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Awareness and behavioral problems in dementia patients: a prospective study

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ABSTRACT

Background: The results of studies of the association between awareness and clinical correlates in patients with dementia are inconclusive. The aims of this study were to investigate whether awareness changed during the course of dementia and to determine whether awareness was associated with certain behavioral symptoms. Specifically, it was hypothesized that relatively intact awareness was related to affective disorders.

Methods: One hundred and ninety-nine patients with dementia were included in a prospective 18-month follow-up study. Behavioral problems were assessed with the Neuropsychiatric Inventory and the Cornell Scale for Depression in Dementia. Awareness was assessed by means of the Guidelines for the Rating of Awareness Deficits.

Results: Cross-sectional analyses showed awareness to be positively associated with age, gender, education and socioeconomic status, and negatively associated with psychosis, apathy, and overall behavioral disorders at baseline. After 1 year, a higher level of awareness was related to depression and anxiety. The level of awareness at baseline also predicted depression and anxiety after 1 year. Awareness decreased during the study.

Conclusions: A higher level of awareness is associated with subsyndromal depression and anxiety, whereas lack of awareness is associated with psychosis and apathy. The level of awareness decreases as dementia progresses. Clinicians should be more alert to changes in awareness in patients with dementia because psychosocial support might help to prevent the development of affective symptoms.

Key words: neuropsychiatric symptoms, Alzheimer's disease, awareness, Neuropsychiatric Inventory, depression, anxiety, apathy

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In recent years there has been a growing interest in the concept of awareness in people with dementia. Several terms have been proposed to describe this phenomenon; however, complexities around the concept and relationships of awareness or insight still exist (Aalten *et al.*, 2005; Clare, 2004b; Markova *et al.*, 2005). In the present study, the term "awareness" is used as synonymous with awareness of memory difficulty and its impact.

Considerable attention has been paid to the role of awareness in dementia and in particular its associations with cognitive function. Less is known about relationships between awareness and behavioral and psychological symptoms of dementia (BPSD). Some studies (Burke *et al.*, 1998; Feher *et al.*, 1991; Harwood *et al.*, 2000; Migliorelli *et al.*, 1995; Seltzer *et al.*, 1995; Sevush and Leve, 1993; Smith *et al.*, 2000; Starkstein *et al.*, 1996; 1997), but not all (Arkin and Mahendra, 2001; Cummings *et al.*, 1995; DeBettignies *et al.*, 1990; Derouesné *et al.*, 1999; Lopez *et al.*, 1994; Michon *et al.*, 1994; Ott *et al.*, 1996a; Reed *et al.*, 1993; Verhey *et al.*, 1993; Zanetti *et al.*, 1999), show intact awareness to be associated with depressive symptoms and with anxiety (Derouesné *et al.*, 1999; Harwood *et al.*, 2000; Verhey *et al.*, 1993), although the latter association was not found by Seltzer *et al.* (1995). There is evidence that decreased awareness may be associated with apathy (Derouesné *et al.*, 1999; Robert *et al.*, 2002; Starkstein *et al.*, 1996; 2001), agitation, irritability (Harwood *et al.*, 2000; Seltzer *et al.*, 1995; Starkstein *et al.*, 1995) and psychosis (Mangone *et al.*, 1991; Migliorelli *et al.*, 1995; Starkstein *et al.*, 1996; 1997).

Moreover, some studies have shown that awareness decreases as dementia worsens (Derouesné *et al.*, 1999; Feher *et al.*, 1991; Harwood *et al.*, 2000; Lopez *et al.*, 1994; Mangone *et al.*, 1991; Migliorelli *et al.*, 1995; Seltzer *et al.*, 1995; Sevush, 1999; Sevush and Leve, 1993; Starkstein *et al.*, 1996; 1997; Vasterling *et al.*, 1995; Verhey *et al.*, 1993; Zanetti *et al.*, 1999), whereas others found no such association (Arkin and Mahendra, 2001; Auchus *et al.*, 1994; Kotler-Cope and Camp, 1995; Michon *et al.*, 1994; Reed *et al.*, 1993; Vasterling *et al.*, 1997). These inconsistencies between studies could be due to the use of small samples of patients, different operationalizations of awareness, and cross-sectional data. There is a need for prospective longitudinal studies of larger cohorts. Although Starkstein *et al.* (1997), Vasterling *et al.* (1997), Derouesné *et al.* (1999), Sevush (1999) and Arkin and Mahendra (2001) performed longitudinal studies of the course of awareness in patients with dementia, their studies included relatively small samples of patients and the period of follow-up was limited.

