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ARTICLE

Relative preservation of facial expression recognition in posterior cortical atrophy

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Abstract

Objective

To compare recognition of facial expression (FE) vs recognition of facial identity (FI) in posterior cortical atrophy (PCA), with the hypothesis that FE recognition would be relatively preserved in PCA.

Methods

In this observational study, FI and expression recognition tasks were performed by 194 participants in 4 groups, including 39 with Alzheimer disease (AD) (non-PCA), 49 with behavioral variant frontotemporal dementia (bvFTD), 15 with PCA, and 91 healthy controls. Between-group differences in test scores were compared.

Results

Patients with PCA performed worse than healthy controls in FI and emotion recognition tasks ($p < 0.001$ for all). Patients with PCA also performed worse than AD and bvFTD groups in FI recognition, with no difference in FE recognition.

Conclusions

Patients with PCA have relatively preserved FE recognition compared to FI recognition, as seen in affective blindsight.

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Glossary

AD = Alzheimer disease; **bvFTD** = behavioral variant frontotemporal dementia; **CATS** = Comprehensive Affect Testing System; **CI** = confidence interval; **HC** = healthy controls; **MAC** = Memory and Aging Center; **MMSE** = Mini-Mental State Examination; **MNI** = Montreal Neurological Institute; **PCA** = posterior cortical atrophy; **UCSF** = University of California, San Francisco; **V1** = primary visual cortex; **VBM** = voxel-based morphometry.

Posterior cortical atrophy (PCA) is a syndrome of early and prominent visual disturbance in the setting of a neurodegenerative illness, most commonly Alzheimer disease (AD).[1–4] Updated research criteria emphasize not only an insidious progression of disordered space or object perception, but also a relative preservation in memory, language, and behavior.[2] This selective higher order visual dysfunction results from focal atrophy of the occipital, posterior parietal, and sometimes posterior temporal cortices.

Preservation of some aspects of vision, usually implicit or unconscious, can persist despite cortical vision loss due to damage in the primary visual cortex (V1).[5] Several different research laboratories and paradigms have since demonstrated the ability of patients with cortical blindness to accurately respond to an emotionally salient stimulus, now referred to as "affective blindsight."[6] Cortically blind patients are able to perceive facial expressions (FEs) to an extent better than chance, to exhibit autonomic changes appropriate to the stimulus, and to unconsciously mirror presented FEs without conscious recognition.[7]

Studies of the neuroanatomical support of affective blindsight suggest that emotionally salient visual information may be relayed from the superior colliculus via the pulvinar towards emotionally relevant structures of the brain, such as the amygdala, thus bypassing V1.[8] Given the presumptive preservation of these pathways in PCA, despite the degeneration of cortical networks for visual processing, single case studies have suggested that recognition of emotionally salient stimuli may be preserved in PCA as in cortically blind patients.[9,10]

Herein, we hypothesized that FE recognition would be relatively preserved in PCA (i.e., similar to other groups), compared to both facial identity (FI) recognition and other tests of visual function.

Methods

Study design

This was an observational study across 4 different populations. Participants with dementia were evaluated initially at the Memory and Aging Center (MAC) of the University of California, San Francisco (UCSF).

Standard protocol approvals, registrations, and patient consents

All study participants provided written consent regarding study participation. The institutional review boards of UCSF approved the study.

Participants

Healthy controls (HC, n = 91), as well as patients with PCA (n = 15), behavioral variant frontotemporal dementia (bvFTD, n = 49), or non-PCA AD (AD, n = 39), were selected from the data repository of UCSF's Memory and Aging Center if they had completed the 2 main tasks of interest (a FI and a FE recognition task) and had also received an MRI scan within 3 months of performing the 2 tasks. All participants were seen between March 5, 2008, and May 5, 2016. Patients with AD and patients with bvFTD were included as reference populations in which the ability to recognize emotions is classically thought to be preserved and impaired, respectively.[11]

Patients with PCA were initially defined by Mendez criteria,[1] and were then further classified by research criteria updated in 2017.[2] The patients with bvFTD were diagnosed based on international criteria,[12] and the patients with AD met National Institute on Aging–Alzheimer's Association criteria.[13] Patients were recruited from a dementia specialty clinic, and normal controls were recruited through newspaper advertisements and local community centers. A multidisciplinary team of neuropsychologists, neurologists, and nurses determined all diagnoses. Patients with white matter lesions deemed to be clinically significant, including a history of stroke, were excluded, as were those with other neurologic or medical comorbidities that might interfere with cognitive performance. Patients were excluded if their Mini-Mental State Examination (MMSE) score was less than 15.

