

Delusions and Patterns of Cognitive Impairment in Alzheimer's Disease

*Frederick W. Bylsma, Ph.D., *Marshal F. Folstein, M.D., **Devangere P. Devanand, M.D.,
†Marcus Richards, Ph.D., †Jacqueline Bello, M.D., §Marilyn Albert, Ph.D.,
and †Yaakov Stern, Ph.D.

*Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University, Baltimore, Maryland; **Department of Neurology and Psychiatry, College of Physicians and Surgeons of Columbia University, New York, New York; †Albert Einstein College of Medicine, Bronx, New York; §Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts, U.S.A.

Summary: Cognitive correlates of delusions were examined in 180 probable Alzheimer's disease (AD) patients. Deluded ($n = 45$) and nondeluded ($n = 135$) AD patients were equally demented, but deluded patients had relatively preserved attention and worse confrontation naming. In an independent sample of AD patients, the finding of better attention in deluded patients was replicated but the naming difference, although in the expected direction, failed to reach significance. Preserved attention and poor naming may be important for the development of delusions in AD patients. **Key Words:** Delusion—Cognition—Alzheimer's disease. NBN 7:98-103, 1994

Delusions are false, personal beliefs that are held by an individual despite incontrovertible evidence to the contrary (1). Delusions are common in patients with neuropsychiatric disorders such as Alzheimer's disease (AD). The patient who Alzheimer presented in his classic paper (2) had a delusional suspiciousness of her husband as her initial symptom. This suspiciousness continued for a period of time. Later, auditory hallucinations were also apparent. As the disease progressed, these symptoms were no longer reported.

Since this early description of psychopathologic symptoms associated with AD, many reports of their prevalence have been published. Prevalence estimates range from 10 to 73%, with the majority of studies reporting rates of 40-60% (3-9). The most common symptom reported is delusion, followed in frequency of occurrence by misidentification and then hallucination. These symptoms occur most often in mildly or

moderately demented patients (3, 4, 9) and have been associated with extrapyramidal signs (10), physical aggression and hostility (4, 5) and with more rapid cognitive decline (10-12) and functional decline (13), but not increased mortality (14).

The factors which predispose AD patients to experience delusions are not well understood. Maher and Ross (15) and others have proposed that delusions are due to cognitive defects, perceptual defects, or both. Pathological causes of delusions are suggested by patient studies. Many medical and neurological conditions are associated with delusions (15, 16). Unilateral pathology of the left hemisphere is common (15, 17-19). In this study we describe the cognitive correlates of delusions in a large group of AD patients.

METHODS

Subjects

A sample of 224 patients with probable AD according to NINCDS-ADRDA criteria (20) were recruited for a longitudinal multi-site study of predictors of decline in AD (21). The purpose of that study is to exam-

Address correspondence and reprint requests to Dr. Frederick W. Bylsma, Department of Psychiatry and Behavioral Science, The Johns Hopkins University School of Medicine, Meyer 218, 600 North Wolfe Street, Baltimore, Maryland, 21205 U.S.A.

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ine the effects of extrapyramidal symptoms, psychopathologic symptoms, and myoclonus on the rate of cognitive and functional decline in AD. Study sites are the Memory Disorders Center at the Neurological Institute of New York (Columbia University; 99 subjects), The Johns Hopkins University School of Medicine (Baltimore; 70 subjects), and the Massachusetts General Hospital (Boston; 55 subjects). The procedures and requirements of the study were explained to each patient and his/her informant. A consent form was signed prior to data collection.

Exclusion criteria were Parkinson's disease, concurrent untreated major depression, and treatment with antipsychotic medications. Any subject being treated with antipsychotic medications had to have a medication-free period of at least one month prior to enrollment. However, these medication could be reinstated immediately after the baseline visit. No subjects in the current study were taking antipsychotic medications at the time of baseline evaluation.

Procedures

For this study, the baseline visit data of all patients enrolled in the longitudinal study were used. At that visit, 209 of the patients were outpatients and 15 were in adult assisted living facilities (21). Two groups were selected for this study: those for whom delusions (as defined below) were the only psychopathologic symptom reported (*Deluded, D*; $n = 45$) and those for whom no delusions, misidentifications, or hallucinations were reported (*Non-Deluded, Non-D*; $n = 135$) (Table 1). The rationale for selecting subjects this way comes from Jaspers (27), who distinguished primary from secondary psychopathological symptoms. Primary symptoms appear in isolation and secondary symptoms are causally related to other psychopathologic symptoms. Jaspers (27) proposed that the pathophysiology and phenomenology of individual symptoms may be obscured if secondary symptoms are considered. Also, Flint, (28), in a recent review of the literature on delusions in dementia, suggests that symptoms 'should be studied separately if we are to better understand their pathophysiology, nature, and natural history and if we are to develop more effective management'.

