HHS Public Access

Author manuscript

J Alzheimers Dis. Author manuscript; available in PMC 2017 February 25.

Published in final edited form as:

J Alzheimers Dis. 2016 February 25; 51(4): 1145–1155. doi:10.3233/JAD-150729.

The Cognitive Change Index as a Measure of Self and Informant Perception of Cognitive Decline: Relation to Neuropsychological Tests

Chatchawan Rattanabannakit[a,e,f], **Shannon L. Risacher**[b,e], **Sujuan Gao**[c,e], **Kathleen A. Lane**[c,e], **Steven A. Brown**[c,e], **Brenna C. McDonald**[a,b,e], **Frederick W. Unverzagt**[d,e], **Liana G. Apostolova**[a,b,e], **Andrew J. Saykin**[a,b,d,e,*], and **Martin R. Farlow**[a,e]

[a]Department of Neurology, Indiana University School of Medicine, Indianapolis, IN, USA [b]Department of Radiology and Imaging Sciences, Center for Neuroimaging, Indiana University School of Medicine, Indianapolis, IN, USA [c]Department of Biostatistics, Indiana University School of Medicine, Indianapolis, IN, USA [d]Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, USA [e]Indiana Alzheimer Disease Center, Indiana University School of Medicine, Indianapolis, IN, USA [f]Division of Neurology, Department of Internal Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract

Background—The perception of cognitive decline by individuals and those who know them well ("informants") has been inconsistently associated with objective cognitive performance, but strongly associated with depressive symptoms.

Objective—We investigated associations of self-report, informant-report, and discrepancy between self- and informant-report of cognitive decline obtained from the Cognitive Change Index (CCI) with cognitive test performance and self-reported depressive symptoms.

Methods—267 participants with normal cognition, mild cognitive impairment (MCI), or mild dementia were included from a cohort study and memory clinic. Association of test performance and self-rated depression (Geriatric Depression Scale, GDS) with CCI scores obtained from subjects (CCI-S), their informants (CCI-I), and discrepancy scores between subjects and informants (CCI-D; CCI-S minus CCI-I) were analyzed using correlation and analysis of covariance (ANCOVA) models.

Results—CCI-S and CCI-I scores showed high internal consistency (Cronbach alpha 0.96 and 0.98, respectively). Higher scores on CCI-S and CCI-I, and lower scores on the CCI-D, were

*Correspondence to: Dr. Andrew J. Saykin, 355 W. 16th St., Suite 4100, Center for Neuroimaging, Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, Indiana 46202, USA. Tel.: +1 317 963 7501; Fax: +1 317 963 7547; asaykin@iupui.edu.

Preliminary results from this study were presented at the Alzheimer's Association International Conference in Copenhagen, Denmark in 2014 (DOI: 10.1016/j.jalz.2014.05.1598).

Authors' disclosures available online (http://j-alz.com/manuscript-disclosures/15-0729r1).

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: http://dx.doi.org/10.3233/JAD-150729.

associated with lower performance on various cognitive tests in both univariate and in ANCOVA models adjusted for age, gender, and education. Adjustment for GDS slightly weakened the relationships between CCI and test performance but most remained significant.

Conclusion—Self- and informant-report of cognitive decline, as measured by the CCI, show moderately strong relationships with objective test performance independent of age, gender, education, and depressive symptoms. The CCI appears to be a valid cross-sectional measure of self and informant perception of cognitive decline across the continuum of functioning. Studies are needed to address the relationship of CCI scores to longitudinal outcome.

Keywords

Alzheimer's disease; cognitive change Index; cognitive performance; subjective cognitive decline; validation

INTRODUCTION

Individuals in preclinical stages of Alzheimer's disease (AD) often self-perceive decline in their cognition more than a decade prior to a subsequent diagnosis of mild cognitive impairment (MCI) or dementia due to AD [1]. This self-perception of decline often plateaus or reverses as the illness progresses to dementia [2, 3]. The term subjective cognitive decline (SCD) has been used to describe this self-perceived decline in cognition over time [2]. Longitudinal studies have shown that cognitively normal individuals with SCD are at a higher risk to progress to MCI or dementia [4–6].

There is evidence that SCD is associated with increased likelihood of biomarker abnormalities consistent with AD, including findings from cerebrospinal fluid (CSF), structural and functional magnetic resonance imaging (MRI), positron emission tomography (PET), and visual contrast sensitivity [7–16]. However, the associations between SCD and concurrent performance on objective cognitive tests have been inconsistent across studies. Since it is acknowledged that depression, anxiety, and personality factors may affect the perception of cognitive decline and objective cognitive performance [2, 17–21], these variables might contribute to the inconsistent results regarding the relationship between SCD and objective cognitive performance.

Confirmation of cognitive decline by an informant was not considered necessary for the classification of SCD in the initial consensus definition [2]. However, there is increasing evidence that report of one's cognitive decline by family members or any other close observer correlates better with objective cognitive performance than self-report [22, 23] and may be a better predictor of subsequent conversion to MCI or dementia [24–26]. Additionally, compared to informant-only or self-only report of cognitive decline, using mutual report by both subjects and informants has been found to give an even better prediction of cognitive decline, with report of decline by both self and informant shown to be associated with an additive degree of risk for dementia [27, 28].

The discrepancy between self and informant reports of cognitive decline can be interpreted as under- or over-estimation of one's cognitive problems by the subject in relation to the

informant. Limited data has been published to date examining the discrepancy between self and informant reports of cognitive decline and their relationship to objective cognitive performance. Edmonds et al. examined this relationship by using the discrepancy score obtained from self- minus informant-report of the measurement of Everyday Cognition (ECog) questionnaire in a cohort that included cognitively normal and MCI participants, and demonstrated that amnestic MCI subjects who underestimate their decline relative to their informants on ECog memory items show worse performance on an objective recall memory test [29]. Moreover, they also demonstrated that underestimation of cognitive problems was associated with CSF AD biomarkers and progression to dementia. So, instead of using reports of cognitive decline from self-only or informant-only, difference scores from these two reports may show a better relationship to objective cognitive performance or predict the risk of cognitive decline.

The Cognitive Change Index (CCI) is a tool used to assess the perception of cognitive decline in memory, executive function, and language domains from both self and informant perspectives. The present 20 item version of the CCI was adapted from a larger item pool used in previous research on cognitive complaints in older adults by Saykin et al. [8] with item selection based primarily on considerations regarding targeted content within and across the three included domains (episodic memory, executive function, and language) as well as analyses (unpublished data) on associations with neuroimaging, cognitive and outcome variables in an independent sample. The CCI Self and Informant questionnaires are available on request from the authors (contact Dr. Saykin at asaykin@iupui.edu). The memory items from the self-report of the CCI are also used in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort study as a criterion to identify subjects with significant memory concern [10] (also see http://www.adni-info.org). The current study aims to examine the association of CCI scores, obtained from participants and their informants, with objective cognitive performance measures, as well as study their association with subjectively rated depression, in a mixed sample of individuals with normal cognition, MCI, and mild dementia. In addition to using the CCI scores reported by self-only or informant-only in our analyses, we also used the difference score obtained from self- minus informant-reports as a proxy measure for the subjects' insight into their cognitive deficits (excessive worry/overestimation versus lack of insight/underestimation) and examined its relationship with cognition, which has received limited attention in prior studies. Finally, we investigated the effect of depressive symptoms on the association between CCI scores and objective cognitive performance.

