Original Research Article

Impairment in Proverb Interpretation as an Executive Function Deficit in Patients with Amnestic Mild Cognitive Impairment and Early Alzheimer's Disease

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Abstract

Background/Aims: Proverb interpretation is assumed to reflect executive functions. We hypothesized that proverb interpretation is impaired in patients with amnestic mild cognitive impairment (aMCI) diagnosed as single-domain impairment by common neuropsychological testing. **Methods:** We compared performance in a proverb interpretation test in single-domain aMCI patients and patients with early Alzheimer's disease (EAD). **Results:** The groups with aMCI and EAD performed significantly worse than healthy controls. Both patient groups gave concrete answers with a similar frequency. However, patients with EAD tended to give senseless answers more frequently. **Conclusions:** Our data suggest that in patients diagnosed as single-domain aMCI, deterioration of executive functions is detectable with subtle and appropriate neuropsychological testing. Implementation of these procedures may improve the early prediction of AD.

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Introduction

Mild cognitive impairment (MCI) is regarded as the transitional state between the cognitive changes in normal aging and early dementia. Initially, memory impairment was a prerequisite for the diagnosis of MCI. Meanwhile, different clinical subtypes of MCI have been

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proposed to extend the concept and include prodromal forms of a variety of dementias: (a) single-domain amnestic MCI (aMCI), (b) multiple-domain aMCI, (c) single-domain non-amnestic MCI, and (d) multiple-domain non-amnestic MCI [1].

Although memory decline is the hallmark of aMCI, impairment in executive functions has also been reported in these patients [2]. Executive functions are superordinate concepts encompassing a spectrum of cognitive functions such as monitoring, controlling, planning, behavior initiation, flexibility, inhibition, and abstract thinking [3]. Impairment in tasks requiring executive control appears to be a reliable predictor of Alzheimer's disease (AD) [4]. In early AD (EAD), the presence of executive dysfunction is common [5].

Set shifting, inhibition abilities and abstract thinking are executive functions which are involved in processes such as proverb comprehension [6, 7]. Proverbs are simple sayings which express a truth, based on common sense or practical experience. Usually, proverbs are metaphoric and cannot be interpreted literally. Impairments in interpreting proverbs are assumed to be associated with executive dysfunction, which leads to an impaired ability to disregard a concrete meaning and understand an abstract figurative meaning [8].

Deficits in understanding proverbs are a hallmark of thought disorder in schizophrenia that is characterized by aspects of concrete thinking [9]. Barth and Küfferle [10] applied a 15-item proverb interpretation test and found that schizophrenic patients interpreted proverbs in a significantly less meaningful and abstract way than patients with depressive disorders. They introduced a qualitative evaluation system using a multiple-choice task. After listening to a verbally presented metaphoric proverb, the patients had to choose 1 of 5 interpretation options given by the investigator. The interpretation categories were based on the assumptions by Benjamin [11], who proposed an interpretation system consisting of two levels, namely (1) 'desymbolization' and (2) 'sense'. Desymbolization involves the level of abstraction necessary when interpreting proverbs. Depending on the level of desymbolization, the interpretation can be partially or completely concrete or abstract. According to the second level of the interpretation system, the interpretation can be meaningful or senseless.

Kempler et al. [12] demonstrated substantial deficits in understanding proverbs even in mildly affected AD patients. In another study, only 30% of the presented proverbs were correctly explained by AD patients [13]. So far, no study has investigated proverb comprehension in patients with MCI.

Recent studies investigated other forms of non-literal language comprehension in AD. Using a sentence-to-picture task, Papagno et al. [7] examined idiom comprehension in patients with mild AD. They presented pictures showing literal and figurative senses of idioms and observed that literal comprehension was normal or only mildly impaired, whereas figurative comprehension was poor. The authors suggested that AD patients may not have lost the ability to understand the figurative meaning but are unable to inhibit the literal meaning. Amanzio et al. [6] investigated patients with mild and advanced AD using a novel metaphor task and found a relationship between metaphor comprehension and performance in the visual planning task from the Behavioral Assessment of Dysexecutive Syndrome test battery, suggesting that the processing of novel metaphors may be negatively affected by executive dysfunction.

In the present study, we investigated proverb interpretation in patients with single-domain aMCI and EAD. We hypothesized that proverb comprehension would best correlate with performance in executive function tasks. Moreover, we hypothesized that proverb interpretation is already impaired in patients with single-domain aMCI, suggesting subtle executive dysfunctions in this group.