Instruments administered. The Columbia University Scale for Psychopathology in Alzheimer's Disease (CUSPAD) (29), a semi-structured interview designed to allow clinicians or trained lay interviewers to assess informant-reported delusions, hallucinations, illusions, misidentifications, behavioral disturbance, and depression in AD patients, was administered. The patient was not present at the interview. The time frame used was the previous month, and was adhered to

TABLE 1. Demographic, cognitive, and functional data for patients with delusions and those with no symptoms [M (SD)]

	Deluded	Non-Deluded
<i>n</i>	45	135
Male/Female	20/25	58/80
Age, years	74.7 (8.7)	71.6 (8.6) ^d
Onset age, years	70.6 (8.9)	67.6 (8.9)
Duration, years	4.0 (2.5)	3.9 (2.4)
% with EPS ^a	37.8	45.7
% Familial ^b	44.4	54.1
Married/unmarried ^c	28/17	87/49
Blessed functional activity scale		
Total	9.2 (3.1)	7.1 (3.0) ^e
Part 1	3.6 (1.4)	3.0 (1.3)
Part 2	0.5 (0.8)	0.5 (0.9)
Part 3	5.2 (2.2)	3.6 (2.1) ^e
Dependency rating	2.3 (0.7)	2.2 (0.8)
Equivalency Institute service	1.7 (0.7)	1.4 (0.6)
CDR rating	1.2 (0.4)	1.2 (0.3)
Hamilton depression index	3.9 (5.2)	2.7 (3.6)

^a Extrapyramidal motor signs.

^b Cases with at least one affected parent or sibling.

^c Unmarried are those currently widowed, divorced, or separated, and those who were never married.

^d $p < .01$.

^e $p < .001$.

with rigor. A psychiatrist and a trained lay person had adequate inter-rater reliability when concurrently rating a single interview ($kappa = .74$ to 1.0 for individual items) or when conducting separate interviews ($kappa = .53$ to .73) (29). This instrument was administered by trained lay interviewers at each study site. Raters from the Johns Hopkins and Massachusetts sites attended day-long training sessions at Columbia University to ensure comparable administration across sites.

Standard probe questions are posed to the informant about specific symptoms (e.g., for *delusions*: "Has he/she stated that someone is stealing things from him/her?"; for *misidentifications*: "Has he/she looked in the mirror and said it was someone else?"; for *hallucinations*: "Has he/she heard voices or sounds when no one is there?"). Informants were asked specifically about patients' delusions of people stealing things, other suspicions, people in the house when no one is there (phantom boarder), that their current house is not their home, that their spouse is being unfaithful, and that they will be abandoned by their spouse or care-taker. An additional question asked about other delusions not previously assessed. If a delusion was endorsed, the informant was queried about the frequency of occurrence and whether the patient would accept the truth if told. Delusions were coded as "transient" if they occurred once or twice a week, or as "persistent" if they occurred three or more

times in a week. For this paper, if either transient or persistent delusions were reported, the subject was said to be deluded.

The same coding scheme was used for misidentifications items (e.g., misidentify spouse, self in mirror, television characters as real). Similarly, informant reports of either vague or clear hallucinations resulted in the item being coded as positive. This method uses the "broad" definition of these psychopathologic symptoms, as defined by Devanand (29). Misidentifications and hallucinations were assessed to flag subjects to be eliminated from further analyses because the focus of this paper is on differences between deluded AD patients and those with neither delusions, hallucinations or misidentifications.

Patients were administered the modified Mini-Mental State Examination (mMMSE) (30, 31). This modified version includes scores for both serial-seven subtractions and spelling "WORLD" backwards in the total score, and adds the following items to the standard Mini-Mental State Examination (MMSE) (32): digit span forward and backwards, adding change (3 pennies, 1 nickel, 1 dime, and 1 quarter), naming the current and previous 4 presidents, a 10-item picture confrontation naming task, an additional sentence repetition item, a two part command to read and obey, and two alternate figures to copy (circle-and-diamond and a cube). The maximum score is 57, comprised of scores on Orientation, Registration, Recall, Digit Span, Attention/Calculation, Presidents, Naming, Language, and Construction subscales.