MATERIALS AND METHODS

Setting and participants

The study was approved by the Indiana University (IU) Institutional Review Board before data access and analysis. We collected data from participants with Mini-Mental State Examination (MMSE) ≥18 from the local National Institute on Aging-Indiana Alzheimer Disease Center (IADC) cohort and the Memory Clinic (MC) of the IU Health Neuroscience Center between January 2013 and November 2014. Individuals who are enrolled in the IADC are volunteer participants recruited via a variety of mechanisms, including community

outreach and advertisements, clinical referral, and participation in studies of familial genetic disorders. Patients seen in the MC are initially evaluated due to clinical memory concerns and may present with problems in other domains as well. After excluding subjects with incomplete CCI data, 267 adults and their informants were included. Demographic, family history, medical history, and neuropsychological assessment data were collected.

Clinical diagnoses of normal cognition, MCI, or dementia were determined by consensus between two or more clinicians. Cognitively normal participants (CN) were defined as having no deficit in instrumental activities of daily living and no evidence of objective cognitive impairment. Diagnosis of MCI was based upon the Petersen criteria [30] and defined as having a report of cognitive change by the participant, informant, and/or clinician with objective cognitive impairment greater than 1.5 standard deviations outside the age-adjusted normative mean in at least one cognitive domain and intact instrumental activities of daily living. Diagnosis of dementia was based upon standard criteria for dementia of the Alzheimer's type or for other non-Alzheimer's dementing disorders including DSM-IV [31], NINCDS-ADRDA [32] for diagnosis of AD, NINDS-AIREN criteria for the diagnosis of vascular dementia [33], Neary consensus on clinical diagnosis criteria for frontotemporal lobar degeneration [34] and McKeith's criteria for the clinical diagnosis of dementia with Lewy bodies [35].

Cognitive and behavioral assessments

Participants underwent detailed neuropsychological evaluation, including measures of general cognition, memory, language, attention, executive function, and visuospatial ability. Only cognitive tests results obtained within three months of the CCI were included in the analysis. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery of neuropsychological tests [36] was used in the MC, while another extensive battery of tests including those from the National Alzheimer's Coordinating Center (NACC) Uniform Data Set was used in the IADC cohort. The test batteries shared the MMSE [37], Animal Fluency [38], Constructional Praxis [39] and Trail Making Test (Parts A and B) [40]. The CERAD incorporates a shorter 15-item Boston Naming Test (BNT) [36] while the full 60-item BNT [41] was used in the IADC cohort. Notably, the two study subject sources used different verbal learning tests: The Rey Auditory Verbal Learning Test (RAVLT) [42] was used in the IADC cohort while the CERAD's word list memory, recall, and recognition test was used in the MC. The CERAD's word list memory test was also used in some IADC participants in addition to the RAVLT. While the Geriatric Depression Scale (GDS) was used in both settings, the shorter 15-item GDS [43] was used in the IADC cohort, while the longer 30-item GDS [44] was used in the MC. As all items in the short 15-item scale were included in the 30-item scale, we transformed the 30-item GDS score into 15-item GDS score using each response in individual items and used only the 15-item GDS score in the present analysis.

Cognitive change index

The CCI consists of two parallel sets of 20 items asking participants and their informants to rate the participant's cognitive function compared to the previous five years. Participants and informants were asked to complete the CCI by responding to each item on a 1 to 5 Likert

scale with higher scores indicating greater decline (1 = no change or normal ability, 2 = minimal change or slight/occasional problem, 3 = some change or mild problem, 4 = clearly noticeable change or moderate problem, 5 = much worse or severe problem). 12 of the 20 CCI items focus on memory performance (e.g., “recalling information when I really try”, “remembering things that have happened recently”), 5 of the 20 items evaluate one’s executive function (e.g., “focusing on goals and carrying out a plan”), and 3 of the 20 items evaluate language (e.g., “understanding conversations”). In the informant-report, there are also questions asking about the informant’s relationship to the participant, including average number of hours per week spent with participant, number of years he/she has known the participant, and confidence in the accuracy of his/her rating. All but one participant and 240 out of 267 informants completed the CCI during in-person visits. The remaining subject/informants completed the questionnaire elsewhere and mailed it in.

The sum of all 20 items of the CCI self-report (CCI-S, range 20 to 100) and the CCI informant-report (CCI-I, range 20 to 100) were used in this study. The difference score between self and informant reports (CCI-D, range −80 to 80) was calculated as CCI-S minus CCI-I to demonstrate the discrepancy between self- and informant-reports. A positive value on the CCI-D indicates that the participant reported more severe cognitive impairment than his or her informant, while a negative value indicates that the informant reported greater cognitive impairment than the participant did.

Statistical analysis

Descriptive statistics of baseline clinical characteristics were calculated for all participants, including frequency and percentage for categorical variables and mean and standard deviation for continuous variables. Clinical characteristics, including age, gender, race, years of education, family history of dementia, diagnosis, CCI scores, and neuropsychological performance scores were compared between recruitment sites (IADC versus MC) using *t*-tests for continuous variables and Fisher’s exact tests for categorical variables. CCI scores and cognitive test scores were also compared between recruitment sites and diagnostic groups using analysis of covariance models (ANCOVA) adjusted for age, education, gender, and diagnosis. Following a significant overall effect, pair-wise comparisons were similarly made and *p*-values were adjusted using Sidak’s multiple comparison method. Associations between CCI-S, CCI-I, and CCI-D scores and objective cognitive tests scores and GDS scores were assessed using Pearson’s correlation coefficients. Partial correlation coefficients derived from ANCOVA models adjusted for various combinations of age, gender, education, GDS, and family history of dementia were also calculated to show the association after eliminating the influence of these covariates. Because of differences in the cognitive assessment by cohort, we calculated Z-scores for the different BNTs and verbal learning tests to combine participants from different cohorts in the analysis. The data used to standardize the 60-item BNT and the RAVLT came from the first exposure to the test of CN participants from the entire population of the IADC. The data used to standardize the 15-item BNT and the CERAD learning and delayed recall came from the control subjects in Morris et al [36]. Statistical analyses were performed using SAS version 9.4.

RESULTS

Participant and informant demographic characteristics

There were 170 (63.7%) participants from the IADC cohort and 97 (36.4%) from the MC. Demographic and cognitive comparisons of the two cohorts can be seen in Table 1. The mean age of all participants was 67.8 ± 11.2 years (range 25.1–91.0 years) and 51.7% were female. There was no difference in age between participants from the two cohorts, but the IADC cohort had a significantly greater proportion of females. The mean education of all participants was 15.6 ± 2.8 years. IADC participants were significantly more educated than participants from the MC. 139 (52.1%) of all participants had a family history of dementia in at least one parent. Participants from the IADC had a significantly higher proportion of parental history of dementia compared to those from the MC. Overall, 149 (55.8%) participants were classified as CN, 96 (36.0%) had a diagnosis of MCI, and 22 (8.2%) had a diagnosis of dementia. The MCI diagnoses consisted of single-domain amnestic MCI (44.8%), multiple-domain amnestic MCI (47.9%), and non-amnestic MCI (7.3%). AD was the main clinical diagnosis in participants with dementia (50.0%), followed by frontotemporal dementia (22.7%), and dementia with Lewy bodies (13.6%). There was a significant difference in the diagnoses between participants from the IADC and the MC. Most participants from the IADC (75.9%) were CN, whereas most participants from the MC (73.2%) had the clinical diagnosis of MCI.

