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Complex activities of daily living in mild cognitive impairment: conceptual and diagnostic issues

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Abstract

Background: the impact of cognitive impairment on activities of daily living (ADL) is being used as a major criterion for differentiating between mild cognitive impairment (MCI) and dementia. The concept of an ADL threshold that separates MCI from dementia, however, appears to be improbable for several reasons.
Objectives: to determine whether complex ADL are impaired in patients with MCI; to examine the usefulness of the assessment of ADL impairment for the diagnosis of MCI; to explore whether both cognitive testing and assessment of impaired ADL are significant predictors of the diagnosis according to the diagnostic gold standard of MCI.
Design: cross-sectional study.
Setting: university-based outpatient clinic.
Subjects: a total of 45 elderly MCI patients diagnosed according to research diagnostic criteria and 30 age-matched cognitively unimpaired controls.
Methods: clinical assessment – Alzheimer's disease Assessment scale, cognitive subscale (ADAS-cog) for the assessment of cognitive functions, Alzheimer's disease Cooperative Study scale for ADL in MCI (ADCS-MCI-ADL) for the assessment of impairments of complex ADL. Statistical evaluation – Mann–Whitney U tests for significant differences on measures of cognition and everyday functioning. Non-parametric correlations for associations between ADL and cognitive ability. Receiver operator curve (ROC) analyses to identify optimal cut-off scores on the ADCS-MCI-ADL and ADAS-cog scales to differentiate between MCI patients and controls. Binary logistic regression analyses to predict the diagnosis of MCI on the basis of the above-mentioned instruments.
Results: patients scored significantly higher than controls on the ADAS-cog scale and significantly lower on the ADCS-MCI-ADL scale. There was a significant negative correlation of the above-mentioned scales in MCI patients ($r = -0.46$, $P<0.01$). Both instruments discriminated well between patients and controls (ADCS-MCI-ADL: optimal cut-off 52 points, sensitivity 0.89, specificity 0.97; ADAS-cog: optimal cut-off 10 points, sensitivity 0.78, specificity 1.0). With regard to the linear predictor in the logistic regression built, both instruments were strong predictors of the diagnosis according to the diagnostic gold standard (ADCS-MCI-ADL: $P = 0.002$; ADAS-cog: $P = 0.041$).
Conclusion: impairment of ADL is already present in MCI. Therefore, intact ADL cannot be used as a criterion to define the syndrome of MCI and to distinguish it from mild dementia. The assessment of complex ADL is probably useful for the diagnosis of MCI.

Keywords: *mild cognitive impairment, activities of daily living, Alzheimer's disease, dementia, elderly*

Introduction

Clinical follow-up studies and neuropathological investigations suggest that mild cognitive impairment (MCI) is often a prodromal state of a neurodegenerative disorder such as Alzheimer's disease (AD) [1]. MCI has been conceptualised as an intermediate state between physiological age-associated cognitive decline and mild dementia. Since cognition deteriorates continuously in most neurodegenerative diseases which

eventually cause dementia, no clear cut-off point exists on any cognitive scale that would separate MCI from dementia. Therefore, the impact of cognitive impairment on activities of daily living (ADL) is being used as a major criterion for the differentiation between MCI and dementia. According to the most frequently used current diagnostic criteria [2], MCI is associated with intact ADL, whereas functional abilities are impaired in dementia and are part of the definition of the syndrome. The underlying assumption is that the ADL remain unimpaired until a certain degree of cognitive deterioration has been reached. The concept of an ADL threshold that separates MCI from dementia is useful for a number of practical reasons. In clinical practice, a clear-cut differentiation between MCI and dementia is important for rapid communication about the disease [3], for management decisions and for counselling carers on present and forthcoming problems. However, different levels of everyday activities have to be distinguished. Basic activities such as bathing, eating and getting dressed remain preserved when first symptoms of cognitive deterioration occur. In contrast, complex ADL such as organising work, managing finances or using public transportation are dependent on intact memory, attention and executive functions, and are likely to decline below previous levels if these cognitive abilities become mildly impaired. Supporting this view, deterioration of complex ADL has been reported in patients with MCI [4]. Furthermore, a close association between measures of cognitive ability and assessments of ADL has been observed in patients with MCI [5], which strongly argues against the assumption of an ADL threshold. Recently, an international working group on MCI agreed that complex functional abilities should be included in the diagnostic process and that slopes of decline may be better measures than deficits relative to age-specific norms [6].

