Biomarker Research Applications in Alzheimer's Disease

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BACKGROUND

- Alzheimer's Disease is a form of dementia characterized by loss of memory, cognitive dysfunction, and changes in brain physiology.
- Literature suggests that age, the presence of the APOE e4 gene and an MCI diagnosis are the three strongest risk factors for the development of Alzheimer's Disease.
- **Research Problem:** Little research has been done regarding an accessible diagnosis, and therapy or drug target for Alzheimer's Disease. Furthermore, the longitudinal progression of AD has not been fully modeled.
- **Research Question:** How can changes in memory, visuospatial ability, the amyloid β 42/40 ratio, and the total hippocampal volume be used to accurately predict the onset and progression of Alzheimer's disease?
- **Hypothesis:** Based on previous research, we hypothesize that memory, visuospatial ability, and the total hippocampal volume will decrease, and the amyloid β 42/40 ratio will change significantly.

METHODS

- Data from the Alzheimer's Disease Neuroimaging Initiative (ADNI database) were analyzed.
- Divided participants into four categories based on genetic risk (e4 carrier or e2/e3 alleles only) and stable diagnosis (cognitively normal or MCI): nl_e23 (normal noncarrier), nl_e4, mci_e23, and mci_e4.
- Three primary data types were analyzed:
  1. Cognitive function (memory and visuospatial tests)
  2. Plasma Aβ42/40
  3. Hippocampal volume (through MRI)
- JASP, Python, and R were used to complete statistical testing (a repeated measures ANOVA) and data visualization.
- Sex, age, and level of education were used as covariates.
- **Participants: 174**
- **Average Age: 77.99**

RESULTS

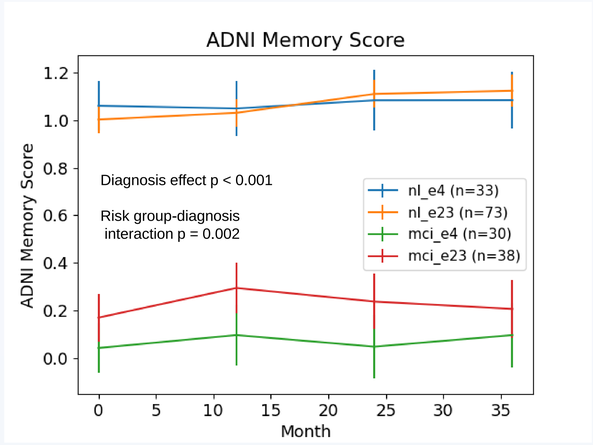

Figure 1. After controlling for age, sex, and education, the difference between individuals with MCI (n=68), scored lower compared to normal individuals (n=103), p < 0.001. The interaction between diagnosis and risk group was also significant (p = 0.002); as the MCI e4 carriers did worse than MCI non-carriers, although no genetic component was observed for normal individuals.

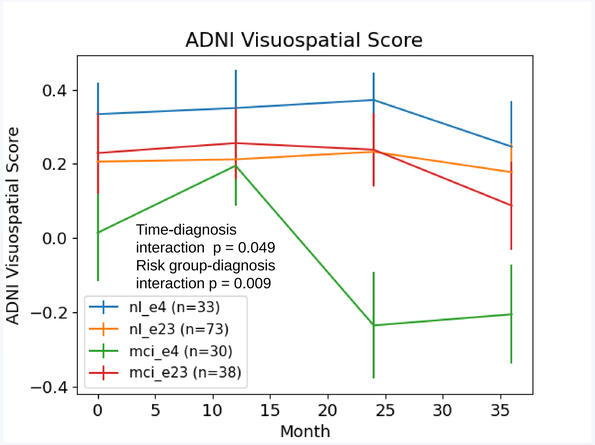

Figure 2. After controlling for age, sex, and education, cognitively normal individuals (n=106) score higher than individuals diagnosed with MCI (n=68), p= 0.049. The interaction between diagnosis and risk group was also significant (p=0.009). Individuals with an MCI diagnosis carrying the e4 gene (n=30) experience a drop in visuospatial ability in month 24, much earlier than other groups.

