

The cognitive profile of posterior cortical atrophy

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Abstract—*Background:* Posterior cortical atrophy (PCA) is a progressive dementia characterized by prominent disorders of higher visual processing, affecting both dorsal and ventral streams to cause Balint's syndrome, alexia, and visual agnosia. *Objective:* To define the cognitive profile of PCA and compare to the typical, primary amnesic dementia of the Alzheimer's type (DAT). *Methods:* The authors used standard cognitive tests and a novel battery designed to reflect dysfunction in both ventral (Object, Face & Color Agnosia Screen [OFCAS]) and dorsal (complex pictures and compound stimuli) visual streams. The authors identified 19 patients with PCA and compared their performance to a matched group of patients with DAT and normal controls. *Results:* Patients with PCA were younger with marked impairment in visuospatial tasks, reading, and writing but relative preservation of memory compared to DAT using standard tests. Dorsal stream signs were most prevalent among the patients with PCA with no pure ventral stream syndromes found. All novel tests distinguished reliably between subjects with complex picture descriptions and processing of compound stimuli showing the most significant differences compared to DAT. *Conclusions:* PCA is predominantly a dorsal stream syndrome, distinct from typical DAT, which involves occipitotemporal regions over time.

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Benson et al. coined the term posterior cortical atrophy (PCA) to describe five patients presenting with progressive visuospatial dysfunction but relatively preserved memory, insight, and judgment.¹ Many additional cases have since been described and the most common features are alexia out of proportion to other language impairments, Balint's syndrome (optic ataxia, ocular apraxia, simultanagnosia), visual agnosia, which is primarily apperceptive, and presenile onset in the 50s and 60s.² The pathology is most often Alzheimer disease (AD) but PCA is described as a distinct clinical syndrome with its own diagnostic criteria.^{3,4}

A basic dichotomy in higher order visual processing is between the ventral "what" and dorsal "where" pathways.⁵ The ventral path mediates object, face, color, and written word recognition and occipitotemporal pathology causes visual agnosias, prosopagnosia, achromatopsia, and alexia. The dorsal stream detects the location and motion of objects in preparation for movement⁶ and occipitoparietal damage results in Balint's syndrome, agraphia, and apraxia. Since all may be present in PCA, it is apparent the syndrome reflects widespread posterior cortical dysfunction and some authors⁷ have argued for classification of PCA into dorsal and ventral subtypes. Our aim in this study was to prospectively describe the cognitive profile of patients with PCA compared to a

typical cohort with primary amnesic AD or dementia of the Alzheimer's type (DAT) to look for distinguishing features and establish the relative burden of deficits in each visual stream. In particular we wanted to establish a battery of tests to help delineate the deficits and offer a quantitative measure of posterior cortical dysfunction reflecting both dorsal and ventral paths. We designed tests of object, face, and color recognition (Object, Face and Color Agnosia Screen [OFCAS]) to focus on the ventral "what" stream. Complex picture descriptions and compound stimuli, testing global vs local processing, were used to detect dorsal stream disruption and we compared the performance on these tests in two patient groups.

Methods. *Subjects.* Subjects with PCA were attendees at the cognitive disorders clinic in London, Ontario, between 1990 and 2004. They were included if they showed gradual onset of cognitive impairment with progressive decline and prominent visuospatial dysfunction but intact primary visual perception. Cardinal features were the presence of some or all elements of Balint's or Gerstmann's (acalculia, agraphia, left-right disorientation, finger agnosia) syndromes, disproportionate alexia, or visual agnosia. Specific other features including prosopagnosia, topographic disorientation, dressing apraxia, aphasia, achromatopsia, neglect, hallucinations, and parkinsonism were identified. All subjects were seen by the same behavioral neurologist (A.K.) and all had neuroimaging performed but are included here on the basis of clinical findings rather than the demonstration of posterior atrophy with CT, MRI, or SPECT.

The reference group comprised patients attending the clinic

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who met National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria for probable AD⁸ and they were matched for disease duration and Mini-Mental State Examination (MMSE) score with the PCA cohort. Since ours are clinical rather than pathologic cohorts these patients are referred to as having DAT to distinguish the typical, primary amnesic, presentation of AD from the pathologic entity that also underlies a major proportion of PCA cases. All DAT subjects presented with progressive memory impairment in the absence of an alternative explanation such as stroke, head injury, or alcohol excess and there was no history of visual hallucinations, parkinsonism, or fluctuations to suggest dementia with Lewy bodies. Neurologic examination at the time of assessment was normal and cranial imaging confirmed the presence of cerebral atrophy and the absence of vascular disease.

