

# SHAPE AND VOLUME OF THE BRAIN CONSIDER AS THE KEY FEATURE FOR ALZHEIMER’S DISEASE

RASIKA BALASURIYA

†Purdue University Fort Wayne Fort Wayne

## ABSTRACT

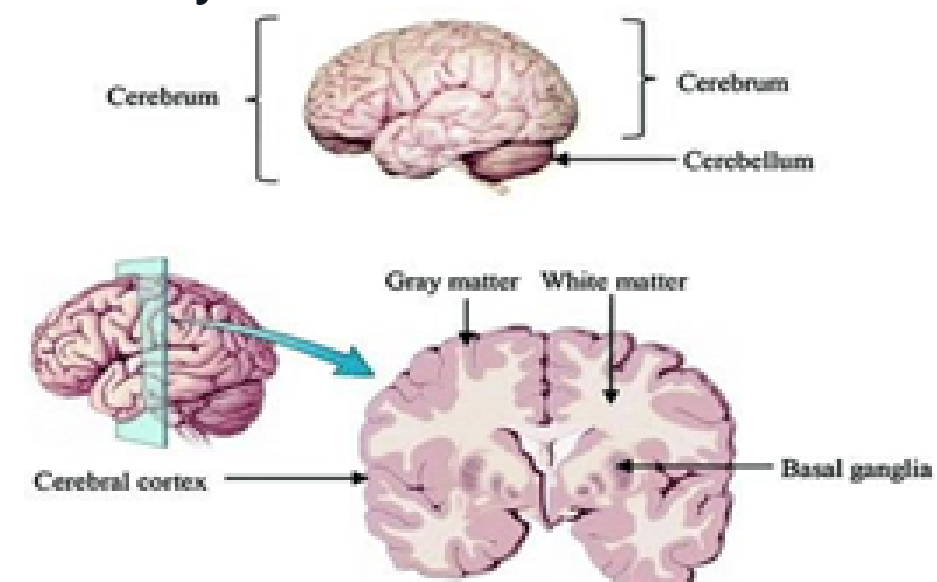
This study analyzes by multiple liner regression method the relationship between brain size and gender. I used 100 participants' MRI scans results using ADNI databases to determine the difference between brain size and gender. I find that, there might be the relationship between average thickness of cortex and gender, as well as size of the Pial Area and gender.

## INTRODUCTION

The brain is one of the complex organs in the body. The healthy brain functions quickly and automatically. However, when problems arise, it can have devastating impact on the individual's physical and mental functioning. According to National Institute of Neurological Disorders and Stroke, which conducts and supports scientific studies in the United States and around the world. According to NINDS, some of the major types of brain disorders include: neurogenetic diseases, developmental disorders, degenerative diseases of adult life, metabolic diseases, cerebrovascular diseases, trauma, convulsive disorders, infectious disease, and brain tumors. Among the brain disorder, Alzheimer's disease (AD) is a progressive, degenerative brain disease and is the most common form of dementia in adults aged 65 and older (Glozman et al., 2017). According to Alzheimer Disease International (ADI), someone in the world develops dementia every 3 seconds and there are over 55 million people worldwide living with dementia in 2020. Worldwide prevalence of AD is expected to rise to over 100 million by 2050 (Brookmeyer et al., 2007). Our world faces a looming global epidemic of Alzheimer's disease as the world's population ages. Therefore, over the years many studies conducted to understand the diseases and developing accurate prognostic indicators using the brain structure. The findings of the many studies reveal overall volume loss and shape changes in specific brain structures, such as the hippocampus, amygdala, corpus callosum, and other regions (Blinkouskaya and Weickenmeier, 2021; Giovann et al., 2008; Glozman et al., 2017; Raji et al., 2009;). The purpose of this study is to understand how shape of the brain can be used to distinguish between patients with AD and healthy individuals.

## METHODS

This study has used the data from the ADNI database. The primary goal of the dataset to collect serial MRI and positron emission tomography (PET) to measure the progression of Mild cognition impairment (MCI) and early AD. The primary goal of this study is to evaluate the effect of age group, gender, on Hemisphere, Gray matter (GM) volume, average thickness of cortex (AvgCortthickness), Pial Area and white area to determine the distinguish between patients with AD and healthy individuals.



In this section, among the 100 participants and were divided into 6 age groups (18-30, 31-40, 41-50, 51-60, 61-70, 71-80). In addition to age group, gender, GM volume, average thickness of cortex and Hemisphere might influence to AD. Since the dataset has multiple variables, this study used multiple liner regression model and concepts with other statical methods to analyze the dataset. All the participants are healthy individuals; therefore, this study is going to examine is there any relationship with gender (male and female) as a dependent variable (predictor) while other variables are explanatory variables.

