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RESEARCH ARTICLE

More than a piece of cake: Noun classifier processing in primary progressive aphasia

Boon Lead Tee[1,2,3] | Lorinda Kwan-Chen Li-Ying[4] | Ta-Fu Chen[5] | Connie TY Yan[6,7] | Joshua Tsoh[6,7] | Andrew Lung-Tat Chan[8] | Adrian Wong[9] | Raymond Y. Lo[10] | Chien Jung Lu[11] | Yu Sun[11] | Pei-Ning Wang[12,13,14] | YiChen Lee[15] | Ming-Jang Chiu[5] | Isabel Elaine Allen[16] | Giovanni Battistella[17] | Thomas H. Bak[18] | Yu-Chen Chuang[12] | Adolfo M. García[3,19,20] | Maria Luisa Gorno-Tempini[1,2,3]

[1]Memory and Aging Center, University of California at San Francisco, San Francisco, California, USA

[2]Department of Neurology, Dyslexia Center, University of California, San Francisco, San Francisco, California, USA

[3]Global Brain Health Institute, University of California, San Francisco, San Francisco, California, USA

[4]Department of Special Education and Counselling, The Education University of Hong Kong, Hong Kong, Hong Kong

[5]Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan R.O.C.

[6]Department of Psychiatry, Prince of Wales Hospital and ShaTin Hospital, Hong Kong, Hong Kong

[7]Department of Psychiatry, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong

[8]Department of Medicine, Queen Elizabeth Hospital, Hong Kong, Hong Kong

[9]Division of Neurology, Department of Medicine and Therapeutics, Chinese University of Hong Kong, Hong Kong, Hong Kong

[10]Department of Neurology, Buddhist Tzu Chi General Hospital, Hualien, Taiwan

[11]Department of Neurology, En Chu Kong Hospital, New Taipei City, Taiwan R.O.C.

[12]Division of General Neurology, Department of Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan R.O.C.

[13]School of Medicine, National Yang Ming Chiao Tung University College of Medicine, Taipei, Taiwan R.O.C.

[14]Brain Research Center, National Yang-Ming Chiao-Tung University, HsinChu, Taiwan R.O.C.

[15]Department of Neurology, National Taiwan University Hospital, HsinChu, Taiwan R.O.C.

[16]Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California, USA

[17]Department of Otolaryngology - Head and Neck Surgery, Massachusetts Eye and Ear and Harvard Medical School, Boston, Massachusetts, USA

[18]School of Philosophy, Psychology and Language Sciences (PPLS), University of Edinburgh, Edinburgh, UK

[19]Cognitive Neuroscience Center, Universidad de San Andrés, Buenos Aires, Argentina

[20]Departamento de Lingüística y Literatura, Facultad de Humanidades, Universidad de Santiago de Chile, Santiago, Chile

Correspondence
Boon Lead Tee, Memory and Aging Center, University of California, San Francisco, 675 Nelson Rising Lane, Suite 190, San Francisco 94158, California, USA.
Email: boonlead.tee@ucsf.edu

Abstract

INTRODUCTION: Clinical understanding of primary progressive aphasia (PPA) has been primarily derived from Indo-European languages. Generalizing certain linguistic findings across languages is unfitting due to contrasting linguistic structures. While PPA patients showed noun classes impairments, Chinese languages lack noun classes. Instead, Chinese languages are classifier language, and how PPA patients manipulate classifiers is unknown.

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METHODS: We included 74 native Chinese speakers (22 controls, 52 PPA). For classifier production task, participants were asked to produce the classifiers of high-frequency items. In a classifier recognition task, participants were asked to choose the correct classifier.

RESULTS: Both semantic variant (sv) PPA and logopenic variant (lv) PPA scored significantly lower in classifier production task. In classifier recognition task, lvPPA patients outperformed svPPA patients. The classifier production scores were correlated to cortical volume over left temporal and visual association cortices.

DISCUSSION: This study highlights noun classifiers as linguistic markers to discriminate PPA syndromes in Chinese speakers.

