Alpha Psychiatry

ORIGINAL ARTICLE
Alpha Psychiatry 2024;25(2):212-219
DOI: 10.5152/alphapsychiatry.2024.231448

Comparison of Cognitive Impairment Diagnosis Criteria in Clinical Settings: Conventional vs. Neuropsychological

ABSTRACT

Background: Theories on Alzheimer disease pathogenesis propose a gap between pathological changes and the onset of clinical symptoms. The early detection of cognitive decline is crucial for the implementation of preventive strategies. Mild cognitive impairment is a transitional stage and an accurate diagnosis is vital. However, the diagnosis of mild cognitive impairment varies due to inconsistent diagnostic criteria. This study aims to explore the effectiveness of comprehensive neuropsychological criteria, including all cognitive domains, for diagnosing cognitive impairment in clinical settings.

Methods: The study included 509 subjects with subjective cognitive complaints between 2017 and 2021. They were diagnosed using the conventional and neuropsychological criteria, and the results were named the complex criteria (conventional criteria–neuropsychological criteria).

Results: Concordance between the conventional and neuropsychological diagnostic criteria diagnoses was 87.82%. Some participants diagnosed with mild cognitive impairment or dementia using the conventional criteria were classified as normal according to the neuropsychological criteria. Notably, the mild cognitive impairment - normal cognition (MCI-NC) and dementia (DEM)-NC (normal cognition) groups exhibited distinct characteristics. The MCI-NC group had higher depression scores ($P = .008$) and better memory performance ($P = .026$) and executive function ($P = .020$) than the MCI-MCI group. The DEM-NC group had better instrumental activities of daily living ($P < .001$) than the DEM-DEM group.

Conclusion: This study highlights the complexity of diagnosing cognitive impairment and the importance of comprehensive criteria. Relying solely on conventional criteria may lead to overdiagnosis. The neuropsychological criteria consider various cognitive domains and better discriminate between individuals with MCIs or other factors that contribute to cognitive difficulties.

Keywords: Neuropsychology, dementia, cognition

Introduction

Theories explaining the pathogenesis of Alzheimer's disease (AD), including the amyloid hypothesis, suggest a large gap between the onset of pathological changes and the onset of clinical symptoms.[1] There is currently no curative treatment for AD. Nevertheless, detecting the disease in its early stages may help slow cognitive decline through the use of preventive measures such as cognitive, physical, and social intervention strategies.[2] Mild cognitive impairment (MCI) is a transitional state between normal age-related memory decline and AD. Conversion rates from MCI to AD ranged from 4% to 23% in community-based samples and from 10% to 31% in clinic-based samples.[3,4] Therefore, several studies have attempted to diagnose MCI accurately and early. Considering the pathological mechanism of AD, early detection of biomarkers such as amyloid and tau is ideal; however, this approach is not suitable for application in all patients in real-world clinical settings due to challenges such as

Hye-Geum Kim[1,2]
Younggyo Kim[3]
Emily C. Edmonds[4,5]
Mark W. Bondi[2,6]

[1]Department of Psychiatry, Yeungnam University Hospital, Yeungnam University College of Medicine, Daegu, Republic of Korea
[2]Department of Psychiatry, University of California San Diego, School of Medicine, La Jolla, CA, USA
[3]Department of Psychology, Yeungnam University Hospital, Daegu, Republic of Korea
[4]Banner Alzheimer's Institute, Tucson, AZ, USA
[5]Departments of Neurology and Psychology, University of Arizona, Tucson, AZ, USA
[6]Veterans Affairs San Diego Healthcare System, San Diego, CA, USA

Corresponding author:
Hye-Geum Kim
✉ psykhg@yu.ac.kr

Received: December 1, 2023
Revision requested: December 21, 2023
Last revision received: January 29, 2024
Accepted: January 29, 2024
Publication Date: April 4, 2024

Cite this article as: Kim H, Kim Y, Edmonds EC, Bondi MW. Comparison of cognitive impairment diagnosis criteria in clinical settings: Conventional vs. neuropsychological. *Alpha Psychiatry.* 2024;25(2):212-219.

cost and accessibility.[5] Recently, the effectiveness of relatively inexpensive plasma-based amyloid and tau tests has been verified, and positive research results have been reported on Multimer Detection System-Oligomeric Amyloid-β measures that can be applied clinically. Consistent reporting should be repeated in the future.[6]

Humans are aging, and the prevalence of dementia is rapidly increasing. In 2011, the largest generation in the history of the U.S. population (Baby Boomers) reached the age of 65 years. By 2030, the proportion of the U.S. population aged 65 years and older is projected to increase significantly, reaching 74 million seniors in the United States. They comprised more than 20% of the total population. The total per capita healthcare and long-term care payments for Medicare beneficiaries with AD and other dementia-related illnesses in 2022 will be nearly 3 times the payments for other Medicare beneficiaries in the same age group from all sources ($43,444 per person for people with AD and other dementias; $14,593 per person for people without dementia).[7] Therefore, a cost-effective method for early diagnosis of dementia is required. A brief screening tool can provide practical and cost-effective assessment.[8] Currently, screening tools are used to detect cognitive impairment, such as the Mini-Mental State Examination (MMSE)[9] and Montreal Cognitive Assessment.[10] The MMSE is the most widely used tool for providing an overall measure of cognitive impairment in clinical, research, and community settings. However, a recent study found no evidence to support the important role of the MMSE as a "stand-alone single-dose test" in identifying patients with MCI who developed dementia.[11]

