Validation, reliability, and psychometric properties of Cognivue®, a quantitative assessment of cognitive impairment

NR-37

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ABSTRACT

Background: Many tools for assessing decline in cognitive function have limited utility due to issues of accuracy, testing bias, and uptake among clinicians. Cognivue® is a brief, easy-to-use, FDA-cleared tool for the adjunctive assessment of risk of cognitive impairment.

Objective: To clinically validate Cognivue® via agreement analysis of impairment risk classifications, retest reliability assessment, and psychometric property comparison.

Methods: Adults (age 55–95 y) at risk for age-related cognitive decline or dementia completed Cognivue®, St. Louis University Mental Status (SLUMS), and other neuropsychological tests including Rey Auditory Verbal Learning Test (RAVLT) & Trail Making Test A/B (TMT-A, TMT-B). Analyses included: regression analyses for agreement and retest reliability, and rank linear regression and factor analysis for psychometric comparisons.

Results: Data were available for 401 subjects who completed ≥1 testing session, and 358 who completed 2 sessions 1–2 weeks apart. Previously determined Cognivue® classification scores were validated, demonstrating good agreement with SLUMS scores (weighted κ = 0.57; 95% CI 0.50–0.63). The study of test-retest reliability showed similar scores across repeated testing for Cognivue® (regression fit: R^2 = 0.81; r = 0.90), and SLUMS (regression fit: R^2 = 0.67; r = 0.82). The Cognivue® classifications of high, low-moderate, and no risk of impairment, did not differ significantly across repeat testing; however, for SLUMS, the relationship between scores and classifications across repeated testing was less robust. The psychometric validity of the Cognivue® cognitive test battery was demonstrated compared to traditional paper & pencil neuropsychological tests. Scores were most closely correlated with measures of verbal processing, manual dexterity/speed, visual contrast sensitivity, visuospatial/executive function, and speed/sequencing.

Conclusions: The Cognivue® validation study demonstrated good agreement between Cognivue® and the SLUMS test; good test-retest reliability of Cognivue® test results; and validated the psychometric properties of the Cognivue® test battery compared to traditional neuropsychological tests.

BACKGROUND

- Tools for assessing cognitive function decline are often limited by lack of validation & consistent retest reliability
- Cognivue® was developed as a physiological & psychophysical computerized tool for automated assessment of brain functioning that is not dependent on traditional question & answer testing
- It is a 10-minute test, FDA-cleared for use as an adjunctive tool to aid in assessing cognitive impairment risk in those 55–95 years of age. It is not intended to be used alone for diagnostic purposes
- Cognivue® uses scores from a sequence of tasks to produce a 1-page report & score

METHODS

Purpose: Clinically validate (Table 1) Cognivue® via:

- Agreement analysis of previously defined impairment risk classifications
- Assessment of retest reliability
- Comparison of psychometric properties vs. other neuropsychological tests

Subjects: Adults (55–95 y) from independent-living communities, at risk for age-related cognitive decline or dementia, invited to participate via posters & email

- Exclusion criteria: limiting motor or visual disabilities, unable to provide informed consent

Tests: Cognivue®, SLUMS, & other neuropsychological tests (Table 1)

- Previous clinical trial (n=92) to determine cut-off scores found:
  - Cognivue® scores ≤50 = SLUMS <21 (impairment)
  - Cognivue® scores 51–74 = SLUMS 21–26 (low-moderate risk)
  - Cognivue® scores ≥75 = SLUMS >27 (no impairment)
- In this validation analysis, low–moderate risk was combined with unimpaired category for each test modality

Analyses: Regression analyses for agreement & retest reliability; rank linear regression & factor analysis for psychometric comparison (Table 1)

METHODS (CONT.)

Table 1. Components of FDA pivotal clinical trial of Cognivue®

Validation of impairment risk classifications	• Purpose: Assess validity of previously defined Cognivue® cut-off scores in larger sample • Methods: Cognivue® & SLUMS scores compared using regression & classification analyses; positive and negative percent agreements (PPA & NPA) calculated
Assessment of retest reliability	• Purpose: Compare scores from repeated administration of Cognivue® to assess retest reliability, compare findings to parallel results from SLUMS • Methods: Repeated Cognivue® & SLUMS testing conducted in 2 sessions 1–2 weeks apart; regression & rank linear regression analysis performed
Assessment of score psychometrics vs. other neuro-psychological tests	• Purpose: Compare scores on Cognivue® and other neuropsychological tests to describe relationships and compare to SLUMS • Methods: 401 participants completed 10 different tests; rank linear regression analysis & factor analysis performed • SLUMS, SLUMS-clock drawing†, SLUMS-animal naming†, RAVLT, TMT-A, TMT-B, Benton JOLO, figural memory, PPB, HVCS, GDS (15-item)

