

# Reliable change scores and their relation to perceived change in memory: Implications for the diagnosis of mild cognitive impairment

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Accepted 10 August 2005

## Abstract

The relation between the subjective report of memory problems and objective evidence of the same has been debated with mixed results appearing in the literature. Less is known about the relation between objective change in test performance and the perceptions of cognitive change from family members/friends and trained clinicians. These relations were explored using 5-year longitudinal data from the population-based Canadian Study of Health and Aging. Statistically reliable deterioration in memory test performance was determined using a standardized regression-based (SRB) approach and a Reliable Change Index (RCI) that accounts for aging and practice effects. Among a subsample of persons with no cognitive impairment (NCI) at baseline, there was a moderate relation between reliable test score decline and ratings made by clinicians and informants. No relation, however, was found with the subjective reports of memory difficulties. These findings hold implications for current mild cognitive impairment (MCI) criteria which include subjective, informant and/or clinician ratings of cognitive decline.

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**Keywords:** Reliable change; Test-retest; Mild cognitive impairment; Subjective memory complaints

Amnesic mild cognitive impairment (MCI), which may be a prodromal state for Alzheimer's disease (Petersen, 2003), has received considerable attention in the field of geriatrics. Several definitions have been proposed for MCI and related constructs, though the most commonly cited criteria include: (1) a memory complaint by the patient, family, or physician; (2) objective evidence of memory impairment in relation to age; (3) largely intact general cognitive functions; (4) essentially preserved activities of daily living; and (5) absence of dementia (Smith, Petersen, Parisi, & Ivnik, 1996). While the diagnosis of MCI is ultimately a matter of clinical judgment, it may be informed by self-reported difficulties, informant reports of memory loss and psychometric test performance.

Several cross-sectional studies have found little or no relation between objectively measured memory deficits and self-report of the same (Bolla, Lindgren, Bonaccorsy, & Bleeker, 1991; Jorm et al., 1994; Jungwirth et al., 2004; O'Connor, Pollitt, Roth, Brook, & Reiss, 1990; Schmidt, Berg, & Deelman, 2001; Sunderland, Watts, Baddeley, & Harris, 1986), although exceptions exist (Podewils, McLay, Rebok, & Lyketsos, 2003). Data from a few longitudinal studies have produced more compelling data linking subjective complaints of cognitive loss to incipient dementia

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and changes in objectively measured cognitive test performance (Jorm, Christensen, Korten, Jacomb, & Henderson, 2001; Martin & Zimprich, 2003; Schmand, Jonker, Hooijer, & Lindeboom, 1996), although these results have also been mixed (Jorm et al., 1997). Informant-reported cognitive decline has been shown to be a more reliable indicator of cognitive loss than self report in some studies (e.g., Tierney, Szalai, Snow, & Fisher, 1996), though it is not without bias. Some informants, for example, may under or overestimate the degree of true change in another individual.

As perceptions of cognitive change can play a central role in the diagnosis of MCI and other cognitive disorders, such as dementia, we sought to examine the relation between the change in memory test performance over time and other common approaches to the identification of cognitive loss (i.e., self report, informant report and clinician judgment) within a large sample of older adults. While several cross-sectional and longitudinal studies have examined perceptions of change in comparison to psychometric test performance, we know of no studies that have examined this relation to statistically reliable test score change over two assessments.

Based on our previous research (Frerichs & Tuokko, 2005), we selected a single memory measure and identified reliable deterioration in test performance using two statistical methods: a simple standardized regression-based (SRB) change score approach and a reliable change index (RCI) that corrects for measurement error and practice/aging effects. Both of these methods have been shown to be useful for classifying normal variability in healthy older adults and were strongly associated with diagnostic change (from normal to dementia). These reliable change scores were then compared to dichotomous ratings of cognitive change made by the individual (self report), the report of a person (typically a family member or friend) providing collateral information about the individual (informant report) and the consensus decision of health care professionals who examined the individual in a clinical evaluation to determine the presence of cognitive loss, as opposed to the diagnostic change (clinician rating).

We expected that statistically reliable deterioration on the memory test scores would be weakly related to the ratings of change provided by the individual and more strongly associated with ratings of loss provided by informants. Since clinicians' judgments are typically based on multiple sources of information, a strong association was expected between their ratings of change and actual change in the memory test scores.