Another problem with the diagnosis of MCI is that there is no consistent diagnostic criteria. Mild cognitive impairment has many competing definitions and criteria.[12] First, several studies used the following criteria: (1) memory complaint; (2) normal activities of daily living (ADL); (3) normal general cognitive function; (4) abnormal memory for age; and (5) not demented. Some studies have specifically defined the degree of cognitive decline as 1.5 standard deviations (SDs) below the age-adjusted norms. Second, the MCI criteria recommended by the International Working Group (IWG) on MCI is as follows: (1) neither normal nor demented; (2) evidence of cognitive deterioration shown by either objectively measured decline and/or subjective self-reported decline and/or informant in conjunction with objective cognitive deficits; and (3) preservation of ADL.[13] Third, the MCI criteria of the Alzheimer Disease Neuroimaging Initiative (ADNI; http://www.adni-info.org), used in many studies, are: (1) subjective memory complaints reported by themselves, study partner, or clinician; (2) objective memory loss defined as scoring below an education-adjusted cut-off score (1.5 SD) on delayed recall of Story A of the Wechsler Memory Scale- Revised Logical Memory Test; (3) global Clinical Dementia Rating (CDR) score of 0.5; and (4) general cognitive and functional performance sufficiently preserved such that a diagnosis of dementia could not be made by the site physician at the time of screening.[14] In addition, the recently revised National Institute on Aging and Alzheimer Association criteria[5] and IWG-2 criteria[15] emphasize neurodegenerative biomarkers and diagnose preclinical stages before MCI.

These conventional criteria for MCI can be problematic because they rely on impairment of a single neuropsychological test, clinical judgment, or limited neuropsychological assessment utilizing a "one test equals one domain" methodology which has been shown to increase the risk of false-positive diagnoses of MCI.[16,17] Additionally, a high false-negative error rate based on the conventional criteria for MCI has been reported, suggesting the risk of missing an MCI diagnosis.[18] These false positives and false negatives may lead to increased medical costs and social burdens.

Jak et al[19] suggested that comprehensive neuropsychological (NP) criteria offer an optimal balance of sensitivity and reliability by using a more liberal >1 SD cutoff for impairment (rather than a 1.5-2 SD cutoff), with the need for at least 2 impaired scores within a cognitive domain. When the NP criteria were applied to the ADNI, an individual was considered to have MCI if any of the following 3 criteria were met: (1) an impaired score, defined as >1 SD below the age-corrected normative mean, on 2 measures within at least one cognitive domain (i.e., memory, language, or speed/executive function); (2) one impaired score, defined as >1 SD below the age-corrected normative mean, in each of the 3 cognitive domains examined; or (3) a Functional Activities Questionnaire score of ≥9 indicating dependence in 3 or more daily activities. Within the ADNI, approximately one-third of the participants diagnosed with MCI using conventional criteria were cognitively normal (CN) when diagnosed using the NP criteria.[17] Moreover, participants who were re-diagnosed with CN using neuropsychological methods had many characteristics, such as imaging findings, genetic biomarkers, and pathological findings that were more consistent with CN than with MCI.[17]

The validity of the NP criteria has been verified in many studies. However, the cognitive domains included in the NP criteria were memory, language, and executive functions, whereas the remaining visuospatial functions and attention abilities were excluded. Previous studies have used data from research groups rather than from subjects in actual clinical settings. Therefore, this study aimed to analyze the results of a periodic comprehensive NP test (all cognitive domains, including attention and visuospatial functions) in subjects who visited the hospital because of subjective cognitive complaints (SCCs) in clinical settings. Accordingly, the purpose of this study was to examine the characteristics and differences when diagnosing NP compared to the conventional criteria commonly used previously.

MAIN POINTS

- *Early detection of cognitive decline is important, but there are no consistent diagnostic criteria.*
- *The conventional criteria are commonly used in clinical practice, but the risk of false positives and false negatives has been reported.*
- *Neuropsychological criteria based on comprehensive neuropsychological test results consider various cognitive domains and better discriminate between individuals with subjective cognitive complaints.*

Material and Methods

Subjects

All subjects were outpatients or inpatients with SCC who visited Yeungnam University Hospital for neuropsychiatric evaluation between January 2017 and February 2021. Among the 1242 participants, an evaluation was performed using the conventional and NP criteria. Three hundred seventy-three participants lacking the data necessary for both criteria were excluded, and a total of 509 subjects

were included. The study was approved by the Institute Review Board (IRB) of Yeungnam University Hospital (Approval IRB No: YUMC 2019-07-028, Date: July 28, 2019). All the participants provided written informed consent.

Neuropsychological Assessment

The data were collected by a psychiatrist and trained psychology graduates. The participants completed a comprehensive neuropsychological assessment evaluating 5 cognitive domains: memory, language, attention, visuospatial, and frontal (executive) functions. All domain scores were considered to follow a normal distribution, and the mean and SD were estimated according to age, education level, and sex, and converted into standard scores.[20] Additionally, the Barthel's ADL (B-ADL),[21] Korean Instrumental ADL (K-IADL),[22] and CDR scales[23] were used to assess daily function and social activity.

