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ORIGINAL COMMUNICATION

Social cognition and behavioral changes in patients with posterior cortical atrophy

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Abstract

Posterior cortical atrophy (PCA) is a rare neurodegenerative condition characterized by progressive visual and visuospatial dysfunction. The consensus criteria state that patients should present "relatively spared behavior and personality" in early stages. However, limited research has focused on these symptoms in PCA. This study compared 157 patients with PCA in early stages of the disease with 352 healthy controls (HC), 202 typical AD (tAD), and 177 logopenic variant primary progressive aphasia (lvPPA) patients from the National Alzheimer's Coordinating Center (NACC) dataset. They were compared using clinician ratings of behavioral symptoms, informant- and clinician-filled questionnaires and patient-facing tests of behavior and social cognition. Results showed that PCA individuals exhibited many behavioral symptoms, the more frequently reported being anxiety, depression, apathy, and irritability. During cognitive testing, clinicians observed disorganized and reactive behaviors, but no insensitive behaviors. Informant reports indicated that PCA patients exhibited higher levels of inhibition and anxiety in response to stimuli associated with non-reward, novelty, and punishment. Social norms knowledge and empathy were overall preserved, although slight decreases in perspective-taking and socioemotional sensitivity were observed on informant-rated questionnaires. Except for more elevated neuropsychiatric symptoms in tAD, the three AD variants had similar profiles. Our findings provide insights into the social cognition and behavioral profiles of PCA, highlighting patterns of preservations and mild impairments, even in the early stages of the disease. These results contribute to a more complete understanding of non-visual symptoms in PCA and have implications for diagnostic and intervention strategies.

Keywords Posterior cortical atrophy · Alzheimer's disease · Social cognition · Behavior · Emotion · Neuropsychology

Introduction

Posterior cortical atrophy (PCA) is a rare neurodegenerative disease characterized by a progressive decline in visual and visuospatial functions [1, 2]. The visual deficits are associated with dysfunctions in parietal, occipital and occipito-temporal regions of the brain. The most common neuropathological cause is Alzheimer disease (AD), although other possible causes are Lewy body dementia, corticobasal degeneration and prion diseases [1]. Since the disease often

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starts between ages 50 and 65 years old, it is often considered an early onset atypical Alzheimer's disease variant. The most frequent clinical manifestations are visual and spatial agnosia, simultanagnosia, constructional dyspraxia, environmental disorientation, oculomotor and dressing apraxia, optic ataxia, alexia, acalculia, apperceptive prosopagnosia and agraphia [1]. In contrast, the most recent consensus criteria state that patients should present relatively spared behavior and personality, memory, language, and executive functions in early stages, although these features may appear in more advanced stages [1].

Nonetheless, some studies have investigated non-visual symptoms in PCA and have observed patterns of impairments in other domains. A majority of PCA patients have reported very mild to mild impairments in episodic memory, language, and attention/executive domains [3]. More precisely, episodic and working memory have been shown to be impaired as early as at clinical presentation [4, 5]. A study by Crutch and colleagues has also shown that PCA patients can have deficits in multiple language domains, including anomia, reduced phonemic fluency and slowed speech as the main deficits [6].

However, behavior and social cognition have rarely been investigated in PCA. Behavioral symptoms are a group of non-cognitive symptoms which can include neuropsychiatric symptoms (agitation, aberrant motor behavior, anxiety, elation, irritability, depression, apathy, disinhibition, delusions, hallucinations, and sleep or appetite changes) and personality changes. These symptoms can be associated with distress among patients with dementia and their caregivers, long-term hospitalization, misuse of medication, and increased health care costs [7]. Social cognition corresponds to a set of mental abilities essential for perception, processing, interpretation, and response to social stimuli. It includes a variety of components such as emotion reading, theory of mind, empathy, moral judgment and socio-emotional semantic knowledge [8–10]. While these domains represent core deficits in other types of neurodegenerative diseases such as the behavioral [11] and semantic behavioral variants of frontotemporal dementia [12], they have also shown to be very useful for the differential diagnosis of many other neurodegenerative diseases such as primary progressive aphasia, Parkinson's disease and amnestic or typical AD (tAD) [13–15]. Social cognition has also been included as a cognitive domain in the DSM-5, highlighting its importance to delineate a full cognitive profile in patients with cognitive difficulties.

While behavior and social cognition are often thought to be relatively well preserved in PCA because they mostly rely on frontal and temporal networks, only a few studies have systematically investigated their substrates in PCA. In terms of neuropsychiatric symptoms in PCA, it has been shown that the most frequent are apathy, anxiety, depression, and irritability, while eating alterations, aberrant motor behaviors, nighttime behavioral disturbances, euphoria, and disinhibition are less frequent [16]. Furthermore, in comparison with tAD, a higher proportion of anxiety symptoms has been reported in PCA [16] which could potentially be explained by the awareness of their medical problem [2]. In terms of facial emotion reading, a relative preservation of facial expression recognition, in comparison to facial identity recognition, is noted in PCA patients [17]. This is consistent with a case study of Gonzalez-Gadea and colleagues (2015), in which a patient with PCA was able to recognize the emotional valence and arousal in most images as well as healthy controls do (except for negative faces), despite a clear difficulty to consciously identify the image [18]. Finally, it has been reported that PCA and logopenic variant of primary progressive aphasia (lvPPA) patients do not differ with regards to behavioral and affective symptoms [19].

