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The language profile of Posterior Cortical Atrophy

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Abstract

Background—Posterior Cortical Atrophy (PCA) is typically considered to be a visual syndrome, primarily characterised by progressive impairment of visuoperceptual and visuospatial skills. However patients commonly describe early difficulties with word retrieval. This paper details the first systematic analysis of linguistic function in PCA. Characterising and quantifying the aphasia associated with PCA is important for clarifying diagnostic and selection criteria for clinical and research studies.

Methods—Fifteen patients with PCA, 7 patients with logopenic/phonological aphasia (LPA) and 18 age-matched healthy participants completed a detailed battery of linguistic tests evaluating auditory input processing, repetition and working memory, lexical and grammatical comprehension, single word retrieval and fluency, and spontaneous speech.

Results—Relative to healthy controls, PCA patients exhibited language impairments across all the domains examined, but with anomia, reduced phonemic fluency and slowed speech rate the most prominent deficits. PCA performance most closely resembled that of LPA patients on tests of auditory input processing, repetition and digit span, but was relatively stronger on tasks of comprehension and spontaneous speech.

Conclusions—The study demonstrates that in addition to the well-reported degradation of vision, literacy and numeracy, PCA is characterised by a progressive oral language dysfunction with prominent word retrieval difficulties. Overlap in the linguistic profiles of PCA and LPA, which are both most commonly caused by Alzheimer's disease, further emphasises the notion of a phenotypic continuum between typical and atypical manifestations of the disease. Clarifying the boundaries between AD phenotypes has important implications for diagnosis, clinical trial recruitment and investigations into biological factors driving phenotypic heterogeneity in AD. Rehabilitation strategies to ameliorate the phonological deficit in PCA are required.

Keywords

Posterior Cortical Atrophy (PCA); Logopenic/Phonological Aphasia (LPA); Alzheimer's disease; language; phonology

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All authors contributed equally to the study concept and design, and approval of the final manuscript. In addition, Drs Crutch and Lehmann conducted the statistical analysis and wrote the paper, and Drs Warren and Rohrer edited and revised the paper.

Competing interests
None of the authors have any conflicts of interest to declare.

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Introduction

Posterior Cortical Atrophy (PCA) is a clinical syndrome characterized by a progressive, dramatic and relatively selective decline in higher-visual processing, and other posterior cortical functions.[1,2] Patients with PCA demonstrate relatively spared episodic memory function in conjunction with prominent impairments of space perception, object perception, alexia, agraphia, acalculia, apraxia, and some or all of the features of Balint's syndrome (simultanagnosia, oculomotor apraxia, optic ataxia, environmental agnosia).[2-7] As the term PCA suggests, the syndrome is associated with posterior tissue loss primarily of the parietal, occipital and temporo-occipital cortices.[8,9] The condition is most commonly associated with the histopathological features of AD, however, a minority of cases of PCA have been attributed to alternative etiologies including corticobasal degeneration (CBD), dementia with Lewy bodies, and prion disease.[4,10-11] In those PCA patients with AD pathology, the distribution of that pathology has been shown to differ from typical AD, with a greater density of senile plaques and neurofibrillary tangles in occipital, posterior parietal, and temporo-occipital cortex and fewer pathological changes in more anterior areas such as prefrontal cortex.[12-13] PCA is typically a young onset condition, most commonly emerging in the 50s and early 60s, but the exact prevalence and incidence remain to be established.

Although most investigations of PCA focus upon the prominent visual syndrome, even the earliest reports of PCA described some early impairment of language skills.[1] Benson and colleagues classified the language impairment observed in their patients as a transcortical sensory aphasia syndrome. However, in the subsequent two decades there have been no systematic investigations of language function in PCA. Limited data on some linguistic skills may be gleaned from several group comparisons of general clinical and neuropsycholgical profiles in PCA and AD. For example, a comparison of PCA and AD which included subtests from the Western Aphasia Battery revealed group differences only on reading and writing tasks, and a classification of anomia in 8/19, Wernicke's aphasia in 3/19 and conduction aphasia in 1/19 PCA patients.[6] One previous study has directly compared patients with PCA, logopenic/phonological aphasia (LPA) and early onset AD (EO-AD).[14] This analysis revealed language problems were a presenting complaint in 5/14 PCA patients compared with 10/10 LPA and 4/16 EO-AD. However cognitive screening tests revealed no difference between PCA and LPA on naming or verbal fluency tasks, and no detailed linguistic evaluation was conducted with the PCA patients. Another case series review of 40 PCA patients indicated an even higher incidence of anomia as a presenting symptom (24/27 patients), though the procedures for determining the presence of anomia were not specified.[2] It has also been suggested that semantic memory is relatively preserved in PCA except on tasks with a visual component, and that PCA patients show equivalent performance on phonemic and semantic fluency tasks, as compared with typical amnestic AD patients who are more impaired on semantic fluency.[15] Semantic fluency performance has also been reported to be better in PCA than AD.[3]