If limitations on complex ADL were present in patients with MCI, the assessment of impairments in everyday life might provide useful complementary information to establish the diagnosis of the syndrome. However, to our knowledge, only a few studies have tried to differentiate between cognitively healthy individuals and patients with cognitive impairment (MCI or dementia) on the basis of ADL. Using a sub-sample of the Canadian Study of Health and Aging, Ebly et al. [7] found significant functional differences between healthy elderly subjects (N = 921), cognitively impaired not demented (CIND, N = 841) individuals and demented patients (N = 1,133). Another comparative study (Doble et al. [8]) of 44 healthy elderly individuals, 24 patients with CIND and 36 with AD found that all three groups differed significantly when their scores on several ADL instruments and their MMSE scores were combined.

The present study had three objectives. First, we wished to determine whether complex ADL are in fact impaired in patients with MCI, using a definition of the syndrome which allowed for such limitations to be present but clearly excluded dementia. Second, we attempted to determine the usefulness of ADL impairments for the diagnosis of MCI. Third, we tried to explore whether both a standard cognitive test and the assessment of impaired ADL were significant predictors of the diagnosis according to the diagnostic gold standard of MCI.

Methods

Study sample and design

The study was carried out at a university-based research unit for cognitive disorders as part of a national collaboration on dementia (Competence Network Dementia [9]). The study refers to 45 patients who sought or were referred for cognitive evaluation and were diagnosed with MCI using research diagnostic criteria developed for this network (Table 1) and who did not meet diagnostic criteria for dementia. For the purposes of the study, we employed a definition of MCI which on the one hand was more explicit than conventional criteria with regard to the level of ADL impairment that was permissible for the diagnosis, and which on the other hand clearly excluded mild stages of dementia. These criteria differ from the frequently used Mayo-Clinic definition [2] in three respects. First, they do not require subjective memory complaints, since this is a poor predictor of objective deterioration of cognitive ability [10]. Second, memory impairment may be absent if at least one other cognitive domain is significantly affected in order to include patients with frontotemporal degenerations and subcortical dementias. Third, although basic ADL are required to be intact, impairment of complex ADL is not a criterion for exclusion from the study. All consecutive evaluations that met the inclusion criteria were entered into the study. There was no selection for patients other than described above.

Cognitive evaluation was based on the Consortium to Establish a Registry for Alzheimer's disease Neuropsychological Assessment Battery (CERAD-NAB), German version [11] which incorporates the Mini-Mental-State Examination (MMSE) [12]. This instrument provides information on verbal and non-verbal learning and memory, verbal fluency, object naming and visuoconstruction. Patients and controls with minor limitations on complex ADL were not excluded from the study. However, to ensure that patients with significant functional impairment including the loss of basic ADL, who might already have crossed the threshold to dementia were not included,

Table 1. Criteria used for the definition of MCI

Inclusion criteria
Cognitive performance of at least 1 SD below the age and education norm in one or more of the following domains: verbal learning and memory, non-verbal learning and memory, verbal fluency, naming, visuoconstruction, information processing speed, executive functions, as demonstrated by the appropriate neuropsychological tests
Decline in cognitive function from a previously higher level of ability
No impairment of basic activities of daily living. More complex activities of daily living may be slightly impaired (B-ADL≤4)
CDR of 0.5 (questionable dementia)
Exclusion criteria
Diagnostic criteria for dementia met
CDR of 1 or higher
Clinically significant psychiatric or neurological disease state which may account for the cognitive impairment

CDR, clinical dementia rating.

patients with an average of more than four points on the Bayer Activities of Daily Living scale (B-ADL) [13] were excluded from the study. This score has been found to discriminate dementia from normal ageing [14] and the potential impairment of complex ADL is in accordance to the latest recommendations of an international group of experts on MCI [6]. Impairment of complex ADL was not a requirement for the diagnosis of MCI, and patients were diagnosable with MCI if they had performed completely normally on everyday tasks. To exclude the impact of physical disabilities on the rating of complex ADL, the informants were given the instruction to report impairment due to cognitive decline only. In most of the cases, informants were the patients' spouses or relatives, who lived in the same household. The assessment was complemented by tests of episodic memory (Wechsler Memory Scale Logical Memory) [15], information processing speed (Trail Making Test A) [16], language [17], constructional ability (Clock Drawing Test) [18] and executive functions (Trail Making Test B) [16]. Interviews were conducted with the informants using the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) [19] to verify deterioration of cognitive ability from a previously higher level. Severity of cognitive decline was rated on the Clinical Dementia Rating (CDR) [20]. A neurological examination, laboratory screening and brain imaging (cranial magnetic resonance imaging) were also performed.