Participant demographics and behavioral scores are listed in tables 1 and 2, respectively. The neuroanatomy of PCA vs the other 2 groups is shown in figure 1. Of the 15 patients with PCA, one met criteria for PCA-Plus by fulfilling criteria for probable corticobasal syndrome. Two more patients with PCA met criteria for possible corticobasal syndrome.[14] Seven of the 15 patients with PCA received amyloid-PET scans, all of which suggested underlying AD pathology.

Task description

We compared performances on FI and expression recognition tasks from the Comprehensive Affect Testing System (CATS),[15] administered by computer with the guidance of trained research assistants. The CATS is a well-validated task that utilizes posed FEs.[16] The tests are composed of 6 emotional expressions (happy, sad, angry, surprised, fearful, and disgusted) as well as a neutral expression, selected due to wide cultural recognition.[17] Facial stimuli are in black and white and are of a uniform size.

In the FI task, 2 faces were shown at the midline of the examinee's field of view. The examinee was then asked to

Table 1 Demographics

	HC (n = 91)	AD (n = 39)	bvFTD (n = 49)	PCA (n = 15)
Sex, % F	59.3	56.4	38.8	60.0
Age, y	59.2 ± 14.7	60.5 ± 10.2	60.3 ± 8.0	59.4 ± 5.15
Education, y	17.1 ± 2.5	16.6 ± 2.7	16.4 ± 3.2	15.2 ± 1.6
CDR[a,b]	0.1 ± 0.2	0.9 ± 0.4	1.2 ± 0.6	0.7 ± 0.2
CDR Sum of Boxes[a,b]	0.1 ± 0.3	5.0 ± 2.3	6.9 ± 3.0	3.4 ± 1.2
Handedness, % R	82.4	88.3	86.3	86.7

Abbreviations: AD = Alzheimer disease (non-PCA); bvFTD = behavioral variant frontotemporal dementia; CDR = Clinical Dementia Rating; HC = healthy control; PCA = posterior cortical atrophy.
Values are mean ± SD or %.
[a] Between all group difference with $p < 0.001$.
[b] Between patient group difference with $p < 0.001$.

decide whether the faces represent the same or different individuals. Portraits were presented in same-sex pairings, both representing the same emotion. Each participant underwent 12 test items, with an equal number of emotion stimuli types.

In the FE task, a face was shown at the top of the screen. Below it, 5 other faces were shown, each expressing a different emotion. The examinee was asked to select which of the 5 faces below matched the expressed emotion of the FE at the top of the screen.

To confirm diagnoses, each participant underwent a comprehensive neuropsychological battery at UCSF's MAC. Selected and relevant measurements include modified Rey-Osterrieth (Benson) figure to test visuospatial abilities,[18] forward and backward digit span to assess working memory,[19] the 9-item California Verbal Learning Task to assess verbal short-term memory,[20] the 15-item Boston Naming Test,[21] and phonemic and category verbal fluency tasks. The Geriatric Depression Scale,[22] MMSE, and Clinical Dementia Rating scores were also collected.[23–25] Each participant provided a detailed neurologic history and underwent a physical examination.

