BISTP6110 Final Project Manuscript: Ben Nguyen - btn2112

Observing Amyloid Beta Levels Relating to Sex and Genetic Risk Factors for Cognitive Impairment in Late Middle-Aged Adults

1 Statistical Analysis (word count: 222)

Amyloid beta (Aβ) positivity status was compared across various strata, including age, waist circumference, years of education, sex, APOE-ϵ4 carrier status, PHQ-9 depression assessment category, and International Physical Activity Questionnaire (IPAQ) category. Aβ positive status is defined as having an Aβ standardized uptake value ratio (SUVR) greater than 1.15, determined by the global mean Aβ SUVR. The global mean Aβ SUVR was calculated the finding the mean of the temporal lobe, parietal lobe, cingulate, and frontal lobe Aβ SUVR mean values.

A multiple logistic regression was also constructed using stepwise selection to determine what the most significant risk factors of Aβ positivity are among age, sex, APOE-ϵ4 carrier status, PHQ-9 category, and IPAQ category at a significance level of 0.15. After determining the most significant factors, they were placed into an adjusted model and compared against a crude model looking at the logistic relationship between only Aβ positivity status and APOE-ϵ4 carrier status. All other tests in this manuscript were conducted at a 0.05 level of significance. The Analysis of Maximum Likelihood Estimate of both models were also compared to each others. The analysis looked at every parameter in each model and their respective coefficient estimate, standard error, 95% odds ratio confidence interval, Wald Chi-Squared Test Statistic, and p-value.

All analyses were carried out using SAS with SAS OnDemand for Academics.

2 Results (word count: 406)

Out of the 265 subjects observed in this dataset, 231 of them were Aβ negative while 34 of them were Aβ positive. One female Aβ negative subject was removed from **Table 1** due to a missing IPAQ category value.

Within this study group, there was a mean age of 64.02 years in the Aβ negative group and a mean age of 63.90 years in the Aβ positive group. The Aβ negative group also has a larger waist circumference measurement than their Aβ positive counterparts at 96.15 cm compared to 95.32 cm. The Aβ positive group had a higher mean education received, however, at 11.12 years compared to their Aβ negative counterparts' 10.34 years. Beyond these categories, the two groups should similarities in the other sections of **Table 1**. Both the Aβ negative and Aβ positive groups were predominantly female (160 and 30 subjects, respectively), within the no symptoms PHQ-category (157 and 22 subjects, respectively), and the high IPAQ category (124 and 23 subjects, respectively).

We wanted to test which variables would be potential confounders between the relationship between APOE-ϵ4 carrier status and Aβ positivity status. To do this a crude logistic model was built with only the intercept and the APOE-ϵ4 carrier status when a subject carried the APOE-ϵ4 allele (-0.9580, 95% OR CI[0.184, 0.800], p=0.0107) (**Table 2**). This was compared to an adjusted logistic model with APOE-ϵ4 carrier status when a subject carried the allele (-0.8746, 95% OR CI[0.197, 0.883], p=0.0223), sex when female (-1.2039, 95% OR CI[0.101, 0.896], p=0.0310), and IPAQ category when high as parameters (-0.6680, 95% OR CI[0.235, 1.120], p=0.0937)(**Table 3**). Comparing the APOE-ϵ4 carrier status slopes between the crude and adjusted models, we observe an 8.71% change in slope between the two models. This means that sex and IPAQ are not potential confounders of APOE-ϵ4 carrier status and Aβ positivity status (**Tables 2 and 3**).

The distribution of Cortical thickness in Alzheimer's disease signature regions was also graphed by sex and APOE-ϵ4 carrier status (**Figures 1 and 2**). The distribution of cortical thickness between males and females both seemed to be normal distributed. The female subjects had a higher mean cortical thickness compared to their male counterparts (**Figure 1**). The distribution of cortical thickness among the two APOE-ϵ4 carrier status groups also to both be approximately normally distributed. Those without the APOE-ϵ4 allele had a slightly higher cortical thickness compared to those who have it.

3 Discussion (word count: 184)

With this analysis, we can sufficiently answer our research question "Are there differences in mean Aβ levels between APOE-ϵ4 carrier statuses or sexes?" In our analysis of maximum likelihood estimate of our adjusted model, we found the 95% odds ratio confidence interval of APOE-ϵ4 status comparing those who do have the allele and those who don't as a predictor of Aβ positivity to be (0.197, 0.883). The 95% odds ratio confidence interval comparing females to males for predicting Aβ positivity status is (0.101, 0.896). Neither of these intervals contain the null value of 1 meaning they are both significant predictors of Aβ positivity status. Therefore, we can also conclude that there are differences in mean Aβ levels among both APOE-ϵ4 carrier statuses and sexes.

One possible limitation with our research and methodology is that we excluded certain variables from our model which may also explain our research question. Some of these variables include histories of stroke, type 2 diabetes, and cancer. Futher research is required to see how these and other variables can affect Aβ status within APOE-ϵ4 carrier statuses and sexes.