In the present study, we prospectively studied 199 patients with dementia for 18 months. Our primary aim was to examine whether awareness is a predictor of behavioral problems, whether specific types of behavior are associated with level of awareness, and how awareness changes during the course of dementia.

We specifically examined the hypothesis that intact awareness is associated with affective disorders, and especially depression.

Methods

Patients

The present study was part of the Maastricht Study of Behavior in Dementia (MAASBED), a study that focuses on the course and risk factors of BPSD. MAASBED is a 2-year prospective study of 199 patients with dementia, who are seen at 6-month intervals. Patients were subsequently referred to the Maastricht Memory Clinic of the University Hospital Maastricht, or the geriatric division of the Regional Institute for Community Mental Health Care (RIAGG), Maastricht.

Patients were included when they met the DSM-IV criteria for dementia (American Psychiatric Association, 1994) and if there was a reliable informant. Of these, 146 patients met the NINCDS-ADRDA (McKhann *et al.*, 1984) (possible, probable) criteria for Alzheimer type dementia, 32 patients the NINCDS-AIREN criteria for vascular dementia (Román *et al.*, 1993), two dementia with Lewy bodies (DLB) (McKeith *et al.*, 1996), and 19 dementia due to multiple etiologies.

Patients were excluded if they were living in a nursing home at the start of the study. Written consent was given by the caregiver and, when possible, by the patient. The Medical Ethics Committee of the University Hospital Maastricht approved this study.

For the present study, data were available for baseline, and 6-, 12- and 18-month follow-up evaluations. After 6 months, 30 patients refused participation and 12 patients had died; after 1 year, nine patients refused participation and 11 patients had died; after 18 months, seven refused participation and 13 patients had died. Complete follow-up data were thus available for 117 patients (58.8%). The 82 patients who did not complete the entire study did not differ from those who attended all follow-up evaluations with regard to age, sex, severity of dementia, severity of behavioral problems, and awareness score at study onset.

Measurements

Behavioral problems

Behavioral problems were assessed with the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994) and the Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos *et al.*, 1988). The NPI is a reliable, informant-based

rating scale developed to assess psychopathology in patients with dementia. The current version (Cummings, 1997) evaluates 12 neuropsychiatric symptoms that are commonly observed in dementia. The severity and frequency of each symptom are scored on the basis of structured questions administered to the patient's caregiver. The score for each symptom is obtained by multiplying severity (1–3) by frequency (1–4). The summed symptom scores give the total NPI score. The validity and reliability of the NPI (Cummings and McPherson, 2001) and its Dutch version (Kat *et al.*, 2002) have been established.

For this study, NPI items were clustered based on a previous principal component analysis study to minimize the number of variables (Aalten *et al.*, 2003). This resulted in three factors: (1) a “mood/apathy” factor, including depression, apathy, night-time behavior disturbances and eating abnormalities (four items, Cronbach's $\alpha = 0.63$); (2) a “hyperactivity factor,” including the symptoms agitation, euphoria, irritability, disinhibition and aberrant motor behavior (five items, $\alpha = 0.73$); and (3) a “psychosis factor,” including hallucinations and delusions (two items, $\alpha = 0.72$). Anxiety was regarded as a separate symptom. The total score for each subsyndrome was calculated by summing the NPI item scores for each factor.

In addition, the CSDD (Alexopoulos *et al.*, 1988) was used to measure mood disturbances and was administered to the caregivers and patients. The CSDD is a 19-item clinician-rated instrument with item scores ranging from 0 (absent) to 2 (severe), with a maximum score of 38 points.