Given the lack of studies that comprehensively describe the performance of PCA patients in terms of behavior and social cognition, there is a clear need of a systematic investigation in this population, especially in the earlier stages of the disease. Most social cognitive domains, such as theory of mind, empathy and the knowledge of social norms have not been investigated in this population. In addition to the potential implications for differential diagnosis, the assessment of social cognition in PCA is crucial to facilitate good communication and interpersonal relations, which has an impact on the mental health and the quality of life of people with social cognitive deficits [14]. These impairments can also affect relatives of those afflicted, increasing the burden and familial stress [20]. Moreover, some brain regions important in social cognition are closely localized to dysfunctional regions in PCA, such as the superior temporal sulcus and temporoparietal junction which are important for theory of mind [10].

Therefore, the current study aims to compare 157 PCA individuals with 352 healthy controls (HC) from the National Alzheimer's Coordinating Center (NACC) on multiple components of social cognition to determine the patterns of behavior and social cognition impairments in PCA. A secondary objective is to determine if these components differ with 202 amnestic Alzheimer and 177 lvPPA individuals. The tests used evaluate neuropsychiatric symptoms, social behavior, empathy, social norms knowledge, and behavioral inhibition. We hypothesize that mild behavioral and social cognitive deficits will be observed in PCA.

Methods

Participants

The sample included cognitively unimpaired older healthy controls (HC), PCA, tAD and lvPPA participants from the

National Alzheimer's Coordinating Center (NACC) database, which were recruited in Alzheimer's Disease Research Centers (ADRC). Patients were diagnosed according to research criteria [6, 21, 22]. This study used data from 46 ADRCs for Uniform Data Set (UDS) visits conducted between September 2005 and December 2022. All participants or their informants provided written informed consent.

From the NACC database, we selected all PCA and lvPPA participants who completed at least one test of social cognition or behavior. Because of the higher number of healthy controls and tAD patients in the NACC database, we selected only those who had at least two tests of social cognition or behavior. Furthermore, we only selected patients (PCA, tAD and lvPPA) with a CDR® Dementia Staging Instrument score of 1 or below, to restrict the analyses to patients in the early stages of the disease. The healthy controls were required to present a CDR® Dementia Staging Instrument score of 0 and about the same age range as PCA, which is between 50 and 83 years old. In the end, 157 PCA, 352 HC, 202 tAD and 177 lvPPA were included in our sample.

Measurement of behavioral symptoms and social cognition

All behavioral and social cognition assessment tools from the Uniform data set version 3 and the Frontotemporal Lobar Degeneration Module (FTLD-MOD) were used for this study [23–26].

Neuropsychiatric inventory-questionnaire (NPI-Q)

The questionnaire is filled by a clinician based on the interview with the informant. It evaluates 12 neuropsychiatric symptom domains (delusions, hallucinations, agitation/aggression, dysphoria/depression, anxiety, euphoria/elation, apathy/indifference, disinhibition, irritability/lability, aberrant motor behaviors, nighttime behavioral disturbances, and appetite/eating disturbances) with "yes" or "no" questions, as well as a severity scale ranging from mild to severe. Only the absence/presence section was used in this study.

Clinician judgment of symptoms

We selected questions relating to the clinician's judgment of behavioral symptoms based on the clinical interview (apathy/withdrawal, depressed mood, visual and/or auditory hallucinations, delusions, disinhibition, irritability, agitation, personality change and anxiety). Each item is answered by a yes or no response.

Behavioral inhibition scale (BIS)

This questionnaire is completed by an informant. It includes seven questions designed to assess the patient's behaviors associated to behavioral inhibition and anxiety. It specifically evaluates traits related to avoiding certain responses and being sensitive to threats (e.g., "Criticism or scolding hurts the subject quite a bit"). It uses a 4-point Likert scale, ranging from "Strongly disagree" to "Strongly agree," [27]. The total score, falling within the range of 7 to 28, is obtained by summing up the responses.

Geriatric depression scale (GDS-15)

The short version of the GDS is a clinician-filled questionnaire evaluating depression based on the answers of the participant. It includes 15 dichotomous items (yes or no) which sums up in a total score between 0 and 15.

Social behavior observer checklist (SBOCL)

In this checklist, the clinician must rate the frequency of 35 specific behaviors (e.g., "Giggled or otherwise made silly, childish comment or noise") using categories such as "never," "once," "2-3xs," or "4+" after engaging with the patient for approximately 30–60 min. These behaviors are categorized into 14 main descriptor items (e.g., "Showed diminished social/emotional engagement"; "not at all," "a little bit," "moderately," "severely") [28]. This assessment yields five scores: a total descriptor score (ranging from 0 to 42), a total checklist behavior score (ranging from 0 to 105), and three behavioral symptom categories derived through cluster modeling across all descriptors: (1) Disorganized (Failed to adapt to structure, Stimulus-bound, Perseverative, Decreased initiation, Fluctuating level of cognitive ability, Diminished social engagement), (2) Reactive (Overly self-conscious, Anxious, Overly dependent, Exaggerated emotional reactivity, Preoccupied with time), and (3) Insensitive (Too little self-consciousness, Insensitive to others' embarrassment, Overly disclosing/inappropriately familiar). Scores for these three descriptors were used in the current study.