Several factors motivate a systematic analysis of language function in PCA. First, there are currently no consensus criteria for PCA,[16] and aphasia is not an exclusion criterion in the

available clinical criteria.[2,3] Thus the boundaries between PCA and other syndromes associated with posterior atrophy such as LPA [17,18] and cortico-basal syndrome [19,20] remain unclear. Whilst existing criteria do provide a sound basis for diagnosis where patients present with truly focal clinical deficits (e.g. selective visual dysfunction), a greater appreciation of the extent and nature of language deficits in PCA will help to disentangle more mixed cases. Second, if we are to understand the factors driving phenotypic heterogeneity associated with diseases such as AD and CBD, it is essential to account for not only prototypical 'pure' clinical presentations but also patients whose phenotype falls between established clinical categories. Third, appreciating the frequency, type and time-course of aphasic deficits in PCA may play an important role in planning disease management and in guiding patient and carer expectations.

The aim of the current paper was to examine and characterise the linguistic profile of PCA. The analysis involved a comparison of PCA patients with both healthy controls and a previously described reference sample of patients with LPA in the domains of auditory input processing, repetition and working memory, lexical and grammatical comprehension, single word retrieval and fluency, and spontaneous speech. It was hypothesised that the aphasic deficits arising in PCA would be primarily phonological in nature given the vulnerability of phonologically coded systems such as auditory verbal short-term memory in individuals with parietal lobe damage. It was also predicted that comprehension and speech production skills would be relatively preserved in PCA given the relative sparing of anterior temporal and inferior frontal regions.

Methods

Participants

The study involved 15 PCA patients and 18 healthy control participants. A reference sample of 7 LPA patients was selected from a previous study of patients with primary progressive aphasia[21]. Demographics and clinical data on all participants are summarized in Table 1. The groups were matched for gender ($P > 0.4$), age ($P > 0.3$), years of education ($P > 0.5$) and disease duration ($P > 0.05$). All clinically affected subjects had attended the Cognitive Disorders Clinic at the National Hospital, London, and the study was approved by the NRES Committee London-Queen Square.

All PCA patients had a clinical diagnosis of PCA owing to probable AD and fulfilled available clinical.[2,3] In addition, all participants fulfilled local neuropsychological criteria for PCA by showing normal range performance on tests of episodic memory and impaired on at least 2 tests of object and space perception, calculation and spelling (see Supplementary material). All were enrolled in a longitudinal clinical study of PCA. Total-tau and Aβ42 cerebrospinal fluid (CSF) biomarker data were available for 3/15 patients; all had raised levels of tau and low Aβ42, a CSF profile previously described in association with pathologically proven Alzheimer's disease.[22]

The LPA reference sample all fulfilled standard diagnostic criteria for primary progressive aphasia (PPA),[23,24] and all demonstrated word-finding pauses in spontaneous speech (in the absence of a motor speech deficit), impaired repetition and comprehension of sentences

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and poor auditory verbal short-term memory.[17,18] LPA patients were only included in the reference sample if screening for mutations in the MAPT, GRN and VCP genes was negative. CSF data were available for 6/7 cases: all had raised levels of tau and 5/6 had low Aβ42.

Neuroimaging data have been reported previously for all participants as part of two separate cross-sectional studies involving larger cohorts of patients with PCA and LPA.[9,21] 1.5T magnetic resonance brain images (MRI) were reanalysed here to provide direct comparisons of the current patients and to provide supportive evidence of the diagnostic classification. Details of the neuroimaging methods can be found in the Supplementary Material.

Neurolinguistic assessment

All subjects completed a battery of neurolinguistic and general neuropsychological tests. Owing to the prominent visual disorders evident in PCA, the linguistic assessment focussed upon tasks with limited visual input and output requirements, consequently excluding reading and writing:

Auditory input processing

(i) PALPA 2 word minimal pairs discrimination test (N=36 items; [25]): A phoneme perception test requiring a judgement as to whether pairs of spoken monosyllabic CVC words are the same (e.g. ‘tack’-‘cat’) or different (e.g. ‘coat’-‘coat’).

(ii) Prosody pair discrimination task (N = 12; [21]): A prosody perception tests requiring a judgement as to whether pairs of CV syllables (e.g. ‘ba’-‘ba’) were the same or different acoustically. On half the trials, syllables contained a single difference in pitch, intensity or duration; on the remaining trials the syllables were acoustically identical. Stimulus parameters were digitally manipulated using Matlab7.0 (www.mathworks.com). The prosody variations used were intended to be easily detectable by normal subjects.

(iii) Linguistic prosody – stress discrimination (N = 14; [26]): Participants heard a spoken phrase with one word stressed (e.g. ‘black and blue’ [stressed word in bold]) and were asked to decide whether the first or second colour term in the phrase was stressed.