Most informants were the participant's spouses or partners (66.9%), followed by children (20.2%), and others (12.9%), including friends, siblings, and other relatives. The mean time that informants spent with participants was 75.4 ± 60.4 hours per week, and they had known participants for a mean of 38.8 ± 15.9 years. 65.3% of all informants rated their confidence in the accuracy of their CCI evaluation as very high, 31.4% as good, 2.5% as low, and 0.8% as very low.

Performance characteristics of CCI and objective neuropsychological performance

Participants from the MC had significantly higher CCI-S and CCI-I scores than participants from the IADC (Table 1). These differences remained significant even after adjusting for age, gender, education, diagnosis, family history of dementia, and GDS ($p = 0.0117$ for CCI-S; $p = 0.0001$ for CCI-I).

After adjusting for age, gender, education, and diagnosis, no difference in cognitive test performance or GDS score was found between participants from IADC and the MC ($p \geq 0.05$) except for the BNT, where participants from the IADC had significantly higher scores ($p = 0.0001$).

Internal consistency of CCI-S and CCI-I and association between these reports

Cronbach alpha scores were 0.96 for the CCI-S and 0.98 for the CCI-I, suggesting good internal consistency. CCI scores obtained from subjects and informants were moderately correlated with each other ($r = 0.53$, $p < 0.0001$). Looking within CCI-I and CCI-S separately, the scores obtained from memory, executive function, and language subscales were significantly correlated with the total score and each subscale score (rs from 0.71 to

0.98, all $p < 0.0001$, Supplementary Table 1). The subjective subscale scores were also significantly correlated with the informant subscale scores (rs from 0.38 to 0.53, all $p < 0.0001$).

CCI scores in each diagnostic subgroup

CCI scores from participants and informants were lowest in the CN group compared to the MCI or dementia groups, as expected (all $p < 0.0001$, except $p = 0.04$ for CCI-S between CN and MCI) (see Table 2 and Fig. 1). CCI-I scores were significantly higher in those with dementia ($p = 0.03$) compared to MCI, whereas the CCI-S did not show a significant difference between these two diagnosis subgroups ($p = 0.97$). CCI-D scores were observed to be positive in the CN subgroup, but the opposite (i.e., CCI-I > CCI-S) was seen in participants with MCI or dementia. Significantly lower CCI-D scores were found in participants with dementia compared to those in the MCI ($p = 0.01$) and CN ($p < 0.0001$) groups. Participants with MCI also had significantly lower CCI-D scores ($p < 0.0001$) than those in the CN group.

Association of CCI scores with neuropsychological test performance

Univariate analysis showed that CCI-S and CCI-I were significantly correlated (all $p < 0.001$; Table 3) with objective tests of global cognition (MMSE, $r = -0.27$ and -0.43), spatial ability (Constructional Praxis, $r = -0.28$ and -0.26), memory (Z-score of verbal learning tests; total learning and delayed recall scores, rs from -0.47 to -0.31), processing speed and executive function (Trail Making Test Parts A and B, seconds to complete, rs from 0.36 to 0.45) and language (Z-score of Boston Naming Test, Animal Fluency, rs from -0.46 to -0.28). Higher CCI-S or CCI-I scores were associated with poorer cognitive performance. CCI-D showed significant ($p < 0.05$) but weaker correlations than CCI-S or CCI-I with all cognitive tests except for Constructional Praxis ($p = 0.57$). As expected, all significant associations between CCI-D and cognitive performance were in the opposite direction compared to the relation of CCI-S and CCI-I scores ($r = -0.16$ and -0.15 for Trail Making Test Parts A and B, and $r = 0.19$ to 0.26 for other cognitive tests) corresponding to loss of insight into one's cognitive deficits among the cognitively impaired. Significant positive associations were shown between the GDS and both the CCI-S ($r = 0.56$, $p < 0.0001$) and CCI-I ($r = 0.39$, $p < 0.0001$), but not between GDS and CCI-D ($p = 0.41$). Adjustments for age, gender, and education did not meaningfully alter the pattern of findings with the exception of the relationship of CCI-D to the Trail Making Test Part A and B which was rendered non-significant.

Effect of depressive symptoms on the association of CCI scores and objective cognitive performance

Most of the relationships between CCI scores and objective cognitive test performances reported above were slightly attenuated but remained significant after adjusting for depressive symptoms as measured by the GDS, except for the relationship between CCI-D and Trail Making Test Part B, which was rendered non-significant (see Table 4). The relationship between CCI-S and MMSE was also attenuated to non-significant after adjusting for age, gender, education, and GDS score.

DISCUSSION

This study reports on the internal consistency and initial concurrent validity of the Cognitive Change Index in a mixed sample of cognitively normal, MCI, and demented participants drawn from a tertiary care memory clinic and a research-based Alzheimer Disease Center. Participant and informant ratings of cognitive impairment on the CCI showed good internal consistency and were related to objective cognitive test scores even after adjusting for demographics and depressive symptoms. Construct validity in the context of the CCI addresses the coherence of the overall cognitive change concept based on self or informant-perceived changes in cognition. One relevant type of external validity can be demonstrated by the correlation of each subscale score with objective tests in the same cognitive domain. We found that subscales of the CCI are highly correlated with objective tests in the same domain, but also correlate with objective tests in other domains. This finding may suggest that a given cognitive complaint may stem from impairment in more than one domain, highlighting the challenge of developing cognitive tests or questionnaires that are “pure” measures of a function.

As expected, participant CCI scores were lowest in the cognitively normal group and elevated in the MCI and dementia groups, which did not differ from each other. Also as expected, informant report of cognitive impairment progressively increased across diagnostic groups with the lowest scores reported for cognitively normal participants and highest scores for demented participants. Lastly, the CCI discrepancy score (CCI-D) showed a clear trend for increasing distance between informant and participant ratings (informant > participant) with increasing cognitive impairment, likely reflecting a progressive deterioration in insight or awareness among participants.

Similar to previous studies, our study demonstrated that self-perceived cognitive decline was highly correlated with psychological symptoms [16, 19, 21, 45–47], and informant-report of subject’s cognitive decline correlated better than self-report to objective cognitive tests [22, 23]. We used the GDS to assess depressive symptoms in our study. Although the GDS may be not an accurate test for depression in patients with dementia [48], evidence has shown that the validity of the GDS depends on the degree of cognitive impairment, such that more severe cognitive impairment may reduce the sensitivity of the GDS in detection of depression [49, 50]. In our study, the mean MMSE is quite high (mean MMSE was 28.2 ± 1.9). Even in our demented participants, who were mostly at a mild level, the mean MMSE was 25.5 ± 3.1. It is very likely that the GDS is valid for this specific application in our study.