Among these neuropsychological tests, the results used in this study were the *z*-scores of 2 tests in each of the 5 cognitive domains for cognitive function and instrumental ADL (IADL) for daily function: (1) Attention: digit span forward and backward tests;[24] (2) Language: fluency and the Boston Naming Test (BNT);[25] (3) Memory: the Seoul verbal learning test (SVLT)—elderly version delayed recall and recognition;[26] (4) Visuospatial functions: the Rey Complex Figure Test (RCFT)[27] copy score and copy time; and (5) Executive functions: the Stroop Test[28] and Trail Making Test (TMT).[29] For each test result, a *z*-score corrected for age, sex, and educational level was used except for language fluency (Table 1).

Conventional Criteria, Neuropsychological Criteria, and Complex Criteria

In this study, diagnoses of normal cognition (NC), MCI, and dementia (DEM) based on conventional criteria were defined as follows: (1) CN is a subject with no test score lower than −1.5 SD; (2) MCI is lower than −1.5 SD in at least one of the tests; and (3) DEM is lower than −1.5 SD in at least one of the tests, and IADL *z*-score is higher than 0.43.[30]

Diagnosis with the NP criteria was as follows: (1) NC is a subject who does not satisfy both (A) and (B) of MCI; (2) MCI is a subject who satisfies the following (A) or (B), and at the same time IADL is higher than 0.09 and lower than 0.43: (A) 2 tests lower than −1 SD within a cognitive domain; (B) at least 1 test lower than −1 SD in all domains; and (3) DEM is a subject who satisfies the MCI criteria and has an IADL above 0.43 (Table 2).[30]

Furthermore, the results of each diagnosis based on the above 2 criteria were grouped together and named the "Complex criteria". For example, if a subject is diagnosed with MCI based on the conventional criteria and with NC based on the NP criteria, the complex criteria would be named MCI-NC.

Table 1. Detailed List of Subscales Used in the Study

Domain	Subscales (*z*-Score)	
Attention	Digit span forward	Digit span backward
Language	Fluency (fluent/non-fluent)	Boston naming test
Memory	SVLT delayed recall	SVLT recognition
Visuospatiall Fx.	RCFT copy score	RCFT copy time
Executive Fx.	Stroop test (color reading)	Trail making test A
Daily Fx.	IADL	

Fx, function; IADL, instrumental activities of daily living; RCFT, the Rey Complex Figure Test; SVLT, the Seoul Verbal Learning Test.

Statistical Analysis

Descriptive statistics and frequency analyses were conducted to examine the demographic information of the participants and groups classified according to the complex criteria. These include mean score and SD of age and educational years, and sex ratio. Descriptive statistics were given with mean (standard deviation) and frequencies with percentages. Then, independent sample *t*-tests and chi-square cross-validations were conducted to compare the differences between MCI-NC and MCI-MCI and DEM-NC and DEM-DEM groups based on the complex criteria for each variable except language fluency. It was compared between the fluent and non-fluent groups using the Fisher's exact test. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS®) version 21.0 for Windows (IBM SPSS Corp., Armonk, NY, USA), and *P*-values < .05 were considered significant.

Results

Demographic Characteristics

This study included 509 participants (316 women and 193 men) who underwent baseline evaluations. The mean and SD of the subjects' age and years of education were 72.17 ± 9.89 years and 7.54 ± 4.57 years, respectively (Table 3). The mean MMSE score was 20.57 ± 4.72 points, CDR-Global Score (GS) was 1.13 ± 0.43, CDR-Sum of Boxes (SOB) score was 5.96 ± 2.89, B-ADL score was 17.29 ± 4.21, I-ADL score was 1.14 ± 0.86, and short version of Geriatric Depression Scale (SGDS) score was 6.34 ± 4.8 (Table 3). When the subjects were diagnosed by the complex criteria, the number of subjects in each group was as follows: NC-NC = 31, MCI-NC = 35, DEM-NC = 24, NC-MCI = 1, MCI-MCI = 93, DEM-MCI = 0, NC-DEM = 2, MCI-DEM = 0, and DEM-DEM = 323 (Figure 1).

Characteristics of the Group Diagnosed as Cognitively Impaired by Conventional Criteria but Normal by NP Criteria: Comparisons of the Groups Diagnosed with Complex Criteria (Conventional Criteria–NP Criteria)

When diagnosed based on the conventional and NP criteria, the concordance rate of the diagnosis was 87.82%. That is, of the total 509 subjects, there were 447 subjects diagnosed with NC-NC, MCI-MCI,

Table 2. Definition of Each Criteria

	Conventional Criteria	NP Criteria
NC	No tests lower than −1.5 SD	MCI criteria (1) and (2) are not satisfied.
MCI	At least 1 test lower than −1.5 SD	(1) Two tests lower than −1 SD within a cognitive domain or (2) At least 1 test lower than −1 SD in all domains, and IADL score between 0.09 and 0.43
DEM	At least 1 test lower than −1.5 SD and IADL score above 0.43	MCI criteria are satisfied and IADL score above 0.43

DEM, dementia; IADL, instrumental activities of daily living; MCI, mild cognitive impairment; NC, normal cognition; SD, standard deviation; NP, neuropsychological.

