Received: 25 January 2023 | Revised: 19 July 2023 | Accepted: 31 July 2023

DOI: 10.1002/dad2.12474

Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Consensus recommendations for clinical assessment tools for the diagnosis of posterior cortical atrophy syndrome from the Atypical AD PIA of ISTAART

Victoria S. Pelak[1] | David F. Tang-Wai[2] | Bradley F. Boeve[3] | Femke H. Bouwman[4] | Jonathan Graff-Radford[3] | Gil Rabinovici[5] | Samantha K. Holden[6] | Ryan A. Townley[7] | Gregory S. Day[8] | Jennifer Whitwell[9] | Rik Ossenkoppele[4,10] | Baayla D. C. Boon[11] | Deepti Putcha[12] | Chiadi U. Onyike[13] | Heather Snyder[14] | Sebastian Crutch[15] | Keir X. X. Yong[15]

[1]Departments of Neurology and Ophthalmology, University of Colorado School of Medicine, Aurora, Victoria, Colorado, USA

[2]Department of Medicine (Neurology), University of Toronto, Toronto, Canada

[3]Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA

[4]Department of Neurology, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

[5]Department of Neurology, University of California San Francisco, San Francisco, California, USA

[6]Department of Neurology, University of Colorado School of Medicine, Aurora, Colorado, USA

[7]Department of Neurology, University of Kansas School of Medicine, Kansas City, Kansas, USA

[8]Department of Neurology, Mayo Clinic Jacksonville, Jacksonville, Florida, USA

[9]Department of Radiology, Division of Neuroradiology, Mayo Clinic, Rochester, Minnesota, USA

[10]Clinical Memory Research Unit, Lund University, Lund, Sweden

[11]Department of Neuroscience, Mayo Clinic Jacksonville, Jacksonville, Florida, USA

[12]Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

[13]Department of Psychiatry, Johns Hopkins Medicine, Baltimore, Maryland, USA

[14]Medical & Scientific Relations, Alzheimer's Association, Chicago, Illinois, USA

[15]UCL Queen Square Institute of Neurology, Dementia Research Centre, London, UK

Correspondence
Victoria S. Pelak, Departments of Neurology and Ophthalmology, University of Colorado School of Medicine, Academic Office 1, Mailstop B-185, 12631 East 17th Avenue, Aurora, CO 80045 USA.
Email: Victoria.Pelak@CUAnschutz.edu

Funding information
John and Joanne Hare Fund

Abstract

INTRODUCTION: Delay in diagnosis of posterior cortical atrophy (PCA) syndrome is common, and the lack of familiarity with assessment tools for identifying visual cortical dysfunction is a contributing factor. We propose recommendations for the approach to the evaluation of PCA clinical features during the office visit, the neuropsychological evaluation, and the research setting. A recommended screening battery for eye clinics is also proposed.

METHODS: Recommendations were developed using results from a web-based survey of members of Alzheimer's Association International Society to Advance Alzheimer's

Research and Treatment (ISTAART) Atypical Alzheimer's Disease Professional Interest Area (PIA), literature review, and consensus by the PCA assessment working party of the Atypical Alzheimer's Disease PIA.

RESULTS: Survey results revealed robust agreement for assessment tool preferences for PCA features, and many respondents indicated that they reserve assessment tools for use only when PCA is suspected. For some PCA features, curated tools were preferred over validated battery tools, particularly for the office visit. Consensus recommendations superseded survey preferences for two core cognitive features within the 2017 PCA diagnostic criteria.

DISCUSSION: These consensus recommendations provide an evaluation framework for PCA clinical features and can facilitate timely and accurate recognition and diagnosis of PCA. Broader use of these tools should be sought, and development and validation of novel PCA clinical outcome assessments are needed to improve our understanding of atypical AD and other dementias and support the inclusion of those with PCA in treatment trials.

KEYWORDS
Alzheimer's disease, assessment tools, Atypical Alzheimer's Disease Professional Interest Area, clinical outcome assessments, PCA clinical features, posterior cortical atrophy

1 | BACKGROUND

Posterior cortical atrophy (PCA) is a clinical-radiological syndrome defined principally by clinical and cognitive features of posterior cortical dysfunction and supported by posterior cortical neuroimaging features of atrophy and/or hypometabolism and/or hypoperfusion. Prospective neuropathological[1–3] and biomarker[4–6] studies have reported evidence of Alzheimer's disease (AD) pathology in most cases, although other pathologies can cause or contribute to PCA, including Lewy body pathology, corticobasal degeneration, and prion disease. The preponderance of PCA recognized as arising from AD is reflected in early descriptions of "progressive visuospatial dysfunction," the "visual variant of AD," "visual-spatial AD," or "biparietal" AD.[7,8] Core features of the PCA syndrome include deficits of space and object perception, elements of Balint and Gerstmann syndrome, apraxia, environmental agnosia, alexia, and homonymous visual field defects, with relative preservation at the onset of anterograde memory, language and executive functions, and behavior and personality.[2,7,9]

Despite increased awareness and attention advanced by the publication of PCA syndrome-defining criteria in 2017,[7] the clinical diagnosis of PCA is often delayed for months or years after initial presentation. Several factors contribute to the delay. First, the unique nature of visual symptoms is difficult for individuals to fully articulate to their health care providers, and ocular disease is usually suspected as the cause. This can lead to repeated trips to eye specialists and changes in eyeglass prescriptions[8] or other approaches that do not improve the visual symptoms. Next, posterior cortical impairment is challenging to identify using traditional cognitive assessment tools.[7,8] Finally, the medical community lacks familiarity with the limited set of assessment tools available for the evaluation of posterior cortical functions.

This work aims to address gaps in familiarity with tools for assessment by providing recommendations for tools to assess PCA clinical features in the clinical and research settings. In addition to increasing awareness, an evaluation framework can facilitate research to advance our understanding of PCA and the mechanisms that drive clinical heterogeneity of disease expression. To accomplish these aims, members of the Atypical AD Professional Interest Area (PIA) of the International Society to Advance Alzheimer's Research and Treatment (ISTAART) were surveyed, and a PCA assessment working group developed consensus recommendations based on survey results and expert opinion. This work follows the model previously employed for the development of the 2017 PCA diagnostic consensus criteria[7] by a PCA working group that ultimately established the Atypical AD PIA.