Interpersonal reactivity index (IRI)

This questionnaire is designed to measure empathy. The informant is asked to answer to 28 questions about the individual being assessed, using a 5-point Likert scale that ranges from "Does not describe well" to "Describes very well" [29]. The version utilized by the NACC is divided into two subscales: empathic concern (e.g., "The subject often has tender, concerned feeling for people less fortunate than me") and perspective taking (e.g. "The subject sometimes

find it difficult to see things from the other guy's point of view"). Each of these subscales produces a score that falls within the range of 7–35.

Revised self-monitoring scale (RSMS)

The RSMS is an empathy questionnaire where the informant responds to 13 questions aimed at assessing the patient's socioemotional sensitivity. It uses a 6-point Likert scale that ranges from "Totally disagree" to "Totally agree," [30, 31]. This questionnaire encompasses items that gauge the individual's sensitivity to expressive behavior, exemplified by questions like "The subject is often capable of accurately interpreting people's genuine emotions through their eye expressions," as well as their ability to modify their self-presentation based on their observations of social feedback from others. Responses are added up to yield a total score ranging from 0 to 65.

Social norms questionnaire (SNQ-22)

In this social cognition task, the participants are tasked with determining the social acceptability of 22 behaviors when they are performed in the presence of a stranger or acquaintance (not a close friend or family member), within the cultural norms of mainstream United States society. For instance, they must determine whether actions like spitting on the floor (not acceptable) or blowing your nose in public (acceptable) are appropriate [32]. The assessment yields three scores: a total score ranging from 0 to 22, a break score (ranging from 0 to 12), indicating accurate identification of behaviors that violate social norms, and an overadhere score (ranging from 0 to 10), representing a control subscale for socially appropriate actions.

Statistical analyses

Data pre-processing and statistical analyses were conducted using R (version 4.3.0). The 4 groups (HC, PCA, tAD and lvPPA) were compared on demographic variables using t tests for the level of education, total MoCa score, age, total CDR® Dementia Staging Instrument score and disease duration. As for race, sex, amyloid status, tau status, dopamine transporter scan and number of APOE alleles, Fisher tests were used.

The total scores of the GDS, the SNQ22 (break and overadhere scores), the SBOCL subscales, the IRI (empathic concern and perspective taking scores), the RSMS total score as well as the BIS total score were compared between the 4 groups (HC, PCA, tAD and lvPPA) using ANCOVAs controlling for age, sex and education. The p values of the post-hoc tests were adjusted for multiple comparisons using the Tukey method.

As for the presence/absence of neuropsychiatric symptoms (NPI) and 11 questions of the Clinician Judgment of Symptoms, logistic regressions controlling for age, sex and education were used to compare PCA with the three other groups. The p-values were adjusted for multiple comparisons using the Bonferroni method (multiplied by three) for each symptom.

Results

Description of participants

In total, 157 PCA, 352 HC, 202 tAD and 177 lvPPA were included in our sample. Participants' demographics and disease characteristics are presented in Table 1. Because a significant proportion of this sample only had UDS data available (i.e. NPI and GDS), and not FTLD-MOD, we also present demographics and disease characteristics of the subsample with at least one test in the FTLD module in Online Resource Table 1. This subsample included 35 PCA, 352 HC, 202 tAD and 51 lvPPA participants. There was no significant difference between demographic data or disease characteristics between the full PCA sample and the PCA subsample. All analyses were conducted on available data for each test.

At the demographic level, a few between-group differences were observed in terms of age, sex and education (Table 1). All analyses are therefore controlled for these three demographic variables. A majority of patients who underwent biomarker testing (cerebrospinal fluid or positron emission tomography for beta-amyloid or tau) showed beta-amyloid positivity (Positive/Negative/Unknown: 45.9%/3.8%/50.3% in PCA; 48.5%/9.4%/42.1% in tAD; 33.9%/7.3%/58.8% in lvPPA) and tau positivity (Positive/Negative/Unknown: 33.1%/5.7%/61.2% in PCA; 31.7%/6.9%/61.3% in tAD; 22.0%/7.3%/70.6% in lvPPA). Expectedly, PCA patients had lower MoCA, CDR® Dementia Staging Instrument scores and had higher rates of amyloid positivity, tau positivity and APOE status in comparison to HC. Furthermore, there were significant differences in terms of disease severity between the three patients' groups. Therefore, when statistically significant differences were identified between two patients' groups, we ran an additional analysis with CDR® Dementia Staging Instrument scores as an additional covariate to confirm that the result was not due to differences in dementia severity.

Behavioral symptoms and social cognition

In terms of behavioral symptoms reported on the NPI, PCA patients showed a frequency of neuropsychiatric symptoms ranging from 3% for euphoria/elation to 42% for anxiety.

