Posterior cortical atrophy (PCA) is a neurodegenerative syndrome that is characterized by a progressive decline in visuospatial, visuoperceptual, literacy and praxic skills. The progressive neurodegeneration affecting parietal, occipital and occipito-temporal cortices which underlies PCA is attributable to Alzheimer’s disease (AD) in the majority of patients. However, alternative underlying aetiologies including Dementia with Lewy Bodies (DLB), corticobasal degeneration (CBD) and prion disease have also been identified, and not all PCA patients have atrophy on clinical imaging. This heterogeneity has led to diagnostic and terminological inconsistencies, caused difficulty comparing studies from different centres, and limited the generalizability of clinical trials and investigations of factors driving phenotypic variability. Significant challenges remain in identifying the factors associated with both the selective vulnerability of posterior cortical regions and the young age of onset seen in PCA. Greater awareness of the syndrome and agreement over the correspondence between syndrome-and disease-level classifications are required in order to improve diagnostic accuracy, research study design and clinical management.

Introduction

Posterior Cortical Atrophy (PCA) is a neurodegenerative condition characterised by a progressive, often dramatic and relatively selective decline in visual processing skills and other functions subserved by parietal, occipital and occipito-temporal regions. Age at onset is typically between 50–65 years and the syndrome is associated with a variety of underlying pathologies. PCA has been recognised for more than two decades, and yet the condition is relatively neglected by researchers. Patients often experience a considerable delay in the time to diagnosis owing to the young age at onset and unusual presenting symptoms. In addition, the term PCA has been applied inconsistently, making it difficult to draw comparisons across studies. Whilst there is an increasing move to define neurodegenerative diseases by their underlying pathology, such progress in relation to PCA is limited currently.
by a lack of specificity in the available diagnostic criteria, and a lack of clarity regarding the relationships between PCA and related syndromic classifications such as aphasic, amnestic and dysexecutive AD phenotypes and corticobasal syndrome (CBS).

This review outlines the clinical, psychological, imaging, epidemiological, genetic and pathological features of PCA. We argue that within pathological subgroups, characterising atypical phenotypes such as PCA will enable the identification of biological factors which promote or protect against pathological changes in specific brain networks. Problems with and possible solutions to current diagnostic and terminological conundrums are considered, with particular reference to implications for future clinical and research trial design involving individuals with PCA. We also aim to increase awareness and improve identification of early and unusual symptoms of PCA, and to provide guidance on the provision of support, care and education for patients, carers and healthcare professionals.

History and Definitions

The term PCA was first introduced to describe patients with predominant deficits in higher-order visual processing, a subset of whom also presented with marked atrophy in parieto-occipital areas. The syndrome outlined was consistent with other early reports of patients with similar clinical characteristics. In the absence of histopathological data, Benson et al felt that the clinical presentation was sufficiently distinct from that of Alzheimer's or Pick's disease as 'to warrant classing them separately until definitive pathologic information becomes available'. Subsequent histopathological studies identified AD as the most common underlying pathology, leading to the synonymous use of the terms PCA, 'biparietal AD', and 'visual variant of AD' in some studies. The term 'progressive posterior cortical dysfunction' has also been used to describe the clinical symptoms in these patients in the absence of clear posterior atrophy. However, PCA is also associated with non-AD pathologies (see 'Pathology'), which has led to suggestions for PCA to be considered a distinct nosological entity with its own diagnostic criteria.

Epidemiology

The prevalence and incidence of PCA are currently unknown, and dependent upon the adoption of consistent diagnostic criteria. Furthermore, any figure is likely to be an underestimate because of poor general awareness of the syndrome's existence. However, Snowden et al. found that that 5% of 523 patients with AD presenting to a single specialist cognitive disorders centre had a visual presentation (also labelled posterior cortical atrophy). Age at onset tends to be much earlier in PCA than in typical amnestic AD, with most studies reporting PCA symptom onset in patients' mid 50s and early 60s although some studies have reported a wider age spread (45–74 years). In terms of gender distribution, some studies have reported no difference in the prevalence based on gender whereas others have reported an over-representation among women.

