

Validation of a New Patient-Reported Outcomes Instrument for Cognitive Impairment

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ABSTRACT

Existing neuropsychological measures have limited sensitivity for mild cognitive impairment (MCI) as well as mild forms of dementia of the Alzheimer's type (DAT). Given evidence that MCI frequently progresses to DAT over time, measurement of MCI is important to the identification of patients who may benefit from early intervention. The patient perspective of the condition, its symptoms and their impact is particularly relevant for a disorder like MCI, where standard measures may not detect deficits. A new instrument, the 55-item Patient Reported Outcomes in Cognition instrument (PROCOG), was developed and evaluated to obtain the patient perspective on MCI and mild DAT. The 5-point Likert scaled items derive from clinical input, patient and informant focus groups in the US and Europe, and from the literature. Total score and scores for 7 subscales can be calculated: memory for recent events, semantic memory, long term memory, cognitive functioning, emotional impact, and social impact of cognitive impairment. Psychometric properties were tested in a sample of 60 MCI patients, 72 mild DAT patients, and 34 controls, age 64+, recruited through outpatient neurology and memory clinics in the US. Item distributions indicated acceptable response spread for most items; most control subjects endorsed the lowest severity options and most DAT subjects endorsed the highest severity options. Scores for MCI patients were intermediate between DAT patients and control group. Internal consistency reliability was excellent for total and subscale scores, ranging from 0.83 to 0.93. Test-retest reliability across 2 weeks was extremely high; intraclass correlations ranged from 0.60 to 0.91. Concurrent validity was supported by moderately high correlation with the QOL-AD (0.56 for all groups combined, $p < 0.05$), a quality of life instrument developed for dementia of the Alzheimer's type (Logsdon et al., 2002). Correlation to the MMSE was -0.39 ($p < 0.05$) for skill loss but lower for the remaining subscales. Results indicate that the PROCOG is a reliable and valid measure for collection of the patient perspective on mild levels of cognitive impairment.

INTRODUCTION

- MCI has been defined as a potentially prodromal phase of dementia of the Alzheimer's Type (DAT) based on clinical presentation and data on progression to DAT over time (Morris et al., 2001; Petersen et al., 1999). Detection and measurement of MCI are therefore of key importance for disease management.
- Neuropsychological measurement can provide detailed information about patient symptom severity but can be time-consuming and may have limited sensitivity for detection of mild to moderate levels of impairment.
- Evaluation of milder cognitive impairment may be enhanced by information on symptoms and their impact on mood, work, and social and daily functioning.
- The PROCOG was developed to address the need for measurement of comprehensive outcomes relevant to cognitive impairment for MCI and mild to moderate DAT.

STUDY OBJECTIVE

Provide empirical data on the psychometric properties of the PROCOG.

PROCOG DEVELOPMENT & TESTING

The PROCOG was developed through review of literature, discussion with experts in the field and focus groups with patients and informants for those patients.

Key psychometric features examined were:



METHODS

Study Design

Data were collected at a single visit from patients recruited from 4 U.S. academic medical centers and memory clinics. Retest data were obtained from 25% of subjects at 2 weeks.

All Patients: Age >64, Center for Epidemiological Studies-Depression Scale (CES-D) <23

Mild DAT Patients: Current diagnosis (last 3 months) of probable DAT (NINCDS-ADRDA) criteria; mild severity based on clinical evaluation.

MCI Patients: Memory complaints with informant corroboration of deficit; self-reported normal general cognitive function; Clinical Dementia Rating (CDR) score of 0.5 (memory box score of 0.5 or 1) within prior 3 months.

Controls: Free of all cognitive complaints and not meeting criteria for DAT or MCI.

Exclusion Criteria: 1) Serious life events in the previous 3 months that may have affected the HRQL of the participant in the judgment of the investigator; 2) Current participation in another research study/clinical trial that includes the use of investigational medications for cognitive indications; 3) History of alcohol or substance abuse consistent with DSM-IV criteria within the past 2 years. NOTE: Subjects could be currently taking prescription or non-prescription medication for their MCI or DAT.