## 1. Method

### 1.1. Participants

All participants in this study were involved in the first two waves of the population-based Canadian Study of Health and Aging (CSHA). The CSHA is a large, multi-centre, multi-disciplinary, epidemiological study of health issues including dementia in people over age 65 in Canada (for more details, see the [Canadian Study of Health and Aging Working Group, 1994, 2000](#)). The first wave of the CSHA (CSHA-1) began in 1991 and the second wave (CSHA-2) in 1996.

In CSHA-1 a total of 10,263 persons from the community and institutions were interviewed regarding health-related issues and were screened for cognitive impairment using the Modified Mini-State Examination (3MS; Teng & Chui, 1987). All participants in institutions, all community participants scoring below 78/100 on the 3MS and a subset of community participants scoring 78 or greater on the 3MS were seen for thorough clinical evaluations ( $n = 2914$ ). During the clinical component of the study, a nurse obtained the informant reports (usually from a family member) about the participant's cognitive functioning and functional abilities using Section H of the Cambridge Examination for Mental Disorders (CAMDEX; Roth, Huppert, Tym, & Mountjoy, 1988). The physical examination was conducted by a physician, and the laboratory blood work was conducted for those participants with suspected dementia or delirium to screen for the identifiable disorders. A trained psychometrician administered a standardized neuropsychological test battery (Tuokko, Kristjansson, & Miller, 1995) to those participants who scored 50 or more on the 3MS from the nurse's evaluation. The neuropsychological test results were interpreted by a neuropsychologist. On the basis of all the available information, CSHA clinicians (including physicians, psychologists and nurses) met during a consensus conference and identified each CSHA participant as having one of the following: no cognitive impairment (NCI), cognitive impairment but no dementia (CIND), or dementia using DSM-III-R criteria (American Psychiatric Association, 1987).

CSHA-1 participants who completed these clinical evaluations were revisited approximately 5 years later during CSHA-2 using similar medical, psychological and diagnostic procedures. During CSHA-2 the nurse also administered the Geriatric Depression Scale (GDS; Brink et al., 1982) to the participant. At the consensus conference, clinicians were provided with all the information collected during the CSHA-2 clinical evaluation. In addition, they were provided

with the 3MS score and the participant's self report of activities of daily living obtained during the CSHA-1 screening examination and asked to indicate whether or not, in their opinion, the participant had exhibited cognitive loss since CSHA-1. These ratings were made by the clinicians at CSHA-2 who were blind to the clinical assessment results from CSHA-1. Attrition due to death ( $n = 1534$ ) or other loss of contact ( $n = 231$ ) reduced the number seen for clinical evaluation at CSHA-2 to 1149 participants.

Individuals selected for analysis in this study met the following inclusion criteria: (1) the completion of the CSHA-1 neuropsychological component (English version); and (2) classification as having NCI at CSHA-1 ( $n = 576$ ). Persons with CIND status (who by definition did not meet the criteria for dementia) were not selected so as to minimize the risk of including persons who had already experienced a significant degree of cognitive impairment. Of the 576 meeting the inclusion criteria, 229 that were alive, took part in CSHA-2 and had complete data on all the relevant variables were selected for this study (49 refused participation, 21 lost to follow-up, 160 died and 116 missing data).

## 1.2. Materials

### 1.2.1. Neuropsychological data

Memory functioning was assessed using a modified version of Buschke's Cued Recall (BCR) paradigm (Buschke, 1984; Tuokko & Crockett, 1989). On this selective reminding task, individuals were shown and asked to name 12 pictured items. Recall was tested over three separate learning trials where cues were provided for those items that were not freely recalled by the individual. For the purpose of this paper, the total number of items recalled over all the learning trials was employed, and the highest possible score was 36. This index has been shown to be sensitive to change over time (Tuokko, Vernon-Wilkinson, Weir, & Beattie, 1991).