The CCI-D had the weakest association with cognitive test scores but it was the only score that was not associated with the GDS. As the CCI-I showed the strongest relationship to objective cognitive performance among the various CCI metrics examined, it may be the most valid score to use in assessing an individual’s perceived cognitive decline, especially in later symptomatic stages of disease. However, there is evidence that level of awareness in subjects with different levels of cognitive impairment (controls, MCI, AD) varies among studies within and between clinical or research-based settings [51]. As our MCI participants had average negative value for CCI-D scores (indicating CCI-I was worse than CCI-S), this

could reflect reduced awareness in our MCI sample and attenuate the association of CCIS and objective cognitive tests. Future studies in other populations may show different results for the correlation between self- and informant-report of cognitive decline and cognitive tests, and such differences may be informative with regard to the role of sample characteristics such as insight and awareness. Furthermore, we also demonstrated that GDS scores can slightly weaken the relationship of the CCI with objective cognitive performance, suggesting that CCI-I scores adjusted for GDS score may be preferred to minimize the influence of depressive symptoms. Alternatively, if GDS or similar data is unavailable, the CCI-D might be preferable to use in analyses, as it was not significantly associated with the GDS. The use of discrepancy scores appears promising and warrants further study.

CCI-S and CCI-I scores were higher in participants from the MC even after adjusting for several potentially important covariates. It is possible that there is a higher level of concern in participants from the MC, which is a medical help-seeking setting, compared to the IADC, which is a clinical research-based setting, resulting in higher CCI ratings for MC participants. Unfortunately, no specific independent data was available from subjects or informants regarding level of memory concern that would permit us to investigate this question further.

A high proportion of our participants had a family history of dementia in at least one parent, which was highest in participants from the IADC. This is likely attributable to greater motivation of individuals with family history of dementia to volunteer for dementia-related research relative to those without such a history. There is limited evidence regarding whether genetic variation affects the concurrent perception of cognitive decline or objective cognitive performance. Risacher et al. examined the effect of APOE ε4 genotype on cognitive complaints, objective cognitive performance, and various AD imaging and CSF biomarkers in participants with normal cognition, SCD and early MCI [10]. They found that APOE ε4 status was not associated with cognitive complaints, but did associate significantly with selected measures of memory and executive performance across diagnostic groups. To investigate the effect of family history of dementia, we used it as a covariate in a multivariate model (also adjusted for age, gender, and education), and found that none of the relationships of CCI scores and objective cognitive performance were significantly altered (Supplementary Table 2).

Among various objective cognitive associations included in our study, only performance on the BNT was significantly superior in participants from the IADC relative to patients from the MC after accounting for the influence of age, gender, education, and diagnosis. However, there is evidence that BNT scores are significantly correlated with estimated verbal intelligence as measured by the Wechsler Adult Intelligence scale–Revised (1981) Vocabulary subtest score or the Gates-MacGinitie Reading Vocabulary Test [52, 53]. As we did not include these tests in our sample, we cannot rule out verbal ability as a factor accounting for the BNT difference between participants from IADC and the MC. However, regarding the significant difference of BNT Z-scores between the two sources of our participants, we investigated the effect of sample (IADC versus MC) by adding it as a covariate in multivariable models, and found that all associations between the CCI and Z-score of BNT were still significant (all $p < 0.01$) (Supplementary Table 3).

There are some limitations to our study. First, this is a cross-sectional study so we could not determine whether CCI scores predict actual decline or disease progression. Future studies of the CCI are needed to address test-retest reliability of each form, the relationships to AD biomarkers, rate of clinical progression, and longitudinal outcomes. These data are needed to establish the utility for risk determination and other clinical applications. It should be also noted that self- and informant measures of perceived cognitive decline may be differentially associated with AD biomarkers and cognitive outcomes in a stage-specific manner, i.e., the pattern of associations may change over the course of progression from normal cognition to MCI or dementia. Secondly, even though our statistical analyses demonstrated that age did not influence our results, on average our participants were relatively young, so these findings may not be generalizable to studies of older individuals. Third, apart from depressive symptoms, we did not have information regarding other psychological or personality variables. Evidence suggests that a subject's anxiety, long-standing personality traits, and/or meaning-in-life also influence SCD [2, 19–21, 45, 54]. Further, it should be noted that informant-reported CCI may be affected by psychological conditions or personality traits of informants as well. Future studies that include more extensive psychological and personality measures in both subjects and informants are warranted.

In conclusion, the CCI shows good internal consistency and moderately strong relationships with objective cognitive performance, and as such appears to be a valid cross-sectional marker of self and informant perception of cognitive decline across the continuum of cognitive function. Future research is needed to determine the relationship of subjective and informant report of cognitive function to longitudinal outcome. Prospective longitudinal cohort studies including the CCI along with AD biomarker measurement in individuals at risk for MCI and dementia would likely provide valuable mechanistic data regarding stage-specific sensitivity and specificity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported in part by grants from the NIH including P30 AG10133, R01 AG19771, R01 LM011360, R00 LM011384, R01 AG040770, R01 AG045157, K01 AG049050 and K02 AG048240; the Indiana CTSI (NIH grants U54 RR025761, RR027710-01, and RR020128), the Alzheimer's Association (New Investigator Research Grant to SLR), the Indiana University Health-Indiana University School of Medicine Strategic Research Initiative and NSF grant IIS-1117335. Support was also provided by The Faculty of Medicine, Siriraj Hospital, Mahidol University, which awarded a fellowship to Dr. Chatchawan Rattanabannakit for doing research in Alzheimer's disease and other dementias at Indiana University School of Medicine, Indianapolis, IN, USA. The authors also thank all staff and participants from the National Institute on Aging–Indiana Alzheimer Disease Center and the Memory Clinic at the Indiana University Health Neuroscience Center for their contribution to this research, especially our nurses, coordinators, and neuropsychologists.

REFERENCES

1. Reisberg B, Prichep L, Mosconi L, John ER, Glodzik-Sobanska L, Boksay I, Monteiro I, Torossian C, Vedvyas A, Ashraf N, Jamil IA, de Leon MJ. The pre-mild cognitive impairment, subjective cognitive impairment stage of Alzheimer's disease. Alzheimers Dement. 2008; 4:S98–S108. [PubMed: 18632010]

2. Jessen F, Amariglio RE, van Boxtel M, Breteler M, Ceccaldi M, Chetelat G, Dubois B, Dufouil C, Ellis KA, van der Flier WM, Glodzik L, van Harten AC, de Leon MJ, McHugh P, Mielke MM, Molinuevo JL, Mosconi L, Osorio RS, Perrotin A, Petersen RC, Rabin LA, Rami L, Reisberg B, Rentz DM, Sachdev PS, de la Sayette V, Saykin AJ, Scheltens P, Shulman MB, Slavin MJ, Sperling RA, Stewart R, Uspenskaya O, Vellas B, Visser PJ, Wagner M. Subjective Cognitive Decline Initiative Working G. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. Alzheimers Dement. 2014; 10:844–852. [PubMed: 24798886]