Table 3. Demographic Characteristics of Each Group Diagnosed by the Complex Criteria

	NC-NC (n = 31)	MCI-NC (n = 35)	DEM-NC (n = 24)	NC-MCI (n = 1)	MCI-MCI (n = 93)	NC-DEM (n = 2)	DEM-DEM (n = 323)	Total (n = 509)
Age (y)	77.48 ± 8.97	71.57 ± 7.86	76.96 ± 7.62	76.00	71.43 ± 8.28	83.50	72.8 ± 8.98	72.17 ± 9.89
Education (y)	5.42 (3.91)	8.44 (5.16)	5.21 (3.89)	6.00	7.80 (4.69)	3.50	7.65 (4.68)	7.54 (4.57)
Female	24 (77.42)	20 (57.14)	15 (62.50)	1	54 (58.06)	2	200 (61.92)	316 (62.08)

Values are presented mean ± SD or number (%).
DEM, dementia; MCI, mild cognitive impairment; NC, normal cognition; NP, neuropsychological.

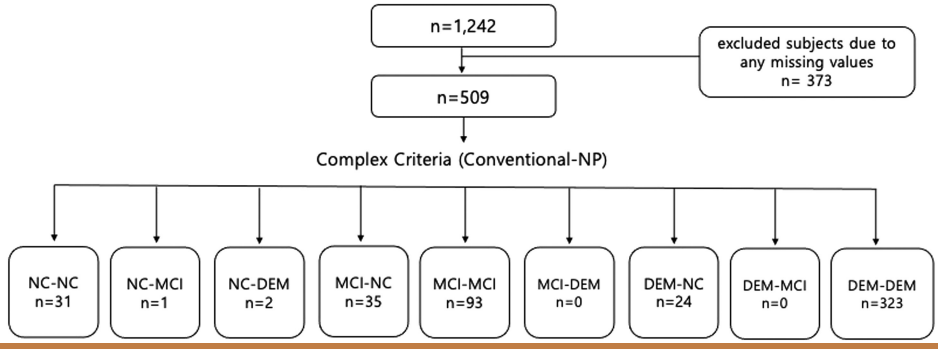

Figure 1. Summary of the evaluation process for all participants.

and DEM-DEM. Based on the NP criteria, some subjects who were diagnosed with MCI (n = 35) or DEM (n = 24) using conventional criteria were diagnosed with NC. To further explore the characteristics of the groups with discrepant diagnoses for each diagnostic criterion, an analysis was conducted comparing them with the groups diagnosed as normal or cognitively impaired using both criteria. This is based on the fact that a subject who receives the same diagnosis in both criteria is likely to actually have that diagnosis.

NC-NC vs. MCI (DEM)-NC: Table 4 shows the results of the comparison between those diagnosed with MCI or DEM using the conventional criteria but diagnosed with NC using the NP criteria and those diagnosed with NC using both criteria. The group diagnosed with MCI using the conventional criteria but diagnosed with NC using the NP criteria (MCI-NC) had significantly higher SGDS scores ($P = .038$). Additionally, they showed significantly lower performance in both the SVLT_delayed_recall ($P < .001$) and SVLT_recognition ($P < .001$). The DEM-NC group, that is the group diagnosed with DEM by conventional criteria but diagnosed with NC by NP criteria, showed significantly lower scores on the MMSE ($P = .033$) and one subtest for each cognitive domain except the language domain: Digit span backward for attention ($P = .040$); RCFT copy score for visuospatial function ($P = .039$); SVLT-delayed recall for memory ($P < .001$); and TMT time for frontal function ($P = .030$).

MCI (DEM)-NC vs. MCI (DEM)-MCI (DEM): The results of the comparison of the characteristics of the MCI-NC group versus the MCI-MCI group and the DEM-NC group versus the DEM-DEM group are summarized in Table 5. That is, comparison between groups diagnosed with MCI or DEM by the conventional criteria but diagnosed with NC by the NP criteria, and groups diagnosed consistently with MCI or DEM by both criteria. First, in the comparison results between the MCI-NC group and the MCI-MCI group, the MCI-NC group had a significantly higher MMSE score ($P = .002$), lower SGDS ($P = .008$), lower IADL ($P < .001$), and lower CDR_GS and SOB ($P < .001$) than the MCI-MCI group. Considering the differences in each cognitive domain, the MCI-NC group had significantly higher SVLT_delayed recall ($P = .026$) and K-TMT time ($P = .020$) scores. Next, in the comparison results between the DEM-NC group and the DEM–DEM group, the DEM-NC group had significantly higher B-ADL ($P < .001$) and lower CDR-GS and SOB ($P = .001$ and $P < .001$) than the DEM–DEM group. In the comparison results for each cognitive domain, the DEM-NC group had significantly higher BNT *z*-scores ($P = .001$), SVLT-recognition scores ($P < .001$), SVLT-delayed recall scores ($P = .035$), Stroop test scores ($P = .001$), and K-TMT-time scores ($P < .001$).

Discussion

The purpose of this study was to determine the characteristics of the NP criteria compared to the conventional criteria commonly used in clinical trials and research. In particular, we aimed to examine the modified NP criteria, which includes all 5 cognitive domains (attention, language, memory, visuospatial function, and executive function) in more detail, and how they serve as a dementia diagnostic tool for subjects in real clinical settings. This study provides valuable insights into the diagnosis of cognitive impairment in a group of older adults in a clinical setting using both the conventional and NP criteria. The results reveal several interesting findings that shed light on the complexity of cognitive impairment diagnoses in older populations.

