Behavioural Neurology, 1989, **2**, 167–182

Semantic Dementia: a Form of Circumscribed Cerebral Atrophy

J. S. SNOWDEN, P. J. GOULDING AND D. NEARY

Department of Neurology, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL, UK

Three patients are described with primary cerebral atrophy in whom progressive breakdown in language and visual perception are attributed to loss of semantic information. This form of dementia is distinct from that of Alzheimer's disease and is assumed to represent a form of circumscribed cerebral atrophy with predominant and early affection of the temporal lobes.

Introduction

It is becoming increasingly evident that primary cerebral atrophy leading to dementia represents a heterogeneous group of conditions, of which Alzheimer's disease, although the most common is only one disorder. Dementia of frontal lobe type is a disorder (or group of disorders) affecting predominantly anterior regions of the brain (Gustafson, 1987; Neary *et al.*, 1988). Commonly, it is associated with progressive personality change and breakdown in social behaviour, impaired judgement, abstraction and planning abilities. Primary linguistic and visuo-spatial skills are relatively intact. The clinical picture contrasts sharply with that of Alzheimer's disease, in which amnesia, visuo-spatial disorientation and aphasia occur in the context of preserved social conduct (Cummings and Benson, 1983; Neary *et al.*, 1986), so that clinical differentiation between the two conditions is possible.

Diagnostic distinctions may not invariably be so precise. A minority of patients with primary cerebral atrophy present with a progressive deterioration in language. The syndrome of progressive aphasia without generalized dementia has been recognized (Mesulam, 1982; Chawluk *et al.*, 1986) and necropsy studies have revealed focal spongiform degeneration and an absence of Alzheimer pathology (Kirshner *et al.*, 1987). However, in Alzheimer's disease too language disorder may predominate and represent the earliest symptom (Foster *et al.*, 1983; Pogacar and Williams, 1984). When prominent language disorder is set against a background of other cognitive difficulties, or when other cognitive difficulties emerge during the course of disease, Alzheimer's disease may be assumed to be the correct diagnosis. Such an assumption may not be warranted.

Three patients are described who presented with progressive and profound language impairment. Historical information together with their impoverished performance on visuo-constructional tasks and apparent amnesia suggested superficially the cognitive picture of Alzheimer's disease.

0953–4180/89/030167 + 16 $3.50/0

Closer examination indicated a pattern of cognitive disorder distinct from that of Alzheimer's disease, characterized by profound loss of semantic information. Increasing behavioural disorder during the course of disease suggested that the condition may be more akin to dementia of frontal-lobe type, and may represent a form of circumscribed cerebral atrophy with prominent emphasis of pathology in temporal rather than frontal regions of the brain.

In all three patients progressive and insidious decline in mental functioning occurred in the absence of neurological symptoms. In no patient was there evidence of vascular or systemic disease. None had abused alcohol or suffered a major head injury. Routine laboratory investigations were normal.

Case Reports

Patient 1 (SL)

A 67-year-old retired male furniture craftsman presented with a 3-year history of "failing memory", with impoverished vocabulary and later poor face recognition. His relatives believed him to be lost in the home since he would carry out activities in inappropriate locations, such as urinating in the bedroom and emptying the dustbin in the garage. Nevertheless he continued to walk to and from Synagogue alone without becoming lost. Although still able to dress himself it was necessary for articles to be arranged for him in order. Otherwise, he would put on inappropriate combinations of clothes, such as two shirts. His formerly placid character was unchanged and he remained physically well. He displayed an appropriate degree of distress regarding his disabilities. There was no family history of dementia.

Physical examination

This was entirely normal. There were no primitive reflexes.

Mental examination

Conduct He displayed a pleasant, sociable disposition. He was fully cooperative and persisted in tasks, looking constantly to the examiner for approval and feedback. He exhibited an appropriate degree of distress at his difficulties. Rate of performance was normal.

Language Articulation, phonation, prosody and rate of speech production were entirely normal. Moreover, his adept and fluent use of social platitudes and gestures of agreement gave the superficial appearance of preserved language skills. However, structured language testing revealed marked difficulties in comprehension and verbal expression. Whilst his sentences, produced effortlessly, were syntactically correct, they were restricted by profound loss of nominal terms. In a name-object matching test of compre-

hension, he could not select correctly the named object from an array, consisting of a key, comb, watch and pen. He failed to point correctly to specified body parts. In the shortened Token test (De Renzi and Faglioni, 1987) he indicated only named colours. He was unable to name common objects to confrontation or from description and made verbal paraphasic errors. In general, responses bore some relationship to the correct word (he responded "knife" for key; "chair" for door; "screwdriver" for razor and "jumper" for sock). On the Boston naming test (Kaplan *et al.*, 1983) he named no items correctly. His naming performance did not benefit from provision of multiple choice alternatives; his selection appeared arbitrary. In a verbal fluency test he could produce no names of animals, even when he appeared to grasp what was required.