Table 1 Demographics data

	HC (N = 352)	PCA (N = 157)	tAD (N = 202)	lvPPA (N = 177)
Years of education	16.01 ± 2.55[c,d]	15.88 ± 2.98[d]	15.51 ± 2.72[a,d]	16.51 ± 2.53[a,b,c]
MoCA	26.91 ± 2.46[b,c,d]	14.39 ± 6.19[a,c]	15.91 ± 6.07[a,b,d]	14.05 ± 6.8[a,c]
Age	63.20 ± 8.18[b,c,d]	65.15 ± 8.26[a,c,d]	60.93 ± 6.81[a,b,d]	67.89 ± 8.27[a,b,c]
Global CDR®	0[b,c,d]	0.83 ± 0.24[a,c,d]	0.75 ± 0.26[a,b,d]	0.58 ± 0.31[a,b,c]
CDR® sum of boxes	0[b,c,d]	4.70 ± 1.73[a,d]	4.53 ± 1.76[a,d]	3.15 ± 2.11[a,b,c]
Disease duration (years)	–	4.69 ± 2.51	4.31 ± 3.14[d]	5.08 ± 2.96[c]
White	90.62%[b,d]	97.45%[a]	90.10%	93.79%[a]
Black or African American	5.40%	1.91%	4.95%	1.13%
American Indian or Alaska Native	0.00%	0.00%	0.50%	0.00%
Native Hawaiian or Pacific Islander	3.69%	0.64%	1.98%	3.39%
Asian	0.28%	0.00%	0.99%	1.69%
Multiracial	0.00%	0.00%	1.49%	0.00%
Male	42.61%[d]	38.22%[c,d]	51.49%[b]	55.93%[a,b]
Female	57.39%	61.78%	48.51%	44.07%
Amyloide-negative	2.84%[b,c,d]	3.82%[a]	9.41%[a]	7.34%[a]
Amyloid-positive	0.28%	45.86%	48.51%	33.90%
Unknown amyloid status	96.88%	50.32%	42.08%	58.76%
Tau-negative	3.12%[b,c,d]	5.73%[a]	6.93%[a]	7.34% [a]
Tau-positive	0.00%	33.12%	31.68%	22.03%
Unknown tau status	96.88%	61.15%	61.39%	70.62%
Dopamine-negative	1.14%	5.10%	3.47%	5.65%
Dopamine-positive	0.00%	0.64%	0.00%	0.00%
Unknown dopamine status	98.86%	94.27%	96.53%	94.35%
No APOE alleles	51.99%[b,c]	30.57%[a]	26.24%[a]	45.20%
1 copy of APOE alleles	25.00%	33.76%	19.31%	27.12%
2 copies of APOE alleles	2.27%	5.73%	8.42%	5.65%
Unknown APOE status	20.74%	29.94%	46.04%	22.03%

Significant differences between groups ($p \leq 0.05$) are denoted as: a = different from HC; b = from PCA; c = from tAD; d = from lvPPA

In comparison to HC, PCA patients presented significantly more disinhibition, apathy, delusions, agitation, depression, anxiety, irritability, hallucinations, motor disturbance, nighttime behavior and eating changes (Table 2, Fig. 1). However, in comparison to tAD, PCA patients presented with less disinhibition, apathy, depression, irritability and eating change (Table 2, Fig. 1). Adding the CDR as covariate in the statistical model to control for disease severity did not modify the significance of these between-patients differences (see Online Resource, Table 3). No differences were observed between PCA and lvPPA for neuropsychiatric symptoms.

Regarding clinician ratings of behavioral symptoms, 60% of PCA patients were flagged as having overall behavioral changes. When looking at specific symptoms, they ranged from 2% (auditory hallucinations and personality changes) to 31% (anxiety) in PCA. In comparison to HC, the clinicians noted significantly more disinhibition, apathy, agitation, depression, anxiety, irritability and general behavior symptoms in PCA patients (Table 2, Fig. 1). Similarly to what was observed on the NPI, there was also significantly more disinhibition, apathy, irritability and personality changes in tAD than PCA (Table 2, Fig. 1). For behavioral inhibition as measured with the BIS, there was a significant difference between PCA and HC. In terms of depressive symptoms as assessed by the GDS-15, they were significantly more elevated in PCA patients in comparison to HC. Adding the CDR as covariate in the statistical model to control for disease severity did not modify the significance of these results. No differences were observed between PCA and lvPPA for clinician-rated behavioral symptoms.

Regarding social cognition, many differences were found between PCA patients and HC (Table 3, Fig. 2). In terms of social behaviors reported on subscales of the SBOCL, there were significant differences between PCA and HC for the disorganized and reactive subscales. Regarding empathy, measured by either IRI or RSMS, significant differences were found between PCA and HC: PCA patients had a lower RSMS total score and a lower perspective-taking score on the IRI compared to HC. Finally, for social norms knowledge, measured by the SNQ, there was a significant