(iv) Linguistic prosody - intonation discrimination task (N = 14; [21]): Participants heard a two-syllable word (name of a food) spoken either declaratively or interrogatively (e.g., ‘apple’ vs ‘apple?’). Participants were requested to decide whether what they heard was a statement (as if read from a list) or a question (as if they were being asked if they wanted the food).

Repetition and working memory

(i) Word Repetition (N=60; [27]): 20 one-syllable, 20 two-syllable and 20 three-syllable words.

(ii) Nonword Repetition (N=20; [25]): 20 nonwords comprising 10 three-letter CVC nonwords and 10 words of one to three-syllables taken from the PALPA 8 nonword repetition task.

(iii) Sentence and Cliché Repetition (N=20; [27]): 10 sentence clichés (e.g. “As blind as a bat”, “A flash in the pan”), and 10 novel sentences (e.g. “She met me at the airport”, “He mended the plug”). Sentence length varied between three and seven words; there was no significant difference in word number between the clichés (4.4 words per sentence) and novel sentences (4.8 words per sentence).

(iv) Digit span: Maximum digit span forwards and backwards was recorded.

Lexical and grammatical comprehension

(i) Lexical comprehension (N=50; [28]): The concrete and abstract synonym comprehension test was administered, requiring participants to judge which of two response words was closest in meaning the probe word: e.g. marquee: tent or palace?). Stimuli were presented in both spoken and written form.

(ii) Grammatical comprehension (N=30; [29]): Participants were read 30 sentences, half containing grammatical errors of verb tense, addition/substitution/deletion of function words or incorrect word order, and requested to judge whether the sentence was grammatically correct.

Single word retrieval and fluency

(i) Graded Naming Test (N=30; [30]): Participants completed the GNT, administered as picture naming task (controls and LPA patients) or a naming to verbal description task (PCA patients). If participants failed to name the target item, a single phoneme cue was provided (followed by a subsequent two-phoneme cue if required for PCA patients).

(ii) Verbal fluency: Participants completed phonemic (F, A, S) and semantic (animals) fluency tests, 60s per trial.

Spontaneous speech—A sample of spontaneous speech was obtained by asking participants to talk about their last holiday. This sample was recorded and subsequently analyzed for total number of words produced, speech rate (words/minute), type-token ratio (number of different words/total number of words), overall word frequency and noun frequency (log CELEX rating). In addition, speech was also analyzed for word-finding pauses: mean and maximum inter-word intervals in the speech sample were obtained using a customised routine running under Matlab® which measured intervals between vocalizations (whether within or between sentences).

Backgrond neuropsychological tasks—All participants also completed: Mini-Mental State Examination,[31] Object Decision from the Visual Object and Space Perception battery (VOSP),[32] Graded Difficulty Spelling test,[33] and limb and orofacial praxis tests from the Apraxia Battery for Adults.[34] PCA patients also completed a more extensive battery of neuropsychological tests of visual function as part of the longitudinal clinical

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study of PCA, including VOSP Fragmented letters, Dot counting and Number location, letter cancellation (Coughlan, unpublished) and usual/unusual view perception.[35]

Statistical analysis

Behavioural composite scores were generated for each of the five domains of linguistic processing. To calculate composite scores, every subtest score was transformed onto a linear scale from 0-100, where 0 represented the minimum and 100 the maximum score obtained by any participant across the three groups. Composite scores represent the mean transformed score across all subtests within each domain. Pair-wise comparisons between groups on each cognitive test were conducted using Wilcoxon-Mann-Whitney ranksum statistics.

Results

Regional differences in cortical thickness between controls, PCA and LPA are shown in Figure 1. Direct and indirect comparisons revealed characteristic patterns of reduced cortical thickness in the patient groups. In the direct comparison, PCA patients had significantly lower cortical thickness in the right occipital lobe, whilst LPA patients had lower cortical thickness in anterior temporal lobe regions.

The mean and standard deviation scores for controls, PCA patients and LPA patients, and pairwise between-group statistical differences, are shown in Table 1. More detailed individual participant scores are shown in Supplementary Table S1. Also shown is the percentage of patients achieving a score equal with or superior to the 2nd worst control participant (≥~10th percentile).

Controls

A correlation matrix of control linguistic test scores revealed significant correlations ($P \leq 0.05$) between tests of prosody (stress and turn-end type: r=0.59), prosody and tasks involving phonological input and output (e.g. concrete synonym comprehension, naming and phonemic fluency: r≥0.48 all), tasks with a semantic processing component (GNT and concrete synonyms: r=0.53; GNT and grammatical comprehension: r=0.56; abstract synonyms and semantic fluency: r=0.54), phonological input and output processes (PALPA2 and phonemic fluency: r=0.46), and fluency measures (semantic and phonemic fluency: r=0.47; semantic fluency and spontaneous speech total words: r=0.59).

