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Zweig *et al* (1988) suggested that this supports the hypothesis that the presence of depression in AD is representative of a biological subtype of the disorder.

Conclusion

The present findings suggest that subjects with features of depression in AD suffer from a less severe form of the illness, but that progression of the disease is the same as in those without depression. A longer follow-up, post-mortem validation of the AD diagnosis, and neuropathological correlates of depression will help clarify the situation and are being pursued on the present sample.

Acknowledgements, references, and authors' details will be found at the end of the fourth paper in this series, this issue, pp. 92–94.

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Psychiatric Phenomena in Alzheimer's Disease. IV: Disorders of Behaviour

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Out of a sample of 178 patients with AD, aggression was present in 20%, wandering in 19%, binge-eating in 10%, hyperorality in 6%, urinary incontinence in 48%, and sexual disinhibition in 7%. Behavioural abnormalities were greater in those with more severe dementia. Temporal-lobe atrophy correlated with aggression, and widening of the third ventricle with hyperorality. Features of the Kluver–Bucy syndrome were commonly seen, but the full syndrome occurred in only one subject. Patients with at least one feature of the Kluver–Bucy syndrome had greater temporal-lobe atropy than those without any of the features.

Behavioural problems in AD, like psychiatric symptoms, have received relatively little attention. However, behavioural difficulties impose a significant burden on carers (Rabins *et al*, 1982) and may result in a subject being admitted to long-term care (Sanford, 1975). While behavioural problems may be related to previous personality traits, they may also be a manifestation of underlying structural brain damage (Fairburn & Hope, 1988*a*).

Rabins *et al* (1982) highlighted the difficulties experienced by care-givers. Of the seven items of behaviour cited as causing serious problems, only one (memory disturbance) could be related to cognitive function. The others (physical violence, hitting, incontinence, catastrophic reactions, suspiciousness, and accusatory behaviour) appeared not to be related to cognitive deficits. Several recent studies have highlighted behavioural disturbances in more detail. Swearer *et al* (1988) evaluated 126 demented patients (57 with AD) who attended an AD research centre. Angry outbursts occurred in over half the sample and violent behaviour was present in 21%. 'Dietary change' (not further specified) accounted for 46% of subjects. Teri *et al* (1988) found wandering in 26% of 127 patients with AD. Subsequently, the same group (Teri *et al*, 1989) presented more detailed results: increased appetite occurred in 20%, wandering in only 5%, and no patient displayed behaviour aimed at "attempting to hurt others". In a community study of aggression (Ryden, 1988) 65% of the 183 subjects were found to be aggressive. However, dementias of any aetiology were included in this sample.

The relationship between some of these changes in behaviour and the Kluver–Bucy syndrome is of

TABLE I
Behavioural disturbance in Alzheimer's disease

	No. (%) with disorder	*Sex ratio (M:F)*	*% of men affected*	*% of women affected*
Aggression ($n=178$)	35 (19.7)	15:20	40	14**
Wandering ($n=178$)	33 (18.5)	7:26	19	21
Urinary incontinence ($n=174$)	83 (47.7)	17:66	47	48
Elements of Kluver–Bucy syndrome (n = 174)				
Binge-eating	17 (9.8)	8:9	22	7*
Hyperorality	11 (6.3)	2:9	6	7
Sexual disinhibition	12 (6.9)	3:9	8	7
Misrecognition of nurses/relatives	77 (44.3)	13:64	36	46
Going into 'rages'	62 (35.6)	13:49	36	45
Hypermetamorphosis	54 (31)	12:42	33	30
Withdrawal/apathy	71 (40.8)	13:58	36	42

*$P<0.01$, **$P<0.001$ (χ^2).

interest. This was originally described following bitemporal lobectomy in monkeys (Kluver & Bucy, 1937). Striking behavioural changes were described:

(a) visual agnosia
(b) strong oral tendencies, with hyperphagia
(c) hypermetamorphosis (an excessive tendency to attend and react to every visual stimulus)
(d) increased sexual behaviour
(e) emotional changes, both withdrawal and apathy, but also loss of fear and 'rage' reactions.

In humans, the syndrome has been described following bilateral removal of the temporal lobes (Terzain & Ore, 1955), in AD (Sourander & Sjogren, 1970), and in Pick's disease (Cummings & Duchen, 1981). Probably the most common feature of the syndrome seen in AD is the increased eating, and this has been said to occur in the absence of other features of the syndrome (Fairburn & Hope, 1988*b*).

