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Original Research Article

Anosognosia and Anosodiaphoria in Mild Cognitive Impairment and Alzheimer's Disease

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Key Words

Dementia · Disease progression · Behavior · Neuropsychology

Abstract

Aims: To evaluate the occurrence of anosognosia (lack of awareness) and anosodiaphoria (insouciance) in mild cognitive impairment (MCI) and Alzheimer's disease (AD) and to evaluate the influence of a worsening of dementia on these phenomena. **Methods:** A self-evaluation scale was used assessing degrees of anosognosia and anosodiaphoria; furthermore, a neuropsychological assessment and statistical analyses with nonparametric tests which could cope with data on an ordinal scale level and small samples were employed. **Results:** Cognitive ability was lower in AD (n = 9) than in MCI patients (n = 12), but AD patients self-rated lower cognitive disabilities, which is interpreted as one relative sign of anosognosia in AD. Awareness of the reasons for cognitive problems was also lower in AD, which is considered as another sign of anosognosia. The main pattern in MCI found that the higher the awareness, the lower the cognitive ability. In AD low awareness paralleled low cognitive functioning. Anosodiaphoria was present in AD but not in MCI. **Conclusion:** According to the literature anosognosia and anosodiaphoria seem to increase with progression of dementia from MCI as a result of right hemispheric alterations.

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Introduction

Consciousness is one of the most difficult neuropsychological concepts to define, since it refers to the essence of being alive as a human being. Thinking is a complex activity, and consciousness has been defined as 'integrated information' [1, p. 216], referring to the psychological mechanisms that continuously interweave ample, always changing, sensory infor-

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mation and make it possible for the individual to keep him or her constantly updated about the information interwoven as a gestalt [2]. Lack of illness awareness or insight may be conceived as a deficit in consciousness and has been studied throughout medical history [3–5]. Babinski [6] in 1914 coined the term anosognosia to characterize a state of a lack of consciousness of left-sided hemiplegia, which he hypothesized originated in a right hemispheric lesion, in one of his patients [7]. Later, anosognosia has come to signify a unawareness of a variety of disturbances in 'sensory, perceptual, motor, affective, or cognitive functioning' [8, p. 570; 9]. Not recognizing being ill may present serious problems for the patients, reducing their willingness to be compliant with treatment and to realize the practical consequences of the disturbance for their everyday life [10].

The neuroanatomical correlates of anosognosia in Alzheimer's disease (AD) have most often been studied with functional imaging [single photon emission computed tomography (SPECT) and positron emission tomography (PET)] [11]. There is a lot of evidence that anosognosia in AD is associated with right-sided abnormalities [8, 10, 12, 13] in the frontal region [12–16]. Aberrant metabolic activity has also been seen in the temporoparietal junction, which has been found to be 'consistent with impairment in self-referential processes and perspective taking in AD' [17, p. 588].

Not many studies have been conducted on the prevalence and neuronal correlates of anosognosia in mild cognitive impairment (MCI) [18], which is a state of failing cognition that may precede a later conversion to AD [19, 20]. However, one study reports the frequency of anosognosia in MCI to be 54% [18]. There are indications that anosognosia intensifies with a worsening of AD [13, 21], and unawareness of memory deficits in MCI has also been suggested as a possible precursor to AD [22]. Data about the prevalence of anosognosia in AD vary considerably. A range between 20 and 80% has been reported [5], but frequencies such as 46.7% of the sample [23] and 43 of 57 patients [12] have also been estimated.

Another trait that Babinski [6] observed in 1914 was that some hemiplegic patients recognized the presence of their paralysis but seemed unconcerned about it and trivialized the malfunction. Babinski named this attitude of insouciance anosodiaphoria, which resembles *la belle indifférence* earlier described by Breuer and Freud [24, p. 135] and which today in DSM-IV is considered as a conversion symptom [25, 26].

Among the neurodegenerative disorders, frontal anosodiaphoria, meaning 'lack of emotional concern' [27, p. 1690], is particularly salient in the behavioral variant of frontotemporal dementia [27, 28]. No study has been found indicating anosodiaphoria in AD. However, since there are strong indications of a frontal involvement in anosognosia in AD, the possibility of anosodiaphoria in AD also needs to be taken into consideration. Another reason is that anosodiaphoria may be mistaken for anosognosia, which can be exemplified by an interpretation of Korsakoff's description [29] in 1889 of severe amnesia as a 'lack of concern' for the symptoms, as a sign of anosognosia [5, p. 7].

