



Domain-general and -specific Cognitive Changes Among Individuals At Genetic Risk For Alzheimers Disease Using Computational Models



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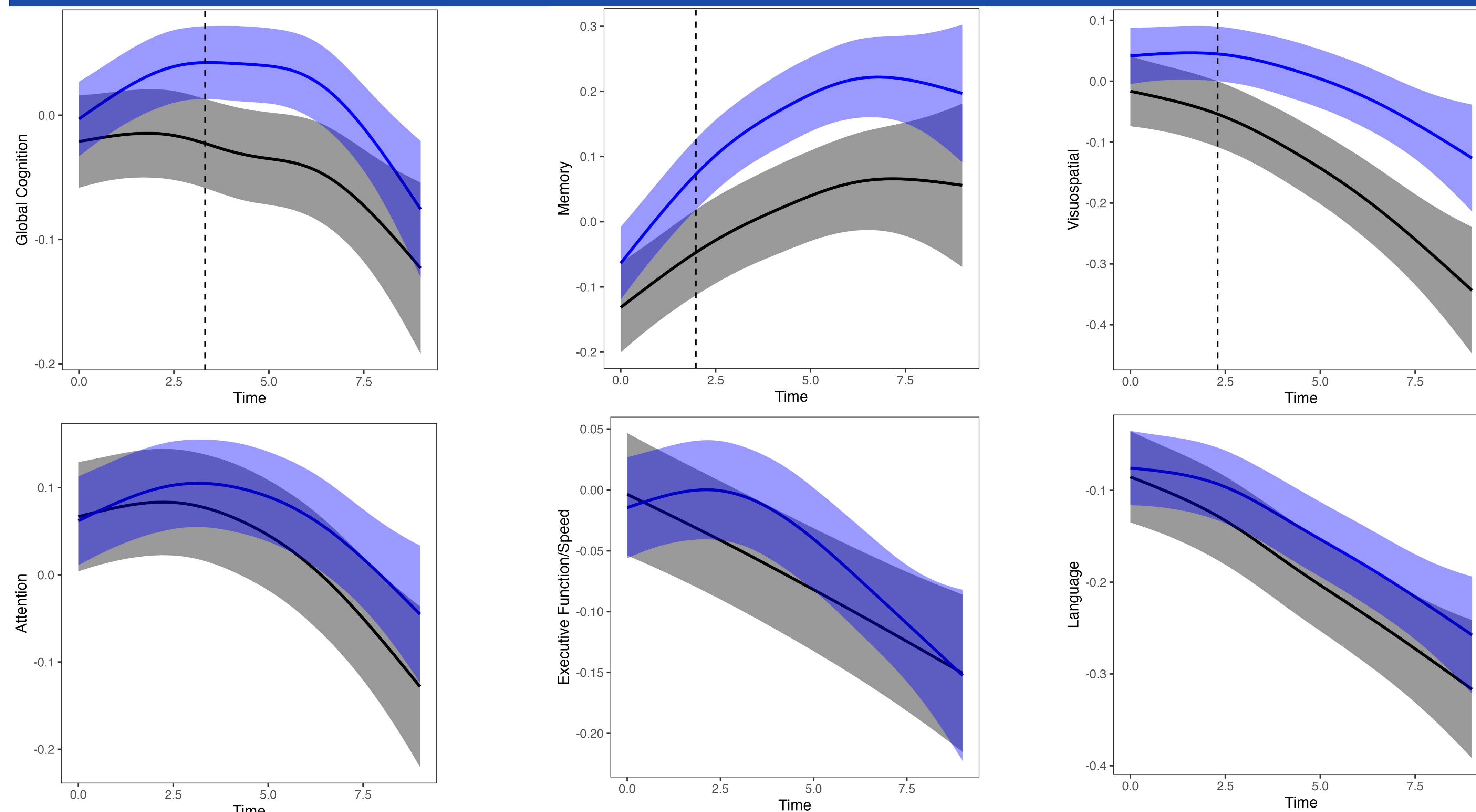
Introduction

- Cognitive decline is a hallmark of aging and Alzheimer's disease (AD).
- Identifying when changes in cognition begin (both globally and within specific domains) with high precision is critical for primary and secondary prevention trials in AD.
- Despite being one of the strongest predictive factors for developing AD, *APOE* $\epsilon 4$ effects on cognition are mixed and generally small.
- Approaches to measuring cognitive change often assume a linear change, which may not be accurate.
- More innovative models that make different assumptions about longitudinal data can better pinpoint when cognitive change begins.

Methods and Materials

- Cognitively normal participants (N = 3902) from the National Alzheimer's Coordinating Center.
- Baseline Age = 68 years old (SD = 9.96)
- *APOE* $\epsilon 4$ carriers (N = 1247) or *APOE* $\epsilon 4$ noncarriers (N = 2655) completed yearly cognitive assessments (Mean = 5).
- Cognitive Composites (Kisela et al. 2020)
 - Memory
 - Language
 - Visuospatial Ability
 - Attention
 - Executive Function/Speed
 - Global Cognition

Results



$\epsilon 4$ Noncarriers $\epsilon 4$ Carriers; Dashed line = point of divergence

Analytic Approach

- Generalized Additive Mixed Models (GAMMs) were used to analyze longitudinal data given their flexibility in modeling how (nonlinear) trends change over time.
- Divergence in cognitive trajectories of the groups was assessed to determine earliest group differences.

Conclusions

- Individuals at genetic risk for developing AD have unique cognitive trajectories from those not at risk for developing AD.
- Key differences in Global cognition appear after ~ 4 years; Memory occur even sooner, just after ~ 2 years.
- **Flexible computational approaches can provide unique insights into staging cognitive changes during preclinical AD.**