The current study presents the results of an investigation into behavioural disturbances in a group of AD patients and relates the changes to cognitive function, CT appearances, and to elements of the Kluver–Bucy syndrome.

TABLE II
Relationship of behavioural disturbance to overall severity of dementia

	Clinical Dementia Rating: % with each behaviour		
	mild (n = 12)	*moderate (n = 77)*[1]	*severe (n = 85)*
Aggression	8.3	16.7	23.5
Wandering	0	10.2	27.0**
Urinary incontinence	8.3	2.6	94 ***
Elements of Kluver–Bucy syndrome			
Binge-eating	8.3	10.4	9.4
Hyperorality	0	0	13.0**
Sexual disinhibition	0	2.6	11.8*
Misrecognition of nurses/relatives	8.3	26.0	65.9***
Going into 'rages'	25	28.6	43.5
Hypermetamorphosis	8.3	28.6	36.5
Withdrawal/apathy	50	28.6	50.1*
Subjects with any features of the Kluver–Bucy syndrome	75	66.2	96.5***

1. One subject who completed the CDR could not be rated for the Kluver–Bucy syndrome.
*$P<0.05$, **$P<0.01$, ***$P<0.001$ (3×2 χ^2).

Method

Subjects

The sample and assessment procedures have been fully described in the first paper of this series (this issue, pp. 72–76). Briefly, the sample consisted of 178 subjects satisfying NINCDS/ADRDA criteria for probable or possible AD. Assessments were made using the CAMDEX, the GMSS, a CT scan and the CDR. Repeat cognitive testing was performed one year later. The mortality rate 30 months after entry to the study was also calculated. All pateints were examined personally by AB.

Behavioural disturbance

The instrument used for the assessment of behaviour disturbance was the Stockton Geriatric Rating Scale (SGRS; Meer & Baker, 1966). This consists of 33 behaviour items,

TABLE III
Behavioural disturbance in Alzheimer's disease and cognitive function[1]

	Aggression		*Wandering*		*Binge-eating*	
	yes	*no*	*yes*	*no*	*yes*	*no*
No. of subjects						
initially	35	143	33	145	17	157
lost to 1-year follow-up	13	86	13	86	10	88
MMSE score (maximum 30)						
initial score	4.5	8.8**	4.3	8.8**	6.8	8.1
change in 1 year[2]	−3.5	−3.5	−3.3	−3.5	−3.5	−3.5
AMTS score (maximum 10)						
initial score	1.0	2.8**	1.1	2.8*	2.0	2.5
change in 1 year	−0.7	−1.3	−0.7	−1.3	−1.3	−1.2
CAMCOG memory score (maximum 27)						
initial score	1.4	3.8**	1.5	3.7*	3.4	3.3
change in 1 year	−2.1	−2.0	−1.3	−2.1	−2.0	−2.0
CAMCOG language (maximum 30)						
initial score	6.5	12.5**	6.5	12.4**	10.2	11.5
change in 1 year	−4.0	−4.5	−4.1	−4.5	−4.9	−4.4
CAMCOG praxis score (maximum 12)						
initial score	2.2	4.4*	2.0	4.4**	3.2	4.1
change in 1 year	−1.5	−1.7	−1.5	−1.7	−1.9	−1.7
CAMCOG total score (maximum 107)						
initial score	13.8	29.6**	14.3	29.3**	23.0	27.1
change in 1 year	−11.1	−12.4	−10.7	−12.5	−12.6	−12.2

1. High scores on the tests indicate preserved cognitive function.
2. Mean change in score for the group over 12 months – the negative sign indicating that a deterioration in cognitive function has taken place.
*$P<0.01$, **$P<0.001$ (Student's t-test).

each of which is answered on a three-point scale of frequency: never or rarely (0), sometimes (1), or often (2). In addition, questions were asked concerning behaviour present in the Kluver–Bucy syndrome. These questions were asked in the same three-point format and are shown in the Appendix. Questions were also asked about wandering and urinary incontinence. Based on 480 individual observations, the test–retest and inter-rater reliability (kappa) for these additional questions was 0.74 and 0.72 respectively. Aggression was defined as behaviour resulting in or liable to result in actual physical harm to another person. Binge-eating, wandering, sexual disinhibition, hyperorality, and urinary incontinence were defined as present if a score of 1 or 2 was obtained on the corresponding question in either the SGRS or the 'Kluver–Bucy Scale'. The questionnaire was completed by AB during a semistructured interview with the person (or persons) in most frequent contact with the patient.