In contrast to his comprehension and naming difficulties his powers of repetition were excellent. He retained a normal digit span of 7 digits, and could repeat without error complex phrases and sentences. He tended to "echo" questions put to him, yet altering the syntax appropriately, despite total lack of understanding, e.g. Question—"What do you stir your tea with?"; Response—"What do I stir my tea with?". Moreover, he could recite overlearnt series, such as the days of the week and months of the year fluently and with facility, providing that the sequence was initiated for him. Similarly he could recite nursery rhymes without error.

He could spell aloud words with regular spellings but tended to produce phonetically regular spellings of irregular words. He read aloud rapidly and without error letters of the alphabet, words and sentences. He wrote his name and address with a clear well-formed script. He could write words and sentences to dictation, although with some spelling errors for irregular words, e.g. "The cat court the mouse". Execution of script was rapid and fluent. In contrast, his understanding of written material was grossly impaired, mirroring his level of aural comprehension. He could not carry out mental calculations, but succeeded in solving written two-digit additions.

His ability to communicate non-verbally by gesture and pantomine appeared superior to his verbal skills, but nevertheless was impaired. Indeed, frequent failure to grasp task requirements, despite repeated visual and manual demonstrations, suggested that he had a comprehension impairment which was not restricted entirely to the verbal domain.

Spatial, perceptual and constructional abilities Spatial localization appeared intact. He negotiated his environment normally. He could locate objects in the room, and had no difficulty finding the exit when leaving. When dressing, he oriented clothing appropriately. He had no difficulty tieing his shoelaces. He could copy non-representational hand postures and track the Money road map (Money *et al.*, 1965). Elementary perception was preserved and he could match shapes without difficulty. His behaviour and test performance indicated generally preserved perceptual identification of objects. He used eating implements appropriately, put on items of clothing on the correct part of the body, selected a pen from other objects to write,

and spontaneously demonstrated use of objects by gesture and pantomime. His ability to appreciate the significance of line drawings was less easy to interpret: performance was hindered by his gross communication difficulties. However, failure to describe the function of an object that he could not name, nor to demonstrate its use by gesture or pantomime suggested problems in identification not explicable solely on a linguistic basis.

He expressed signs of familiarity when shown faces of celebrities, but it was not clear whether he appreciated their identity: for one photo, he correctly selected "Edward Heath" from 3 alternative names, but then referred to subsequent pictures of politicians by the same name.

He demonstrated normal manual dexterity. He manipulated objects normally and completed simple Koh's block constructions. His excellent ability to copy motor rhythms tapped out to him mirrored his preserved verbal repetition skills. Copying of line drawings was hampered by poor comprehension: he tended to write down the verbal instruction as it was given, mirroring his tendency to repeat questions orally. In addition, having drawn a design he tended to perseverate it, despite the presentation of other templates. Nevertheless, his fluent and effortless strokes, together with the preserved spatial relationships between parts of a design, suggested that where failures occurred these could not be attributed to failures of spatial appreciation or motor execution.

Abstraction His conceptual powers could not be formally assessed owing to his communication difficulties. In a Weigl's block task (de Renzi *et al.*, 1966) he failed to grasp what was required, despite demonstrations. Nevertheless, when presented with Token test items he spontaneously grouped together those of the same shape, suggesting some ability to classify at a relatively elementary perceptual level.

Investigations

Electroencephalography was normal. Computed tomography revealed generalized cerebral atrophy.

Progression

He was reviewed regularly over the following 4 years, during which time an insidious deterioration was noted although his pattern of disability was essentially similar.

His conversational speech diminished over the next year, and was limited to stereotyped social remarks, and paraphrased iterations of the examiner's remarks. His comprehension of language was nil, and he had increasing difficulty understanding non-verbal methods of communication. He could name no object correctly and responses were now generally unrelated to the correct word, e.g. "comedian" for saucer, "briefcase" for watch, and "chimpanzee" for cup. In contrast, he preserved the capacity to repeat and to recite overlearnt series. Indeed, he could effectively complete numerical

series such as "2,4,6, ...", "10,20,30 ..." and "20,19,18 ...". He could recite rhymes and prayers.

He appeared to have increasing difficulty appreciating the significance of objects, and would fail to use them appropriately. However, he would arrange objects, blocks and shapes into aesthetically pleasing designs, suggesting normal apperceptive powers. There was no evidence of impaired spatial localization, nor loss of manual skills, although increased perseveration was noted on constructional tasks.

Two years later he lacked initiative and required supervision for all activities of daily living. Nevertheless, he remained physically well, and was free from neurological signs. He displayed an affable, smiling demeanour, and chuckled when spoken to. He did not speak spontaneously, although occasionally responded "yes" as a social automatism. He would no longer repeat. Nevertheless he was still able to count, and recite the days of the week and months of the year if these series were initiated for him. He could no longer recite entire nursery rhymes, although when given one line could generally produce the next. Sometimes he substituted for the correct phrase a syntactically correct although entirely meaningless line, rhyming with the preceding line. He would pick up objects and examine them, rotating and turning them, indicating normal manipulative abilities. Yet, he demonstrated no understanding of their meaning and made no attempt to use them. In contrast, if an action was initiated for him, such as combing his hair with a comb, he could continue the action alone.

Single photon emission tomography using 99mTc-HM-PAO, carried out 7 years after onset of illness, revealed bilateral reduction in uptake of tracer in the anterior cerebral hemispheres (Fig. 1).