Eighteen healthy control subjects were selected from relatives of patients attending the cognitive disorders clinic. They were all well physically and none had memory complaints or a history of stroke, head injury, or alcohol excess. Most controls were spouses of the DAT reference group allowing us to control for sociodemographic factors and likely exposure to famous faces, a component of the OFCAS. They served as a normal reference group for performance on face recognition and complex picture descriptions.

Cognitive assessments. **Object, Face and Color Agnosia Screen.** Object Recognition (includes object naming, word picture matching, superordinate categories, odd one out; max score 130): The test material consists of 40 Snodgrass pictures of common objects with 10 each in the four categories of fruit, furniture, clothing, and animals. Object Naming (max score 40): The first task begins by asking the subject to name the items depicted in each picture. Since our interest was in visual recognition rather than naming ability per se, a half credit was given for correct identification without naming, as for example with the response "a pet that barks" instead of "dog." Phonologic and semantic cues were not employed. Word Picture Matching (max score 40): To further control for the effects of aphasia on naming ability the same pictures were arranged randomly in a group of 10 and the patient is asked to select the correct referent. This is repeated three times covering all 40 pictures. Sorting into Superordinate Categories (max score 40): To test semantic knowledge and recognition without reliance on verbal responses the pictures are randomly presented one at a time and the subjects are asked to sort them into their four superordinate categories of fruit, furniture, clothing, and animals. Odd One Out (max score 10): This test is similar to the Palms and Pyramids test⁹ of nonverbal visuospatial processing but with the reverse response, asking for differences rather than similarities. A set of three pictures are presented to the subject and they are asked to pick the odd one out; the condition is repeated nine times.

Face Recognition (includes naming famous faces, name picture matching, facial expressions; max score 30): The test material consists of 20 photographs of famous people, some of whom are still alive (Queen Elizabeth II, Alan Alda) and others from the more remote past (John F. Kennedy, Winston Churchill) but in all cases appropriate for the ages of patients largely in their 50s to 70s. Naming Famous Faces (max score 10): Photographs are presented one at a time and subjects are asked to identify them by name. Again, to make allowance for any mild anomia a half credit is given for correct identification without naming such as "the English/British Prime Minister" for Margaret Thatcher. Name Picture Matching (max score 10): To reduce the reliance on verbal responses the subject is then presented with the other 10 photographs in an array and asked to point to the famous person named. Facial Expressions (max score 10): Recognition of facial expressions probes the processing of emotional expressions from non-familiar faces. Preserved ability here implies intact facial feature perception. It was tested using 10 photographs of actors showing faces that are happy, sad, angry, or neutral. Each photograph is presented and the subject asked to choose which of the four emotions is displayed from a multiple-choice format. Only the face recognition subtests of the OFCAS were standardized with normal controls, as they would reach a ceiling in other measures.

Color Recognition (includes color naming, color matching, verbal-semantic color associates; max score 30): The testing process is designed to distinguish among the three main syndromes of color processing, namely achromatopsia, color agnosia, and color anomia. The test material consists of two identical sets of

cards in 10 prototypical colors (red, purple, green, pink, yellow, orange, blue, black, brown, white). Color Naming (max score 10): Color perception, recognition, and naming are tested by presenting subjects with one card at a time and asking them to identify the 10 colors. Color Matching (max score 10): As a nonverbal test of color perception the subject is then presented with the two sets of cards arranged in two random arrays, side by side, and they are asked to match cards from each pile according to color. Verbal-Semantic Color Associates (max score 10): Finally, subjects are asked 10 questions designed to test their conceptual knowledge of color items, for example, "what color is tangerine?"

Complex Pictures. Eight color pictures of varying complexity, depicting scenes such as a boardroom meeting and an ice-hockey match, are presented to the subject one at a time. They are asked the question: "what do you see in this picture?" to guide them to identify as many items as they can from the picture and then give their impression of the overall scene. The scoring system was to award one point for each major item in the picture and five points for the overall impression, yielding scores between 8 and 13 for each picture and an overall maximum of 78.