Table 2 Differences between groups for behavioral symptoms

	Comparison	Z value	*p* value
Disinhibition—NPI	PCA—HC	− 4.314	< 0.001*
	PCA—tAD	3.013	0.008*
	PCA—lvPPA	1.002	0.949
Apathy—NPI	PCA—HC	− 7.239	< 0.001*
	PCA—tAD	4.028	< 0.001*
	PCA—lvPPA	0.159	2.620
Delusions—NPI	PCA—HC	− 3.788	< 0.001*
	PCA—tAD	1.247	0.637
	PCA—lvPPA	− 1.880	0.180
Agitation—NPI	PCA—HC	− 6.096	< 0.001*
	PCA—tAD	1.941	0.157
	PCA—lvPPA	− 0.921	1.071
Depression—NPI	PCA—HC	− 5.786	< 0.001*
	PCA—tAD	3.191	0.004*
	PCA—lvPPA	0.258	2.389
Anxiety—NPI	PCA—HC	− 7.476	< 0.001*
	PCA—tAD	1.982	0.143
	PCA—lvPPA	0.412	2.041
Irritability—NPI	PCA—HC	− 4.741	< 0.001*
	PCA—tAD	3.315	0.003*
	PCA—lvPPA	− 0.311	2.268
Hallucinations—NPI	PCA—HC	− 3.524	0.001*
	PCA—tAD	− 1.083	0.836
	PCA—lvPPA	− 2.041	0.124
Euphoria—NPI	PCA—HC	− 2.002	0.136
	PCA—tAD	0.970	0.996
	PCA—lvPPA	1.226	0.661
Motor disturbance—NPI	PCA—HC	− 5.184	< 0.001*
	PCA—tAD	2.067	0.116
	PCA—lvPPA	− 2.016	0.131
Nighttime behaviors—NPI	PCA—HC	− 4.145	< 0.001*
	PCA—tAD	2.086	0.111
	PCA—lvPPA	− 0.647	1.552
Eating changes—NPI	PCA—HC	− 4.880	< 0.001*
	PCA—tAD	3.169	0.005*
	PCA—lvPPA	0.321	2.245
Disinhibition—clinician	PCA—HC	− 2.962	0.009*
	PCA—tAD	2.397	0.050*
	PCA—lvPPA	0.967	1.001
Apathy—clinician	PCA—HC	− 4.423	< 0.001*
	PCA—tAD	3.898	< 0.001*
	PCA—lvPPA	0.026	2.938
Delusions—clinician	PCA—HC	− 0.019	2.955
	PCA—tAD	− 0.168	2.599
	PCA—lvPPA	− 1.881	0.180
Agitation—clinician	PCA—HC	− 3.603	0.001*
	PCA—tAD	1.911	0.168
	PCA—lvPPA	0.829	1.222
Depression—clinician	PCA—HC	− 6.857	< 0.001*
	PCA—tAD	1.989	0.140
	PCA—lvPPA	− 0.794	1.281
Anxiety—clinician	PCA—HC	− 6.284	< 0.001*
	PCA—tAD	1.939	0.157
	PCA—lvPPA	− 0.350	2.178
Irritability—clinician	PCA—HC	− 5.062	< 0.001*
	PCA—tAD	4.087	< 0.001*
	PCA—lvPPA	0.738	1.382
Visual hallucinations—clinician	PCA—HC	− 0.019	2.955
	PCA—tAD	− 0.909	1.091
	PCA—lvPPA	− 1.653	0.295
Auditory hallucinations—clinician	PCA—HC	− 0.008	2.982
	PCA—tAD	− 0.325	2.236
	PCA—lvPPA	− 0.336	2.211
Personality changes—clinician	PCA—HC	− 1.296	0.585
	PCA—tAD	2.934	0.010*
	PCA—lvPPA	0.521	1.808
Overall behavior—clinician	PCA—HC	− 9.537	< 0.001*
	PCA—tAD	2.386	0.051
	PCA—lvPPA	− 1.076	0.846

Results from logistic regressions controlling for age, sex and education. Significant differences between PCA and other groups are denoted as: *p ≤ .05 (Bonferroni-corrected p value)

difference between PCA and HC on the overadhere score. However, no differences were found between the three patients' groups in any of the social cognition assessment tools.

Discussion

The main aim of this study was to compare PCA patients in the early stages of the disease with HC across various aspects of social cognition and behavioral symptoms to identify the patterns of preservation and impairments in these domains in PCA. We observed higher frequencies of disinhibition, apathy, delusions, agitation, depression, anxiety, irritability, hallucinations, motor disturbance, nighttime behavior and eating changes in PCA compared to HC, using a neuropsychiatric questionnaire and clinician-based ratings. PCA patients were also described as more avoidant and sensitive to threats on an informant-filled questionnaire. During cognitive testing, disorganized and reactive behaviors were frequently observed by clinicians. While slight decreases in perspective-taking and socioemotional sensitivity were observed on informant-rated questionnaires, empathic concern was preserved on the same questionnaire, insensitive

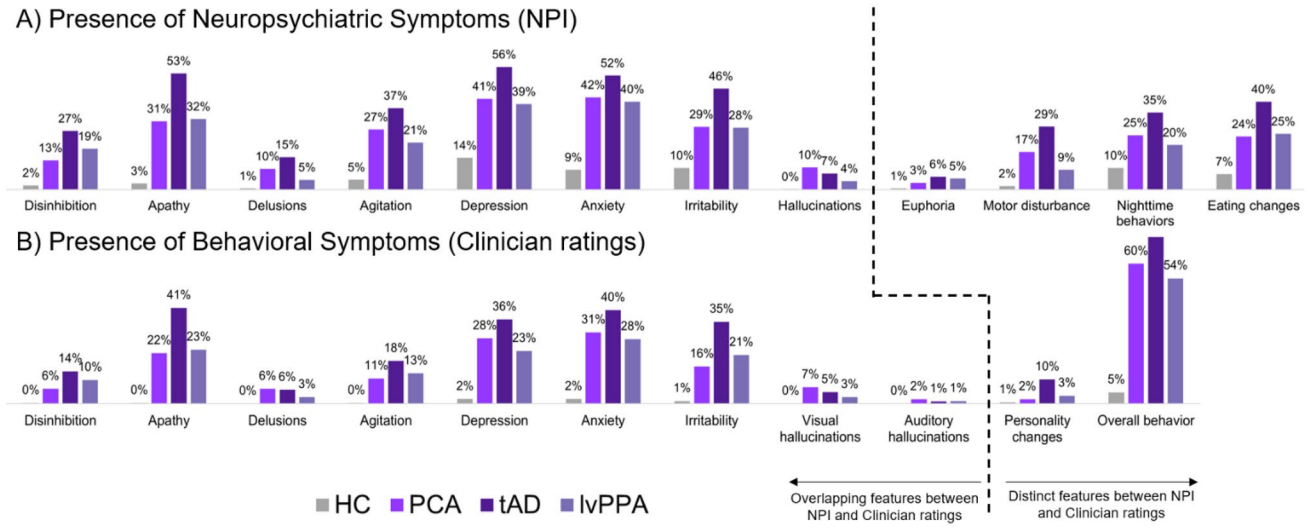

Fig.1 Presence of behavioral symptoms. On the left side of the line, you can see overlapping features between the questionnaires and on the right side of the line the distinct features