Awareness

Awareness was assessed by means of the Guidelines for the Rating of Awareness Deficits (GRAD) (Verhey *et al.*, 1993; Zanetti *et al.*, 1999). The GRAD is a semistructured interview in which the degree of awareness is assessed by comparing the patient's and the caregiver's information about the patient's history. Impaired awareness is defined as the absence of knowledge or recognition of cognitive deficits and its impact. It is rated on a four-point scale, ranging from 4 (intact), 3 (mildly disturbed), 2 (moderately disturbed) to 1 (absent).

Procedure

In addition to general information on demographics, disease duration (years), level of education, socioeconomic status (SES) and medical history gathered from the primary caregivers, trained research assistants administered cognitive tests to the patients. The Mini-mental State Examination (MMSE) (Folstein *et al.*, 1975) was administered as a measure of cognitive decline and the Global Deterioration Scale (GDS) as a measure of severity of dementia (Reisberg *et al.*, 1982).

Statistical analyses

Statistical analyses were performed with the Statistical Package for Social Sciences, version 10. To determine whether awareness was related to behavioral disorders during the 18-month follow-up, logistic regression analyses were performed on the three subsyndromes of the NPI and the CSDD, with awareness as the independent variable. The subsyndromes were dichotomized by median split. Separate analyses were also performed for the symptoms anxiety, depression and apathy, as measured by the NPI.

Cross-sectional analyses were performed for each assessment time, correcting for age, sex, SES and severity of dementia (GDS). Longitudinal analyses were performed looking at baseline GRAD as predictor of the subsyndromes and separate symptoms. Age, sex, SES and GDS were again included as covariates, as were the baseline scores for the subsyndromes.

To test differences in descriptive sample characteristics between the four awareness groups, one-way analysis of variance (ANOVA), χ^2 -tests and Kruskal–Wallis tests were used as appropriate. To determine whether awareness decreased with time, ANOVA with repeated measures with time (baseline, 6-, 12- and 18 months) as the within-subject factor was computed. All significance tests were performed at a two-tailed α level of 0.05.

Results

Patient characteristics and relationships with awareness

At baseline, 83 men (41.7%) and 116 women (58.3%) were included in the study (see Table 1). The mean age was 76.4 ± 8.0 years (range 53–96 years). Most patients had a relatively low education and SES. The mean disease duration was 3.0 ± 2.2 years. The average MMSE score was 18.1 ± 4.7 at baseline and declined significantly at each follow-up, to reach 16.0 ± 6.1 after 18 months. The GDS score increased significantly during follow-up, indicating that severity of dementia increased over time.

A series of one-way ANOVAS found significant effects of age on awareness at baseline ($F(3,198) = 2.73$, $p = 0.05$) and 1 year ($F(3,143) = 3.14$, $p = 0.03$), showing younger age to be associated with intact awareness. Intact awareness was also associated with lower GDS ($p < 0.001$) and higher MMSE scores ($p = 0.01$ or $p < 0.001$ at 6 months) at all assessments, indicating that awareness is negatively associated with severity of dementia. There were also sex differences, with men having a more intact insight at baseline ($\chi^2 = 25.5$, d.f. = 3, $p < 0.001$) and at 1 year ($\chi^2 = 8.06$, d.f. = 3, $p = 0.05$). Kruskal–Wallis tests revealed positive associations between education and SES at the first three assessments, indicating

Table 1. Means (\pm S.D.) and proportion (%) of patient characteristics by level of awareness at each assessment