Global vs Local Processing. Navon Letters (max score 30): The test material consists of 10 compound figures in which a larger global letter is composed of a repeated different, smaller letter.¹⁰ The subject is shown each letter and instructed to report exactly what he or she sees. No time limit is applied and the stimulus is presented until the subject responds. In the event of an incorrect or incomplete response the subject is cued with the question "do you see anything else?" A quantitative scoring system was adopted with three points for a correct response, two points if cuing was required, and a single point if only one element (large or small letter alone) is reported despite cuing.

The Hooper Visual Organization Test¹¹ was administered to all three cohorts (max score 30). It consists of 30 pictures of more or less recognizable cut-up objects and the subject is required to name each object in turn. It calls upon the same perceptual functions as Object Assembly (WAIS-R), testing perceptual integration/organization, recognition, and naming, but is relatively little influenced by aphasia.¹²

Statistical analyses using one-way analyses of variance were performed with group membership (PCA vs DAT vs normal controls) as the between subjects factor. Tukey HSD was used for post hoc tests and an independent samples *t* test was used where the data compared only DAT and PCA groups. Logistic regression with the enter method was used to predict group membership between PCA and DAT patients. SPSS version 10.1 (SPSS Inc., Chicago, IL) was used for all analyses. The research ethics board of the University of Western Ontario approved the study.

Results. Subjects. The 19 subjects with PCA (9 men and 10 women) had an average onset at 59 years of age (range 47 to 80 years, SD 8.4 years) and their clinical characteristics are summarized in table 1. The first symptoms were referable to posterior cortical areas in 13 subjects with problems reading, writing, getting lost, and difficulty seeing or recognizing objects in front of them. Mild memory loss was the first symptom in the remainder but was soon overshadowed by prominent visuospatial dysfunction. Five subjects reported a history of dementia in a first-degree relative. First assessment, 4.5 ± 1.6 years after onset of symptoms, revealed an average MMSE score of 14.3 ± 6.4 (range 2 to 25). Alexia and agraphia out of proportion to other language difficulties were the most common findings, present in 18 cases. Sixteen had acalculia, while left/right disorientation was evident in six, finger agnosia in four, and a full Gerstmann's syndrome in just three cases at the time of assessment. Simultanagnosia was present in 17, optic ataxia in 15, ocular apraxia in 6, and the full Balint's syndrome in 5. Other findings were dressing apraxia ($n = 12$), topographic/spatial disorientation ($n = 9$), visual agnosia ($n = 9$), prosopagnosia ($n = 4$), and hemianopia ($n = 1$). Visuo-perceptive deficits were so severe in three cases that they were described as cortically

Table 1 Clinical characteristics of 19 subjects with PCA

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Onset age, y	52	53	80	51	54	63	65	52	55	69	70	50	59	49	65	63	61	57	47
Duration to examination, y	3	4	3	4	5	3	6	6	2	5	1	6	8	3	6	6	5	5	6
Sex	M	M	M	M	F	F	M	F	F	M	F	M	F	F	F	F	M	M	F
MMSE	NA	16	13	9	8	25	16	16	12	9	23	6	9	18	2	21	16	15	23
Balint																			
Simultanagnosia	+	+	+	++	+	+	+	+	+	+	+	+	+	+		+	+	+	+
Optic ataxia	+	++	+	++	+	+	+	+	++	+	+	+	+	+		+	+	+	+
Ocular apraxia			+	++			++	+	++	+	+		+						++
Spatial disorientation	+	++			+	+		+	+				+	+				+	+
Visual agnosia	+	++	+	++	+		+	+	++			+			+			+	+
Prosopagnosia		+		+									+			+			
Dressing apraxia	+	+	+	++	++		+		+	++	+	+	+	+	+			+	+
Alexia	+	+	+	+	+	+	+	+	++	+	+	+	+	+	+	+	+	+	+
Gerstmann																			
Acalculia	+	+	+	+	+	+		+	+	+		+		+	+	+	+	+	+
Agraphia	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			+	+
L/R disorientation	+	++	+	+				+	+				+						
Finger agnosia		++		+				+	+									+	
Achromatopsia	++																		
Color agnosia							++		++										
Hemianopia	++							+	++										
Cortical blindness	++	++			+				+						+				
Neglect							++		++	+				+					
Parkinsonism			+			++	+		++				+						+
Fluctuation						++	++			++			+						+
Hallucinations	++					++				++			+			+	+		
Limb apraxia	+	++	+	+	++	+	+	+	++	+	+	+	+	+	+			+	+
PCA on imaging	+	+	+	+		+	+	+	+		+	+		+		+	+	+	+