Functional abilities were assessed using the Blessed Dementia Rating Scale (BDRS) (22). Dementia severity was rated, using a modified version of the Clinical Dementia Rating scale (CDR), as either absent [0], mild [1], moderate [2], severe [3], profound [4], or terminal [5] (21). The Hamilton Depression Scale was administered in a semi-structured interview format with both the patient and informant (23) to index the severity of depressive symptoms. Patients' dependence on care-giver assistance was rated on a scale ranging from 0 (no assistance required) to 5 (total dependence) based upon an interview with the care-giver. An estimate of the equivalent institutional care level (limited home care, supervised adult setting, or a health-related facility) for that patient was also made based upon the latter data. The Dependence Scale and the Equivalent Institutional Service scales are described in detail by in another paper (24). Extrapyr- amidal motor signs (EPS) were assessed in a standard way using a modified version of the Unified Parkinson's Disease Rating Scale. This instrument codes for the presence and severity of resting tremor, rigidity, bradykinesia, gait disturbance, postural change and

facial appearance, as well as for dyskinesia and myo- clonus and has been shown to be reliable in this sub- ject population (25). History of dementia in the par- ents and siblings of the patient was reviewed using a semi-structured interview (26).

Data analysis. Patient groups were contrasted, by *Chi-square* or analysis of variance (ANOVA) with *post hoc* Scheffe or paired *t*-tests as warranted, on de- mographic, cognitive, and functional measures.

RESULTS

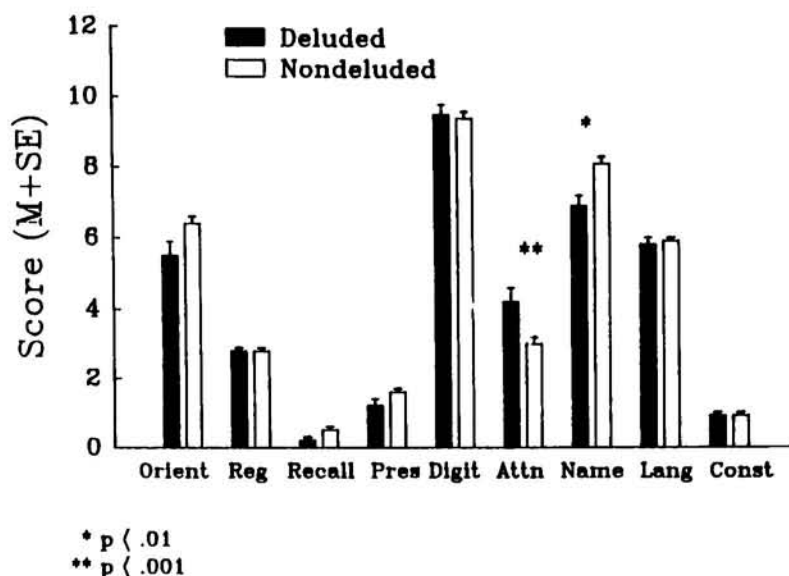
Twenty subjects (4 deluded, 16 nondeluded) were taking antidepressants, 8 subjects (1 deluded, 7 non- deluded) were taking sedative hypnotics, 5 subjects (1 deluded, 4 nondeluded) were taking thyroid medica- tions, and 6 nondeluded subjects were taking ergot medicines. The majority of subjects in each group [37 of 45 (87%) of deluded subjects; 100 of 135 (76%) of nondeluded subjects] were taking no psychotropic medicines at the time of baseline assessment.

Delusions were reported as the only psychopatho- logic symptom for 45 patients (D group) or 24.9% of the sample. The most frequently reported delusion was of someone stealing things (28 patients; 56% of all delusions) followed by 'other' delusions (11 patients; 24% of delusions), delusions of abandonment (7 pa- tients; 16% of all delusions), and finally somatic delu- sions (4 patients; 9% of all delusions). Five cases (11% of all deluded cases) reported more than one type of delusion. No psychopathologic symptoms were found in 135 AD cases, and these subjects constitute the non-deluded group (Non-D). The remaining 44 cases had misidentifications or hallucinations and were not included in the analyses below.

