Empirically-Derived Subtypes of Mild Cognitive Impairment: The Vanderbilt Memory & Aging Project

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Background & Objective

- Recent cohort studies have dichotomized mild cognitive impairment (MCI) to include:
  - Early MCI with subjective cognitive decline and normal neuropsychological performance, and
  - Late MCI with subjective cognitive decline and impaired neuropsychological performance.
- These categorizations lack empirical validation.
- This study statistically derived MCI subtypes using an innovative approach, latent class analysis (LCA), which identifies unobservable subtypes of related classes within a population.

Methods

- Participant data were drawn from the Vanderbilt Memory & Aging Project, a case-control longitudinal study investigating vascular health and brain aging.
- At screening, participants were diagnosed with NC or MCI (Albert et al., 2011) via consensus conference following a comprehensive assessment.
- At enrollment, participants completed a comprehensive neuropsychological protocol. See **Table** for MCI participant characteristics.

Analytical Plan & Results

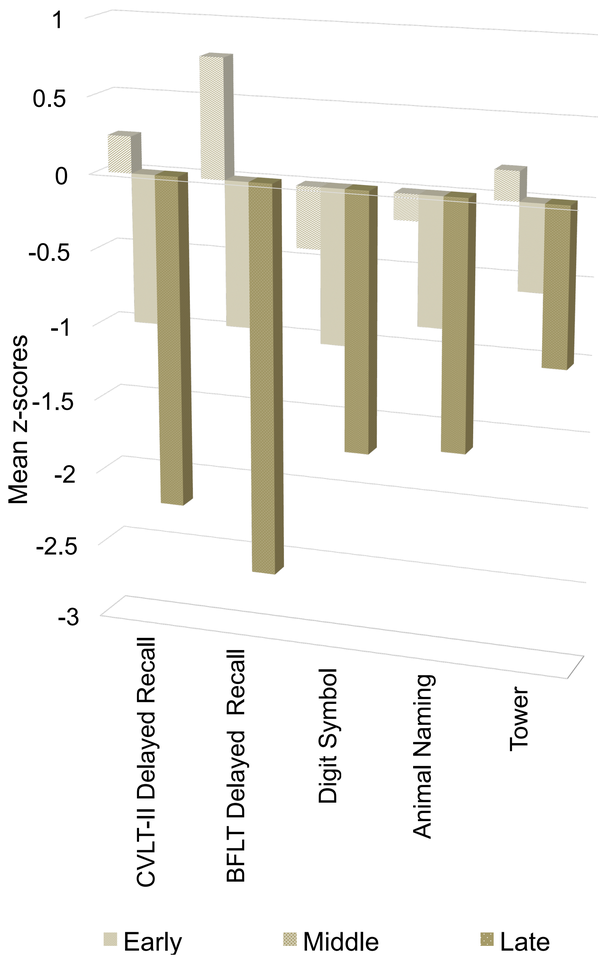
- MCI participant raw neuropsychological performances were converted to z-scores based on age-, sex-, and race-matched NC participant performances.
- Adjusting for age, sex, and education, LCA yielded 3 distinct classes based on the z-score neuropsychological performances.
- Neuropsychological performances were compared using Kruskall-Wallis tests for the 3 classes. Results suggested the classes aligned with 3 subtypes of cognitive severity. See **Table** and **Figure** for results.

Table. Participant Characteristics

	Early n=33	Middle n=57	Late n=29	Total n=119
Age, years	70±5	74±7	75±8	73±7
Sex, % female	39	40	45	41
Education, years	16±3	16±3	15±3	16±3
CVLT-II Trials 1-5 Total Learning	-0.3±0.8	-1.7±0.7§	-2.6±0.8‡	-1.6±1.2
CVLT-II Delayed Recall	-2.2±0.7	-1.0±0.8§	0.2±0.8‡	-1.0±1.2
CVLT-II Discriminability	-0.2±1.2	-0.8±0.8§	-2.0±1.0‡	-0.9±1.2
BFLT Trials 1-5 Total Learning	0.7±0.6	-0.8±0.5§	-1.7±0.6‡	-0.6±1.1
BFLT Delayed Recall	0.8±0.6	-1.0±0.8§	-2.6±0.8‡	-0.9±1.4
BFLT Discriminability	0.02±0.6	-1.3±0.7§	-3.0±1.3‡	-1.3±1.4
BNT 30-Item	-0.8±1.4	0.2±0.8§	0.8±1.4‡	0.4±3.9
Animal Naming	-0.2±1.1	-0.8±0.7§	-1.6±1.1‡	-0.9±1.1
WAIS-IV Digit Symbol Coding	-0.4±1.1	-1.0±1.1§	-1.7±0.8‡	-1.0±1.1
DKEFS Number Sequencing*	0.32±1.1	1.0±1.5§	2.2±3.1‡	1.1±2.0
DKEFS Number-Letter Switching*	0.2±1.0	1.7±2.1§	4.4±5.2‡	1.9±3.3
DKEFS Tower	0.2±0.9	-0.6±0.9§	-1.0±1.1‡	-0.5±1.1
DKEFS Color-Word Inhibition*	0.7±1.3	1.5±1.6§	3.2±2.9‡	1.7±2.1

Note. CVLT-II=California Verbal Learning Test-II; BFLT=Biber Figure Learning Test; BNT=Boston Naming Test; DKEFS=Delis-Kaplan Executive Function System; WAIS-IV=Wechsler Adult Intelligence Scale, 4th Edition; *=higher scores denote worse performance; §= different from Early; ‡= different from Early and Middle, all at $p<0.05$.

Figure. Representative Results for MCI Classes



Conclusions

- Finding suggest MCI severity subtypes can be empirically derived from neuropsychological performances.
- Results are consistent with prior research identifying MCI subtypes using cognitive profiles (e.g., Libon et al., 2011).
- Future work will assess biomarker and risk factor profile differences as well as longitudinal outcomes, such as diagnostic conversion, among MCI subtypes.

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