Results

Table I outlines the frequency with which the main behavioural disturbances were seen. As there were no differences in the frequency of behavioural disturbance in subjects with 'probable' or 'possible' AD, the results are reported for the group as a whole. Three signs of the Kluver–Bucy syndrome were relatively uncommon (binge-eating, hyperorality, and sexual disinhibition). The other four signs were more common. Incontinence occurred in nearly half the sample. Aggressive subjects were more likely to be on neuroleptic medication but there was no association between binge-eating and the prescribing of neuroleptics.

Table II shows the prevalence of the behavioural abnormalities in relationship to the overall severity of dementia as assessed by the CDR. As would be expected, behavioural disturbances became more common as severity of dementia increased. The exceptions were binge-eating, hypermetamorphosis, and 'rages'. There was a non-significant trend for aggression to increase with severity of dementia. Thirty-four per cent of in-patients were aggressive compared with 11% of those at home and 4% in residential homes ($P<0.001$, χ^2 test). Of the 83 subjects with incontinence, 47% were dead at 30-month follow-up, compared with 23% who were not incontinent ($P<0.001$, χ^2 test).

Table III details patterns of cognitive function in subjects with and without aggression, wandering, and binge-eating. Patients with aggression and wandering were significantly more cognitively impaired on all measures than those without. However, there was no significant difference in cognitive function in those with or without binge-eating.

TABLE IV
Behavioural disturbance in Alzheimer's disease: summary of CT findings

	Present	*Absent*	
Aggression			
No. of subjects	22	114	
Temporal lobe atrophy: no. of subjects			
absent	0	11	*2
mild	13	58	
moderate	7	44	
severe	2	1	
Wandering			
No. of subjects	22	114	
Size of Sylvian fissure (mean ± s.d.): cm^2			
right	8.8 ±2.9	7.1 ±2.7	**1
left	9.7 ±2.9	8.2 ±2.9	*1
total	18.6 ±5.4	15.3 ±5.2	***1
Hyperorality			
No. of subjects	5	132	
Size of 3rd ventricle (mean ± s.d.): cm^2	2.55 ± 0.91	1.89 ± 0.61	**1
Frontal-lobe atrophy			
absent	1	34	***2
mild	3	78	
moderate	0	19	
severe	1	1	
Occipital-lobe atrophy			
absent	2	53	***2
mild	1	65	
moderate	1	14	
severe	1	0	

1. Student's *t*-test.
2. χ^2 test.
*$P<0.05$, **$P<0.02$, ***$P<0.01$.

Deterioration in cognitive function over the one-year follow-up showed no differential decline in any of the groups. Cognitive function in patients with the other behavioural disturbances showed a similar (significant) pattern to those with aggression and wandering and have not been detailed separately.

Associations with CT findings have been summarised in Table IV. Aggression was associated with more temporal-lobe atrophy, wandering with increased size of the Sylvian fissure, and hyperorality with size of the third ventricle. Hyperorality was also associated with frontal, parietal and occipital atrophy, but was not associated with temporal-lobe atrophy. There were no differences on the CT measures in those with or without sexual disinhibition. Patients with incontinence had significantly more atrophy in all regions and more ventricular enlargement than continent patients (mean VBR 16.9 ± 6.0 v. 13.7 ± 4.4, respectively, $P<0.001$, Student's *t*-test). The 142 subjects with at least one feature of the Kluver–Bucy syndrome were more likely to have moderate or severe atrophy of the temporal lobes (χ^2 with Yates' correction, $P<0.04$).

The relationship between the seven elements of the Kluver–Bucy syndrome was analysed. The findings were as follows:

TABLE V
Factor analysis of behaviour associated with the Kluver–Bucy syndrome

	Factor 1	*Factor 2*	*Factor 3*
Sexual disinhibition	***0.67***	−0.15	0.00
Visual agnosia	***0.38***	0.19	−0.61
Hyperorality	***0.72***	0.18	0.25
Withdrawal/apathy	***0.56***	0.14	−0.29
'Rage' behaviour	−0.17	***0.83***	0.00
Hypermetamorphosis	0.25	***0.63***	−0.03
Binge-eating	0.24	0.10	***0.81***

Bold italic type indicates components of factors.