PCA vs controls

PCA patients performed significantly more poorly than controls on tests of prosody processing, nonword, sentence and cliché repetition, digit span, naming and verbal fluency, some aspects of spontaneous speech (speech rate and word frequency), spelling, and lexical and grammatical comprehension. However, PCA patients demonstrated relatively preserved performance in several linguistic domains: there were no significant differences between PCAs and controls on tests of auditory-verbal minimal pair discrimination or word repetition (possibly owing to ceiling effects), and some aspects of spontaneous speech (total words, type-token ratio and pause length). Furthermore, despite groupwise comparisons of sentence repetition performance reaching formal statistical significance, it is of note that only 2/15

PCA patients scored less that 90% correct on the sentence repetition task. Synonym comprehension scores may also constitute an underestimate of PCA comprehension performance, as owing to impaired perception, there were considerable working memory demands involved in answering auditorily-presented questions (e.g. Which is more similar to a marquee, a tent or a palace?).

Several features were of particular note in the PCA linguistic profile. Based on 10th percentile cut-off scores, anomia and phonemic fluency were the most common linguistic deficits with 93% of PCA patients failing the Graded Naming Test and 100% of patients failing the 'P' fluency task. These patients also demonstrated a strong phonemic cueing effect on the Graded Naming Test (PCA: 0 vs 1 phoneme: Signtest P = 0.003; 0 vs 2 phonemes: P = 0.005; Controls: 0 vs 1 phoneme: P = 0.001). Spontaneous speech was characterised by occasional word finding pauses and occasional phonemic errors, but there was no evidence of motor speech impairment. PCA patients also scored significantly lower than controls on the MMSE and all object and space perception background tests.

LPA vs controls

LPA patients scored significantly lower than controls on every test administered. The only tests on which 50% or more of LPA patients managed to exceed the 10th percentile control performance level were the auditory-verbal minimal pairs discrimination test and the type-token measure of spontaneous speech. There was no evidence of agrammatism or apraxia of speech in the spontaneous speech analysis. LPA patients also achieved significantly lower scores than controls on the MMSE but not on the object perception background test.

PCA vs LPA

PCA patients achieved numerically higher scores than LPA patients on every linguistic task. Group differences were statistically significant in the areas of prosody (only the turn-end type task), word and sentence repetition, naming, verbal fluency, lexical and grammatical comprehension, and all measures of spontaneous speech except word frequency. The only test on which LPA patients were significantly better than PCA patients was the VOSP Object Decision test. PCA and LPA performance was very closely matched (and significantly impaired relative to controls) on tests of spelling and upper limb praxis, highlighting the vulnerability of dominant parietal circuits in both groups.

Comment

Overall, PCA patients were significantly worse than controls in all of the linguistic domains tested (auditory input processing, repetition/working memory, comprehension, retrieval/fluency, and spontaneous speech). Nonetheless the profile of impairment across the five domains was not uniform. The relative aphasic profiles of the two patient groups were examined by comparing the mean composite ranking score for PCA patients, LPA patients and controls in each of the five domains (see Figure 2). Among the patients assessed, PCA patients showed lowest ranking scores for auditory input processing and repetition/working memory, whilst LPA patients showed lowest ranking scores for comprehension, naming/fluency, and spontaneous speech. This suggests that in PCA the emergent aphasia is milder than that exhibited by LPA patients and characterised by proportionally greater impairment

of auditory input processing and working memory (associated with parietal and posterior temporal regions) than comprehension and production skills (associated with more anterior temporal and frontal regions).

Discussion

Progressive deterioration of visual, literacy and numeracy skills is the typical cognitive hallmark of PCA. However gradual erosion of oral language skills is an important yet rarely studied clinical feature. In the current study, the language skills of 15 PCA patients were compared with 7 LPA patients and 18 healthy controls across five broad linguistic domains: auditory input processing, repetition and working memory, lexical and grammatical comprehension, single word retrieval and fluency, and spontaneous speech. At the level of formal group statistical comparisons, PCA patients demonstrated significant impairments in subtests across all five domains, including prosody processing, nonword, sentence and cliché repetition, digit span, synonym comprehension, grammaticality judgements, naming, semantic and phonemic fluency, and some aspects of spontaneous speech (speech rate and word frequency). However, the aphasic symptoms in which most PCA patients exhibited impaired performance (defined by scores falling below the 10^{th} percentile control cut-off) were marked anomia (93%) and reduced phonemic fluency (100%). There were also some areas of relative sparing, such as auditory-verbal minimal pair discrimination, word repetition and some aspects of spontaneous speech (total words, type-token ratio and pause length). In the patient group comparisons, PCA patients were superior to LPA patients on all tasks except the object perception background test. PCA performance most closely resembled LPA performance on tests of auditory input processing, repetition and digit span, but was more distinct on tasks of comprehension and spontaneous speech (see Figure 2). This suggests PCA patients had particular difficulty on linguistic tasks mediated by or involving the manipulation and retrieval of different types of phonological information.