He died a few months later aged 71 of a myocardial infarction. Necropsy was not undertaken.

Patient 2 (EB)

A 60-year-old housewife presented with a two-year history of progressive difficulty in word finding and comprehension. In conversation she would substitute words belonging to the same semantic category, or relied on non-specific descriptive terms. She could no longer name familiar people, and appeared moreover to have difficulty in recognizing them and appreciating the context of her acquaintance with them. Perceptual and spatial abilities were otherwise thought to be normal. She had become rather more irritable than formerly and less scrupulous about her appearance, but her behaviour and social conduct were generally appropriate. She was aware of her language difficulties and displayed an appropriate degree of distress. She was known to suffer from chronic bronchitis, but this was not sufficient to cause respiratory failure.

Physical examination

On general examination there was evidence of obstructive airways disease,

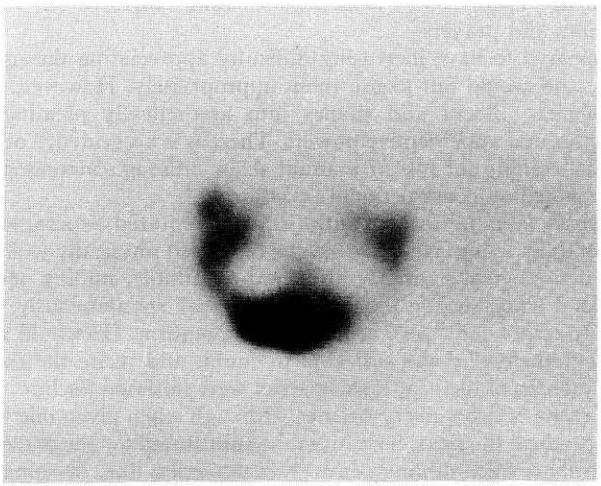

FIG. 1. SPET scan of patient 1. Image shows transaxial section at mid-ventricular level. Frontal lobes are uppermost and the left hemisphere is seen on the right. There is severe reduction in uptake of tracer in both anterior cerebral hemispheres, with a smaller abnormality in the left parietal region.

but no signs of ventilatory failure. Neurological examination revealed postural tremor of the hands of long-standing, and bilateral palmomental reflexes.

Mental examination

Conduct She displayed a pleasant, sociable demeanour and cooperated fully. She was mildly anxious.

Language Articulation, prosody, phonation and rate of speech production were entirely normal. Output was fluent, effortless and syntactically correct and social conversation revealed no abnormality. In response to direct questions mild circumlocutions hinted at word finding difficulty. More profound deficits became apparent however when assessing comprehension and naming. In particular, she had difficulty understanding nominal terms and in naming objects to confrontation and from description. In contrast, her understanding of prepositions denoting a spatial relationship was well preserved. Token test performance (De Renzi and Faglioni, 1978) was impaired as a result of her lack of understanding of shape names. If these were eliminated by commands such as "put that one under/on/next to that one" performance was error free. She could answer correctly questions involving complex syntax such as "If the tiger is killed by the lion which animal is dead?", whilst failing to understand the meaning of the word

"tiger". Thus, when couched in grammatical sentences, her understanding appeared generally well preserved; indeed, she could often infer the sense despite failure to understand individual nouns. In naming, she substituted generic terms or semantically related words: she described Margaret Thatcher's occupation as "senior careers officer" and then "labour councillor". In a verbal fluency test, she produced only 4 animals names, but 15 words beginning with F, each in one minute.

In contrast to her nominal difficulties, her ability to recite overlearnt series and her powers of repetition were normal. She read aloud fluently, although with a tendency to read phonetically, irregularly spelt words. Phonetic regularisations of spellings were noted also in her oral spelling and writing. Her understanding of written material mirrored her aural comprehension, with difficulty most evident for nominal terms. She could carry out two-digit mental and written additions and subtractions without difficulty.

Perceptuo-spatial and constructional abilities Elementary perceptual and spatial abilities were well preserved. She had no difficulty matching by shape, colour and size, and carried out a line drawing and face matching task normally. She demonstrated no difficulty in spatial localization, could navigate her environment and find her bed on the hospital ward. She could trace the Money road map (Money *et al.*, 1965) and place towns correctly on a map of Great Britain. Her copies of line drawings, accomplished with ease, showed preserved spatial configuration and relationship between elements. Her appropriate use of objects indicated moreover that she understood the significance of objects that she could not name. She demonstrated normal manual dexterity and had no difficulty manipulating objects. She reproduced hand postures, sequences of hand positions and motor rhythms with ease.

Memory She was well oriented for time and place and could provide an accurate account of day-to-day events. In contrast she performed poorly on formal memory tests. Verbal memory tests were avoided since performance would inevitably be impaired as a result of her language difficulties. On the Warrington face recognition test (Warrington, 1984) she scored at chance level.

Investigations

Electroencephalography was normal. Computed tomography revealed cerebral atrophy with widening of the sylvian fissures (Fig. 2). Single photon emission tomography using 99mTc-HM-PAO revealed a selective anterior hemisphere abnormality (Fig. 3).

