Progressive biparietal atrophy: an atypical presentation of Alzheimer's disease

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Abstract

Objectives—To define the clinical, neuropsychological, and radiological features of bilateral parietal lobe atrophy.

Methods—Four patients underwent a comprehensive longitudinal neuropsychological assessment, as well as MRI and HMPAO-SPECT.

Results—The consistent findings in the patients were early visuospatial problems, agraphia of a predominantly peripheral (or apraxic) type, and difficulty with bimanual tasks, all of which outweighed deficits in memory and language until later in the course of the illness. As the disease progressed, impairments in the phonological aspects of language and in auditory-verbal short term memory were often striking, perhaps reflecting spread from the parietal lobe to perisylvian language areas. Three patients went on to develop a global dementia and fulfilled the criteria for a clinical diagnosis of probable Alzheimer's disease; the fourth patient has only recently been identified. Neuroimaging disclosed bilateral parietal lobe atrophy (MRI) and hypoperfusion (SPECT), which was out of proportion to that seen elsewhere in the brain. One patient has died and had pathologically confirmed Alzheimer's disease with particular concentration in both superior parietal lobes.

Conclusions—Bilateral biparietal atrophy is a recognisable clinical syndrome which can be the presenting feature of Alzheimer's disease. Although the label "posterior cortical atrophy" has been applied to such cases, review of the medical literature suggests that this broad rubric actually consists of two main clinical syndromes with features reflecting involvement of the occipitotemporal (ventral) and biparietal (dorsal) cortical areas respectively.

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It is now well established that, in most patients with Alzheimer's disease, impairment in anterograde episodic memory is the earliest neuropsychological deficit.¹⁻³ The profound deficit in new learning reflects the fact that the initial acquisition of plaques and tangles

occurs in the transentorhinal region which effectively deafferentates the hippocampal complex.⁴ In a previous study, we have suggested that the breakdown of semantic memory, which in some patients begins not long after the episodic deficit, reflects spread of disease into more lateral neocortical regions which are critical for the representation of long term knowledge.² Involvement of the posterior association cortices is also common as the disease progresses, resulting in deficits in visuospatial, perceptual, and praxic abilities.⁵

Against this background of the typical amnesic presentation, it is important, particularly with the fast approaching advent of disease modifying drugs, to know whether Alzheimer's disease can present with other focal cognitive syndromes. Primary progressive aphasia usually occurs in the context of various non-Alzheimer forms of dementia⁵⁻⁸ but there are now several reports of patients with pathologically verified Alzheimer's disease presenting with progressive aphasia of either a fluent or a non-fluent type.⁸⁻¹¹

In addition to progressive aphasia, there are also a growing number of reports of patients with progressive occipitoparietal atrophy—so-called posterior cortical atrophy; such patients present with either visual agnosias (alexia, achromatopsia, apperceptual object agnosia), features of Balint's syndrome (visual disorientation, optic apraxia, and simultanagnosia), or apraxic disorders.^{5, 12-23} In most cases, pathological confirmation of the diagnosis has been unavailable: a very few cases of histologically established Alzheimer's disease have shown predominantly occipitoparietal neurofibrillary tangles and neuritic plaques, but no behavioural or neuropsychological data, other than the presence of Balint's syndrome, were reported.^{5, 24} To date, there have been only three reported patients with histologically confirmed Alzheimer's disease presenting with posterior cortical atrophy, all of whom had striking deficits in visuo-perceptual processing suggestive of the occipitotemporal, rather than the parietal variant of this syndrome.^{12, 18, 21} We argue in the discussion that posterior cortical atrophy comprises two fairly distinct clinical syndromes which present with symptoms reflecting involvement of the occipitotemporal (ventral) and occipitoparietal (dorsal) streams of visuo-perceptual ("what") and visuomotor ("where") processing respectively.^{25, 26}

This report describes four patients with progressive cerebral dysfunction associated with bilateral parietal lobe atrophy. Initially, all four patients presented with striking deficits in

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writing, hand coordination, and general visuospatial skills which overshadowed deficits in language and memory. Three showed rapidly progressive deterioration to a state of generalised dementia. Postmortem examination of one of these patients provided histopathological confirmation of Alzheimer's disease.