### 1.2.2. Clinically significant change data

Dichotomous ratings (i.e., cognitive loss and no cognitive loss) of clinically significant change were obtained from three sources: (1) subjective report of change; (2) report of change provided by a knowledgeable informant (usually a family member); and (3) clinicians' judgment of cognitive loss (not necessarily a complete diagnostic change). The subjective report of change was obtained from the participants' responses to the item "Do you feel that you have more problems with memory than most?" from the GDS. The second report of change was derived from Section H of the CAMDEX where informants reported whether the participant had no difficulty or any difficulty (i.e., slight or great) in remembering recent events. The third source of information concerning the cognitive change was consensus clinician judgment at CSHA-2 as to whether or not the participant had exhibited cognitive loss since CSHA-1. Again, the clinicians who participated in making this judgment were blind to the clinical assessment results from CSHA-1.

## 1.3. Data analyses

The main statistical analyses described below were completed with SPSS (SPSS Inc., 1998). Two statistical methods for measuring reliable change were calculated using the total retrieval score from the BCR. These methods have been shown to be accurate with respect to both classification of normal samples and identification of diagnostic change (Frerichs & Tuokko, 2005). The regression-based prediction of follow-up test scores was calculated using a simple SRB change score approach (McSweeney, Naugle, Chelune, & Luders, 1993). The equation was developed using the reference sample of persons who exhibited NCI at CSHA-1 and CSHA-2 ( $n = 166$ ) (see Frerichs & Tuokko, 2005). Baseline performance was the only entered predictor for SRB change scores. The RCI that corrects for measurement error and practice effects (Chelune, Naugle, Luders, Sedlak, & Awad, 1993) was defined as  $((X_2 - X_1) - (M_2 - M_1))/S.D.$ , where  $X_1$  was the individual's score at baseline,  $X_2$  the individual's score at follow-up 5 years later,  $M_1$  the group mean pretest score,  $M_2$  the group mean post-test score and S.D. the observed standard deviation of the difference scores. Classification ratings from the regression equation and the RCI were dichotomized to reflect the presence or absence of statistically reliable deterioration in the test scores. The criterion for reliable change was  $z = -1.645$  (one tailed).

The sensitivity, specificity, positive predictive value, negative predictive value and overall correct classification rate were calculated (Essex-Sorlie, 1995). These values were all expressed as percentages. In this study, reliable deterioration in memory test performance was used as "gold standard" against which the reports of cognitive loss (i.e., subjective report, informant report, consensus rating) were compared.

To determine the statistical significance of the associations between reliable change and clinically significant indices of change, the dichotomous data were analyzed using chi-square tests of significance with alpha set at a conservative 0.01 level (Type I error rate = 1%). An odds ratio (OR) was also calculated to provide a measure of the degree of association between reliable deterioration in test score performance and clinically significant change. An OR reflects the probability or likelihood of cognitive loss when there is evidence of reliable deterioration in test scores versus the incidence of cognitive loss when there is no reliable deterioration. Values near one indicate a lack of association and values over three indicate strong positive associations (Bieliaskas, Fastenau, Lacy, & Roper, 1997).

## 2. Results

Descriptive data for the 229 participants who were selected for inclusion in this study are presented in Table 1. Participants were predominantly Caucasian, ranged in age from 65 to 98 and had 10 years of education on average. Female participants comprised 59% of the sample. The majority of individuals in the sample did not have any reported declines in memory functioning from the perspective of the individuals themselves, an informant and clinicians (see Table 1).

Chi-square analyses revealed that the subjective reports of memory difficulties were not significantly associated with reliable decrements in memory test performance determined using the SRB and RCI methods ( $ps > .05$ ). Pearson product-moment correlation coefficients for these associations were low (RCI:  $r = 0.128$ ; SRB:  $r = 0.089$ ). By contrast, both informant and clinician reports of loss in cognition did have a significant relation with declining memory test performance ( $ps < .001$ ). Correlations between the test score change and informant reports of decline ranged from  $r = 0.36$  (RCI) to  $r = 0.39$  (SRB). Clinician ratings and test score change ranged from  $r = 0.46$  (RCI) to  $r = 0.48$  (SRB). A summary of the classification accuracy statistics and ORs for the RCI and SRB methods are listed in Tables 2 and 3, respectively.