	TOTAL GROUP	AWARENESS SCORE				<i>p</i> *
		1	2	3	4	
Sex (% male)						
Baseline (<i>n</i> = 199)	41.7	12.5	41.3	40.0	73.5	<0.001
6 months (<i>n</i> = 155)	43.2	35.3	33.9	54.5	57.1	0.08
1 year (<i>n</i> = 144)	40.3	36.4	35.6	38.5	76.9	0.05
18 months (<i>n</i> = 126)	39.7	36.6	34.0	48.3	66.7	0.31
Education (1–8)†						
Baseline	2.3 ± 1.7	1.6 ± 1.2	2.0 ± 1.4	2.3 ± 1.8	3.4 ± 2.2	0.001
6 months	2.3 ± 1.7	2.1 ± 1.4	1.7 ± 1.1	2.9 ± 2.1	3.1 ± 2.0	0.001
1 year	2.3 ± 1.7	1.9 ± 1.4	2.0 ± 1.5	2.7 ± 1.8	3.7 ± 2.2	0.006
18 months	2.3 ± 1.6	1.9 ± 1.3	2.3 ± 1.7	2.7 ± 1.7	3.0 ± 2.0	0.12
SES (1–6)‡						
Baseline	2.1 ± 1.6	1.5 ± 1.2	2.0 ± 1.6	2.1 ± 1.4	3.1 ± 1.9	<0.001
6 months	3.1 ± 1.9	1.8 ± 1.3	1.6 ± 1.1	2.7 ± 1.8	3.1 ± 1.9	<0.001
1 year	2.2 ± 1.6	1.8 ± 1.3	1.8 ± 1.4	2.7 ± 1.8	3.4 ± 1.8	<0.001
18 months	2.2 ± 1.6	1.8 ± 1.4	2.2 ± 1.6	2.5 ± 1.7	2.7 ± 1.9	0.10
Age						
Baseline	76.4 ± 8.0	79.3 ± 8.8	77.2 ± 7.0	75.3 ± 7.8	74.6 ± 8.7	0.05
6 months	76.7 ± 8.1	78.6 ± 7.5	77.3 ± 8.1	76.1 ± 8.0	73.6 ± 9.0	0.15
1 year	77.2 ± 8.1	79.1 ± 7.5	77.1 ± 8.6	77.9 ± 7.6	71.2 ± 7.3	0.03
18 months	77.4 ± 8.0	78.4 ± 7.0	78.3 ± 8.1	75.9 ± 9.1	71.3 ± 5.4	0.12
GDS						
Baseline	4.1 ± 0.7	4.6 ± 0.7	4.2 ± 0.7	4.0 ± 0.6	3.8 ± 0.7	<0.001
6 months	4.6 ± 0.8	5.0 ± 0.8	4.7 ± 0.8	4.3 ± 0.7	4.1 ± 0.6	<0.001
1 year	4.7 ± 0.7	5.2 ± 0.6	4.6 ± 0.6	4.7 ± 0.6	4.2 ± 0.7	<0.001
18 months	4.9 ± 0.7	5.2 ± 0.6	4.9 ± 0.6	4.6 ± 0.7	4.3 ± 0.5	<0.001
MMSE						
Baseline (<i>n</i> = 193)	18.1 ± 4.7	17.2 ± 4.4	17.2 ± 5.0	18.0 ± 4.1	20.6 ± 4.9	0.01
6 months (<i>n</i> = 147)	17.1 ± 5.4	14.0 ± 5.6	16.4 ± 4.1	18.9 ± 5.2	20.2 ± 5.5	<0.001
1 year (<i>n</i> = 118)	16.1 ± 5.8	14.0 ± 5.7	15.5 ± 5.2	16.5 ± 6.3	20.5 ± 4.7	0.01
18 months (<i>n</i> = 98)	16.0 ± 6.1	13.6 ± 5.7	15.6 ± 6.4	19.0 ± 5.3	18.6 ± 3.7	0.01
Disease duration						
Baseline (<i>n</i> = 187)	3.0 ± 2.2	3.0 ± 2.5	3.0 ± 2.2	3.1 ± 2.1	3.0 ± 2.0	0.995
6 months (<i>n</i> = 147)	3.6 ± 2.2	3.5 ± 2.6	3.6 ± 2.1	3.6 ± 2.2	3.4 ± 2.0	0.979
1 year (<i>n</i> = 135)	4.0 ± 2.2	4.6 ± 3.0	3.8 ± 1.8	4.0 ± 2.2	4.0 ± 2.3	0.46
18 months (<i>n</i> = 118)	4.5 ± 2.2	4.7 ± 2.7	4.6 ± 1.9	4.4 ± 2.2	3.6 ± 1.1	0.67

SES = socioeconomic status; GDS = Global Deterioration Scale; MMSE = Mini-mental State Examination.