Statistical analyses

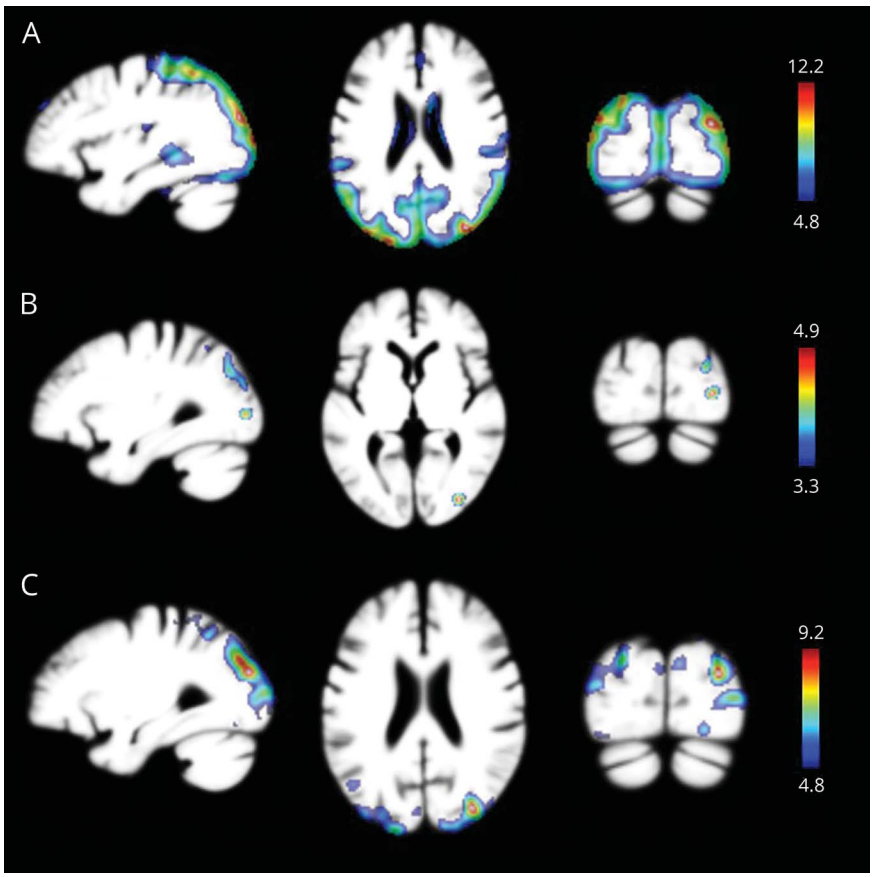
Statistical analyses were performed in Stata 13.0.[26] Age, disease severity (Clinical Dementia Rating [CDR] Sum of Boxes score), education, and sex were considered as potential

Table 2 Behavioral scores of participants

	HC (n = 91)	AD (n = 39)	bvFTD (n = 49)	PCA (n = 15)
MMSE[a,b]	29.1 ± 0.9	23.0 ± 3.4	25.4 ± 3.5	23.9 ± 4.0
California Verbal Learning Test, 30 seconds[a,b]	7.8 ± 1.9	3.6 ± 2.2	5.1 ± 2.4	5.4 ± 1.9
California Verbal Learning Test, 10 minutes[a,b]	7.5 ± 1.9	2.2 ± 2.4	4.0 ± 2.9	4.3 ± 2.3
Boston Naming Test, abbreviated[a]	14.3 ± 1.0	12.3 ± 2.6	12.6 ± 3.0	11.4 ± 1.5
Phonemic fluency[a,c]	16.8 ± 4.7	9.4 ± 4.3	8.3 ± 4.5	12.2 ± 4.6
Semantic fluency[a]	23.3 ± 5.3	11.3 ± 4.6	12.5 ± 6.4	12.0 ± 3.5
Digit span backwards[a,c]	5.6 ± 1.2	3.2 ± 1.3	3.9 ± 1.3	3.2 ± 0.9
Benson copy[a,b]	15.4 ± 1.0	12.3 ± 4.1	14.5 ± 1.4	4.8 ± 4.1
Benson delay[a,b]	12.5 ± 3.0	4.2 ± 3.1	7.2 ± 4.1	3.5 ± 2.8
Calculations[a,c]	4.6 ± 0.6	3.2 ± 1.2	3.9 ± 1.1	2.6 ± 1.2
Geriatric Depression Scale score[d]	4.1 ± 4.3	6.7 ± 4.4	6.8 ± 5.7	6.5 ± 2.9

Abbreviations: AD = Alzheimer disease (non-PCA); bvFTD = behavioral variant frontotemporal dementia; HC = healthy controls; MMSE = Mini-Mental State Examination; PCA = posterior cortical atrophy.
Values are mean ± SD.
[a] Between all group difference with $p < 0.001$.
[b] Between patient group difference with $p < 0.001$.
[c] Between patient group difference with $p < 0.05$.
[d] Between all group difference with $p < 0.05$.