Univariate analysis of variance (ANOVA) compar- ing the deluded cases with the Non-D cases using sub- ject Group as the independent factor, revealed no dif- ferences across groups for current age, age of onset, or duration of disease. The groups had equal numbers of males and females, married and unmarried cases, cases with concurrent extrapyramidal motor signs, and "familial" cases (at least one affected parent or sibling) (Table 1).

Patients with delusions were rated as more func- tionally impaired than the Non-D patients on the BDRS ($F = 17.22$, $df = 1,181$, $p < .001$). Deluded patients had more "disturbance of personality" (BDRS Section 3; $F = 19.43$, $df = 1,181$, $p < .001$) being rated as more stubborn, self-centered, irritable, and emotionally labile than nondeluded patients. There were no group differences on Part 1 (memory and performance) or Part 2 (feeding, dressing and toi- letting) of the BDRS, the dependency rating scale, es- timated equivalent institutional service required or

FIG 1. Profile of modified Mini-Mental State Exam subscale scores for the initial sample (Abbreviations: Orient = Orientation; Regis = Registration of 3 words; FWD = Digit Span forward; BKWD = Digit Span backwards; Attn = Attention/Calculation; Pres = Current and previous 4 presidents; Name = 10-item naming task; Lang = Language; Const = Construction).



on CDR ratings. Similarly, on the Hamilton Depression Scale, deluded and nondeluded patients were not distinguishable.

Severity of dementia as indexed by mMMSE scores was not significantly different across groups ($F = 2.14, df = 1,181, ns$) indicating that the deluded patients were not more demented overall than nondeluded patients. However, an analysis of performance on each mMMSE subscale revealed selective differences across groups (Fig. 1). Specifically, deluded patients scored significantly better on the Attention/Calculation items (serial seven subtractions, spell "WORLD" backwards, and add change) ($F = 7.89, df = 1,181, p < .001$) but significantly worse on the ten-item Naming scale ($F = 15.07, df = 1,181, p < .001$) than nondeluded patients.

Replication study. Archival data from an independent sample of AD patients was examined to assess the generalizability of these findings. The subjects were taken from among those reported on by Deutsch et al. (4) in a study examining the relationship between delusions, hallucinations, and physical aggression. All subjects were being followed in the Johns Hopkins Alzheimer's Disease Research Center. Patients with dementia of equivalent severity as the patients in the cohort above were identified. Each of these patients had been administered the standard MMSE and a 30-item Boston Naming Test (33). These data were used to examine the generalizability of the finding of better attention/calculation and worse naming in AD patients with delusions relative to those with no delusions.

A group of 8 AD patients with delusions as their only psychopathologic symptom and a group of 25 nondeluded patients were identified. The patients were similar in age, duration of disease, and Mini-

Mental State score (Table 2). Modified MMSE scores were not available for these patients. However, a regression formula to compute mMMSE scores from standard MMSE scores was used to generate estimated mMMSE scores for this group of patients. These estimated values correspond closely to those for the first cohort, indicating similar dementia severity across samples of AD patients.

Analysis of the Attention/Calculation item of the MMSE (serial sevens subtraction) revealed a significant group effect ($F = 3.38, df = 1,31, p < .05$) with deluded patients scoring higher ($M = 1.9, SE = 0.7$) than nondeluded patients ($M = 1.0, SE = 0.3$). However, the groups were not significantly different on the naming task, although differences were in the expected direction (AD-Del: $M = 14.9, SE = 2.6$; Non-D: $M = 18.9, SE = 1.2$) ($F = 1.10, df = 1,31, ns$). These results support the finding of relatively preserved attention in AD patients with delusions when compared to nondeluded AD patients, but are only suggestive of relatively worse naming.

DISCUSSION

Psychopathologic symptoms were examined in 224 probable AD patients. Ninety-nine (44%) patients

TABLE 2. Demographic and clinical data for subjects in the replication study [M(SD)]

	Deluded	No symptoms
n	8	25
Age, years	72.8 (5.2)	71.5 (8.6)
Onset age, years	68.6 (5.0)	67.2 (8.3)
Duration, years	4.1 (2.3)	4.3 (1.5)
Mini-Mental State	16.9 (3.8)	16.6 (1.9)
Estimated mMMSE scores	33.6 (2.9)	33.3 (3.6)

were reported by their informants to have experienced some psychopathologic symptom during the month preceding the clinic visit, a level comparable to previous reports (3, 4, 6). Of the 99 patients, 45 were reported to evidence only delusions. On the mMMSE these deluded patients had relatively preserved attention but worse naming ability than patients with no psychopathologic symptoms. Relatively preserved attention was also noted in an independent sample of 8 deluded AD patients, attesting to the generalizability of the finding. In that sample, differences in naming ability were in the expected direction (worse in deluded patients), but the groups were not significantly different on this measure.

