



Influence of nutritional status on cognitive, functional and neuropsychiatric deficits in Alzheimer's disease

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ABSTRACT

Nutrition is an important issue for elderly people, especially in patients with dementia. It is also related to clinical outcome, such as cognition, autonomy and behavior. The present study investigated the role of nutritional status on cognitive, functional and neuropsychiatric deficits in patients with Alzheimer's disease (AD). Forty-nine patients underwent neuropsychological, nutritional and neuropsychiatric assessments. The sample was divided into at risk of malnutrition (21 patients) and well-nourished (28 patients) according to the Mini Nutritional Assessment (MNA) score. The groups were similar for clinical and demographic variables, except for MNA score and age. The mean body mass index (BMI) was higher than the normal range. Patients at risk of malnutrition showed greater impairment, both in simple and instrumental activities of daily living (ADL and IADL) and a more severe ideomotor praxis deficit than well-nourished patients. Neuropsychiatric symptoms showed significant differences in hallucination, apathy, aberrant motor behavior and night-time subscales of Neuropsychiatric Inventory (NPI). These symptoms were more severe in patients at risk of malnutrition. Logistic regression analysis showed that malnutrition was an important risk factor for the onset of apathy. We hypothesized that changes in dietary habits and intake and the onset of these disorders reflect the involvement of a common neuroanatomical network.

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1. Introduction

AD is a progressive dementia in which memory deficit is one of the earliest and most pronounced symptoms. As the disease progresses other cognitive functions, such as language and general intellectual performance, also become impaired. The decline in cognition is associated with a progressive loss of functional autonomy (Morris and Kopelman, 1986).

As well as the neuropsychological symptoms of dementia, eating disorders are another very common problem (Rivière et al., 1999). Hyperphagia, hyporexia, sweet cravings, choice of food, refusal and severe feeding difficulties are the prevalent eating patterns. Weight loss is also frequent, increasing the risk of infection and skin ulcers and decreasing the AD patient's quality of life. The severity of weight loss follows disease progression and is considered a predictor of patient mortality (Gillette-Guyonnet et al., 2005).

Various mechanisms may be responsible for weight loss. It could be associated with a change in food intake owing to reduced

functional capability. White et al. (1997a,b) proposed that weight variations reflected a dysfunction in the body's weight variation system. Other authors (Grundman et al., 1996) showed that in patients with AD the mesial temporal cortex (MTC) is atrophied compared with controls and is associated with lower BMI and low cognitive function. Since MTC plays a fundamental role in eating behavior, memory and emotions, changes in MTC could contribute to weight loss through changes in eating behavior or cognitive and behavioral impairment. Several recent epidemiological studies examined weight loss in AD. The results of White et al. (1997b) showed that nearly twice as many subjects with AD experienced a weight loss of 5% or more compared with controls.

Problems encountered in feeding subjects with AD relate not only to the quantity, but also to the quality of foods consumed (Greenwood et al., 2005). Other studies (Ikeda et al., 2002) have highlighted the changes in appetite, in food preference and in eating habits in these patients. Subjective and objective measures indicate that patients with dementia show an increased preference for sweet foods, leading to a greater intake of carbohydrates and less proteins (Mungas et al., 1990; Keene and Hope, 1997). Therefore, the risk of malnutrition is associated not only to a reduced food intake but especially to a diet poor in foods containing proteins.

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The nutritional status has been associated with cognitive status in many studies (Jorissen and Riedel, 2002; Dumont et al., 2005). Significant correlations were found between the under-nourished status and cognitive, behavioral disturbances and caregiver distress (Broker et al., 2003). Vellas et al. (2005) reported a more rapid aggravation of the disease in under-nourished patients with a rapid loss on the Mini Mental State Examination (MMSE) (Folstein et al., 1975) (three points or more in 1 year). Similarly, increased dependence at 1 year was more frequent in subjects at risk of undernutrition at inclusion. The aim of our study was to evaluate the role of nutritional status on cognitive, functional and neuropsychiatric deficits in a sample of patients with AD.

2. Subjects and methods

2.1. Subjects

All patients, consecutively admitted to our Alzheimer's Disease Unit in Southern Italy between 2001 and 2003, were assessed. Only patients with a diagnosis of AD according to NINCDS-ADRDA (McKhann et al., 1984) were included. Exclusion criteria were a history of head injury, substance abuse or dependence and a history of psychiatric disturbances before the onset of dementia. A total of 49 outpatients were enrolled in the study. Written informed consent was obtained for all patients. The study was approved by the internal ethic committee.

Table 1 reports some demographic and clinical features. All patients underwent mental status examination, neuropsychological, neurological and neuroradiological examinations and nutritional and neuropsychiatric assessments. Patients were divided into two groups according to nutritional status: group 1 = patients at risk of malnutrition (MNA < 23.5) and group 2 = well-nourished patients (MNA $\geq$ 23.5).