Instruments

PROCOG: 55 items on memory symptoms, cognitive functioning (e.g., executive function, navigation), social functioning, leisure time, self-esteem, mood, and functional status. Likert scale from 0 – 4. Higher values indicate greater severity. A total score is computed as the sum of all items (range: 0 – 220). 7 subscales were identified based on exploratory factor analysis (oblique rotation). Subscale scores are calculated as the mean value of all items within the subscale: Affect/self-esteem, Skill loss, Semantic memory, Memory for recent events, Cognitive functioning, Social impact, Long-term memory (1-item).

SAMPLE ITEMS

Do family members or friends say you repeat the same stories or jokes?
Because of your memory or thinking problems, how often have you cut back on social activities outside the home?
Do you walk into a room and forget why you went there?

Demographics: Basic socio-demographic data. Retest participants were asked 2 questions regarding changes in physical or cognitive health status between the initial completion and the retest.

Neuropsychological Assessments:

Mini-Mental State Exam (MMSE) (Folstein et al., 1975): Evaluate gross cognitive function; **Wechsler Memory Scale Word List Delayed Recall** (Wechsler, 1997a) shown to be a meaningful predictor of longitudinal progression to dementia; **Verbal Fluency:** List all words beginning with "S" (30 sec); **Wechsler Adult Intelligence Scale (WAIS) Digit Span** (Wechsler, 1997b); **WAIS Similarities** (Wechsler, 1997b) for executive functioning.

Depression and Quality of Life Assessments:

Centers for Epidemiological Studies – Depression Scale (CES-D) (Radloff and Teri, 1986; Radloff, 1977) – 20 item self-administered 4-point Likert scale.

Quality of Life-AD Measure (QOL-AD) (Logsdon et al., 1999; 2002) – 13 item self-administered 4-point Likert scale.

METHODS (CONT'D)

Psychometrics

Item and Subscale Analysis: Distributional properties, inter-item correlations.

Internal Consistency Reliability: Cronbach's formula for coefficient alpha, alpha with item deleted.

Test-Retest Reliability and Reproducibility: Intraclass correlations coefficients (ICC), Pearson's correlation coefficients, and change scores.

Concurrent Validity: Pearson's correlation coefficients.

Scaling Success: Item correlated significantly higher with its hypothesized scale (corrected for overlap) than with another scale (MAP program; Hays and Hayashi, 1990).

RESULTS

Subjects

165 patients were recruited: 60 MCI, 72 mild DAT, 33 cognitively intact. See Table 1.

Table 1. Subject Characteristics

	MCI N=60	DAT N=72	Control N=33
Age (Mean ± SD)	76.1 ± 6.7	79.1 ± 6.0	75.8 ± 5.5
Gender (% Male)	57%	53%	39%
Education			
Some College	20%	14%	18%
Postgraduate Degree	27%	25%	18%
Retired	78%	92%	85%

Psychometric Performance of the PROCOG

Item Performance:

- Missing data was minimal in the MCI and control groups, higher in the DAT group.
- Item-to-item correlations were generally acceptable (>0.20) and positive.
- No single item showed evidence of poor performance across all diagnostic groups.
- Many items were not expected to apply to control subjects. The data support this: >55% control subjects responded at the floor value to 41 of the 55 items. In contrast, only 12 items had floor effects for >55% of DAT patients.

Internal Consistency Reliability: Cronbach's alpha values were 0.95 or above.

Test-Retest Reliability and Reproducibility: The mean total score of the PROCOG was 52.1 at T1 and 53.0 at T2 (ns) (mean 10.5 (±3.6) days between, range: 5-18 days). The ICC for the PROCOG total score was 0.90.