3. Buelow MT, Tremont G, Frakey LL, Grace J, Ott BR. Utility of the cognitive difficulties scale and association with objective test performance. Am J Alzheimers Dis Other Demen. 2014; 29:755–761. [PubMed: 24928819]

4. Reisberg B, Shulman MB, Torossian C, Leng L, Zhu W. Outcome over seven years of healthy adults with and without subjective cognitive impairment. Alzheimers Dement. 2010; 6:11–24. [PubMed: 20129317]

5. Kryscio RJ, Abner EL, Cooper GE, Fardo DW, Jicha GA, Nelson PT, Smith CD, Van Eldik LJ, Wan L, Schmitt FA. Self-reported memory complaints: Implications from a longitudinal cohort with autopsies. Neurology. 2014; 83:1359–1365. [PubMed: 25253756]

6. Mitchell AJ, Beaumont H, Ferguson D, Yadegarfar M, Stubbs B. Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: Meta-analysis. Acta Psychiatr Scand. 2014; 130:439–451. [PubMed: 25219393]

7. Visser PJ, Verhey F, Knol DL, Scheltens P, Wahlund LO, Freund-Levi Y, Tsolaki M, Minthon L, Wallin AK, Hampel H, Burger K, Pirttila T, Soininen H, Rikkert MO, Verbeek MM, Spiru L, Blennow K. Prevalence and prognostic value of CSF markers of Alzheimer's disease pathology in patients with subjective cognitive impairment or mild cognitive impairment in the DESCRIPA study: A prospective cohort study. Lancet Neurol. 2009; 8:619–627. [PubMed: 19523877]

8. Saykin AJ, Wishart HA, Rabin LA, Santulli RB, Flashman LA, West JD, McHugh TL, Mamourian AC. Older adults with cognitive complaints show brain atrophy similar to that of amnestic MCI. Neurology. 2006; 67:834–842. [PubMed: 16966547]

9. Jessen F, Feyen L, Freymann K, Tepest R, Maier W, Heun R, Schild HH, Scheef L. Volume reduction of the entorhinal cortex in subjective memory impairment. Neurobiol Aging. 2006; 27:1751–1756. [PubMed: 16309795]

10. Risacher SL, Kim S, Nho K, Foroud T, Shen L, Petersen RC, Jack CR Jr, Beckett LA, Aisen PS, Koeppe RA, Jagust WJ, Shaw LM, Trojanowski JQ, Weiner MW, Saykin AJ. Alzheimer's Disease Neuroimaging Initiative (ADNI). APOE effect on Alzheimer's disease biomarkers in older adults with significant memory concern. Alzheimers Dement. 2015; 11:1417–1429. [PubMed: 25960448]

11. Wang Y, Risacher SL, West JD, McDonald BC, Magee TR, Farlow MR, Gao S, O'Neill DP, Saykin AJ. Altered default mode network connectivity in older adults with cognitive complaints and amnestic mild cognitive impairment. J Alzheimers Dis. 2013; 35:751–760. [PubMed: 23481685]

12. Scheef L, Spottke A, Daerr M, Joe A, Striepens N, Kolsch H, Popp J, Daamen M, Gorris D, Heneka MT, Boecker H, Biersack HJ, Maier W, Schild HH, Wagner M, Jessen F. Glucose metabolism, gray matter structure, and memory decline in subjective memory impairment. Neurology. 2012; 79:1332–1339. [PubMed: 22914828]

13. Amariglio RE, Becker JA, Carmasin J, Wadsworth LP, Lorius N, Sullivan C, Maye JE, Gidicsin C, Pepin LC, Sperling RA, Johnson KA, Rentz DM. Subjective cognitive complaints and amyloid burden in cognitively normal older individuals. Neuropsychologia. 2012; 50:2880–2886. [PubMed: 22940426]

14. Merrill DA, Siddarth P, Saito NY, Ercoli LM, Burggren AC, Kepe V, Lavretsky H, Miller KJ, Kim J, Huang SC, Bookheimer SY, Barrio JR, Small GW. Self-reported memory impairment and brain PET of amyloid and tau in middle-aged and older adults without dementia. Int Psychogeriatr. 2012; 24:1076–1084. [PubMed: 22335970]

15. Risacher SL, Wudunn D, Pepin SM, MaGee TR, McDonald BC, Flashman LA, Wishart HA, Pixley HS, Rabin LA, Pare N, Englert JJ, Schwartz E, Curtain JR, West JD, O'Neill DP, Santulli RB, Newman RW, Saykin AJ. Visual contrast sensitivity in Alzheimer's disease, mild cognitive impairment, and older adults with cognitive complaints. Neurobiol Aging. 2013; 34:1133–1144. [PubMed: 23084085]

16. Schultz SA, Oh JM, Koscik RL, Dowling NM, Gallagher CL, Carlsson CM, Bendlin BB, LaRue A, Hermann BP, Rowley HA, Asthana S, Sager MA, Johnson SC, Okonkwo OC. Subjective memory complaints, cortical thinning, and cognitive dysfunction in middle-aged adults at risk for AD. Alzheimers Dement (Amst). 2015; 1:33–40. [PubMed: 25938132]
17. Smith GE, Petersen RC, Ivnik RJ, Malec JF, Tangalos EG. Subjective memory complaints, psychological distress, and longitudinal change in objective memory performance. Psychol Aging. 1996; 11:272–279. [PubMed: 8795055]
18. Yaffe K, Blackwell T, Gore R, Sands L, Reus V, Browner WS. Depressive symptoms and cognitive decline in non-demented elderly women: A prospective study. Arch Gen Psychiatry. 1999; 56:425–430. [PubMed: 10232297]
19. Reid LM, Maclullich AM. Subjective memory complaints and cognitive impairment in older people. Dement Geriatr Cogn Disord. 2006; 22:471–485. [PubMed: 17047326]
20. Elfgren C, Gustafson L, Vestberg S, Passant U. Subjective memory complaints, neuropsychological performance and psychiatric variables in memory clinic attendees: A 3-year follow-up study. Arch Gerontol Geriatr. 2010; 51:e110–e114. [PubMed: 20211500]
21. Slavin MJ, Brodaty H, Kochan NA, Crawford JD, Trollor JN, Draper B, Sachdev PS. Prevalence and predictors of “subjective cognitive complaints” in the Sydney Memory and Ageing Study. Am J Geriatr Psychiatry. 2010; 18:701–710. [PubMed: 21491631]
22. Gavett R, Dunn JE, Stoddard A, Harty B, Weintraub S. The Cognitive Change in Women study (CCW): Informant ratings of cognitive change but not self-ratings are associated with neuropsychological performance over 3 years. Alzheimer Dis Assoc Disord. 2011; 25:305–311. [PubMed: 22086219]
23. Rami L, Mollica MA, Garcia-Sanchez C, Saldana J, Sanchez B, Sala I, Valls-Pedret C, Castellvi M, Olives J, Molinuevo JL. The Subjective Cognitive Decline Questionnaire (SCD-Q): A validation study. J Alzheimers Dis. 2014; 41:453–466. [PubMed: 24625794]
24. Slavin MJ, Sachdev PS, Kochan NA, Woolf C, Crawford JD, Giskes K, Reppermund S, Trollor JN, Draper B, Delbaere K, Brodaty H. Predicting cognitive, functional, and diagnostic change over 4 years using baseline subjective cognitive complaints in the Sydney Memory and Ageing Study. Am J Geriatr Psychiatry. 2014; 9:906–914. [PubMed: 25441053]
25. Rabin LA, Wang C, Katz MJ, Derby CA, Buschke H, Lipton RB. Predicting Alzheimer’s disease: Neuropsychological tests, self-reports, and informant reports of cognitive difficulties. J Am Geriatr Soc. 2012; 60:1128–1134. [PubMed: 22690986]
26. Caselli RJ, Chen K, Locke DE, Lee W, Roontiva A, Bandy D, Fleisher AS, Reiman EM. Subjective cognitive decline: Self and informant comparisons. Alzheimers Dement. 2014; 10:93–98. [PubMed: 23562429]
27. Gifford KA, Liu D, Lu Z, Tripodis Y, Cantwell NG, Palmisano J, Kowall N, Jefferson AL. The source of cognitive complaints predicts diagnostic conversion differentially among nondemented older adults. Alzheimers Dement. 2013; 10:319–327. [PubMed: 23871264]
28. Gifford KA, Liu D, Carmona H, Lu Z, Romano R, Tripodis Y, Martin B, Kowall N, Jefferson AL. Inclusion of an informant yields strong associations between cognitive complaint and longitudinal cognitive outcomes in non-demented elders. J Alzheimers Dis. 2015; 43:121–132. [PubMed: 25061054]
29. Edmonds EC, Delano-Wood L, Galasko DR, Salmon DP, Bondi MW. Alzheimer’s Disease Neuroimaging I. Subjective cognitive complaints contribute to misdiagnosis of mild cognitive impairment. J Int Neuropsychol Soc. 2014; 20:836–847. [PubMed: 25156329]
30. Petersen RC, Morris JC. Mild cognitive impairment as a clinical entity and treatment target. Arch Neurol. 2005; 62:1160–1163. discussion 1167. [PubMed: 16009779]
31. American Psychiatric Association. DSM-IV, Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: APA Press; 1994.
32. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer’s disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer’s Disease. Neurology. 1984; 34:939–944. [PubMed: 6610841]

