Cross-Sectional Cognitive Profiles Better Reflect Everyday Functioning Trajectories than HAND

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Background

Context
- Mild cognitive difficulties remain prevalent among people with HIV (PWH) despite widespread use of modern antiretroviral therapy (ART).
- HIV-associated neurocognitive disorder (HAND) criteria constitute a threshold-based diagnostic framework for categorizing cognitive impairment severity.

Problem
- In the modern ART era, cognitive and functional variability among PWH is subtle and multidimensional, exceeding the resolution of HAND criteria – limiting functional risk stratification and targeted intervention planning.

Solution
- Model-based approaches offer a framework for characterizing cognitive heterogeneity and its relationship to functional outcomes beyond HAND classification.

Methods

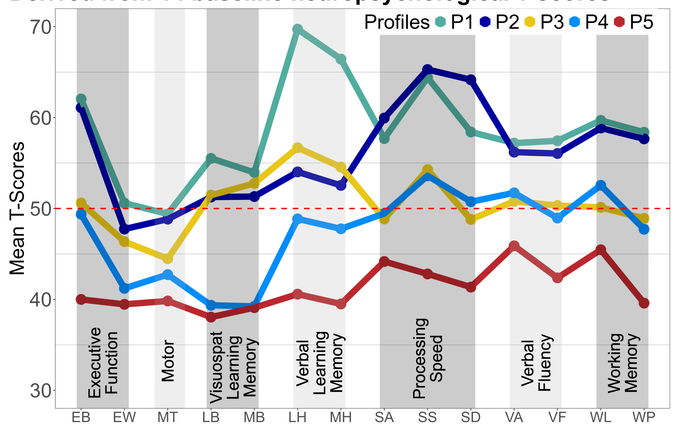
Data
- N = 476 adults (358 PWH, 118 demographically matched people without HIV)
- Baseline comprehensive neuropsychological testing
- Performance-based assessment of functioning using the Texas Functional Living Scale (TFLS)
- HAND classification based on Frascati criteria:
  Sample: 75% Normal, 21% ANI, 3% MND, <1% HAD – reflecting a predominantly cognitively healthy cohort (ART-treated/well-managed HIV among PWH)

Mixture Modeling Applications
- Latent Profile Analysis (LPA): identifies multivariate, cross-sectional cognitive phenotypes without diagnostic cut points.
- Growth Mixture Modeling (GMM): Identifies latent functional trajectory classes that differ in baseline level and rate of change.
- Single-Class Latent Growth (Random-Slopes Model): Estimates continuous individual-level TFLS intercepts and slopes.

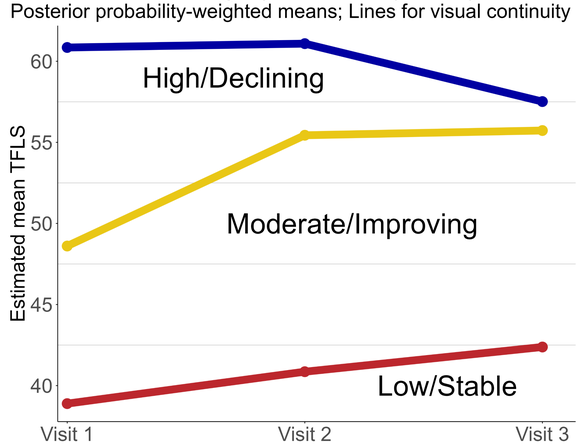
Data-driven cognitive profiles more clearly differentiated everyday functioning, functional impairment risk, and change over time than standard clinical diagnoses

Results

LPA Profiles: Neurocognitive Patterns
Derived from 14 baseline neuropsychological T-scores

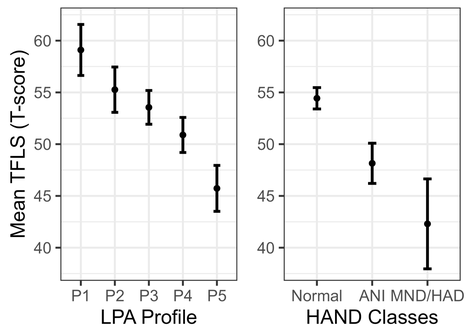


Mean Functioning by GMM Trajectory
Posterior probability-weighted means; Lines for visual continuity



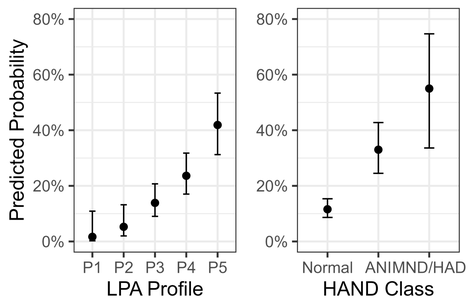
Baseline everyday functioning showed graded separation across LPA profiles, with weaker differentiation by HAND

Baseline Functioning by Framework



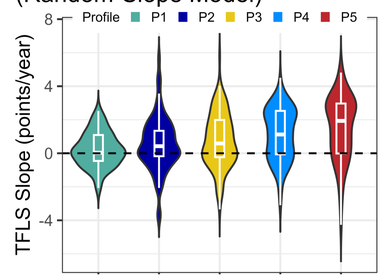
Functional impairment risk increased stepwise across LPA profiles but showed weaker separation by HAND

Probability Functional Impairment (TFLS ≤ 40)



Individual slopes differed systematically across LPA profiles, with progressively greater functional change in lower-performing profiles

TFLS Slopes by LPA Profile (Random-Slope Model)



Conclusions

LPA identified distinct cognitive profiles reflecting meaningful heterogeneity in multivariate neuropsychological performance that is obscured by broad HAND diagnostic categories.

These LPA profiles more clearly stratified everyday functioning, risk of functional impairment, and longitudinal functional change, with progressively greater vulnerability observed in lower-performing profiles.

Notably, despite HAND's explicit incorporation of functional impairment in its diagnostic criteria, HAND classifications showed weaker differentiation of functional level and change than data-driven LPA profiles.

Together, these findings demonstrate that model-based approaches reveal meaningful cognitive-functional heterogeneity beyond threshold-based diagnoses — and may help detect prodromal cognitive and functional vulnerability in NeuroHIV.

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