

Digital Cognitive Tools for Stage 2 Alzheimer's Disease Detection

NIA-AA 2024 Framework: Systematic Review

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KEY TAKE AWAY

Brain amyloid pathology begins before overt clinical impairment, and Stage 2 Alzheimer's disease may be missed by conventional paper-and-pencil tests. Digital cognitive tools can capture subtle abnormalities such as reaction-time variability, altered learning curves, practice effects, and high-frequency longitudinal change. In this systematic review, these tools showed promising diagnostic performance and relevant associations with Alzheimer's biomarkers.

INTRODUCTION

- Alzheimer's disease pathology starts years before dementia symptoms emerge.
- Under the NIA-AA 2024 framework, Stage 2 refers to biologically defined disease with subtle objective change, often while traditional cognitive scores remain within normal limits.
- Standard tests may show ceiling effects and may not capture micro-level cognitive fluctuations.
- Digital cognitive tools (DCTs) offer scalable, repeatable, high-resolution assessment.
- Aim: to evaluate the diagnostic accuracy of DCTs and their association with Alzheimer's biomarkers in preclinical and early clinical populations.

Figure 1. AD continuum and opportunity for detection

Preclinical (at-risk/biomarker no symptoms) → Stage 2 (subtle cognitive change; objective decline) → Stage 3/Dementia (symptoms and functional impact)

Years

DCTs can detect Stage 2 changes before overt clinical impairment.

METHODS

- Design: systematic review following PRISMA 2020.
- Databases: PubMed, Scopus, and Web of Science.
- Search period: 2010–2025.
- Population: cognitively unimpaired, subjective cognitive decline (SCD), mild cognitive impairment (MCI), and early Alzheimer's disease cohorts.
- Focus: Stage 2 and Stage 3 AD continuum.
- Outcomes extracted: tool format, cognitive domain, population tested, sensitivity, specificity, AUC/accuracy, longitudinal prediction, and biomarker associations.
- Records identified: n = 550.
- Studies included in qualitative synthesis: n = 20.

Figure 3. PRISMA 2020 flow diagram

Records identified through database searching (n = 550)

Records after duplicates removed (n = 420)

Full-text records (n = 420) → Records excluded (n = 390)

Full-text articles assessed for eligibility (n = 30) → Articles excluded with reasons (n = 10)

Studies included in qualitative synthesis (n = 20)

RESULTS

Digital cognitive tools demonstrated promising diagnostic performance in differentiating cognitively normal individuals from those with MCI or early AD. In Stage 2 populations, DCTs identified subtle deficits such as loss of practice effects and increased intra-individual reaction-time variability. Remote and repeated assessments improved ecological validity and longitudinal sensitivity.

Table 1. Summary of diagnostic performance for selected computerized cognitive tools

Tool (Format)	Main Cognitive Domain(s)	Population Tested	Sensitivity	Specificity	AUC / Accuracy
UCSF Brain Health Assessment (BHA) iPad battery	Memory, executive function, language processing speed	MCI vs cognitively normal older adults	84%	85%	AD dementia: 100% sensitivity; 98% specificity.
CAMCI, self-administered battery	Attention, memory, executive functions, visuospatial skills	MCI vs CN	86%	94%	-
CANTAB Paired Associate Learning (PAL)	Visual episodic memory	MCI vs CN	83%	82%	-
Cogstate Brief Battery (CBB)	Psychomotor speed, attention, visual learning, working memory	MCI vs CN; AD dementia vs CN	41–80% for MCI; 53–100% for AD dementia	85–86%	Sensitive to Aβ+ decline
BrainCheck	Multidomain	MCI vs CN	86%	83%	AUC = 0.84
MyCog	Memory and executive function composite	Cognitive impairment (MCI / mild dementia) vs normal controls	72–83%	79–91%	AUC = 0.89
Altoida DNS, AR neurofunctional test	Spatial navigation, motor planning, IADL behavior	Preclinical AD / amyloid+ cognitively normal, MCI due to AD	-	-	Up to 84% accuracy predicting progression to prodromal AD about 6 years before symptoms
AI Digital Clock Drawing Test (DCT)	Visuospatial construction and executive planning	Dementia vs CN	83%	87%	Meta-analytic pooled values

Results Summary

- Most multidomain batteries showed good discrimination in MCI vs cognitively normal adults.
- In Stage 2 cohorts, repeated digital measures detected subtle decline despite preserved traditional test scores.
- Remote/high-frequency assessments improved ecological validity and longitudinal sensitivity.
- AR spatial-navigation tools showed especially strong predictive performance in selected cohorts.
- Altoida DNS reports predictive accuracy rather than traditional sensitivity/specificity.

CONCLUSIONS

- Digital cognitive tools are promising instruments for identifying subtle cognitive change in biologically defined early Alzheimer's disease.
- Their greatest value lies in repeated and longitudinal measurement rather than single cross-sectional scores.
- Combining DCTs with biomarkers such as amyloid and p-tau217 may support earlier and more precise risk stratification.
- Future work should improve standardization, reporting quality, and external validation.

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Figure 2. Examples of digital cognitive tasks

Reaction-time tasking

Learning curves & practice effects

Spatial navigation (AR / VR)

Visuoconstruction (Clock drawing)

Attention & working memory

Physiological & behavioral signals

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