Progression

Her comprehension and naming difficulties deteriorated over the following two years. Moreover, she appeared increasingly to fail to appreciate the

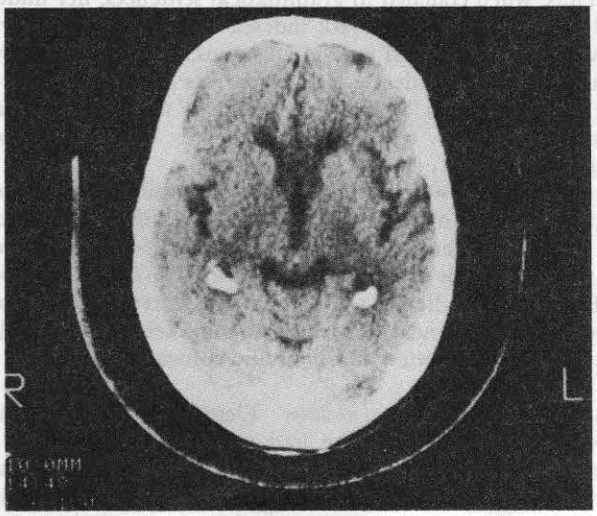

FIG. 2. Computed tomogram of patient 2. There is cerebral atrophy, with widening of the sylvian fissures, greater on the left.

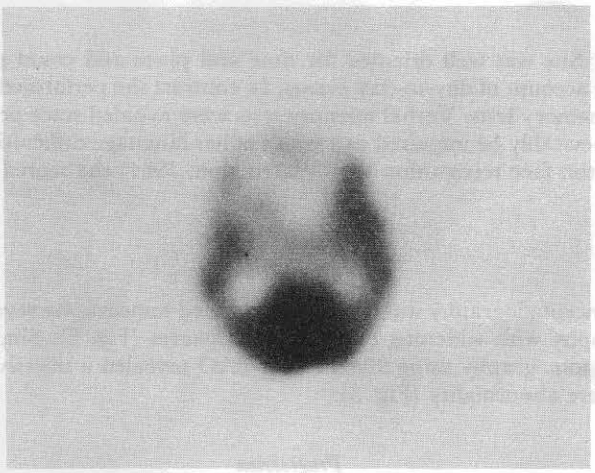

FIG. 3. SPET scan of patient 2. Image shows transaxial section at mid-ventricular level. There is reduced uptake of tracer in both frontal lobes.

significance of objects. When shopping, she did not know whether certain foodstuffs were to her liking or not. Whilst she could still reckon change, she no longer understood the significance of the pound coin. She continued to keep a diary, although entries revealed increasing spelling errors. Her social conduct had become uncharacteristically disinhibited and she would speak to strangers and create scenes in public. She was unusually stubborn and argumentative. She adopted an increasingly stereotyped daily routine and became annoyed if this was upset. She would "clock watch" and continually provide a commentary on the time, e.g. "It's three fifty-six, four minutes to four o'clock". She had developed a fondness for chocolates, which she ate in great abundance. She continued to dress herself and could lay the table. She would spend much of her day playing patience or dominoes at which she continued to excel.

Mental examination confirmed a profound impairment in comprehension of nominal terms and in word finding in the context of well preserved ability to repeat and recite overlearnt series. She increasingly employed generic terms, such as "water" to refer to all types of liquid, suggesting the possibility of impoverishment in the conceptual distinction between members of a semantic category. On the Boston naming test (Kaplan *et al.*, 1983) she scored only 4/60. She could read aloud but made occasional phonetic errors particularly in reading irregularly spelt words. For the Glushko lists of common one-syllable words (Glushko, 1979) she pronounced correctly 88% of regular words and 76% of exception words. She read correctly no words from the Nelson Adult Reading Test (Nelson and O'Connell, 1978), composed of relatively low frequency orthographically irregular, mainly polysyllabic words. She was still able to produce a clear well-formed script, despite the presence of orthographic errors. She carried out three-figure written additions and subtractions accurately.

She continued to demonstrate well preserved apperceptive and spatial abilities. She had no difficulty carrying out same–different object and face matching tasks, even when faces were presented from different orientations. On the Boston faces test (Levin *et al.*, 1975) she scored within the normal range. If coloured blocks were sorted for her with respect to their colour or shape she could classify additional blocks appropriately. She was left-right orientated and performed without error the Mannequin test (Ratcliffe, 1979), even when the figure was inverted, requiring a mental spatial rotation. She could count dots displayed on a video monitor, and showed a normal "chunking" strategy. In contrast, she failed to recognize faces of celebrities and could not match names to faces in a multiple choice task. In addition, performance was profoundly impaired in a task which required the sorting of pictures of dogs and cats into their relevant animal category, and one that required the matching of a taste with a particular fruit suggesting that her purported "semantic" deficit was not limited to the verbal domain. A more detailed analysis of her semantic impairment will be the subject of a future report.

She remained fully orientated for time and place and could give an adequate account of recent autobiographical events.

Repeat SPET imaging of the brain two years after initial imaging revealed further reduction in uptake in the anterior cerebral hemispheres.

