Superior test-retest reliability of cognitive assessment with Cognivue® vs SLUMS during an 18-month longitudinal study

John Andrefsky, MD, FAHA, D, ABSM[1]; Diego Cahn-Hidalgo, MD[2]; Reina Benabou, MD, PhD[3]
[1]University Hospital Parma Medical Center, Parma, OH; [2]Internal Medicine, Rochester, NY; [3]Cognivue Inc., Victor, NY

ABSTRACT

Background: Cognivue is an FDA-cleared computerized testing tool designed to assess early signs of cognitive impairment. In an FDA clearance study, Cognivue demonstrated good agreement with the St. Louis University Mental Status (SLUMS) and other neuropsychological tests, and superior test re-test reliability compared to SLUMS across 2 sessions, 1 to 2 weeks apart (Cognivue regression fit: $R^2 = 0.81$, r = 0.90); SLUMS regression fit: $R^2 = 0.67$, r = 0.82). Further follow-up long-term data analysis within this cohort was done to study Cognivue's test re-test reliability vs SLUMS over time.

Objective: To compare the test-retest reliability of Cognivue with that of the SLUMS test over the course of 18 months.

Methods: 238 subjects from the FDA clearance study enrolled in the longitudinal study. They underwent the Cognivue test and SLUMS at 3 sessions over the course of 18 months (6, 12, 18 months post-FDA study). An analysis of rank linear regression test-retest reliability was performed for both tests. In a separate sub-analysis, the medical records of those subjects were analyzed to determine the correlation, if any, between comorbidities or medication usage and Cognivue score.

Results: Among these 238 patients, Cognivue demonstrated similar linear regression scores across comparisons (test session 1&2: regression fit: $R^2 = 0.76$; r = 0.87; test session 1&3: regression fit: $R^2 = 0.72$; r = 0.85; test session 1&4: regression fit: $R^2 = 0.73$; r = 0.86). The SLUMS test demonstrated greater variability in regression scores across test sessions (test session 1&2: regression fit: $R^2 = 0.63$; r = 0.79; test session 1&3: regression fit: $R^2 = 0.43$ r = 0.65; test session 1&4: regression fit: $R^2 = 0.64$; r = 0.80).

In the subanalysis, medical records of 203 subjects were analyzed. Overall, an increased co-morbidity count significantly decreased subjects' Cognivue scores (correlation -0.21; P=0.01). Cardiopulmonary comorbidities had the largest impact on a patient's Cognivue score (78.0 score for those without this comorbidity vs 67.1 score for those with; P<0.001). Use of anti-HTN medications was significantly correlated with a decrease in subjects' Cognivue scores (correlation -0.2; P=0.02).

Conclusions: Cognivue demonstrated maintained superior test re-test reliability compared to SLUMS over a period of 18 months after the FDA clearance study. An increased comorbidity count and cardiopulmonary comorbidities significantly decreased a subject's Cognivue score over time.

BACKGROUND

- Existing neuropsychological tests have limitations that may affect test scores, including subjectivity, the potential for respondents to learn answers with repeated use, and an inability to track small changes in cognitive ability over time[1-3]
- Cognitive issues may be related to a number of causes, including life-style-related risk factors, underlying disease states, and prescription drug side effects[4-8]
  - Timely identification of cognitive issues may allow healthcare providers to intervene by treating the underlying cause or managing relevant pharmacotherapies, possibly reversing or improving the initial cognitive issue[5,6,8]
- Cognivue (Figure 1) is a computerized testing tool rooted in adaptive psychophysics that is FDA-cleared for use as an adjunctive aid to assess early signs of cognitive impairment.[9] (Table 1) Cognivue is not intended to be used alone for diagnostic purposes
  - Cognivue produces a 2-page report with the participant's overall score and subsequent breakdown into 6 key cognitive domains and speed parameters (Figure 2)
- In the FDA clearance study, Cognivue demonstrated overall good agreement with SLUMS and other neuropsychological tests in addition to superior test re-test reliability compared to SLUMS across 2 sessions, 1 to 2 weeks apart (Cognivue regression fit: $R^2 = 0.81$, r = 0.90); SLUMS regression fit: $R^2 = 0.67$, r = 0.82)[9]
- A longitudinal study was conducted to explore the test re-test reliability of both methods over a period of 18 months

Figure 1. The Cognivue device, shown closed (left) and open (right)

BACKGROUND (CONT.)