Figure 1 Brain morphometric differences among patients with posterior cortical atrophy (PCA), healthy controls (HC), patients with Alzheimer disease (AD), and patients with behavioral variant frontotemporal dementia (bvFTD)



Heat map references for T values are on the right. (A) Volumetric differences were found between HC and bvFTD at the critical T value of 4.82 based on the permutation method (Tmax 12.17) in the cluster and permutation method in the right middle occipital gyrus. (B) No difference was found between AD and PCA at the critical T value of 5.06. A difference was found between AD and PCA at $p < 0.001$ based on the cluster and permutation method, with a corrected p value of 0.0410, and a Tmax of 4.82. (C) Differences were found between bvFTD and AD in the right superior occipital gyrus with the critical T value of 4.82 (Tmax 9.22).

confounders in all analyses. Using a preselected value of $p < 0.05$ for significance, we compared potential covariates between groups using analysis of variance for continuous and χ^2 testing for nominal variables. The CDR Sum of Boxes score differed between groups ($p < 0.001$), and was included as a covariate in future regressions.

Based on performances in healthy controls, Z scores were created for the FI task, the FE task, and the Benson figure copy task. For each individual, a difference score was then created for the main tasks of interest by subtracting the FI task from the FE task. The more positive the difference score (FE – FI), the greater the extent to which facial emotion recognition is spared relative to FI recognition.

Multiple regression was used first to investigate between-group differences in the primary variables (e.g., FE recognition Z scores). To then compare the extent to which the facial emotion recognition score differed from the identity recognition score within each group, we investigated between-group differences in FE – FI using the Tukey-Kramer method of post hoc comparisons. All comparisons were first assessed across all groups including controls, and then between patient groups only.

Neuroimaging

As a confirmatory step to characterize our patient population, we performed neuroimaging analysis with voxel-based morphometry. Within 3 months of the experimental session, all of those with PCA underwent a structural MRI scan on a 1.5, 3, or 4T Magnetom VISION system (Siemens Inc., Iselin, NJ). A volumetric magnetization-prepared rapid gradient echo MRI sequence (repetition time/echo time/inversion time = 10/4/300 ms) provided T1-weighted whole brain images, with 15-degree flip angle, coronal orientation perpendicular to the double spin echo sequence, 1.0 × 1.0 mm^2 in-plane resolution, and 1.5 mm slab. As the timespan of data collection was broad, magnet strength varied between individuals, and so this was included as a covariate in later analyses. Scans with excessive movement artifacts on visual inspection were not processed for voxel-based morphometry (VBM) analysis, and any such cases were removed from all analyses.

VBM preprocessing and analysis were performed using the VBM8 toolbox (dbm.neuro.uni-jena.de/vbm/) and SPM8 software (fil.ion.uc.ac.uk/spm/software/spm8). Following bias correction and tissue classifications, segmented images were normalized to the Montreal Neurological Institute (MNI) coordinate system space with a 1.0 mm cubic

resolution using affine and nonlinear transformations via the Diffeomorphic Anatomical Registration using the Exponentiated Lie Algebra (DARTEL) method.[22,27] Default measures of the VBM8 toolbox were used in all preprocessing steps, except for the addition of a light clean-up procedure in the morphologic filtering step.[28] The spatially normalized, segmented, and modulated gray matter images were smoothed with an 8-mm full width at half maximum isotropic Gaussian kernel.

A multiple regression analysis was performed with age, sex, MMSE, magnet strength, and total intracranial volume as covariates, comparing whole brain volumes of patients with PCA to those of healthy controls matched by age, sex, and magnet strength. We also compared with bvFTD and AD, using the CDR Sum of Boxes score as a covariate to adjust for disease severity.

The resulting statistical parametric map was thresholded at $p < 0.001$, and then corrected for multiple comparisons at $p < 0.05$ based on custom-fit error distribution and clustering based on 1,000 permutations.[29] The resulting T-maps were superimposed on the MNI single subject brain using automated anatomical labeling included in MRIcron (sph.sc.edu/comd/rorden/mricro.html). Descriptive imaging results are available in table 1.

Data availability

De-identified data included in this study are available for the purposes of replicating methods and results upon request by other qualified investigators to the senior author of this publication.

