

Benchmarking Trajectories Of Digital Speech Measures Against Brain Atrophy Pattern: A Longitudinal Study In At-risk Alzheimer's Disease

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Background

Digital speech-based assessment is emerging as a scalable tool for clinical trial screening and referral strategies in early Alzheimer's disease (AD)¹. Our previous studies established its biological grounding through cross-sectional associations with regional brain volumes and functional connectivity^{2,3}. However, its practical utility in capturing longitudinal atrophy trajectories for monitoring and disease progression prognosis remains limited.

AIMS: We investigated whether changes in speech-derived measures over 15 months reflect regional brain atrophy patterns across years in an at-risk population for AD.

Method

- 198 participants (HC, SCD, MCI) with 1,099 automated telephone-based assessments (semantic verbal fluency and verbal learning tasks) over 15 months.
- Speech-based cognitive scores and task-level latent factors were derived; individual speech slopes were estimated via latent growth curve models.
- Speech slopes were associated with regional gray matter atrophy from 624 MRI scans over several years using linear mixed-effects models.
- Non-inferiority of speech slopes was tested against multi-year cognitive scores in association with atrophy patterns.

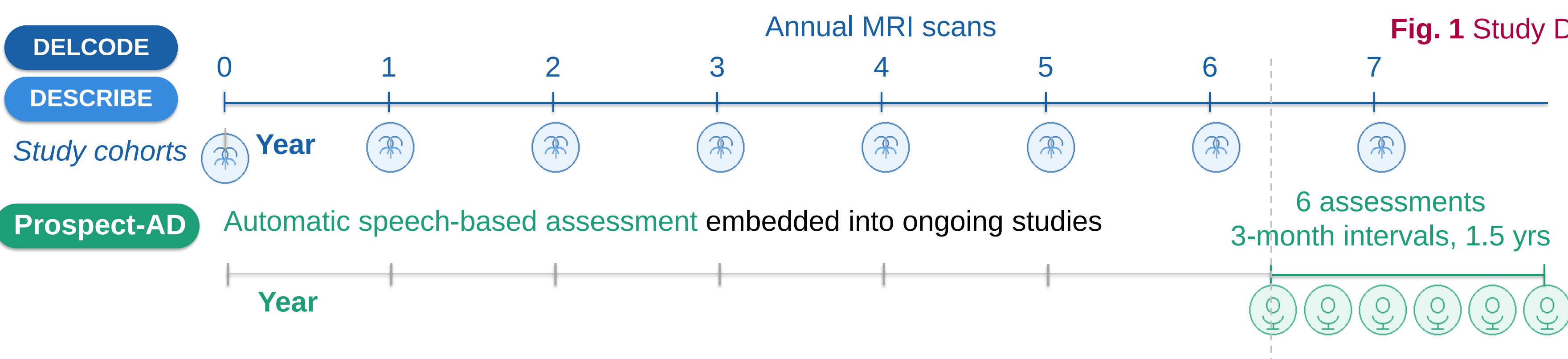
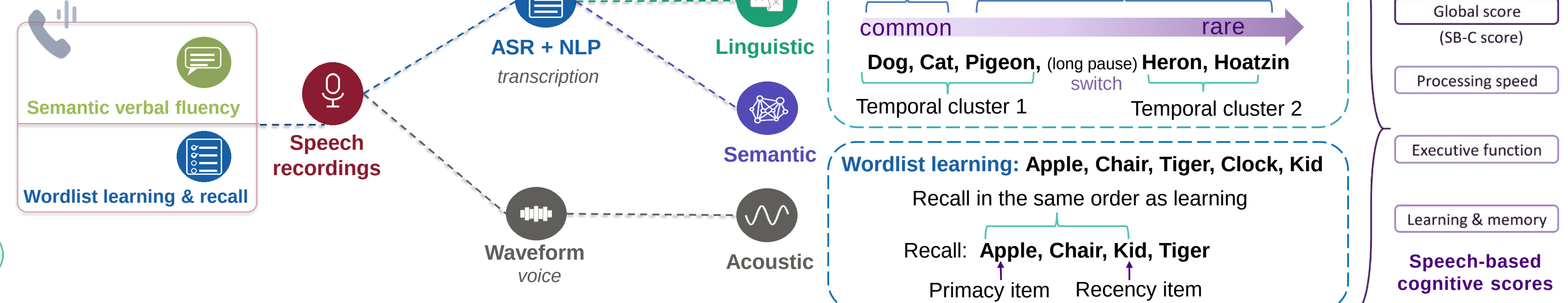


Fig. 1 Study Design



Results

- Speech change rates showed significant associations with atrophy exclusively in AD-signature, with SBC Processing Speed and Memory showing the broadest coupling.
- 15-month remote speech slopes were non-inferior to multi-year traditional cognitive scores in 70% of comparisons (56/80 pairs).

