Association of variant Apolipoprotein E (ApoE) alleles to decline in cognitive function with aging demonstrated through network modeling

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Abstract

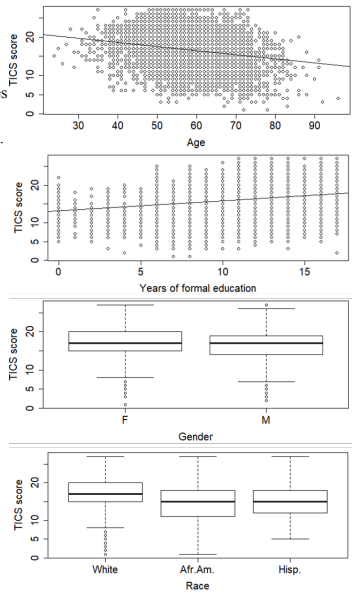
The gene ApoE has been shown to have an influence on age-related cognitive decline. The three variant alleles (e2, e3, and e4) have been associated with different outcomes. Previous research shows that in ApoE4 individuals, age is negatively correlated to cognitive function. ApoE3 has a neutral effect on cognitive function. Suggestive data has shown ApoE2 to have a protective property on one's cognition; cognition tends to be more consistent as one ages.

Using data from the Health and Retirement Study (HRS), biostatistical analysis was performed to find a potential link between ApoE, demographic variables, and cognitive function. Understanding how ApoE correlates with the demographic variables through network modeling and eliminating confounding variables will assist in more accurate predictive analysis of one's risk for Alzheimer's disease.

Introduction

Self-reported data tends to be noisy, causing false bias within a dataset. Eliminating confounding factors in predictive models is essential to an accurate model. Our goal was to eliminate confounding factors by using path-analysis to fit a series of linear and logistic regression models to break down correlation between covariates into separate parts. Data used is provided by the HRS; the HRS is a longitudinal study with the goal of better understanding the aging of the U.S. population. The HRS obtained a cognitive score of each participant via Telephone Interview for Cognitive Status (TICS). A reduced data set that included only baseline TICS scores was used in this study.

From the dataset some initial relationships between the variables used in the progression of models were conveyed using simple plots.



Relationships displayed

- Negative correlation between Age and TICS scores
- Positive correlation between years of formal education and TICS scores
- Median of females' and males' TICS scores generally the same
- African-Americans' and Hispanics' median scores are significantly lower than whites'

Methods

Statistical analysis.

- Path-analysis used. A series of regression models were fitted to break correlation between multiple covariates into smaller parts.
- Regression analysis using stepwise regression in Rstudio.

Network modeling.

- Network created using Bayesware Discoverer to display relationship between each variable and the TICS score

Results

The models:

Stepwise regression based on Bayesian information criterion (BIC) values was applied to obtain an accurate model. This process was repeated with each covariate as the response until the last model consisted of race as the response and ApoE as the only predictor.

Model 1: smallTICS= 22.03838 -0.09527Age -0.84889sex +2.27513ED -2.58928Afr.Am. -2.39990Hisp.

Predictor	P-Value
Age	2.00E-16
Education	2.00E-16
sex	2.00E-16
Afr. Am.	2.00E-16
Hisp.	2.00E-16

Model 2 Age= 58.3292 +2.5197sex -2.1826ED -0.8781Afr.Am. -2.7249Hisp.

Predictor	P-Value
Education	2.00E-16
sex	2.00E-16
Afr. Am.	0.00014
Hisp.	3.94E-15

Model:3 ED= -0.1733 +0.2098sex -0.5283Afr.Am. -0.2875Hisp.

Predictor	P-Value	Odds Ratio	95% CI
Sex	1.05E-07	1.233	(1.142, 1.333)
Afr. Am.	2.00E-16	0.524	(0.524, 0.663)
Hisp.	0.00179	0.75	(0.627, 0.896)

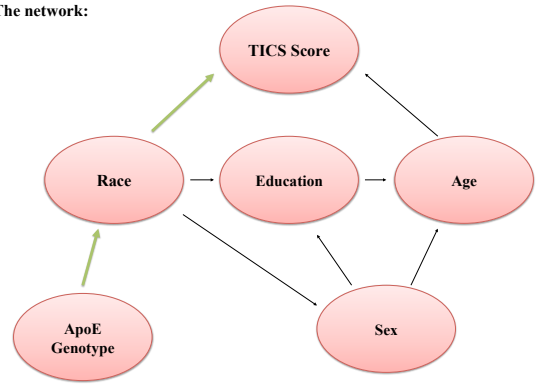
Model 4: sex= -0.2510 -0.2853Afr.Am. -0.1482Hisp.

Predictor	P-Value	Odds Ratio	95% CI
Afr. Am.	0.00000154	0.751	(0.688, 0.844)
Hisp.	0.105	0.862	(0.720, 1.031)

Model 5: RACE= -1.6422 +0.7668e2/e2 +0.1477e2/e3+0.8681e2/e4 +0.2843e3/e4 +0.6576e4/e4

Predictor	P-Value	Odds Ratio	95% CI
e2e2	0.00427	2.153	(1.245, 3.587)
e2e3	0.05969	1.159	0.922, 1.350)
e2e4	2.33E-10	2.382	(1.814, 3.105)
e3e4	0.00000307	1.392	(1.179, 1.497)
e4e4	0.0000106	1.93	(1.431, 2.572)

The network:



Frequencies of ApoE in different races:

	e3e3	e2e2	e2e3	e2e4	e3e4	e4e4
Whites	0.61014	0.00549	0.12496	0.0206	0.2189	0.01991
Afr. Am.	0.47693	0.01278	0.14336	0.05039	0.27466	0.04187
Hisp.	0.68182	0.00379	0.08144	0.02273	0.19886	0.01136

	e3e3	e2e2	e2e3
Whites	0.82386	0.00742	0.16873
Afr. Am.	0.75336	0.02018	0.22646
Hisp.	0.88889	0.00494	0.10617

	e3e3	e3e4	e4e4
Whites	0.7187	0.25785	0.02345
Afr. Am.	0.60107	0.34615	0.052773
Hisp.	0.76433	0.22293	0.01274

Conclusion

ApoE and Race

- Consistent relationship
- ApoE2 and ApoE4 higher in African Americans

Fixing variables within a network allowed interactions to be studied

This project has aided in the understanding of the distribution of ApoE and its relationship in different races. Manipulation of the network in the software has provided better insight to covariate interactions and the ultimate effect they have on TICS scores. This project also demonstrated the possibility of fixing variables to eliminate noise and bias within a data set.

References and Acknowledgments

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Associations:

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