Patients and methods

PATIENTS

The patients, all of whom presented to the memory and cognitive disorders clinic at Addenbrooke's Hospital, Cambridge, were two men and two women with an age range from 54 to 73 years. All patients received a standard neurological examination and an extensive neuropsychological evaluation.

NEUROPSYCHOLOGICAL TESTS

The followings tests were given to all four patients whenever possible.

Global measures

- (a) Mini mental state examination (MMSE);
- (b) dementia rating scale (DRS).²⁷

Language tests

(a) National adult reading test (NART); (b) letter fluency for words beginning with F, A, and S; (c) test for reception of grammar;²⁸ (d) reading of 126 pairs of monosyllabic regular and exception words varying in frequency, plus 40 non-words;²⁹ (e) writing and oral spelling of 36 words;²⁹ (f) phoneme segmentation and blending tasks which require the patient to delete the first sound of a single syllable spoken stimulus and say what remained, and add a single phoneme onset to the "rime" of a single syllable spoken stimulus and say the result. Forty eight real and non-word stimuli were used. A rhyme production task required the patient to produce a rhyme in response to each of 24 target words.³⁰

Memory tests

(a) digit span; (b) logical memory (immediate and delayed story recall); (c) recall of the Rey complex figure; (d) the recognition memory test.³¹

Perceptual tests

Benton's judgement of line orientation test;³² an object matching (unusual views) test.³³

Semantic knowledge tests

(a) the Pyramids and palm trees test;³⁴ (b) the semantic battery of Hodges and coworkers^{6, 35} which employs one consistent set of stimulus items and assesses input and output from central representational knowledge about the same group of items via different sensory modalities. It contains 48 items representing three categories of animals (land animals, sea animals, and birds) and three categories of manmade items (household items, vehicles, and musical instruments) matched for category prototypicality and word frequency. Of the seven subtests in the battery the following four were used in this study: (a) category flu-

ency for each of the main categories plus two lower order categories (breeds of dog and types of boat), (b) naming of all 48 pictures without cues, (c) naming in response to a verbal description (for example "what do we call a large grey animal with a trunk?"), for half of the 48 items, (d) semantic features questionnaire consisting of 192 (eight per item) yes-no questions half of which explore knowledge of physical features (size, shape, colour, etc) and half tap knowledge of non-perceptual attributes (habitat, diet, uses, etc).

Case reports

CASE 1

A 56 year old right handed woman who had worked as a teacher, presented in 1992 with a two year history of dyspraxic difficulties, deficits in writing, and visuosperceptual problems. She was unable to write because of difficulty manipulating a pen but her oral spelling was relatively well preserved and she was able to read. Her husband reported that until very recently her memory for day to day events was good; she was able to provide details concerning recent family events and to keep track of appointments. More recently, she had developed problems with dressing and would put her clothes on the wrong way round and inside out. By the time she was assessed by us there were features of severe visual disorientation, such that she was unable to locate and pick up a knife and fork. Although her visual acuity (6/6 bilaterally), colour vision (as measured by Ishihara charts), and visual fields were intact, she had difficulty reaching in space and showed a degree of simultanagnosia; she could recognise and identify small objects and parts of large pictures but she had difficulty synthesising together the parts of scenes. Clinically, her language was well articulated and fluent with mild anomia and preserved single word repetition. Comprehension of nominal terms seemed intact but she showed deficits when attempting to follow sequential commands.

Neuropsychological examination disclosed widespread cognitive impairment (table) She performed extremely poorly on tests of visuospatial ability, obtaining a score of zero on the line orientation test and a chance level score on the unusual views (object matching) test. She was virtually unable to copy the Rey complex figure. Her ability to perform both transitive and intransitive hand gestures was extremely poor even when they were demonstrated by the examiner.

Language and semantic testing showed deficits in both comprehension and verbal output. She performed poorly on all of the semantic memory measures and her understanding of syntax was also severely impaired as evidenced from her score on the test for reception of grammar.