## ANALYSIS AND RESULTS

Use Gender as a predictor variable in the regression model into a dummy variable. Since it is categorical variable that can take on two different values (male or female), this study uses only dummy variable for the gender ( $K-1 = 2-1 = 1$ ;  $K$  – number of categorical variables). The analysis was performed using statistical software MATLAB and Excel. Following syntaxes use to create categorical array with two elements that belong to the categories (male and female).

```
>> esSEX=ismember(Data.Sex,'m').
>> esSex=double(esSEX);
>> rsSEX=array2table(esSex,'VariableName',{'SexC'});
>> Data=[Data rsSEX]
```

Also, this study used the same syntax to convert into dummy variables for the hemisphere ( $K-1 = 2-1 = 1$ ) and age groups ( $K-1 = 6-1 = 5$ ). Table 1 illustrated the converted dataset with dummy variables.

SexC	AvgCortThickness	PialArea	WhiteArea	GreyMatterVol	GroupC	HemisphereC
0	0.45223	6169.1	5596.0	1440.2	1	0
0	0.45224	6123.9	5646.2	1227.8	1	0
0	2.79194	41089	32210	1.1616e+05	1	0
0	2.78471	40782	32074	1.2455e+05	1	0
0	2.45244	33422	27019	1.1027e+05	1	0
0	2.71597	33162	26819	1.0933e+05	1	0
0	2.78752	25119	18692	74279	1	0
0	2.7159	24591	18644	69219	1	0
0	2.4704	17045	12649	55141	1	0
0	2.8947	12640	1071	52040	1	0
0	2.6723	2441.4	2479.7	1761.4	1	0
0	3.1044	2425.7	2511.9	2125.2	1	1
1	0.5131	1.1007e+05	94010	1.1007e+05	6	0
1	1.2378	90273	75047	1.7470e+05	6	1

Table 1: the new dataset with categorical variables for gender(sex)-SexC and age groups-GroupC and HemisphereC (left or right)

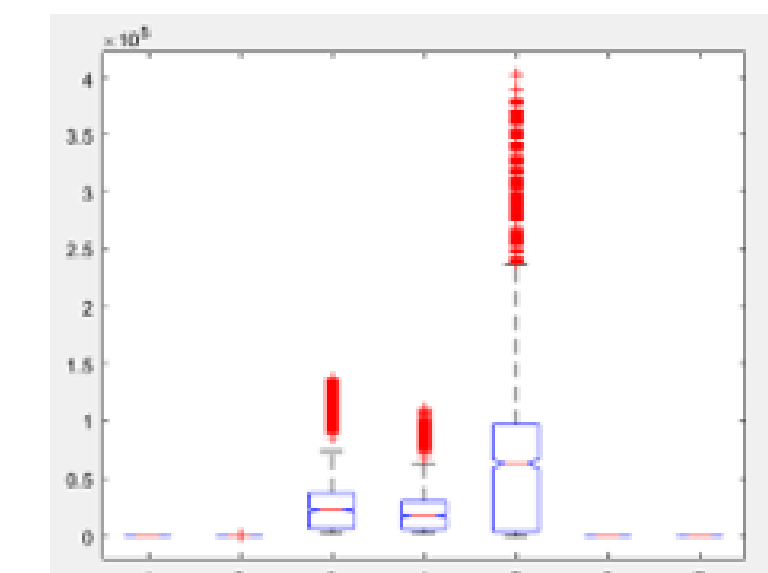


Figure 1: 1-SexC, 2-AvgCortThickness, 3-PialArea, 4- White Area, 5- GreymatterVol, 6-GroupC, 7 -HemisphereC

```
>> R = corrcocof(DatasetN)
```

R =	Sex	AVGCortThi	PialArea	WhiteArea	GreymatVol	AgeG	Hemishhere
	1.0000	-0.0230	0.0444	0.0469	0.0473	0.0477	0
	-0.0230	1.0000	0.2602	0.2498	0.3170	-0.1366	0.0156
	0.0444	0.2602	1.0000	0.9991	0.9904	-0.0385	-0.0020
	0.0469	0.2498	0.9991	1.0000	0.9847	-0.0262	-0.0013
	0.0473	0.3170	0.9904	0.9847	1.0000	-0.0852	-0.0070
	0.0477	-0.1366	-0.0385	-0.0262	-0.0852	1.0000	0
	0	0.0156	-0.0020	-0.0013	-0.0070	0	1.0000

Table 3: The coefficients table

According to the Table 3 above the correlation with each coefficient, we can see some type of relationships with the predictor variable(gender) and Pial Area , white Area, Greymatter Volume as well as the age of each individual. Therefore, we have to interpret the best linear relationship model with gender(Male/Female) with explanatory variables.

model = Gender

Linear regression model:  
 $y \sim 1 + x1 + x2 + x3 + x4 + x5 + x6$

Estimated Coefficients:

	Estimate	SE	tStat	pValue
(Intercept)	0.53858	0.054202	9.9365	1.5181e-22
x1	-0.074097	0.02127	-3.4837	0.00050943
x2	-0.00014282	2.1614e-05	-6.6078	5.4839e-11
x3	0.00013462	2.1137e-05	6.3688	2.5597e-10
x4	1.2981e-05	1.9706e-06	6.5872	6.2759e-11
x5	0.016826	0.0074702	2.2524	0.024448
x6	0	0	NaN	NaN

x1 - AVGCortThi x2-PialArea x3- WhiteArea x4- GreymatVol x5- AgeG x6-Hemishhere

Number of observations: 1440, Error degrees of freedom: 1434  
Root Mean Squared Error: 0.487  
R-squared: 0.0364, Adjusted R-Squared: 0.033  
F-statistic vs. constant model: 10.8, p-value = 3.07e-10

Figure 2: The Linear regression model gender as dependent variable and all other explanatory variable.