Patient 3(LB)

A 66-year-old housewife presented with a two-year history of rapidly progressive failure of intellect, characterized by memory loss, difficulty in communication and impaired vision. Her social conduct was well preserved, and she became upset by her difficulties. There were no physical symptoms. Her mother died from dementia aged 73, and a brother was also said to have mental problems.

Physical examination

She was physically well, without neurological signs.

Mental examination

Conduct She had a pleasant, sociable demeanour, but became distressed when confronted with her difficulties, into which she retained some insight.

Language Articulation, phonation, prosody and rate of speech production were normal. Utterances were fluent and grammatically correct but severely limited in information content, being restricted principally to social platitudes and stereotyped phrases, e.g. "You're nice. Yes, you are, very nice" and "I'm not right, I just can't remember a thing, not a thing, it's not right". She tended to echo questions put to her, altering the syntax appropriately, but demonstrated no understanding of what she had been asked. She had virtually no understanding of nominal terms, and could not point to named common objects in front of her. In contrast she could point to named colours and consistently designated her own left and right. Naming of objects to confrontation and from description was nil. She could not name digits. Production of overlearnt series such as counting was relatively well preserved. She could write her own name, and simple words to dictation, although there was a strong tendency to perseverate earlier words. She could not read, nor convey information by gesture and pantomime.

Perceptuo-spatial and constructional abilities Evaluation was hindered by her profound communication disorder. However, her responses in tasks requiring the identification of line drawings and faces of celebrities suggested that difficulties could not solely be explained in terms of language impairment. She frequently denied knowledge of the meaning of an object. In contrast, she could match shapes and visual patterns suggesting that putative perceptual problems lay in the semantic "associative" rather than "apperceptive" domain. She could count dots presented in random display on a video monitor, suggesting an appreciation of the overall spatial layout of dots and an ability to keep track of which dots had already been counted.

Memory This could not be formally assessed.

Investigations

Electroencephalography revealed a mild excess of slow wave activity most apparent over the left fronto-temporal region. Computed tomography revealed cerebral atrophy. A cortical biopsy of the right temporal lobe showed no specific pathology, and in particular there were no senile plaques or neurofibrillary tangles to indicate a diagnosis of Alzheimer's disease. Biochemical analysis showed no reductions in choline acetyltransferase: activity or acetylcholine synthesis, supporting the conclusion that she was suffering from a non-Alzheimer form of dementia.

Progression

She deteriorated gradually over the following two years. Her comprehension and word finding were nil, and she was formally untestable. However, she continued to utter stereotyped phrases and articulation, prosody and phonation were entirely normal. She had become more irritable and aggressive than formerly. She remained physically well, without evident neurological signs. She died of bronchopneumonia four years after onset of illness. Necropsy was not undertaken.

Discussion

The three patients share a similar neuropsychological picture, characterized by progressive loss of semantic connotation. Although presenting symptoms emphasize difficulty in naming, the disorder is not modality specific, but involves a loss of symbolic meaning affecting both verbal and non-verbal domain. The language disorder has characteristics of a transcortical sensory aphasia (Goldstein, 1917; Benson, 1979). Fluent, well-articulated speech with normal syntax, preserved repetition skills, and excellent recitation of overlearnt information, contrast with profoundly impaired comprehension and naming. Verbal paraphasias are prevalent, but not literal paraphasias or neologisms. Echolalia is marked. Relative preservation of reading, writing and spelling contrasts with failure to understand the sense of what has been read, written or spelt. Errors tend to be phonetic regularizations of irregularly spelt words. A similar picture has been reported previously in sporadic patients with primary degenerative dementia and those patients have been the subject of detailed neuropsychological investigation (Schwartz *et al.*, 1979, 1980; McCarthy and Warrington, 1986; Baxter and Warrington, 1987). The designation "anomic" dementia has been adopted by some authors (Schwartz *et al.*, 1979, 1980) to describe the condition. However, the underlying aetiology remains unknown.

There are strong grounds for assuming that the disorder is a form of primary cerebral degeneration. Insidiously progressive and profound

mental changes occur in the absence of notable neurological signs and in the context of physical well-being. Patients exhibit no risk factors for cerebrovascular disease. Computed tomographic abnormalities are limited to cerebral atrophy.

The pattern of disability, particularly if derived from historical information alone, might be confused with that of Alzheimer's disease. Complaints of "failing memory", language difficulties and disorientation in familiar surroundings suggest at first sight cortical hemisphere deficits typical of Alzheimer's disease. However, there are important distinctions. Symptoms of memory failure in these patients refer largely to a loss of semantic knowledge, in particular about the meaning of words. They refer much less to the memory of personally relevant events (episodic memory), which is so strikingly affected in Alzheimer's disease. Whilst the language disorder of Alzheimer's disease has been likened by some authors to a transcortical sensory aphasia (Cummings *et al.*, 1985; Kertesz *et al.*, 1986) it does not mirror the classical descriptions. Echolalia in Alzheimer's disease is not a prominent feature. Recitation of overlearnt sequences and nursery rhyme completion is impaired (Cummings *et al.*, 1985). A reduction in repetition span accompanies onset of language disturbance. Literal paraphasias occur. Logoclonia is common in advanced disease (Cummings and Benson, 1983). Calculation and writing skills are impaired early in Alzheimer's disease, contrasting with the relative preservation of those abilities in patient 2 of the present report.