She attempted the written condition of the 36 word spelling test but the test had to be abandoned after 12 items. All of her responses were illegible although the occasional letter was appropriately formed. By contrast, when given the oral spelling condition of the same

Performance on neuropsychological test battery (maximum scores in parentheses)

	Case 1 Dec 92	Case 2 Dec 92	Case 3 Aug 92	Case 4 Feb 95
MMSE (30)	14	10	7	26
DRS (144)	79	68	56	142
Semantics:				
Category fluency (eight categories)	42	19	18	107
Naming (48)	28	32	16	36
Naming to description (24)	16	10	6	22
Word picture matching (48)*	40	45	45	45
Sem feature questions (172)‡	159	160	160	—
Pyramids and palm trees (52)‡	36	39	38	49
Language:				
Letter fluency (FAS)	13	10	2	36
Comprehension, TROG (80)†	45	54	44	76
Reading, regular words (126)	124	106	110	125
Exception words (126)	120	96	94	122
Non-words (40)	29	23	15	38
Oral spelling (36)	27	10	1	35
Visuospatial skills:				
Line orientation (30)	0	0	0	23
Object matching (40)‡	23	26	27	35
Key figure copy (36)	1	5	0	7.5
Memory and attention:				
Digit span forward/ back	3/2	4/2	3/2	6/3
Recognition, words (50)‡	33	26	23	49
Faces (50)‡	34	39	38	38
Stories, immediate/delayed recall (25)	3/1	2.5/0	4.5/3.5	6.5/6

Chance levels of performance *0.125; †0.25; ‡0.5.

test she succeeded in correctly spelling 27 out of 36 items. Although her performance on this test was poorer than that of control subjects (who correctly spell an average of 35 of 36 words), it was clearly better than her performance on the written condition of this task. She made equal numbers of errors on regular and exception words and her error types consisted of letter omissions or substitutions. Although she attempted a letter copying task she was completely unable to copy in either upper or lower case. This profile of results suggests that the dysgraphia was of a peripheral (apraxic) rather than central (linguistic) type. By contrast with her performance on writing tasks her reading ability was well preserved.

There was also evidence that her verbal and non-verbal episodic memory were impaired and her immediate memory span was reduced to three digits forwards and two backwards.

Brain SPECT showed greatly decreased perfusion in the superior parietal lobes bilaterally.

After 1992 there was a rapid and global decline in cognitive function, particularly on tasks requiring hand coordination or motor function, such that she became totally unable to dress, feed, or toilet herself. Her language abilities also declined dramatically, with largely phonological errors both in spontaneous conversation and on naming tasks; she also performed poorly on tests of rhyme production (12/24) and phoneme blending (10/48). Her oral spelling had dramatically deteriorated and she was only able to spell four out of 36 words correctly. Her errors consisted of perseverations and bizarre letter strings.

She died in December 1994. Neuropathological examination was carried out according to the CERAD protocol. The brain showed a moderate degree of generalised cerebral gyral atrophy, with a particular emphasis on both superior parietal lobules (especially the right). The medial occipital lobe showed some thinning of the visual cortex, and the white matter beneath it was reduced.

Microscopic examination found severe nerve cell loss in the parietal cortex and a smaller loss in the medial temporal areas. There was also extensive neuritic plaque formation and numerous neurofibrillary tangles in archicortex and cerebral neocortex, with particularly severe parietal involvement. The neuropathological changes fulfilled the CERAD diagnostic criteria for definite Alzheimer's disease.

In summary, the course of her disease was atypical with the onset characterised by severe difficulties with writing, hand coordination, and visuospatial skills.

CASE 2

A 54 year old right handed man who left school with three A levels and most recently worked as a garden designer, presented in 1992 with a three year history of difficulty performing everyday tasks requiring manual or visuospatial abilities. He had developed problems in dressing, and his difficulty in drawing and following plans had led him to abandon his hobbies. Twelve months before being seen by us he had apparently lost the ability to write but had continued to be an avid book reader. Both the patient and his family reported preservation of day to day memory and personality.

As with patient 1, although he presented with symptoms suggesting a focal form of dementia, he too rapidly progressed to a stage of more global dementia. He performed extremely poorly on all tests of visuospatial ability and was completely unable to attempt the block design subtest from the Wechsler adult intelligence scale revised.