The majority of patients with PCA are clearly distinguishable from those with PPA, and indeed would not meet diagnostic criteria for PPA, by virtue of language difficulty not being the most prominent clinical feature.[36] Despite some deficits in naming, speech rate and repetition, there are at least two ways in which this aphasic syndrome differs from patients with LPA. First, the aphasic syndrome in PCA is milder than that exhibited by LPA, with subtle language impairments often apparent at presentation but not being the most notable clinical feature. Second, PCA patients exhibited proportionally greater impairment of single word retrieval, auditory input processing and working memory (associated with parietal and posterior temporal regions) than comprehension, spontaneous speech and speech production skills (associated with more anterior temporal and frontal regions). At a practical level, the 10^{th} percentile cut-off analyses indicate that the tests which best distinguish the linguistic impairment shown by PCA and LPA patients are sentence repetition, grammaticality judgement and the presence of lengthy pauses in spontaneous speech.

An auditory-verbal short term memory deficit has been hypothesised to be the critical mechanism underpinning the LPA syndrome.[17,18] This claim is based on neuropsychological evidence of digit span, sentence repetition and syntactic comprehension deficits (affecting both simple and complex sentence constructions) and neuroimaging

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evidence of left posterior temporal and inferior parietal atrophy). However, given previous evidence of strong dissociations between list and sentence recall which show the need to consider auditory-verbal short-term memory performance and articulation skills separately, [27,37] we are cautious of attributing the linguistic profile observed in PCA to a single cognitive deficit. The ceiling levels of performance demonstrated by PCA patients on single word repetition tasks involving low frequency, polysyllabic words suggest that speech production deficits are largely absent in this cohort. The fact that PCA patients showed preserved single word repetition but failed single nonword repetition tasks, which draw more heavily upon phonological skills owing to the absence of supportive lexical-semantic information, may reflect their weak auditory-verbal short term memory. However, it remains an open question whether poor nonword repetition in PCA, together with poor performance on the linguistic and non-linguistic prosody perception tasks, is influenced by damage to more basic acoustic perceptual mechanisms.[38]

In addition to impairment of phonologically-coded auditory-verbal short term memory, access to or retrieval of phonological information may also be the primary deficit underpinning the anomia observed in PCA. Anomia (examined by naming to verbal description) and phonemic fluency (impaired in 100% of PCA patients) were arguably the most significant clinical deficits revealed by the current study of language in PCA. The type of naming errors observed (mainly circumlocutory or omission, with occasional literal paraphasias) and relative absence of comprehension and articulatory deficits suggest that anomia in PCA is most commonly attributable to failure to activate the appropriate phonological output lexicon.[39] In addition, PCA patients demonstrated a strong phonemic cuing effect when unable to retrieve the uncued target word, suggesting that additional phonological information had a beneficial effect upon the selection or activation of the target word form. It should be noted that the LPA patients and controls were tested by naming to confrontation not description so results are not directly comparable, but the large differences between groups are unlikely to be accounted for by the difference in presentation mode. There have been no investigations into rehabilitation strategies for aphasia in PCA, but the overlap in linguistic profiles suggests that such patients may benefit from intensive word retrieval and phonological training described previously in individuals with LPA or progressive non-fluent aphasia.[40,41]