At a separate visit within 4 weeks after the initial examination, the Alzheimer's disease Cooperative Study scale for ADL in MCI (ADCS-MCI-ADL) [21] was administered by an independent rater. This interview was developed to assess impairment of everyday tasks in non-demented individuals with high sensitivity. It covers 18 areas. The overall score varies between zero (worst performance) and 57 (best performance). The Alzheimer's disease Assessment Scale, cognitive subscale (ADAS-cog) [22] was performed at this visit by the same independent rater. This interview is the most frequently used cognitive assessment battery in clinical trials of antidementia drugs. It consists of 11 tasks including the assessment of memory, comprehension, orientation in time and place, praxis and attention. Scores vary between zero and 70 points with higher scores indicating poorer performance.

The study also included 30 age-matched control subjects without cognitive complaints who were the patients' spouses or friends and were recruited from the same unit. They had not been referred for cognitive evaluation and had no history of neurological or psychiatric illness. The same assessment instruments were used for patients and controls. Controls with impaired ADL were not excluded. Both patients and controls gave their written informed consent after the purpose and the procedures of the study had been fully explained. The study protocol was approved by the local ethics committee. The research reported complies with the ethical rules for human experimentation as stated in the Declaration of Helsinki.

Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 11.5 (SPSS Inc., Chicago, IL). Absolute frequencies were compared between patients and controls using chi-square tests. To determine whether complex ADL scores were impaired in patients with MCI compared to controls, median values were examined for statistically significant differences using non-parametric Mann–Whitney U tests. Associations between ADL and cognitive ability were analysed using non-parametric correlations (Spearman's rank correlation coefficient). In addition, a scatter plot of the relationship between ADCS-MCI-ADL and ADAS-cog scores was generated. Non-parametric correlations were also computed between B-ADL and ADCS-MCI-ADL scores. To determine the usefulness of ADL impairments for the diagnosis of MCI, a receiver operator curve (ROC) analysis was applied to the sample in order to identify cut-off scores on the ADCS-MCI-ADL and the ADAS-cog scales which differentiated best between patients and controls with respect to the 1-norm. The area under the ROC-curve (AUC) was used to determine the accuracy of each instrument in differentiating between patients and controls. AUC values of less than 1.0 (perfect test) refer to excellent (>0.9), good (>0.8), fair (>0.7) and poor (>0.6) accuracy. Binary logistic regression analyses were used to predict the diagnosis according to the research diagnostic criteria for the diagnosis of MCI on the basis of both instruments and respective cut-off values. All *P*-values given are unadjusted, two-sided and subject to a significance level of 5%. After correction for multiple testing, significance remains unchanged.

Results

Description of the study population

There were no statistically significant differences between patients and controls with regards to gender distribution, age or years of formal education. Patients scored significantly lower on the MMSE scale and significantly higher on the ADAS-cog scale than the controls, showing a greater impairment of cognitive functions. Patients also had a significantly higher average score on the B-ADL scale and a significantly lower score on the ADCS-MCI-ADL scale, indicating a greater degree of ADL impairment. Patients showed a rather great range both on scales of cognition and daily functioning consistent with the well-documented heterogeneity of the syndrome (Table 2). There was a modest but statistically significant negative correlation of the ADCS-MCI-ADL and ADAS-cog scores in MCI patients ($r = -0.46$, $P<0.01$, Figure 1). B-ADL and ADCS-MCI-ADL scores were also significantly correlated in patients ($r = -0.61$, $P<0.01$).

Results of the ROC analyses

The results of the ROC analyses displayed in Figure 2 show that both instruments discriminated well between patients and controls (ADCS-MCI-ADL: optimal cut-off at 52 points with a sensitivity of 0.89 and a specificity of 0.97;

Table 2. Description of study sample.