Results

Measurements of interest

All 3 patient groups differed from the healthy controls in FI recognition (PCA: $\beta = -3.47$, T = −9.81, $p < 0.001$, confidence interval [CI] [−4.17 to −2.78]; AD: $\beta = -0.57$, T = −2.35, $p = 0.02$, CI [−1.05 to −0.09]; bvFTD: $\beta = -1.46$, T = −6.47, $p < 0.001$, CI [−1.90 to −1.01]; $R^2 = 0.38$) in unadjusted analysis. After inclusion of the CDR Sum of Boxes score as a covariate, differences remained between HC and patients with frontotemporal dementia and patients with PCA (PCA: $\beta = -3.26$, T = −8.36, $p < 0.001$, CI [−4.34 to −2.49]; AD: $\beta = -0.28$, T = −0.81, $p = 0.417$, CI [−0.95 to 0.40]; bvFTD: $\beta = -1.04$, T = −2.58, $p = 0.011$, CI [−1.83 to −0.24]; $R^2 = 0.31$). All groups differed from controls in FE recognition both before covariate inclusion (PCA: $\beta = -3.05$, T = −4.09, $p < 0.001$, CI [−4.52 to −1.58]; AD: $\beta = -2.92$, T = −5.61, $p < 0.001$, CI [−3,93 to −1.90]; bvFTD: $\beta = -4.00$, T = −8.42, $p < 0.001$, CI [−4.52 to −1.58]; $R^2 = 0.32$) and after covariate inclusion (PCA: $\beta = -2.43$, T = −2.96, $p = 0.003$, CI [−4.05 to −0.81]; AD: $\beta = -2.02$, T = −2.82, $p = 0.005$, CI [−3.43 to −0.6]; bvFTD: $\beta = -2.74$, T = −3.23, $p < 0.001$, CI [−4.41 to −1.07]; $R^2 = 0.32$). However, no differences in FE recognition were found between patients with PCA, patients with bvFTD, and patients with AD ($\beta = -0.62$, T = −1.60, $p = 0.11$, CI [−1.38 to 0.14] before covariate inclusion, $\beta = -0.26$, T = −0.61, $p = 0.54$, CI [−1.11 to 0.58] after covariate inclusion). In contrast, patients with PCA performed worse than the other 2 patient groups (bvFTD and AD) in FI recognition (AD: $\beta = -2.90$, T = −5.67, $p < 0.001$, CI [−3.91 to −1.89]; bvFTD: $\beta = -2.01$, T = −4.05, $p < 0.001$, CI [−3.00 to −1.02]; $R^2 = 0.24$ before covariate inclusion; AD: $\beta = -2.99$, T = −5.73, $p < 0.001$, CI [−4.01 to −1.95]; bvFTD: $\beta = -2.22$, T = −4.06, $p < 0.001$, CI [−3.3 to −1.13]; $R^2 = 0.25$ after covariate inclusion) (table 3 and figure 2).

By investigating difference scores, we confirmed that patients with PCA had a greater ability to recognize FE vs FI when compared to any other group both before covariate inclusion (HC: $\beta = -3.70$, T = −6.86, $p < 0.001$, CI [−4.76 to −2.63]; AD: $\beta = -4.02$, T = −6.85, $p < 0.001$, CI [−5.19 to −2.87]; bvFTD: $\beta = -3.20$, T = −5.61, $p < 0.001$, CI [−4.32 to −2.07]; $R^2 = 0.22$) and after covariate inclusion (HC: $\beta = -3.65$, T = −6.11, $p < 0.001$, CI [−4.83 to −2.47]; AD: $\beta = -4.05$, T = −6.75, $p < 0.001$, CI [−5.23 to −2.86]; bvFTD: $\beta = -3.24$, T = −6.11, $p < 0.001$, CI [−4.83 to −2.47]; $R^2 = 0.22$) (figure 3).

Discussion

We hypothesized that patients with PCA would have relative sparing of FE recognition (i.e., similar to other groups) when compared to FI recognition (i.e., different from other groups). Our results support this hypothesis.