The purpose of this report is to describe the methods, results, and consensus recommendations for PCA assessment in three settings: office visits (i.e., physician or provider's clinic visit), neuropsychology evaluations, and research studies, and we also propose recommendations for a rapid screening battery for use in eye care clinics (i.e., offices of ophthalmologists and optometrists), since visual acuity is not affected early in the course of PCA

2 | METHODS

2.1 | Survey design

We developed a web-based survey to capture preferences by ISTAART Atypical AD PIA members for the clinical approach, tasks, tests,

tools, and stimuli (henceforth referred to as "assessment tools") in the evaluation of PCA clinical features in three settings: the office visit, neuropsychology evaluation, and research studies. Information regarding respondent background and experience assessing and caring for people with PCA was also captured. For the full survey, see Supplemental Material.

The assessment tools listed in the survey were selected by a core group of experts (V.P., D.T.W., S.C., B.B., C.O., and K.Y.). Survey items sought responses regarding preferences for assessment tools for 12 of 16 core features of PCA as delineated in the 2017 PCA diagnostic criteria (see Table 1).[7] Four core features were not included because they rely on the neurologic examination (oculomotor apraxia, optic ataxia, and limb apraxia [non-limb kinetic]) or history (dressing apraxia). The survey included questions concerning non-criteria specified PCA clinical features of impaired dominant parietal skills related to spelling, gestures, and digit span; early visual (cortical) processing deficits (i.e., shape discrimination, shape detection, and size discrimination); visual crowding; and central achromatopsia.

Write-in options and "free text" comment sections were available. The frequency of use for each preferred assessment tool could be indicated by the respondent using one of the following designations: almost always (>90%), frequently (>50 to 90%), occasionally (20% to 50%), rarely, or never.

We included additional questions regarding preferences for evaluating global cognition and cognitive domains and functions that initially exhibit relative sparing in PCA. We also included quesitons related to the respondent's approach to examining ocular structures, early visual pathway functions (such as visual acuity, visual field, and pseudoisochromatic color vision testing), as well as early visual (cortical) processing, including shape detection, shape discrimination, and size discrimination.

2.2 | Statistical analysis

Analysis of the frequency of use of tools to assess space perception versus object perception deficits was performed using the T-test, to evaluate differences in assessment frequencies for dorsal visual pathway (occipitoparietal) and ventral visual pathway (occipitotemporal).

2.3 | Survey of ISTAART Atypical AD PIA members

Consent Statement: The study was approved by the Colorado Multiple Institutional Review Board (COMIRB) and consent was not required.

Invitation to take the online survey was distributed to the members of the ISTAART Atypical AD PIA ($N = 538$ members at that time). Survey data were collected anonymously using a web-based application (Research Electronic Data Capture) that is Health Insurance Portability and Accountability Act (HIPAA) compliant. The survey was available for 3 months between (approximately) August 1, 2020, and November 1, 2020).

RESEARCH IN CONTEXT

1. **Systematic review**: The authors identified the need for a common framework for posterior cortical atrophy (PCA) feature assessment through discussions at business meetings of the Atypical Alzheimer's Disease (AD) Professional Interest Area. A literature review (PubMed) revealed a lack of data regarding validation of assessment tools for use in PCA.
2. **Interpretation**: Data from a survey of the Atypical AD PIA membership show clear preferences and robust agreement for preferred clinical assessment tools for PCA clinical features. Based on survey results and expert consensus, a PCA Assessment working group from the Atypical AD PIA provides recommendations for assessment tools for PCA features, including each of the core cognitive features in 2017 PCA criteria, and a rapid screening battery for cortical visual dysfunction for use in eye clinics.
3. **Future directions**: Development and validation of clinical outcome assessments for PCA are needed for accurate prognosis, management, and clinical trial inclusion of those with PCA.

2.4 | Formation of the PCA assessment working group

The PCA assessment working group was formed by members of the Atypical AD PIA who responded to an invitation to participate and by past and current members of the Atypical AD Executive Board.

3 | RESULTS

3.1 | Survey respondents: background and general approach

Fifty-five members (10.2%) of the ISTAART Atypical AD PIA completed the survey, and respondent background and preferences for the general approach to PCA clinical feature assessment are described in Table 2. Seventy percent of all respondents were in practice for more than 10 years, most were neurologists (60%), and the majority had assessed and/or cared for at least five people with PCA in the prior 2 years.

When PCA is suspected, 75% of respondents indicated a reliance on assessment tools that they do *not* routinely use to assess other individuals with cognitive impairment. Forty percent of respondents reported that before cognitive evaluation in those suspected of having PCA, they do not personally evaluate, or request evaluation by an eye

TABLE 1 Summary of the diagnostic criteria and consensus classification for posterior cortical atrophy [7].

Core PCA syndrome features (all 3 must be present)	Insidious onset, gradual progression, prominent early disturbance of visual functions, other posterior cortical functions, or both
Core PCA cognitive features (at least 3 must be present as an early or presenting feature)	1. Space perception deficit 2. Simultanagnosia 3. Object perception deficit 4. Constructional dyspraxia 5. Environmental agnosia 6. Alexia 7. Left/right disorientation 8. Acalculia 9. Apperceptive prosopagnosia 10. Agraphia 11. Homonymous visual field defect 12. Finger agnosia *13. Oculomotor apraxia *14. Optic ataxia *15. Limb apraxia (not limb-kinetic) *16. Dressing apraxia *Features not included in the survey
Core PCA neuroimaging features (supportive of diagnosis)	Prominent occipitoparietal or occipitotemporal atrophy or hypometabolism or hypoperfusion on MRI, FDG-PET, or SPECT
Other cognitive domains (all must be evident)	Relatively spared: anterograde memory function, speech and non-visual language functions, executive functions, and behavior and personality
Exclusions	Unable to explain symptoms based on the following: afferent visual dysfunction, afferent visual lesions, vascular lesions, brain tumor or other mass lesions, or any other causes

Abbreviations: FDG-PET, Fludeoxyglucose (18F)-positron emission tomography; MRI, magnetic resonance imaging; PCA, posterior cortical atrophy; SPECT, single photon emission computed tomography.

specialist, of ocular structures or early visual pathway functions that include the funduscopic examination, visual acuity, perimetric visual field assessment, pseudo-isochromatic color vision testing, shape and size discrimination, and shape detection. Among the 60% of respondents who do assess ocular structures and early visual functions, or rely on others to do so, most indicated that visual acuity for each eye is tested (81.8%), followed by shape discrimination testing (54.5%), pseudo-isochromatic color plate testing (i.e., Ishihara) (48.5%), funduscopic examination (45.5%), perimetric visual field testing (36.4%), shape detection testing (30.3%), and size discrimination testing (30.3%).

