Clinical Correlations

Pilot Study: SLUMS Correlation

A conservative approach to cognitive assessment

Objective

To determine if the Cognivue® clinical scores correspond to the SLUMS 3-level classification of cognitive impairment.

Method

92 subjects ages 55-95 who were at risk for age-related cognitive decline or dementia were given the Cognivue and SLUMS test.

Key Findings

- Cognivue scores ≤50, provide a standard that's consistent with cognitive impairment.
- Cognivue scores ≥75, are consistent with no cognitive impairment.

Cognivue is easy to use and provides a useful part of a full medical work-up for cognitive impairment.

Comparison of the Cognivue® quantitative assessment tool and SLUMS to classify the risk of cognitive impairment

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ABSTRACT

Background: Cognivue® was developed based on clinical experience and NIH funded laboratory research into the neural mechanisms of functional impairment in aging and dementia. The computerized testing tool provides an automated brain functional assessment tool not tied to traditional question & answer testing. Cognivue® consists of 3 sub-batteries of 10 separately scored sub-tests presented in a 10 minute automated sequence. These include basic motor & visual ability (visuo-motor and visual salience), perceptual processing (letter, word, shape, and motion discrimination), and memory processing (letter, word, shape, and motion memory).

Objective: To determine the Cognivue® cut-off scores corresponding to the St. Louis University Mental Status (SLUMS) 3-level classification for risk of cognitive impairment.

Methods: Adults (age 55-95 y) at-risk for age-related cognitive decline or dementia were invited via posters and email to complete the SLUMS and Cognivue® tests. Optimization analyses by positive percent agreement (PPA) and negative percent agreement (NPA), as well as by accuracy and error bias were conducted.

Results: 92 subjects, at 5 sites, completed SLUMS (reference standard) and Cognivue® tests. Based on SLUMS score, 50% were not impaired (>26), 38% were intermediate (26–21), and 12% were impaired (<21). Analyses using 2 measures of objective function (inaccuracy and error bias), showed that a SLUMS cut-off score of <21 (impairment) corresponded to a Cognivue® score of 54.5 (NPA = 0.92; PPA = 0.64). The SLUMS cut-off score of >26 (no impairment) corresponded to a Cognivue® score of 78.5 (NPA = 0.5; PPA = 0.79). Based on the results of 2 separate analysis techniques, results showed that Cognivue® scores between 55–64 corresponded to SLUMS scores for impairment, and Cognivue® scores between 74–79 corresponded to SLUMS scores for no impairment.

Conclusions: Cognivue® scores ≤50 provide a conservative standard for high risk of impairment that will avoid misclassification of an individual as impaired. Cognivue® scores ≥75 provide a conservative cut-off for no risk of impairment that will avoid misclassification of an individual as not unimpaired.

BACKGROUND

- Many tools for assessing cognitive function decline are limited by issues of measurement efficacy, testing bias, or lack of uptake by clinicians
- Cognivue® was developed based on clinical experience and NIH-funded laboratory research into neural mechanisms of functional impairment in aging & dementia
- Cognivue® is a computerized testing tool that provides an automated brain functional assessment tool not tied to traditional question & answer testing. It only takes 10 minutes to complete
- Cognivue® is FDA-cleared for use as an adjunctive tool to aid in assessing cognitive impairment risk in those 55–95 years of age
  - Not intended to be used alone for diagnostic purposes
- Basic research (neurophysiological studies) created the scientific foundation for Cognivue® technology:
  - Learning & memory in development & aging
  - Cortical information processing
  - Influences of multi-stimulus interactions on cortical signal processing (focus on attentional & task effects on cortical neurons)
- Clinical research on aging & dementia contributed to the experimental foundations of Cognivue® technology:
  - 21 published studies, conducted predominantly at University of Rochester Medical Center with NIH funding or at the company (Cognivue, Inc.)

