

Proteomic Markers Of Heterogeneous Cognitive Decline In Alzheimer’s Disease Investigated Using Digital Twins

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Proteomic-based Gemini digital twins enable improved prediction of Alzheimer's disease progression and cognitive decline beyond clinical covariates, while identifying biological pathways related to synaptic dysfunction, neuroinflammation, oxidative stress, and impaired cellular homeostasis that may contribute to disease progression.

INTRODUCTION

METHODS

RESULTS

CONCLUSIONS

Rates of cognitive decline in Alzheimer’s disease (AD) vary across individuals and predicting progression and linking it to underlying biology remain challenging. **Aitia’s Gemini digital twin (GDT)** modeling framework was applied to large-scale proteomic data from **Global Neurodegeneration Proteomics Consortium (GNPC)** to investigate biologically informative predictors of cognitive progression rates.

Gemini Digital Twins Pipeline

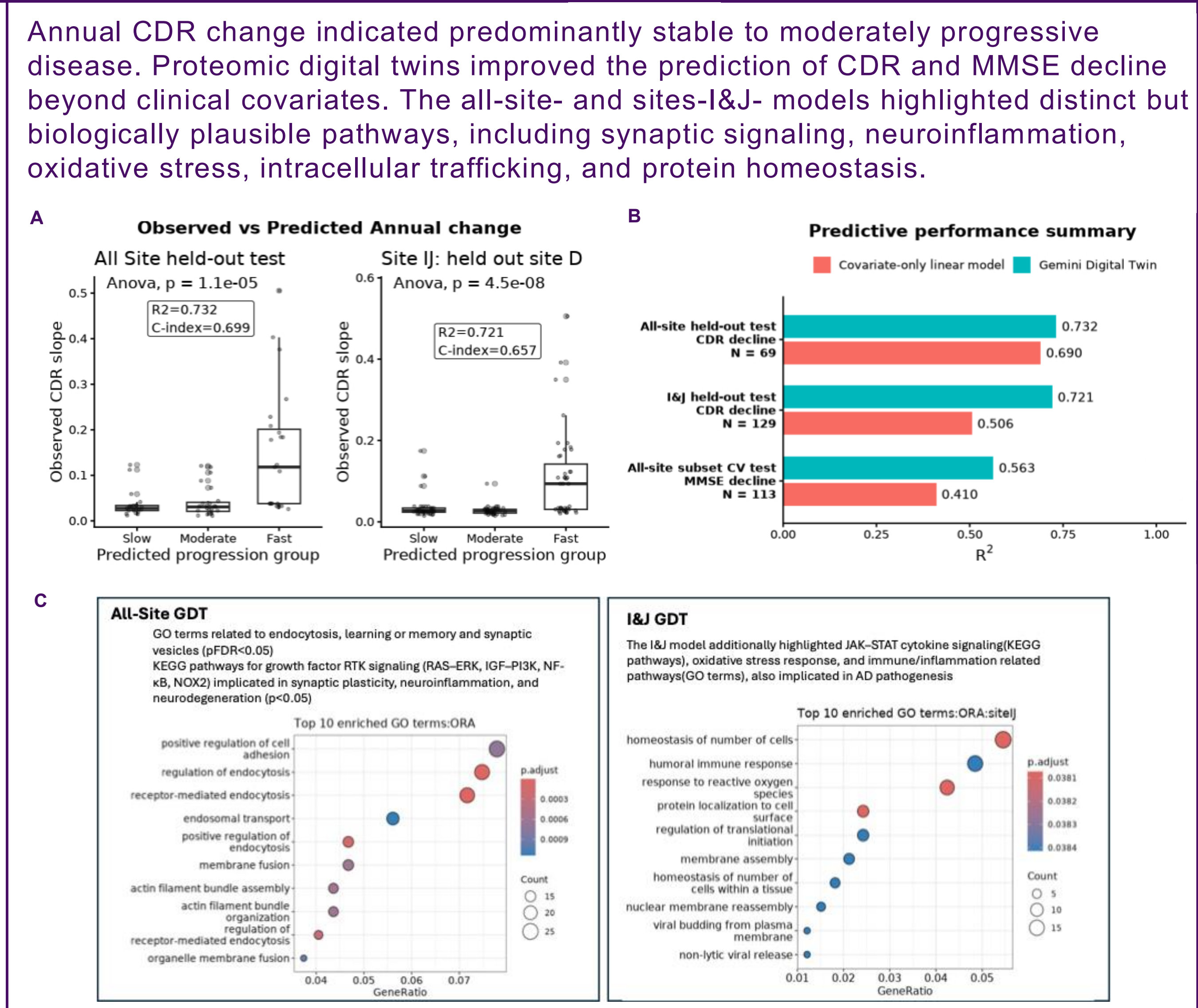
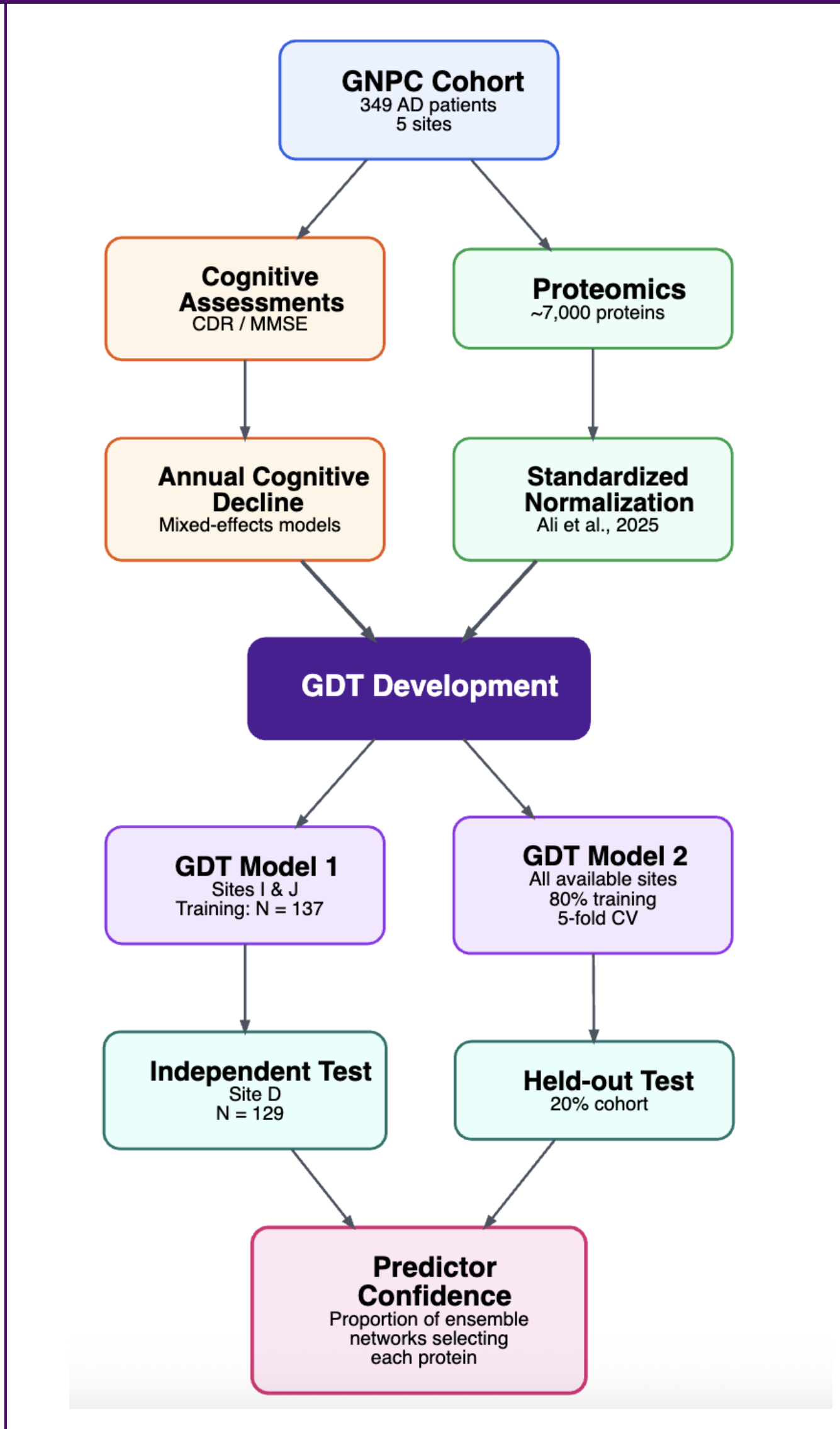
1 Multi-modal Data
Proteomics
Genomics
Imaging
Clinical
...

2 Gemini Digital Twin
Ensemble of Bayesian Network Models
Molecular
Clinical
Genetic
...

3 In silico Counterfactual Experiments
Input
Do(input = value)
Intervention (Do-operation)
Outcome
Simulated given Do(input = value)

4 Predicted Patient Outcomes
Cognitive Decline
Time
Predicted Outcome (Distribution)

5 Strong Drivers, Biomarkers, Subpopulations & Pathways
Causal Confidence
Patient Subpopulations
Biological Pathways & Biomarkers



Aitia’s GDT framework enables modeling of cognitive decline using GNPC proteomic profiles with **improvements in prediction** beyond clinical covariates, while offering biologically informative signals related to disease progression, particularly in synaptic and inflammatory pathways. Future work will focus on refining these models by explicitly accounting for site-specific variation within the **causal network framework**, while preserving biologically relevant disease progression signals.

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