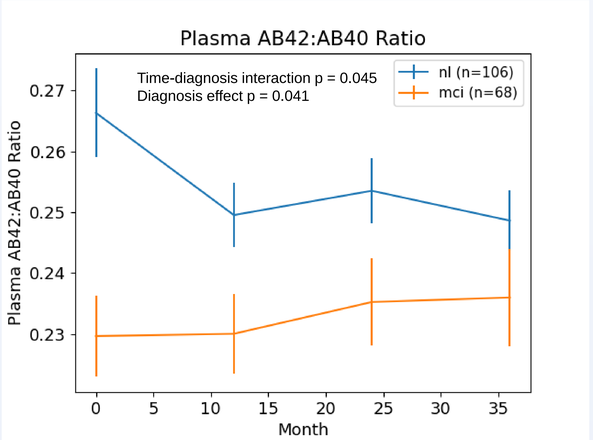

Figure 3. After controlling for age, sex, and education, cognitively normal individuals (n=106) have a higher amyloid β 42/40 ratio than individuals diagnosed with MCI (n=68), p = 0.041. However, this difference diminishes over time (p=0.045).

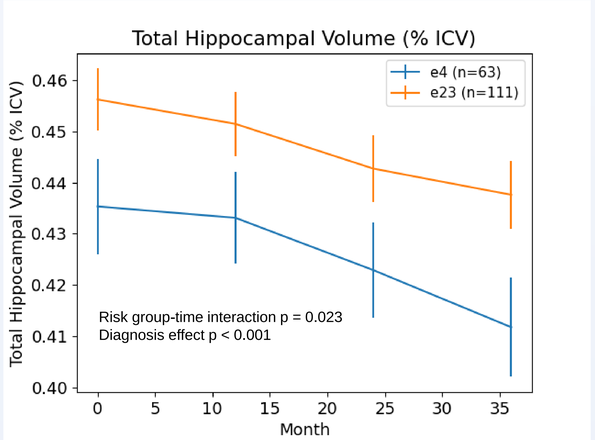

Figure 4. After controlling for age, sex, and education, the total hippocampal volume of e4 carriers (n=63) is greater than that for noncarriers (n=111), p < 0.001. The effect is also significant over time (p = 0.023), with greater hippocampal volume loss in e4 carriers, most prominent at the 36-month timepoint.

LIMITATIONS

- Our data lacks sufficient information regarding underrepresented racial and ethnic groups, as well as non-English speakers
- ADNI's data from prior studies were heavily focused on the Caucasian population in the United States, making it difficult to observe a wider range of data regarding other races and ethnicities

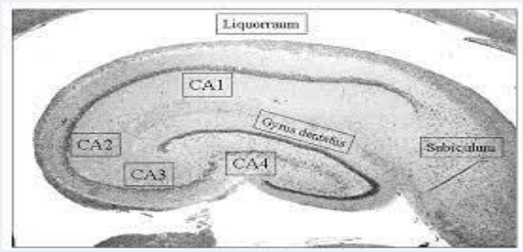

Figure 5. Hippocampus Structure

CONCLUSION

- The impact of the e4 allele on memory and visuospatial ability over time may be strong in people who show early cognitive decline, independent of age, sex and education.
- Hippocampal volume loss is greater in people who carry the e4 allele independent of covariates.
- It is unclear if plasma biomarkers reflect brain pathology.

FUTURE GOALS

- In order to produce more inclusive results, data should be collected from a diverse, nation-wide range of racial and ethnic groups with varying backgrounds in terms of economic status, gender, and educational background.
- Future directions include gathering data from surrounding communities in order to yield a larger scope of data and produce equally comprehensive results that can be applied and benefit more individuals and doing outreach to discuss results with the local community.
- Further directions include applying machine learning to provide a prediction and progression model for AD and expansion of the variable set to include more biomarkers.

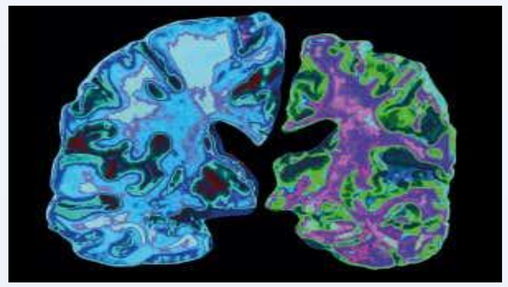

Figure 6. Normal brain (left) and Alzheimer's affected brain (right) with evident neuronal damage

REFERENCES