The current study suggests that detailed linguistic assessment in PCA may contribute to the ‘deep-phenotyping’ required to refine the diagnostic boundaries between PCA and other syndromes associated with posterior atrophy. The idea of considerable overlap in the linguistic profiles of PCA and LPA is consistent with the broader notion that atypical focal phenotypes of AD such as (the majority of patients with) PCA and LPA represent points in a spectrum or continuum of clinical manifestations of the disease.[7,14] Whilst phenotypic outliers undoubtedly exist (e.g. patients with a relatively pure occipital lobe degeneration), [42] the hypothesis of a common posterior parietal/posterior cingulate/precuneus site of pathological onset in early onset AD irrespective of subsequent phenotype remains appealing given the available evidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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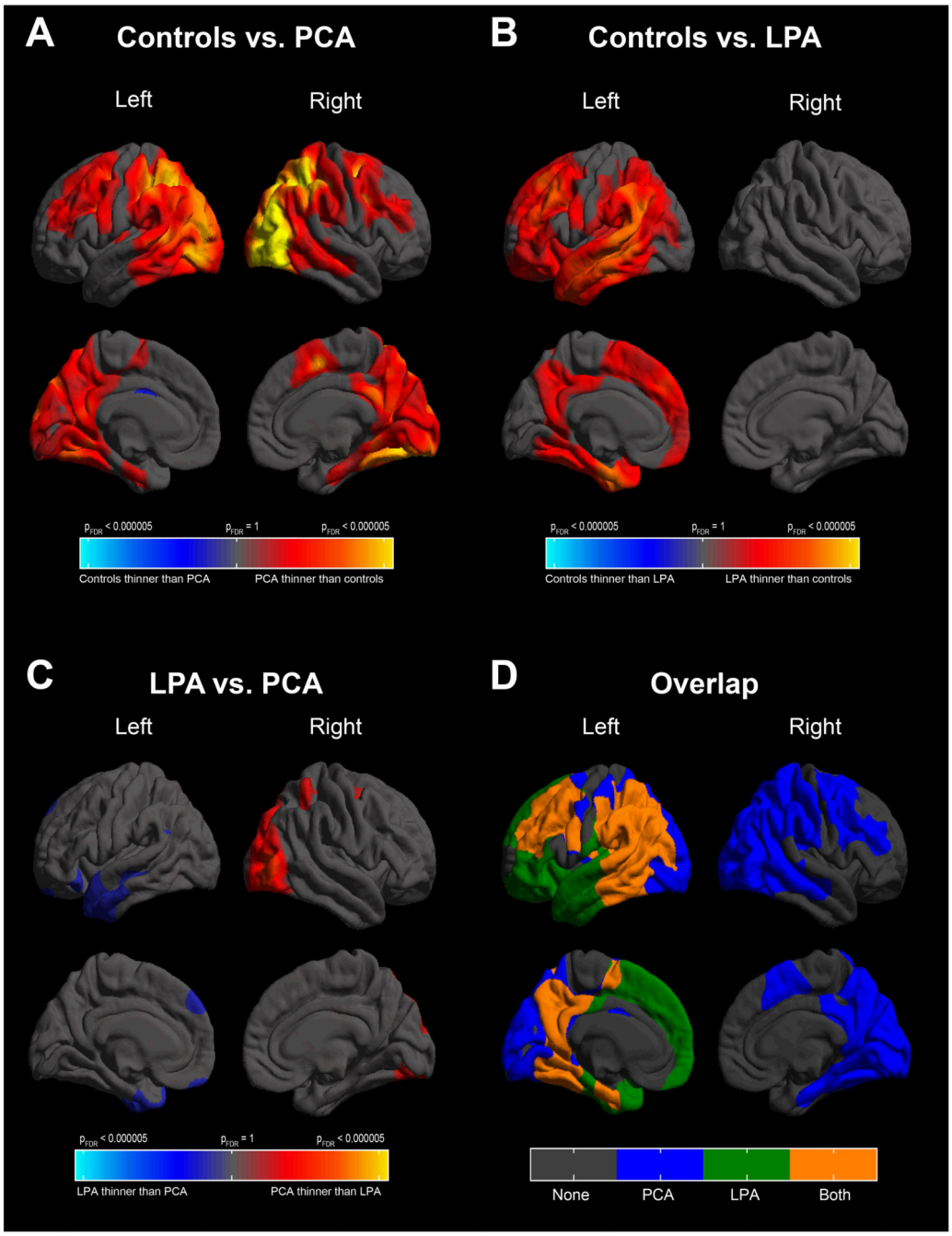

Figure 1.

A-C) Regional differences in cortical thickness between A) PCA and controls, B) LPA and controls, and C) LPA and PCA. Colour scales represent FDR-corrected p values thresholded at a 0.05 significance level. Red and yellow represent lower cortical thickness in the patient groups compared with controls, and PCA compared with LPA, whereas dark and light blue represent greater cortical thickness. **D)** Overlap map of lower cortical thickness in PCA and LPA compared with controls. Blue represents areas which are reduced in PCA only, green

shows regions reduced in LPA only, and orange shows areas reduced in both PCA and LPA compared with controls.