Table 1  
Description of 229 persons with NCI at CSHA-1

Age at CSHA-1 (years)	Mean = 77.46 S.D. = 6.28	Range = 65–98
Education (years)	Mean = 10.99 S.D. = 3.94	Range = 0–25
Gender	94 males	135 females
Subjective rating of memory at CSHA-2	22 reported loss	207 no loss
Informant rating of memory at CSHA-2	42 reported loss	187 no loss
Clinician rating of memory at CSHA-2	66 reported loss	163 no loss

NCI: no cognitive impairment and CSHA: Canadian Study of Health and Aging.

Table 2  
Examination of statistically significant decline on the BCR Total Retrieval score (as defined using the Reliable Change Index with correction for measurement error and practice/aging effects) in relation to multiple perspectives of clinically relevant change ( $n = 229$ )

Report	SENS	SPEC	PPV	NPV	CA	OR
Self report	17.9	92.1	31.8	84.5	79.5	2.55 95% CI [0.96–6.75]
Informant report	48.7	87.9	45.2	89.3	81.2	6.90 95% CI [3.21–14.81]
Clinician rating	74.4	80.5	43.9	93.9	79.5	11.99 95% CI [5.37–26.78]

SENS: sensitivity; SPEC: specificity; PPV: positive predictive value; NPV: negative predictive value; CA: classification accuracy; and OR: odds ratio.

Table 3  
Examination of statistically significant decline on the BCR Total Retrieval score (as defined using the Simple Regression Based method) in relation to multiple perspectives of clinically relevant change ( $n = 229$ )

Report	SENS	SPEC	PPV	NPV	CA	OR
Self report	15.4	91.6	27.3	84.1	78.6	1.98 95% CI [0.72–5.43]
Informant report	51.3	88.4	47.6	89.8	82.1	8.04 95% CI [3.73–17.35]
Clinician rating	76.9	81.1	45.5	94.5	80.3	14.26 95% CI [6.23–32.65]

SENS: sensitivity; SPEC: specificity; PPV: positive predictive value; NPV: negative predictive value; CA: classification accuracy; and OR: odds ratio.

Table 4

Number of individuals with varying degrees of BCR Raw Test score change relative to perceived ratings of cognitive change

Reported loss	Raw BCR Test score change (Time 2 – Time 1)			
	–30 to –21	–20 to –11	–10 to –1	0 to 10
<b>Subjective ratings</b>				
Loss ( <i>n</i> = 22)	0	2	17	3
No loss ( <i>n</i> = 207)	4	15	112	76
<b>Informant ratings</b>				
Loss ( <i>n</i> = 42)	3	11	22	6
No loss ( <i>n</i> = 187)	1	6	107	73
<b>Clinician ratings</b>				
Loss ( <i>n</i> = 66)	4	16	34	12
No loss ( <i>n</i> = 163)	0	1	95	67

The classification accuracies for the SRB method of determining reliable change were slightly higher (i.e., 82.1% and 80.3% for informant and clinician, respectively) than those yielded in relation to the RCI correcting for measurement error and practice/aging effects (i.e., 81.2% and 79.5% for informant and clinician, respectively). The SRB method in relation to the clinician's reports of cognitive loss resulted in the highest OR (OR = 14.26 (95% CI = 6.23, 32.65)). Overall, these findings provided support for the study hypotheses regarding the relation between self, informant and clinician reports of cognitive loss and change score classification (see Table 4).

### 3. Discussion

Reliable declines on test scores were moderately related to informant and clinician ratings of change but weakly related to subjective ratings of change in this study. The latter finding is consistent with the cross-sectional studies that have shown little to no relation between objectively defined memory deficits and subjective memory loss (Bolla et al., 1991; Jorm et al., 1994; Schmidt et al., 2001; Sunderland et al., 1986). Others have speculated on the reasons for this lack of association (Schmidt et al., 2001) but we can only speculate that this pattern may reflect the diminished insight among persons with memory deficits who may tend to overestimate their abilities.

Notably, our findings pertaining to subjective memory complaints do not fit with those obtained in a few other longitudinal studies (Jorm et al., 2001; Martin & Zimprich, 2003). One reason for this discrepancy might be related to the differences in the cognitive measures that were employed. Martin and Zimprich (2003), for example, looked at age-related cognitive change using measures of fluid intelligence and did not specifically examine memory performance in their study. Jorm et al. (2001) did examine memory, which they operationalized using a three-item recall task, an address recall task and a word recognition measure. While the use of a memory measure(s) other than the BCR may have yielded different results, our preliminary analysis of other memory test data that were also collected as part of the CSHA do not support this contention.