PCA = posterior cortical atrophy; MMSE = Mini-Mental State Examination; + = present at initial assessment; ++ = present later.

blind. The visual agnosia detected in our series was of the apperceptive type; meaning visual recognition of objects was impaired with retained knowledge through the verbal or tactile modalities with poor copying and visual matching. These patients tended to have longer disease durations than those without visual agnosias (5.1 years vs 4.2 years) though this was not significant (*t* test, *p* > 0.05). Deficits of color perception were not evident at initial assessment. Delusions such as Capgras, Fregoli, or the phantom border were present in five cases while four had well-formed visual hallucinations. Fifteen subjects had evidence of focal posterior cortical atrophy on imaging while generalized atrophy was present otherwise. None of our patients had early (within 2 years of onset) signs of visual hallucinations or parkinsonism. Two patients demonstrated the alien limb phenomenon while another had marked asymmetry of limb apraxia and a fourth showed diagonal dyspraxic movements. Three patients were seen on just one occasion, the other 16 were followed for an average of 3.4 ± 2.7 years with the development of additional elements of Balint's syndrome (n = 5), apperceptive visual agnosia (n = 3), color agnosia (n = 2), unilateral

neglect (n = 2), cortical blindness (n = 2), and achromatopsia (n = 1). Seven cases are known to be dead after 9.1 ± 3.7 years of illness (range 4 to 16 years); pathology is available on six and will be reported separately.

We recruited 11 patients with typical, primary amnesic DAT (seven women, four men) with an average disease onset at 67.4 ± 7.2 years (range 52 to 75 years), older than the PCA cohort (*t* test vs PCA, *p* = 0.01) but with similar disease durations (4.4 ± 1.4 years; *t* test vs PCA, *p* = 0.9). Eighteen relatives of clinic attendees (13 women, 5 men) served as normal controls at an average age of 67.1 ± 7.9 years, which was not different from the other two groups (range 52 to 79 years, Tukey post hoc vs DAT and PCA, *p* > 0.05).

Cognitive profiles. Background neuropsychological testing. Background neuropsychological data for the patients with PCA were available in the form of the Dementia Rating Scale¹³ (n = 11), the Western Aphasia Battery¹⁴ (n = 13), the WAIS-III/R (n = 8), and the Frontal Behavioral Inventory¹⁵ (n = 6). The average DRS score (max = 144) was 83.5 ± 27.0 with the greatest impairment (scores expressed as a % of maximum subtest score) in measures of construction (26.7%), initiation/perseveration (48%), and

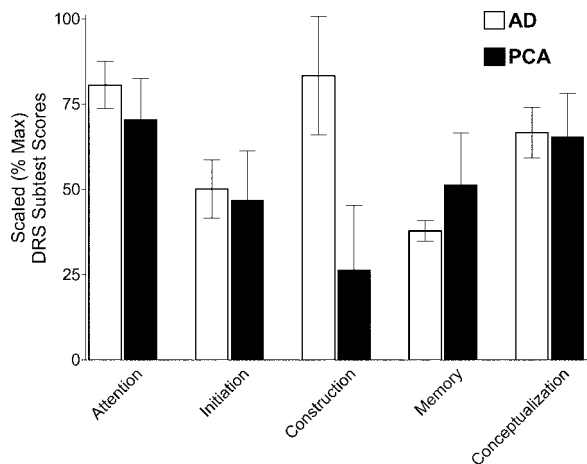


Figure 1. Bar graph showing mean and 95% CIs for Dementia Rating Scale (DRS) subtest scores. Scores are scaled as a % of the maximum achievable in each subtest. Patients with posterior cortical atrophy show impaired construction and borderline better memory performance compared to those with Alzheimer disease.