KEYWORDS
Chinese language, lemma, lexical syntactic attributes, noun classifier, primary progressive aphasia

Highlights

- Noun classifier processing varies in the different primary progressive aphasia (PPA) variants. Specifically, semantic variant PPA (svPPA) and logopenic variant PPA (lvPPA) patients showed significantly lower ability in producing specific classifiers. Compared to lvPPA, svPPA patients were less able to choose the accurate classifiers when presented with choices.
- In svPPA, classifier production score was positively correlated with gray matter volume over bilateral temporal and left visual association cortices in svPPA. Conversely, classifier production performance was correlated with volumetric changes over left ventral temporal and bilateral frontal regions in lvPPA.
- Comparable performance of mass and count classifier were noted in Chinese PPA patients, suggesting a common cognitive process between mass and count classifiers in Chinese languages.

1 | BACKGROUND

Primary progressive aphasia (PPA) is a spectrum of neurodegenerative diseases predominantly involving specific speech and/or language deficits.[1] Three main PPA variants have been described: semantic variant PPA (svPPA), non-fluent/agrammatic variant PPA (nfvPPA), and logopenic variant PPA (lvPPA).[2] To date, most clinical evidence on PPA comes from speakers of linguistically closely related Germanic and Romance languages.[3–5] However, there are > 7000 languages worldwide, with marked variations in linguistic features that can influence clinical presentation.[6] Accordingly, investigation of language-specific features beyond the confines of the English language is crucial to promote global equity and expand our understanding to the neural mechanisms of PPA. This study investigates Chinese, a classifier language lacking noun classes, to examine noun classifiers as markers for lemma processing impairments, which manifest as noun class inflection errors in Indo-European–speaking PPA patients.

In various Indo-European, Semitic, and Bantu languages, noun classification is based on semantic, morphological, and/or phonological properties represented via inflections or bound morphemes (e.g., gender, such as "camarero" [waiter] and "camarera" [waitress] in Spanish; countability, such as "lemon" and "lemonade" in English; plurality, such as "kitabu" [a book] and "vitabu" [books] in Swahili). These noun classes generally abide certain grammatical agreements, such as the adjectives "many" and "much" for countable and uncountable English nouns (e.g., many houses vs. much milk), or the articles "la" and "el" for feminine and masculine Spanish nouns (e.g., el gato vs. la casa), respectively. Across languages, noun classes range from several dozen (e.g., Bantu languages) through three (e.g., German, Russian) or two (e.g., French, Hindi) to none (e.g., Chinese, Thai).[7] Noun class inflection deficits have been reported in PPA cohorts in Indo-European languages. For example, English-speaking svPPA patients struggle with the inflections of low-frequency irregular nouns, while lvPPA and nfvPPA patients have difficulties with pseudo-noun inflections.[8]

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Spanish-speaking individuals with svPPA fail at matching gendered articles with phonologically exceptional nouns (e.g., pairing the feminine article "la" with masculine nouns ending with "a," such as "problema," as final "a" usually denotes feminine gender).[9] Access to noun gender information is also deteriorated in French-speaking svPPA patients.[10]

Many East and Southeast Asian languages lack distinct gender, countable/uncountable, or singular/plural noun forms. Instead, they categorize nouns via classifiers, namely, words with independent meanings that specify quantity (e.g., "two slices of bread" vs. "two loaves of bread") and/or offer semantic reference (e.g., "a bar of chocolate" vs. "a cup of chocolate").[7] Unlike Indo-European languages in which classifiers are reserved for non-countable/mass nouns (e.g., "water" or "sand"), classifier languages like Chinese mandate classifier use whenever numerals or determiners precede nouns, regardless of noun countability.[11] Classifiers can be copious, reaching up to 902 classifiers in Chinese languages.[12] Most Chinese classifiers are specific to nouns based on physical or inherent attributes, albeit with substantial arbitrariness.[13,14] For instance, 把 /ba3/ is the designated classifier for "knife" (刀 /dao1/), "fire" (火/huo3/), and "salt" (鹽/yan2/), although these nouns lack semantic or physical similarities. Moreover, Chinese nouns can evoke different meanings depending on the accompanying classifier. For example, the noun "book" (書 /shu1/) is preceded by本 for "one book," 套for "book series," and 堆、叠、排for "book stacks organized in various manners." As both noun classifiers and noun classes share the function of categorizing nouns, some linguists consider them concordial linguistic counterparts, specifically as lexical–syntactic attributes (i.e., lemma).[13,15]