* Based on one-way ANOVA, χ^2 analysis was used for sex and the Kruskal–Wallis test for education and SES.

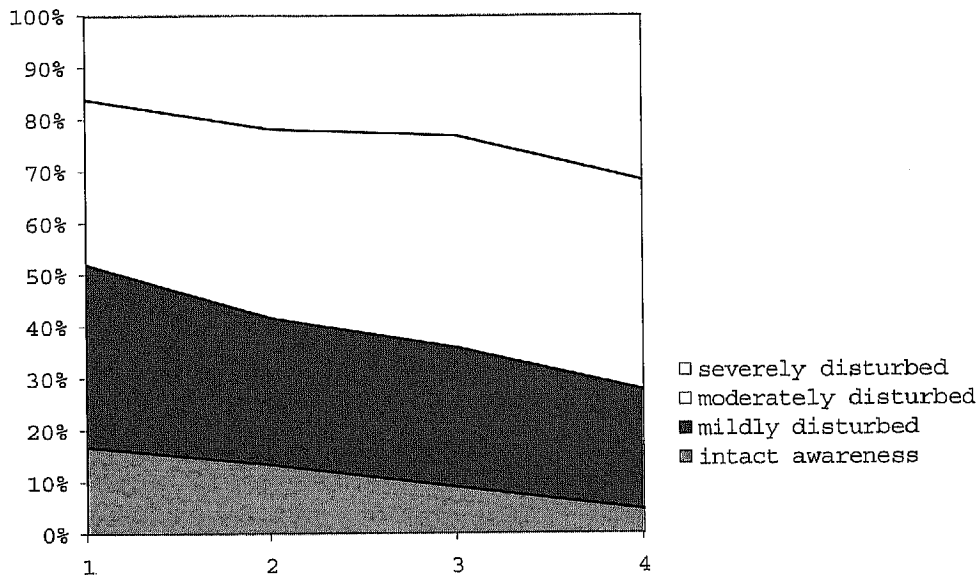
† Ranging from primary education to university degree.

‡ Ranging from untrained work to higher profession.

Table 2. Cross-sectional analysis; associations between levels of awareness and behavioral disorders at baseline and after 1 year

	BASELINE (<i>n</i> = 199)			1 YEAR (<i>n</i> = 144)		
	OR	<i>p</i>	95% CI	OR	<i>p</i>	95% CI
Mood/apathy	0.84	0.32	0.60–1.18	1.21	0.39	0.79–1.84
Hyperactivity	0.78	0.15	0.55–1.10	1.05	0.84	0.68–1.60
Psychosis	0.66	0.03	0.46–0.95	0.85	0.46	0.56–1.30
Anxiety	0.99	0.97	0.71–1.40	1.95	0.01	1.23–3.08
Depression	1.24	0.22	0.88–1.76	1.63	0.03	1.05–2.55
Apathy	0.61	0.01	0.43–0.86	0.98	0.94	0.64–1.50
NPI total	0.61	0.01	0.43–0.87	1.17	0.49	0.76–1.79
CSDD	1.13	0.49	0.80–1.58	1.15	0.51	0.76–1.75

OR = odds ratio; 95% CI = 95% confidence interval; NPI = Neuropsychiatric Inventory; CSDD = Cornell Scale for Depression in Dementia.

**Fig. 1.** Relative proportional distribution of GRAD scores

higher levels of awareness in patients with higher education levels and higher SES. Disease duration was not associated with the level of awareness.

