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Awareness of cognitive deficits and clinical competence in mild to moderate Alzheimer's disease: their relevance in clinical practice

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Abstract Awareness of cognitive deficits and clinical competence were investigated in 79 mild to moderate Alzheimer's disease patients. Awareness was assessed by the anosognosia questionnaire for dementia, and clinical competence by specific neuropsychological tests such as trail making test-A, Babcock story recall test, semantic and phonemic verbal fluency. The findings show that 66 % of the patients were aware of memory deficits, while the 34 % were unaware. Deficit in awareness correlated with lower scores on the Mini Mental State Examination test that, in the score range from 24.51 to 30 and from 19.50 to 24.50, appeared to be a significant predictor of level of awareness. None of the AD patients had fully preserved clinical competence, only 7 patients (9 %) had partially preserved clinical competence and 72 patients (91 %) had completely lost clinical competence. All the patients with partially preserved clinical competence (9 %) were aware of their

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Department of Philosophy, Pedagogy and Psychology, University of Verona, Lungadige Porta Vittoria 17, Verona, Italy memory deficit. The study indicates that neuropsychological tests used for the assessment of executive functions are not suitable for investigating clinical competence. Therefore, additional and specific tools for the evaluation of clinical competence are necessary. Indeed, these might allow clinicians to identify AD patients who, despite their deficits in selected functions, retain their autonomy of choice as well as recognize those patients who should proceed to the nomination of a legal representative.

Keywords Awareness · Clinical competence · Alzheimer's disease · Memory · Dementia · Executive functions · Neuropsychological assessment

Introduction

Alzheimer's disease (AD) is characterized by deterioration of cognitive abilities, behavioural disorders and decline in daily living abilities. Awareness of these cognitive deficits and decision-making capacities (clinical competence) may be altered in the early stages of AD [1] with the intensity of deficit changing during the course of the dementia [2].

Anosognosia represents a complex and multifaceted entity, as demonstrated in patients affected by stroke, Huntington's and Parkinson's diseases, traumatic brain injury and schizophrenia [3, 4].

In AD, anosognosia is described as a lack of awareness in impairments in activities of daily life or in neuropsychological deficits, particularly memory deficits [5]. Estimates of anosognosia prevalence in AD change in different studies, varying from 80 [6] to 42 % [5].

Neuroimaging studies highlight the link between anosognosia and metabolic changes in the right frontal and orbito-frontal, temporal and bilateral temporo-parietal

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areas [7] and cingulate cortex [8]. Nevertheless, nowadays these results are of unclear validity [1].

A correlation between anosognosia and performances in neuropsychological tests for executive functions (e.g. WCST, Fluency, Stroop) and memory (e.g. Story recall, Rey 15-items memory test) as well as with behavioural disorders (e.g. apathy) has been found, but the results are controversial and not conclusive [4, 9, 10]. Thus, the involvement of factors other than neuropsychological has been suggested [5].

Clinical Competence (CC) has been conceptualized in terms of patients' competence to make treatment-related decisions [11]. Four core components have been identified in CC [11]: (1) *understanding*, the ability to comprehend information relevant to the decision; (2) *appreciation*, the ability to apply information to one's own situation; (3) *reasoning*, the ability to compare potential consequences of various decisions; (4) *expression of choice*, the ability to communicate a choice.

In the specific literature concerning the assessment of CC, the debate on the use of specific semi-structured interviews or neuropsychological tests is open. The former has the great limitation of the unavoidable subjectivity with results depending on the single examiner. In contrast, although neuropsychological tests are less ecologic, they offer more objective measures. Thus, the identification of tests that specifically examine functions connected to CC is crucial. Recent studies suggest that tests assessing executive functions and story recall may respond to this question.

Indeed, in AD, deficits in CC are considered to be associated to damage of the executive frontal system (attention, action planning, monitoring of task, inhibition of automatic responses) and deficits in logic memory [12].

This study investigates the eventual existence of relationship between awareness and CC in mild to moderate AD and its changes in the different stages of the disease. In addition, it analyses the correlations between these functions and individuals' age, global cognition level and cognitive functions.

Indeed, since the loss of cognitive capacities is progressive in AD, clinicians need to consider not only the patient's deficits, but also residual patient's autonomy. This allows to define and share with the single subject the existential, therapeutic and care proposals as long as possible. When the patient will no longer be able to decide for his/herself, an in depth assessment of awareness and CC will permit to advance the use of legal instruments.