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Table 1. Demographic data and cognitive status

	HC	aMCI	EAD
Subjects	32	12	22
Female	17	5	13
Male	15	7	9
Age, years	71.9 ± 6.0	75.3 ± 6.5	75.1 ± 7.0
Education, years	12.0 ± 3.4	12.7 ± 3.1	12.1 ± 3.6
MMSE score	29.1 ± 1.0	28.1 ± 1.3	24.0 ± 1.7

Values are numbers or mean $\pm$ SD.

Methods

Subjects

Sixty-six subjects (35 women, 31 men) with a mean age of 73.6 ± 6.5 years (range: 60–93 years) participated in this study and were divided into 3 groups: healthy controls (HC), patients with single-domain aMCI, and patients with EAD. Patients were recruited from the Memory Clinic of the Department of Psychiatry and Psychotherapy of the University Hospital of Tübingen. The study was approved by the local ethics committee, and written informed consent was obtained from each individual. The HC group consisted of patients' relatives or friends who did not have a history of neurological or psychiatric disease or any signs of cognitive decline, as confirmed by clinical interview.

Patients with AD and aMCI underwent physical, neurological, and psychiatric examinations. In addition, electroencephalography and computed tomography or magnetic resonance imaging of the brain were performed. Routine laboratory tests included lues serology and analysis of vitamin B_{12}, folic acid, and thyroid-stimulating hormone levels. Neuropsychological testing of all patients was performed using the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-plus) test battery [14].

aMCI was defined using the Mayo criteria, which include the presence of a memory complaint by the patient or a reliable informant, impaired memory function for age and education, preserved general cognitive function (MMSE score $\geq$ 26) [15], intact activities of daily living, and the absence of dementia. All 12 patients with MCI were, by definition, patients with single-domain aMCI [1]. No other cognitive impairments were detected by detailed neuropsychological testing.

All patients with AD met the diagnostic criteria of probable AD according to the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association [16] and had a score of 4 on the Global Deterioration Scale [17]. All patients and control subjects were native German speakers, had normal or corrected-to-normal visual acuity and sufficient hearing ability. None of the participants had a physical handicap influencing the ability to perform the required tasks or an indication of neurological or psychiatric disorders not related to their diagnosis.

The demographic data and the mean MMSE scores of the 3 groups are shown in table 1. One-way analyses of variance (ANOVA) of mean age ($F_{(2, 63)} = 2.07$; $p = 0.135$) and education ($F_{(2, 63)} = 0.21$; $p = 0.809$) showed no significant group differences. The 3 groups did also not differ according to gender distribution ($\chi^2[2] = 0.94$; $p = 0.623$). As expected, one-way ANOVA was highly significant for the MMSE score ($F_{(2, 63)} = 97.00$; $p < 0.001$). Post-hoc tests showed significant differences between all 3 groups in the expected order of EAD < MCI < HC.

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Table 2. The 10 items of the proverb interpretation test

1	While the cat's away, the mice will play. (Wenn die Katze aus dem Haus ist, tanzen die Mäuse auf dem Tisch.)
2	There's honor among thieves. (Eine Krähe hackt der anderen kein Auge aus.)
3	Harm set, harm get. (Wer anderen eine Grube gräbt, fällt selbst hinein.)
4	Even a blind hen sometimes finds a grain of corn. (Auch ein blindes Huhn findet manchmal ein Korn.)
5	Strike while the iron is hot. (Man soll das Eisen schmieden, solange es heiss ist.)
6	If the child has drowned, one covers the well. (Wenn das Kind ertrunken ist, deckt man den Brunnen zu.)
7	Too many cooks spoil the broth. (Viele Köche verderben den Brei.)
8	A burned child dreads the fire. (Ein gebranntes Kind scheut das Feuer.)
9	No rose is so beautiful that it does not finally wilt. (Keine Rose ist so schön, dass sie nicht endlich welke.)
10	If the fox wants to catch geese, he wags his tail. (Wenn der Fuchs Gänse fangen will, so wedelt er mit dem Schwanz.)

Neuropsychological Assessment

The investigator performing the neuropsychological assessment was blinded to the clinical diagnosis.