Awareness and behavioral disorders

CROSS-SECTIONAL ANALYSES

Logistic regression analyses were performed to determine whether awareness and behavioral disorders were associated (Table 2). At baseline, low levels of awareness were associated with psychosis [odds ratio (OR) = 0.66; *p* = 0.03; 95%

Table 3. Distribution of awareness scores across assessments and changes from baseline

	CHANGE IN AWARENESS SCORES FROM BASELINE				DISTRIBUTION AT EACH ASSESSMENT
	1	2	3	4	
Baseline					
GRAD1					32 (16.1)
GRAD 2					63 (31.7)
GRAD 3					70 (35.2)
GRAD 4					34 (17.1)
Total <i>n</i>		After			199
6 months					
GRAD1	18 (69.2)	11 (25.0)	5 (9.3)	0	34 (21.9)
GRAD 2	6 (23.1)	28 (63.6)	21 (38.9)	1 (3.2)	56 (36.1)
GRAD 3	1 (3.8)	4 (9.1)	24 (44.4)	15 (48.4)	44 (28.4)
GRAD 4	1 (3.8)	1 (2.3)	4 (7.4)	15 (48.4)	21 (13.5)
Total <i>n</i>	26	44	54	31	155
1 year					
GRAD 1	13 (61.9)	12 (25.0)	8 (16.0)	0	33 (22.9)
GRAD 2	6 (28.6)	33 (68.8)	17 (34.0)	3 (12.0)	59 (41.0)
GRAD 3	2 (9.5)	3 (6.3)	21 (42.0)	13 (52.0)	39 (27.1)
GRAD 4	0	0	4 (8.0)	9 (36.0)	13 (9.0)
Total <i>n</i>	21	48	50	25	144
18 months					
GRAD 1	15 (75.0)	17 (39.5)	8 (18.6)	0	40 (31.7)
GRAD 2	4 (20.0)	23 (53.5)	18 (41.9)	6 (30.0)	51 (40.5)
GRAD 3	1 (5.0)	3 (7.0)	15 (34.9)	10 (50.0)	29 (23.0)
GRAD 4	0	0	2(4.7)	4 (20)	6 (4.8)
Total <i>n</i>	20	43	43	20	126

Values are given as *n* (%).

Awareness scores: 1 = severely disturbed; 2 = moderately disturbed; 3 = mildly disturbed; 4 = intact. GRAD = Guidelines for the Rating of Awareness Deficits.

confidence interval (95% CI) = 0.46–0.95] and apathy (OR = 0.61; $p = 0.01$; 95% CI = 0.43–0.86), and a higher NPI total score (OR = 0.61; $p = 0.01$; 95% CI = 0.43–0.87). There were no significant associations at 6 months. After 1 year, awareness was positively related to anxiety (OR = 1.95; $p = 0.01$; 95% CI = 1.23–3.08) and depression (OR = 1.63; $p = 0.03$; 95% CI = 1.05–2.55). The subsyndromes mood/apathy and hyperactivity were not associated with level of awareness, and neither was awareness nor the CSDD score.

AWARENESS AS PREDICTOR OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS

The baseline level of awareness was positively associated with anxiety after 1 year (OR = 1.76; $p = 0.01$; 95% CI = 1.13–2.76) and 18 months (OR = 1.85;

$p = 0.02$; 95% CI = 1.13–3.02). At 1 year, intact awareness at baseline was also associated with greater depression (OR = 1.55; $p = 0.05$; 95% CI = 1.00–2.39). No other longitudinal relationships were found between baseline awareness and other behavioral disorders.

Course of awareness

ANOVA with repeated measures showed a significant time effect ($F(3,348) = 23.81$, $p < 0.001$), indicating that the level of awareness decreased significantly during the follow-up. At baseline, 34 of 199 patients (17.1%) had an intact awareness, and 70 patients (35.2%) had a mildly disturbed awareness, so at baseline around 50% of the patients had intact or mildly disturbed awareness (see Figure 1 and Table 3). At the 18-month follow-up the awareness of most patients with either mild or intact awareness had decreased, whereas that of most patients with severely disturbed awareness remained stable. Around just a fifth of patients with intact awareness at baseline continued to have this 18 months later. Awareness improved in three patients at subsequent assessments from severely disturbed to mildly disturbed or intact awareness. Changes in medication use in these patients were not responsible for this improvement of awareness.