Neuropsychological features

The most frequently cited neuropsychological deficits in PCA are visuospatial and visuo perceptual impairments, alexia and features of Balint's syndrome (simultanagnosia, oculomotor apraxia, optic ataxia, environmental agnosia) and Gerstmann's syndrome (acalculia, agraphia, finger agnosia, left/right disorientation). Working memory deficits and limb apraxia have also been emphasised. Longitudinal studies have shown that anterograde memory, executive functions and linguistic skills, which are sometimes strikingly preserved in the earlier stages of the disease, gradually deteriorate in some patients as they progress to a more global dementia state.
Although higher order visual problems such as object and space perception problems are more commonly reported, many such difficulties are at least partially underpinned by deficits in more basic visual processing (e.g. form, motion, colour, point localisation). In a detailed comparison of basic and higher order perception, all PCA patients demonstrated impairment in at least one basic visual process, emphasising the vulnerability of fundamental aspects of vision associated with occipital cortical dysfunction. This study also revealed specific correlations of basic visual processing with higher-order visuospatial and visuoperceptual skills, but not with non-visual parietal functions (such as calculation and spelling), suggesting the specific involvement of visual networks in PCA.

In combination, the basic and higher order visual deficits in PCA have predictable consequences on performance on general neuropsychological tests, e.g. performance IQ is often up to 30–40 points lower than verbal IQ scores. Performance on cognitive tasks with any significant visual component (e.g. visual memory recall, Trail Making, Stroop test) are vulnerable to impairment and misinterpretation, and thus accurate assessment requires the selection of tasks which minimise visual demands (e.g. auditory-verbal memory tasks, naming from verbal description).

Many patients with PCA also experience unusual symptoms or ‘positive perceptual phenomena’ including abnormally prolonged colour after-images; reverse size phenomena; the perception of movement of static stimuli; and in one case even 180° upside-down reversal of vision (see Figure 1). Reading skills may be limited by numerous processes, including visual disorientation (e.g. getting lost on the page), reverse size phenomena (i.e. accurately perceiving small but not large print), and visual crowding (impaired identification of the constituent individual letters of a word owing to excessive integration of visual features from surrounding letters). The condition may also lead to primary peripheral dyslexias. Anecdotally, individuals with PCA frequently report heightened sensitivity to glare from shiny surfaces, and experience a range of localised sensation and pain phenomena and disturbances of balance and bodily orientation which may potentially be linked to deranged visuo-vestibular interactions.

Questions remain over whether PCA should be considered a unitary clinico-anatomical syndrome or rather a collection of related but distinct syndromic subtypes. Extrapolating from basic neuroscientific evidence of distinct cortical streams which process different types of visual information, it has been suggested that separate parietal (dorsal), occipitotemporal (ventral) and primary visual (striate cortex; caudal) forms of PCA exist. However, these claims are based on findings from single case reports. Subsequent neuropsychological case series studies have failed to find evidence to support a pure ventral stream syndrome, and have revealed considerable overlap in the neuropsychological profiles and patterns of cortical thinning in patients with behaviourally-defined predominant dorsal or ventral stream impairments. Rather, these findings suggest that phenotypic differences may be more appropriately considered to represent points on a continuum of variation within PCA.

Clinical features

The clinical presentation of PCA is influenced by several factors, including the time taken before an individual presents to medical services or is referred to a cognitive specialist; the individual's specific pattern of deficits; in some cases the underlying pathology; and each patient's psychological response to their symptoms. The relative rarity of PCA, the sometimes unusual nature of its symptoms, and the relatively young age at onset leads to misdiagnosis of many patients as depressed, anxious or even malingering in the early stages of the disease. Early anxiety is at least anecdotally a common feature, perhaps reflecting that...
patients with PCA typically have relatively intact insight into there being a problem, even if its nature is unclear. Even to experienced cognitive neurologists, the initial history may be more suggestive of anxiety, until examination reveals impairment referable to parietal and/or occipital lobe function. Patients are frequently first referred to opticians and ophthalmologists believing that an ocular abnormality is responsible for their visual symptoms, sometimes even leading to unnecessary medical procedures such as cataract surgery.