Tab. 1 Datasets

a. Speech dataset				
	Mean (SD)	Overall N=198	HC N=27	SCD N=107
Number of speech tests		5.6 (1.1)	5.6 (0.8)	5.7 (0.9)
				MCI N=64
				5.3 (1.3)
b. MRI-speech dataset				
	Mean (SD)	Overall N=108	HC N=20	SCD N=58
Number of MRI scans		5.8 (2.5)	7.7 (1.1)	5.8 (2.5)
				MCI N=30
				4.5 (2.4)

Conclusion: Automated speech-based monitoring holds promise as a scalable, neurobiologically grounded tool for tracking AD-related atrophy patterns in at-risk populations.

Next Steps: Replication in larger, more diverse populations is needed to evaluate generalizability and advance implementation for clinical trial screening and disease monitoring.

Fig. 2 Associations between remote speech change rates and regional brain atrophy trajectories

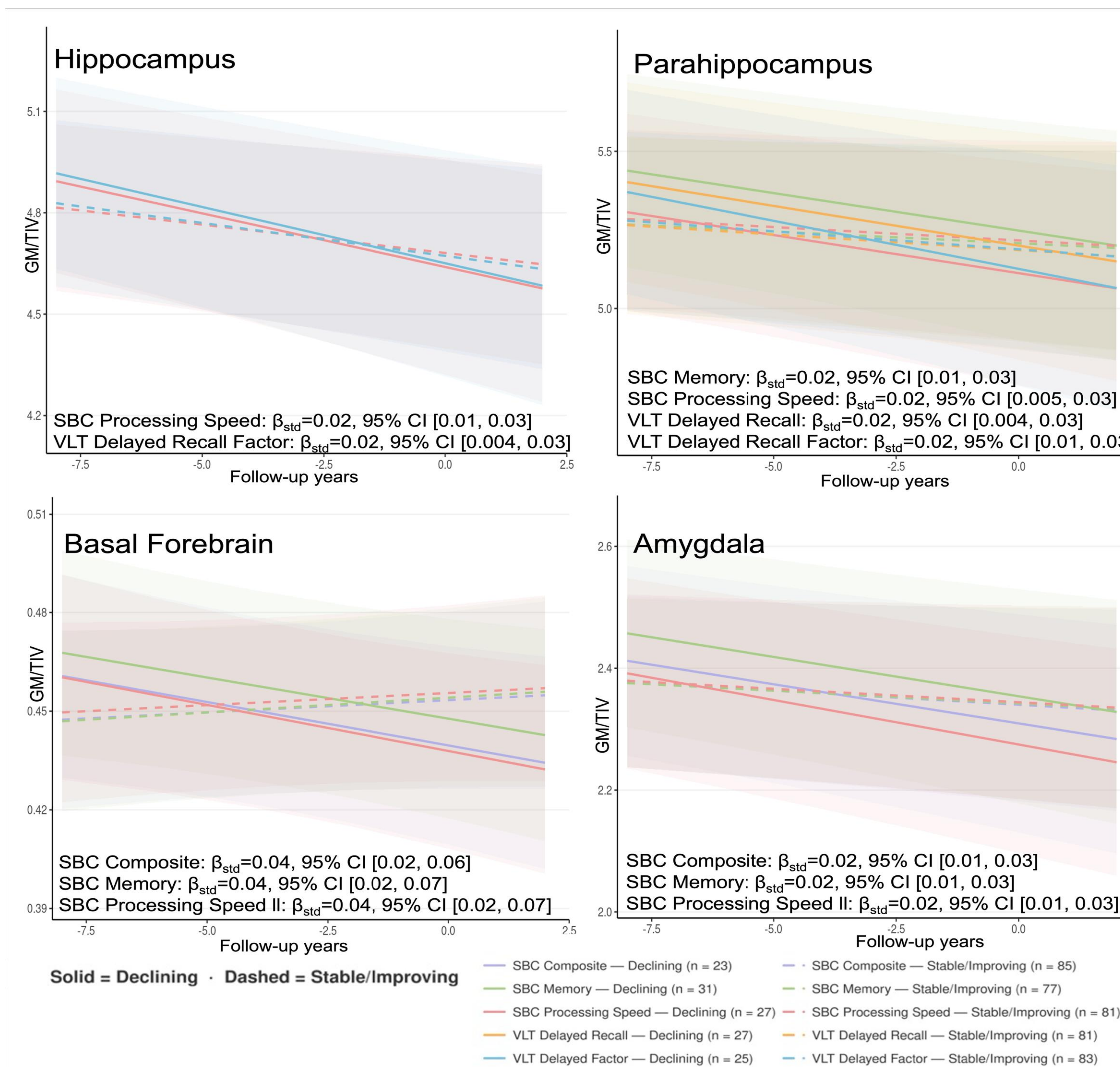
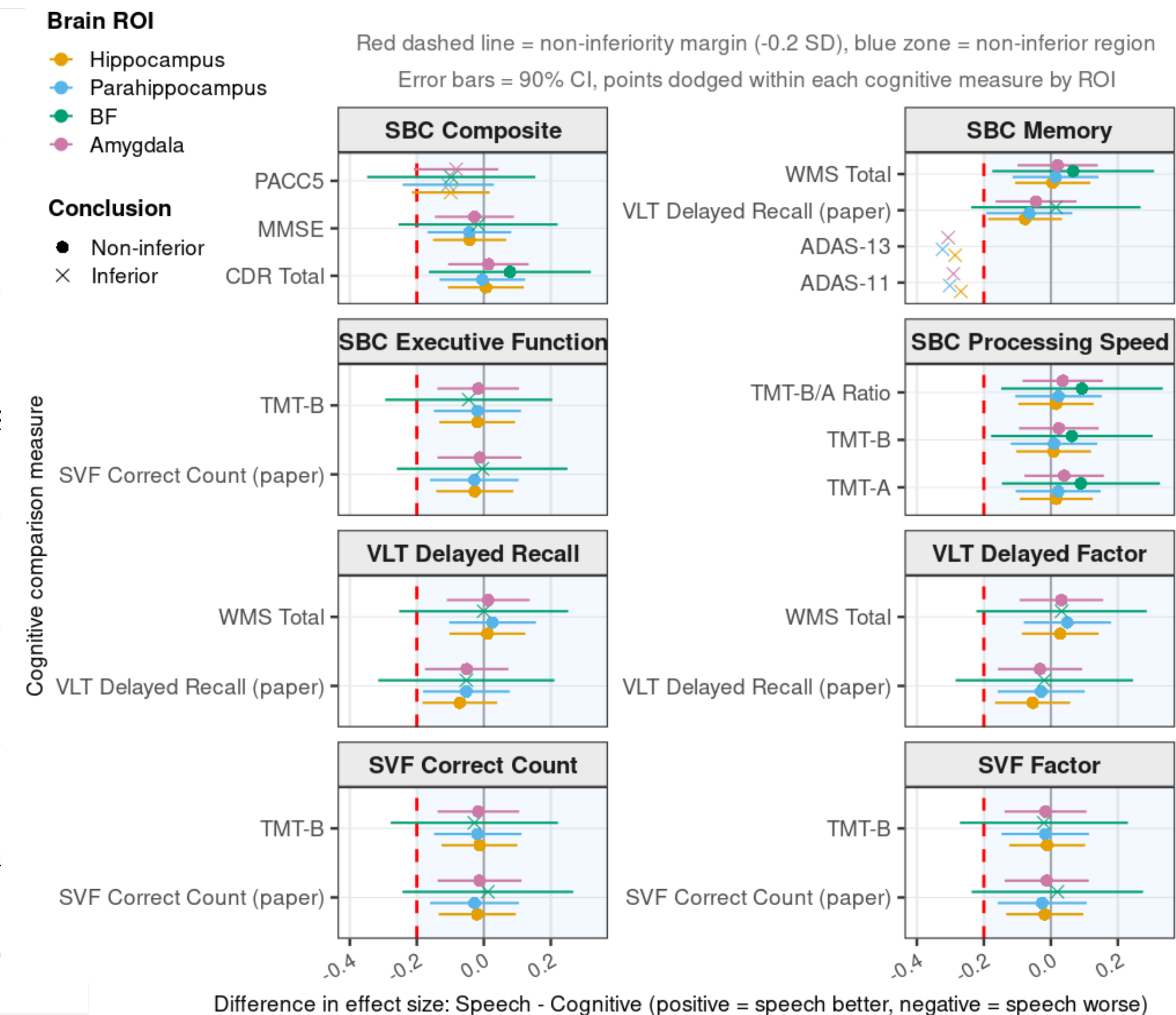


Fig. 3 Non-inferiority of remote speech change rates relative to traditional cognitive change rates in associating brain atrophy trajectories



References: ¹Miller MJ, Saito N, Conti CC, et al. The ADNI4 Digital Study: Remote, unsupervised cognitive assessment to identify cognitive impairment in digitally recruited populations. *Alzheimers Dement*. 2025;21(Suppl 3):e099537. Published 2025 Dec 24. doi:10.1002/alz.70857_099537

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