Discussion

The main question of this study was whether awareness was related to behavioral problems in patients with dementia. We found that high levels of awareness at baseline were predictive for anxiety at 12 and 18 months, and depression at 12 months. These associations were also found at 12 months, cross-sectional. Starkstein *et al.* (1997) and Derouesné *et al.* (1999) found awareness to be a predictor of the emergence of depression and “emotional deficit” (including anxiety symptoms), after a mean interval of 16 and 21 months, respectively. Combined, the studies suggest that awareness is a predictor for depressive symptoms and anxiety. Other authors, in cross-sectional studies, have found depression to be more common among patients with higher levels of awareness (Burke *et al.*, 1998; Feher *et al.*, 1991; Harwood *et al.*, 2000; Migliorelli *et al.*, 1995; Seltzer *et al.*, 1995; Sevush and Leve, 1993; Smith *et al.*, 2000; Starkstein *et al.*, 1996; 1997), whereas others have not (Arkin and Mahendra, 2001; Cummings *et al.*, 1995; DeBettignies *et al.*, 1990; Derouesné *et al.*, 1999; Lopez *et al.*, 1994; Michon *et al.*, 1994; Ott *et al.*, 1996a; Reed *et al.*, 1993; Verhey *et al.*, 1993; Zanetti *et al.*, 1999). Some authors found that less severe forms of depression, such as dysthymia, were associated with greater awareness (Migliorelli *et al.*, 1995; Starkstein *et al.*, 1997) and suggested that dysthymia represented an emotional response to progressive cognitive decline, whereas

major depression was associated with a biological etiology unrelated to awareness. A recent review indicated that awareness is only related to subsyndromal depression (Aalten *et al.*, 2005). Further studies should address this issue. A positive association between awareness and anxiety has been reported less often (Derouesné *et al.*, 1999; Harwood *et al.*, 2000; Verhey *et al.*, 1993). Like depression, feelings of anxiety may be the result of a psychological reaction to painful insight into cognitive decline.

The negative association between psychosis and awareness we found in this study has been reported previously (Mangone *et al.*, 1991; Migliorelli *et al.*, 1995; Starkstein *et al.*, 1996; 1997) and may be explained from a psychopathological perspective. Because of impaired reality testing abilities related to cognitive decline, patients with low levels of awareness might be less able to recognize changes in themselves or in their environment. As a result, they may compensate for this by incorrect rationalizations resulting in psychosis. An alternative explanation is that both awareness and psychosis are related to dysfunction of certain brain structures or systems that are themselves variably affected by the progression of dementia.

We, like others (Derouesné *et al.*, 1999; Robert *et al.*, 2002; Starkstein *et al.*, 1996; 2001), found awareness to be negatively associated with apathy at baseline. Patients who are unaware of their deficits may be less reactive to their environment and to their needs and emotions, resulting in apathy. Loss of awareness, as well as psychosis and apathy, has been related to neuropathological changes in right frontal and related subcortical structures (Mega *et al.*, 2000; Migliorelli *et al.*, 1995; Ott *et al.*, 1996b; Reed *et al.*, 1993). The shared neuropathological substrates may be the reason why fewer inconsistencies are reported between studies assessing these relationships in early stages of dementia.

Awareness did not, however, seem to be predictive for the subsyndrome mood/apathy and the CSDD. This may be because the NPI subsyndrome and the CSDD include both apathy and depression, which have opposite relationships to awareness. In addition, like the symptom depression, in our study both mood/apathy and the CSDD did not specifically measure dysthymia.

Previous studies have found higher levels of unawareness to be associated with agitation (Harwood *et al.*, 2000) and irritability (Seltzer *et al.*, 1995), which are symptoms included in our "hyperactivity" subsyndrome. Subanalyses (not reported here) found negative associations between awareness and agitation at baseline and after 6 months. Although some authors suggest that lack of awareness is greater in patients with Alzheimer's disease than in those with dementia of other etiologies (DeBettignies *et al.*, 1990; Wagner *et al.*, 1997), we and others (Verhey *et al.*, 1995; Zanetti *et al.*, 1999) found no evidence for this.