However, varying noun categorization approaches implicate different linguistic (lexical, semantic, morphosyntactic) systems that are differentially affected across PPA syndromes, raising questions as to how PPA symptoms related to lemma vary across these languages. We hypothesized that Chinese-speaking PPA patients, particularly svPPA patients with semantic knowledge deficits and lvPPA patients with lexical retrieval impairment, exhibit difficulties in noun classifier processing. Moreover, considering the limited neuroanatomical evidence on Chinese classifiers,[16–18] we also investigated structural magnetic resonance imaging (MRI) correlates of behavioral performance across groups. Finally, in an exploratory fashion, we assessed whether mass and count classifiers have varying performance.

RESEARCH-IN-CONTEXT

1. **Systematic review**: The authors reviewed the literature on noun classifiers and/or primary progressive aphasia (PPA) using PubMed and Google Scholar. Prior studies showed that English PPA patients have inflection morphology difficulties, while French and Spanish PPA patients struggle with noun class processing. Linguists considered noun classifiers and noun classes as concordial linguistic counterparts. Chinese languages lack noun classes, while noun classifiers are mandatory when numerals or determiners precede nouns. No existing study investigates the production of noun classifiers in PPA patients.
2. **Interpretation**: Our findings showed noun classifiers as a promising marker in discriminating PPA variants in Chinese-speaking individuals and offered insights into the neural basis of classifier processing.
3. **Future direction**: This study informs the diagnostic approach to Chinese-speaking PPA patients and underlines the importance of culturally and linguistically appropriate tests. Future research is needed to develop novel tests for PPA syndromic differentiation in languages with varying linguistic structures.

2 | METHODS

2.1 | Participants

This prospective cross-sectional study included 74 native Chinese (Cantonese or Mandarin) speakers: 22 were cognitively normal, the remaining 52 met current diagnostic criteria for svPPA ($n = 12$), nfvPPA ($n = 11$), or lvPPA ($n = 29$).[1,2] Participants either received ≥ 6 years formal education in the Chinese languages or all their formal education in Chinese if they had < 6 years of formal education. We excluded participants with other neurodegenerative diseases, a history of brain surgery, major brain trauma requiring hospitalization; oropharyngeal disorders affecting articulation; profound visual or hearing impairments; or a Mini-Mental State Exam score (MMSE)[19] < 10. We recruited participants from seven sites in Hong Kong, Taiwan, and the United States, and the study protocol was approved by the relevant institutional review boards (Table in supporting information).

2.2 | Neuropsycholinguistic assessment

Neuropsycholinguistic assessments that were performed across all recruitment sites included the MMSE[19] and the Chinese Language Assessment for PPA (CLAP) battery.[20] The CLAP battery encompasses confrontation naming, single-word comprehension, semantic association, syntax comprehension, repetition, and motor speech tests. In the CLAP confrontational naming test, we tasked participants to name 48 pictures with high concreteness but varying word frequency. For single-word comprehension test, participants were provided the name of 15 objects or animals verbally and asked to identify the target stimuli from six pictures of the same semantic category. For CLAP semantic association tests, participants were shown 30 sets of three words or pictures, with the target stimulus positioned on top of the other two stimuli. Participants were then requested to identify the words or pictures that best matched the target stimulus. In the syntax comprehension test, participants were presented with 30 Chinese

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sentences with pictures that vary in syntactic constructional meanings. Participants were then asked to select the picture that accurately represents the sentence. In the repetition task, we tasked participants to repeat sensical and non-sensical phrases and sentences ranging from three to eleven Chinese characters in length. For the motor speech evaluation, we asked participants to repeat 15 four-character phrases five times, and the phrases were designed to differ either in lexical tone, place, or manner of articulation. Assessments were conducted in each participant's dominant language (Cantonese or Mandarin) by board-certified neurologists, neuropsychologists, speech-language pathologists, or supervised research staff, all of whom are native Chinese speakers.