3.2 | Survey results

3.2.1 | Agreement on preferred assessment tools

For nearly all PCA features and all settings, there was clear agreement on the first and second preferences for assessment tools. (See Table S1 for the top-ranked assessments.) *Office setting*: there was a separation between the second preference and the next ranked option by 1 to 18 respondents, except for *object perception* impairment, which had two options ranked after the first preference with an equal number of respondents. *Neuropsychological evaluation setting*: there was a separation by one to five respondents between the second-ranked option and next ranked option for all features except *early visual processing deficits* (five respondents for each option after the first ranked preference), and *alexia* (six respondents each for two options after the first ranked option). *Research setting*: there was no separation between the top three options for *simultanagnosia* and *object perception deficit*, whereas all other features had separation by one or two respondents between the first and the next preferred options.

3.2.2 | Preferences for assessment tools

For the evaluation of several PCA clinical features, more respondents preferred curated stimuli over any single stimulus or assessment tool from a validated battery, such as the Visual Object and Space Perception Battery (Warrington E.K., James M. (1991) Bury St Edmunds, England: Thames Valley Test Company) or from a standardized battery, such as the Cortical Vision Screening Test (https://www.corvist.org/). This was true for the office visit setting for *space perception deficit*, *simultanagnosia*, *object perception deficit*, *alexia*, *early visual (cortical) processing deficits*, and *central achromatopsia*. For the neuropsychology setting, more respondents preferred curated stimuli over any validated battery stimulus for *alexia* and *central achromatopsia*, whereas preferences for curated versus standardized battery stimuli were equal for *early visual (cortical) processing deficits*. (See Table S2.)

TABLE 2 Survey respondent background and response to general approach for posterior cortical atrophy assessment.

Survey question (paraphrased if necessary)	Total respondents (% of total responding to question)
Total completing the survey	55
What is your specialty?	
Neurologist	33 (60%)
Psychiatrist	3 (5.5%)
Neuropsychologist	10 (18.2%)
Geriatrician	3 (5.5%)
Research scientist with patient contact	6 (10.9%)
Research scientist without patient contact	0
How many years in practice?	
1–4	8 (16%)
5–10	7 (14%)
>10	35 (70%)
How many PCA patients have you cared for and/or assessed in past 2 years?	
0	4 (7.3%)
1–4	21 (38.2%)
5–10	14 (25.5%)
>10	16 (29.1%)
If PCA is suspected, do you use tasks and tests you do not always use for cognitive assessments?	
Yes	42 (75%)
No	14 (25%)
Do you or an allied health professional assess early visual pathway function before proceeding with more complex visual pathway testing?	
Yes, I complete all early visual pathway testing	8 (14.6%)
Yes, an ophthalmologist or optometrist completes some or all early visual pathway testing	13 (23.6%)
Yes, the assessment is completed by me and an ophthalmologist or optometrist	12 (21.8%)
No, early visual pathway function assessment is not completed prior	22 (40%)

3.2.3 | Frequency of use for preferred assessment tools

More than 50% of respondents indicated that they use preferred assessment tools "almost always (>90%)" or "frequently (50% to 90%)," in at least one setting, for the following PCA features: *space perception deficit* (65.7% of respondents), *simultanagnosia* (69.5%), *constructional dyspraxia* (84.8%), *alexia* (69.9%), *right/left disorientation* (93.0%), *acalculia* (63.8%), *agraphia* (88.5%), *homonymous hemianopia* (57.1%), and *finger anomia* (71.7%). Less than 50% of respondents reported using their preferred assessment tools "*almost always*" or "*frequently*" for *object perception* (45.4%) and *apperceptive prosopagnosia* (37.7%). More respondents reported using their preferred tools "always or frequently" for space perception assessments compared to object perception assessment (58.1% vs 37.4%, $p < 0.001$), whereas more respondents reported using preferred tools "occasionally or rarely" for assessing object perception compared to space perception (32.2% vs 62.6%, $p < 0.00001$) (see Figure 1).

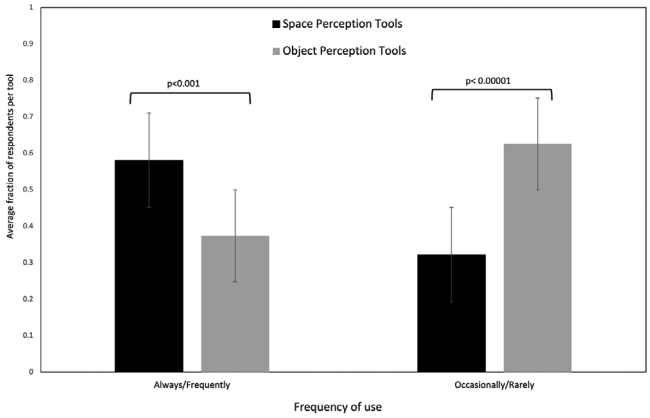


FIGURE 1 Frequency of use of preferred tools for space and object perception assessment. Data reveal that more respondents use their preferred tools for space perception assessment "always or frequently" than for object perception assessment. In turn, more respondents use preferred object perception tools "occasionally or rarely" compared to use of preferred space perception tools.

For PCA non-criteria features, preferred assessments tools were "almost always or frequently" used by more than 50% of respondents for *other dominant parietal dysfunction* (85.9%), whereas less than 50% of respondents indicated "almost always or frequently" for preferred tools for *central achromatopsia* (45%), *early visual (cortical) processing deficits* (48%), and *visual crowding* (32.3%).