Proverb Interpretation Test

Ten common German proverbs were selected from the proverb interpretation test by Barth and Küfferle [10] (table 2) and verbally presented to the subjects. In contrast to the original version by Barth and Küfferle [10], the subjects were asked to provide their own interpretation of the proverb meaning instead of choosing the appropriate meaning from five interpretation options because we wanted to avoid recognition effects. Each explanation was assigned to 1 of the 5 categories according to the scoring system by Barth and Küfferle [10]. An example is shown in table 3. The participants scored 1 point for a correct interpretation (type I), 2 points for a meaningful and partially concrete solution (type II), 3 points for a meaningful and concrete interpretation (type III), 4 points for a senseless and concrete solution (type IV), and 5 points for a senseless and abstract interpretation (type V). Thus, for all 10 proverbs, a score of 10 indicated a completely correct interpretation, whereas a score of 50 revealed a completely poor performance.

Cognitive Test Battery

Cognitive functions were evaluated in all patients using a comprehensive neuropsychological test battery consisting of subtests and short forms of commonly used neuropsychological measures (CERAD-plus) [10]. Executive function was tested with the Trail Making Test part A (TMT A) and part B (TMT B). Concept formation as a part of executive function

Table 3. Categorization of proverb interpretation depending on the two levels 'desymbolization' and 'sense' into type I–V

| | | Desymbolization | | |
		Abstract	Partially concrete	Concrete
Sense	Meaningful	Type I: When no controlling person is present, you can do what you want.	Type II: When nobody is there to look after you, the mice can do what they want.	Type III: Cats eat mice. Mice hence cannot celebrate till the cat has left home.
	Senseless	Type V: When nobody is there, you can do anything alone.	No type available	Type IV: When the cat and the mice are absent, then the house is completely unattended.

Test item: 'While the cat's away, the mice will play'.

was assessed by a semantic and phonological verbal fluency task. The copy condition of the Rey-Osterrieth Complex Figure test was used to test for deficits in visuospatial planning ability. A total of 18 details were assessed with regard to their presence, placement, and completeness with 0–2 points, according to the 36-point evaluation system by Osterrieth. Evaluation guidelines as described by Taylor were applied [18]. Language abilities were evaluated with the 15-item subset of the Boston Naming Test. For testing visuospatial abilities, the subjects had to copy the four geometric figures of the CERAD test battery. Verbal short-term (immediate recall) and long-term (delayed recall) memory functions were assessed with the word list of the CERAD test battery. Figurative memory was tested with the delayed recall of the four geometric figures of the CERAD test battery.

Data Analysis

The SPSS-15 statistical package for Windows was used for data analysis. Data are shown as means ± SD. To assess group differences according to age, education, and MMSE score, one-way ANOVA was performed. Because the data from the HC and MCI groups in the proverb interpretation test were not normally distributed and variances were heterogeneous, the non-parametric Kruskal-Wallis test was applied to detect group differences. The Student-Newman-Keuls test was used for post-hoc comparisons. The χ^2 test was used to detect differences in gender distribution. The performance of the patient groups in the cognitive test battery were expressed as raw data and z-scores. Student's t test was used to compare the raw data of the aMCI and EAD groups in the cognitive test battery.

Correlation analyses between the subtests of the cognitive test battery were performed using Pearson's tests. Additionally, three types of stepwise linear regression analyses were carried out to identify which of the neuropsychological test parameters were the best variables to predict outcome in proverb interpretation in the patient groups. First, we determined the best neuropsychological test parameters to predict meaningful and abstract proverb interpretation (number of type I solutions as dependent variable). Second, we computed the test parameters which correlated best with the portion of senseless solutions. The portion of senseless solutions was determined by the ratio of the senseless solutions (type IV and type V solutions) to all solutions besides the meaningful and concrete ones (type I + type IV + type V solutions). Third, we determined the neuropsychological variables which correlated best with the portion of concrete solutions. The portion of concrete solutions was calculated

Table 4. Group differences of performance in the proverb interpretation test

	HC	aMCI	EAD	$\chi^2[2]$	p
Proverb interpretation test	12.4 (2.1)	17.9 (5.3)[a]	24.4 (11.1)[a]	27.6	<0.001

Means (SD) are given for the proverb interpretation test. [a] Significant difference compared to HC (p < 0.05).