It obvious the all the P values are less than the  $\alpha=5\%$  (0.05) there are 4 explanatory variables which are significant variables for the gender (predictor variable).

## ANALYSIS AND RESULTS

According to the resulting P values of individual models (male/Female) , the relationship with those explanatory variables with females are more significant than the relationship with male.

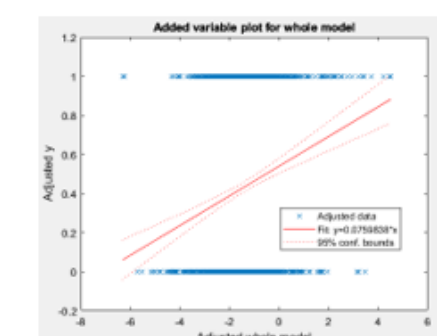


Figure 5: The plot for linear regression model for gender as dependent variable

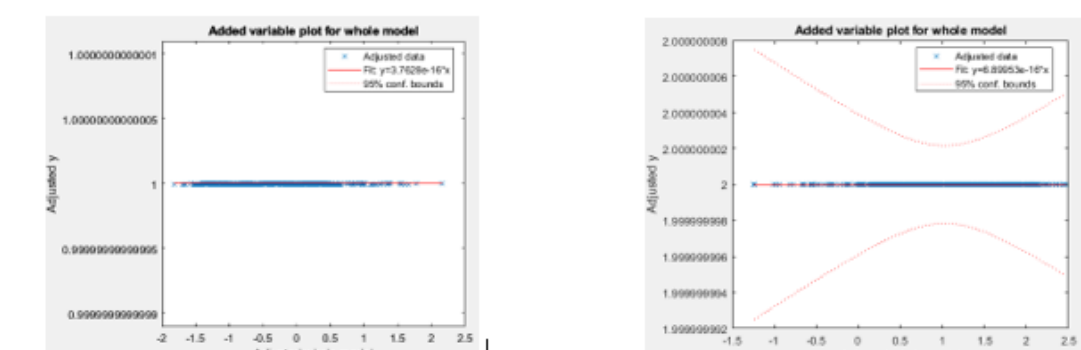


Figure 6: The plot for the regression model Female as dependent variable  
Figure 7: The plot for the regression model Male as dependent variable

## DISCUSSION

According to the study, there may be the relationship between average thickness of cortex and gender, as well as size of the Pial Area and gender. Females are higher risk of developing AD than males. Studies (Nebel et al., 2018 show that females are more likely to develop AD due to stress, cardiovascular disease, and mental health issues. There is a need for continued evaluation of differences in AD progression. Finally understanding the how certain area of the brain and gender differences impact on AD will help on proper treatment of AD, including differences requirements in care for male and female AD patients.

## References

- C A. Raji, O L. Lopez, L H. Kuller, O T. Carmichael, and J T. Becker. Age, Alzheimer disease, and brain structure. *Neurology*, 73(22): 1899–1905, 2009.
- Giovanni B Frisoni, Rossana Ganzola, Elisa Canu, Udo Rüb, Francesca B Pizzini, Franco Alessandrini, Giada Zoccatelli, Alberto Beltramello, Carlo Caltagirone, and Paul M Thompson. Mapping local hippocampal changes in Alzheimer's disease and normal ageing with MRI at 3 Tesla. *Brain*, 131(12): 3266–3276, 2008.
- Rebecca A Nebel, Neelum T Aggarwal, Lisa L Barnes, Aimee Gallagher, Jill M Goldstein, Kejal Kantarci, Monica P Mallampalli, Elizabeth C Mormino, Laura Scott, Wai Haung Yu, Pauline M Maki, and Michelle M Mielke . Understanding the impact of sex and gender in Alzheimer's disease: A call to action. *Alzheimers Dement*. 14(9): 1171–1183, 2018.
- Ron Brookmeyer, Elizabeth Johnson, Kathryn Ziegler-Graham, and H Michael Arrighi. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*, 3, 186-191, 2007.
- Tanya Glozman, Justin Solomonb, Franco Pestillic, and Leonidas Guibas. Shape-Attributes of Brain Structures as Biomarkers for Alzheimer's Disease. *Journal of Alzheimer's Disease*, 56: 287–295, 2017.
- The Alzheimer's Disease Neuroimaging Initiative (ADNI). OpenData for the Independent morphological variables correlate to aging, Mild Cognitive Impairment, and Alzheimer's Disease manuscript. URL <https://zenodo.org/record/5750619.Yxj8>.
- Yana Blinkouskaya and Johannes Weickenmeier. Brain Shape Changes Associated with Cerebral Atrophy in Healthy Aging and Alzheimer's Disease. *Frontiers in Mechanical Engineering*, 7: 705653, 2021.