behaviors were absent during cognitive testing and personality changes were almost never reported by clinicians. Altogether, these results suggest no major changes in empathy in PCA patients. Social norms knowledge was preserved in PCA patients, although they tended to be overly cautious when determining whether a behavior is socially inappropriate or not. The second aim of this study was to assess whether these behavioral and social cognitive components exhibited variations when comparing with other AD variants, namely tAD and lvPPA. The three AD variants had very similar profiles of social cognitive performance, with the exception for differences in the frequency of neuropsychiatric symptoms. More precisely, we observed more frequent apathy, depression, irritability and eating changes in tAD in comparison to PCA.

While PCA is characterized by predominant impairments in visual and visuospatial functions, our study, as well as a few others before, highlight the relevance of investigating non-predominant impairments in other cognitive domains. Our results suggest that mild behavioral and social cognition impairments are observed in PCA, even in early stages of the disease, similarly to what has been observed in language, memory and executive functioning [3–6]. This is an essential nuance to consider for clinicians applying the most recent consensus criteria for PCA, which state that patients should present relatively spared behavior and personality in early stages, although these features may appear in more advanced stages [1]. While it is true that behavioral and social cognition features may not be as severe as visual impairments, they are still present, and our study significantly contributes to the precise delineation of profiles of impairments and preservations within this domain. This is helpful in establishing clearer expectations regarding which impairments to anticipate, and it underscores the importance of not dismissing a PCA diagnosis solely based on the presence of behavioral and social cognition features.

More precisely, and consistently with previous studies, we found that anxiety, depression, apathy and irritability are the most frequent neuropsychiatric symptoms in PCA [16, 33], as well as the most easily detected by clinicians. However, we also found higher frequencies of disinhibition, delusions, agitation, hallucinations, motor disturbance, nighttime behavior and eating changes in PCA, which were all present in more than 10% of patients. Consistently with these results, patients were also described as presenting more behavioral inhibition and anxiety, specifically trait response avoidance and sensitivity to threat (i.e., worry), using the BIS. Interestingly, when comparing the frequencies of the same neuropsychiatric behaviors as measured by a formal questionnaire versus clinician ratings, we observed significantly higher rates with the NPI questionnaire (Fig. 1). This underscores the importance of thorough questioning to avoid overlooking symptoms that may be crucial for disease management.

In terms of social behaviors during testing, disorganized and reactive behaviors were frequently observed by clinicians, but insensitive behaviors were not. Disorganized behaviors might be related to the executive impairments observed in PCA patients [3–5], as well as brain damage that can extend to frontal and fronto-parietal networks [34]. The heightened reactive behaviors and absence of insensitive behaviors are also consistent with previous literature. In fact, increased emotional reactivity and contagion have been reported in individuals with AD previously, albeit not

Table 3 Differences between groups for social cognition and GDS-15

	Group	Mean	F value	*p* value	Partial eta-squared
BIS total score	HC (N = 284)	16.67 ± 3.85[b,c,d]	18.341	< 0.001	0.104
	PCA (N = 20)	19.4 ± 4.15[a]			
	tAD (N = 158)	19.37 ± 3.90[a]			
	lvPPA (N = 36)	18.78 ± 3.23[a]			
GDS-15	HC (N = 343)	1.62 ± 2.11[b,c,d]	22.364	< 0.001	0.081
	PCA (N = 139)	3.13 ± 2.65[a]			
	tAD (N = 172)	3.37 ± 3.25[a]			
	lvPPA (N = 132)	2.9 ± 2.8[a]			
Disorganized—SBOCL	HC (N = 351)	0.08 ± 0.28[b,c,d]	43.120	< 0.001	0.174
	PCA (N = 34)	0.74 ± 1.15[a]			
	tAD (N = 201)	0.92 ± 1.31[a]			
	lvPPA (N = 51)	0.97 ± 1.31[a]			
Reactive—SBOCL	HC (N = 351)	0.18 ± 0.46[b,c,d]	34.923	< 0.001	0.146
	PCA (N = 34)	0.91 ± 1.21[a]			
	tAD (N = 201)	0.81 ± 1.06[a]			
	lvPPA (N = 51)	0.8 ± 0.92[a]			
Insensitive—SBOCL	HC (N = 351)	0.05 ± 0.36[c]	4.949	0.002	0.024
	PCA (N = 34)	0.10 ± 0.36			
	tAD (N = 201)	0.20 ± 0.57[a]			
	lvPPA (N = 51)	0.18 ± 0.43			
Empathy concern—IRI	HC (N = 278)	28.36 ± 5.39[c]	8.799	< 0.001	0.054
	PCA (N = 19)	28.74 ± 5.10			
	tAD (N = 154)	25.73 ± 6.49[a]			
	lvPPA (N = 36)	25.25 ± 5.31			
Perspective taking—IRI	HC (N = 278)	24.76 ± 6.18[b,c,d]	31.306	< 0.001	0.168
	PCA (N = 19)	19.95 ± 6.18[a]			
	tAD (N = 154)	18.94 ± 6.57[a]			
	lvPPA (N = 36)	18.89 ± 5.82[a]			
RSMS total score	HC (N = 282)	45.9 ± 10.14[b,c,d]	49.751	< 0.001	0.239
	PCA (N = 19)	32.32 ± 9.21[a]			
	tAD (N = 158)	33.73 ± 11.33[a]			
	lvPPA (N = 36)	33.75 ± 12.77[a]			
SNQ22—break score	HC (N = 342)	0.40 ± 0.67[c,d]	8.804	< 0.001	0.045
	PCA (N = 23)	0.78 ± 1.17			
	tAD (N = 176)	0.73 ± 1.15[a]			
	lvPPA (N = 33)	1.09 ± 1.70[a]			
SNQ22—overadhere score	HC (N = 342)	1.74 ± 1.51[b,c,d]	20.484	< 0.001	0.100
	PCA (N = 23)	3.13 ± 1.98[a]			
	tAD (N = 176)	2.94 ± 2.21[a]			
	lvPPA (N = 33)	2.85 ± 1.91[a]			