Another explanation for the lack of agreement between our findings and those obtained in other studies could relate to the statistical analyses. Whereas Jorm et al. (2001) and Martin and Zimprich (2003) used structural equation modeling to find group trends in their data, we used indices of statistically reliable test score change in our study. It could be argued that the sizable raw score change needed to qualify as a statistically 'reliable' change may have had the effect of weakening any association with subjective memory complaints. Of course, if this held true, we would not have expected to find such a strong relation between the memory test score changes and ratings provided by informants and clinicians.

Our finding of a relation between informants' reports of cognitive loss and reliable memory test score change in this study is consistent with the findings from Tierney et al.'s (1996) study, though their sample was clinic-based rather than population-based. While the strength of the associations was overall modest, clinicians' ratings of loss were more strongly associated with memory test score deterioration than informants' ratings, regardless of which change score method was used. To the best of the authors' knowledge, no other study has demonstrated that reliably determined change on neuropsychological tests is related to the judgments of cognitive loss.

These findings have implications for the diagnostic criteria that are frequently used to identify MCI. We believe that the diagnosis of MCI may be the most reliable and accurate when informed by informant data, clinician judgment and psychometric test data. Though subjective reports of memory decline should not be dismissed as irrelevant (as they may be related to the development of dementia in some individuals), they appear to be less specific indicators of future decline in any given individual than informant and clinician ratings. Refining the criteria for amnesic MCI in a manner that excludes or at least places less emphasis on subjective memory complaints may enhance our ability to detect those individuals who will ultimately progress to dementia over time. We believe that informant and clinician judgments should remain the key components of the MCI criteria, and our findings may be seen as a step toward validating their inclusion. It is, however, important to note that reliable change was not perfectly associated with any index of clinical significance used in this study and is probably best viewed as one component of determining clinically significant change (Beutler & Moleiro, 2001).

We acknowledge that there are limitations to our research. The first relates to attrition (a threat in most longitudinal studies) and in particular, the small sample sizes of the groups identified with cognitive loss over time. Although the CSHA is a population-based study of older adults across Canada, the small number of individuals who showed cognitive loss and completed the neuropsychological assessment at follow-up may not be representative of all persons experiencing cognitive loss. The extent to which these study findings can be generalized, then, may be limited. A second issue is the manner in which cognitive loss was operationalized in this study. We defined change from the perspective of the individual, an informant and clinicians using single questions with dichotomized responses. While this is not substantially different from some other studies that have examined subjective memory complaints, there may be better methods for measuring the reports of cognitive decline, such as the use of detailed questionnaires pertaining to memory functioning. In addition, we examined only one measure of memory, albeit one that has been shown to be particularly related to clinically significant change (Frerichs & Tuokko, 2005) and the use of other or additional memory measures may have yielded different findings.

As an area of future research, we encourage the continued examination of the relations between the varied perspectives of clinical change and objective test score change using a broader array of cognitive measures and symptom reports. Though the debate regarding the value of subjective memory complaints in the prediction of dementia may not be settled, further research will help us to better understand and refine those features and changes that are most likely to herald progressive cognitive decline in later years.

## Acknowledgements

The Canadian Study of Health and Aging was funded by the Seniors' Independence Research Program, through the National Health Research and Development Program (NHRDP) of Health Canada (project no. 6606-3954-MC(S)). Additional funding was provided by Pfizer Canada Incorporated through the Medical Research Council/Pharmaceutical Manufacturers Association of Canada Health Activity Program, NHRDP (project no. 6603-1417-302 (R)), Bayer Incorporated, the British Columbia Health Research Foundation (project no. 38 (93-2) and no. 34 (96-1)). The study was coordinated through the University of Ottawa and the Division of Aging and Seniors, Health Canada. The authors would like to thank all persons involved in the Canadian Studies of Health and Aging. The Alzheimer Society of British Columbia provided training support to the first author. A research personnel award from the Canadian Institutes of Health Research, Institute of Aging provided support to the second author in the preparation of this manuscript.

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