METHODS

Purpose: Compare Cognivue® quantitative assessment tool & SLUMS to determine cut-off scores to classify risk of cognitive impairment

Subjects: Adults (55-95 y) from assisted & independent-living communities, at-risk for age-related cognitive decline or dementia, invited via posters and email to complete SLUMS and Cognivue® tests

Tests:

- Cognivue® quantitative assessment tool includes (Table 1):
  - 3 sub-batteries (visuo-motor ability, perceptual processing, & memory processing) presented in automated sequence over 10 minutes

METHODS (CONT.)

Tests (cont.):

- SLUMS (reference standard)
  - 11-item questionnaire with scores ranging from 0 to 30
  - Designed to measure orientation, memory, attention, & executive functions
- Stratification: >26 = unimpaired; 26–21 = mild cognitive impairment; <21 = impaired

Analyses: 2 different optimization methods used to determine cut-off values for Cognivue® scores corresponding to SLUMS classifications for risk of impairment

- 1st analysis used minimization algorithm to optimize PPA & NPA between Cognivue® & SLUMS scores in the objective function:
  1) NPA = (true negative [TN]/false positive [FP] + TN) x 100%
  2) PPA = (true positive [TP]/false negative [FN] + TP) x 100%
- 2nd minimization algorithm used accuracy & error bias measures in the objective function:
  1) Inaccuracy = 1- (TP + TN/total)
  2) Error bias = contrast ratio (difference/sum) of FPs & FNs

Table 1. Components of Cognivue® quantitative assessment tool

Sub-battery & Sub-test	Description of assessment
Basic motor & visual ability	
Adaptive motor control test	• Visuo-motor responsiveness using speed & accuracy measures • Ability to control rotatory movement of CogniWheel™ in response to rotational visual stimuli
Visual salience test	• Basic visual processing functions • Ability to identify wedge filled by random pattern of black & white dots shown on neutral (gray) background
Perceptual processing	
Letter Discrimination	• Measures perceptual processing of different forms, despite addition of increasing amounts of clutter • Discriminate real English letters from variety of non-letter, letter-like shapes
Word Discrimination	• As above • Discriminate real 3-letter words from 3-letter non-words
Shape Discrimination	• As above • Discriminate a circle filled with a common shape from rest of display filled with other common shapes
Motion Discrimination	• As above • Discriminate a circle filled with 1 direction of dot motion from rest of display filled with another direction of dot motion
Memory processing	
Letter memory	• Memory using specialized sets of visual stimuli • Ability to recall which letter presented as pre-cue, and then select that letter from display of alternative items, despite addition of increasing amounts of clutter • Select correct letter of English alphabet
Word memory	• As above • Select correct 3-letter word
Shape memory	• As above • Select correct shape
Motion memory	• As above • Select correct direction of motion

RESULTS

- 92 subjects total, at 5 sites, completed both SLUMS & Cognivue® tests
- Scores for participants shown in Figure 1, and based on SLUMS score:
  - 50% not impaired (>26)
  - 38% intermediate (26–21)
  - 12% impaired (<21)

1st analysis

- SLUMS impairment cut-off score (<21) minimized to 0.297 at Cognivue® score of 63.5 (NPA = 0.80; PPA = 0.79)
- SLUMS unimpairment cut-off score (>26) minimized to 0.324 at Cognivue® cut-off of 73.5 (NPA = 0.68; PPA = 0.67)

RESULTS (CONT.)