The symptoms reported by a patient with PCA are likely to reflect broadly their individual pattern of neuropsychological impairment. Visual symptoms are perhaps more likely than other posterior deficits to be volunteered, with individuals describing difficulties reading lines of text, judging distances (often leading to repeated minor car accidents or problems parking), identifying static objects within the visual field, or problems with stairs and escalators. Visual symptoms such as light sensitivity or visual distortions may be mistaken for migraine. Careful history taking may reveal some of the more unusual visual phenomena described above, including the presence of prolonged after-images or visual crowding. Individuals may volunteer problems using common objects reflecting dyspraxia, or progressive difficulty with calculations or spelling. The presence of other neurological symptoms, including visual hallucinations (reported in up to 25% of PCA patients)\textsuperscript{19, 21, 43}, and rapid eye movement sleep behaviour disorder may be suggestive of underlying dementia with Lewy bodies (DLB). Very occasionally, there may be a history consistent with occipital lobe seizures.

Careful bedside testing can elicit signs of disproportionate parietal/occipital dysfunction, including but not limited to visual disorientation, difficulties resolving degraded stimuli, ideational and/or ideomotor dyspraxia, dyscalculia, and problems with spelling. The physical examination in most cases of PCA is unremarkable, although in the presence of severe cortical visual problems interpretation of visual acuity and visual fields may be difficult, with hemianopia often misdiagnosed owing to the presence of higher-order visual attentional problems. Finger myoclonus is also not uncommon: Snowden et al. reported similar frequencies of extrapyramidal signs (41%), myoclonus (24%) and grasp reflex (26%) in PCA compared with those found in typical AD\textsuperscript{18}. Nonetheless, the presence of features of clear symmetrical motor parkinsonism (suggestive of Lewy body pathology), or prominent asymmetric myoclonus and dystonia (suggestive of corticobasal degeneration) may give important clues to the underlying aetiology, although there are currently relatively sparse pathological data on which these clinical observations can be confirmed.

**Neuroimaging**

Increasingly sophisticated image analysis tools have been used to localize and quantify (typically group) differences in patterns of atrophy in patients with PCA compared either with controls or with patients with typical AD. Cross-sectional voxel-based morphometry (VBM) has revealed widespread grey matter differences between PCA patients and healthy controls, with the most significant reductions found in regions of the occipital and parietal lobes, followed by regions in the temporal lobe\textsuperscript{24, 30}. Direct comparison between PCA and typical AD using both VBM and cortical thickness measures have demonstrated greater right parietal and less left medial temporal and hippocampal atrophy in PCA. It should be noted that a number of studies report asymmetric atrophy patterns in PCA (R>L), but these differences may reflect selection biases in the diagnosis and recruitment of patients with prominent visual dysfunction. Limited diffusion tensor imaging (DTI) data also suggest PCA reduces the integrity of white matter tracts in posterior brain regions\textsuperscript{44–46}. However, considerable regional overlap in atrophy has also been reported, with regions including the posterior cingulate gyri, precuneus, and inferior parietal lobe being affected in both PCA and
Such findings suggest that PCA, when underpinned by AD, exists on a spectrum of variation with other AD phenotypes. Fluid registration of longitudinally-acquired structural MR images illustrates the evolution of PCA (see Figure 3), with group studies indicating that, by five years symptom duration, atrophy is widespread throughout the cortex including medial temporal lobe structures.

Data from functional imaging studies using single photon emission computed tomography (SPECT) and fluorodeoxyglucose positron emission tomography (FDG-PET) are largely consistent with structural changes in parieto-occipital areas (see Figure 2). In addition to posterior regions, FDG-PET has revealed specific areas of hypometabolism in the frontal eye fields bilaterally which may occur secondary to loss of input from occipitoparietal regions and underpin ocular apraxia in PCA. A limited number of studies have also assessed patterns of amyloid deposition using Pittsburgh compound B (PIB)-PET in PCA. Single case studies and small series have reported increased Aβ accumulation predominantly in the occipital and parietal lobes relative to individuals with typical AD. However, two studies that compared PIB uptake in larger groups of PCA patients to typical AD reported that there was no significant difference in amyloid deposition between PCA and typical AD, with both groups showing diffuse PIB uptake throughout frontal, temporoparietal and occipital cortex (see Box 1).