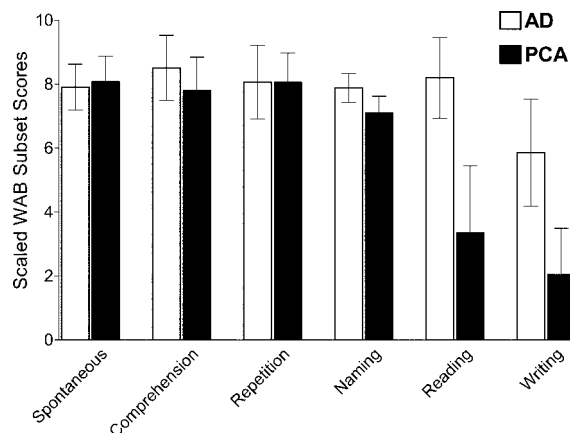


Figure 2. Bar graph showing mean scaled (max = 10) subtest scores on the Western Aphasia Battery (WAB) for patients with posterior cortical atrophy and patients with Alzheimer disease. Error bars indicate 95% CIs for the mean. Patients with posterior cortical atrophy perform worse on reading and writing compared to other language areas.

memory (51.2%). Relatively less impaired were tests of conceptualization (65.4%) and attention (70.5%). Compared with DAT controls (figure 1), the patients with PCA scored lower on tests of construction (PCA 1.6 ± 1.8 vs AD 5.0 ± 1.5 , $p = 0.0001$) and showed a strong trend toward better performance on memory testing (PCA 12.8 ± 6.0 vs DAT 9.4 ± 1.1 , $p = 0.08$).

Performance on the WAB revealed an Aphasia Quotient (AQ) of 75.4 ± 16.3 . Tests of reading (3.3 ± 3.1) and writing (2.0 ± 2.1) revealed the greatest impairment and were lower than all other sections of the WAB (one-way analysis of variance [ANOVA], Tukey post hoc tests, $p < 0.001$). Individual analysis revealed a classification of anomic aphasia in eight, Wernicke's aphasia in three, and conduction aphasia in one. Comparison with DAT controls revealed similar scores in terms of overall AQ as well as subtests of spontaneous speech, naming, comprehension, and repetition (figure 2). The PCA cohort however had poorer performance on tests of reading (PCA 3.3 ± 3.1 vs DAT 8.2 ± 1.6 , $p = 0.0005$) and writing (PCA 2.0 ± 1.3 vs DAT 5.8 ± 2.2 , $p = 0.001$).

Full-scale IQ on the WAIS was 77.9 ± 7.8 with a marked discrepancy between verbal IQ (91.1 ± 9.0) and performance IQ (62.5 ± 7.2 , paired t test, $p < 0.001$). The FBI revealed relatively mild disturbances in behavior at the time of testing and an average score of 12.8 ± 6.8 , which is well within the range usually seen in patients with DAT (<30). One other patient developed behavioral disturbance 4 years after testing and scored 36 on the FBI, which is above the usual cut-off for DAT, however with more negative behaviors than disinhibition.

HVOT showed a graded performance with lowest scores among patients with PCA (6.5 ± 4.9 , $n = 3$), highest scores for normal controls ($n = 18$, 25.8 ± 2.6), and intermediate scores for DAT (14.6 ± 6.3 , $n = 10$). Post hoc tests revealed between-group differences on all comparisons (PCA vs DAT, $p < 0.05$; PCA vs controls, $p < 0.001$; DAT vs controls, $p < 0.001$). We performed baseline tests of tactile and visual naming using 20 objects from the Western Aphasia Battery in patients with DAT and patients with

PCA without a clear visual agnosia. The PCA ($n = 7$) and AD ($n = 11$) groups performed similarly on their ability to name objects presented by touch (PCA, 14.7 ± 4.7 vs DAT, 16.6 ± 4.2 , $p = 0.4$). There was no difference in relative ability to name by touch compared to visual presentation in either PCA ($p = 0.7$) or DAT ($p = 0.8$).

Object, Face and Color Agnosia Screen. Complete OFCAS data were available for 9 of the PCA cohort and 11 patients with DAT (table 2) with both groups matched for disease duration ($p = 0.53$) and MMSE scores ($p = 0.73$) but again the patients with PCA were younger at onset. The face recognition section of the OFCAS was also administered to 18 controls to give an indication of normal performance. Other OFCAS sections were not tested on controls, as we would expect near perfect scores and a ceiling effect. The total OFCAS score (max = 190) was lower for patients with PCA compared to those with typical DAT. Patients with PCA also scored lower on subtests of object and face recognition compared to patients with DAT. No group difference was detected for tests of color recognition. Face recognition for the control group was significantly higher than both patient groups. A cut-off score of 120/190 correctly assigned 2/3 of patients with PCA and 100% of patients with DAT. Logistic regression analysis was performed using age at onset and OFCAS subset scores of object, face, and color recognition as predictor variables. This model accounted for between 52.8% and 70.6% of the variance in-group status with 88.9% of the patients with PCA and 100% of the patients with DAT successfully predicted.

