Cognivue Clarity® in the Detection of Biomarker-Confirmed Mild Cognitive Impairment and Alzheimer's Disease

James E. Galvin, MD, MPH[1]; Michael J. Kleiman, PhD[2]; Heather M. Harris[3,*]; Paul W. Estes[3]

[1]University of Miami Miller School of Medicine; Cognivue Advisory Board Member; [2]University of Miami Miller School of Medicine; [3]Cognivue Working Group, Cognivue Inc., Victor, NY. *Presenting author.

KEY TAKEAWAY: **Cognivue Clarity® discriminated healthy controls from those with Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD), strongly correlated with AD biomarkers, and had strong psychometric properties.**

BACKGROUND

Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI) treatment and prevention trials are underway; however, recognition of potentially eligible individuals can be challenging, which leads to delayed recruitment and high screen failure. Digital biomarkers that can accurately identify MCI and AD and correspond to AD biomarkers could greatly facilitate enrollment and track disease progression and/or response to treatment.

Cognivue *Clarity*® is an FDA-cleared 10-minute, digital cognitive testing platform using adaptive psychophysics to capture global and domain-specific performance (Figure 1). The test generates a report that can be used by clinicians to assess cognitive status.

The Bio-Hermes Study generated a first-of-its-kind, "head-to-head" comparison of a broad set of AD biomarkers. The Cognivue *Clarity* device was included as part of the study's assessments to explore the utility of several leading biomarkers.

Figure 1. The Cognivue *Clarity* device.

DESIGN/METHODS

The Bio-Hermes study, funded by the Global Alzheimer's Platform Foundation®, enrolled healthy controls, as well as patients with MCI and AD. Assessments included sociodemographics, Cognivue *Clarity*, plasma AD biomarkers, and amyloid positron emission tomography (PET) scans. Cognivue *Clarity's* psychometric properties, diagnosis discrimination, correlations with AD biomarkers, and diagnostic power were analyzed.

RESULTS

The entire Bio-Hermes study included 1,001 participants, including 417 controls, 311 participants with MCI, and 273 participants with probable AD. Participants had a mean age of 72.0.9+6.7 years and 15.4±2.8 years of education. 56.2% of participants were female and 23.8% were from underrepresented minorities (75.6% Non-Hispanic White, 11.3% Black, 11.4% Hispanic, 1.8% Asian).

The mean Mini–Mental State Examination (MMSE) score was 26.6+2.9 and mean Cognivue *Clarity* score was 62.9+17.4. Cronbach's alpha among the whole sample was 0.879 (95% CI: 0.867-0.890), supporting high reliability.

Cognivue *Clarity* scores differed between ethnoracial groups in the study (Table 1).

	Non-Hispanic White	Non-Hispanic Black	Hispanic	p-value
Age	72.5 (6.6)	70.2 (6.2)	71.2 (6.9)	.001[a]
Cognivue	63.9 (17.4)	59.1 (14.4)	58.2 (18.6)	<.001[b]
MMSE	27.0 (2.7)	25.3 (3.0)	25.2 (3.2)	<.001[b]
Centiloid Level	30.2 (47.9)	23.4 (37.9)	29.9 (45.8)	.399

Post-hoc analyses:
[a] Non-Hispanic Blacks are different from Non-Hispanic Whites.
[b] Non-Hispanic Whites are different from Non-Hispanic Blacks and Hispanics.

Table 1. Cognivue *Clarity* differences by sociodemographic characteristics in the entire Bio-Hermes study sample (mean [SD] or %).

In the entire study sample, Cognivue *Clarity* demonstrated discrimination between diagnosis groups (Figure 2) and was able to detect the presence of amyloid (Figure 3).

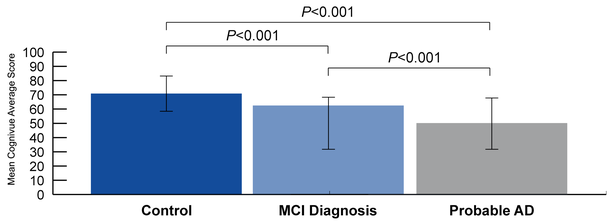

Figure 2. Mean average score with Cognivue *Clarity* by diagnosis group.

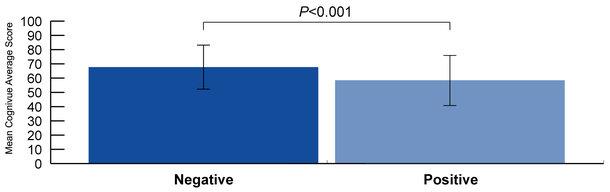

Figure 3. Mean average score with Cognivue *Clarity* to meet threshold for Amyvid scan.

Cognivue *Clarity* was analyzed in 555 biomarker-confirmed participants (297 Controls, 113 MCI, 145 AD) with a mean age of 71.9±6.6 years and 15.6±2.8 years of education. 56.4% of participants were female and 21.7% were from underrepresented minorities. Participants had a mean MMSE score of 26.6±3.0, and a mean Cognivue *Clarity* score of 64.0±17.4. Cronbach's alpha was 0.882 (95%CI: 0.867-0.897), indicating high reliability.