Methods

affected by mild to moderate AD according to McKahnn criteria [13] or "prodromal AD" according to NINCDS-ADRDA criteria [14]. In these latter, the "prodromal AD" identifies individuals presenting with specific cognitive symptoms (not involving limitations in IADL) in addition to positive CSF or neuroimaging biomarkers consistent with AD pathology.

The patients received comprehensive neurologic evaluation as well as blood tests (thyroid function, homocysteine, vitamin B_{12} and folic acid dosage), brain MRI or CT, neuropsychological (Battery for Mental Deterioration) [15] and functional assessment (Instrumental Activities of Daily Living Scale-IADL, Index of Independence in Activities of Daily Living-ADL) [16, 17]. 33 % of them was treated with AchE or memantine.

Patients and their relatives agreed to participate in the study, which was approved by the local Ethics Committee (n 2,238).

The inclusion criteria were: absence of behavioural disorders, a MMSE [18] score $\geq 15/30$, age between 65 and 85 years, education ≥ 5 years, preserved verbal comprehension.

Subjects with a history of head injury, psychiatric disorders (e.g. depression-Geriatric Depression Scale [19]) or neurological diseases were excluded.

Procedure

On the basis of a previous classification [20], the patients were stratified in three classes of MMSE values: 15-19.50, 19.51-24.50 and 24.51-30 and in four classes of age: 65-69 (*n* 7), 70-74 (*n* 16), 75-79 (*n* 23) and 80-85 (*n* 33).

Awareness was evaluated by Anosognosia Questionnaire for Dementia (AQ-D) [20]. It consists of 30 questions assessing intellectual functions and changes in interests and personality and identifies four factors concerning deficits in: IADL, basic ADL, depression, disinhibition. Form A is answered by the patient alone, by means of a four points scale (never = 0, always = 3), while an identical thirdperson referred Form B is answered by the caregiver. The diagnosis of anosognosia is defined as a \geq 2 point differential on four or more items in the IADL domain [5, 9].

For the rating of CC, we followed the indications and scores criteria resulting from the consensus document of the Italian ISS (Istituto Superiore di Sanità) [21], which suggests the use of tests investigating logic memory (Babcock Story Recall Test: BRST [22]), executive functions (TMT-A [23]) and verbal fluency (Semantic and Phonemic Verbal Fluency: SVF and PVF [15]). Indeed, these functions have previously identified as good predictor of capacity to consent in mild AD [24].

CC was classified as follows: *preserved* scores above the cut-off in all tests, *partially preserved* scores above the cut-

off in two tests, *impaired* scores under the cut-off in all tests (see Table 2).

Statistical analysis

We used the Pearson's coefficient (r) to evaluate association between awareness (AQ-D) and age, MMSE and neuropsychological tests, the Mann–Whitney to compare the two subscales (intellective functions and behaviour) of AQ-D, the Kruskal–Wallis to evaluate the difference among MMSE classes, and t tests to evaluate the differences in mean age between aware and unaware patients.

A logistic regression was employed to evaluate the association between dichotomized awareness status (awareness/unawareness) and MMSE (3 levels, reference 15–19.50) controlling for gender (reference male), age, education, ADL (reference ADL <3), IADL (male, 5 functions: reference IADL <3; female, 8 functions: reference IADL <5). Results were summarized as odds ratios (with 95 % confidence interval).

Statistical analyses were performed with the SPSS and STATA software (significant value at p < 0.05).

Results

Clinical and demographic patients' data are showed in Table 1.

Awareness

Sixty-six percentage of patients (n = 52) were rated as aware and 34 % (n = 27) as unaware for memory loss. Unaware patients showed median scores significantly lower than aware patients in both the cognitive (median value for unaware vs. aware patients: 5.5 vs. 10 p = 0.0016) and behavioural (median value for unaware vs. aware patients: 1.5 vs. 4 p = 0.0079) subscales. Between the two groups there was no statistically significant difference in age $(79.1 \pm 4.6 \text{ and} 76.8 \text{ years} \pm 5.7, \text{ respectively})$ (t = 1.771, p = 0.081).

A correlation was found between AQ-D scores and MMSE scores (AQ-D $R_s = -0.293$, p = 0.009), indicating a role for general cognitive level in awareness.