In this study, the diagnostic concordance rate was 87.82% when diagnosed using the conventional and NP criteria. This suggested that the 2 criteria generally agreed with the diagnosis. However, it was necessary to further explore the remaining 12% of participants. One of the most noteworthy results was that some subjects who were diagnosed with MCI or DEM using the conventional criteria were diagnosed with NC using the NP criteria. In other words, there were cases in which individuals were diagnosed as cognitively impaired by the

Table 4. Comparison of Cognitive and Functional Characteristics by Group Diagnosed by the Complex Criteria: Comparison Between Those Diagnosed with MCI or DEM by Conventional Criteria but Diagnosed with NC by NP Criteria and Those Diagnosed with NC by Both Criteria

	NC-NC	MCI-NC	*df*	*P*	NC-NC	DEM-NC	*df*	*P*
MMSE, mean (SD)	23.91 (4.01)	25.15 (3.69)	51	.437	23.91 (4.01)	19.60 (3.89)	37	.033*
SGDS	3.08 (2.47)	6.00 (4.00)	60	.038*	6.00 (4.00)	7.00 (5.06)	50	.619
B_ADL	18.45 (3.21)	18.33 (3.82)	56	.935	18.45 (3.21)	19.90 (0.32)	39	.173
I_ADL	0.53 (0.59)	0.09 (0.15)	32	.052	0.53 (0.59)	1.17 (0.90)	46	.067
CDR_GS	0.77 (0.26)	0.54 (0.32)	63	.065	0.77 (0.26)	0.95 (0.16)	52	.079
CDR_SOB	3.32 (1.89)	2.31 (1.95)	62	.213	3.32 (1.89)	4.30 (1.32)	53	.187
Attention								
Digit_span_forward	−0.36 (0.73)	0.11 (1.17)	62	.254	−0.36 (0.73)	−0.34 (0.61)	53	.948
Digit_span_backward	0.09 (0.85)	−0.55 (1.22)	61	.162	0.09 (0.85)	−0.91 (1.24)	44	.040*
Language								
Naming_K_BNT	0.38 (0.82)	−0.37 (1.14)	57	.086	0.38 (0.82)	−0.17 (0.66)	51	.111
Visuopatial Fx								
RCFT_copy	0.01 (0.69)	−1.09 (2.21)	40	.128	0.01 (0.69)	−1.24 (1.75)	28	.039*
RCFT_copy_time	0.27 (0.80)	−0.58 (1.53)	56	.114	0.27 (0.80)	0.00 (1.16)	43	.538
Memory								
SVLT_delayed_recall	0.31 (0.73)	−1.02 (0.84)	64	<.001**	0.31 (0.73)	−1.19 (0.83)	52	<.001**
SVLT_recognition	0.13 (0.80)	−1.47 (1.29)	51	<.001**	0.13 (0.80)	−0.33 (0.57)	53	.149
Frontal Fx								
StroopTest	−0.06 (1.10)	−0.96 (1.12)	64	.059	−0.06 (1.10)	−0.83 (1.37)	39	.167
K_TMT_time	−0.50 (1.61)	−1.16 (1.56)	39	.315	−0.50 (1.61)	−2.02 (1.09)	27	.030*
	NC-NC	**MCI-NC**	χ^2	*P*	**NC-NC**	**DEM-NC**	χ^2	*P*
Language fluency, n (%)								
Fluent	11 (100.0%)	12 (92.3%)	0.883	1.000	11 (100.0%)	10 (100.0%)	-	-
Non-fluent	0 (0.0%)	1 (7.7%)			0 (0.0%)	0 (0.0%)		

BNT, Boston Naming Test; BADL, Basic Activities of Daily Living; CDR, Clinical Dementia Rating; DEM, dementia; GS, global score; IADL, Instrumental Activities of Daily Living; K-TMT, Korean trail making test; MCI, mild cognitive impairment; MMSE, Mini-Mental State Exam; NC, normal cognition; RCFT, the Rey complex figure test; SD, standard deviation; SOB, sum of boxes; SGDS, short version of Geriatric Depression Scale; SVLT, the Seoul verbal learning test; NP, neuropsychological; Fx, Function.
*Significant at the .05 level.
**Significant at the .01 level.

conventional criteria but were classified as normal according to the NP criteria. This is the critical point of interest in this study.

This study examined the characteristics of 2 main groups with discrepant diagnoses: MCI-NC (diagnosed as MCI by conventional criteria but NC by NP criteria) and DEM-NC (diagnosed as dementia by conventional criteria, but NC by NP criteria). When performing this analysis, we assumed that subjects with a consistent diagnosis were more likely to be diagnosed. MCI-NC individuals had significantly higher SGDS and poorer performance on memory-related tests than the NC–NC group. This suggests that they may experience cognitive deficits due to factors such as depression, rather than true MCI. Individuals with DEM-NC exhibited lower MMSE scores and poorer performance in various cognitive domains except for language. This indicates that they might have cognitive difficulties but may not meet the criteria for dementia as per the NP approach. The group diagnosed with DEM according to the conventional criteria can be interpreted as the group that showed findings lower than the standard on one scale in each area. The NP criteria are meaningful in that they aim to compensate for the vulnerability of "one test equals one domain".[16,17] Using actuarial-based neuropsychological methods, we avoid the difficulty of interpreting individually impaired scores on a single cognitive test and apply a cutoff score for impairment that optimizes classification rates, this may reduce overinterpretation and minimize the chance of false-positive diagnosis of MCI or DEM.[31-33]