Thus, there are indications that anosognosia is present in MCI and in dementia, particularly in AD, where it has been regarded as an early symptom of AD, and that anosodiaphoria is particularly indicative of the behavioral variant of frontotemporal dementia. Although behavioral and neuropsychiatric symptoms in AD are well documented [5, 30, 31], seemingly no attention has been paid to the probability of anosodiaphoria in this disorder. There also seems to exist a risk that anosodiaphoria may be mistaken for anosognosia. No study of anosodiaphoria in MCI has been found.

The aim of the present study has been to contribute to the conceptual clarity concerning the distinction between anosognosia and anosodiaphoria, to investigate whether there are signs of anosognosia as well as anosodiaphoria in MCI and AD and to evaluate the influence of progression of cognitive, mnemonic and executive disabilities on the level of anosognosia and anosodiaphoria in MCI and AD.

Table 1. Demography of MCI and AD patients

Group	n	Gender (F/M)	Age (F/M), years	p value	Age group (F + M), years	p value	Education (F/M), years	p value	Education group (F + M), years	p value
MCI	12	5/7	72.8/74.1	n.s.	73.6	0.05	13.2/17.1	n.s.	15.5	0.04
AD	9	8/1	79.6/85.0	-	80.2		11.9/13.0	-	12.0	

Values represent means. F = Females; M = males.

Materials and Methods

Participants

The participants were recruited among clinical MCI and AD outpatients at the Colorado Springs Neurological Associates, PC (CSNA), Colorado Springs, Colo., USA. The MCI sample was mixed insofar as the subjects exhibited different degrees of memory decline and deterioration of other cognitive functions. The enrollment of the subjects was nonconsecutive because of the largely varying degrees of cognitive decline among the patients. A consecutive enrollment would have risked that patients that were not testable due to intellectual disabilities would have been contacted in vain.

Patients finally included were those that were willing to participate, who were estimated to be able to perform on the tests and where relatives were positive about their participation. All the patients in the study had been informed about their diagnoses during the previous visits to their physician.

The initial sample included 31 patients with cortical as well as subcortical changes. However, the number of the patients with suspected frontotemporal pathology (2 patients), Parkinson's disease (3 patients) and ischemic disorders (5 patients) that were available during the data-collecting phase of the study (1 month, 2011) was too small, and therefore they had to be excluded from the study. The final sample consisted of 12 MCI patients and 9 AD patients (table 1). A follow-up study is planned with an increased number of patients in each of the mentioned diagnostic categories.

The mean age of the MCI group was significantly lower than that of the AD group. The educational level was generally rather elevated and significantly higher in the MCI group than in the AD group. Analyses of the effects of gender on education in the AD group were not meaningful, since the distribution of the sexes was uneven, with an overrepresentation of females in this diagnostic category.

Diagnostic Criteria

Patients were diagnosed according to the requirements of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) [32]. Indications for MCI were a decrease in cognition for age, and for AD they were an insidious onset of memory/cognitive/orientation/behavioral symptoms, imaging evidence [magnetic resonance imaging (MRI)] of cerebral atrophy, a spacious third ventricle, slowing of the posterior dominant rhythm on EEG (alpha less than 8.5 Hz) and normal National Institutes of Health (NIH) laboratory screening, including serology for *Treponema pallidum* (syphilis). Definite AD diagnosis must be based on autopsy [33].

Definitions

Cognitive awareness was understood here as a state of mind where information from different sensory systems is put together to a mental entirety [1]. Anosognosia was thus defined as a loss of or an abated awareness of symptoms, their roots and implications for life, and anosodiaphoria was defined as a reduction or a lack of botheration for this altered state of mind and situation [28]. The inclusion of the association with illness and consequences for everyday life in the anosognosia definition is based on an elaboration of a previous study [34]. For reasons of simplicity, anosognosia was used synonymously with expressions such as a lack of insight and a lack of awareness, and anosodiaphoria with expressions such as unconcern, insouciance and their equivalents. A thorough elaboration of the semantic correspondence of these synonyms would go beyond the scope of this investigation.

