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A linear mixed model analysis of the APOE4 gene with the logical memory test total score in Alzheimer's disease

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OUTLINE

- Introduction
- Significance of the study
- Objectives
- Study Design
- Methodology
- Analysis
- Data Modeling
- Results
- Conclusion
- The Way Forward
- References

INTRODUCTION

What is Alzheimer's Disease (AD)?

Alzheimer's disease is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills, and eventually, the ability to carry out the simplest tasks (National Institute of Aging, 2016).

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SIGNIFICANCE

What's in the news about the disease?

Biogen Inc. has halted trials on Alzheimer's disease because of failed improvement.

https://www.statnews.com/2019/03/21/biogen-eisai-alzheimer-trial-stopped/

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OBJECTIVES

- To determine if Logical Memory Examination Test Scores can also be used to measure Alzheimer's disease(AD).

- To measure the longitudinal effect of apolipoprotein E epsilon 4 (APOE4) genotype on the logical memory test total score in AD.

- To select the best model for measuring longitudinal changes in logical memory test score in linear mixed model analysis while controlling for the effects of sex and age.

STUDY DESIGN

- Longitudinal study.

- Data on study participants was obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI).

METHODOLOGY

The study consisted of 2167 cognitive normal (CN) patients, 4472 mild cognitive impairment (MCI) and 844 Alzheimer's Disease patients.

METHODOLOGY cont.

- 3309 females and 4174 males were monitored and their performance was recorded.
- Episodic memory of the study participants was monitored based on a short story told to the participants.
- The participants were asked to recall what was told.

ANALYSIS

- Statistical analysis was done using SAS and graphical representations was done using Tableau.
- The 7483 participants were monitored from baseline to 8 years down the line.
- The mean age of the participants before the study was 74.0 years.
- The mean age of the participants at the end of the study was 73.7 years.
- 98.5% of the participants with AD were APOE4 carriers. The corresponding rates of APOE4 carriers in MCI and CN groups were 97.34% and 98.3% respectively.

DATA MODELING

Table 1: Descriptive statistics

Variable	CN		MCI		AD/DEMENTIA	
	Before	After	Before	After	Before	After
Sample size(n)	2167	2449	4472	3118	844	1647
Sex(%Female)	1069(49.33)	1265(56.25)	1867(41.75)	1235(39.61)	373(44.19)	707(42.93)
APOE4 carriers (%)	2130(98.3)	2332(95.22)	43.53(97.34)	3088(99.03)	831(98.46)	1636(99.33)
Mean Age ± SD	74.75(5.6)	73.79 (6.02)	72.3(6.82)	72.98(7.49)	75.05 (7.67)	74.31(7.37)
Education ± SD	16.33(2.69)	16.43(2.64)	16.26 (2.66)	15.97(2.8)	15.16(2.98)	15.47(2.9)
LDELTOTAL ± SD	13.58(4.38)	13.88(3.91)	9.13(4.23)	7.44(4.89)	1.06(2.01)	1.47(2.73)