We also investigated whether the level of awareness is associated with major demographic variables and how awareness changes during the course of

dementia. We found that higher levels of awareness were associated with younger age, mild/moderate severity of dementia, male sex, and higher education and SES level. Most studies have not found awareness to be associated with age (Arkin and Mahendra, 2001; DeBettignies *et al.*, 1990; Feher *et al.*, 1991; Harwood *et al.*, 2000; Lopez *et al.*, 1994; Reed *et al.*, 1993; Sevush and Leve, 1993; Starkstein *et al.*, 1997; Vasterling *et al.*, 1995; 1997), although some have (Derouesné *et al.*, 1999). The association with male sex was also found by Sevush and Leve (1993). Our finding that a preserved awareness was associated with more intact cognitive functioning, as measured with the MMSE and GDS, supports previous research (Derouesné *et al.*, 1999; Feher *et al.*, 1991; Harwood *et al.*, 2000; Lopez *et al.*, 1994; Mangone *et al.*, 1991; Migliorelli *et al.*, 1995; Seltzer *et al.*, 1995; Sevush, 1999; Sevush and Leve, 1993; Starkstein *et al.*, 1996; 1997; Vasterling *et al.*, 1995; Verhey *et al.*, 1993; Zanetti *et al.*, 1999). To our knowledge, this study is the first to show awareness to be associated with education and SES. Patients with higher educational and occupational backgrounds may have more knowledge regarding characteristics and impact of dementia, and are therefore better able to perceive and interpret their own cognitive deterioration. We did not find duration of illness to be associated with level of awareness, in line with most other studies (Derouesné *et al.*, 1999; Mangone *et al.*, 1991; Reed *et al.*, 1993; Sevush and Leve, 1993; Vasterling *et al.*, 1995; 1997).

Impaired awareness was common and, at baseline, 82.9% of the patients in our study had some degree of impaired awareness, as found by others (Derouesné *et al.*, 1999; Reed *et al.*, 1993; Sevush, 1999; Verhey *et al.*, 1993). Awareness decreased with time in most patients with either mild or intact awareness at baseline, whereas it tended to be stable in most patients with more severe limitations of awareness at baseline. Three patients showed an improvement in awareness at subsequent assessments, as found by other researchers (Arkin and Mahendra, 2001; Derouesné *et al.*, 1999). This supports the view that awareness is not simply a symptom of a disease that becomes progressively more severe and suggests that psychological and social factors contribute to the manifestation of disturbed awareness (Clare, 2004a).

Although the results of this study were in some respects ambiguous, taken together with previous studies our findings suggest that a relatively intact awareness is associated with subsyndromal depression and anxiety, and that lower levels of awareness are related to psychosis and apathy. The strengths of the present study are its prospective design, the use of a structured instrument for assessing behavioral problems, and the inclusion of a representative clinical sample that is larger than in previous studies. The discrepancies between our and other studies may be attributed, at least in part, to differences in theoretical and conceptual formulations and methods of measuring awareness and behavioral

problems. In addition, a weakness of our study is the use of the four-point rating scale of the GRAD, which may be too general to assess a complex phenomenon such as awareness. However, the use of a clinician rating method has the advantage of allowing a rapid assessment of awareness, and assessing awareness in the context of an interview might allow for comprehension to be checked and answers to be explored in more detail. Nevertheless, it is important for future work to focus on developing better conceptual frameworks and methodological approaches of awareness that are of use to clinicians and can contribute to enhancing the quality of care for people with dementia and their families (Aalten *et al.*, 2005; Clare, 2004a; Clare *et al.*, 2005).

Our findings can help clinicians to determine which of their patients are at risk of developing depression or anxiety. Clinicians should be more alert to changes in awareness in patients with dementia, and often psychological support is of importance as it may help to reduce depression and anxiety in patients with an intact awareness. Other studies are needed to investigate whether psychological approaches to depression and anxiety are effective, with emphasis on biological interventions for the treatment of major depression, psychosis and apathy.

Conflict of interest

None.

Description of author's roles

Both Frans Verhey and Jelle Jolles had a role in formulating the research question, designing the study and writing the article. Pauline Aalten was the main researcher and psychologist of this study, and, along with Marjolein de Vugt, participated in formulating the research question, designing the study, carrying it out, analyzing the data and writing the article. Evelien van Valen collected the data and assisted with writing the article. Richel Lousberg helped with the statistical analyses of the study.

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