The apparent disorientation in patient 1 of the present series is most readily explained in terms of loss of perceptual knowledge. That is, his inappropriate behaviour with respect to different locations appears to result from failure to appreciate the significance of those locations. That he was able to negotiate his environment with ease, and walked to and from Synagogue alone suggests relative preservation of spatial localization and navigational abilities. The relative preservation of spatial abilities contrasting with impoverished perceptual associative abilities was suggested also in the three patients by neuropsychological testing. In contrast, in Alzheimer's disease, defective spatial localization and appreciation is prominent, perceptual understanding remaining relatively preserved till late in the course of disease (Neary *et al.*, 1986). Thus, Alzheimer patients may need to search for rooms in the home, yet having done so typically recognize their connotation.

The dissociation between perceptual and spatial abilities is well established and there is evidence that distinct brain regions mediate these abilities (Eslinger and Benton, 1983; Newcombe *et al.*, 1987; Ungerleider and Mishkin, 1982). That the parietal regions play a crucial role in spatial function is reflected in the consistent finding in Alzheimer patients with clinical features of spatial disorder of parietal lobe reductions in uptake of tracer on brain imaging by positron emission tomography (PET) (Foster *et al.*, 1984; Duara *et al.*, 1986) and single photon emission tomography (SPET) (Neary *et al.*, 1987; Johnson *et al.*, 1988). It is noteworthy that in the two patients presented here who underwent SPET imaging, neither showed the "parietal" reductions in uptake demonstrated in Alzheimer patients (Neary *et al.*, 1987).

All three patients described remained remarkably free from neurological signs and did not exhibit the extrapyramidal features which invariably emerge in Alzheimer's disease with disease progression (Molsa *et al.*, 1984). The normal electroencephalograms seen in two patients are also atypical of Alzheimer's disease, in which slowing of wave forms is characteristic (Neary *et al.*, 1986). Support for the view that these patients have a condition other than AD comes from the results of cortical biopsy of the right frontal lobe in patient 3. Senile plaques and neurofibrillary tangles, the pathological hallmarks of AD, were absent. Moreover, biochemical analysis did not show the abnormalities of choline acetyltransferase activity and acetylcholine synthesis shown to be characteristic of AD (Bowen *et al.*, 1976; Sims *et al.*, 1980).

The prominence of symptoms of language disturbance in all three patients suggests a possible association with the syndrome of slowly progressive aphasia (Mesulam, 1982; Chawluk *et al.*, 1986; Kirshner *et al.*, 1987). Anomia is a prominent feature of that condition, as it is in the present cases. Calculation abilities may be relatively well preserved. In common with the present cases, patients retain insight into their disability and exhibit signs of distress. However, certain features set them apart. First, with respect to the language disorder, agrammatism and non-fluent features of the type seen in Broca's aphasia have been reported in slowly progressive aphasia (Mesulam, 1987), whereas preservation of syntax is a potent feature of the patients in the present report. Echolalia, preservation of repetition and automatic production of overlearnt sequences recorded in the present patients have not been notable features of patients with progressive aphasia. Second, in patients with progressive aphasia the deficit is confined to the verbal domain: in the present patients the semantic disorder encompasses both loss of meaning of words and of objects. In keeping with this clinical distinction, the present patients exhibit bilateral abnormalities on SPET imaging, whilst defects confined to the left hemisphere have been reported in PET studies of cases with slowly progressive aphasia (Chawluk *et al.*, 1986).

The three patients share some similarities with those with dementia of frontal lobe type (DFT) (Neary *et al.*, 1988). Although personality change and breakdown in social conduct were not notable presenting features, increasing apathy was observed in patient 1 and disinhibition in patient 2 as the disease progressed. Patient 2 demonstrated an abnormal fondness for sweets, which has been noted commonly in patients with DFT (Neary *et al.*, 1988) but not Alzheimer's disease. Whilst anomia in DFT may be a relatively subsidiary feature, nevertheless the pattern of breakdown is similar to that described above: patients resort increasingly to use of generic terms and verbal stereotypes, and verbal (semantic) paraphasias occur. The absence of neurological signs and normal electroencephalogram are also reminiscent of DFT. It is of interest that the SPET scan appearance of patient 1, showing profound loss of uptake in the anterior cerebral hemispheres, is typical of patients with DFT (Neary *et al.*, 1987). In patient 2, only a mild abnormality was present. The two patients differed with respect to disease severity; patient 1 was scanned shortly before his death and his dementia was substantially more advanced than that of patient 2.

Disruption to semantic knowledge has been associated with damage to the temporal lobes (Wilkins and Moscovitch, 1978; Gainotti *et al.*, 1982) and a similar clinical picture to that described here has been reported in post-encephalitic patients who show damage to the mesial temporal areas (Warrington and Shallice, 1984; De Renzi *et al.*, 1987). One might expect that in the present cases too the temporal regions would be the principal site of pathology. Limited resolution of SPET results in poor sensitivity to abnormalities in temporal regions (Reed *et al.*, 1989), so that putative early involvement of temporal lobe structures remains inferential. Nevertheless, the widespread anterior hemisphere abnormality in patient 1 and progressive involvement of the anterior hemispheres in patient 2 indicate a disorder predominantly of the fronto-temporal cortex. One might speculate that the "semantic dementia" described in this paper represents a form of circumscribed cerebral atrophy, and a possible variant of DFT. The clinical presentation of loss of semantic connotation rather than of personality change and conduct disorder may reflect the regional distribution of pathological change with early emphasis on temporal rather than frontal lobes.

