Differences in Longitudinal Changes in Brain-Age Gap Between Individuals with Normal Cognition, Mild Cognitive Impairment, and Alzheimer's Disease

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INTRODUCTION

- Early identification of potential neurocognitive decline is crucial for the timely management to counter the adverse effects on independent living of older people.
- ***Brain-Age Gap (BAG)***, an index generated by a computational algorithm based on neuroimaging data, is useful for reflecting the discrepancy between an individual's chronological age and predicted brain age.
- The larger the BAG, the higher the chance of age-inappropriate neurocognitive decline (Karim et al., 2022).

OBJECTIVE

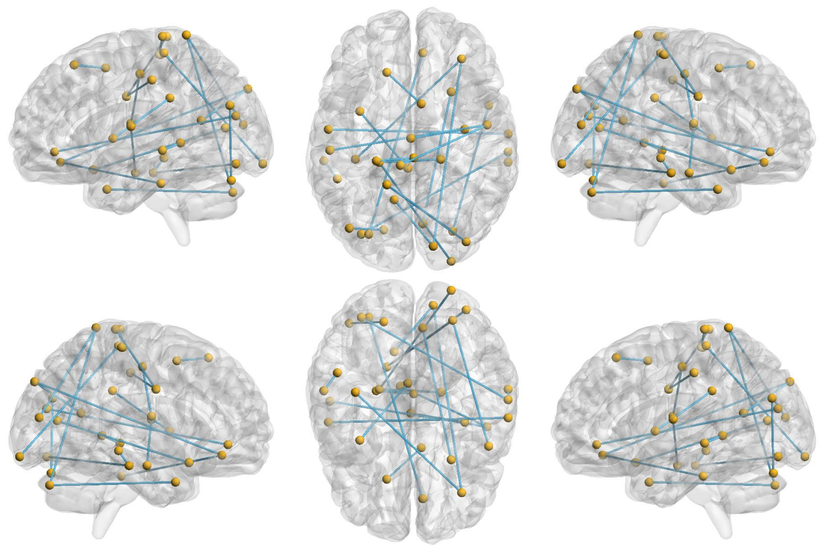
- **To investigate the difference in cross-sectional and longitudinal Brain-Age Gap across the spectrum of healthy to pathological cognitive aging.**

METHODS

Participants were recruited and assessed longitudinally at 63 sites in the US and Canada under the cohort of **Alzheimer's Disease Neuroimaging Initiative** (ADNI, https://adni.loni.usc.edu). We screened out participants with at least **three** rounds of MRI scanning with time intervals **longer than 90 days** between each of the two time points.

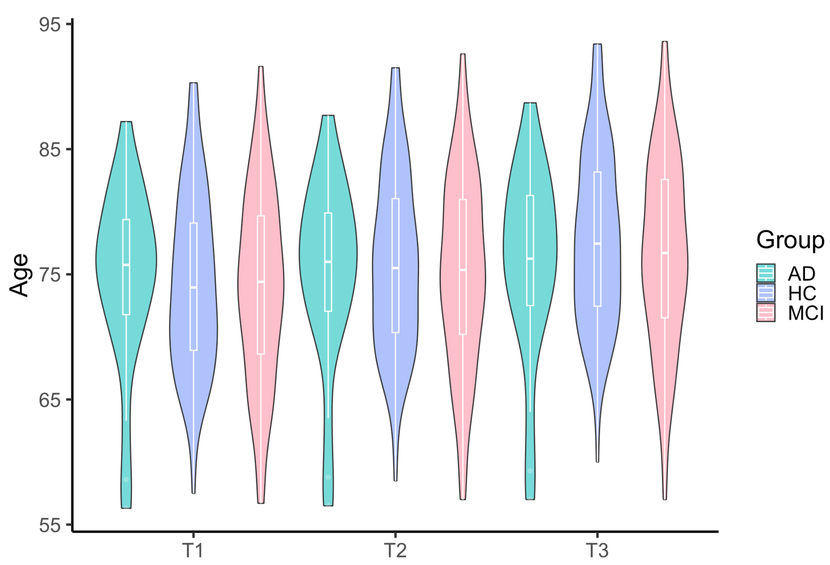
Extracting Resting-State Functional Connectivity Matrix ⇨ Support Vector Regression Modeling Training ⇨ Calculate Brain-Age Gap and Its Longitudinal Changes ⇨ Statistical Analysis

- The resting-state functional connectivity matrix at three time points was extracted based on the power-264 functional brain atlas (Power et al., 2013) and served as features for machine-learning model training.
- Additionally, the functional connectivity matrix from healthy controls from a single-time-point MRI data (N = 201, Mean Age = 71.31, SD = 8.20) was extracted for model training.
- Brain-Age Prediction Model was trained and optimized using Support Vector Regression (SVR) .
- We applied the best-performance Brain-Age Prediction Model to gain the predicted brain age and the Brain-Age Gap for cognitively healthy individuals (N = 104), people with Mild Cognitive Impairment (N = 138), and Alzheimer's Disease (N = 26).
- Longitudinal changes in quantified as the standard deviation of the BAG across three times.