2.2. Cognitive evaluation

Cognitive functions were examined using the MMSE (Folstein et al., 1975; Magni et al., 1996). All patients were assessed using Mental Deterioration Battery (Carlesimo et al., 1996). This battery consists of eight simple verbal and visual-spatial tasks: Rey's Auditory Verbal Learning Test (RAVLT); Phonemic Word Fluency; Phrase Construction; Raven's Colored Matrices; Immediate Visual Memory; Copying Drawings; Copying Drawings with Landmarks.

In addition to MDB, we used the following tests: Prose recall; Semantic Word Fluency; Token Test; Attentive Matrices; Ideomotor Apraxia Test (Spinnler and Tognoni, 1987); Naming Test of Aachener Aphasia Test (Luzzatti et al., 1996).

2.3. Nutritional status evaluation

MNA was administered to assess nutritional status at the initial visit (Guigoz et al., 2002). The MNA is an assessment tool that can be used to identify geriatric (>65 years) patients at risk of malnutrition. It consists in 18-item questionnaire comprising

anthropometric measurements (BMI, mid-arm and calf circumference, weight loss) combined with a questionnaire on diet (number of meals consumed, food and fluid intake and feeding autonomy), a global assessment (life-style, medication, mobility, presence of acute stress and presence of dementia or depression) and a self-assessment (self-perception of health and nutrition). An MNA score <17 indicates a status of malnutrition, an MNA score <23.5 indicates a risk of malnutrition and a score >23.5 denotes good nutritional status. The MNA is well validated and correlates highly with clinical assessment and objective indicators of nutritional status.

2.4. Functional assessment

Functional autonomy was evaluated at the initial visit using the Activities of Daily Living scale (ADL) (Katz et al., 1963) and Instrumental Activities of Daily Living scale (IADL) (Lawton and Brody, 1969).

2.5. Psychiatric evaluation

Neuropsychiatric symptoms were evaluated using the NPI (Cummings et al., 1994). Twelve behavioral domains are evaluated in this test: delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability/lability, aberrant motor activity, night-time behavioral disturbances and appetite/eating disorders. The NPI is based on screening questions used to ask the caregiver whether the patient's behavior has changed since the onset of dementia and, if so, whether the altered behavior was present during the last month. In the affirmative, the domain is then explored with subquestions about the specific features of the behavioral disturbances. The caregiver must rate the severity of the neuropsychiatric disturbances on a scale from 1 to 3, and the frequency from 1 to 4. For each behavioral domain the score is the product of the frequency and severity. Total score is the sum of the subscale scores.

The NPI has been shown to have good content and concurrent validity, as well as adequate test-retest, between rater reliability and internal consistency (Cummings et al., 1994). The NPI also shows changes in patients at the different phases of illness (Mega et al., 1996). The Italian version of the NPI was validated by Binetti et al. (1998) in AD patients and has demonstrated comparable psychometric properties.

2.6. Data analysis

Differences between demographic and clinical data of well-nourished patients and those at risk of malnutrition were analyzed using the Student's *t*-test and chi-square analyses as appropriate. The MMSE and other neuropsychological and functional test scores were compared in the two groups using the Mann-Whitney *U*-test.

The bootstrap analysis (Angelelli et al., 2004) was used to compare NPI mean scores between groups. The bootstrap is a non-parametric re-sampling technique that allows a probability

Table 1
Demographic and clinical features of the study population

	AD patients (N = 49)	Well-nourished (N = 28)	At risk of malnutrition (N = 21)	Comparison of groups
Age (years) (mean $\pm$ S.D.)	73.89 $\pm$ 7.42	71.8 $\pm$ 6.8	76.6 $\pm$ 7.5	$t_{(47)} = -2.32$, $p < 0.05$
Education (years) (mean $\pm$ S.D.)	5.84 $\pm$ 3.92	5.7 $\pm$ 3.9	5.9 $\pm$ 4	$t_{(47)} = -0.17$, n.s.
Gender (male/female)	17/32	7/21	10/11	$\chi^2 = 1.8$, d.f. = 1, n.s.
MNA (mean $\pm$ S.D.)	23.5 $\pm$ 3.22	25.75 $\pm$ 1.13	20.5 $\pm$ 2.58	$t_{(47)} = 9.61$, $p < 0.001$
Weight	65.03 $\pm$ 9.37	66.8 $\pm$ 9.1	63.1 $\pm$ 9.5	$t_{(43)} = 1.34$, n.s.
BMI	26.73 $\pm$ 4.12	27.4 $\pm$ 3.8	26 $\pm$ 4.4	$t_{(43)} = 1.15$, n.s.
Onset (months) (mean $\pm$ S.D.)	24.12 $\pm$ 16.7	23.1 $\pm$ 16.6	25.5 $\pm$ 17.1	$t_{(47)} = -0.48$, n.s.

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