33. Roman GC, Tatemichi TK, Erkinjuntti T, Cummings JL, Masdeu JC, Garcia JH, Amaducci L, Orgogozo JM, Brun A, Hofman A, et al. Vascular dementia: Diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology. 1993; 43:250–260. [PubMed: 8094895]
34. Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Freedman M, Kertesz A, Robert PH, Albert M, Boone K, Miller BL, Cummings J, Benson DF. Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. Neurology. 1998; 51:1546–1554. [PubMed: 9855500]
35. McKeith IG, Dickson DW, Lowe J, Emre M, O'Brien JT, Feldman H, Cummings J, Duda JE, Lippa C, Perry EK, Aarsland D, Arai H, Ballard CG, Boeve B, Burn DJ, Costa D, Del Ser T, Dubois B, Galasko D, Gauthier S, Goetz CG, Gomez-Tortosa E, Halliday G, Hansen LA, Hardy J, Iwatsubo T, Kalaria RN, Kaufer D, Kenny RA, Korczyn A, Kosaka K, Lee VM, Lees A, Litvan I, Londos E, Lopez OL, Minoshima S, Mizuno Y, Molina JA, Mukaetova-Ladinska EB, Pasquier F, Perry RH, Schulz JB, Trojanowski JQ, Yamada M. Consortium on DLB. Diagnosis and management of dementia with Lewy bodies: Third report of the DLB Consortium. Neurology. 2005; 65:1863–1872. [PubMed: 16237129]
36. Morris JC, Heyman A, Mohs RC, Hughes JP, van Belle G, Fillenbaum G, Mellits ED, Clark C. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part I. Clinical and neuropsychological assessment of Alzheimer's disease. Neurology. 1989; 39:1159–1165. [PubMed: 2771064]
37. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–198. [PubMed: 1202204]
38. Goodglass, H.; Kaplan, E. The assessment of aphasia and related disorders. Philadelphia, PA: Lea & Febiger; 1983.
39. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. Am J Psychiatry. 1984; 141:1356–1364. [PubMed: 6496779]
40. Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. Percept Mot Skills. 1958; 8:271–276.
41. Kaplan, E.; Goodglass, H.; Weintraub, S.; Goodglass, H. Boston naming test. Philadelphia: Lippincott Williams & Wilkins; 2001.
42. Schmidt, M. Rey Auditory Verbal Learning Test: A Handbook. Los Angeles: Western 550 Psychological Services; 1996.
43. Sheikh, JI.; Yesavage, JA. Geriatric Depression Scale (GDS): Recent evidence and developent of a shorter verison. In: Brink, TL., editor. Clinical Gerontology: A Guide to Assessment and Intervention. NY: The Haworth Press; 1986. p. 165-173.
44. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO. Development and validation of a geriatric depression screening scale: A preliminary report. J Psychiatr Res. 1982; 17:37–49. [PubMed: 7183759]
45. Stewart R. Subjective cognitive impairment. Curr Opin Psychiatry. 2012; 25:445–450. [PubMed: 23037961]
46. Reid M, Parkinson L, Gibson R, Schofield P, D'Este C, Attia J, Tavener M, Byles J. Memory complaint questionnaire performed poorly as screening tool: Validation against psychometric tests and affective measures. J Clin Epidemiol. 2012; 65:199–205. [PubMed: 21889305]
47. Koppara A, Wagner M, Lange C, Ernst A, Wiese B, Konig HH, Brettschneider C, Riedel-Heller SG, Luppa M, Weyerer S, Werle J, Bickel H, Mosch E, Pentzek M, Fuchs A, Wolfsgruber S, Beauducel A, Scherer M, Maier W, Jessen F. Cognitive performance before and after the onset of subjective cognitive decline in old age. Alzheimers Dement (Amst). 2015; 1:194–205.
48. Snow AL, Kunik ME, Molinari VA, Orengo CA, Doody R, Graham DP, Norris MP. Accuracy of self-reported depression in persons with dementia. J Am Geriatr Soc. 2005; 53:389–396. [PubMed: 15743279]
49. Kafonek S, Ettinger WH, Roca R, Kittner S, Taylor N, German PS. Instruments for screening for depression and dementia in a long-term care facility. J Am Geriatr Soc. 1989; 37:29–34. [PubMed: 2642498]

50. McGivney SA, Mulvihill M, Taylor B. Validating the GDS depression screen in the nursing home. J Am Geriatr Soc. 1994; 42:490–492. [PubMed: 8176142]

51. Roberts JL, Clare L, Woods RT. Subjective memory complaints and awareness of memory functioning in mild cognitive impairment: A systemic review. Dement Geriatr Cogn Disord. 2009; 28:98–109.

52. Harry A, Crowe SF. Is the Boston Naming Test still fit for purpose? Clin Neuropsychol. 2014; 28:486–504. [PubMed: 24606169]

53. Hawkins KA, Bender S. Norms and the relationship of Boston Naming Test performance to vocabulary and education: A review. Aphasiology. 2002; 16:1143–1153.