4 Tables and Figures

Table 1: Summary Statistics of the Distribution of Aβ Positivity Status Over Various Strata

Variable	**Aβ[1] Negative (n=231)**	**Aβ Positive (n=34)**
Mean age (years)	64.02	63.90
Waist circumference (cm)	96.15	95.32
Mean education obtained (years)	10.34	11.12
Sex		
Male (n=75)	71 (30.74%)	4 (11.76%)
Female (n=190)	160 (69.26%)	30 (88.24%)
APOE-ϵ4[2] carrier status		
No (n=190)	172 (74.46%)	18 (52.94%)
Yes (n=75)	59 (25.54%)	16 (47.06%)
PHQ-9[3] category		
No symptoms (n=177)	157 (67.97%)	22 (64.71%)
Minimal symptoms (n=49)	44 (19.05%)	5 (14.71%)
Mild symptoms (n=27)	21 (9.09%)	6 (17.65%)
Moderate symptoms (n=6)	6 (2.60%)	0 (0%)
Severe symptoms (n=4)	3 (1.30%)	1 (2.94%)
IPAQ[4] category		
Low (n=53)	47 (20.35%)	6 (17.65%)
Moderate (n=65)	60 (25.97%)	5 (14.71%)
High (n=147)	124 (53.68%)	23 (67.65%)

[1]Amyloid beta
[2]Allele that is a significant risk factor for cognitive impairment
[3]Patient Health Questionnaire-9: a depressive symptom scale and diagnostic tool
[4]International Physical Activity Questionnaire

Table 2: Analysis of Maximum Likelihood Estimate of Crude Model

Parameter	**Estimate**	**SE[5]**	**OR 95% CI[6]**	**Wald[7] χ^2**	**p-value**
Intercept	-2.2629	0.2477	-	83.4879	< 0.0001
APOE-ϵ4 carrier status (yes)	-0.9580	0.3752	(0.184, 0.800)	6.5187	0.0107

[5]Standard error
[6]Odds ration 95% confidence interval
[7]Wald Chi-Squared test statistic

Table 3: Analysis of Maximum Likelihood Estimate of Adjusted Model

Parameter	**Estimate**	**SE**	**OR 95% CI**	**Wald χ^2**	**p-value**
Intercept	3.5974	0.6103	-	34.7439	< 0.0001
APOE-ϵ4 carrier status (yes)	-0.8746	0.3826	(0.197, 0.883)	5.2239	0.0223
Sex (female)	-1.2039	0.5580	(0.101, 0.896)	4.6549	0.0310
IPAQ category (high)	-0.6680	0.3986	(0.235, 1.120)	2.8088	0.0937

Figure 1: Distribution of Cortical Thickness Between Sexes

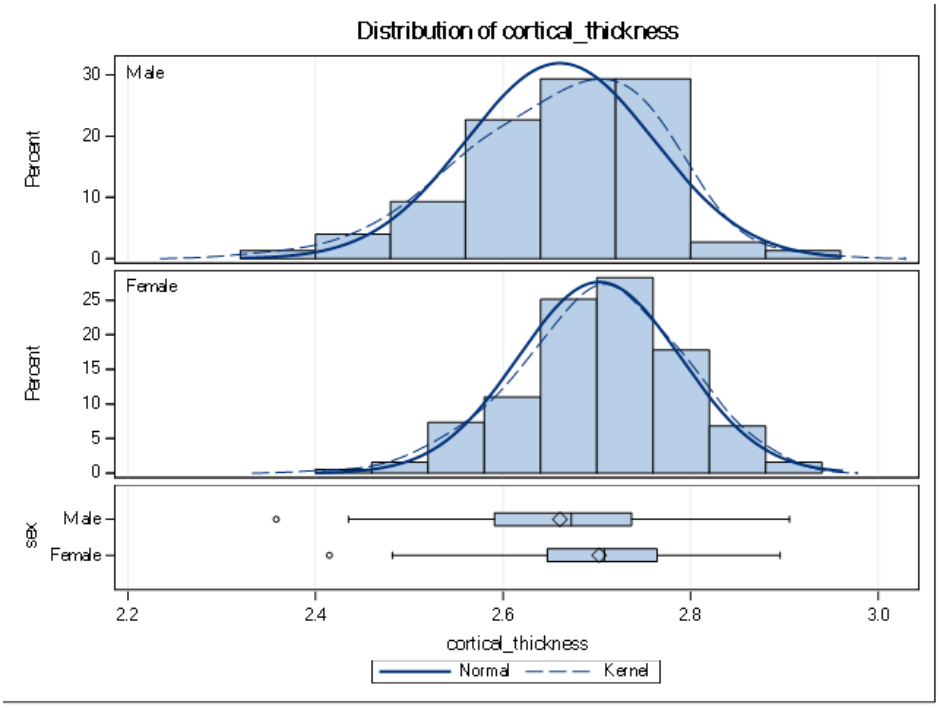

Figure 2: Distribution of Cortical Thickness Between APOE-ϵ4 Carrier Status