On language tests he showed considerable word finding difficulties and made frequent phonological paraphasic errors. His comprehension of simple commands was good but he had difficulty with more complex tasks. On the written version of the 36 item spelling test he obtained a score of 8, but by contrast with patient 1, his oral spelling was not much better (10/36). Although he often produced well formed letters at the beginning of a word, the

rest of the word was usually illegible. His performances on regular and exception words were equivalent. He was unable to copy single letters or words. This profile suggests a combined central and peripheral dysgraphic disorder. Like patient 1 he performed poorly on a test of rhyme production (15/24) and was unable to complete the phoneme blending task.

It was difficult to assess his memory in view of his language and spatial problems but there was evidence that this too was impaired. For example, his orientation was poor, his digit span was reduced, and his performance on a simplified version of the recognition memory test was impaired.

Brain SPECT in 1992 showed focal hypoperfusion of the left temporoparietal region with less reduction in the right parietal region.

Since 1992 he has shown a steady and global decline in cognitive function including a considerable impairment on tests of semantic knowledge. His spontaneous language output is now largely unintelligible due to hesitations, phonological approximations, and neologisms. By contrast with this picture of universal impairment, his reading of both words and non-words remains well preserved.

Brain MRI in 1994 showed a mild degree of generalised atrophy with pronounced atrophy in the parietal lobes. Of note was the preservation of the medial temporal complex. As with patient 1, he fulfilled the criteria for a clinical diagnosis of probable Alzheimer's disease, but once again, the onset of his disease was atypical with prominent apraxia and visuospatial problems.

CASE 3

A 68 year old right handed man who had lectured in an art college, complained in 1987 of difficulty performing manual tasks and an inability to write. In particular, he was unable to tie his shoelaces, had changed to wearing clothes with no buttons, and could no longer perform simple bimanual tasks such as washing up, peeling vegetables, or gardening. His writing had deteriorated to such an extent that he could only sign his initials and was otherwise unable to write. His memory at this stage was reported by the patient and his family to be normal and there was no change in personality.

Although he initially presented with focal symptoms suggestive of biparietal pathology, he progressed over the next five years to a stage of more global dementia. In 1992, when first assessed in Cambridge, neuropsychological examination found evidence of generalised impairment. As in the two previous patients, his performance on all tests of visuospatial ability was extremely impaired and he showed gross impairment on tests of limb praxis involving both transitive and intransitive gestures.

On language assessment, he showed considerable impairment of syntactic comprehension, and there was also evidence that his semantic knowledge was fundamentally impaired on both verbal and non-verbal tests. He was completely unable to write and could spell orally only one out of 36 words correctly,

indicating a combined central and peripheral agraphia. He performed poorly on the rhyme production task (12/24) and could not manage to do phoneme blending at all.

Since 1992 his language output has become progressively more dysfluent and dominated by phonological errors. His reading skills have also declined, whereas his performance on semantic tests which do not require speech has stayed about the same. Brain SPECT showed biparietal reduction in perfusion and MRI in 1994 disclosed notable asymmetry in the degree of cerebral atrophy with left parietal and temporal lobes being particularly involved. He fulfils the criteria for a clinical diagnosis of probable Alzheimer's disease although the pathological basis of his disease remains a little uncertain. The presentation of his disease was, however, very atypical, being dominated by difficulties with praxis, writing and somewhat later, spoken language.

CASE 4

A 73 year old right handed woman who worked as a special needs teacher presented in 1994 with a four year history of writing difficulties and problems reaching for things in space. Having been a keen letter writer she had progressively lost the ability to write using joined up (lower case) script; the process of writing had become slow and laborious, and the product was difficult to read because it was shaky and characterised by incomplete letters and letter omissions. She had compensated by printing in upper case letters. More recently, she had experienced difficulty dressing and found that she often knocked over objects when reaching, and described that when she was looking at things in space "they seem to disappear". Reading had become difficult as the lines seemed "jumbled" and she complained of difficulty scanning across lines. Neurological examination showed normal visual acuity (6/6), colour vision, and visual fields.