Sub-analysis showed that patients with PCA were similarly impaired in naming living and non-living things (paired t test, $p = 0.35$) while patients with DAT performed better in naming non-living things (paired t test, $p = 0.007$). Within tests of face recognition the patients with PCA performed similarly to patients with DAT on familiar face naming and pointing but both patient groups were impaired compared to normal controls (one-way ANOVA, post hoc Tukey HSD, $p < 0.001$). On tests of facial expression the performance in patients with DAT

Table 2 Comparison of OFCAS scores for PCA, DAT, and normal controls

	PCA	DAT	Controls	p Value
No.	9	11	18	—
Onset age, y, mean ± SD	60.1 ± 6.8	67.4 ± 7.2	—	0.034
Duration, y, mean ± SD	4.8 ± 1.1	4.4 ± 1.4	—	NS
Age, y, mean ± SD	64.8 ± 7.2	71.7 ± 7.6	67.1 ± 7.9	NS
MMSE	14.8 ± 5.6*	15.5 ± 4.2*	29.2 ± 0.8*	<0.001
OFCAS				
Objects	73.4 ± 42.1	116.2 ± 14.2	—	0.005
Faces	12.8 ± 6.2	18.1 ± 6.1	27.8 ± 1.5	<0.001,*† 0.035‡
Colors	25.0 ± 6.7	27.4 ± 3.2	—	NS
Total (max = 190)	111.2 ± 51.8	161.7 ± 19.4	—	0.008

* PCA vs controls.

† DAT vs controls.

‡ PCA vs DAT.

OFCAS = Object, Face and Color Agnosia Screen; PCA = posterior cortical atrophy; DAT = dementia of Alzheimer type; MMSE = Mini-Mental State Examination.

and controls was similar while the patients with PCA performed poorly compared to both the reference (DAT) and control groups (one-way ANOVA, post hoc Tukey HSD, $p < 0.001$). Analysis of the DAT group performance showed a graded performance (repeated measures ANOVA, $p < 0.001$). Facial expression description was better than name picture matching (post hoc Tukey HSD, $p < 0.05$), which in turn was better than famous face naming (post hoc Tukey HSD, $p < 0.01$). Tests of color perception/matching, naming, and color knowledge were similar in PCA and DAT groups (t test, $p > 0.05$).

Complex pictures. Complex picture data were available for 8 patients with PCA and 10 patients with DAT as well as 18 normal controls (table 3). Again, the patients with PCA and patients with DAT were matched for disease duration and MMSE scores; however, in this subgroup there was no difference in age at onset between the patients with DAT and patients with PCA. A cut-off score of 37/78 correctly assigned 80% of each patient group. Logistic regression using each of the individual complex picture scores as predictor variables accounted for 62% to 83% of

the variance and successfully categorized 87.5% of the patients with PCA and 90% of the patients with DAT.

Global vs local processing. Quantitative analysis of Navon figure discrimination revealed the poorest performance in patients with PCA (9.0 ± 1.7 , $n = 4$) and intermediate performance in patients with DAT (22.2 ± 7.4 , $n = 10$) compared to controls (29.0 ± 2.9 , $n = 18$). Post hoc tests showed between-group differences on all comparisons (PCA vs DAT, $p < 0.001$, PCA vs controls, $p < 0.001$, DAT vs controls, $p < 0.01$). Patients with PCA also made errors of local precedence, in other words, consistently identifying only the smaller constituent letters. Cuing in these patients did not change performance and they never reported the global letter even when told it existed or indeed what it was. Patients with DAT tended to make errors of local precedence by failing to recognize the larger letter ($n = 5$) with only one patient showing the reverse pattern. In all DAT cases cuing improved performance. Only one control (MMSE = 27) did not give a perfect score by failing to recognize the smaller letter (error of global precedence) though all errors were corrected with cuing.

Table 3 Comparison of performance in complex picture description for PCA, DAT, and normal control groups

	PCA	DAT	Controls	p Value
n	8	10	18	—
Onset age, y	61.4 ± 5.4	66.7 ± 7.6	—	0.12
Duration, y	4.9 ± 1.8	4.4 ± 2	—	0.65
Age, y	66.1 ± 6.4	71.1 ± 7.7	67.1 ± 7.9	0.31
MMSE	18.0 ± 4.8	15.8 ± 4.8	29.2 ± 0.9	<0.001*†
Complex pictures (max = 78)	27.6 ± 22.4	52.8 ± 15.9	75.1 ± 1.4	<0.001*†‡

Values are mean ± SD.