**Genetics**

To date there have been no reports of a PCA phenotype associated with autosomal dominant familial AD, but a recent case series described the PCA syndrome in familial prion disease associated with 5-octapeptide insertion into the prion protein (5-OPRI). Available PCA case series suggest that there is no significant difference in the number of patients with a positive family history of dementia in PCA compared with typical AD. Some studies have found significant differences in apolipoprotein E (ApoE) genotypes in patients with PCA versus amnestic AD. Other studies, however, have reported no difference in ApoE between PCA and typical AD (see also for estimates in typical AD, and for healthy controls; see Table 1 for a summary ApoE ε4 prevalence data in PCA, AD and controls). Discrepancies between these studies may reflect differences in factors such as inclusion criteria used to define PCA and typical AD, and age at onset. In particular the lack of pathological confirmation is a major limitation in these studies; questions remain as to whether ApoE ε4 drives the degenerative pattern in patients with AD (i.e. to or away from medial temporal structures); whether the lower frequency of ApoE ε4 in PCA seen in some studies is due to patients with non-AD pathology; or whether different (as yet unrecognised) genetic factors underlie PCA compared to typical late onset AD. Studies using larger sample sizes, consistent definitions of PCA, and post-mortem confirmation of diagnosis will be required to obtain more conclusive results; it will be of considerable interest to assess the frequencies of other genetic risk factors for sporadic AD determined in genome wide association studies.

**Pathology**

Pathological studies have all shown that AD is the most common underlying cause of PCA. However, a small number of cases are attributable to other aetiologies such as corticobasal degeneration (CBD), prion disease (including CJD and familial fatal insomnia), and subcortical gliosis. In the largest series to date, Renner et al. reported pathological data of 21 PCA patients of whom 13 (62%) had AD, 2 had AD-Lewy Body variant pathology (10%), 1 had AD with coexisting Parkinson's disease (5%), 1 had DLB with coexisting subcortical gliosis (5%), 2
had CBD (10%), and 2 had prion disease (10%, CJD and FFI)\textsuperscript{15}. Tang-Wai et al. reported 7/9 (78%) PCA patients had AD pathology, whereas the remaining 2 (22%) had CBD\textsuperscript{21}.

Although the patterns of the distribution of pathology has been shown to be different in PCA compared with typical AD, the exact pattern of the pathological changes is inconsistent and based on very small numbers of cases. Some studies have demonstrated differences in both plaques and neurofibrillary tangles between PCA and typical AD\textsuperscript{10, 12, 72}, whereas others have found no differences in plaque distribution\textsuperscript{15, 21}. For example, Levine et al. reported the pathological findings of 1 PCA patient who showed greatest density of senile plaques and neurofibrillary tangles in occipitoparietal regions, and lowest density in frontal lobe regions\textsuperscript{10}. Hof et al. reported similar findings with plaques and tangles found predominantly in primary visual and visual association areas around the occipito-parieto-temporal junction, whereas frontal regions such as the prefrontal cortex showed very low densities of pathological changes\textsuperscript{72, 73}. In contrast, Tang-Wai et al. compared pathological changes in 9 PCA patients with 30 typical AD patients. The PCA group showed significantly higher density of neurofibrillary tangles in visual and visual association cortices and fewer tangles and senile plaques in the hippocampus and subiculum. However, density of senile plaques in other cortical areas was comparable in both groups\textsuperscript{21}. Reasons for the discrepant findings in these autopsy studies may include differences in inclusion criteria and demographic characteristics (such as age and disease severity) as well as differences in the methods used to quantify the pathological changes (such as different staining techniques, and discrimination between diffuse and neuritic plaques).

Studies assessing CSF biomarkers (A\beta\textsubscript{1–42}, T-tau and P-tau\textsubscript{181}) have reported similar findings in PCA compared with AD\textsuperscript{27, 56, 60, 74}, supporting previous reports that PCA is typically associated with underlying AD pathology.