By contrast with the other three patients, neuropsychological examination did not find evidence of global impairment. She showed mild impairment on some tests of visuospatial ability such as the line orientation test and an object matching test. However, she performed very poorly on the Rey figure and failed all of the subtests from the visual object and space perception battery³⁶ except for the initial screening test (figure-ground discrimination) and the number location subtest.

Her scores on tests of language comprehension and reading were within normal limits but she showed mild impairments in language output, particularly on picture naming tests. Performance on rhyme and phoneme blending tasks was normal at presentation. As noted above, her writing was difficult to read when she used joined up script, but when asked to write to dictation using separate lower or upper case letters, she could write legibly. She was also able to copy upper and lower case letters but made two errors when asked to transcribe upper case into lower case letters. Given the written version of the 36 item spelling test

Brain MRI for patient 4: coronally oriented T1 weighted images through the anterior (A) and posterior temporal region (B) showing mild global atrophy but well preserved hippocampal complex. Slices through the posterior parietal region (C and D) show dramatic bilateral superior parietal atrophy with compensatory dilation of the lateral ventricles.

and allowed to print her responses, she made only one error, indicating that her spelling was well preserved and suggesting that her dysgraphia is peripheral rather than central.

On memory tests, her verbal recognition memory was intact but her recognition memory for faces was impaired. She also performed poorly on the logical memory test but without the accelerated forgetting which is typically seen in patients with Alzheimer's disease.

Brain SPECT in 1994 showed pronounced bilateral hypoperfusion in the posterior parietal lobes and mild bilateral reduction in the temporal lobes. Brain MRI in 1995 (figure) showed striking bilateral atrophy in the superior parietal lobes with compensatory dilatation of the lateral ventricles and a few scattered periventricular lucencies of doubtful significance. By contrast, the temporal lobes, particularly the hippocampus and related structures, seemed normal.

Follow up neuropsychological testing six months later disclosed a generally stable performance. Her dyspraxic difficulties had, however, worsened and were causing her some distress. For example, she was finding it so difficult to use a knife and fork that she was too embarrassed to eat out in restaurants. Her dressing dyspraxia had worsened, and she was finding it difficult to tell the time on her non-digital watch.

In conclusion, patient 4 presented with writing deficits and visuospatial problems which overshadow more subtle deficits in language output and memory.

Discussion

We have described four patients whose illness

began with features of progressive biparietal pathology. The onset of their illness was characterised by visuospatial problems, dyspraxia, and dysgraphia. In three of the patients, other cognitive deficits have become apparent, particularly in the phonological aspects of language and in auditory-verbal short term memory. This pattern may indicate spread of the disease from parietal areas to the perisylvian language area, particularly the superior temporal gyrus. The fourth patient does not show evidence of global intellectual decline but has selective cognitive deficits involving visuospatial functions and writing. Brain MRI showed particularly notable bilateral parietal lobe atrophy in three of the patients and post-mortem examination of patient 1 showed Alzheimer's disease with particular involvement of the parietal lobes. The clinical features conform to what has been termed posterior cortical atrophy although, for reasons outlined below, we prefer the term progressive biparietal atrophy.

The term posterior cortical atrophy was first used by Benson *et al*¹³ to describe five patients presenting with slowly progressive disorders of higher visual function without evidence of basic sensorimotor dysfunction or impaired visual acuity. All five patients met the criteria for a diagnosis of probable Alzheimer's disease but confirmatory pathology was not available. The patients initially complained of difficulty reading, visual distortion, problems with object recognition, and a tendency to get lost even in familiar surroundings. All five were unable to copy simple drawings. Their insight and memory seemed relatively well preserved until later in the course of the illness. Over a three to five year period, three patients devel-

oped a full blown Balint's syndrome (visual disorientation, optic apraxia, and simultanagnosia) implying bilateral parietal-occipital involvement. All five patients eventually developed the four components of Gerstmann's syndrome (finger agnosia, right/left disorientation, agraphia, and acalculia) suggestive of spread of the pathology to the angular gyrus area. Radiological findings (CT and MRI) in three patients showed cortical degeneration with particular involvement of the posterior cerebral hemispheres. On the basis of these findings, Benson *et al*¹³ suggested that their patients' disease initially involved occipital and parietal association cortices then progressed to the angular gyrus or its connections bilaterally.