The pathological changes associated with DFT are non-specific and consist of atrophy affecting predominantly fronto-temporal regions, gliosis and mild spongiform change (Brun, 1987). Senile plaques and neurofibrillary tangles are absent. The neuronal inclusions and swollen cells pathognomonic of Pick's disease are only rarely seen. Similar pathological findings have been reported with respect to slowly progressive aphasia (Kirshner *et al.*, 1987; Taboada *et al.*, 1986). It is possible that DFT, slowly progressive aphasia and the semantic dementia described in this paper are all forms of non-Alzheimer cerebral degeneration which share a similar neuropathological substrate. Variations in the clinical presentation and progression may reflect the topographical emphasis and distribution of underlying pathology. The precise nature of pathological change in these conditions remains to be explored.

References

Baxter, D. M. and Warrington, E. K. (1987). Transcoding sound to spelling: single or multiple sound unit correspondence? *Cortex*, **23**, 11–28.

Benson, D. F. (1979). "Aphasia, Alexia and Agraphia". Clinical Neurology and Neurosurgery Monographs. pp. 87–90. Churchill Livingstone, New York.

Bowen, D. M., Smith, C. B., White, P. and Davison, A. N. (1976). Neurotransmitter-related enzymes and indices of hypoxia in senile dementia and other abiotrophies. *Brain*, **99**, 459–496.

Brun, A. (1987). Frontal lobe degeneration of non-Alzheimer type. 1 Neuropathology. *Archives of Gerontology Geriatrica*, **6**, 193–208.

Chawluk, J. B., Mesulam, M. M., Hurtig, H., Kushner, M., Weintraub, S., Saykin, A., Rubin, N., Alavi, A. and Reivich, M. (1986). Slowly progressive aphasia without generalized dementia: studies with positron emission tomography. *Annals of Neurology*, **19**, 68–74.

Cummings, J. L. and Benson, D. F. (1983). "Dementia: a Clinical Approach". pp. 35–72. Butterworths, Boston.

Cummings, J. L., Benson, D. F., Hill, M. A. and Read, S. (1985). Aphasia in dementia of the Alzheimer type. *Neurology*, **35**, 394–397.

DeRenzi, E. and Faglioi, P. (1978). Normative data and screening power of a shortened version of the token test. *Cortex*, **14**, 41–49.

De Renzi, E., Faglioni, P., Savoiardo, M. and Vignolo, L. A. (1966). The influence of aphasia and of the hemisphere side of the cerebral lesion on abstract thinking. *Cortex*, **2**, 399–420.

De Renzi E., Liotti, M. and Nichelli, P. (1987). Semantic amnesia with preservation of autobiographical memory. A case report. *Cortex*, **23**, 575–597.

Duara, R., Grady, C., Haxby, J., Sundaram, M., Cutler, N. R., Heston, L., Moore, A., Schlageter, N., Larson, S. and Rapoport, S. I. (1986). Positron emission tomography in Alzheimer's disease. *Neurology*, **36**, 879–887.

Eslinger, P. J. and Benton, A. L. (1983). Visuoperceptual performances in aging and dementia: clinical and theoretical implications. *Journal of Clinical Neuropsychology*, **5**, 213–220.

Foster, N. L., Chase, T. N., Fedio, P., Patronas, R. A., Brooks, R. A. and Di Chiro, G. (1983). Alzheimer's disease: focal cortical changes shown by positron emission tomography. *Neurology*, **33**, 961–965.

Foster, N. L., Chase, T. N., Mansi, L., Brooks, R., Fedio, P., Patronas, N. J. and di Chiro, G. (1984). Cortical abnormalities in Alzheimer's disease. *Annals of Neurology*, **16**, 649–654.

Gainotti, G., Miceli, G., Silveri, M. C. and Villa, G. (1982). Some anatomo-clinical aspects of phonemic and semantic comprehension disorders in aphasia. *Acta Neurologica Scandinavica*, **66**, 652–665.

Glushko, R. J. (1979). The organization and activation of orthographic knowledge in reading aloud. *Journal of Experimental Psychology: Human Perception and Performance*, **5**, 674–691.

Goldstein, K. (1917). "Die Transkortikalen Aphasien". Gustav Fischer, Jena.

Gustafson, L. (1987). Frontal lobe degeneration of non-Alzheimer type 11. Clinical picture and differential diagnosis. *Archives of Gerontology Geriatrica*, **6**, 209–223.

Johnston, K. A., Holman, L. B., Mueller, S. P., Rosen, T. J., English, R., Nagel, J. S. and Growdon, J. H. (1988). Single photon emission computed tomography in Alzheimer's disease. *Archives of Neurology*, **45**, 392–396.