As in the entire study sample, Cognivue *Clarity* scores differed between ethnoracial groups in the biomarker sample (Table 2).

	Non-Hispanic White	Non-Hispanic Black	Hispanic	p-value
Age	72.3 (6.7)	69.9 (6.2)	70.7 (6.2)	.042[a]
Cognivue	64.8 (17.5)	62.3 (13.6)	59.6 (18.4)	.195
MMSE	26.9 (2.9)	25.8 (3.1)	25.9 (3.5)	<.001[c]

Post-hoc analyses:
[a] Non-Hispanic Blacks are different from Non-Hispanic Whites.
[b] Hispanics are different from Non-Hispanic Whites.
[c] Non-Hispanic Whites are different from Non-Hispanic Blacks and Hispanics.

Table 2. Cognivue *Clarity* differences by sociodemographic characteristics in the biomarker study sample (mean [SD] or %).

In post-hoc analyses, Cognivue *Clarity* scores were different between the control, MCI-AD, and AD groups, while MMSE scores were different between MCI-AD and AD groups only (Table 3).

	Control	MCI-AD	AD	p-value
Cognivue	71.9 (12.5)	60.1 (16.2)	49.4 (17.4)	<.001
MMSE	28.4 (1.5)	27.0 (1.9)	22.8 (2.6)	<.001
C2N AB42/40	0.101 (.009)	0.089 (.006)	0.091 (.008)	<.001
C2N APS	16.4 (19.4)	59.4 (26.4)	55.9 (29.3)	<.001
Lilly Amyloid PET	0.958 (0.06)	1.376 (0.21)	1.461 (0.21)	<.001
Lilly pTau217	0.171 (0.06)	0.356 (0.23)	0.474 (0.26)	<.001
Quanterix pTau181	16.2 (7.5)	24.1 (11.0)	30.6 (18.5)	<.001
pTau181/AB42	0.327 (0.14)	0.544 (0.27)	0.688 (0.38)	<.001
pTau217/AB42	0.0035 (0.001)	0.0080 (0.005)	0.107 (0.006)	<.001

Table 3. Cognivue *Clarity* differences by biomarker groups (mean [SD]).

Cognivue *Clarity* average and subtest scores robustly differentiated (p<0.001) between healthy controls (71.9±12.5), MCI (60.1±16.2) and AD (49.4±17.4) in the biomarker sample (Figure 4).

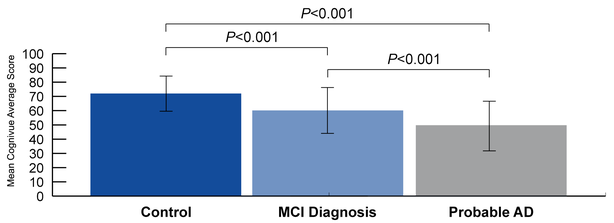

Figure 4. Mean average score with Cognivue *Clarity* by diagnosis group among participants in the biomarker-confirmed sample.

Cognivue *Clarity* was moderately correlated with AD plasma and imaging biomarkers (p<.001), while AD biomarkers were moderately correlated with each other (p<.001). Cognivue *Clarity* demonstrated similar associations with AD plasma and imaging biomarkers as biomarkers have with each other (Table 4).

	Cognivue	AB42/40	APS	SUVR	Ptau217	Ptau181	Ptau181/AB42
AB42/40	.253						
APS	-.339	-.819					
SUVR	-.486	-.455	.584				
Ptau217	-.426	-.381	.417	.608			
Ptau181	-.287	-.319	.350	.454	.546		
Ptau181/AB42	-.307	-.386	.409	.513	.550	.946	
Ptau217/AB42	-.443	-.411	.442	.629	.958	.503	.588

Table 4. Correlations between Cognivue *Clarity* and biomarkers.

CONCLUSIONS

Cognivue Clarity discriminated healthy controls from MCI and AD, strongly correlated with AD biomarkers, and had strong psychometric properties. Individuals with Cognivue Clarity average scores <70 were 7.5-fold more likely to be impaired. Cognivue Clarity can be used to screen individuals for cognitive impairment, enrich clinical trial inclusion, and track disease progression.

FUNDING

This study was funded by grants from AbbVie, Aural Analytics, C2N, Cognivue, EMTherapro, GNS Healthcare, IXICO, Lilly, Linus, Merck, Quanterix, Retispec, Roche, Soma Logic, University of Gothenburg, Global Alzheimer's Platform Foundation® (GAP), Alzheimer's Drug Discovery Foundation (ADDF), Gates Ventures, and Pentara Corporation.

CONTACT

Heather M. Harris,
Executive Director, Science, Medical Affairs, and Research, Cognivue
Email: hharris@cognivue.com