54. Steinberg SI, Negash S, Sammel MD, Bogner H, Harel BT, Livney MG, McCoubrey H, Wolk DA, Kling MA, Arnold SE. Subjective memory complaints, cognitive performance, and psychological factors in healthy older adults. Am J Alzheimers Dis Other Demen. 2013; 28:776–783. [PubMed: 24363073]

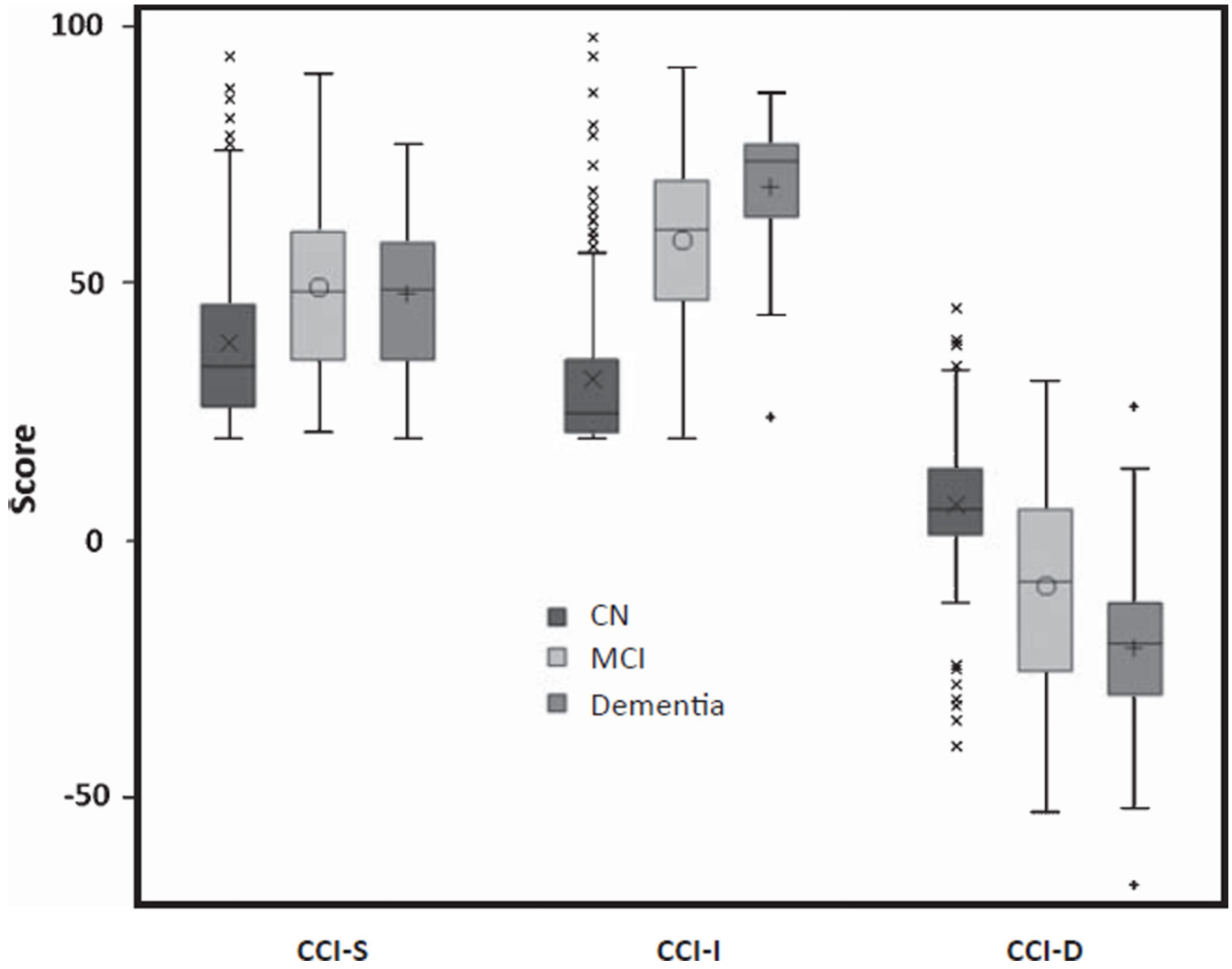

Fig. 1.

Box plot showing the performances of each CCI score in each diagnostic subgroup. CCI, Cognitive Change Index; CCI-S, Self-report score of CCI; CCI-I, Informant-report score of CCI; CCI-D, Difference in CCI score from self-report minus informant-report; CN, cognitively normal; MCI, mild cognitive impairment.

J Alzheimers Dis. Author manuscript; available in PMC 2017 February 25.

Table 1

Demographic and cognitive comparisons of the two cohorts

Characteristics	IADC		Memory Clinic		*p*-value	Adjusted *p*-value†
	n	Value	*n*	Value		
Age at visit, years, Mean ± SD	170	67.9 ± 11.7	97	67.6 ± 10.3	0.8304	n/a
Female gender, n (%)	170	99 (58.2)	97	39 (40.2)	0.0052 *	n/a
Race, n (%)	170		96		0.2941	n/a
White		162 (95.3)		93 (96.9)		n/a
African American		8 (4.7)		2 (2.1)		n/a
Asian		0 (0.0)		1 (1.0)		n/a
Education, years, Mean ± SD	167	16.1 ± 2.7	93	14.8 ± 2.7	0.0002	n/a
History of dementia in parents, n (%)	168	116 (69.0)	91	23 (25.3)	<0.0001	n/a
Diagnosis, n (%)	170		97		<0.0001	n/a
Normal cognition		129 (75.9)		20 (20.6)		
Mild cognitive impairment		25 (14.7)		71 (73.2)		
Dementia		16 (9.4)		6 (6.2)		
CCI Scores, Mean ± SD						
CCI-S: Self	170	39.0 ± 14.6	97	50.6 ± 18.9	<0.0001 *	0.0117 *
CCI-I: Informant	170	36.0 ± 20.2	97	58.8 ± 16.5	<0.0001 *	<0.0001 *
MMSE, Mean ± SD	170	28.4 ± 2.0	97	27.8 ± 1.6	0.0075 *	0.9903
Constructional Praxis, Mean ± SD	161	9.9 ± 1.3	43	9.5 ± 1.3	0.0778	0.1347
Z-score of initial verbal learning total, Mean ± SD	148	−0.6 ± 1.2	43	−1.1 ± 1.1	0.0105 *	0.7399
Z-score of verbal learning delayed recall, Mean ± SD	155	−0.5 ± 1.4	43	−1.0 ± 1.0	0.0115 *	0.4288
Trail Making Test Part A, seconds, Mean ± SD	167	33.2 ± 19.1	42	39.8 ± 16.6	0.0435 *	0.5807
Trail Making Test Part B, seconds, Mean ± SD	167	88.3 ± 59.4	41	103.4 ± 56.2	0.1432	0.9089
Animal fluency, Mean ± SD	170	20.5 ± 6.1	43	16.6 ± 4.9	0.0001 *	0.2098
Z score of BNT, Mean ± SD	167	0.0 ± 1.0	43	−1.1 ± 2.0	0.0005 *	0.0001 *
15-item GDS, Mean ± SD	168	2.0 ± 2.3	93	2.8 ± 3.4	0.0297 *	0.9517

†Adjusted for age, gender, education and diagnosis,

*Significance with $p < 0.05$,

IADC, Indiana Alzheimer Disease Center; CCI, Cognitive Change Index; MMSE, Mini-Mental State Examination; BNT, Boston Naming Test; GDS, Geriatric Depression Scale; n/a, not applicable.