Kaplan, E., Goodglass, H. and Weintraub, S. (1983). The Boston Naming Test. Lea and Febiger, Philadelphia.

Kertesz, A., Appell, J. and Fisman, M. (1986). The dissolution of language in Alzheimer's disease. *Canadian Journal of Neurological Sciences*, **13**, 415–418.

Kirshner, H. S., Tanridag, O., Thurman, L. and Whetsell, W. O. (1987). Progressive aphasia without dementia: two cases with focal spongiform degeneration. *Annals of Neurology*, **22**, 527–532.

Levin, H. S., Hamsher, K de S. and Benton, A. L. (1975). A short form of the test of facial recognition for clinical use. *Journal of Psychology*, **91**, 223–228.

McCarthy, R. and Warrington, E. K. (1986). Phonological reading: phenomena and paradoxes. *Cortex*, **22**, 359–380.

Mesulam, M. M. (1982). Slowly progressive aphasia without generalized dementia. *Annals of Neurology*, **11**, 592–598.

Mesulam, M. M. (1987). Primary progressive aphasia—differentiation from Alzheimer's disease (editorial). *Annals of Neurology*, **22**, 533–534.

Molsa, P. K., Marttila, R. J. and Rinne, U.K. (1984). Extrapyramidal signs in Alzheimer's disease. *Neurology*, **34**, 1114–1116.

Money, J., Alexander, D. and Walker, H. T. (1965). "Manual for a Standardised Road-map of Direction Sense". Johns Hopkins University Press, Baltimore.

Neary, D., Snowden, J. S., Bowen, D. M., Sims, N. R., Mann, D. M. A., Benton, J. S., Northen, B., Yates, Y. P. O. and Davison, A. N. (1986). Neuropsychological syndromes in presenile dementia due to cerebral atrophy. *Journal of Neurology, Neurosurgery and Psychiatry*, **49**, 163–174.

Neary, D., Snowden, J. S., Northen, B. and Goulding, P. (1988). Dementia of frontal lobe type. *Journal of Neurology, Neurosurgery and Psychiatry*, **51**, 353–361.

Neary, D., Snowden, J. S., Shields, R. A., Burjan, A. W. I., Northen, B., Macdermott, N., Prescott, M. C. and Testa, H. J. (1987). Single photon emission tomography using 99mTc-HM-PAO in the investigation of dementia. *Journal of Neurology, Neurosurgery and Psychiatry*, **50**, 1101–1109.

Nelson, H. and O'Connell, A. (1978). Dementia: the estimation of premorbid intelligence levels using the new adult reading test. *Cortex*, **14**, 234–244.

Newcombe, F., Ratcliffe, G. and Damasio, H. (1987). Dissociable visual and spatial impairments following right posterior cerebral lesions: clinical, neuropsychological and anatomical evidence. *Neuropsychologia*, **25**, 149–161.

Pogacar, S. and Williams, R. S. (1984). Alzheimer's disease presenting as slowly progressive aphasia. *Rhode Island Medical Journal*, **67**, 181–185.

Ratcliffe, G. (1979). Spatial thought, mental rotation and the right cerebral hemisphere. *Neuropsychologia*, **17**, 49–74.

Reed, B. R., Davis, C. A., Jagust, W. J., Seab, J. P., Ober, B. A. and Budinger, T. F. (1989). Early abnormalities of regional cerebral blood flow and cognitive function in Alzheimer's disease. *Neurology*, **39**, (suppl) 168.

Schwartz, M. F., Marin, O. S. M. and Saffran, E. M. (1979). Dissociations of language function in dementia: a case study. *Brain and Language*, **7**, 277–306.

Schwartz, M. F., Saffran, E. M. and Marin, O. S. M. (1980). Fractionating the reading process in dementia: evidence for word-specific print-to-sound associations. *In* "Deep Dyslexia". (Eds M. Coltheart, K. Patterson, and J. C. Marshall). pp. 259–269. Routledge & Kegan Paul, London.

Sims, N. R., Bowen, D. M., Smith, C. C. T., Flack, R. H. A., Davison, A. N., Snowden, J. S. and Neary, D. (1980). Glucose metabolism and acetylcholine synthesis in relation to neuronal activity in Alzheimer's disease. *Lancet*, **i**, 333–335.

Taboada, E., Dickson, D., Horoupian, D. and Davis, P. (1986). Clinicopathologic and neurochemical studies of one case of dysphasic dementia. *Journal of Neuropathology and Experimental Neurology*, **45**, 323.

Ungerleider, L. G. and Mishkin, M. (1982). Two cortical visual systems. *In* "Analysis of Visual Behaviour" (Eds D. J. Ingle, R. J. W. Mansfield and M. S. Goodale). pp. 549–586. MIT Press, Cambridge, Massachusetts.

Warrington, E. K. (1984). "Recognition Memory Test". NFER-Nelson Publishing Co., Windsor.

Warrington, E. K. and Shallice, T. (1984). Category specific semantic impairments. *Brain*, **107**, 829–854.

Wilkins, A. and Moscovitch, M. (1978). Selective impairment of semantic memory after temporal lobectomy. *Neuropsychologia*, **16**, 73–79.