Since this initial description by Benson *et al*,¹³ several groups have reported similar patients.^{5 12 14–21 24} Although all of these patients have been grouped under one general class, a finer grained analysis of this and earlier relevant medical literature in fact suggests two broad presentations of posterior cortical atrophy which reflect the predominant site of pathology—that is, occipitotemporal and biparietal—although in many patients features of both eventually develop.

Those in the occipitotemporal group present with complaints of visual distortion, difficulty with object recognition, topographical agnosia, and alexia. Examination typically shows restricted visual fields or unilateral extinction on bilateral stimulation, impaired colour vision and stereopsis, deficits in object recognition, prosopagnosia, and alexia (either letter by letter reading or attentional alexia). In the original study by Benson *et al*,¹³ three of the five patients presented in this way. Similar patients were reported in the ophthalmological literature by Cogan¹⁹ and by Kiyosawa and colleagues.²² The second group described five patients with prominent visual symptoms; four had difficulty reading because they could not stay on the correct line of print and complained of visual distortion. As the disease progressed other prominent symptoms included environmental agnosia and simultanagnosia, and three patients developed mild to moderate expressive dysphasia. Most showed atrophy of the posterior cerebral hemispheres on MRI, and PET studies showed significant decreases in glucose uptake in occipital areas with sparing of the primary motor and sensory cortex. Very similar cases of “slowly progressive visual agnosia” with features of apperceptual agnosia, prosopagnosia, and alexia were reported by De Renzi.²³

The nature of the reading disorder associated with this form of posterior cortical atrophy was described by Freedman *et al*²⁰ in a report of a 54 year old man who was found to have the characteristics of letter by letter reading (pure alexia) and subsequently developed profound constructional problems, agraphia, a complete Gerstmann's syndrome, and severe aphasia with compromised naming and comprehension. Brain PET showed symmetric bilateral occipitotemporal hypoperfusion but pathological confirmation of the diagnosis was not available.

More recently, three pathologically verified cases of Alzheimer's disease presenting with progressive visual loss and other features of occipital pathology have been reported.^{12 18 21} In a remarkable 12 year longitudinal study, Levine and colleagues²¹ reported a 59 year old man who presented with what they termed “the visual variant of Alzheimer's disease”. He complained of difficulty in reading, driving, and locating items by sight and was found to have constricted visual fields, widespread visuospatial deficits, and an attentional dyslexia. Intellect and memory were initially preserved but declined along with the visual deficits over a 12 year period. Towards the end of his illness he developed aphasic difficulties with word finding problems and occasional phonological paraphasias. Postmortem examination confirmed Alzheimer's disease with particular involvement of the posterior cingulate cortex (area 23), primary visual cortex (area 17), and visual association cortex (area 18 and 20). In terms of the suggested dichotomy, this occipitotemporal subgroup manifest either impairment in basic visual abilities, reflecting involvement of primary visual cortex, or disruption of the ventral stream of higher order visual processing which is vital for object, face, and written word identification.²⁶

The second major category of patients with posterior cortical atrophy is that with features of parietal lobe dysfunction which is usually bilateral, although often asymmetric. Unlike those with early occipitotemporal involvement, such patients initially complain of visuospatial problems, agraphia, and dyspraxia. With progression they may manifest a full blown Balint's syndrome but show preservation of visual fields, basic perceptual abilities, object recognition, and reading. These deficits reflect interruption of the dorsal stream of visuomotor processing which is critical for object location and visually guided movements,²⁵ and damage to areas of the parietal lobe which are involved with general motor programming and writing.

Features of parietal lobe pathology are well recognised in the context of Alzheimer's disease, and indeed most patients with moderately severe dementia show such signs³⁷; but the fact that Alzheimer's disease may occasionally present in this way has not been clearly established. In a series of elegant neuropathological studies Hof and colleagues^{5 24} showed that patients with Alzheimer's disease who had prominent features of Balint's syndrome showed involvement of the dorsal occipitoparietal pathways, which are known to be critical for visuospatial and perceptual-motor processing; because clinical details of the cases were not included, it is unclear whether these patients presented with Balint's syndrome or merely developed such features during the course of their disease. A similar problem exists in interpreting the findings of Mendez *et al*¹⁷ who investigated visuospatial and perceptual abilities in 30 mildly to moderately demented patients with probable Alzheimer's disease. They identified six patients who met the criteria for Balint's syn-

drome. Other more general neuropsychological data were not reported, but on the basis of their scores on the MMSE it seems likely that this subgroup also had other substantial cognitive deficits.