Living in the past, or shortcomings in adapting one's self-image to current circumstances, has been mentioned as a component of anosognosia in AD [35]. In frontotemporal dementia and AD patients 'a failure to update their self image after disease onset' has been identified as a characteristic trait for the diseases [36, p. 632]. Therefore, orientation about one's own age and reminiscence about one's profession (previous or current) have been included in the interview (see below) as relevant aspects of the anosognosia complex.

Measures

Anosognosia and Anosodiaphoria

A structured interview was conducted to assess the levels of anosognosia and anosodiaphoria, the Anosognosia and Anosodiaphoria scale (A&A scale, Appendix 1). The interview guide is a revision and a development of a previously published guide used for assessing the loss of insight into frontotemporal dementia [34]. In the present study, it consisted of ten questions, where the answers were self-rated by the patients. The awareness part of the scale, aimed at catching signs of anosognosia, consisted of two questions concerning autobiographical data (question 1: age, question 2: earlier or present profession; the correctness of the answers to the question about present or previous profession was checked against the charts or with relatives). One question (question 3) about how the days are spent and whether the patient has made any changes in his or her way of living was asked to establish whether the patient thought that everything was as before and kept up old interests despite obvious signs that this would not be cognitively possible. The fourth question concerned awareness of the diagnosis, and there was a follow-up question (question 5) about what was understood about the diagnosis. The next question (question 6) was pertinent to subjectively experienced degrees of cognitive symptoms and the following question (question 7) to self-rated degrees of problems associated with cognition. Question 8 concerned the reasons for cognitive problems and whether problems noted could be associated with a relevant diagnosis or illness. The last question (question 10) in this section was about measures taken to adapt. Patients experiencing cognitive disabilities may have a need for adjustments, and alterations can therefore serve as a sign of awareness. If a patient does not subjectively experience any difficulties, although they may objectively be present, he or she may not find that there is any need for change whatsoever [34]. The anosodiaphoria subscale included a question where the patients were asked to rate their feelings in terms of worries about their cognition (question 9).

The interview questions were asked according to the protocol, and the participants were then requested to make self-ratings according to the scoring alternatives, which were explained verbally by the examiner. In that way, the subjective experiences of the participants were assessed. The scores usually ranged from 1 to 3 points.

Estimations made by close informants may be used as a basis for comparisons with self-reports. A discrepancy score between self-evaluations and caregivers' ratings can serve as an indication of anosognosia [37]. Since no informant scoring was available in the present study, evaluations of the occurrence of anosognosia and anosodiaphoria in MCI and AD were made through comparisons of the self-ratings on the A&A scale between the groups themselves and versus their neuropsychological test scores. Comparisons with neuropsychological test scores have also been a previously used method to assess anosognosia [8]. Here, the relation between the cognitive performance levels in MCI and AD was compared to obtain an estimate of which level could be considered as lower and which as higher. Relatively low awareness scores versus comparatively low cognitive performance levels have served as indications of anosognosia. Relatively low rates on the emotional evaluative part of the scale and comparatively low cognitive levels have been used as criteria of anosodiaphoria.

Neuropsychological Assessment

The cognitive level, including memory, was investigated with a short battery of neuropsychological tests, comprising semantic memory: Information (Wechsler Adult Intelligence Scale – 4th ed., WAIS-IV [38]); spatial thinking/executive function: Clock Drawing (free-hand drawing of ten past eleven [39]), Rey-Osterrieth Complex Figure, copying [40, 41]; executive function: verbal creativity/fluency: Controlled Oral Word Association Test (FAS) [42]; spatial creativity: Design Fluency (DF) [43] and psychomotor function/visual scanning/set shifting with Trail Making Test (TMT), parts A and B, number of connections [44]; working memory: rote memory – Digit Span Forward, rote memory/mental flexibility – Digit Span Backward (WAIS-IV) [38]; verbal and spatial episodic memory: Rey Auditory Verbal Learning Test (RAVLT) – learning, delayed recall 30 min and noting repetitions of already mentioned words in the wordlist as well as confabulations [41], and Rey-Osterrieth (immediate recall [40, 41]). Finally, after the testing had been concluded, the participants were asked to recall as many tasks as possible that they had been doing during the investigation; this was classified as a task for recall from the verbal episodic memory (for scoring principles, see Appendix 1). The recall task about what had been done during the test session was inspired by the Rivermead Behavioral Memory Test.