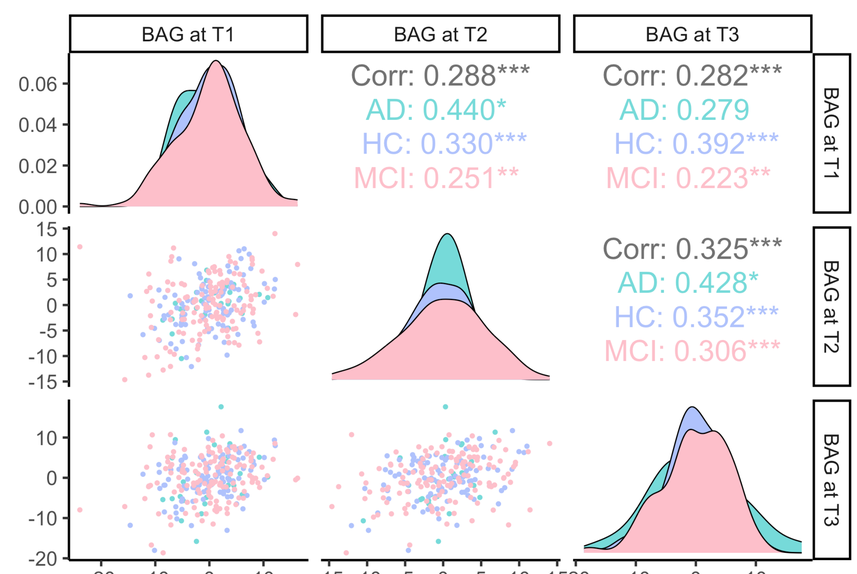
21 pairs of functional connectivity based on Power264 template were selected as features for SVR model

RESULTS



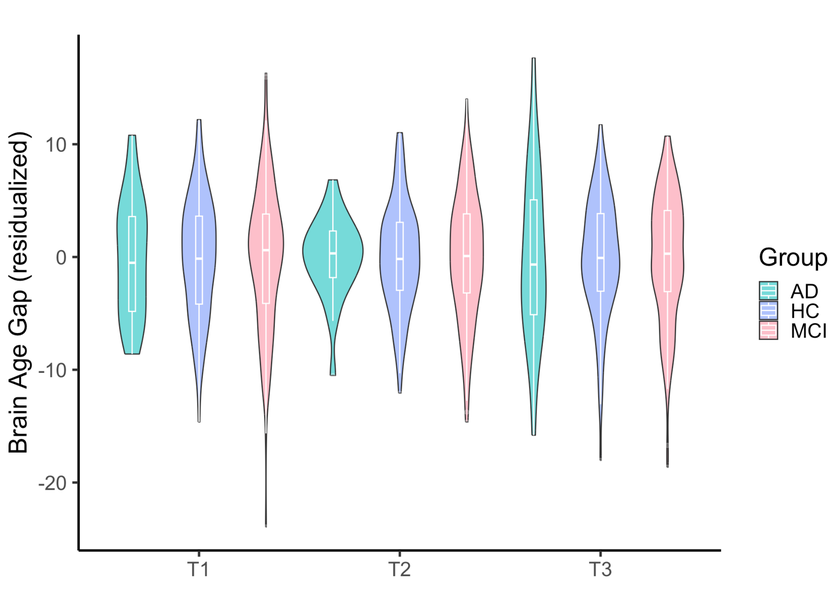
No difference in *Age* among three groups at three times.

F (2, 265) = 0.144, *p* = 0.866 at T1, *F* (2, 265) = 0.233, *p* = 0.792 at T2, *F* (2, 265) = 0.798, *p* = 0.451 at T3.

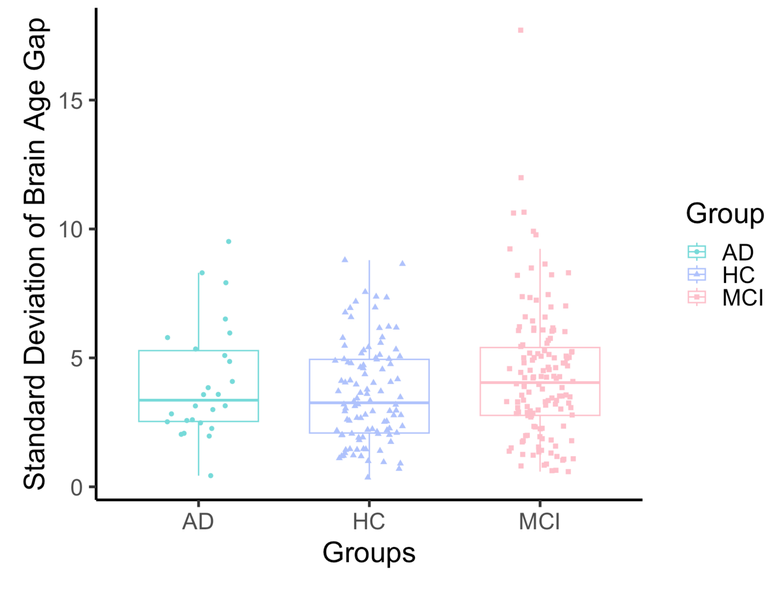


Brain-Age Gap at three time points are highly correlated.

*Note: * p < 0.05, ** p < 0.01, *** p < 0.001*



No difference in *Brain-Age Gap* among three groups at three times. *F* (2,265) < 0.001, *p* = 1 for T1-3



The standard deviation is significantly higher in MCI (M =4.33) compared to HC (M = 3.61), *p* = 0.045. But there is no difference between AD (M = 4.05) and HC (*p* = 0.65) or MCI and AD (*p* =0.84).

CONCLUSION

- Longitudinal changes in Brain-Age Gap would be a more sensitive biomarker compare to cross-sectional values.
- Future investigation into the underlying biological correlates contributing to the observed longitudinal changes is worthwhile.
- It also provides a quantifiable supplementary index that facilitates the monitoring of neurocognitive decline to facilitate timely and personalized interventions.

ACKNOWLEDGEMENTS

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