Table 2

CCI scores by diagnosis subgroup in the pooled sample (Mean ± SD (Range))

CCI scores	Cognitively normal (CN)	Mild Cognitive Impairment (MCI)	Dementia (D)	*p*-value	Significant Pairs (Sidak adjusted $p < 0.05$)
CCI-S: Self	38.5 ± 15.9 (20, 94)	49.5 ± 17.3 (21, 91)	47.9 ± 14.8 (20, 77)	<0.0001	CN<MCI, D
CCI-I: Informant	31.5 ± 16.1 (20, 98)	58.5 ± 16.8 (20, 92)	68.6 ± 15.7 (24, 87)	<0.0001	CN< MCI, D; MCI <D
CCI-D: CCI-S minus CCI-I	7.0 ± 14.0 (−40, 45)	−9.0 ± 19.5 (−53, 31)	−20.8 ± 20.9 (−67, 26)	<0.0001	D< CN, MCI; MCI <CN

J Alzheimers Dis. Author manuscript; available in PMC 2017 February 25.

Table 3

Association of CCI scores with objective cognitive tests and depression scale

Objective tests	Pearson correlation coefficient (r) and *p*-value				Partial correlation coefficient (r) and *p*-value after adjusting for age, gender and education			
	n	CCI-S	CCI-I	CCI-D	n	CCI-S	CCI-I	CCI-D
MMSE	267	−0.27* $p < 0.0001$	−0.43* $p < 0.0001$	0.24* $p < 0.0001$	260	−0.23* $p = 0.0002$	−0.38* $p < 0.0001$	0.22* $p = 0.0004$
Constructional Praxis	204	−0.28* $p < 0.0001$	−0.26* $p = 0.0002$	0.04 $p = 0.57$	200	−0.28* $p < 0.0001$	−0.24* $p = 0.0007$	0.02 $p = 0.80$
Z-score of initial verbal learning total	191	−0.33* $p < 0.0001$	−0.47* $p < 0.0001$	0.26* $p = 0.0003$	187 $p < 0.0001$	−0.32* $p < 0.0001$	−0.44* $p = 0.003$	0.22*
Z-score of verbal learning delayed recall	198	−0.31* $p < 0.0001$	−0.44* $p < 0.0001$	0.24* $p = 0.0006$	194	−0.29* $p < 0.0001$	−0.42* $p < 0.0001$	0.22* $p = 0.002$
Trail Making Test Part A, time (s)	209	0.36* $p < 0.0001$	0.42* $p < 0.0001$	−0.16* $p = 0.02$	206	0.35* $p < 0.0001$	0.39* $p < 0.0001$	−0.12 $p = 0.08$
Trail Making Test Part B, time (s)	208	0.42* $p < 0.0001$	0.45* $p < 0.0001$	−0.15* $p = 0.03$	205	0.42* $p < 0.0001$	0.43* $p < 0.0001$	−0.10 $p = 0.14$
Animal fluency	213	−0.38* $p < 0.0001$	−0.46* $p < 0.0001$	0.19* $p = 0.005$	209	−0.35* $p < 0.0001$	−0.41* $p < 0.0001$	0.15* $p = 0.03$
Z score of BNT	210	−0.28* $p < 0.0001$	−0.41* $p < 0.0001$	0.23* $p = 0.0009$	207	−0.27* $p = 0.0001$	−0.40* $p < 0.0001$	0.22* $p = 0.002$
GDS	261	0.56* $p < 0.0001$	0.39* $p < 0.0001$	005 $p = 0.41$	255	0.55* $p < 0.0001$	0.42* $p < 0.0001$	0.02 $p = 0.70$

CCI, Cognitive Change Index; CCI-S, self-report score of CCI; CCI-I, informant-report score of CCI; CCI-D, Difference in CCI score from self-report minus informant-report; MMSE, Mini-Mental State Examination; BNT, Boston Naming Test; GDS, Geriatric Depression Scale;

*significance with $p < 0.05$.

Table 4

Association of CCI scores with objective cognitive tests after adjusting for GDS

Objective tests	Partial correlation coefficient (r) and *p*-value after adjusting for GDS				Partial correlation coefficient (r) and *p*-value after adjusting for age, gender, education and GDS			
	n	CCI-S	CCI-I	CCI-D	n	CCI-S	CCI-I	CCI-D
MMSE	255	−0.16* $p = 0.01$	−0.36* $p < 0.0001$	0.25* $p < 0.0001$	255	−0.09 $p = 0.14$	−0.31* $p < 0.0001$	0.24* $p = 0.0001$
Constructional Praxis	198	−0.24* $p = 0.0007$	−0.20* $p = 0.006$	0.02 $p = 0.83$	198	−0.21* $p = 0.003$	−0.17* $p = 0.02$	0.00 $p = 0.95$
Z-score of initial verbal learning total	185	−0.28* $p = 0.0001$	−0.43* $p < 0.0001$	0.23* $p = 0.002$	185	−0.21* $p = 0.004$	−0.37* $p < 0.0001$	0.21* $p = 0.005$
Z-score of verbal learning delayed recall	192	−0.24* $p = 0.0008$	−0.40* $p < 0.0001$	0.22* $p = 0.002$	192	−0.17* $p = 0.02$	−0.34* $p < 0.0001$	0.21* $p = 0.004$
Trail Making Test Part A, time (s)	204	0.29* $p < 0.0001$	0.36* $p < 0.0001$	−0.15* $p = 0.03$	204	0.22* $p = 0.001$	0.28* $p < 0.0001$	−0.11 $p = 0.13$
Trail Making Test Part B, time (s)	203	0.41* $p < 0.0001$	0.44* $p < 0.0001$	−0.13 $p = 0.07$	203	0.35* $p < 0.0001$	0.36* $p < 0.0001$	−0.09 $p = 0.20$
Animal fluency	206	−0.33* $p < 0.0001$	−0.41* $p < 0.0001$	0.17* $p = 0.02$	206	−0.25* $p = 0.0003$	−0.33* $p < 0.0001$	0.14* $p = 0.04$
Z score of BNT	204	−0.19* $P = 0.008$	−0.35* $p < 0.0001$	0.22* $p = 0.001$	204	−0.16* $p = 0.02$	−0.33* $p < 0.0001$	0.21* $p = 0.003$

CCI, Cognitive Change Index; CCI-S, self-report score of CCI; CCI-I, informant-report score of CCI; CCI-D, Difference in CCI score from self-report minus informant-report; MMSE, Mini-Mental State Examination; BNT, Boston Naming Test;

*significance with $p < 0.05$.