Sample characteristics	Patients ($N = 45$)	Controls ($N = 30$)	P values
Females : males	21:24	14:16	0.386
Education[a]	11.36 ± 2.51	12.50 ± 2.85	0.168
Age[a]	69.17 ± 8.30	66.67 ± 9.27	0.182
MMSE[a] (range)	26.88 ± 1.42 (25–29)	29.27 ± 0.69 (28–30)	<0.001
ADAS-cog[a] (range)	15.47 ± 6.78 (4–33)	6.00 ± 1.93 (2–9)	<0.001
ADCS-MCI-ADL (range)[a]	41.38 ± 9.85 (10–57)	55.93 ± 1.68 (50–57)	<0.001
B-ADL average score[a] (range)	2.82 ± 0.96 (1–4)	1.00 ± 0.0 (1)	<0.001

[a]Mean ± standard deviation. Mini-Mental-State Examination (MMSE) normal range: 1–30. Alzheimer's disease Assessment scale (ADAS-cog) normal range: 0–70. Alzheimer's disease Cooperative Study scale for Activities of Daily Living in Mild Cognitive Impairment (ADCS-MCI-ADL) normal range: 0–57. Bayer Activities of Daily Living (B-ADL) normal range: 0–10.

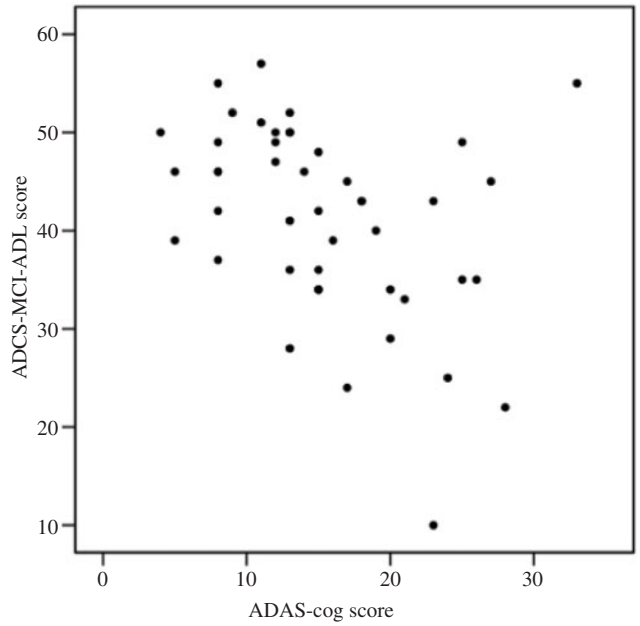

Figure 1. Scatterplot of the relationship between ADCS-MCI-ADL and ADAS-cog scores.

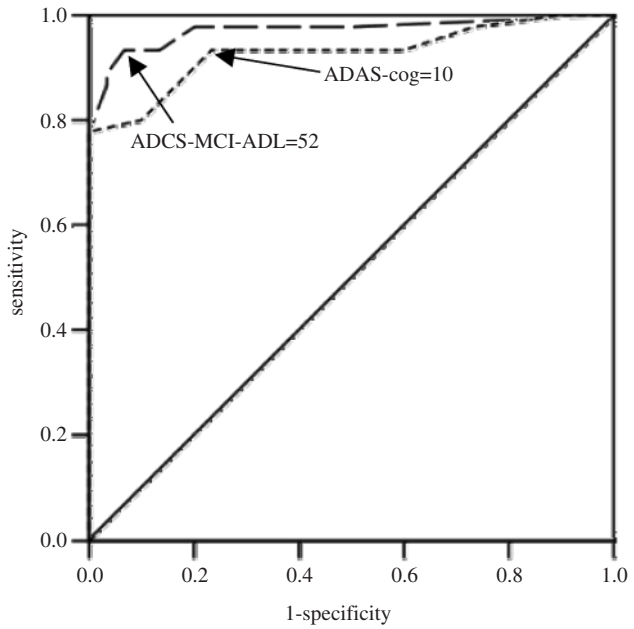

Figure 2. ROC curves for ADCS-MCI-ADL and ADAS-cog. The optimal cut-points on the receiver operator curve (ROC) are defined as the minimal distance to (0/1) with respect to the 1-norm and are indicated by arrows. The line with long dashes represents all possible cut-points of the Alzheimer's disease Cooperative Study scale for Activities of Daily Living in Mild Cognitive Impairment (ADCS-MCI-ADL). The line with short dashes indicates all possible cut-points of the Alzheimer's disease Assessment Scale (ADAS-cog). The solid line is the line for a random test. A positive classification on the graph is having the more severe of the two categories.

ADAS-cog: optimal cut-off at 10 points with a sensitivity of 0.78 and a specificity of 1.0). The discriminating accuracy of the ADCS-MCI-ADL was slightly superior to the ADAS-cog (AUC 0.97 vs. 0.93). However, this difference was not statistically significant.