* PCA vs controls.

† DAT vs controls.

‡ PCA vs DAT.

PCA = posterior cortical atrophy; DAT = dementia of Alzheimer type; MMSE = Mini-Mental State Examination.

Discussion. Visual problems are prevalent in DAT with pathology extending from the anterior visual system causing optic nerve degeneration to higher order centers causing impairment in visuoconstructive tasks, topographic disorientation, and object and face agnosia.^{16,17} Detailed testing reveals deficits in color discrimination, stereoacuity, contrast sensitivity, face recognition, and motion perception,¹⁸ though paradoxically patients with DAT report fewer visual symptoms to physicians compared to other healthy elderly individuals,¹⁹ suggesting these symptoms are relatively mild. In contrast, patients with PCA present with prominent visuospatial symptoms, which are disabling in themselves. While distinctive abnormalities such as Balint's syndrome are recognized in AD, they are rare—one retrospective survey of 2,500 autopsies (diagnoses not specified) from psychiatric and geriatric hospitals in Geneva over 60 years documented Balint's syndrome clinically in just eight patients with pathologically confirmed AD.²⁰

In this study we identified 19 cases with the clinical syndrome of PCA, detailed their clinical and neuropsychological profile, and performed a pilot study using a novel visuospatial battery to compare their performance with a typical cohort of patients with primary amnesic DAT. We found an equal proportion of women to men and an onset of symptoms before the age of 60, which is earlier than typical DAT. The most common features were alexia out of proportion to other language difficulties, agraphia, simultanagnosia, and optic ataxia. A complete Balint's syndrome was detected in five individuals while the full Gerstmann's syndrome was found in three cases. Unilateral neglect and visual field defects were the least common findings overall. None of our patients had early visual hallucinations and parkinsonism to suggest a diagnosis of dementia with Lewy bodies. However, later in the course of their illness, five patients met the McKeith criteria²¹ for probable DLB by the presence of two of the three core features of spontaneous parkinsonism, fluctuations, or visual hallucinations. The presence of prominently asymmetric limb apraxia and alien limb phenomena raise the possibility of CBD, which has been described as both a clinical accompaniment and confirmed pathologic cause of PCA.^{22,23} Despite the presence of additional motor signs these patients with features of DLB and CBD appeared to have otherwise identical cognitive deficits to other patients with PCA on the tests used. Consistent with their symptoms, background neuropsychometry in our PCA cohort revealed the greatest deficiencies in performance IQ and tests of construction with relatively preserved memory compared to patients with DAT, while any behavioral disturbance was mild. The aphasias detected were predominantly mild, fluent, and post-sylvian in nature. Otherwise overall language ability was no different from DAT controls and the majority of patients with PCA were classed as anomic but with disproportionate impairment in

the posteriorly located language tasks of reading and writing. Visual agnosia was a relatively less frequent finding affecting just under half of the PCA cohort and prosopagnosia was detected in a fifth of cases. The duration of illness tended to be longer in those with agnosia compared to those without, suggesting that it develops later than other features of PCA. In addition, the lack of difference in tactile compared to visual naming argues against the presence of a subtle visual agnosia in other patients with PCA. Certainly patients with prominent aphasias were longer into their illness than others (6.1 years vs 3.7 years, *t* test, $p = 0.006$), implying relative preservation of language until later in the course of the illness. While alexia is the most common abnormality and can reflect ventral stream dysfunction, it is important to remember that simultanagnosia, which accompanied alexia in all but two cases, will also seriously disrupt reading abilities in these patients. The almost universal finding of agraphia with alexia also suggests that occipitoparietal rather than occipitotemporal pathology is the substrate for reading difficulties in these patients. Despite these prominent posterior cortical symptoms, most but not all of our cases had clear evidence of corresponding atrophy on CT or MRI, a finding described in other series,^{4,24} casting doubt on the validity of an anatomically derived name for a clinically defined syndrome.