The study further compared individuals within the NP criteria: MCI-NC vs. MCI-MCI and DEM-NC vs. DEM-DEM. MCI-NC individuals had better MMSE scores, lower depression scores, and higher scores on delayed recall and executive function tasks than MCI-MCI individuals. This suggests that MCI-NC individuals may have milder cognitive impairments and better overall cognitive functioning. Looking at the characteristics of the groups diagnosed with NC in the NP criteria, these are characteristics that have been repeatedly mentioned as risk factors that can predict the onset of AD in the existing literature. Many studies have reported that memory tests are the best predictors of future cognitive impairment. For example, the Selective Reminding Test,[34,35] the Free and Cued Selective Reminding Test,[36] the California Verbal Learning Test,[37] Various recall tests, including the Rey Auditory Verbal Learning Test[38] and the Story Recall Test,[39-41] have been used in many studies to predict cognitive decline. In addition, many studies have shown that it is useful when combining memory tests with executive function tests or language tests; for example, predictions are made with high accuracy when an episodic memory test is combined with a naming test or verbal fluency test.[42] These results suggest that a risk group with characteristic cognitive

Table 5. Comparison of Cognitive and Functional Characteristics by Group Diagnosed by the Complex Criteria: Comparison of Those Diagnosed with MCI (DEM) by the Conventional Criteria but Diagnosed with NC by the NP Criteria and Those Diagnosed with MCI (DEM) by Both Criteria

	MCI-NC	MCI-MCI	*df*	*P*	DEM-NC	DEM-DEM	*df*	*P*
MMSE, mean (SD)	25.15 (3.69)	21.51 (3.42)	64	.002**	19.60 (3.89)	19.45 (4.07)	20	.910
SGDS	3.08 (2.47)	5.81 (4.03)	74	.008**	7.00 (5.06)	7.13 (4.69)	27	.937
B_ADL	18.33 (3.82)	19.54 (1.04)	30	.302	19.90 (0.32)	16.15 (4.55)	30	<.001**
I_ADL	0.09 (0.15)	0.27 (0.10)	49	<.001**	1.17 (0.90)	2.24 (3.34)	27	.317
CDR_GS	0.54 (0.32)	0.93 (0.17)	60	<.001**	0.95 (0.16)	1.22 (0.48)	57	.001**
CDR_SOB	2.31 (1.95)	4.74 (1.41)	66	<.001**	4.30 (1.32)	6.84 (2.51)	62	<.001**
Attention								
Digit_span_forward	0.11 (1.17)	−0.19 (1.02)	68	.374	−0.34 (0.61)	−0.83 (1.08)	38	.167
Digit_span_backward	−0.55 (1.22)	−0.81 (1.08)	73	.468	−0.91 (1.24)	−1.23 (1.24)	30	.435
Language								
Naming_K_BNT	−0.37 (1.14)	−1.12 (1.45)	105	.096	−0.17 (0.66)	−1.90 (1.68)	54	.001**
Visuopatial Fx								
RCFT_copy_score	−1.09 (2.21)	−2.46 (2.71)	110	.107	−1.24 (1.75)	−3.15 (3.46)	60	.088
RCFT_copy_time	−0.58 (1.53)	−0.14 (1.50)	91	.370	0.00 (1.16)	−0.48 (1.44)	32	.316
Memory								
SVLT_delayed_recall	−1.02 (0.84)	−1.85 (1.02)	63	.026*	−1.19 (0.83)	−1.84 (0.93)	27	.035*
SVLT_recognition	−1.47 (1.29)	−1.96 (1.54)	104	.310	−0.33 (0.57)	−2.24 (1.83)	59	<.001**
Frontal Fx								
StroopTest	−0.96 (1.12)	−1.67 (1.22)	68	.073	−0.83 (1.37)	−2.38 (1.39)	26	.001**
K_TMT_time	−1.16 (1.56)	−3.12 (2.63)	108	.020*	−2.02 (1.09)	−4.37 (4.23)	58	<.001**
	MCI-NC	**MCI-MCI**	χ^2	*P*	**DEM-NC**	**DEM-DEM**	χ^2	*P*
Language, n (%)			2.904	.260			0.901	1.000
Fluency								
Fluent	12 (92.3%)	37 (100%)			10 (100.0%)	88 (91.7%)		
Non-fluent	1 (7.7%)	0 (0.0%			0 (0.0%)	8 (8.3%)		

BADL, Basic Activities of Daily Living; BNT, Boston Naming Test; CDR, Clinical Dementia Rating; DEM, dementia; GS, global score; IADL, Instrumental Activities of Daily Living; K-TMT, Korean trail making test; M, mean; MMSE, Mini-Mental State Exam; MCI, mild cognitive impairment; NC, normal cognition; RCFT, the Rey complex figure test; SD, standard deviation; SOB, sum of boxes; SGDS, short version of Geriatric Depression Scale; SVLT, the Seoul verbal learning test; NP, neuropsychological; Fx, Function.
*Significant at the .05 level.
**Significant at the .01 level.

changes in AD can be more accurately identified when diagnosed using the NP criteria.

DEM-NC individuals had better IADL scores and lower global and functional impairment scores than DEM–DEM individuals. This indicates that individuals with DEM-NC may have less severe functional impairments despite cognitive difficulties. These findings highlight the importance of considering both cognitive and non-cognitive factors, such as depression and daily functioning, when diagnosing cognitive impairment in older adults. The NP criteria seem to differentiate individuals with milder cognitive impairments or those whose cognitive difficulties may be more related to factors other than neurodegenerative diseases.[43] Clinicians should exercise caution when diagnosing cognitive impairment and consider the broader context of cognitive and functional status.