Kruskal–Wallis shows a statistically significant difference in AQ-D scale score between all classes of MMSE (H = 7.32, df = 2, p = 0.026). A logistic regression model confirmed that only the variable MMSE (24.51–30, 19.51–24.50) is a significant predictor of the expected outcome, i.e. to have awareness of cognitive deficits (odds ratio = 6.16, p = 0.007 in the MMSE range 24.51–30 and odds ratio = 4.26, p = 0.038 in MMSE range 19.51–24.50).

Nevertheless, although in the MMSE class 15–19.51, 79 % of patients were classified as unaware, also in the other classes of MMSE the deficit of awareness results to be present. In specific, we found as unaware the 50 % of subjects and in the MMSE class 24.51–30, the 30 %.

Other variables (gender, age, education, IADL and ADL) were not significant predictors of outcome (aware vs. unaware) (Table 2). Indeed, clinical and demographical data of the three classes (Table 1) indicate that the age and education were absolutely comparable between the three groups.

Clinical competence

As shown in Table 3 scores in the neuropsychological tests were below cut-off, except for the SVF in the MMSE class >24.50 and the PVF in all the groups. However, in this task, 10 patients in MMSE class 15-19.50, 11 in class 19.51-24.50 and 6 in class >24.50 were below cut-off.

None of the patients showed fully preserved CC, with only seven patients (9 %) being rated as partially competent and 72 (91 %) as having completely lost CC.

As shown in Table 4, Pearson's correlation coefficient revealed a significant correlation between AQ-D and neuropsychological tests, indicating that awareness and

 Table 1
 Demographic and clinical characteristics of the subjects are reported separately for the three classes of mini mental state examination (MMSE) scores

	MMSE 15–19.50 (<i>n</i> = 19)		MMSE 19.51–24.50 (<i>n</i> = 26)		MMSE 24.51–30 (<i>n</i> = 34)		TOT 15–30 (<i>n</i> = 79)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	77.68	4.49	78.65	6.07	76.88	5.48	77.7	5.46
Education (years)	7.47	3.79	8.19	4.51	7.26	3.59	7.6	3.93
Instrumental activities daily living ^a	3.83	1.88	2.75	1.98	2.45	2.18	2.89	2.09
Basic activities daily living ^a	1.61	1.81	1.04	1.42	1.03	1.51	1.17	1.56

TOT value referred to the whole sample, SD standard deviation

^a No. of functions compromised

cognitive functions are strictly connected. It is noteworthy that the patients with partially preserved CC were all aware of their cognitive deficits.

Discussion

In the early stage of AD great variability in prevalence and severity of anosognosia has been reported [5]. This has relevant impact within ethics and forensic medicine, in communication of diagnosis and doctor-patient relationship.

We found only 34 % of our patients to be unaware of cognitive, functional and behavioural deficits. The discrepancy with respect to other studies may depend on various elements. Firstly, the general cognitive level in our patients was higher (MMSE 23.30 \pm 3.73) than in other studies (i.e. 6) with a part of subjects having a MMSE score >24. Nevertheless, it is noteworthy that clinical rating studies have not found a consistent relationship between anosognosia in AD and length of illness, dementia severity

Table 2 Odds ratios (with 95 % confidence interval) were obtained by a logistic regression controlling for gender (reference: male), age (years), education (years of education), MMSE (3 levels: 15–19.50, 19.51–24.50, 24.51–30, reference 15–19.50)

Awareness outcome	Odds ratio	p > z	[95 % CI]	
Gender	1.695062	0.385	0.5149232	5.579931
Age	0.9835903	0.732	0.8948399	1.081143
Education	0.8786776	0.107	0.7507999	1.028336
MMSE (19.51-24.50)	4.266705	0.038	1.082376	16.81927
MMSE (24.51-30)	6.160709	0.007	1.637166	23.18295
IADL	0.3362443	0.100	0.0918526	1.230888
ADL	1.942257	0.369	0.4561046	8.270827

Table 3 Patients mean score at neuropsychological tests

or memory impairment severity [25] neither with demographic variables [7]. In addition, our most interesting result concerns the percentages of anosognosic patients in the 19.51–24.50 and 24.51–30 MMSE classes, the 50 and 30 %, respectively. This indicates that the minor gravity of disease cannot represent a guarantee for clinicians concerning patient's awareness. This needs to be specifically investigated, in order to avoid any overestimation of subject abilities to recognize their deficits.