Coslett, Saffran, and coworkers^{14,38} have explored the nature of the cognitive deficits seen in a series of patients presenting with progressive parietal lobe dysfunction, whose major symptoms of simultanagnosia and visual disorientation have been attributed to impairments in visual processing with a "narrowing of the attentional spotlight". Although these patients once again eventually fulfilled criteria for a clinical diagnosis of probable Alzheimer's disease, pathological verification has not yet been provided.

The consistent findings in the four cases presented here—pronounced visuospatial problems, agraphia, and dyspraxia, which outweighed deficits in memory and language until later in the course of the illness—are in keeping with the site of pathology shown on MRI and SPECT—namely, the parietal lobes. It should be stressed, however, that only patient 4 had a pure biparietal syndrome when first formally assessed. In the other three patients, the history obtained from the patients' relatives was stereotyped and atypical of Alzheimer's disease with sparing of episodic memory but neuropsychological testing showed more widespread deficits.

We have so far obtained a pathological diagnosis in only one of our patients. It is not yet possible, therefore, to determine whether all four patients have the same underlying pathology. According to the medical literature, a variety of degenerative processes may occasionally produce posterior cerebral dysfunction including Alzheimer's disease,²¹ subcortical gliosis—a lobar atrophy similar to Pick's disease¹⁸—and Creutzfeldt-Jakob disease.^{15,18} The close similarity of the cognitive deficits and the neuroradiological findings in our patients, and the slowly progressive course, leads us to hypothesise that all four have Alzheimer's disease. Rather than apply the general label posterior cortical atrophy, we prefer the more specific term progressive biparietal syndrome.

Two aspects of our patients which are particularly atypical of Alzheimer's disease, and which have not previously been highlighted in patients with posterior cortical atrophy, are the severe dysgraphia and breakdown in phonological processing. The writing disorder in patients with Alzheimer's disease is generally mild, at least at presentation, and is often dominated by deficits in spelling (rather than letter formation). The most common pattern is one of lexical or surface dysgraphia in which performance is better on words with regular spelling to sound correspondence than on irregularly spelt words.³⁹ In a group study, we have recently confirmed the relative normality of spelling and writing processes in many patients with mild Alzheimer's disease.⁴⁰ Although some of the patients in this group exhibited a surface dysgraphic profile and others demonstrated deficits in letter formation

characteristic of peripheral dysgraphia, in all cases the degree of impairment was mild compared with the four patients reported here who were practically unable to write early in the course of their disease. Two patients (1 and 4) displayed a fairly pure peripheral dysgraphia in that oral spelling was remarkably superior to written spelling and was unaffected by the regularity of the word; the other two patients (2 and 3) had a more complex disorder with elements of both central and peripheral dysgraphia.

The other notable feature in the three more impaired patients was their prominent phonological impairment. In typical Alzheimer's disease, the language deficit reflects a breakdown in lexicosemantic processing resulting in progressive anomia, reduced information content, disproportionate impairment in semantic category based tests of verbal fluency, and impaired comprehension of low frequency words.^{41–43} Phonological errors are rare, except in advanced disease. Aphasic disorders have been noted in some studies of patients with posterior cortical atrophy but have not been explored in any detail. The patients reported here showed progressively severe phonological breakdown as evidenced by phonological paraphasic errors in spontaneous speech and picture naming. Their dramatically reduced digit span was probably attributable to impairment in the phonological, rather than the executive, component of working memory, as supported by their poor performance on tests of phonological competence.

In conclusion, although memory and language impairment are usually the earliest signs of Alzheimer's disease, the predominant and presenting symptoms can in some cases involve dyspraxia, agraphia, and visuospatial problems.

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