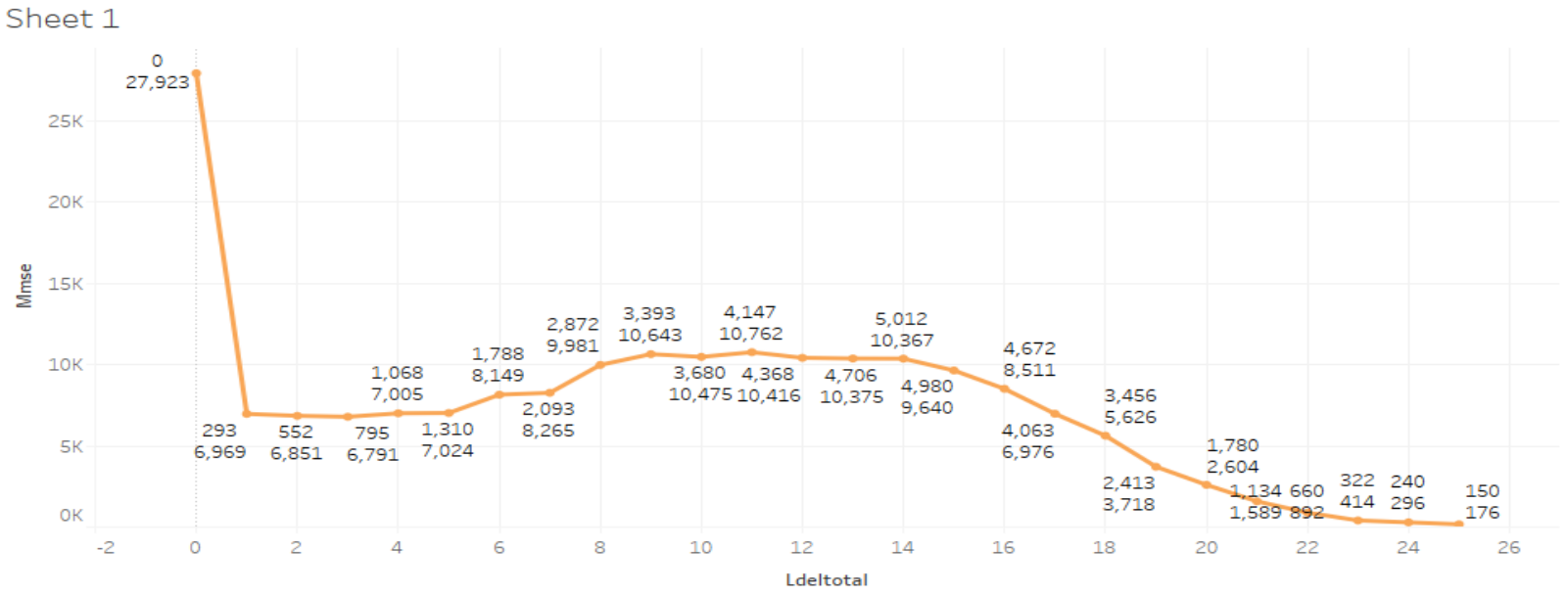
DATA MODELING cont.

Table 2: Model selection

STRUCTURE	AIC	BIC	Chi-Square	P-value
Unstructured (UN)	37067.3	37438.1	7458.57	<.0001
Compound Symmetry (CS)	37771.3	37858.5	6650.57	<.0001
Autoregressive AR (1)	37659.5	37670.4	6755.98	<.0001
Heterogeneous ARH (1)	37596.9	37651.4	6834.58	<.0001
Heterogeneous CS	37565.3	37619.8	6866.2	<.0001
Variance Component	44413.5	44418.9	0	1

RESULTS

Fig. 1: Comparison between Minimal Mental State Examination Scores and Logical Memory Test Scores



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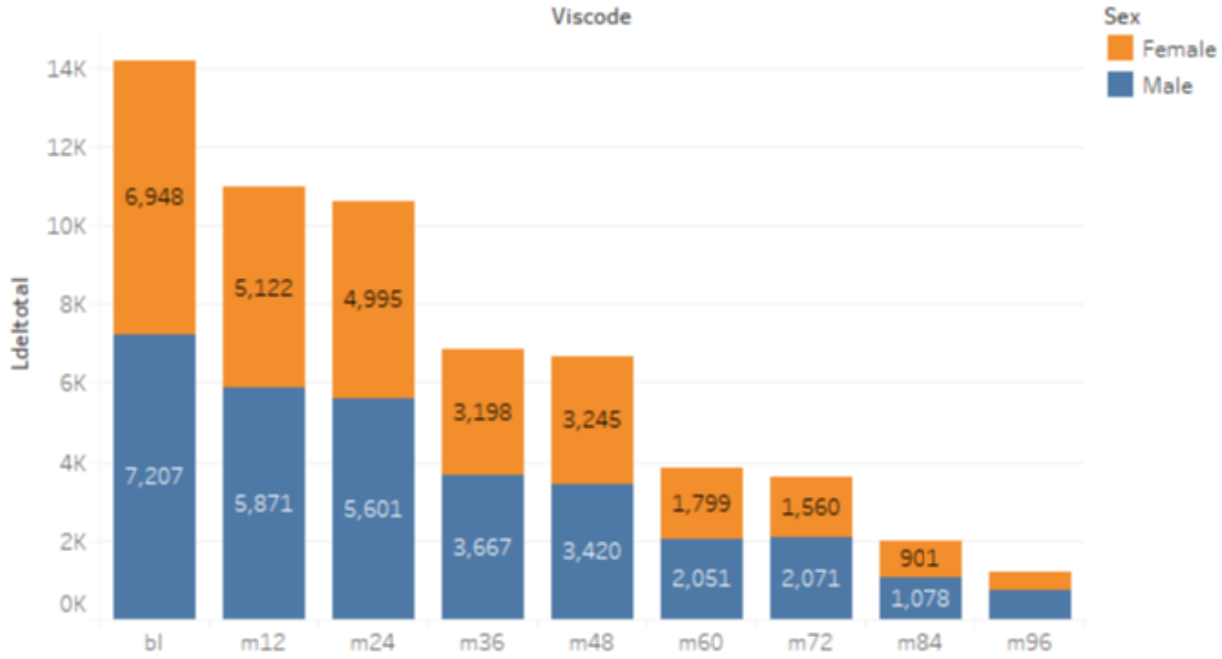
RESULTS cont.