A second aspect concerns the assessment tools that differ between the studies, varying from clinician impressions [26] to specific self-assessment scales or tasks and clinical insight rating [27]. The AQ-D has been demonstrated to be highly informative and valid with respects to the construct of awareness of cognitive and behavioural difficulties in AD [5] and our data confirm its consistence with respect to neuropsychological tests.

The correlation between general cognitive level, scores in neuropsychological tests and awareness found in our study confirms the literature, where the severity and prevalence of anosognosia are reported to increase with progression of disease ([20, 28], but see also [1, 26]).

Although decision-making impairment is common in AD, many patients appear to be capable of making their own medical decisions; to clarify this apparent contradiction, evidence-based assessments of their capacity to consent to medical treatment are necessary. In the last decades the debate about the assessment of capacity to give consent has been intense [21].

Studies about decision-making abilities are usually carried out in two main ways [29]: using interviews and questionnaires that investigate the four components of competence [8, 30] or by means of tests for cognitive functions, in particular investigating executive functions, verbal fluency and logic memory [21, 31]. We have chosen the second approach, which guarantees high degree of

No. of patients (79)	MMSE 15–19.50 $(n = 19)$		MMSE 19.51–24.50 ($n = 26$)		MMSE 24.51–30 ($n = 34$)	
Neuropsychological tests (cut-off test)	Mean	SD	Mean	SD	Mean	SD
SVF (>25)	20.52	5.89	21.11	7.45	26.61	6.33
PVF (>17)	18.78	9.16	20.00	9.51	25.26	9.64
TMT-A (<94)	238.52	83.80	175.69	85.69	161.17	91.98
BRST (>11.5)	0.34	0.96	1.18	1.71	2.04	2.13

SVF Semantic verbal fluency, PVF Phonemic verbal fluency, TMT-A Trail making test-A, BRST Babcock story recall test, SD Standard deviation

 Table 4
 Correlation between AQ-D and neuropsychological tests

Pearson's correlation	PVF	SVF	TMT-A	BRST
AQ-D	$0.460 \ (p = 0.000)$	$0.424 \ (p = 0.000)$	$0.225 \ (p = 0.046)$	$0.367 \ (p = 0.001)$

objectivity and is recommended by the Italian ISS (Istituto Superiore di Sanità).

We found CC impairment in the 91 % of the patients, a percentage higher than that reported in previous studies which reported percentage ranged broadly from 45.5% [32], to 68 % [31], to 79 % [8]. This variability may depend on the different samples selected (i.e. 31) and evaluation tools employed. Nevertheless, our results suggest that even patients with very mild dementia and awareness spared may show substantial deficits in decision-making capacity. This apparently odd data may be due to different tools employed for assessment, i.e. a question-naire for detecting awareness and neuropsychological tests for CC.

Nevertheless, we suggest an alternative hypothesis, rising from the idea of awareness as a multifaceted syndrome. The "intellectual" awareness has been described [33, 34], to indicate subjects who know to be affected by an illness, but are not aware of its consequences. In other words, they correctly verbally describe their symptoms, but do not make decisions according with their pathological conditions (e.g. they go to supermarket without a shopping list being amnestic). For making good decisions, "anticipatory" awareness is necessary, which permits to anticipate the effects of different actions. It is thus possible that intellectual but not anticipatory awareness is spared in patients of our sample who appear to be awareness but not competent. Indeed, in order to make decisions and to be competent, anticipatory awareness concerning subjective abilities is necessary.

The concept that capacity to give consent is related to performance on cognitive functions tasks has been criticized [35]. These tests are designed for diagnosis of dementia, which is in itself necessarily linked to loss of ability. Since almost all our patients fail in CC, we suggest to consider the limitation associated with the use of common tests (TMT-A, BRST, PVF and SVF) for specific analysis of residual capacities in AD patients. More specific tasks need to discriminate various eventual profiles and the subcomponents of CC.

This study presents some limitations, mainly due to the small sample and the use of different assessment instruments (self-referred questionnaires and neuropsychological tests). Moreover, although our innovative result consists of the identification of CC deficits in very mild stages of AD, only a longitudinal approach may confirm an eventual evolution connected with the progression of the disease.

Conclusion

In sum, our data confirm that cognitive deficits in executive function, memory and language may mediate the association between capacity and awareness but also suggest that the two constructs may be differently impaired in patients. More specific tasks need to better understand the various components of CC and the specific profile of competence that each subject may present, with deficits and residual abilities.

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