Statistical Analyses

Data were analyzed with IBM SPSS Statistics, version 19. Demographic information was evaluated with Student's *t* test. Internal consistency and reliability of the scale were tested with Cronbach's alpha, where rates between 0.70 and 0.95 have been identified as acceptable, but where an alpha value of 0.90 has been suggested as an acceptable upper limit [45]. Since the neuropsychological information was on the ordinal scale level and the samples sizes were small, data have been investigated with nonparametric methods. Differences between MCI and AD patients on the A&A scale and on neuropsychological tests were assessed with the Mann-Whitney *U* test. The relationships between the scores on the A&A scale and cognitive test results were estimated with Spearman's rank correlation coefficient test. The significance level was $p = 0.05$. The study was approved by the Memorial Health System, Colorado Springs, Colo., USA (IRB No. 110305).

Results

Cronbach's alpha for all the items on the A&A scale except item 9, which concerned anosodiaphoria, was 0.76, and this indicates a good internal consistency and reliability of the instrument. The mean ranks of the answers to the interview questions showed that the ratings

Table 2. Scores of MCI and AD patients on the A&A scale

Question	Group	Median	Min–Max	Mean rank	p value
<i>Awareness</i>					
1 (age)	MCI	3	2–3	13.1	0.03
	AD	2	1–3	8.2	
2 (profession)	MCI	3	1–3	12.1	n.s.
	AD	3	1–3	9.6	
3 (change in spending days)	MCI	3	2–3	12.6	n.s.
	AD	2	2–3	8.8	
4 (diagnosis)	MCI	3	1–3	12.9	n.s.
	AD	1	1–3	8.4	
5 (diagnostic understanding)	MCI	3	1–3	12.6	n.s.
	AD	1	1–3	8.8	
6 (degree of cognitive symptoms)	MCI	2	1–3	12.9	0.05
	AD	2	1–2	8.5	
7 (degree of problems)	MCI	2	1–3	11.5	n.s.
	AD	2	1–2	10.3	
8 (reasons for cognitive problems)	MCI	2	1–4	13.0	0.04
	AD	1	1–2	8.3	
10 (adjustment)	MCI	2	1–3	11.1	n.s.
	AD	2	1–3	10.9	
<i>Emotional evaluation</i>					
9 (feelings about cognition)	MCI	2	1–3	12.3	n.s.
	AD	1	1–3	9.2	

Medians, minimum and maximum scores, mean ranks, and differences in mean ranks between MCI and AD are shown.

on the awareness items were generally higher in the MCI group than in the AD group, although they were significant only for three of the ten items. The MCI patients were considerably better oriented about their own age (question 1), rated a higher degree of cognitive shortcomings (question 6) and could more often associate their cognitive problems with a relevant diagnosis and illness (question 8) than the AD patients (table 2).

Neuropsychological performance levels (table 3) according to the mean ranks were significantly higher in MCI than in AD patients on tests of general knowledge/semantic memory (Information) and selectively higher on tests of spatial thinking/executive function (Clock Drawing, Rey-Osterrieth), executive/psychomotor function: spatial creativity (DF), set shifting (TMT B), short-term memory – rote memory/mental flexibility (Digit Span Backward (B), repetition), two aspects of verbal episodic memory (RAVLT), and recall of the tasks which had been performed during the test session as well as visuospatial episodic memory (Rey-Osterrieth).

All the items on the A&A scale were significantly correlated to different constellations of neuropsychological tests (table 4) except for the Rey-Osterrieth Complex Figure, copying condition, the number of connections on the set shifting test, TMT B and RAVLT, delayed recall (30 min) as well as the number of repetitions of the words on RAVLT, delayed recall, where no associations with the scale items were found.

The correlation analysis between significantly differentiating A&A scale items (questions 1, 6 and 8) and significantly differentiating neuropsychological test results indicated more numerous associations in the AD group than in the MCI group. Totally, in the AD group six of the ten comparisons revealed more numerous correlations than in the MCI group (table 4).

