from 60 to 96 years see (Tab. 7).

The radial temporal horn width has the mean 7.34 mm on the right side, while on the left side is 8.33 mm see (Tab. 8). The lower measurement of rTHW on the right side is 6.87 mm and the upper of rTHW on the right side is 7.81mm. The lower measurement of rTHW on the left side is 7.75 mm and the upper rTHW on the left side is 8.01 mm see (Tab. 9). The mean of right rTHW in patients with age  $\geq 75$  is 7.17 mm and the left rTHW in the same age group is 7.98 mm. The mean of right rTHW in patients with age  $< 75$  is 7.50 mm and the left rTHW in the same age group is 8.66 mm see (Tab. 10).

One-Sample Statistics				
	N	Mean	Std. Deviation	Std. Error Mean
Rt. rTHW	60	7.346667	1.8220371	.2352240
Lt. rTHW	60	8.335000	2.2455851	.2899038

Rt. rTHW = right radial temporal horn width, Lt. rTHW = left radial temporal horn width.

Table 8: rTHW mean and standard deviation.

One-Sample Test						
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Rt. rTHW	31.233	59	.000	7.3466667	6.875985	7.817349
Lt. rTHW	28.751	59	.000	8.3350000	7.754904	8.915096

Rt. rTHW = right radial temporal horn width, Lt. rTHW = left radial temporal horn width.

Table 9: The upper and lower measurements of rTHW.



Group Statistics					
	Age Group	N	Mean	Std. Deviation	Std. Error Mean
Rt. rTHW	>=75 Years	29	7.172414	1.7519166	.3253227
	< 75 Years	31	7.509677	1.8993604	.3411352
Lt. rTHW	>=75 Years	29	7.982759	2.2182794	.4119241
	< 75 Years	31	8.664516	2.2566270	.4053022

Rt. rTHW = right radial temporal horn width, Lt. rTHW = left radial temporal horn width.

**Table 10:** The age groups in relation to rTHW.

Gender	Lt. rTHW	MTA grade	H Rt. Hpo	W Rt. Hpo	H Lt. Hpo	W Lt. Hpo	Rt. rTHW	
Male	Mean	8.8094	2.13	10.6344	12.2344	10.5813	12.8250	7.6188
	N	32	32	32	32	32	32	32
	Std. Deviation	2.13487	1.070	1.73793	2.54249	1.93215	2.48868	1.81169
Female	Mean	7.7929	2.39	9.9000	11.8071	10.5964	12.0107	7.0357
	N	28	28	28	28	28	28	28
	Std. Deviation	2.28359	1.133	1.96601	2.37267	1.84942	2.51047	1.81602
Total	Mean	8.3350	2.25	10.2917	12.0350	10.5883	12.4450	7.3467
	N	60	60	60	60	60	60	60
	Std. Deviation	2.24559	1.099	1.86877	2.45335	1.87798	2.51122	1.82204

H Rt. Hipo = height of right hippocampus, W Rt. Hipo = width of right hippocampus, H Lt. Hipo = height of left hippocampus, W Lt. Hipo = width of left hippocampus, Rt. rTHW = right radial temporal horn width, and Lt. rTHW = left radial temporal horn width.

**Table 11:** The relation between AD and gender.

Coefficients <sup>a</sup>						
Model	Unstandardized Coefficients		Standardized Coefficients		t	Sig.
	B	Std. Error	Bela			
1	(Constant)	3.596	1.599		2.249	.029
	Age	.034	.016	.255	2.075	.043
	H Rt. Hpo	-.080	.085	-.136	-.937	.353
	W Rt. Hpo	-.128	.061	-.285	-2.088	.041
	H Lt. Hpo	-.064	.085	-.109	-.753	.455
	W Lt. Hpo	-.068	.062	-.156	-1.105	.274

a. Dependent Variable: MTA grade

H Rt. Hipo = height of right hippocampus, W Rt. Hipo = width of right hippocampus, H Lt. Hipo = height of left hippocampus, and W Lt. Hipo = width of left hippocampus.

**Table 12:** MTA relation with linear hippocampal measurements.

## Discussion

The most common grade is grade one in 19 patients opposite to the hypothesis because the average age of the sample is 70.58 years. The grade zero was

never found in any patient because all the patients are geriatrics above 60 years and normal aging alone is responsible to cause some atrophy in the brain generally. Male patients have a higher rTHW and linear hippocampal measurements than females, but it is not an accurate comparison between genders. The hippocampal dimensions and temporal horn width are related to the size of organ in gender more than the AD severity in gender. Usually in health individual, the organs in males are bigger and larger than females. The average MTA score for female patients is 2.39, while in male is 2.13. The MTA score and severity of AD in female is higher than male similar to the hypothesis and similar to the AD report of Saudi Ministry of Health.<sup>2</sup>

The severity of AD affects the left side more than the right side which can be related to the dominant hemisphere. The majority of the patients in the sample are males compare to the Saudi report which indicate that female patients are more affected by AD more than male opposite to the findings in this paper.<sup>2</sup> Left hippocampus is affected by AD more than the right side which is opposite to Tarroun's findings in France (Tarroun et al., 2007).<sup>6</sup> Tarroun et al took the measurements at the anterior and posterior part of the hippocampus, but not at the level of the corpus of the hippocampus which explains the low measurements in height among AD patients. In addition, the common grade among this sample is grade one which shows the mean of hippocampal height a 10.58 mm on the left and 10.29 mm on the right side. Tarroun's finding is a  $6.6 \pm 1.1$  mm on the of hippocampal height on the right and  $6.76 \pm 1.1$  mm on the left side (Tarroun et al., 2007).<sup>6</sup>

According to (Varon et al., 2015) who conducted a research on ANDI database AD patients found that visual rating system has 83% sensitivity and 56% specificity for patients who are  $\geq$  stage 3 compare to the volumetric measurements which has 83% sensitivity and 78% specificity.<sup>7</sup> (Varon et al., 2015) concluded that MTA is a good diagnostic tool, but according to Varon's findings, MTA cannot diagnosis or predict AD in of any patient in stage 0, 1, and 2 because of the low specificity.<sup>7</sup> What they found supports what was found in this research see (Tab. 6). The sensitivity is the ability to identify who is not normal, while the specificity is the ability to identify who is normal. The necessity to identify the normal person is more impor-

tant than identifying the abnormal person. MTA must change from visual grading system to a system that depend on measurable values and specific ranges for each grade. RR can be used as criteria for the new MTA scale.

## Conclusion

The suggestions and recommendations for any future studies, is to focus on transforming the MTA grading system to a system that depend on measurable values. Add the width of the hippocampus to the MTA grading system criteria. Provide a simple software's that can measure the hippocampal volume in a simple clinical sittings.

**Conflict of Interest:** None.

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