Table 5. Group differences of performance in the cognitive test battery

Neuropsychological parameter	aMCI		EAD		t [33]	p
	raw value	z-score	raw value	z-score		
Boston Naming Test (max. 15)	13.9 (1.4)	–0.2	13.0 (1.8)	–1.0	1.48	0.148
CERAD word list, immediate recall (max. 30)	17.0 (2.7)	–0.5	11.4 (3.6)	–2.4	4.51	<0.001
CERAD word list, delayed recall (max. 10)	4.5 (1.2)	–1.0	1.7 (1.6)	–2.1	5.12	<0.001
CERAD figures, copy (max. 11)	9.8 (1.4)	–0.8	10.1 (1.3)	–0.8	–0.57	0.573
CERAD figures, delayed recall (max. 11)	7.8 (2.1)	–0.7	3.5 (2.9)	–1.9	4.14	<0.001
TMT A, s[a]	46.0 (11.7)	0.0	75.1 (33.5)	–1.5	–2.64	0.014
TMT B, s[a]	114.6 (34.4)	0.1	252.4 (72.9)	–1.8	–5.62	<0.001
TMT B/A, s	2.5	0.1	3.4	–0.8	–4.89	<0.001
Semantic fluency	18.9 (5.2)	–0.2	11.9 (5.4)	–1.6	3.67	<0.001
Phonological fluency	13.6 (5.0)	0.8	12.2 (6.0)	0.4	0.57	0.572
ROCF (max. 36)	31.9 (5.1)		24.1 (8.9)		2.79	0.009

Means (SD) are given for all tests (raw data). ROCF = Rey-Osterrieth Complex Figure test; max. = maximum. [a] Failure in coping with the task was evaluated with a maximal time limit of 180 s in the TMT A and 300 s in the TMT B.

by the ratio of the concrete solutions (type II + type III + type IV solutions) to all solutions besides the abstract and senseless ones (type I + type II + type III + type IV solutions). In each of the three regression analyses, the MMSE performance was included into the regression model to control for the influence of patients' general level of cognitive status. The significance level was set at p < 0.05.

Results

Quantitative Analysis of Performance in the Proverb Interpretation Test
The results of the 3 groups in the proverb interpretation test are shown in table 4. The HC group performed significantly better than the aMCI (p < 0.05) and EAD groups (p < 0.05). Mean scores of the EAD group were significantly worse than mean scores of the aMCI group (p < 0.05).

Qualitative Analysis of Performance in the Proverb Interpretation Test (fig. 1)
All 32 HC subjects (100.0%) successfully interpreted the proverbs in a meaningful way (type I–III). However, 17% of the HC subjects' answers showed at least partially concrete tendencies.
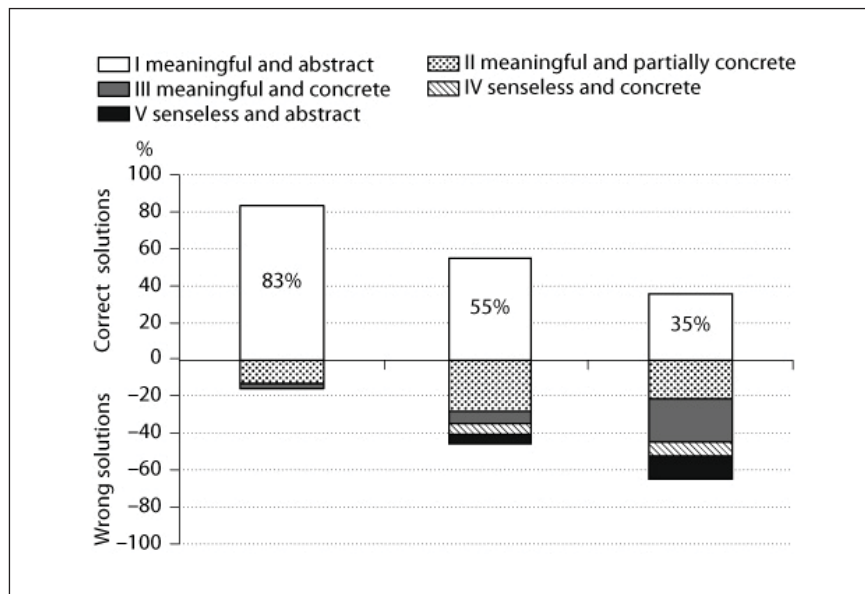
Fig. 1. Qualitative analysis of the proverb interpretation test. Percentage of answers of type I–V in HC and patients with aMCI and EAD.