Mean scores on the Behavioral Inhibition Scale (BIS), the Geriatric Depression Scale, the Social Behavior Observer Checklist (SBOCL), the Interpersonal Reactivity Index (IRI), the Revised Self-monitoring Scale (RSMS) and the Social Norms Questionnaire (SNQ-22). Results from ANCOVAs controlling for age, sex and education. Significant differences between groups are denoted as: a = different from HC; b = from PCA; c = from tAD; d = from lvPPA at $p \leq .05$ (Tukey-corrected p values for post-hoc tests)

specifically in patients with PCA, and it has been shown to be associated with increased functional connectivity within the salience network in AD patients [35–37]. Future studies should investigate this association in PCA. Finally, it is quite interesting to note that the heightened reactivity might be captured using a brief and straightforward observation

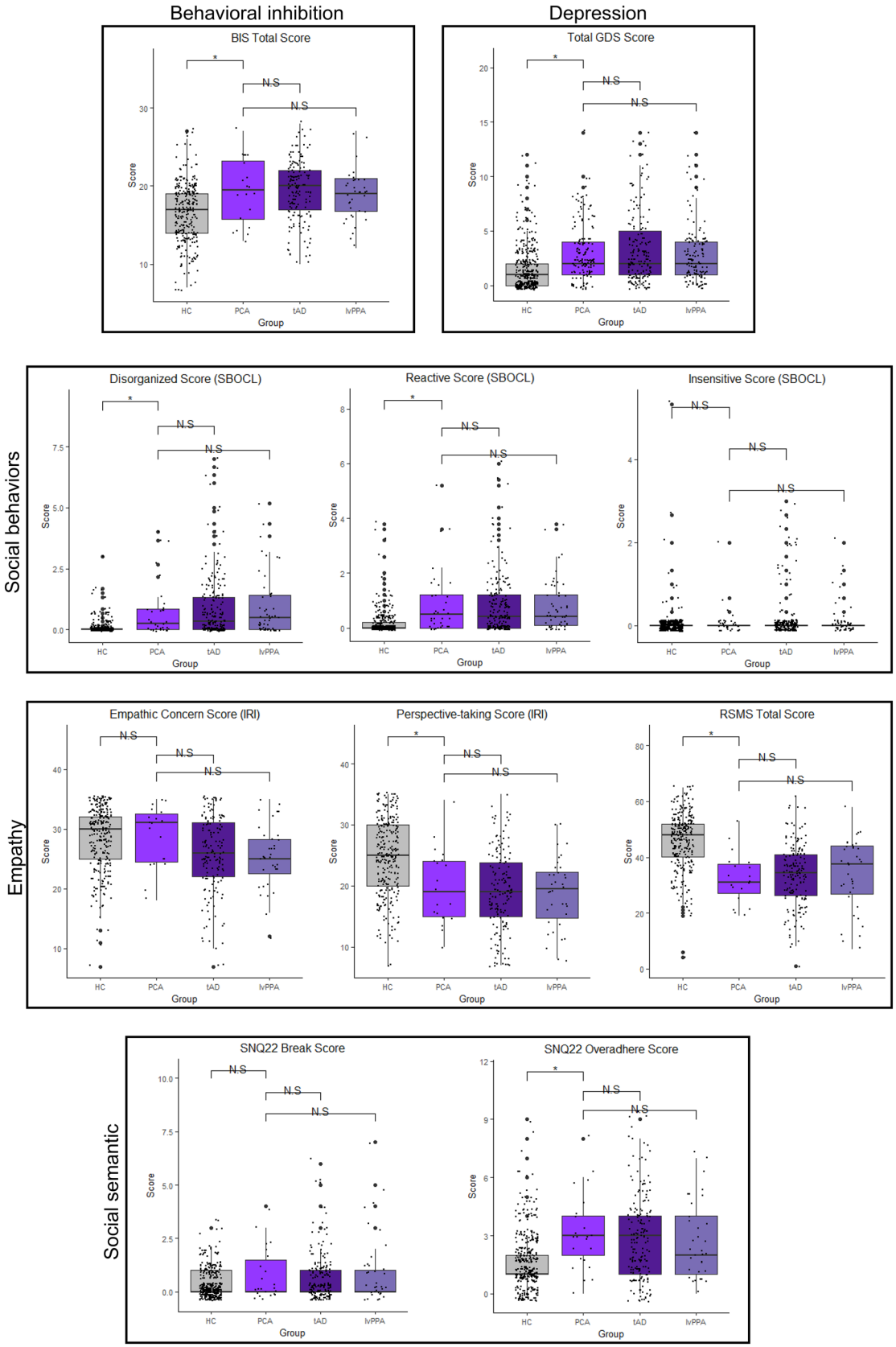

Fig. 2 Comparisons of social cognition measures and GDS-15 total scores between PCA and other groups. Significant differences between PCA and other groups are denoted as: *p ≤ .05 (Tukey-corrected p-values for post-hoc tests) *N.S* not significant