†Scored separately from overall SLUMS; GDS: Geriatric Depression Scale; HVCS: Hamilton-Veale Contrast Sensitivity; JOLO: judgment of line orientation; PPB: Purdue Peg Board; RAVLT: Rey Auditory Verbal Learning Test; SLUMS: St. Louis University Mental Status; TMT: Trail Making Test

RESULTS

- 401 subjects completed ≥1 testing session; 358 completed 2 sessions 1–2 weeks apart
- Based on SLUMS score, 27% were impaired (<21), 43% were intermediate (26–21), and 30% were not impaired (>26)

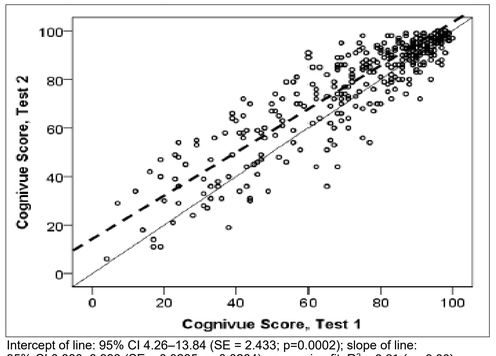
Validation analyses

- Previously determined Cognivue® classification scores were validated in a sample of 401 subjects who completed ≥1 testing session
  - PPA = 56% (95% Wilson interval [WI] 0.47–0.65)
  - NPA = 95% (95% WI 0.91–0.97)
  - Weighted κ = 0.57 (95% CI 0.50–0.63)
- The data suggest significant categorical relationship between Cognivue® & SLUMS scores
- Analysis omitting intermediate groups as being indeterminate showed stronger relationship between Cognivue® & SLUMS categories for impaired or unimpaired
  - PPA = 82% (95% WI 0.72–0.89), NPA = 98% (95% WI 0.93–0.99)

Retest reliability analyses

- 358 subjects completed repeated Cognivue® & SLUMS testing in 2 sessions 1–2 weeks apart
- Test-retest reliability analyses showed similar scores across repeated testing
  - Cognivue® (regression fit: R^2 = 0.81; r = 0.90) (Figure 1)
  - SLUMS (regression fit: R^2 = 0.67; r = 0.82)

Figure 1. Scatterplot showing Cognivue® 1st (abscissa) & 2nd test scores (ordinate) co-plotted with Deming regression line (dashed)



Intercept of line: 95% CI 4.26–13.84 (SE = 2.433; p=0.0002); slope of line: 95% CI 0.880–0.993 (SE = 0.0285; p=0.0264); regression fit: R^2 = 0.81 (r = 0.90)

RESULTS (CONT.)

- Cognivue® agreement analysis revealed strong correlation between subject classification by 1st & 2nd Cognivue® tests
  - PPA = 89%, NPA = 93%; intraclass correlation (ICC) of tests 1 & 2 = 0.99 (p<0.001)
- SLUMS analysis also showed strong agreement between subject classification by 1st & 2nd SLUMS tests
  - PPA = 87%, NPA = 87%; ICC = 0.87 (p<0.001)
- Cognivue® classifications of high, low-moderate, and no risk of impairment, did not differ significantly across repeat testing
- Analysis of 3 classifications separately: 89% PPA for high risk of impairment, 57% PPA for low-moderate, and 87% PPA for no risk (Table 2)

Table 2. Proportion of subjects classified in each risk category by 1st and 2nd Cognivue® tests

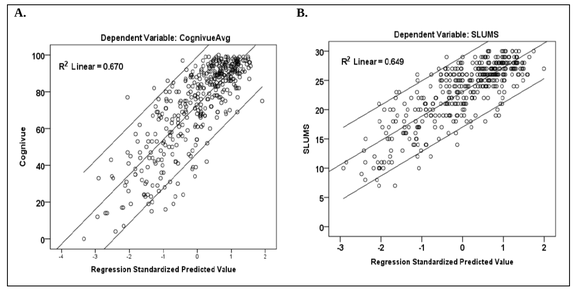
	1st TEST			
2nd TEST	**High risk**	**Low to mod. risk**	**No risk**	**Total**
High risk	**42 (89%)**	21	0	63
Low to mod. risk	5	**41 (57%)**	32	78
No risk	0	10	**207 (87%)**	217
Total	47	72	239	358