Figure 1. Scatterplot of SLUMS & Cognivue® scores for 92 study participants

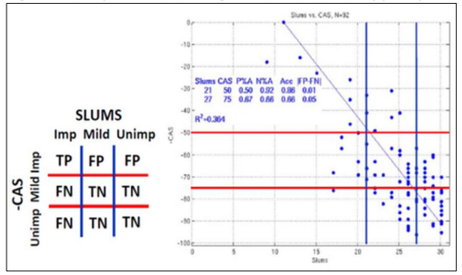

Table to left of scatter plot provides key for relating plot to participant classifications. Above upper horizontal red line shows Cognivue® scores <50, to left of the left vertical blue line shows SLUMS scores <21 denoting high risk of impairment. Below bottom horizontal red line shows Cognivue® scores >75, to right of the right vertical blue line shows SLUMS >27 denoting low risk of impairment. Classification analyses results included in table enclosed in scatter plot.
ACC: accuracy; CAS: Cognivue® assessment system; FN: false negative; FP: false positive; N%A: negative percent agreement; P%A: positive percent agreement; SLUMS: St. Louis University Mental Status; TN: true negative; TP: true positive

2nd analysis

- SLUMS cut-off score <21 (impairment) = Cognivue® score 54.5 (NPA = 0.92; PPA = 0.64)
- SLUMS cut-off score >26 (no impairment) = Cognivue® score 78.5 (NPA = 0.5; PPA = 0.79)

Combined findings

- Based on 2 separate analysis techniques, it was determined that:
  - Cognivue® scores of 55-64 = SLUMS scores for impairment (0-20)
  - Cognivue® scores of 74-79 = SLUMS scores for no impairment (27-30)
- Cognivue® cut-off scores (Figure 2) of:
  - **≤50** provide conservative standard for **high risk of impairment** and avoid misclassification of individual as impaired
  - **≥75** provide conservative cut-off for **no risk of impairment** and avoid misclassification of individual as not unimpaired
- Cognivue® scores between ranges classifying impairment & unimpairment = SLUMS scores of 21-26

Figure 2. Summary of Cognivue® cut-off score analysis

	SLUMS cut-off scores	Cognivue® cut-off scores
High risk of impairment	<21	≤50
Low to moderate risk of impairment	21-26	51-74
No risk of impairment	>26	≥75

CONCLUSIONS

- Cognivue® scores ≤50 and ≥75 consistent with conservative standards for high risk of impairment and no risk of impairment, respectively
- Cognivue® is an easy to use, computerized cognitive assessment aid, which provides a useful adjunctive part of a full medical work-up for cognitive impairment

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.

FDA Clearance Study

Objective

To further validate the reliability and psychometric properties of Cognivue® and to demonstrate the safety and effectiveness of Cognivue as an adjunctive tool to be used by licensed practitioners.

Method

401 subjects ages 55-95 who were at risk for age-related cognitive decline or dementia were given the Cognivue test, SLUMS, and a series of other neuropsychological tests (RAVLT, TMT-A, TMT-B). They were each tested twice within 2-4 weeks.

Key Findings

- Cognivue demonstrated significant correlation between the clinical scores of Cognivue and the SLUMS test.
- Good test-retest reliability of Cognivue test results.
- The psychometric properties of the Cognivue test battery compared to traditional neuropsychological tests.

Cognivue is easy to use and provides a useful part of a full medical work-up for cognitive impairment.

Cold Spring Harbor Laboratory

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

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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 re-test 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 re-test 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 & re-test 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 re-test reliability	• Purpose: Compare scores from repeated administration of Cognivue® to assess re-test 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

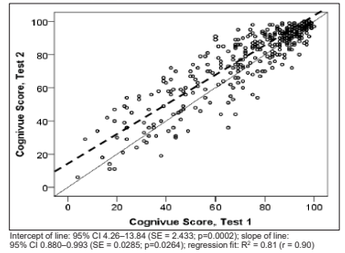
RESULTS

- 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)

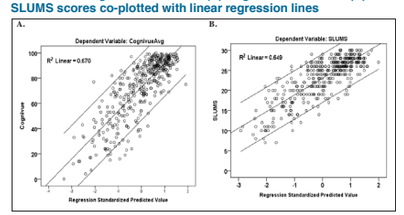
Table 2. Proportion of subjects classified in each risk category by 1st and 2nd Cognivue® tests

	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.

This study was supported by Cognivue, Inc.