In the aMCI group, 90% of all answers were meaningful (type I–III). However, only 55% of the solutions in the aMCI group were abstract and meaningful (type I). In 10% of the cases, answers were senseless (type IV and V). Post-hoc tests showed that patients with aMCI gave answers with concrete tendencies ($p < 0.05$) and senseless answers ($p < 0.05$) significantly more often than HC subjects.

In 79% of the cases, patients with EAD successfully interpreted the proverbs in a meaningful way (type I–III), but in 44% of the cases, the interpretations were meaningful with concrete tendencies (type II and III). However, 21% of the interpretations were senseless (type IV and V). Patients with EAD gave answers with concrete tendencies ($p < 0.05$) and senseless answers ($p < 0.05$) significantly more often than HC subjects. No significant differences between the EAD and the aMCI groups were observed concerning answers with concrete tendencies ($p = 0.135$). Patients with EAD gave senseless answers more often than patients with aMCI; however, the difference just failed to reach statistical significance ($p = 0.082$).

Performance in the Cognitive Test Battery
Table 5 shows the results of the aMCI and EAD groups in the cognitive test battery. Patients with EAD performed significantly worse than aMCI patients in the immediate and delayed recall of the CERAD word list, in the semantic fluency task, the TMT A, TMT B, TMT B/A, the Rey-Osterrieth Complex Figure test, and the delayed recall of the CERAD figures. No differences were detected between the aMCI and EAD groups in the Boston Naming Test, the phonological fluency task, or the copying of the four geometric figures of the CERAD test battery.

Correlation and Regression Analyses of Performance in Proverb Interpretation and Cognitive Test Battery according to Patient Groups
In the aMCI and EAD groups, meaningful and abstract interpretation of the proverbs correlated best with the TMT B ($r = -0.682$; $p < 0.001$). The better the TMT B was managed,

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Table 6. Stepwise linear regression analyses for the MCI and EAD patients

Predictor	Correct solutions (type I)				Portion of senseless solutions				Portion of concrete solutions			
	Step	β	t	p	Step	β	t	p	Step	β	t	p
MMSE	C	–0.170	–0.894	0.381	C	0.042	0.206	0.839	C	0.023	0.112	0.912
BNT		–0.148	–0.962	0.347		0.209	1.199	0.244		0.169	0.986	0.335
CERAD word list, immediate recall		0.065	0.276	0.786	1	–0.458	–2.385	0.026		–0.211	–1.002	0.328
CERAD word list, delayed recall	2	0.416	2.360	0.028		–0.261	–1.088	0.289		–0.382	–2.078	0.050
CERAD figures, copy condition		0.083	0.549	0.589		0.007	0.045	0.965		–0.055	–0.328	0.746
CERAD figures, delayed recall		0.151	0.759	0.456		–0.311	–1.702	0.104		–0.323	–1.742	0.096
TMT A		–0.141	–0.821	0.421	2	0.413	2.357	0.028		0.164	0.816	0.423
TMT B	1	–0.564	–3.023	0.006		0.085	0.354	0.727	1	0.679	3.376	0.003
TMT B/A		0.144	0.783	0.442		0.026	0.132	0.897		–0.082	–0.401	0.692
Semantic fluency		–0.172	–0.921	0.368		0.296	1.303	0.207		0.107	0.513	0.613
Phonematic fluency		0.199	1.393	0.178		–0.072	–0.393	0.698		–0.112	–0.678	0.505
ROCF, copy condition		–0.025	–0.153	0.880		–0.056	–0.320	0.752		0.022	0.117	0.908

The portion of senseless errors is the ratio of type IV + type V solutions to type I + type IV + type V solutions; the portion of concrete solutions is the ratio of type II + type III + type IV solutions to type I + type II + type III + type IV solutions.

BNT = Boston Naming Test; ROCF = Rey-Osterrieth Complex Figure test; Step = step at which repressor entered the model; β = beta coefficient; C = MMSE was the control variable.

the more type I solutions were provided. Stepwise linear regression analyses showed that 29.1% of the variance for meaningful and abstract interpretations (type I) were explained by the TMT B. In addition, 10.8% of the variance were explained by the delayed recall of the CERAD word list (table 6).

The portion of senseless solutions (ratio of type IV + type V solutions to type I + type IV + type V solutions) correlated best with the immediate recall of the CERAD word list (r = –0.484; p < 0.01). The worse the immediate recall of the CERAD word list was managed, the more senseless solutions occurred. Stepwise regression analysis showed that 16.6% of the variance could be explained by the immediate recall of the CERAD word list. TMT A significantly accounted for 13.3% of the variance in patients' senseless solutions (table 6).