(a) 18.4% had none of the symptoms, 29.3% had only one of the symptoms, 24.7% had 2, 17.2% had 3, and 8.6% had 4; only one patient had all 7
(b) a Spearman correlation showed significant correlations between disinhibited sexual behaviour and hyperorality (0.30, $P<0.001$), hypermetamorphosis and apathy (0.23, $P<0.001$), and binge-eating and hyperorality (0.24, $P<0.001$)

(c) a principal-components analysis followed by a factor analysis with a varimax-rotation revealed three factors accounting for 57.1% of the variance; factor loadings of >0.35 were regarded as significant but visual inspection of the data reveals that this arbitrary definition was justified (Table V)
(d) a Cronbach's α coefficient to assess internal consistency was low (0.43) confirming that the scale was not assessing a unifying construct.

Therefore, the individual items on the scale were significantly associated with each other but the scale was assessing three different factors. Binge-eating appeared to be least associated with the other items.

Discussion

The main results of this study are:

(a) behavioural disturbances occurred in a significant proportion of AD patients
(b) the majority were directly associated with more severe disease, as measured in terms of cognitive function and overall severity
(c) some had anatomical correlates as measured by CT
(d) the complete Kluver–Bucy syndrome, even in advanced AD, was rare, but individual items associated with the syndrome were common and tended to be inter-related, with the exception of binge-eating.

Proportion of patients with behavioural disturbance

Aggression is the behaviour causing most distress to carers, both at home and in hospital. The proportion of patients who are aggressive varies according to the definition used. The one used in the present study (behaviour liable to cause physical injury to others) is very similar to that used by Swearer *et al* (1988) and the percentage of aggressive subjects is almost identical (20% of the current study, 21% by Swearer *et al*). Likewise, Reisberg *et al* (1987) found 'violence' to occur in 19% of their sample. Ryden (1988) found 65% of a community sample of 183 subjects to have at least one form of aggression (most commonly verbal aggression). Closer inspection of her results show that acts which would be deemed aggressive in other studies were much less frequent, for example, pushing/shoving (21%), pinching/squeezing (15%), and hitting/punching (14%). Thus, it would appear that predominantly physical, as opposed to verbal, aggression showed a rate remarkably consistent, at around 20%.

The neurophysiological basis for aggression is unknown, but human and animal studies have suggested circuits involving the medial nuclei of the hypothalamus (Moyer, 1971), the amygdala (Hitchcock & Cairns, 1973; Heath & Mickle, 1960), and hippocampus (Green *et al*, 1957). Two observations suggest that a link may exist between aggression and neurochemical changes in AD. First, there is evidence that the circuits mediating aggression are cholinergic (Smith *et al*, 1970) and the cholinergic deficit in AD is well recognised (Rossor *et al*, 1984). Second, serotonin metabolites have been shown to be reduced in aggressive patients with depression (Branchey *et al*, 1984) and schizophrenia (Lemoine *et al*, 1984). A reduction in serotonin metabolites has also been demonstrated in AD (e.g. Adolfsson *et al*, 1979).

Wandering has received less attention as a disruptive behaviour in AD – it was not even included as an item in the original Stockton Geriatric Rating Scale (Meer & Baker, 1966). However, it has been cited by over 70% of families as being a problem (Rabins *et al*, 1982). The only other study to offer a predetermined definition of wandering is that by Teri *et al* (1988), who found the behaviour in 26% of the 127 subjects. It was commoner (over 50%) in subjects with severe dementia (defined as a MMSE score of less than 10). Both the frequency of wandering and association with severe dementia have been replicated in the present study.

Urinary incontinence is another major problem for both relatives (Rabins *et al*, 1982) and care staff (Meer & Baker, 1966). The prevalence rate in outpatients varies from 16% to 40% (Rabins *et al*, 1982; Swearer *et al*, 1988). In one study (Teri *et al*, 1988) its presence was clearly related to the severity of dementia. This is in agreement with the present work, in which the vast majority of those rated as 'severe' were incontinent. The grave prognostic significance of the feature has also been shown, with 47% of incontinent patients having died within 30 months.

Binge-eating is one of the features of the Kluver–Bucy syndrome (Sourander & Sjogren, 1952). Increased eating in dementia has been described (Hope *et al*, 1989) but was not considered to be associated with other signs of the Kluver–Bucy syndrome. Morris *et al* (1989) found increased eating in 26% of 33 patients with dementia. However, the sample was mixed, with 27 subjects suffering from AD and six from other dementias. Swearer *et al* (1988) found 'dietary change' (either decreased or increased eating) in 46% of their subjects. Binge-eating differed from other behaviours described here in that the proportion of the subjects exhibiting this feature did not increase with the severity of dementia. There appeared to be no association with other features of the Kluver–Bucy syndrome, except with the related disorder of hyperorality, which is not surprising.