Table 3. Performance of MCI and AD patients on neuropsychological tests

Cognitive test	Group	Median	Mean rank	p value
<i>Semantic memory</i>				
Information	MCI	12.0	13.5	0.03
	AD	4.0	7.6	
<i>Visuospatial/executive function</i>				
Clock Drawing	MCI	5.0	13.2	0.05
	AD	4.0	8.1	
CF, copying, points	MCI	31.5	13.5	0.03
	AD	24.0	7.6	
<i>Executive and psychomotor function</i>				
FAS, totally	MCI	25.0	12.1	n.s.
	AD	13.0	9.6	
DF, no correct	MCI	26.0	14.2	0.006
	AD	2.0	6.7	
DF, no figurative	MCI	2.0	11.1	n.s.
	AD	1.0	10.8	
TMT A, connections	MCI	24.0	12.1	n.s.
	AD	24.0	9.6	
TMT B, connections	MCI	22.5	12.8	0.03
	AD	7.0	7.1	
<i>Short-term memory</i>				
Digit Span F, total sum	MCI	10.0	11.8	n.s.
	AD	9.0	9.9	
Digit Span B, total sum	MCI	7.0	13.3	0.05
	AD	6.0	7.9	
<i>Verbal episodic memory</i>				
RAVLT, learning, no words	MCI	24.0	13.5	0.03
	AD	14.0	7.6	
RAVLT, learning, no repetitions	MCI	0.50	13.0	0.05
	AD	0.00	8.4	
RAVLT, learning, no confabulations	MCI	0.50	11.8	n.s.
	AD	0.00	9.9	
RAVLT, recall, no words	MCI	5.0	13.1	0.003
	AD	0.00	5.7	
RAVLT, recall, repetitions	MCI	0.00	10.0	n.s.
	AD	0.00	10.0	
Recall of testing tasks	MCI	4.5	14.3	0.005
	AD	0.00	6.7	
<i>Visuospatial episodic memory</i>				
CF, recall, points	MCI	7.5	13.8	0.02
	AD	2.0	7.2	

Medians, mean ranks and differences between mean ranks between MCI and AD are shown. CF = Rey-Osterrieth Complex Figure; Digit Span F = forward; Digit Span B = backward.

In the MCI category the analysis showed that the higher the awareness of age (question 1), the higher the verbal episodic memory (RAVLT). In the AD group there was a positive correlation between awareness of age and general knowledge/semantic memory (Information), and spatial creativity (DF). Knowledge about one's own age also correlated positively with spatial episodic memory in the AD category.

Table 4. Correlations between significantly different items on the A&A scale and significantly different neuropsychological tests for MCI and AD patients

Question	Group	Cognitive test	p value	r
<i>Awareness</i> 1 (age)	MCI	RAVLT, learning	0.02	0.648
	AD	Information	0.04	0.688
		DF, correct	0.04	0.699
		CF, recall, points	0.02	0.763
6 (degree of cognitive symptoms)	MCI	–	–	–
	AD	DF, correct	0.02	0.746
8 (reasons for cognitive problems)	MCI	Information	0.02	–0.679
		Clock Drawing	0.002	–0.788
	AD	–	–	–

CF = Rey-Osterrieth Complex Figure.

In MCI the estimation of the degree of cognitive problems (question 6) was not associated with any result in the neuropsychological tests. In AD there was a relationship meaning that the larger the amount of subjectively experienced cognitive problems, the higher the spatial creativity (DF). The MCI patients were more prone to associate their cognitive decline with illness (question 8) than the AD patients, and there was a negative association showing that the higher the insight into the roots of the mental decline, the lower the general knowledge and spatial orientation (Clock Drawing). In the AD group there were no associations between this question and cognition.

The pattern in the relations between the nonsignificant items on the A&A scale and the levels on significantly differentiating neuropsychological tests was the same as between the significant A&A items and the cognitive tests, i.e. more numerous correlations in AD than in MCI (table 5). There were no connections between the awareness of profession (question 2) and cognition in the MCI group, but there were connections in the AD group, where it correlated positively with the test of semantic memory and the spatial episodic memory.

