Age at Onset and Pre-Morbid IQ Influence Early Progression Rates in AD

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Background

- We have reported that patients with Alzheimer Disease (AD) followed in the Baylor Alzheimer Disease and Memory Disorders Center (ADMDC) progress at variable rates after their initial visit.[1]
- The future progression rate can be predicted from a simple calculation of their progression rate prior to their initial ADMDC visit (the "pre-progression rate")[2, 3]

$$\frac{30 - \text{MMSE Score at Initial visit}}{\text{Physician's Estimate of Symptom Duration}}$$

- We wished to identify predictors of this calculated pre-progression rate.

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Methods

- Patients of the ADMDC were enrolled after consenting to longitudinal follow up
- Standardized baseline assessment includes
  - a standardized physician's assessment of symptom duration (inter-rater reliability rho=.95, p<.001)
  - laboratory testing (including APOE genotype)
  - Neuroimaging
  - neuropsychological testing including the MMSE and the American Adult reading Test (AMNART)
  - Clinical history, including a quantitative assessment of previous anti-dementia drug exposure, expressed as months on treatment divided by total months since symptom onset
- Variables hypothesized to predict the pre-progression rate: age at onset, pre-morbid IQ (the AMNART score), sex, race (white vs. non-white), prior anti-dementia drug exposure, and presence of one or two APOE ε 4 alleles. (Note we did not include education, since this variable is included in the calculation of the AMNART score).
- Linear regression analysis was used to assess the relationship between the pre-progression rate, expressed as a continuous variable, and the hypothesized predictors.

Results

- Only age at onset of symptoms and the AMNART score (pre-morbid IQ) were independent predictors of the pre-progression rate.
- For every 5 point increment in AMNART score, the pre-progression rate declined by .35 points per year
- For every 5-year increase in age, the pre-progression rate increased by .17 points per year.
- Together, these two variables accounted for 7% of the variance in the pre-progression rate.

Table 1. Patient Characteristics (n=641)

Variable	Mean (±Stand. Dev.) or (Percent)
Age at Onset (Clinician Estimate)	69.2 ± 8.6
Sex (% female)	68.2%
Education (years)	13.6 ± 3.6
Race (white, non-white)	87.3%
Calculated Pre-progression Index (points/year)	3.69 ± 3.12
Calculated Pre-progression Index (categorical)	
• Fast	23.7%
• Intermediate	39.5%
• Slow	36.8%
AMNART	107.6 ± 10.3
APOE ε4 Alleles	
• 0	63.5%
• 1 or 2	36.5%
Exposure to Anti Dementia Medication Before First ADMDC Visit (yes/no)	42.6%
Anti Dementia Drug Exposure (months) / Symptom Duration (months)	.12 ± .22

Results (cont.)

Table 2. Multiple Linear Regression Results for Predictors of Pre-progression Rate

Variable	Regression Coefficient (Beta)	Standard Error	p-value
AMNART (5-point increments)	.344	.064	<.001
Age at Symptoms Onset (5-point increments)	.162	.077	.036
Sex (reference=female)	.421	.276	.128
Race (reference=non-white)	.045	.448	.314
APOE ε4 Positive (reference=Yes)	.073	.269	.784
Anti-Dementia Drug Exposure Index	.096	.569	.866

Conclusions

- Higher pre-morbid IQ appears to slow the rate of AD progression from the time symptoms first become apparent. This study extends the findings we reported previously regarding the important role of the AMNART score in predicting rate of decline in AD patients[4].
- Having at least one APOE ε4 allele does not seem to influence the rate of decline after symptoms are observed in this cohort. Only one patient had two APOE ε4 alleles, so we were not able to examine the effect of one versus two alleles.

References

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