2.3 | Noun classifier task

Chinese classifiers do not entail grammatical inferences, hence deficits in classifier processing cannot be represented by the morphological inflections of nouns or classifiers. Therefore, we examined classifier processing in Chinese speakers with svPPA, nfvPPA, lvPPA, and cognitively normal controls by examining their ability to spontaneously produce and select specific classifiers. The classifier production task involved 25 high-frequency concrete nouns (denoting animals and objects) with varying specific classifiers (Table S2 in supporting information). Because the same Chinese noun can be matched with varying classifiers when in different forms (e.g., 片for "banana slices," 根for "one single banana," 把/串for "a bunch of bananas," 株/棵for "banana trees"), items were presented in both words and pictures, to specify the form of the objects. To better examine participants' ability to produce classifiers, participants were asked to avoid two general classifiers: 個 for things and 隻 for animals. Among them, 20 were considered count classifiers for nouns with high countability (e.g., "one horse" 一匹馬), and five were mass classifiers for uncountable nouns (e.g., "a glass of water"一杯 水), with example provided in Figure S1 in supporting information.

When participants were unable to produce the correct classifier, we administered a choice recognition task, whereby participants were shown four classifiers and asked to choose the correct one. A classifier recognition score was computed as the percentage of accurate choices among the inaccurate responses. To examine whether performance was influenced by lexical properties of the stimuli, we obtained the character/word frequency of nouns and classifiers from the Human Cognition Project (http://humanum.arts.cuhk.edu.hk/Lexis/chifreq/). The mean log frequency values, represented in parts per million and standardized using Zipf's law,[21] were 5.07 ± 0.79 for nouns and 4.69 ± 0.43 for classifiers in Taiwan; and 5.01 ± 0.99 for the nouns, and 4.66 ± 0.47 for classifiers in Hong Kong.

2.4 | Statistical analysis

Demographic and neuropsycholinguistic data, as well as classifier scores, were compared among groups via analyses of variance for continuous variables (with Bonferroni correction for multiple comparisons) and with the Pearson chi-squared test for categorical variables. Classifier production and recognition scores were adjusted by age and education using general linear models. Using Pearson correlations, we examined whether these scores were associated with semantic and lexical measures from the CLAP battery. To investigate the influence of lexical properties of nouns and classifiers on classifier task performance, we used general linear model analyses for each PPA group separately, wherein the accuracy of classifier production served as the outcome variable, while the character frequency of classifiers and the word frequency of nouns were included as covariates. This allowed us to evaluate the individual contributions of these lexical properties on the overall performance of the classifier task. Statistical analyses were conducted using IBM SPSS Statistics 27.0, at an alpha level of 0.05.