The OFCAS and complex pictures comprise a novel battery designed to offer a quantitative measure of disturbances in posterior cortical areas with elements to reflect both dorsal (complex pictures) and ventral (OFCAS) streams of visuospatial processing. It is straightforward to use and takes approximately 60 minutes to complete. In this series we performed a pilot study to examine the clinical utility of this battery in the two distinct patient groups of PCA and DAT. Matching for disease duration, global cognitive deficits, and language disturbance, the OFCAS detected significantly greater impairment in object and face recognition among the PCA cohort compared to those with DAT. Although not part of our original hypothesis the OFCAS did facilitate comparisons in performance between living and non-living percepts, a frequently described example of category-specific semantic impairment. The sensory-functional theory suggests that each category is identified according to different attributes.²⁵ By this theory living things depend more on their perceptual attributes and visual knowledge for identification than non-living things, which are determined more by their functional properties. One might therefore expect poorer identification of living things among patients with PCA; however, analysis revealed no difference in performance for either category (paired *t* test, $p = 0.35$). An alternative theory using computer simulations has shown that intercorrelated features (such as having gills and having fins) are more often active in the representations of living than non-living things.²⁶ It is also suggested that the concepts represented by these intercorre-

lated features are robust in the face of mild damage but more sensitive to more generalized, severe damage. This model would therefore predict preserved knowledge of living things in early DAT while more advanced disease would see the pattern reversed.²⁷ Consistent with this our DAT cohort, who could be classified as moderately severe, showed poorer identification of living compared to non-living things (paired *t* test, *p* = 0.007).

Face analysis was impaired in patients with PCA but the finding of impaired performance compared to the DAT reference group on tests of facial expression alone with similar scores on pointing and naming suggests a primarily apperceptive deficit in these patients. In contrast, the relative preservation of facial expression detection (scored at normal control levels) in DAT cases with impaired recognition by pointing and naming suggests preserved pre-semantic, perceptual processes.²⁸ Although a slightly more difficult test, the poorer performance on face naming compared to name picture matching suggests an additional impairment in semantic and post-semantic processes involving lexical activation in patients with DAT.²⁹ Tests of color recognition and processing gave similar results in both sets of patients, reflecting the absence of achromatopsia or color agnosia initially in our PCA cohort, again suggesting relative preservation of the inferior occipital region and occipitotemporal junction.³⁰

Similarly, tests of complex picture description showed graded performances, which were best in normal controls, intermediate in DAT, and worst among the PCA cohort. Performance on this test was notable for the slow detection of individual elements of the pictures and poor interpretation of the overall scene, which is typical of simultanagnosia. A subdivision of simultanagnosia has been proposed³¹ along similar lines of dorsal and ventral streams based on cognitive profile and lesion location. Dorsal simultanagnosia is characterized by preserved recognition but the inability to *perceive* more than one object at a time with slowness shifting between them. Ventral simultanagnosia in contrast can *recognize* only one object at a time although other objects are seen. A striking illustration of dorsal simultanagnosia in our patients was their interpretation of Navon letters, which are typically used to demonstrate interhemispheric specialization in global and local processing. From their descriptions during testing it was clear that patients with PCA perceived only one smaller letter at a time and they consistently failed to recognize the global letter even when they were told it existed and even what it was.

Overall, the combination of clinical findings and test results suggest the greatest burden of symptoms in PCA lies in the dorsal stream, consistent with functional imaging studies showing selective hypometabolism of the occipito-parietal regions in this group compared to DAT.³² The clinical deficits then spread to involve the ventral stream and primary visual cortex and forward to perisylvian areas to

cause aphasias as the illness progresses. Also, the clinical profile and performance on testing suggest a distinct syndrome in comparison to DAT with different mechanisms underlying apparently similar deficits, such as recognition of famous faces. Both the OFCAS and complex pictures show distinct levels of performance for each set of patients, which offers a reliable discrimination between patients with PCA and patients with DAT and suggests face validity for these tests as measures of posterior cortical function. They also allow qualitative interpretation of performance, giving insights into the mechanisms underlying the deficits. A limitation of our study is the lack of distinct dorsal and ventral patient groups to allow us to examine the reliability of the OFCAS and complex pictures in distinguishing between dorsal and ventral stream dysfunction. Nonetheless our study offers further evidence for considering PCA as a distinct clinical entity distinguished by its clinical and cognitive profile and also by its younger age at onset. Further testing with the OFCAS and complex pictures in other patient groups is warranted to establish inter-rater and retest reliability and to confirm validity, particularly as a longitudinal measure of decline.

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