### Diagnostic and research criteria

Two sets of diagnostic criteria for PCA have been proposed\textsuperscript{17, 21}. Proposed core features for a diagnosis of PCA include: (i) insidious onset and gradual progression; (ii) presentation of visual deficits in the absence of ocular disease; (iii) relatively preserved episodic memory, verbal fluency and personal insight; (iv) presence of symptoms including visual agnosia, simultanagnosia, optic ataxia, ocular apraxia, dyspraxia and environmental disorientation; and (v) absence of stroke or tumour. Supportive features include alexia, ideomotor apraxia, agraphia, acalculia, onset before the age of 65 years and neuroimaging evidence of posterior cortical atrophy or hypoperfusion.

Whilst these criteria have proved useful in a number of clinical and research contexts, they are based on clinical experience at single centres and have not been validated more widely. In the absence of objective evidence linking clinical phenotype to underlying pathology, there continues to be inconsistency, with the term PCA being used as a descriptive, syndromic term and as a diagnostic label. Such inconsistencies present a number of problems in the evaluation of differential diagnoses and particularly in the design and interpretation of research studies and clinical trials. First, whilst a syndromic classification may be adequate for some types of research study (e.g. brain-behaviour, behavioural intervention), other investigations require direct consideration of the likely underlying pathology (e.g. clinical trials of disease-specific medicinal products). Second, there is currently no evidence base on which to adjudicate whether pharmacological treatments for AD are effective in individuals with PCA attributable to probable AD, or whether individuals with PCA should be included/excluded from conventional AD clinical trials (e.g. because of the potential unsuitability of study outcome measures [e.g. visual memory tasks] selected for patients with more typical amnestic or global clinical presentations). Third,
current criteria provide no guidance as to the degree of specificity required for a diagnosis of PCA. For example, in the relatively large series reported by Renner et al (2004), 9/27 patients presented with the PCA syndrome as a relatively isolated disorder, whereas in 18/27 it was the prominent feature of a more generalised dementia\textsuperscript{15}. A number of studies have suggested PCA, where attributable to probable AD, lies on a phenotypic continuum with other typical and atypical AD phenotypes (e.g. amnestic AD, global cognitive impairment, logopenic/phonological aphasia)\textsuperscript{18, 23, 32}, but the boundaries between such phenotypes are defined imprecisely. Fourth, the 'presentation of visual complaints' is a core feature of existing criteria but some patients with neurodegenerative conditions present with predominant impairment of other posterior cortical functions such as calculation, spelling and praxis\textsuperscript{6, 18, 27, 48, 75}; such individuals could be considered to fall within the PCA spectrum. Fifth, the value of biomarkers may differ in PCA compared to typical AD or DLB (e.g. relative absence of hippocampal atrophy). This is particularly important given the increasing incorporation of such biomarkers in disease-specific diagnostic criteria\textsuperscript{76, 77}.

Future resolution of these issues and development of clinical and research criteria for the definition of PCA are likely to require consensus opinion from multiple specialist centres supported by objective evidence of the relationship between clinical presentation, neuroimaging and CSF biomarkers, and histopathological data. Establishing the relative likelihood of different pathologies in large, multi-centre datasets would improve the discrimination of potential disease subtypes necessary for trials involving disease-modifying compounds. One possible approach would be to apply a range of criteria to a multi-centre dataset to determine sets of inclusion/exclusion criteria which identify specific disease subgroups (e.g. PCA-AD). Consensus criteria might also investigate frameworks for operationalising criteria in terms of a quantifiable set of diagnostic markers, for the purpose of determining entry into research studies and to improve comparability of data between institutions.

Management

Although there are no published reports that assess the effectiveness of acetyl cholinesterase inhibitors (e.g. donepezil, rivastigmine and galantamine) in PCA, these are frequently, and (given that AD is statistically the most likely underlying pathology) in our view appropriately, administered. Clinical experience and limited single case reports suggest some clinical benefit\textsuperscript{78}, most likely in patients with underlying AD or DLB pathology. It may also be appropriate to consider anti-depressant medication in patients with persistent low mood, and levodopa/carbidopa trials in patients with parkinsonism.