3.3 | Consensus for PCA assessment working group recommendations

3.3.1 | Meetings and discussions

The first PCA working group meeting was held virtually (December 2020, Total $N = 13$ participants) and featured an open discussion of goals and priorities. Topics included inherent and practical challenges associated with PCA assessment, priorities for assessment (diagnostic and prognostic, phenotyping, validation, and outcome measures), limitations of existing tools, proprietary issues, and time constraints for testing. At a follow-up meeting (March 2021, Total $N = 17$ participants) survey results were reviewed further and the plan for finalizing recommendations was made. It was agreed that shared resources for PCA assessment tools were important.

The working group acknowledged the resourcefulness of clinicians and emphasized the need to avoid being overly prescriptive.

Other themes discussed were the gap in data regarding assessment tool sensitivity and specificity and the need for further investigations, particularly for staging and longitudinal assessments. The group acknowledged that the inclusion of people with PCA in treatment trials will ultimately depend on validated clinical assessments tools and a need for the development and validation of clinical assessments to complement available fluid and imaging biomarkers.

3.3.2 | Consensus recommendations

A semi-quantitative and expert consensus approach was used to build recommendations for assessment in the three settings and a rapid screening battery for eye clinics. The working group considered assessment tool preference totals, frequency of use for assessment tools, proprietary issues (i.e., licensing and costs), and time constraints for each setting.

The final consensus recommendations are shown in Table 3. The percentage of respondents choosing one or more of the tools within the final recommended was greater than 75% for 80% of the recommendations (see Table S3 for details). Recommendation for a rapid screening battery for eye clinics is shown in Table 4. Recommendations for each PCA feature consist of three assessment tool options listed in the order of preference for each setting. Some features have fewer than three options because of the limited number of assessment tools or approaches available.

3.3.3 | PCA working group recommendations distinct from survey results

Recommendations by the working group that superseded survey preferences are noted for the following: apperceptive prosopagnosia, homonymous hemianopia, central achromatopsia, early visual (cortical) processing deficits, and global cognitive measures. Factors contributing to this are discussed further.

Apperceptive prosopagnosia. Diagnosis of the apperceptive variant of prosopagnosia involves demonstrating prosopagnosia (i.e., inability to know that a face has been seen before) due to impaired facial coding of facial features/structures.[10] By contrast, associative prosopagnosia is the inability to link a face to memories, despite intact facial coding.[11] The apperceptive variant of prosopagnosia is a core PCA feature in the 2017 criteria, whereas associative prosopagnosia is not. Using these distinctions, the working group recommends starting with assessments that determine the presence or absence of impaired facial coding to diagnose apperceptive prosopagnosia. These include the CORVIST Face Perception tests, the Cambridge Face Perception Test, or the Glasgow Face Matching Test, which are recommended for all three settings.

Alternatively, an examiner can assess for prosopagnosia starting with the survey respondent preferences of the Cambridge Face Memory Test or the Wechsler Memory Scale-III Faces (neuropsychology and research settings) or a set of curated images of famous faces for recognition (office setting). Once prosopagnosia is established with these tools, testing for apperceptive prosopagnosia should proceed using the tests recommended above and in Table 3. When using a famous faces collection, we recommend considering the educational, cultural, and generational backgrounds of an individual. Of the 24 respondents who prefer the use of famous faces, 16 respondents (66.7%) reported that they do not adjust the collection for an individual's background.

Homonymous visual field loss. Confrontational visual field testing (i.e., finger counting in each quadrant) was preferred by respondents for the assessment of homonymous visual field loss. The working group recommends that threshold perimetry be used if confrontational finger counting is normal or inconclusive in the office setting, and threshold perimetry is recommended as the first choice in the research setting. Visual field threshold perimetry determines the brightness threshold for a small stimulus (typically a 4 mm^2 circle of white light) at numerous locations throughout the visual field for each eye separately, as presented by a computer algorithm. Threshold perimetry is recommended because it is a standardized, systematic approach that has greater sensitivity to abnormal sensory thresholds (i.e., the weakest stimulus that can be detected) than finger counting.

Central achromatopsia. Survey respondents preferred pseudoisochromatic plate testing and the use of color association questions (i.e., "What color is a stop sign?"). However, central achromatopsia is the impaired perception of the distinction between different chromatic hues due to cortical dysfunction. The use of pseudoisochromatic color plate testing can be abnormal in the presence of simultanagnosia, and reporting the color of things involves semantic knowledge and imagery. For these reasons, the working group recommends pseudoisochromatic plates as a third option in the office visit and the neuropsychology evaluation setting, with a color hue discrimination test and a color hue matching test as the first and second options. For the research setting, standardized color hue discrimination tests (Farnsworth Munsell color hue or CORVIST hue discrimination tests) are recommended.

Early visual (cortical) processing deficits and visual crowding. For the research setting, curated images were preferred by respondents. Instead, the working group recommends the use of validated tools within the CORVIST for size discrimination, shape discrimination, shape detection, and crowding.

Measures of global cognition. The Mini-Mental State Examination and Montreal Cognitive Assessment were preferred by more survey respondents (N = 44 respondents) than Addenbrooke's Cognitive Examination-III (ACE-III) (N = 10). The advantage to the ACE-III, however, is that there is adequate testing of multiple domains, including the visuospatial/perceptual domain, to allow for comparison between domains (ACE-III is available for free). Specifically, visuospatial/perceptual testing on the ACE-III includes two items for copy, clock drawing, dot counting, and fragmented letter recognition. Thus the working group recommends the ACE-III in all settings, although time constraints could limit its use in the office visit setting.

TABLE 3 Posterior cortical atrophy assessment working group recommendations for posterior cortical atrophy feature assessment.