checklist completed by a clinician following testing. Our study therefore highlights the clinical relevance of the SBOCL in PCA patients.

Consistently with these findings, results from the informant-rated IRI suggested a preserved empathic concern and a very mildly reduced perspective-taking in PCA. This result might be explained by the fact that perspective-taking is strongly related to executive abilities such as working memory, mental set switching, and inhibitory control, which are often impaired in PCA [38–40]. While looking at item-level data on the IRI, PCA patients were described as having lower perspective-taking on two particular items which were related to looking at both sides of a disagreement or a question before making a decision, which might particularly implicate executive functioning. In contrast, the informant-filled RSMS provided conflicting results, more specifically a significantly reduced socioemotional sensitivity in PCA patients. Nonetheless, previous studies have shown that the RSMS detects very subtle changes in socioemotional sensitivity, even in HC [31]. Furthermore, the RSMS detects slight changes in all other neurodegenerative disorders including primary progressive aphasia, progressive supranuclear palsy and AD, although nowhere near the impairments observed in behavioral variant of frontotemporal dementia [9]. Overall, when combining observations from the NPI, SBOCL, IRI and RSMS, we can conclude of a relative preservation of empathy in PCA patients,

At the semantic level, there seems to be no deficits in knowledge of social norms among PCA patients in the only patient-facing test of the study. The increased overadhere score in the SNQ22 could be caused by confusion, general cognitive deficits or anxiety which makes them comply more than what is socially expected.

Besides a few differences in rates of neuropsychiatric symptoms, behavioral symptoms and social cognition do not appear particularly useful in distinguishing PCA, tAD & lvPPA. More precisely, disinhibition, apathy, depression, irritability and eating changes seem to be the more frequently observed in tAD vs PCA, while there seems to be no differences between PCA and lvPPA. Previous studies suggested higher anxiety in PCA [16, 33] but we did not replicate this result in our study using a larger sample size. Nonetheless, it is still relevant to investigate social cognition in tAD and lvPPA, as impairments have been reported before [13, 41, 42] and in the current study. Furthermore, behavioral and social cognitive assessment will be critical in the diagnosis of other atypical variants such as behavioral variant of AD (bvAD), and potentially dysexecutive AD (dAD) [43, 44]. Behavioral and social cognitive symptoms are at the core of bvAD, since it is characterized by two of the classic bvFTD symptoms (behavioral disinhibition, apathy or inertia, loss of empathy or sympathy, hyperorality and dietary changes) in the context of positive AD biomarkers. A recent study from Singleton et al. (2023) found deficits in emotion recognition, empathy based on informant and knowledge of social norms with a higher break score in this population [45]. While patients with dAD are described as showing predominant executive dysfunctions (working memory, cognitive flexibility, and cognitive inhibitory control) in the absence of predominant behavioral features, more detailed studies are needed to clarify this profile. Future studies should compare all AD variants on behavioral and social cognitive features.

This study has some limitations. First, although our study includes a large sample size and extensive test battery, missing data was observed in the PCA group, particularly for the FTLD-MOD social cognition tasks. Secondly, there were some demographic differences between the four groups, which were controlled in subsequent statistical analyses. Thirdly, within the FTLD-MOD, there is only one patient-facing social cognition assessment tool, indicating the necessity for additional research that extends beyond clinician observations and questionnaires completed by informants. Developing this kind of test would be important to ensure that the perspective of the informant or the clinician fits with objective social deficits of PCA patients. Due to the visual deficits in PCA, a lot of existing social cognitive tests would be inappropriate in this population. However, using auditory stimuli to measure social cognition could represent a good avenue. For example, emotion recognition tasks could use emotional bursts and affective prosody [46, 47] and theory of mind could use short auditory scenarios instead of written vignettes. A physiological approach could also be particularly interesting to test emotional reactivity in PCA patients.

In conclusion, our study reveals the nuanced nature of social cognition and behavioral symptoms in PCA. It also emphasizes the need to avoid oversimplification by recognizing that behavior, personality, and social cognition are multifaceted domains. Even in clinical syndromes where they are not the predominant symptoms, evaluating social cognition can be pivotal for improving communication and interpersonal relationships, thereby enhancing mental health and overall quality of life. The experiences of PCA patients, such as the individual in Harding et al.'s (2018) study who described the challenges of daily interactions ("I'm usually quite okay here but the minute I step outside the door it all goes mad… Life goes a bit strange,yes… (…) dealing with… interacting with people, in general, no, it's not great, not great… (…) I'm much less comfortable and avoid, now, going unless I really need to go into town."), underscore the importance of tailored interventions and support [48].

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Declarations

Conflicts of interest The authors declare that they have no conflict of interest.

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