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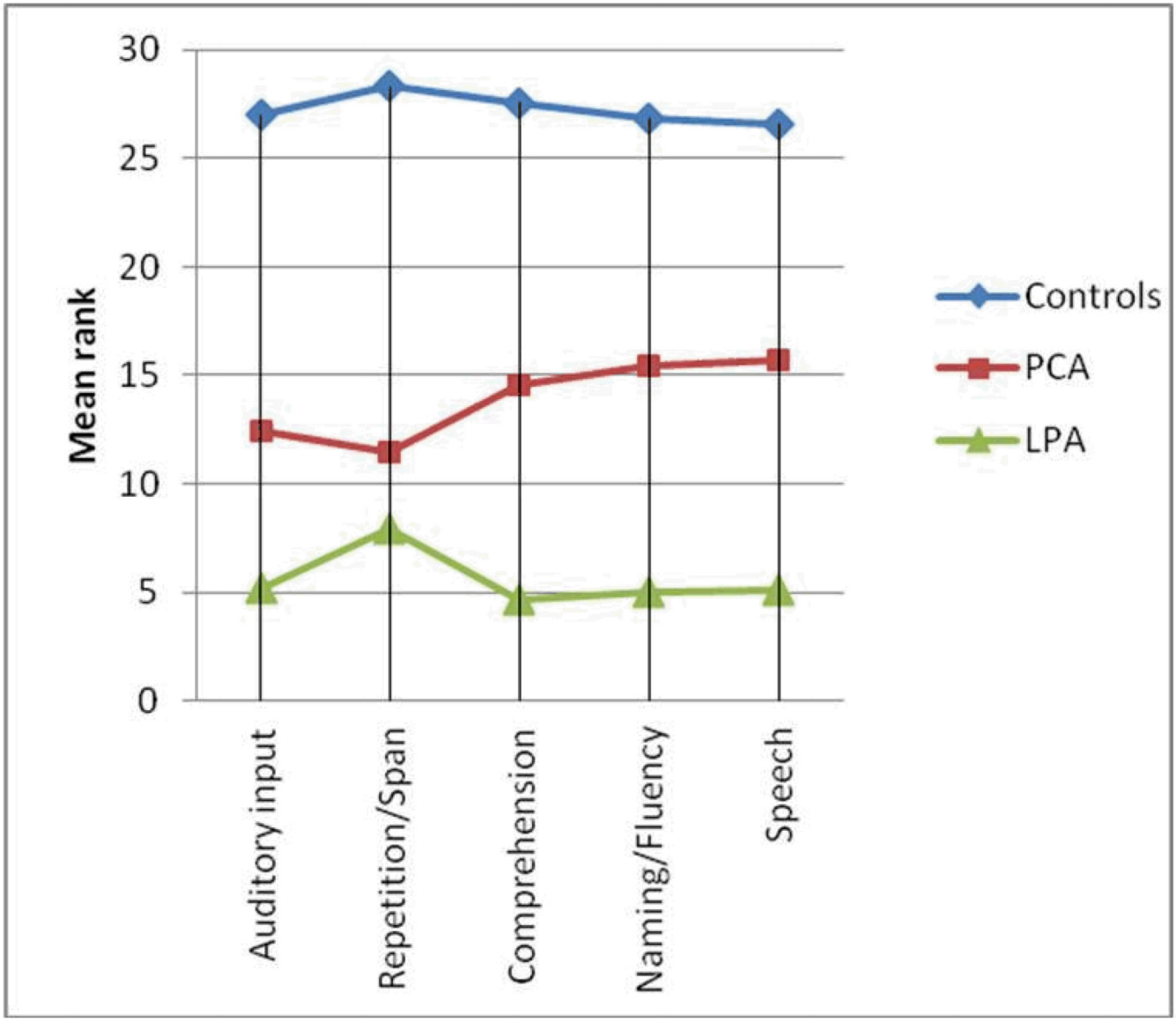

Figure 2.

Mean composite ranking scores for each participant group across the domains of auditory input processing, repetition/working memory, comprehension, naming/fluency, and spontaneous speech.

Table 1

Demographic data and the mean (and standard deviation) neuropsychological scores for controls, PCA patients and LPA patients, and pairwise between-group statistical differences.