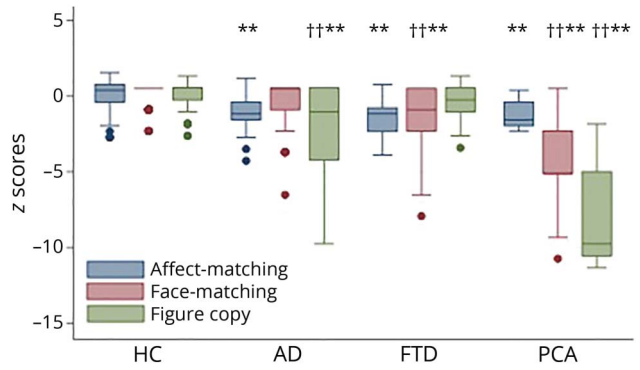
The partially unconscious nature of emotional processing has been recognized in scientific literature for decades.[30] The

Table 3 Measures of interest, including mean ± SD (median)

	HC (n = 91)	AD (n = 39)	bvFTD (n = 49)	PCA (n = 15)
CATS face discrimination[a,b]	11.8 ± 0.5 (12)	11.2 ± 1.2 (12)	10.3 ± 1.8 (11)	8.3 ± 2.3 (8)
CATS affect matching[a]	15.1 ± 2.5 (16)	12.2 ± 2.9 (12)	11.1 ± 2.9 (11)	12.1 ± 2.3 (11)
Difference of *Z* scores[a,b]	−0.2 ± 1.2 (−0.1)	−0.5 ± 2.0 (−0.9)	0.3 ± 2.6 (−0.3)	3.5 ± 2.9 (3.6)

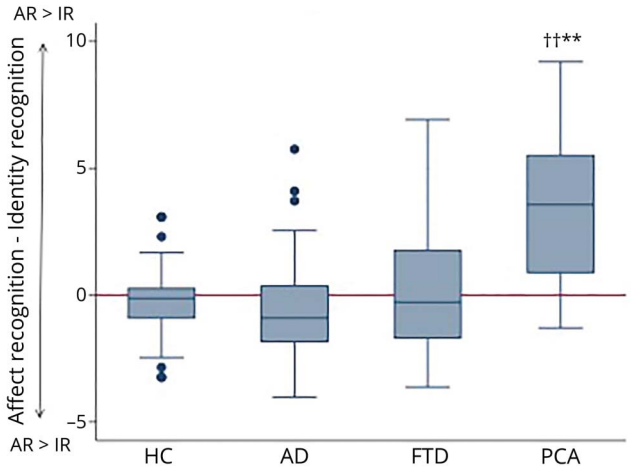
Abbreviations: AD = Alzheimer disease (non-PCA); bvFTD = behavioral variant frontotemporal dementia; CATS = Comprehensive Affect Testing System; HC = healthy control; PCA = posterior cortical atrophy.
PCA differs from patient groups in face identity, but not in affect recognition.
[a] Between all group difference with $p < 0.001$.
[b] Between patient group difference with $p < 0.001$.

Figure 2 Facial expression recognition, facial identity recognition, and figure copy tasks compared between groups



All scores have been normalized for comparison on a similar scale. AD = Alzheimer disease (non-PCA); FTD = behavioral variant frontotemporal dementia; HC = healthy control; PCA = posterior cortical atrophy. ** Between all group difference with $p < 0.001$; †† between patient group difference with $p < 0.001$.

Figure 3 Difference between normalized facial identity and affect recognition scores compared between groups



The zero line indicates an equal ability to recognize facial identity and affect, based on scores. Above the zero line indicates more ability to recognize affect than identity. AD = Alzheimer disease (non-PCA); FTD = behavioral variant frontotemporal dementia; HC = healthy control; PCA = posterior cortical atrophy. ** Between all group difference with $p < 0.001$; †† between patient group difference with $p < 0.001$.

term blindsight was first introduced in 1974,[31] describing a patient with some retained visual function despite having a damaged visual cortex, a phenomenon also described in other primates.[29] In 1999, a patient with a left V1 injury and a corresponding right visual field deficit was described, who was able to discriminate FEs presented in the blind right visual field at an above-chance level.[32] This affective blindsight has since been demonstrated using a variety of methods.[7] In 2009, researchers described an increased skin conductance response in a patient with PCA who was shown emotionally negative pictures.[10] In 2015, a report was presented on a woman with PCA who, despite showing decreased explicit visual recognition, retained some implicit awareness of image-associated valence and arousal.[9]