PCA core features in diagnostic criteria [7]	Approach, tasks, tests, and/or stimuli recommendations for use in three clinical settings (ordered according to survey results and working group consensus)		
	Office visit assessment	**Neuropsychology assessment**	**Research assessment**
Broad visual assessment	Visual acuity for each eye, ocular examination of anterior and posterior segments of both eyes, and assessment of early visual (cortical) processing should be performed before diagnosing PCA.	Visual acuity for each eye, ocular examination of anterior and posterior segments of both eyes, and assessment of early visual (cortical) processing should be performed before diagnosing PCA.	Visual acuity for each eye, ocular examination of anterior and posterior segments of both eyes, and assessment of early visual (cortical) processing should be performed before diagnosing PCA.
Space perception deficit	1. Visual scanning or visual search with cancellation 2. Line bisection 3. ACE-III dot counting	1. Block Design 2. JoLO 3. Visual scanning or visual search with cancellation	1. VOSP number location 2. VOSP dot counting 3. VOSP cube analysis
Simultanagnosia	1. Cookie Theft picture 2. Other complex scene or image interpretation (photographs, line drawings, ^Arcimboldo paintings, beach or picnic scenes, and images from Queen Square Screening Test for Visual Deficits) 3. Navon figures (letters or shapes)	1. Rey–Osterrieth Complex Figure Copy 2. Poppelreuter-Ghent Overlapping Figures 3. Other complex scene or image	1. Rey–Osterrieth Complex Figure Copy 2. Pseudoisochromatic Plates (Ishihara or Hardy-Rand-Rittler) 3. Complex scene or image (including Cookie Theft picture)
Object perception deficit	1. Line drawing 2. Single letters 3. Photographs	1. Fragmented letters (ACEIII or CORVIST) 2. Object ecision 3. CORVIST unusual/usual views	1. VOSP Object decision Task 2. VOSP Silhouettes 3. VOSP Progressive Silhouettes
Constructional dyspraxia	1. Clock drawing 2. Intersecting pentagons copy 3. Necker cube copy	1. Rey–Osterrieth Complex Figure Copy 2. Benson Complex Figure Copy 3. Clock drawing or Mattis Dementia Rating Scale: constructional subscale	1. Clock drawing 2. Intersecting pentagons copy 3. Benson Complex Figure Copy
Environmental agnosia	No tasks, tests, or stimuli to recommend (assess by history)	No tasks, tests, or stimuli to recommend (assess by history)	No tasks, tests, or stimuli to recommend (assess by history)
Alexia	Examinee to read aloud 1. a single word 2. a paragraph 3. regular and irregular words	Examinee to read aloud 1. regular and irregular words 2. single word 3. paragraph	Examinee to read aloud 1. regular and irregular words 2. single word 3. paragraph
Left/right disorientation	Examinee to point to left and/or right side of body (egocentric) and Examinee to point to left and/or right side of body of examiner (allocentric)	Examinee to point to left and/or right side of body (egocentric) and Examinee to point to left and/or right side of body of examiner (allocentric)	Ask examinee to point to left and/or right side of body (egocentric) and Examinee to point to left and/or right side of body of examiner (allocentric)

(Continues)

TABLE 3 (Continued)

PCA core features in diagnostic criteria [7]	Approach, tasks, tests, and/or stimuli recommendations for use in three clinical settings (ordered according to survey results and working group consensus)		
	Office visit assessment	**Neuropsychology assessment**	**Research assessment**
Acalculia	1. Verbal calculations (given spontaneously by examiner) 2. Written calculations (given spontaneously by examiner) 3. Verbal calculations (from prepared script)	1. Verbal calculations (from prepared script) 2. Written calculations (from prepared script) 3. Written calculations (given spontaneously by examiner)	1. Verbal calculations (from prepared script) 2. Written calculations (from prepared script) 3. Verbal calculations (given spontaneously by examiner)
***Apperceptive prosopagnosia**	1. CORVIST Faces test 1 and test 2 2. Cambridge Face Perception Test 3. Glasgow Face Matching Test Alternatively, establish prosopagnosia (using Cambridge Face Memory Test or Famous faces appropriate to education, culture, and generation of examinee), and then proceed with one or more of three options above	1. CORVIST Faces test 1 and test 2 2. Cambridge Face Perception Test 3. Glasgow Face Matching Test Alternatively, establish prosopagnosia (using Cambridge Face Memory Test or Wechsler Memory Scale-III Faces,) and then proceed with one or more of three options above	1. CORVIST Faces test 1 and test 2 2. Cambridge Face Perception Test 3. Glasgow Face Matching Test Alternatively, establish prosopagnosia (using Cambridge Face Memory Test or Wechsler Memory Scale–III Faces), and then proceed with one or more of the three options above
Agraphia	Examinee to write: 1. sentence chosen by examinee 2. sentence chosen and verbalized by examiner 3. sentence by copy	Examinee to write: 1. sentence chosen by examinee 2. sentence chosen and verbalized by examiner 3. sentence by copy	Examinee to write: 1. sentence chosen by examinee 2. sentence chosen and verbalized by examiner 3. sentence by copy
Finger agnosia	Examiner points to a finger for examinee to name that is 1. on the examinee 2. on the examiner 3. on a drawing	Examiner points to a finger for examinee to name that is 1. on the examinee 2. on a drawing 3. on the examiner	Examiner points to a finger for examinee to name that is 1. on the examinee 2. on the examiner 3. on a drawing
***Homonymous hemianopia**	Confrontation visual field testing, and If confrontation testing normal or inconclusive, automated threshold visual field perimetry (24° or 30°) or Goldmann visual field perimetry with isopter sizes V, III, and I	An option for the neuropsychologist is to provide the recommendation that visual field testing should be done to assess for a homonymous visual field defect	1. Automated threshold visual field perimetry (24 or 30°) 2. Goldmann visual field perimetry with isopter sizes V, III, and I

(Continues)

TABLE 3 (Continued)