It is important to determine whether these results obtain because of subject characteristics or methodological deficiencies. The samples used were large, independent groups of patients with probable AD diagnosed according to modern criteria. Subjects were specifically selected to have mild dementia. They were carefully examined using reliable methods and instruments to rule out competing etiologies of dementia. There were multiple referral sources, and subjects were recruited at three sites in different cities. Therefore, it is unlikely that a systematic bias of ascertainment would make these samples atypical of clinically evaluated cases of AD. However, since all cases were selected from among patients seen at clinical centers, they might differ from typical cases in the community.

The cognitive examination was limited, consisting of the subscales of the mMMSE in the initial sample, and the standard MMSE and a 30-item form of Boston Naming Test in the replication sample. However, the mMMSE and MMSE items used to assess attention and calculation (serial sevens, mental additions, reverse spelling, digit span) tap the 'Encode' component of attention as described by Mirsky (34). While certainly not exhaustive, the language items (reading and obeying instructions, sentence repetition, and confrontation naming) assess essential aspects of language comprehension. The semi-structured informant interview assessment of delusion was state of the art at the time of the survey.

Previous studies did not separate AD patients with primary delusions from those with delusions secondary to mood disorder or hallucination. In this investigation, patients currently deluded, but with no other psychopathologic symptoms, were contrasted with patients with no psychopathologic symptoms. In addition, misidentifications were not included as delusions. These differences in subject grouping method and symptom definition may explain the difference between our finding and those of other published reports. In those studies patients with delusions, regard-

less of whether other symptoms were also present, were compared to patients without delusions (11, 36, 17). These latter studies found deluded AD patients to be more cognitively impaired than those with no psychopathology. In contrast, we found that delusions were not related to more severe dementia in general, but were associated with relatively preserved attention and impaired naming. This pattern of impairment suggests that there may be a particular distribution of pathological changes in the brains of deluded AD patients that differs from that of nondeluded patients. Testing this hypothesis would require MRI scans from large samples of deluded and nondeluded patients. These data were not available for the current study.

The majority of delusions AD patients were reported to experience are like those described by Cummings (18): simple, nonsystematic, and unelaborated paranoid delusions. Several mechanisms have been proposed for delusion formation (35). One proposal is that they arise from the application of normal thought processes to explain anomalous perceptual experiences (15). As such, it is the aberrant nature of the data to be analyzed, not the analytic process itself that is most important in the etiology of delusion. It is unlikely that this explanation can hold true for delusions in AD patients, since the condition is defined by cognitive disorder. It is unclear whether perceptual aberrations contribute to the experience of delusions in AD. Delusions occur early in the course of the disease (3, 4, 9) when perceptual disturbance is minimal. Perhaps the expression of delusion in AD patients results from the application of anomalous cognitive processes to normal perceptual experiences. If so, it may be that the observed imbalance between attention and naming performance predisposes certain AD patients to experience delusions.

A pertinent question about the etiology of delusions in AD patients is their relationship to the memory deficits which characterize the disorder. That is, are the patients showing evidence of delusion because they cannot remember things? This is of particular relevance for suspicious and paranoid delusions (people stealing things), which are typically the most prevalent. An analysis comparing patients with 'suspicious' delusions to those with other types of delusions showed no significant differences on the memory items of the mMMSE, or on any other mMMSE or clinical variable. In addition, patients without psychopathologic symptoms were as impaired on the memory items as were the deluded AD patients. This suggests that memory deficits are not the basis of suspicious delusions in AD patients.

In conclusion, this study compared AD patients with delusions as their only psychopathologic symp-

tom to AD patients with no psychopathologic symptoms. The two groups were similar in demographic characteristics. However, the deluded patients were more functionally impaired. In addition, despite similar overall cognitive performance, the deluded patients were noted to have significantly better attention but worse naming than the nondeluded patients. This pattern of cognitive strengths and deficits may predispose AD patients to delusion. This hypothesis requires confirmation with more extensive assessment of both attention and language functions in independent samples of AD patients.

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