We confirmed the relative preservation of FE recognition vs the recognition of FI among patients with PCA, which demonstrated that the difference between these 2 abilities was greater in patients with PCA than in patients with AD or patients with bvFTD. Although the ability to recognize facial identities was lower in patients with PCA than in any other group, the ability to recognize FE did not differ from other patients with dementia, including AD or bvFTD. It should be noted that contrary to our expectations,[33] while patients with PCA, patients with bvFTD, and patients with AD all differed from HC in FE recognition, patients with bvFTD did not differ from patients with AD in FE recognition. This unexpected similarity between bvFTD and AD in our study likely reflects 2 factors. First is the clinical, neuroanatomical, and histopathologic heterogeneity of patients with bvFTD.[34] It is possible that our sample of patients with bvFTD includes a higher proportion of a bvFTD class in which FE recognition is relatively spared compared to other FTD subtypes. This heterogeneity may also explain why FE recognition was not worse than FI recognition in this bvFTD group, though an identity recognition deficit in bvFTD has been described.[35] Second, the mean age of our AD population was 60, which is considerably younger than the national average, and those with early-onset AD are more likely to have behavioral or dysexecutive phenotypes similar to bvFTD.[36] Such an atypical AD group in our study may explain the lack of difference on the emotion recognition measure. Patients with PCA, however, stood apart from both patients with bvFTD and patients with AD in the extent to which recognition of FEs differed from recognition of FI. While not equal to FE recognition in controls, the relative preservation of FE recognition in spite of pronounced visuospatial deficits in PCA raises questions about the underlying mechanisms, and about how this sparing may contribute to the overall clinical picture of PCA.

Patients with PCA are essentially socially and emotionally normal, with perhaps some increased anxiety.[37,38] Clinically, patients with PCA are often noted to be empathetic and interpersonally appropriate. A lack of ability to accurately read FEs has commonly been associated with disorders that disrupt normal social function, such as autism,[39] bvFTD,[34] and schizophrenia,[40] and deficits in FE recognition in these disorders have been anatomically correlated with cortical regions relatively spared in PCA. While this study is not powered for mediation analysis, relative preservation of emotion recognition may allow patients with PCA to interact in socially appropriate ways, despite their visual deficits.

In this study we systematically evaluated emotion recognition vs other tasks of visuospatial ability in a group of patients with

PCA compared to both HC and patients with other forms of neurodegenerative disease, including AD (non-PCA) and bvFTD. The chosen stimuli mitigate against features such as color and motion, which can influence affective blindsight.[6] Although our sample size is relatively small, it is reasonable for a rare disorder.

Patients were selected from a data repository of others with PCA—however, many of the patients had not done the tasks of interest, raising the possibility of selection bias, although their participation in visuospatial tasks was essentially random. Our results could also theoretically be more liable to a response bias vs other strategies, such as psychophysiologic measurements or use of response times.

Future studies could incorporate different stimuli, explore whether the effect differs between emotion types, and measure reaction times and physiologic changes. A larger sample size may allow correlation between the relative preservation of affect recognition and caregiver perception of patient empathy, interpersonal skills, and outcomes for both the patient with PCA and caregiver, as well as correlates with neuroimaging.

People with PCA have relatively preserved FE recognition compared to FI recognition. Future studies may investigate the neural substrate supporting this phenomenon as well as how preservation of FE recognition relates to social interaction.

Author contributions

P.S. Pressman: study concept and design, analysis and interpretation. K. Gola: study concept and analysis. S. Shdo: analysis and interpretation. B. Miller: study supervision. C. Fredericks: critical revision of the manuscript for important intellectual content. C. Mielke: analysis and interpretation. V. Pelak: critical revision of the manuscript for important intellectual content. Katherine Rankin: study supervision.

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Disclosure

P.S. Pressman, K. Gola, and S. Shdo report no disclosures relevant to the manuscript. B. Miller has served as director on the medical advisory board of the Larry H. Hillblom Foundation, medical director of the John Douglas French Foundation, and scientific director of the Tau Consortium. C. Mielke, C. Fredericks, V. Pelak, and K. Rankin report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

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