Other PCA features (not in criteria) and global measures	Office visit assessment	Neuropsychology assessment	Research assessment
***Early visual processing deficits**	1. Shape discrimination (curated stimuli) 2. Size discrimination (curated stimuli) 3. Shape detection (curated stimuli)	1. CORVIST Shape Discrimination test 2. CORVIST Size Discrimination test 3. CORVIST Shape Detection test	1. CORVIST Size Discrimination test 2. CORVIST Shape Discrimination test 3. CORVIST Shape Detection test
***Central achromatopsia**	1. Color hue discrimination test (Farnsworth Munsell or CORVIST Hue Discrimination) 2. Color hue matching of curated items 3. Ishihara color plates (*Note*: color naming or association test should not be used to assess central achromatopsia, and Ishihara color tests can be abnormal due to simultanagnosia)	1. Color hue discrimination test (Farnsworth Munsell or CORVIST hue discrimination) 2. Color hue matching of curated items 3. Ishihara color plates (*Note*: color naming or association test should not be used to assess central achromatopsia, and Ishihara color tests can be abnormal due to simultanagnosia)	Color hue discrimination test (Farnsworth Munsell or CORVIST Hue Discrimination test) (*Note*: color naming or association test should not be used to assess central achromatopsia, and Ishihara color tests can be abnormal due to simultanagnosia)
***Visual crowding**	1. Single letter visual acuity versus 3 to 5 letter per line visual acuity 2. Target letter (and/or digit) report in crowded versus uncrowded format 3. Read string of crowded letters (and/or digits) and compare to uncrowded string	1. CORVIST Crowding test 2. Single letter visual acuity versus 3 to 5 letter per line visual acuity 3. Target letter (and/or digit) report in crowded versus uncrowded format or read string of crowded letters (and/or digits) and compare to uncrowded string	1. CORVIST Crowding test 2. Single letter visual acuity versus 3 to 5 letter per line visual acuity or target letter (and/or digit) report in crowded versus uncrowded format 3. Read string of crowded letters (and/or digits) and compare to uncrowded string
Other dominant parietal dysfunction	1. Digit span forward and backward 2. Gesture production 3. Spelling from prepared list presented verbally by examiner	1. Digit span forward and backward 2. Spelling from prepared list presented verbally by examiner 3. Gesture production	1. Digit span forward and backward 2. Spelling from prepared list presented verbally by examiner 3. Gesture production
***Longitudinal global cognitive assessment**	See text for further discussion. 1. ACE III (used with mild or moderate impairment or throughout course) 2. MoCA Full version (commonly used with mild or moderate impairment) 3. MMSE Standard version (commonly used throughout course) 4. MoCA Basic version (used throughout course or with mild to moderate impairment)		

Note: Arcimboldo paintings are images of portrait paintings by 16th century Italian artist Giuseppe Arcimboldo that consist of smaller objects, such as fruits and vegetables, which create the global portrait image. Recommendations are given for three clinical settings, and options are listed in order of preference. Use of more than one of the available options per feature might be necessary to confirm the presence or absence of a feature. The working group recommendations that superseded survey results are indicated with an asterisk* in the first column. See posterior cortical atrophy Assessment Toolkit for images and instructions that support assessment recommendations.

Abbreviations: ACE-III, Addenbrooke's Cognitive Examination-III; BORB, Birmingham object recognition battery; CORVIST, Cortical Vision Screening Test; JoLO, judgment of line orientation; VOSP, visual object and space perception battery.

TABLE 4 Recommendations for rapid screening battery for cortical visual dysfunction for eye clinics.

Visual field perimetry and at least two of the following are recommended for screening in eye clinics:
1. Interpretation of Poppelreuter-Ghent Overlapping Figure(s)
2. Interpretation of Navon figure(s)
3. Copy an intersecting pentagon figure
4. Read two short paragraphs: one in cursive and one not in cursive
5. Test for visual crowing using the Cortical Vision Screening Test (CORVIST) crowding test
6. If there is no evidence of ocular cause for visual symptoms, have patient complete the Colorado posterior cortical questionnaire [17]

Further instructions and stimuli can be found at: https://neurologyevent.ucdenver.edu/documents/EyeClinicVisualCorticalScreening.pdf

4 | DISCUSSION

We provide recommendations for assessment tools to evaluate clinical features of PCA and global cognition in clinical and research settings, as well as a rapid screening battery for eye clinics. The recommendations are organized around the core cognitive features in the 2017 PCA criteria and additional features of posterior cortical visual dysfunction. We did not make recommendations for the assessment of cognitive domains that are relatively spared in PCA, given that the majority of survey respondents indicated "no preferences." We provide survey response data from those who had preferences in Table S3. Guidance for tools that minimize reliance on visual perception for the assessment of relatively spared domains in PCA awaits future explorations and dedicated study of the topic.

Approximately 10% of the members (55 members) responded to the survey, and it is noteworthy that the consensus criteria published in 2017 was based on 38 survey respondents.[7] Overall, we believe that the respondents represent those with significant clinical experience in assessing and caring for patients with the rare syndrome of PCA. There was a robust agreement for preferred assessment tools used "frequently or almost always."

Of interest, less than half of respondents chose tools they use "frequently or almost always" for *object perception deficits* and *apperceptive prosopagnosia*. There was a significantly greater fraction of respondents who use their preferred tools "almost always or frequently" to assess dorsal visual pathway (occipitoparietal) functions compared to ventral visual pathway (occipitotemporal) functions. The reasons for this might include familiarity and availability of ventral pathway assessment tools; further work to explore this potential gap is needed.

When PCA is suspected, respondents use assessment tools that they do *not* routinely use for individuals with cognitive impairment not suspected of having PCA. This highlights the importance of dissemination of recommendations to increase familiarity with assessment tools beyond experts. It also underscores the potential that reserving assessment tools only for those suspected of having PCA increases the risk of under-recognition of dementia-related visual impairment and reduces our ability to understand phenotypic heterogeneity and to accurately describe individuals who fall in the middle of a phenotypic continuum. For example, individuals with an "equivalent" degree of impairment in memory and visual domains can be missed. Clinicians, neuropsychologists, and researchers must take notice of whether their cognitive batteries lack adequate assessment of visual posterior cortical functions and work to remedy gaps to better serve patients and the field.