Fig. 2: Gender difference in Logical Memory Test Scores monitored for 9 years



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RESULTS cont.

- Table 2: APOE4 was significantly associated with logical memory test scores (p-value <0.0001) using linear mixed model analysis.

- The missing observations was 490.

- Fig. 1: A positive relationship was observed from the plot of Logical Memory Test scores against Minimal Mental State Scores.

- Fig. 2: Males obtained higher scores compared to females across all time points from the plot of time (viscode) against the logical memory scores.

CONCLUSION

- The small p-value(p-value<0.0001) informs us that the logical memory examination scores is associated with APOE4 with the occurrence of Dementia.

- The positive relationship (fig. 1) indicates that logical memory examination scores have the ability just like the known MMSE score to detect whether a patient is at risk of getting Dementia.

- The lower logical memory scores obtained for women at all time points (fig. 2) is an indication that females are more likely to be affected by Alzheimer's Disease compared to males.

THE WAY FORWARD

Further research may be required to determine whether logical memory test score is better than minimal mental state examination scores in predicting the transition from Alzheimer's Disease to Dementia.

REFERENCES

- Albert, M. S., Moss, M. B., Tanzi, R., & Jones, K. (2001). Preclinical prediction of AD using neuropsychological tests. *Journal of the International Neuropsychological Society,7*(5), 631-639. doi:10.1017/s1355617701755105
- Baek, M. J., Kim, H. J., Ryu, H. J., Lee, S. H., Han, S. H., Na, H. R., . . . Kim, S. (2011). The usefulness of the story recall test in patients with mild cognitive impairment and Alzheimers disease. *Aging, Neuropsychology, and Cognition,18*(2), 214-229. doi:10.1080/13825585.2010.530221
- Ballard, C., Gauthier, S., Corbett, A., Brayne, C., Garland, D., & Jones, E. (2011). Alzheimer's disease. *The Lancet, 377*(9770), 1019-1031. doi:10.1016/s0140-6736(10)61349-9
- Battista, P., Salvatore, C., & Castiglioni, I. (2017). Optimizing neuropsychological assessments for cognitive, behavioral, and functional impairment classification: A machine learning study. *Behavioral Neurology, 2017*, 1-19. doi:10.1155/2017/1850909
- Biswas, A. (2008). *Statistical advances in the biomedical sciences clinical trials, epidemiology, survival analysis, and bioinformatics*. Hoboken, NJ: Wiley.A.E Van der viles et al., Most rapid cognitive decline in ApoE ε4 negative Alzheimer's disease with early onset.
- Corder, E., Saunders, A., Strittmatter, W., Schmechel, D., Gaskell, P., Small, G., Pericak-Vance, M. (1993). Gene dose of apolipoprotein E type 4 allele and the risk of alzheimer's disease in late onset families. *Science, 261*(5123), 921-923. doi:10.1126/science.8346443
- Gatz, M., Reynolds, C. A., Fratiglioni, L., Johansson, B., Mortimer, J. A., Berg, S., Pedersen, N. L. (2006). Role of genes and environments for explaining alzheimer disease. *Archives of General Psychiatry,63*(2), 168. doi:10.1001/archpsyc.63.2.168
- Lange, K. L., Bondi, M. W., Salmon, D. P., Galasko, D., Delis, D. C., Thomas, R. G., & Thal, L. J. (2002). Decline in verbal memory during preclinical alzheimer's disease: Examination of the effect of APOE genotype. *Journal of the International Neuropsychological Society, 8*(07). doi:10.1017/s1355617702870096
- Nutterupham, K., Saykin, A., Rabin, L., Roth, R., Wishart, H., Pare, N., & Flashman, L. (2008). Verbal fluency performance in amnestic MCI and older adults with cognitive complaints. *Archives of Clinical Neuropsychology,23*(3), 229-241. doi:10.1016/j.acn.2008.01.005
- Small, J. A., Kemper, S., & Lyons, K. (2000). Sentence repetition and processing resources in alzheimer's disease. *Brain and Language, 75*(2), 232-258. doi:10.1006/brln.2000.2355

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THANK YOU

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