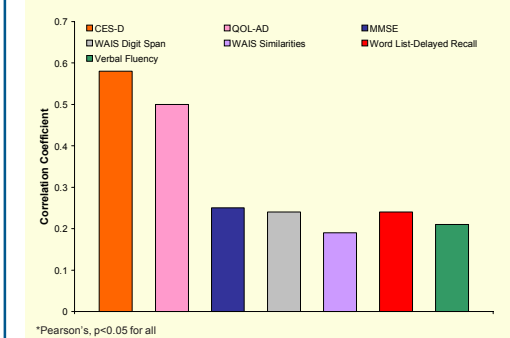
Concurrent Validity: See Figure 1.

RESULTS (CONT'D)

Subscale Evaluation: *For all subjects combined, scaling success was >90% for all subscales. See Table 2. *The internal consistency reliability (Cronbach's alpha) of the subscales was 0.82 or above. *Reproducibility of the subscales was supported by high ICCs from first assessment to second assessment. Score differences between assessment time points were near zero. *Concurrent validity: QOL-AD was statistically significantly correlated with most PROCOG subscales. See Figure 2.

Discriminant Validity of Subscales: Control subjects were distinct from either MCI or DAT patients, with the exception that the long term memory did not distinguish between the groups. Skill loss and memory for recent events subscales showed the most separation between MCI and DAT patients.

Figure 1. PROCOG Total Score Concurrent Validity* (MCI, DAT, and Control Participants)



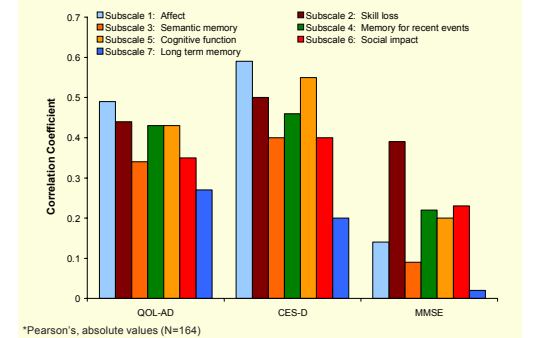
*Pearson's, $p < 0.05$ for all

Table 2. Scaling Success and ICC* (MCI, DAT, and Control Participants)

Subscale	Scaling success	ICC
Affect	100.0	0.83
Skill loss	97.0	0.91
Semantic memory	100.0	0.83
Memory for recent events	95.8	0.86
Cognitive function	91.7	0.81
Social impact	96.3	0.84
Long term memory	n/a	0.50
PROCOG total score	96.6	0.90

*: % with higher or significantly higher scale vs. non-scale-total correlation
N=33

Figure 2. PROCOG Subscale Concurrent Validity* (MCI, DAT, and Control Participants)



*Pearson's, absolute values (N=164)

DISCUSSION

- Psychometric performance of the PROCOG was good to excellent across diagnostic groups:
 - Internal consistency reliability was well above the 0.70 value established as acceptable.
 - Test-retest reliability was high, with total score and nearly all item scores remaining stable across the 2-week retest period.
 - Concurrent validity was good with moderate to high correlation to QOL-AD and CES-D.
- Even in the absence of diagnosed cognitive impairment, control subjects reported use of memory strategies, misplacing objects, and difficulty remembering names of new people. Even against this baseline, the profile of responses for DAT and MCI patients was more severe.
- The PROCOG showed particular strength in measurement of emotional impact of symptoms.
- The PROCOG measures "complex ADLs" (e.g., handling finances and participating in specific leisure activities) which are of key importance in MCI and early DAT.

CONCLUSION

- The PROCOG provides a method for collecting unique information on the impact of cognitive impairment from the perspective of individuals with mild memory and cognition deficits.
- The PROCOG provides valid, reliable data on symptom severity and symptom impact based on the patient's perspective.
- The PROCOG is suitable for use with mild cognitive impairment and mild to moderate DAT.

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