- For SLUMS, relationships between scores & classifications across repeated testing were less robust than those for Cognivue®
- Analysis of 3 classifications separately: 87% PPA for impaired, 55% PPA for intermediate, and 51% PPA for unimpaired

Psychometric analysis

- 401 subjects completed ≥1 testing session, including Cognivue®, SLUMS, and other neuropsychological tests
  - Rank scores on each test were plotted against their ranks on SLUMS scores and against their ranks on Cognivue® scores with linear regression lines, the lines' parameters, and their 95% CIs (data not shown)
- Data were condensed using factor analysis of neuropsychological test scores
  - Tests grouped by relations between scores across participants
- Factor analysis converged in 6 iterations to yield 5-factor solution (Table 3), Cognivue® scores most closely correlated with:
  - Verbal processing (animal naming, RAVLT)
  - Manual dexterity & speed (Peg Board)
  - Visual acuity (contrast sensitivity)
  - Visuospatial & executive function (Trails B, JOLO)
  - Speed & sequencing (Trails A)
- 5-factor scores for each subject used in multiple linear regression analysis (Figure 2A & B)
  - Cognivue®: adjusted linear R^2 = 0.67
  - SLUMS: adjusted linear R^2 = 0.65

Figure 2. Scatterplot showing regression standardized predicted values including all 5 factors and (A) Cognivue® scores or (B) SLUMS scores co-plotted with linear regression lines



RESULTS (CONT.)

Table 3. Factor analysis component matrix for neuropsychological test scores

	Component				
	1	**2**	**3**	**4**	**5**
SLUMS-clock drawing	.420	.338	.038	.367	-.049
SLUMS-animal naming	**.529**	.346	.146	.365	-.125
RAVLT-A-1	**.718**	.209	.034	.128	-.040
RAVLT-A-2	**.820**	.204	.080	.157	-.138
RAVLT-A-3	**.832**	.193	.120	.190	-.057
RAVLT-A-4	**.847**	.200	.143	.184	-.040
RAVLT-A-5	**.863**	.210	.080	.182	-.013
RAVLT-B-1	**.579**	.213	.104	.178	-.060
RAVLT-A-6	**.852**	.134	.093	.170	-.051
RAVLT-A-7	**.860**	.159	.117	.164	-.040
RAVLT-hits	**.670**	.052	.128	.252	-.003
RAVLT-fps	-.408	-.017	-.111	-.041	.125
Peg Board-Left	.247	**.796**	.297	.120	-.090
Peg Board-Right	.297	**.752**	.206	.160	-.186
Peg Board-Bimanual	.293	**.822**	.230	.134	-.137
Contrast-Left	.146	.133	**.801**	.110	-.068
Contrast-Right	.160	.156	**.802**	.094	-.106
Contrast-Binocular	.189	.183	**.833**	.132	-.153
TMT-B-Time	-.312	-.088	-.213	**-.788**	.116
TMT-B-Errors	-.266	-.072	-.197	**-.815**	.085
Benton JOLO	.185	.196	-.024	**.499**	-.344
TMT-A-Time	-.115	-.185	-.158	-.150	**.862**
TMT-A-Errors	-.081	-.058	-.134	-.068	**.902**
Figural memory	.272	.243	.202	.376	.047
GDS	-.119	-.341	.207	-.329	-.008

Cognivue® scores most closely correlated with verbal processing (animal naming, and RAVLT – **RED**), manual dexterity & speed (Peg Board – **BLUE**), visual acuity (contrast sensitivity – **GREEN**), visuospatial & executive function (Trails B and JOLO – **PURPLE**), and speed & sequencing (Trails A – **YELLOW**).

Fps: frames per second; GDS: Geriatric Depression Scale; JOLO: judgment of line orientation; RAVLT: Rey Auditory Verbal Learning Test; SLUMS: St. Louis University Mental Status; TMT: Trail Making Test

CONCLUSIONS

- FDA pivotal clinical trial demonstrated validity, reliability, and psychometric properties of Cognivue®
- Validation study confirmed agreement between SLUMS & Cognivue® classifications of risk of impairment
  - Cognivue® can inform an impression that patient is or is not impaired
- Retest reliability study demonstrated Cognivue® repeated testing of older adults resulted in similar scores, and similar test subject classifications
- Psychometric profile of Cognivue® most closely correlated with verbal processing, manual dexterity & speed, visual acuity, visuospatial & executive function, and speed & sequencing, and was in general agreement with that of SLUMS
- Cognivue® is an easy-to-use, computerized cognitive assessment aid, which provides a useful adjunctive part of a full medical work-up to detect early signs of cognitive impairment in patients 55–95 years of age

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.

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