Regarding question 3, the analysis indicated negative correlations in MCI, meaning the higher the number of changes that had been made because of cognitive malfunction, the lower the spatial orientation. In AD the positive association with DF appeared also in connection with question 1. Concerning awareness of diagnosis (question 4), there was a negative association in MCI, implying the higher the knowledge of diagnosis, the lower the general knowledge and spatial orientation. In AD the awareness of diagnosis was positively related to different aspects of episodic memory. In MCI the understanding of the meaning of the diagnosis (question 5) was negatively correlated with the same tests as in question 4. In AD the associations meant the higher the diagnostic understanding, the higher parts of the verbal episodic memory. The evaluation of the degree of problems associated with cognitive decline (question 7) in the MCI category was positively related to spatial as well as verbal episodic memory. Data also revealed that the higher the experienced degree of problems in AD, the higher the executive function (DF) and results on the test of verbal episodic memory. The adjustment subscale (question 10) showed no associations in MCI, but they were shown in AD with spatial orientation/executive ability, and short-term and verbal episodic memory.

Question 9 disclosed no associations with cognition in MCI, but in AD there were positive relations to spatial creativity and verbal episodic memory.

Table 5. Correlations between nonsignificantly different items on the A&A scale and significantly different neuropsychological tests for MCI and AD patients

Question	Group	Cognitive test	p value	r
<i>Awareness</i>				
2 (profession)	MCI	–	–	–
	AD	Information	0.02	0.735
		CF, recall	0.04	0.702
3 (change in spending days)	MCI	Clock Drawing	0.01	–0.689
	AD	DF, correct	0.02	0.740
4 (diagnosis)	MCI	Information	0.03	–0.617
		Clock Drawing	0.01	–0.689
	AD	RAVLT, learning	0.03	0.707
		Recall, testing tasks	0.01	0.779
5 (diagnostic understanding)	MCI	Information	0.03	–0.617
		Clock Drawing	0.01	–0.689
	AD	RAVLT, learning	0.03	0.725
		Recall, testing tasks	0.01	0.798
7 (degree of problems)	MCI	CF, recall	0.008	0.719
		Recall, testing tasks	0.002	0.802
	AD	DF, correct	0.01	0.796
		RAVLT, learning	0.003	0.866
10 (adjustment)	MCI	–	–	–
	AD	Clock Drawing	0.02	0.746
		Digit Span B, total sum	0.04	0.685
		Recall, testing tasks	0.02	0.739
<i>Emotional evaluation</i>				
9 (feelings about cognition)	MCI	–	–	–
	AD	DF, correct	0.04	0.685
		RAVLT, learning	0.003	0.857

Discussion

The MCI patients subjectively experienced a higher degree of cognitive deficits than the AD patients, although the neuropsychological testing showed that semantic memory, spatial thinking, spatial creativity, set shifting, selectively short-term memory and essential parts of the episodic memory were considerably higher in MCI than in AD. Likewise, the awareness of age was higher in MCI than in AD, which means that the autobiographical memory in this respect was better preserved in MCI than in AD. This supports the clinical diagnoses of the participants in these diagnostic groups.

The understanding that the current cognitive problems were due to a specific diagnosis or illness was also higher in MCI than in AD, that is the MCI patients could anchor their intellectual shortcomings in a disease or diagnosis in quite another way than the AD patients, who – if they to some extent admitted deficiencies – more often did not know where their deficits originated from.

There were more associations between the A&A scale items and neuropsychological performance levels in AD than in MCI. One striking trait in the correlation analyses is that the MCI pattern is characterized by associations between on the one hand the A&A scale items and on the other hand memory and spatial functions. In AD a similar pattern appears, but with

the addition of associations with tests of frontal lobe functions (DF, RAVLT repetitions – a sign of dysexecutivity – and short-term memory). This may signify a progression of the neurodegeneration in the AD group to a frontal lobe engagement.

In the current study MCI patients rated larger cognitive problems than AD patients (question 6). Previous findings concerning self-ratings of cognitive hardship are contradictory. Lamentations about loss of memory have been found to increase concomitantly with cognitive decline in MCI [46], which fits well with the pattern in the MCI group, where the negative correlations generally imply that the higher the awareness is, the lower is the cognitive ability. This pattern of negative correlations disappears in AD, where the associations are positive and predominantly so with episodic memory and executive functions.