Results of the logistic regression analyses

With regard to the linear predictor in the logistic regression built by entering the two diagnostic tests to a null model in a stepwise fashion, both ADCS-MCI-ADL and ADAS-cog were strong predictors of the diagnosis according to the diagnostic gold standard (ADCS-MCI-ADL: $P = 0.002$; ADAS-cog: $P = 0.041$).

Discussion

Our results demonstrate that patients with MCI perform significantly poorer than age- and gender-matched cognitively unimpaired controls on informant interviews on complex ADL. This result is consistent with previous studies showing that patients with questionable dementia (CDR rating of 0.5) are more impaired on informant-reported ADL [7, 8, 23, 24]. Furthermore, we found a strong correlation between patients' level of cognitive performance and their ability to carry out everyday tasks. This finding is consistent with the findings of several recent studies which show that patients with MCI have limitations in various situations of everyday life due to their memory impairment, especially in

tasks requiring episodic memory [25]. It is unlikely that our finding of ADL impairment in MCI patients can be attributed to including patients who had already progressed to dementia. Patients were excluded from the study who met ICD-10 criteria for dementia [26], who were rated 1 or higher on the Clinical Dementia Rating [20], and who had a score on a standard ADL scale that was suggestive of dementia [14]. This operational criterion was necessary because the original definition of MCI specified neither provides measures for the assessment of ADL nor levels of performance consistent with the diagnosis of MCI [27]. Even though the impairment of complex ADL was not required for the diagnosis of MCI in our study, there was not one single patient whose ADL were unimpaired. Furthermore, our sample was entirely comparable to patient populations enrolled in other MCI studies. In a recent study evaluating donepezil and vitamin E in patients with the amnestic subtype of MCI [28], patients were of similar age (mean value 72.9, standard deviation 7.3), had a comparable cognitive level as assessed by the MMSE (mean value 27.27, standard deviation 1.8) and the ADAS-cog scales (mean value 11.26, standard deviation 4.4), and had a similar degree of ADL impairment (ADCS-MCI-ADL: mean value 46.06, standard deviation 4.7). Additionally, in a recent publication by Geslani *et al.* [27], which used an operational definition of the Mayo-Clinic criteria to explore the conversion rate of MCI to AD, the patients also showed similar demographic (age: mean value 73.07 years, standard deviation 7.72; education: mean value 12.67 years, standard deviation 3.24) and test characteristics (MMSE: mean value 26.58, standard deviation 2.20).

We also found that cognitive testing and informant-based interviews on everyday functioning both discriminated very well between MCI patients and healthy controls. Both instruments were almost equal predictors of the diagnosis according to research diagnostic criteria of MCI. These results provide further proof that the impairment of complex ADL is an essential component of the MCI syndrome and should therefore be included in the diagnostic process. Detailed information on the impairment of MCI patients in the particular items of the ADCS-MCI-ADL scale is published elsewhere [4].

Our study also has several limitations. First, the participants are unlikely to be representative of the entire population with MCI, since they were relatively young, well educated, physically healthy, and were recruited at a university centre. Second, the CERAD-NAB used as part of the expert diagnosis and the ADAS-cog used for the evaluation of the present results are similar in some aspects. Therefore training effects will have possibly occurred in the successive administration of both instruments. In this case, training effects would have occurred both in the patient and the control group. Third, the ADAS-cog may not be the most sensitive test for the identification of minor cognitive impairments, although it has been used previously in studies including patients with MCI [28].

In conclusion, if one uses a definition of MCI which does not a priori exclude any impairment of ADL and clearly excludes mild stages of dementia, it becomes apparent that impairment of ADL is present before the conventional threshold of dementia is reached. As a consequence, intact ADL cannot be used as a criterion to define the syndrome of MCI nor to distinguish it from mild dementia since not only cognitive abilities worsen in a majority of MCI patients [29], but also their ability to perform everyday tasks. Therefore, the assessment of complex ADL is probably useful for the diagnosis of MCI. However, as the group of MCI patients is highly heterogeneous, deficits in complex ADL may represent MCI in general, but may not be specific to those who are likely to develop dementia. Ongoing longitudinal studies on larger patient samples will allow more specific characterisations.

Key points

- Impairment of complex ADL is already present before the conventional threshold of dementia is reached.
- Intact complex ADL cannot be used as a criterion to define the syndrome of MCI nor to distinguish it from mild dementia.
- Not only cognitive abilities worsen in a majority of MCI patients, but also their ability to perform everyday tasks.
- The assessment of complex ADL is probably useful for the diagnosis of MCI.

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