An important broad recommendation we include is to ensure measurement of visual acuity, examination of anterior and posterior segments of both eyes, and assessment of early visual (cortical) processing before diagnosing PCA. The survey revealed that these evaluations are not always performed, despite 2017 PCA criteria that stipulate that the diagnosis of PCA is excluded if there is evidence of anterior afferent visual causes for symptoms.[7] In addition, early visual (cortical) processing deficits impact the assessment of other PCA features. It is important to note that data reveal that visual impairment from eye disease is a risk factor for age-related cognitive decline, and recognition and treatment of visual impairment can improve the trajectory of cognitive decline.[12–14]

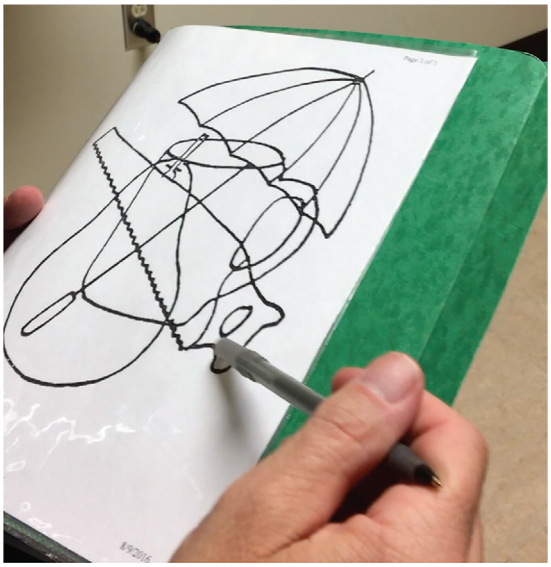
Survey responses indicated a preference for curated tools for some PCA features, particularly in the office setting. This could reflect a lack of access to, or familiarity with, validated batteries with appropriate stimuli. However, a very limited number of stimuli and tools are available, which creates the impetus to curate stimuli that increase sensitivity to detect impairment. One concern is the lack of standardized methods for presentation and interpretation of results. Although this approach is not uncommon in the office setting, this finding reveals a gap in clinical trial readiness for people with PCA syndrome, regardless of the underlying pathology targeted. The recommendations reflect consideration for the use of valid tools whenever appropriate, and further work is needed to validate preferred assessment tools and develop practical and valid assessment batteries that capture posterior cortical dysfunction.

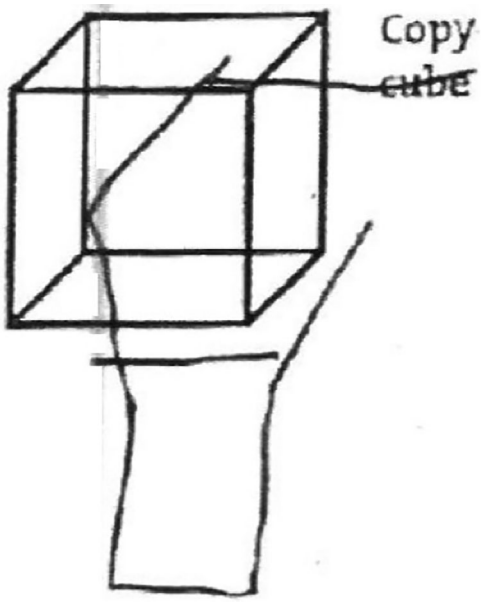
A novel PCA testing toolkit with example stimuli and instructions that reflect these recommendations is in development by one of the authors (K.Y.).[15] Similarly, instructions and stimuli for the recommended rapid screening battery for eye clinics are available at this link: Eye Clinic Rapid Visual Cortical Screening. We also include a video demonstrating the interpretation of a Poppelreuter-Ghent Overlapping Figures image by a person with PCA (see Box 1).

Dissemination of these recommendations will rely on clinicians and researchers in the field to share them with colleagues in neurology, neuropsychology, psychiatry, gerontology, ophthalmology, and optometry. We encourage investigators to use the recommendations as an impetus to develop and validate novel PCA assessment tools and batteries for screening, diagnosis, staging, phenotyping, and clinical outcome assessments for treatment trials.

Box 1: Patient presentation and video demonstrating impaired perception of Poppelreuter-Ghent Overlapping Figures

A previously healthy 52-year-old man presented with a report of 1 year of difficulty reading his own handwriting and getting lost while driving. He had a normal eye examination, and he was referred after a Brain MRI scan was normal. Assessment tools rapidly identified constructional dyspraxia (severely impaired cube copy, below right) and impaired interpretation of Poppelreuted-Ghent Overlapping Figures (video, below left). Further evaluation and neuropsychology assessment identified multiple PCA core features (space and object perception deficits, simultanagnosia, alexia, acalculia, agraphia, homonymous hemianopia) with relative sparing of memory, language, and executive domains, and no behavioral or personality changes were noted. The video demonstrates the use of a four-figure Poppelreuter-Ghent Overlapping Figures image, and the patient was only able to properly perceive two of four objects. He was asked to continue reporting what he was seeing after he paused, but portions of the other figures were confusing to him. Poppelreuter-Ghent Overlapping Figures with a greater number of overlapping figures and/or increased figure rotation can be used to increase the difficulty of the test, if needed.





In summary, the current work follows previous multicenter efforts to improve the characterization of core clinical-radiological features of the PCA syndrome, and it supports the objective to create a common evaluation framework for PCA that was endorsed by the preceding PCA working group that developed the 2017 PCA criteria.[7,16] The framework we provide can facilitate timely and accurate recognition and diagnosis of PCA, support investigations of longitudinal profiles of the PCA syndrome, and foster the development of validated measures that capture posterior cortical dysfunction. Such assessment tools are critical to advancing our understanding of the pathophysiology of dementias and accelerating treatment trials. Future initiatives will be aimed at advancing this evaluation framework.

ACKNOWLEDGMENTS

We wish to thank the Alzheimer's Association and Jodi Titner for support of the PCA assessment working group virtual meetings. This study was supported by the John and Joanne Hare Fund for Accelerating PCA Research at the University of Colorado School of Medicine and the University of Colorado Alzheimer's and Cognition Center.