Sexual disinhibition was seen in 7% of the current sample. Like binge-eating, this is considered by some an integral part of the Kluver–Bucy syndrome (Cummings & Duchen, 1981). An identical frequency of sexual disinhibition has been reported by Kumar *et al* (1988).

Association with severity of dementia

The majority of behavioural disturbances, unlike psychiatric symptoms (see papers I–III, this issue, pp. 72–86), were positively associated with the degree of dementia. Thus, such behaviour is likely to be a result of advanced cerebral pathology, and so the neuropathological substrates may be qualitatively and quantitatively different from those of psychiatric symptoms.

The distinction between disturbed behaviour and specific psychiatric symptoms in AD is often not made (Reisberg *et al*, 1987; Teri *et al*, 1988). There was no evidence that disturbed behaviour was the result of prescribed medication.

Relationship with CT findings

Many of the behavioural disturbances were associated with regional changes in the CT scans. More specifically, aggressive subjects had more atrophy of the temporal lobes, confirming an earlier report (Swigar *et al*, 1985). Hyperorality was associated with widening of the third ventricle and atrophy of the frontal and occiptal lobes. The proximity of the hypothalamus to the third ventricle and its function as a regulator of dietary intake may suggest that damage to this leads to increased oral tendencies.

Signs of the Kluver–Bucy syndrome were associated with temporal-lobe atrophy.

The Kluver–Bucy syndrome

Sourander & Sjogren (1970) described individual components of this syndrome as having frequencies of over 70% in 132 cases of AD verified post-mortem. Abnormal sexual behaviour was the least frequent, with a rate of 17%. However, the various features were not operationally defined and no indication was given of the proportion of cases exhibiting two or more of the components. It has been argued that the full syndrome is unlikely to occur in humans, as it is specific for other primates and that the abnormal sexual behaviour is the least likely to occur (Pilleri, 1966; Sourander & Sjogren, 1970). Both these observations have been confirmed by the present study. The seven features have been shown to have a degree of inter-relationship, but the association was not strong and three individual factors emerged, with binge-eating being isolated, confirming the impression of Fairburn & Hope (1988*b*). It should also be noted that some of the symptoms were not exclusively related to temporal-lobe damage.

One of the problems in the present assessment of the Kluver–Bucy syndrome involves the way in which behaviour seen in animals was assessed in humans using a rating scale. For instance, it was very difficult to translate unequivocally abnormal sexual behaviour in the monkey (defined originally as increased sexual activity involving forms of heterosexual, homosexual and autosexual behaviour) to the sort of disturbance seen in our patients and to incorporate this into a rating scale. We nevertheless felt it was worth attempting this and we think that the questions asked did seem appropriate, although there might obviously have been an overlap between this type of behaviour and that as seen in patients with frontal-lobe damage. Emotional changes have been described as two main types: withdrawal/apathy and rage reactions. It was felt that both of these should be included in the current scale. Further investigations of these behavioural abnormalities are required to assess how they change over time and how they correlate with neuropathological findings. Both these issues are being pursued in a prospective study of this population.

Conclusion

It has been found that behavioural disturbances are common accompaniments of AD and more sophisticated investigations are required to elucidate the structural and functional basis underlying them and the impact they have on patients and their carers.

Appendix I

Questions related to behaviour associated with the Kluver–Bucy syndrome

(a) The patient's sexual behaviour (exposing self, obscene sex language, masturbation, propositioning others) is:
  0 – never appropriate
  1 – sometimes inappropriate
  2 – often inappropriate.

(b) The patient recognises well-known nurses and relatives:
  0 – almost always
  1 – sometimes
  2 – almost never.

(c) The patient goes into rages:
0 – never or rarely
1 – sometimes
2 – frequently.

(d) The patient is distractable and immediately explores things around him/her when they happen (e.g. always going up to the door when someone comes in):
0 – never or rarely
1 – sometimes
2 – often or always.

(e) The patient tends to 'binge' with food (i.e. eating very quickly and stuffing food in his/her mouth):
0 – never or rarely
1 – sometimes
2 – often or always.

(f) The patient tries to put objects (other than food) in his/her mouth:
0 – never or rarely
1 – sometimes
2 – frequently.

(g) The patient seems withdrawn and apathetic:
0 – never or rarely
1 – sometimes
2 – a lot of the time.

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