In the literature there is evidence that MCI patients overrate their cognitive shortcomings, when contrasted with evaluations made by close informants [37]. Since there was no control group, or caregivers' assessments, to compare with in the present study, it is impossible to judge whether the expressed higher levels of cognitive deficits or problems in the MCI group are signs of an overestimation of deficits or not. However, relative to the MCI patients, the AD patients underrated their cognitive symptoms, an observation that is strengthened by their cognitive skills being in several respects lower than those of the MCI patients. This relative underreporting of intellectual insufficiencies in AD is here interpreted as a sign of anosognosia, which is congruent with earlier findings that anosognosia is associated with a reduced awareness of memory due to frontal lobe disturbances [47]. Thus, there is also evidence of a frontal lobe engagement in anosognosia even in AD, not just in frontotemporal dementia [11, 17].

From a definitional point of view, an overrating of deficits does not qualify as a sign of anosognosia, since anosognosia is the same as a reduction or lack of awareness in the sense of not being aware of a loss. An overrating of difficulties could rather be a sign of an increase in anxiety, which together with an increase in aggression-hostility and a decline in extraversion has been documented with Swedish Universities Scales of Personality as changes of personality traits in subjective cognitive impairment and MCI [48].

It has also been found that subjects with suspected dementia/MCI tend to overvalue their memory capabilities relative to healthy controls [49]. An overestimation of skills has likewise been traced in AD, where it has been demonstrated that this group of patients tends to exaggerate their visuospatial and memory capabilities relative to controls. However, self-evaluation mistakes were even made by the control subjects, who underrated their levels of attention and overrated well-overlearned, automatized motor performance and eyesight [50], which underlines the difficulties to obtain reliable control data in this field.

The awareness of the roots of cognitive decline (question 8) is considerably lower in AD than in MCI. Compared to the fact that all AD patients had been informed about their diagnoses and consistently had lower cognitive levels than the MCI patients, this may be interpreted as another sign of anosognosia in the AD group. The AD patients may to some extent be aware of their cognitive symptoms, but they do not know where they come from. It is a kind of knowledge 'that is all in the air'.

Memory impairment itself has also been reported as a reason for anosognosia in MCI as well as AD [51–53], and it has been described as self-evident that it is impossible to be updated on malfunction if the event when the cognition did not work has fallen into oblivion [47]. This indicates that anosognosia can also be due to a loss of memory and not just to executive frontal lobe retrieval dysfunctions. Unawareness of memory deficits [53] due to posteromedial hypoperfusion characteristic for AD changes has also been suggested as a marker for future progression to AD [22].

There were no significant differences between the diagnostic groups in the degree of anosodiaphoria (question 9), but in the AD group the correlation analysis indicated that the

lower/higher the worries about cognition, the lower/higher the objective measures of spatial creativity and verbal episodic memory, which here is conceived as a sign of anosodiaphoria in AD. Anosodiaphoria has mostly been studied in frontotemporal dementia. As reported by Mendez and Shapira [28], most findings indicate that a hypoperfusion in the right frontal area may account for anosognosia in this disorder.

The increase in AD to a more or less global influence of cognitive dysfunctions on the awareness and emotional reactions may reflect the progressive nature of this neurodegenerative disorder. The longer the disease progresses, the larger the effects of executive and other types of cognitive dysfunctions on awareness and emotional engagement. The finding that anosognosia seems to be related to the severity of AD is consistent with several previous studies [7, 15, 54–57]. Considering the overweight in connections between executive and memory functions foremost in AD and to some extent even in MCI, the results are however most consistent with earlier findings that not just the degree of dementia can explain anosognosia in AD, but that frontal lobe dysfunctions and memory decline may be particularly decisive parameters behind anosognosia [12, 58].

Limitations of the study are the restricted number of participants and the lack of data from close informants as a basis for comparisons with the patients' self-ratings, which limits the possibilities to evaluate the occurrence of anosognosia/anosodiaphoria in MCI and AD and of course reduces the generalizability of the results. One way to solve the problem with the lack of informant data would have been to see which of the patients had developed AD at follow-up and use the others as controls (in enlarged samples). However, so far no systematic monitoring of a possible conversion to dementia has been done. The test of disease progression is to be carried out in the follow-up study, which has not yet started. To match the restricted numbers of participants in the present study, data have been analyzed with nonparametric methods, known to be robust techniques for the use in small samples [59], that is in groups with less than 20 participants [41]. Nonparametric methods are tailored to deal with small samples, also taking into consideration often-appearing problems associated with restricted numbers of participants, such as skewness in the normal distribution, and allowing sporadic differences to be significant (which may disappear in larger samples). In contrast, many of the patterns found in the study fit well with previous findings in the literature, which indicates that the present results do not seem to stem from occasional significances originating in statistical anomalies due to small sample sizes. Another limitation is the fact that the A&A scale just includes one item concerning anosodiaphoria and should have comprised more questions concerning this topic. Despite the limited attention to this topic in the scale, this single item all the same revealed an association with cognitive decline in the AD group.