Table 1. Sample screens of Cognivue subtests

Sub-battery	Sub-test	Sample screen
Visuo-motor	Adaptive motor	
	Visual salience	
Perception	Letter discrimination	
	Word discrimination	
	Shape discrimination	
	Motion discrimination	

Sub-battery	Sub-test	Sample screen
Memory	Letter memory	
	Word memory	
	Shape memory	
	Motion memory	

Figure 2. Sample Cognivue reports

METHODS

Subjects: 238 subjects from the FDA pivotal clinical trial for Cognivue were enrolled in this longitudinal study.
- Subjects in the FDA pivotal trial were adults (55–95 y) from independent-living communities, at risk for age-related cognitive decline or dementia[9]
  - Exclusion criteria: limiting motor or visual disabilities, unable to provide informed consent[9]

Tests:
- Subjects underwent the Cognivue test and the SLUMS test at 3 sessions over the course of 18 months (6, 12, 18 months post-FDA study)
  - Cognivue quantitative assessment tool includes 3 sub-batteries (visuo-motor ability, perceptual processing, and memory processing) presented in automated sequence over 10 minutes (Table 1)
  - SLUMS (reference standard):
    - 11-item questionnaire with scores ranging from 0 to 30
    - Designed to measure orientation, memory, attention, and executive functions

Analyses: Two datasets were used for this analysis:
- Longitudinal study data set
- FDA pivotal trial data set analyzed for comparison purposes

The following analyses were performed:
- Rank linear regression test-retest reliability
  - Analysis compared test sessions 1 and 2, 2 and 3, and 3 and 4
  - Analysis also compared test sessions 3 and 4 with test session 1 as a baseline
  - Analysis was designed to show linear regression (R^2) and correlation (r)
- Sub-analysis of medical records to determine the correlation, if any, between comorbidities or medication usage and Cognivue score
  - Subjects who participated in the longitudinal study and/or the FDA pivotal trial were included
    - These subjects sent medical records for supplemental data, which was then formatted to analyze co-morbidities, medications, surgeries, and other statistics (blood pressure, blood work test results, etc.)
  - Cognivue score at a subject's earliest visit and that at a follow-up visit were compared

RESULTS

- In the longitudinal study data set, 238 unique subjects with multiple sessions each completed Cognivue and SLUMS tests over a period of 18 months

Retest reliability analyses
- Cognivue demonstrated superior test-retest reliability by a significant margin (Figure 3)

Progressive test session comparisons (Table 2):
- Among these 238 patients, test-retest reliability analyses showed similar scores across repeated testing with Cognivue:
  - Test session 1&2: regression fit: $R^2 = 0.76$; r = 0.87
  - Test session 2&3: regression fit: $R^2 = 0.73$; r = 0.85
  - Test session 3&4: regression fit: $R^2 = 0.78$; r = 0.88
- The SLUMS test demonstrated greater variability in regression scores across test sessions:
  - Test session 1&2: regression fit: $R^2 = 0.63$; r = 0.79
  - Test session 2&3: regression fit: $R^2 = 0.53$ r = 0.73
  - Test session 3&4: regression fit: $R^2 = 0.60$; r = 0.77
- In an additional comparison of Cognivue results between test sessions 4 and 5, Cognivue demonstrated regression fit of $R^2 = 0.74$ and correlation of r = 0.86

Table 2. Correlation and regression across test sessions

Test	Test Session 1&2		Test Session 2&3		Test Session 3&4	
	Correlation (r)	Linear Regression (R^2)	Correlation (r)	Linear Regression (R^2)	Correlation (r)	Linear Regression (R^2)
Cognivue	0.872	0.761	0.852	0.726	0.884	0.782
SLUMS	0.793	0.628	0.726	0.527	0.771	0.595