Due to poor awareness of the syndrome's existence, patients with PCA often receive limited or inappropriate care and advice, catering to problems which are less significant to the individual (e.g. memory problems) whilst critical perceptual difficulties (e.g. many activities in day centres and nursing homes are visually mediated) are often not considered. The relative preservation of skills such as memory, language and insight in PCA, especially in the mild to moderate stages of the disease, enable patients to take advantage of peer support meetings and group, couple and individual psychological therapies where the need exists. Support group meetings are particularly useful for reducing social isolation, sharing of the experience of what is often a particularly long and difficult route to diagnosis, and for exchanging practical tips and coping strategies and advice. Patients with PCA often benefit from resources designed primarily for the blind and partially sighted, such as mobile phones with simplified displays, voice recognition software, talking books and watches, culinary aids, and lamps to increase ambient light levels in the home. Referral to an occupational therapist or sensory team may be appropriate to help maximise function. It may also be necessary for an individual to be referred to an ophthalmologist in order to register as
partially sighted under statutory invalidity schemes, which may provide access to financial and social benefits and services. Driving a car is clearly not appropriate for many patients with PCA, and particularly those with prominent visual disturbance. Physical therapy can also be helpful for patients with parkinsonism and gait disturbance. Little empirical evidence exists examining the impact of management strategies in PCA, but a rehabilitation programme which included psychoeducation, compensatory strategies, and cognitive exercises was tested in a single individual with PCA, resulting in small improvements in visuo-perceptual functioning.

Conclusions

Posterior cortical atrophy is a debilitating and under-recognised focal degenerative syndrome which is associated with a range of different disease pathologies. The core features of the syndrome are sufficiently homogeneous to justify considering PCA an independent nosology, with AD as the most common underlying cause. However a lack of consistency in the classification of PCA is likely to continue unless diagnostic criteria and terminology are standardized. The proposed criteria in this review attempt to take both the clinical and histopathological features of PCA into account, and to introduce quantifiable behavioural inclusion criteria for research studies involving PCA. Better understanding and awareness of the syndrome among the medical and lay communities is necessary to improve diagnosis, treatment and support services provided to individuals with PCA and their families. Dissecting out the distinctive patterns of structural, functional, cognitive and genetic changes in PCA may lead to new insights into the pathogenesis and clinical features of typical AD, and to more general mechanisms of visual network function and degeneration. Dedicated trials are needed to assess the effectiveness of pharmacological and non-pharmacological interventions in PCA, and to identify factors driving phenotypic variability in this small but significant population of patients typically with early onset dementia.

Acknowledgments

This work was undertaken at UCLH/UCL who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centres funding scheme. The Dementia Research Centre is an Alzheimer's Research UK Co-ordinating Centre and has also received equipment funded by the Alzheimer's Research UK. SC is supported by an Alzheimer's Research UK Senior Research Fellowship and Equipment Grant; ML is supported by the Alzheimer's Society; JMS is a UK HEFCE Clinical Senior Lecturer and receives grant support from Alzheimer's Research UK; GDR receives research support from the NIH [NIA K23-AG031861 (PI)]; the Alzheimer's Association, and the John Douglas French Alzheimer's Foundation; NCF is supported by an MRC (UK) Senior Clinical Fellowship, and MNR and NCF hold National Institute for Health Research (NIHR) Senior Investigator awards.

Reference List


Search strategy and selection criteria

References for this Review were identified through searches of PubMed with the search terms “Posterior Cortical Atrophy”, “biparietal Alzheimer’s disease”, “visual dementia”, and “Balint’s syndrome dementia” for articles published between 1970 and November 2011. Articles were also identified through searches of the authors’ own files. Only papers published in English were reviewed, with the exception of historical manuscripts (pre-1988). The final reference list was generated on the basis of originality and relevance to the broad scope of this Review.
Panel: case study