CONFLICT OF INTEREST

V.S.P.: Research is supported by National Institutes of Health (NIH), the John and Joanne Hare Fund for Accelerating PCA Research, University of Colorado Alzheimer's and Cognition Center, the North American Neuro-ophthalmology Society, and Institutional support from the Lewy Body Dementia Association; also received support from the American Academy of Neurology for editorial work, royalties from Up-to-Date, Inc., the Alzheimer's Association for the Longitudinal Early-Onset Alzheimer's Disease Study Patient Advocacy Committee, and Biogen and Eisai. B.F.B.: Honorarium for the Tau Consortium. Institutional research grant support: Alector, Biogen, Transposon, Cognition Therapeutics, GE Healthcare; Institutional NIH grant support: P30 AG062677, U19 AG063911, R01 AG038791, U01 NS100620, U19 AG071754, U24 AG056270. Institutional foundation support: Lewy Body Dementia Association, American Brain Foundation. Institutional philanthropic support: Mayo Clinic Dorothy and Harry T. Mangurian Jr. Lewy Body Dementia Program, the Little Family Foundation, the Ted Turner and Family Functional Genomics Program. G.R.: Research support from NIH, Alzheimer's Association, American College of

Radiology, Rainwater Charitable Foundation, Avid Radiopharmaceuticals, GE Healthcare, Genentech, Life Molecular Imaging. In the last 36 months, he has served as a paid consultant on scientific advisory boards for Alector, Eli Lilly, Roche, Genentech, GE Healthcare, Merck, and as a paid member of Data and Safety Monitoring Board for Johnson & Johnson. He is an Associate Editor for *JAMA Neurology*. R.A.T.: Honoraria as an advisory board member from C2N Diagnostics. G.S.D.: Research is supported by NIH (K23AG064029, U01AG057195, U19AG032438), the Alzheimer's Association, and Chan Zuckerberg Initiative. He serves as a consultant for Parabon Nanolabs Inc, as a Topic Editor (Dementia) for DynaMed (EBSCO), and as the Clinical Director of the Anti-NMDA Receptor Encephalitis Foundation (Inc, Canada; uncompensated). He is the co-Project PI for a clinical trial in anti-NMDAR encephalitis, which receives support from Horizon Pharmaceuticals. He has developed educational materials for PeerView Media, Inc., and Continuing Education Inc. He owns stock in ANI Pharmaceuticals. Dr. Day's institution has received support from Eli Lilly for Dr. Day's development and participation in an educational event promoting early diagnosis of symptomatic Alzheimer's disease. B.D.C.B.: Receives funding from Alzheimer Nederland (#WE.15-2019-13, #WE.03-2021-15). C.U.O.: Research support from Alector, Transposon, and Denali, and consulting work from Acadia, Reata—consulting. H.S.: Full-time employee of the Alzheimer's Association and spouse employed by Abbott Laboratories. K.Y. is an Etherington PCA Senior Research Fellow and is funded by the Alzheimer's Society, grant number 453 (AS-JF-18-003) and a NIH grant (R01EY027964), and reports support from Roche outside the submitted work. All other authors report no conflict-of-interest disclosures. Author disclosures are available in the Supporting Information.

ORCID

Victoria S. Pelak https://orcid.org/0000-0003-3147-8595
Keir X. X. Yong https://orcid.org/0000-0002-9708-3599

REFERENCES

1. Renner JA, Burns JM, Hou CE, McKeel DW Jr, Storandt M, Morris JC. Progressive posterior cortical dysfunction: a clinicopathologic series. *Neurology*. 2004;63(7):1175-1180.
2. Tang-Wai DF, Graff-Radford NR, Boeve BF, et al. Clinical, genetic, and neuropathologic characteristics of posterior cortical atrophy. *Neurology*. 2004;63(7):1168-1174.
3. Alladi S, Xuereb J, Bak T, et al. Focal cortical presentations of Alzheimer's disease. *Brain*. 2007;130(Pt 10):2636-2645.
4. Seguin J, Formaglio M, Perret-Liaudet A, et al. CSF biomarkers in posterior cortical atrophy. *Neurology*. 2011;76(21):1782-1788.
5. de Souza LC, Lamari F, Belliard S, et al. Cerebrospinal fluid biomarkers in the differential diagnosis of Alzheimer's disease from other cortical dementias. *J Neurol Neurosurg Psychiatry*. 2011;82(3):240-246.
6. de Souza LC, Corlier F, Habert MO, et al. Similar amyloid-beta burden in posterior cortical atrophy and Alzheimer's disease. *Brain*. 2011;134(Pt 7):2036-2043.
7. Crutch SJ, Schott JM, Rabinovici GD, et al. Consensus classification of posterior cortical atrophy. *Alzheimers Dement*. 2017;13(8):870-884.
8. Graff-Radford J, Yong KXX, Apostolova LG, et al. New insights into atypical Alzheimer's disease in the era of biomarkers. *Lancet Neurol*. 2021;20(3):222-234.
9. Mendez MF, Ghajarania M, Perryman KM. Posterior cortical atrophy: clinical characteristics and differences compared to Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2002;14(1):33-40.
10. Corrow SL, Dalrymple KA, Barton JJ. Prosopagnosia: current perspectives. *Eye Brain*. 2016;8:165-175.
11. Barton JS, Davies-Thompson J, Corrow SL. Chapter 10 - Prosopagnosia and disorders of face processing. *Handb Clin Neurol*. 2021;178:175-193.
12. Lee CS, Gibbons LE, Lee AY, et al. Association Between Cataract Extraction and Development of Dementia. *JAMA Intern Med*. 2022;182(2):134.
13. Nagarajan N, Assi L, Varadaraj V, et al. Vision impairment and cognitive decline among older adults: a systematic review. *BMJ Open*. 2022;12(1):e047929.
14. Maharani A, Dawes P, Nazroo J, Tampubolon G, Pendleton N, group SE-CW. Cataract surgery and age-related cognitive decline: A 13-year follow-up of the English Longitudinal Study of Ageing. *PLoS One*. 2018;13(10):e0204833.
15. Yong K, Willoughby AA. PCA Testing Toolkit 2021 [updated 02/08/2021. https://osf.io/mwx63
16. Bellio M, Oxtoby NP, Walker Z, et al. Analyzing large Alzheimer's disease cognitive datasets: Considerations and challenges. *Alzheimers Dement*. 2020;12(1):e12135.
17. Holden SK, Pelak VS, Sooy T, et al. Development of the Colorado posterior cortical questionnaire within an Alzheimer's disease study cohort. *J Clin Exp Neuropsychol*. 2022:1-11.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Pelak VS, Tang-Wai DF, Boeve BF, et al. Consensus recommendations for clinical assessment tools for the diagnosis of posterior cortical atrophy syndrome from the Atypical AD PIA of ISTAART. *Alzheimer's Dement*. 2023;15:e12474. https://doi.org/10.1002/dad2.12474