Comparisons with test session 1 (Table 3):
- Using test session 1 as a baseline, Cognivue showed similar scores in test re-test reliability analysis:
  - Test session 1&3: regression fit: $R^2 = 0.72$; r = 0.85
  - Test session 1&4: regression fit: $R^2 = 0.73$; r = 0.86
- SLUMS showed greater variability in regression scores vs test session 1:
  - Test session 1&3: regression fit: $R^2 = 0.43$ r = 0.65
  - Test session 1&4: regression fit: $R^2 = 0.64$; r = 0.80
- In an additional comparison of Cognivue results between test sessions 1 and 5, Cognivue demonstrated regression fit of $R^2 = 0.68$ and correlation of r = 0.83 (Figure 4)

Table 3. Correlation and regression vs first test session

Test	Test Session 1&3		Test Session 1&4	
	Correlation (r)	Linear Regression (R^2)	Correlation (r)	Linear Regression (R^2)
Cognivue	0.848	0.719	0.856	0.733
SLUMS	0.652	0.425	0.798	0.637

Medical records subanalysis
- In the subanalysis, medical records of 203 subjects who participated in the longitudinal study and/or the FDA pivotal trial were analyzed

Comorbidities analysis:
- Subjects had an average number of 4.98 comorbidities
  - Comorbidities were categorized as being endocrine-, cardiopulmonary-, mood disorder-, sleep disorder-, or bone-related in nature
- Overall, an increased co-morbidity count significantly decreased subjects' Cognivue scores (correlation -0.21; P=0.01)
- Among comorbidity categories, cardiopulmonary comorbidities had the largest impact on a patient's Cognivue score (78.0 score for those without this comorbidity vs 67.1 score for those with; P<0.001)

Medications analysis:
- Subjects took an average number of 6.07 medications
- Of these medications, use of anti-HTN medications was significantly correlated with a decrease in subjects' Cognivue scores (correlation -0.2; P=0.02)

RESULTS (CONT.)

Figure 3. Cognivue score – Demings regression: Test session 1 vs 2

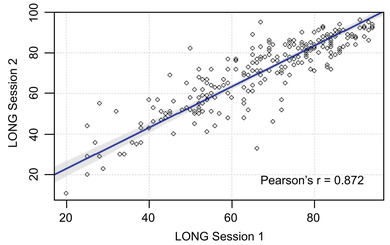
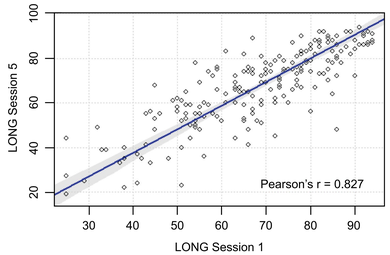


Figure 4. Cognivue score – Demings regression: Test session 1 vs 5



CONCLUSIONS

- This longitudinal study demonstrated that Cognivue maintained superior test re-test reliability compared to SLUMS over a period of 18 months after the FDA clearance trial
- An increased comorbidity count and cardiopulmonary comorbidities significantly decreased a subject's Cognivue score over time

References:
1. Connor et al. *J Prev Alzheimers Dis*. 2018;5:188-196.
2. Collie et al. *Br J Sports Med*. 2001;35:297-302.
3. Segal-Gidan. *Clin Rev*. 2013;23:12-18.
4. Alzheimer's Association. *Alzheimers Dement*. 2018;14:367-429.
5. World Health Organization. *WHO guidelines*. 2019.
6. Livingston et al. *Lancet*. 2017;390:2673-2734.
7. American Diabetes Association. *Diabetes Care*. 2019;42(Suppl.1):S139–S147.
8. Foster et al. *Neurology*. 2019;93(16):705-713.
9. Cahn-Hidalgo et al. *World J Psych*. 2020;10(1):1-11.

INDICATIONS FOR USE: Cognivue testing is indicated as an adjunctive tool for evaluating perceptual and memory function in individuals aged 55–95 y. It is not intended to be used as a stand-alone device to identify the presence or absence of clinical diagnoses. Cognivue is intended to be used by medical professionals qualified to interpret the results of a cognitive assessment examination.

This study was supported by Cognivue, Inc.