A 62 year-old right-handed woman with four years of progressive visuospatial dysfunction. Her first symptom was difficulty seeing when driving at night. In the following years she frequently “dented” her car when parking, tended to “bump” into doors on her right side and had trouble locating items even when they were directly in front of her. She reported problems reading, trouble distinguishing between currency bills and difficulty deciding whether to push or pull a door in order to open it. When she watched television, images appeared to “move slowly.” She was referred to the cognitive neurology clinic by an ophthalmologist who had ruled-out primary ocular disease. On neurologic evaluation she was fully oriented and was an excellent historian. On visual fields testing she was inconsistent counting fingers in the right hemifield. Pupillary responses and extraocular movements were normal, though she was slow initiating saccades and had difficulty reaching for items under visual guidance. Her physical neurologic examination was otherwise normal. On cognitive testing MMSE was 26/30, and she showed severe impairment when copying intersecting pentagons and the Benson figure (Figure 2A). She was able to name colours correctly but showed moderate difficulty matching faces. She had severe difficulty reading, which was improved by spelling words out loud, and had mild deficits in confrontation naming (improved with cues) and category fluency. Verbal memory, phonemic fluency and attention were intact. She could not complete many tasks due to visual dysfunction. Brain MRI showed marked atrophy in bilateral parietal, posterior temporal and lateral occipital cortex (Fig 2B, top row), and FDG-PET (Fig 2B, middle row) showed hypometabolism in the same regions, left worse than right. Frontal cortex, medial temporal cortex and hippocampus were spared. PIB-PET showed diffuse cortical uptake throughout posterior and anterior cortical regions alike (Figure 2B, bottom row), consistent with underlying amyloid-beta plaques.
Figure 1.
Visual dysfunction in posterior cortical atrophy. Individuals with posterior cortical atrophy have difficulty identifying objects and faces, particularly when they consist of many parts or are viewed from an unfamiliar (non-canonical) perspective. Eye-tracking studies contrasting scene perception in healthy individuals (A) and people with posterior cortical atrophy (B) suggest that patients have poor top-down guidance and control of oculomotor function. Circles represent fixation locations and circle size represents fixation duration. Patients with posterior cortical atrophy fixate prominent features initially (e.g., dome on pier), but subsequently fixate relatively uninformative aspects of the scene (e.g., sea or sky) and miss important contextual details (e.g., beachfront or near the end of the pier). Images from Tim Shakespeare and Sebastian Crutch (unpublished).
Figure 2.
Neurological testing (A) and brain imaging (B) of a 62-year-old woman with visuospatial dysfunction. Images are in neurological orientation. See the panel for a description of the case history and imaging findings.
Figure 3.
Registered serial MR images showing axial views of an individual with PCA at four time points (ages 59–63 years old). Repeat scans were fluid-registered to the baseline image and colour-coded voxel-compression maps were produced. The scale shows the percentage volume change per voxel (−20 to 20%) with green and blue representing contraction and yellow and red representing expansion.
Table 1

Overview of prevalence of ApoE ε4 in PCA, AD and controls. Shown are data from 7 studies that have reported ApoE ε4 frequency in PCA, and compared these with typical (or sporadic) AD and controls.

<table>
<thead>
<tr>
<th>Study</th>
<th>PCA</th>
<th>AD</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total N</td>
<td>Age at onset</td>
<td>ApoE ε4-frequency</td>
</tr>
<tr>
<td>Mendez et al. 2002</td>
<td>15</td>
<td>58.2 (5.1)</td>
<td>8</td>
</tr>
<tr>
<td>Tang-Wai et al. 2004</td>
<td>40</td>
<td>60.5 (8.9)</td>
<td>27</td>
</tr>
<tr>
<td>Schott et al. 2006*</td>
<td>10</td>
<td>56.1 (4.1)</td>
<td>10</td>
</tr>
<tr>
<td>Snowden et al. 2007*</td>
<td>24</td>
<td>58.0 (4.0)</td>
<td>-</td>
</tr>
<tr>
<td>Migliaccio et al., 2009</td>
<td>14</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td>Baumann et al. 2010</td>
<td>9</td>
<td>56.7 (7.6)</td>
<td>9</td>
</tr>
<tr>
<td>Rosenbloom et al. 2011</td>
<td>12</td>
<td>57.5 (7.4)</td>
<td>9</td>
</tr>
</tbody>
</table>

*reported significant difference in ApoE ε between PCA and AD
†Farrer et al. 1997
‡Saunders et al. 1993
¶Pendleton et al. 2002
§for whole PCA and AD groups, age at onset for subsample of patients with ApoE unknown, except Schott et al. and Baumann et al.
¥amnestic AD; proportion ε4-positive in memory/semantic AD group = 80