This study has some limitations, including a single assessment point and a relatively narrow focus on cognitive and functional measures. Longitudinal data and a more comprehensive assessment of comorbid conditions will provide a more comprehensive understanding. Since this study was conducted on individuals who visited a university hospital and decided on their own to undergo neurocognitive tests, they did not represent the entire population. However, these subjects were not simply recruited for research, but may represent persons with SCC that can be encountered in actual clinical settings.

In conclusion, this study underscores the complexity of diagnosing cognitive impairment in older adults, and the importance of using comprehensive criteria that consider various factors. These findings suggest that relying solely on the conventional criteria may lead to overdiagnosis, emphasizing the need for a more nuanced approach to understand cognitive decline in populations with SCC. Further research is required to explore long-term outcomes and clinical implications of these discrepant diagnoses.

Availability of Data and Materials: *The data that support the findings of this study are available on request from the corresponding author.*

Ethics Committee Approval: *This study was approved by the Ethics Committee of Yeungnam University Hospital (Approval Number: YUMC 2019-07-028; Date: July 28, 2019).*

Informed Consent: *Informed consent was obtained from the patients who agreed to take part in the study.*

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – H.G.K.; Design – H.G.K., Y.K.; Supervision – H.G.K., Y.K., E.C.E., M.W.B.; Resource – H.G.K.; Materials – H.G.K., Y.K.; Data Collection and/or Processing – H.G.K., Y.K.; Analysis and/or Interpretation – H.G.K., Y.K., E.C.E., M.W.B.; Literature Search – H.G.K., Y.K.; Writing – H.G.K.; Critical Review – H.G.K., Y.K., E.C.E., M.W.B.*

Declaration of Interests: *The authors have no conflicts of interest to declare.*

Funding: *This study was supported by the 2022 Yeungnam University Research Grant.*