The portion of concrete solutions (ratio of type II + type III + type IV solutions to type I + type II + type III + type IV solutions) correlated best with the performance in the TMT B (r = 0.581; p < 0.005). The worse the TMT B was managed, the more concrete solutions occurred. Stepwise regression analysis showed that the TMT B accounted for 28.8% of the variance of the portion of concrete solutions. None of the other neuropsychological procedures significantly explained additional variance (table 6).

Discussion

Our finding of a significant impairment in proverb interpretation in patients with aMCI diagnosed as single-domain impairment by common neuropsychological testing suggests that, in addition to the impairment in episodic memory in patients with single-domain aMCI, deficits in abstract thinking and response inhibition exist. This observation indicates a deterioration of aspects of executive function that are detectable with subtle and adequate neuropsychological testing in this group. Recently, Traykov et al. [19] reported that patients with aMCI performed significantly worse than healthy controls in the Stroop Test and the

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Modified Card Sorting Test, but not in the TMT, the Digit Symbol Test, or the verbal fluency task, indicating specific impairments in response inhibition and rule compliance in these patients. Perry et al. [20] suggested that subcomponents of executive function, such as selective attention and response inhibition, may be particularly sensitive to the neurodegenerative process of developing AD, whereas other executive domains, such as planning ability, working memory, and verbal fluency, may be relatively preserved.

Longitudinal studies of MCI patients showed that, in addition to amnestic deficits, executive dysfunction is a good predictor for subsequent incipient AD [21]. Recent studies have suggested that patients with multiple-domain aMCI have a higher probability to develop AD than patients with single-domain aMCI [22]. Other authors have reported a decline in multiple cognitive domains before the diagnosis of AD [23]. Thus, the implementation of more subtle neuropsychological tests in the assessment of patients with aMCI may be useful for predicting AD.

A staging of neuropathological changes related to AD was provided by Braak and Braak [24]. Initially, the transentorhinal cortex is affected by neuritic plaques (stages I–II). Subsequently, the limbic areas become involved (stages III–IV), and finally, plaques are found in the isocortical areas (stages V–VI). Atrophy of the medial temporal lobe in patients with MCI and EAD has been described [25]. Executive dysfunction is most frequently associated with damage to the frontal lobe [26]. However, early involvement of frontal brain regions in the neurodegenerative process of AD has not been reported. Thus, early executive dysfunction may be due to disruption of connecting fibers rather than frontal atrophy. Because executive functions are likely represented in a decentralized cortical neural network, they may be susceptible to disconnection [27]. Early damage to connecting fibers in AD has been described in recent studies [28].

Our qualitative analysis of the proverb interpretation test showed that the aMCI and EAD groups provided significantly more concrete answers than the HC subjects. With respect to this aspect of performance, patients with aMCI and EAD did not differ, which indicates a similarity in both groups with regard to a failure to inhibit literal meaning and to activate figurative meaning [6, 7, 12, 13].

Stepwise regression analysis showed that the best predictor for concrete proverb interpretation in the patient groups was the TMT B. The TMT is a common measure for determining cognitive flexibility and planning ability [29]. Especially, part B of the TMT is considered a common and sensitive measurement of cognitive flexibility in geriatric assessment [14, 30]. Thus, our data indicate that patients with aMCI and EAD show concrete interpretation of proverbs due to impairment of executive function.

Both patient groups gave significantly more senseless answers than the HC subjects. Although the difference was not significant, the EAD group tended to give senseless answers more often than the aMCI group. Regression analysis showed that the senseless interpretations were best predicted by performance in episodic short-term memory tasks. Thus, we conclude that the complete loss of sense for proverb interpretation in AD patients depends on more severe impairment in memory function.

In summary, in patients clinically classified as having single-domain aMCI, we found impairment in proverb interpretation, indicating a decline in specific aspects of executive function in this group. In particular, deterioration of abstract thinking and response inhibition appears to accompany reduced episodic memory performance. Thus, we estimate that a notable percentage of patients clinically diagnosed as single-domain aMCI may show a wider spectrum of cognitive impairment if subtle neuropsychological testing is performed. As MCI patients with deficits in memory functions and other cognitive domains have a higher risk to develop AD than patients with aMCI only, the implementation of these procedures may contribute to the early prediction of AD.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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