To conclude, regardless of an in many respects lower cognitive ability than in MCI, the AD patients rated lower cognitive disabilities relative to the MCI patients, which is here interpreted as one sign of anosognosia in AD. The awareness of the reasons for cognitive problems was also lower in AD, which is considered as another sign of anosognosia in this disease group. Symptoms of anosodiaphoria were present in AD but not in MCI. Anosognosia and anosodiaphoria seem to increase with the progression of MCI to dementia but in a context of aggravating neurodegeneration; especially dysexecutivity and memory dysfunction seem to account for anosognosia as well as anosodiaphoria. The general outcome of the study is well consistent with previous findings in the field [12].

Babinski's hypothesis [6] in 1914 that anosognosia may be associated with right hemispheric lesions has repeatedly been confirmed in the literature. Since previous findings have mostly identified right hemispheric changes as the roots of anosognosia as well as anosodiaphoria, it is plausible that the signs of anosognosia and anosodiaphoria in the present study may reflect an involvement of an underlying right-sided neurodegeneration, probably with

different right-sided regional localization for these two types of abnormalities. Empirical neuroimaging evidence is necessary to confirm this assumption.

One suggestion for future research is the development of an anosognosia-anosodiaphoria scale that allows the establishment of cutoff values between what should be considered as normal levels of self-rating of disabilities and associated aspects and what should be considered as deviant, allowing to evaluate what should be understood as an absence of and degrees of anosognosia and anosodiaphoria. Cutoff scores for when cognitive decline starts to influence awareness would also be very useful.

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Disclosure Statement

The authors declare no financial conflicts of interest with regard to this study.

Appendix 1

Protocol

Date of the investigation _____

Subject code: _____

Introduction

During this investigation I am going to ask you questions, and to ask you to perform tasks. Some of the tasks are answered verbally, others with the help of paper and pencil. Do you have any questions?

Interview

1. How old are you?

-
- | | | |
|--------------------------|--------------------------------|-------------------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Correct | Not correct – one year's error | Not correct – several years' errors |
| 3 points | 2 points | 1 point |

2. Which were your previous professions? (If the patient still works, he/she is asked about the present profession)

- | | | |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Correct | Not correct | Does not remember |
| 3 points | 2 points | 1 point |

3. How do you spend your days? (If necessary: What is your favorite pastime?) Are these the same things you enjoyed in the past or have these activities changed?

- | | | |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Significantly changed | Same as before | Does not know/remember |
| 3 points | 2 points | 1 point |

4. Has your doctor given you a diagnosis? Which?

- | | | |
|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Relevant diagnosis | Irrelevant diagnosis | Does not remember |
| 3 points | 2 points | 1 point |

5. What do you understand about the diagnosis?

- | | | |
|--------------------------|--------------------------|-----------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Good understanding | Partial understanding | Does not know what it means |
| 3 points | 2 points | 1 point |

6. How do your thinking and memory work for you?

- | | | |
|------------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Prominent cognitive symptoms | Some cognitive symptoms | No cognitive symptoms |
| 3 points | 2 points | 1 point |

7. Is this problematic to you?

Yes, very problematic
3 points

Yes, to some extent
2 points

No problems at all
1 point

8. What do you think are the reasons for your cognitive problems?

Association with relevant
diagnosis and illness
4 points

Association with a relevant diagnostic
name, but without knowing the
implications of the diagnosis
3 points

Association with illness,
but no diagnosis
2 points

Does not
know
1 point

9. How do you feel about your thinking and memory?

Worried (specified)
3 points

Generally but vaguely worried
2 points

Not worried
1 point

10. Have you adjusted to your problems?

Yes, considerably
3 points

Yes, to some extent
2 points

No adaptation at all
1 point

Thank you.

Now we are turning to the task solutions.

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