				% patients ≥10th %ile		Group differences (p values)		
	Controls Mean (SD)	**PCA Mean (SD)**	**LPA Mean (SD)**	**PCA**	**LPA**	**PCA vs Controls**	**LPA vs Controls**	**PCA vs LPA**
Gender (M:F)	9:9	5:10	4:3	-	-	0.34	0.75	0.29
Age	67.9 (5.4)	64.2 (8.2)	65.1 (6.4)	-	-	0.12	0.32	0.46
Disease duration	-	6.0 (2.2)	4.4 (1.0)	-	-	-	-	0.07
Background neuropsychology								
MMSE (/30)	29.7 (0.8)	19.3 (5.1)	15.9 (5.8)	0%	0%	<0.0001	<0.0001	0.24
Graded Difficulty Spelling (/30)	25.8 (2.7)	9.1 (8.1)	5.8 (5.6)	0%	0%	<0.0001	0.0007	0.57
Limb apraxia (ABA3a; /50)	49.9 (0.2)	40.4 (8.7)	39.8 (6.9)	8%	20%	<0.0001	0.0002	0.69
Orofacial apraxia (ABA3b; /50)	50.0 (0.0)	45.9 (3.8)	43.2 (5.4)	8%	20%	<0.0001	<0.0001	0.37
VOSP Object Decision (/20)	17.5 (2.3)	11.4 (5.2)	16.0 (2.4)	47%	100%	0.0006	0.1	0.05
VOSP Incomplete Letter (/20)	*18.8 (1.4)*[a]	4.6 (4.8)	NT	*0%*[a]	-	*sig**	-	-
Unusual views (/20)	*17.1 (3.0)*[b]	2.9 (3.5)	NT	*0%*[b]	-	*<0.0001*	-	-
Usual views (/20)	*19.7 (0.5)*[b]	11.1 (7.1)	NT	*20%*[b]	-	*<0.0001*	-	-
VOSP Number Location (/10)	*9.4 (1.1)*[a]	2.8 (3.3)	NT	*13%*[a]	-	*sig**	-	-
VOSP Dot Counting (/10)	*9.9 (0.2)*[a]	4.6 (3.2)	NT	*13%*[a]	-	*sig**	-	-
A cancellation – Time (s)	*20.5 (6.5)*[c]	82.9 (35.2)	NT	*0%*[c]	-	*sig**	-	-
Auditory input processing								
PALPA2 Minimal pairs (/36)	35.4 (0.9)	34.6 (2.1)	31.3 (5.2)	87%	50%	0.13	0.02	0.15
Prosody - Pair discrimination (/12)	11.3 (0.8)	9.4 (1.2)	8.2 (1.1)	21%	0%	0.0001	0.0005	0.07
Prosody - Stress input (/14)	13.9 (0.3)	12.2 (2.0)	10.2 (3.8)	57%	20%	0.0003	0.0007	0.20
Prosody - Turn-end type (/14)	13.2 (1.1)	10.8 (2.1)	8.0 (2.2)	62%	20%	0.0003	0.0006	0.03
Repetition and working memory								
Word Repetition (/60)	60.0 (0.0)	59.9 (0.3)	51.1 (10.6)	93%	43%	0.27	0.0006	0.006
Nonword Repetition (/20)	20.0 (0.0)	17.9 (3.1)	15.9 (4.0)	60%	14%	0.004	<0.0001	0.12
Cliché Repetition (/10)	10.0 (0.0)	9.0 (1.5)	6.1 (4.4)	53%	29%	0.001	0.0001	0.12
Sentence repetition (/10)	10.0 (0.0)	9.3 (1.0)	4.6 (4.1)	53%	0%	0.001	<0.0001	0.002
Digit span forwards (max)	6.9 (0.6)	5.3 (1.3)	4.0 (1.8)	47%	29%	0.0006	0.0001	0.09
Digit span backwards (max)	4.9 (0.6)	2.5 (0.9)	2.4 (1.3)	20%	14%	<0.0001	0.0006	0.62
Lexical and grammatical comprehension								
Concrete synonyms (/25)	24.3 (0.8)	21.1 (2.8)	16.6 (1.6)	43%	0%	0.0007	0.0001	0.002
Abstract synonyms (/25)	24.3 (1.1)	20.9 (3.4)	14.1 (1.9)	57%	0%	0.001	0.0001	<0.001
Grammaticality judgement (/30)	28.6 (1.4)	25.8 (2.8)	17.9 (6.2)	73%	14%	0.002	0.0002	0.005

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	Controls Mean (SD)	PCA Mean (SD)	LPA Mean (SD)	% patients ≥10th %ile PCA	% patients ≥10th %ile LPA	Group differences (p values) PCA vs Controls	Group differences (p values) LPA vs Controls	Group differences (p values) PCA vs LPA
Single word retrieval and fluency								
GNT + 0 phonemic cues (/30)	25.2 (2.2)	10.0 (8.3)	1.5 (1.8)	7%	0%	<0.0001	0.0003	0.02
GNT + 1 phonemic cues (/30)	26.6 (2.1)	11.9 (9.6)	1.8 (1.6)	13%	0%	0.0003	0.0003	0.03
GNT + 2 phonemic cues (/30)	NT	14.1 (10.4)	NT	-	-	-	-	-
Phonemic fluency (FAS)	50.9 (16.2)	20.7 (15.8)	5.3 (2.2)	0%	0%	0.0001	0.002	0.02
Semantic fluency (Animals)	19.4 (5.4)	7.5 (4.4)	5.3 (2.2)	13%	0%	<0.0001	0.002	0.11
Spontaneous speech								
Total words (N)	339.6 (181.2)	217.8 (106.0)	114.4 (62.9)	50%	0%	0.11	0.0002	0.04
Speech rate (words/minute)	133.9 (22.9)	110.3 (31.3)	63.1 (19.5)	42%	0%	0.02	0.0001	0.002
Type token ratio	0.5 (0.1)	0.5 (0.1)	0.6 (0.0)	83%	71%	0.61	0.04	0.03
Mean pause length	1.0 (0.2)	1.0 (0.2)	1.5 (0.3)	92%	29%	0.68	0.0008	0.01
Max pause length	2.6 (0.8)	2.6 (1.0)	4.9 (1.7)	75%	43%	0.98	0.002	0.01
Word frequency	2.5 (0.1)	2.8 (0.2)	3.0 (0.1)	17%	0%	0.0001	0.0001	0.12
Noun frequency	1.8 (0.1)	2.2 (0.2)	2.0 (0.2)	25%	43%	<0.0001	0.01	0.19

NT = not tested;

sig* = large group differences evident but raw data from published normative sample unavailable for calculation of precise p value. Shaded cells indicate significant group differences.

[a] Normative data from Warrington and James (1991)

[b] Normative data from Crutch (unpublished)

[c] Normative data from Coughlan (unpublished);