References

1. Karran E, Mercken M, De Strooper B. The amyloid cascade hypothesis for Alzheimer's disease: an appraisal for the development of therapeutics. *Nat Rev Drug Discov*. 2011;10(9):698-712. [CrossRef]
2. Rosas AG, Stögmann E, Lehrner J. Neuropsychological prediction of dementia using the neuropsychological test battery Vienna–A retrospective study. *Brain Disord*. 2022;5:100028. [CrossRef]
3. Bennett DA, Schneider JA, Bienias JL, Evans DA, Wilson RS. Mild cognitive impairment is related to Alzheimer disease pathology and cerebral infarctions. *Neurology*. 2005;64(5):834-841. [CrossRef]
4. Lu Y, Liu C, Yu D, et al. Prevalence of mild cognitive impairment in community-dwelling Chinese populations aged over 55 years: a meta-analysis and systematic review. *BMC Geriatr*. 2021;21(1):10. [CrossRef]
5. Frisoni GB, Winblad B, O'Brien JT. Revised NIA-AA criteria for the diagnosis of Alzheimer's disease: a step forward but not yet ready for widespread clinical use. *Int Psychogeriatr*. 2011;23(8):1191-1196. [CrossRef]
6. Pyun JM, Ryu JS, Lee R, et al. Plasma amyloid-beta oligomerization tendency predicts amyloid PET positivity. *Clin Interv Aging*. 2021;16:749-755. [CrossRef]
7. No authors. Alzheimer's disease facts and figures. *Alzheimers Dement*. 2020;2020.
8. Kerwin DR. How to prevent a delayed Alzheimer's diagnosis. *J Fam Pract*. 2009;58(1):9-15.
9. 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(3):189-198. [CrossRef]
10. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695-699. [CrossRef]
11. Arevalo-Rodriguez I, Smailagic N, Roqué-Figuls M, et al. Mini-Mental State Examination (MMSE) for the early detection of dementia in people with mild cognitive impairment (MCI). *Cochrane Database Syst Rev*. 2021;7(7):CD010783. [CrossRef]
12. Ganguli M, Chang CC, Snitz BE, Saxton JA, Vanderbilt J, Lee CW. Prevalence of mild cognitive impairment by multiple classifications: the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) project. *Am J Geriatr Psychiatry*. 2010;18(8):674-683. [CrossRef]
13. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment--beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med*. 2004;256(3):240-246. [CrossRef]
14. Petersen RC, Aisen PS, Beckett LA, et al. Alzheimer's Disease Neuroimaging Initiative (ADNI): clinical characterization. *Neurology*. 2010;74(3):201-209. [CrossRef]
15. Dubois B, Feldman HH, Jacova C, et al. Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria. *Lancet Neurol*. 2014;13(6):614-629. [CrossRef]
16. Edmonds EC, Delano-Wood L, Clark LR, et al. Susceptibility of the conventional criteria for mild cognitive impairment to false-positive diagnostic errors. *Alzheimers Dement*. 2015;11(4):415-424. [CrossRef]
17. Bondi MW, Edmonds EC, Jak AJ, et al. Neuropsychological criteria for mild cognitive impairment improves diagnostic precision, biomarker associations, and progression rates. *J Alzheimers Dis*. 2014;42(1):275-289. [CrossRef]
18. Edmonds EC, Delano-Wood L, Jak AJ, et al. "Missed" mild cognitive impairment: high false-negative error rate based on conventional diagnostic criteria. *J Alzheimers Dis*. 2016;52(2):685-691. [CrossRef]
19. Jak AJ, Bondi MW, Delano-Wood L, et al. Quantification of five neuropsychological approaches to defining mild cognitive impairment. *Am J Geriatr Psychiatry*. 2009;17(5):368-375. [CrossRef]
20. Kang Y, Na D, Hahn SJI. Hbr, co c. *Seoul Neuropsychol Screen Battery*. 2003.
21. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud*. 1988;10(2):61-63. [CrossRef]
22. Won CW, Rho YG, SunWoo D, Lee YS. The validity and reliability of Korean Instrumental Activities of Daily Living (K-IADL) scale. *J Korean Geriatr Soc*. 2002;6(4):273-280.
23. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. *Int Psychogeriatr*. 1997;9(suppl 1):173-6; discussion 177. [CrossRef]
24. Schroeder RW, Twumasi-Ankrah P, Baade LE, Marshall PS. Reliable digit span: A systematic review and cross-validation study. *Assessment*. 2012;19(1):21-30. [CrossRef]
25. Williams BW, Mack W, Henderson VW. Boston naming test in Alzheimer's disease. *Neuropsychologia*. 1989;27(8):1073-1079. [CrossRef]
26. Ryu HJ, Yang DW. The Seoul neuropsychological screening battery (SNSB) for comprehensive neuropsychological assessment. *Dement Neurocogn Disord*. 2023;22(1):1-15. [CrossRef]
27. Shin MS, Park SY, Park SR, Seol SH, Kwon JS. Clinical and empirical applications of the Rey–Osterrieth complex figure test. *Nat Protoc*. 2006;1(2):892-899. [CrossRef]
28. Bench CJ, Frith CD, Grasby PM, et al. Investigations of the functional anatomy of attention using the Stroop test. *Neuropsychologia*. 1993;31(9):907-922. [CrossRef]
29. Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M, Capitani E. Trail making test: normative values from 287 normal adult controls. *Ital J Neurol Sci*. 1996;17(4):305-309. [CrossRef]
30. Kang SJ. The reliability and validity of the Korean Instrumental Activities of Daily Living (K-IADL). *J Korean Neurol Assoc*. 2002;20(1):8-14.
31. Saxton J, Snitz BE, Lopez OL, et al. Functional and cognitive criteria produce different rates of mild cognitive impairment and conversion to dementia. *J Neurol Neurosurg Psychiatry*. 2009;80(7):737-743. [CrossRef]
32. Kliegel M, Zimprich D, Eschen A. What do subjective cognitive complaints in persons with aging-associated cognitive decline reflect? *Int Psychogeriatr*. 2005;17(3):499-512. [CrossRef]
33. Reid LM, Maclullich AM. Subjective memory complaints and cognitive impairment in older people. *Dement Geriatr Cogn Disord*. 2006;22(5-6):471-485. [CrossRef]
34. Lehrner J, Gufler R, Guttmann G, et al. Annual conversion to Alzheimer disease among patients with memory complaints attending an outpatient memory clinic: the influence of amnestic mild cognitive impairment and the predictive value of neuropsychological testing. *Wien Klin Wochenschr*. 2005;117(18):629-635. [CrossRef]
35. Devanand DP, Liu X, Tabert MH, et al. Combining early markers strongly predicts conversion from mild cognitive impairment to Alzheimer's disease. *Biol Psychiatry*. 2008;64(10):871-879. [CrossRef]
36. Peters F, Villeneuve S, Belleville S. Predicting progression to dementia in elderly subjects with mild cognitive impairment using both cognitive and neuroimaging predictors. *J Alzheimers Dis*. 2014;38(2):307-318. [CrossRef]
37. Rabin LA, Paré N, Saykin AJ, et al. Differential memory test sensitivity for diagnosing amnestic mild cognitive impairment and predicting conversion to Alzheimer's disease. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2009;16(3):357-376. [CrossRef]

38. Eckerström C, Olsson E, Bjerke M, et al. A combination of neuropsychological, neuroimaging, and cerebrospinal fluid markers predicts conversion from mild cognitive impairment to dementia. *J Alzheimers Dis*. 2013;36(3):421-431. [CrossRef]
39. Galton CJ, Erzinçlioglu S, Sahakian BJ, Antoun N, Hodges JR. A comparison of the Addenbrooke's Cognitive Examination (ACE), conventional neuropsychological assessment, and simple MRI-based medial temporal lobe evaluation in the early diagnosis of Alzheimer's disease. *Cogn Behav Neurol*. 2005;18(3):144-150. [CrossRef]
40. Didic M, Felician O, Barbeau EJ, et al. Impaired visual recognition memory predicts Alzheimer's disease in amnestic mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2013;35(5-6):291-299. [CrossRef]
41. Guarch J, Marcos T, Salamero M, Gastó C, Blesa R. Mild cognitive impairment: a risk indicator of later dementia, or a preclinical phase of the disease? *Int J Geriatr Psychiatry*. 2008;23(3):257-265. [CrossRef]
42. Albert MS, Moss MB, Tanzi R, Jones K. Preclinical prediction of AD using neuropsychological tests. *J Int Neuropsychol Soc*. 2001;7(5):631-639. [CrossRef]
43. Wei MY, Levine DA, Zahodne LB, Kabeto MU, Langa KM. Multimorbidity and cognitive decline over 14 years in older Americans. *J Gerontol A Biol Sci Med Sci*. 2020;75(6):1206-1213. [CrossRef]