2.5 | Brain–behavior correlations

To explore the neural mechanism of noun classifier production, we examined the neural correlates in participants who completed the CLAP battery and MRI within 3 months. As only svPPA and lvPPA patients exhibited significantly lower noun production scores compared to the control group (as detailed in Sections 3.2 and 3.3), separate voxel-based morphometry (VBM) analyses were conducted for these two groups, alongside controls. Given the ceiling performance of nfvPPA patients on noun classifier measures, neural correlation analysis was not performed in this group. This comprised 9 participants with svPPA, 24 patients with lvPPA, and 13 cognitively normal controls. MRI sequences were acquired with 3T scanners using the Alzheimer's Disease Neuroimaging Initiative 3 (ADNI 3; http://adni.loni.usc.edu/adni-3/) protocol. The ADNI 3 protocol encompassed a high-resolution T1-weighted 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) structural scan with the following parameters: 200 to 211 sagittal slices, repetition time (TR) = 2300 ms, echo time (TE) = 2.98 ms, inversion time = 900 ms, flip angle 9-11 degree, field of view (FOV) = 256 mm3, matrix size = 256 × 256, in-plane voxel size 1.0 × 1.0 mm2, slice thickness = 1 mm. The neuroimaging data were pre-processed with Computational Anatomy Toolbox in the Statistical Parametric Mapping software operating under MATLAB 2019a. The T1-weighted images were bias-field corrected, skull stripped, and categorized into gray matter (GM), white matter, or cerebrospinal fluid using a segmentation approach based on an adaptive maximum a posteriori technique. GM probability maps were non-linearly normalized to the Montreal Neurologic Institute space using DARTEL, modulated via the Jacobian determinant from the spatial normalization, and smoothed by an isotropic Gaussian kernel of 8 mm full width at half-maximum. We studied the correlations between cortical volume and classifier production scores using voxel-wise multiple linear regression models by covarying for diagnosis, sex, age at assessment, years of education, testing language (Mandarin or Cantonese), and total GM volume ($P < 0.05$ family-wise error corrected at cluster level, $k > 100$).

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TABLE 1 Demographic characteristics and neuropsychological performances of the study participants ($n = 74$).

	svPPA ($n = 12$)	nfvPPA ($n = 11$)	lvPPA ($n = 29$)	Control ($n = 22$)	*P* value
Demographics					
Age at examination (years)	69.2 (5.9)	66.6 (6.4)	70.0 (7.7)	65.1 (6.9)	0.094
Sex					0.057
Female	4 (33.3)	7 (63.6)	9 (31.0)	14 (63.6)	
Male	8 (66.7)	4 (36.4)	20 (69.0)	8 (36.4)	
Years of education	13.9 (5.8)	12.9 (3.3)	11.0 (4.2)[c]	15.9 (4.0)[c]	0.002
Handedness					0.226
Right	12 (100)	10 (90.9)	29 (100)	21 (95.5)	
Left	0 (0)	1 (9.1)	0 (0)	0 (0)	
Ambidextrous	0 (0)	0 (0)	0 (0)	1 (4.5)	
Global cognition					
MMSE	21.9 (3.8)[a]	25.5 (4.1)[b,f]	20.2 (5.3)[c,f]	29.6 (1.1)[a,b,c]	<0.001
Speech and language					
Picture naming (0–48)	9.9 (11.7)[a,d,e]	40.8 (9.8)[d,f]	30.5 (13.3)[c,e,f]	47.3 (1.0)[a,c]	<0.001
Single word comprehension (0–15)	7.8 (3.6)[a,d,e]	13.5 (2.0)[d]	12.3 (2.7)[c,e]	14.6 (0.7)[a,c]	<0.001
Semantic association: picture (0–15)[g]	8.8 (3.4)[a,d,e]	13.4 (2.2)[d]	13.1 (2.1)[c,e]	15.0 (0)[a,c]	<0.001
Semantic association: word (0–15)[h]	8.7 (3.5)[a,d,e]	13.8 (2.2)[d]	13.3 (1.8)[c,e]	15.0 (0)[a,c]	<0.001
Multi-character multi-repetition: place of articulation (0–100)[i]	80.8 (11.9)[a,d]	63.6 (20.3)[b,d]	67.4 (16.5)[c]	96.8 (4.6)[a,b,c]	<0.001
Multi-character multi-repetition: manner of articulation (0–100)[i]	82.8 (10.3)[d]	57.5 (20.7)[b,d,f]	74.1 (15.2)[c,f]	90.8 (12.3)[b,c]	<0.001
Multi-character multi-repetition: tone of articulation (0–100)[i]	95.1 (3.8)[d,e]	61.7 (27.2)[b,d,f]	79.8 (12.3)[c,e,f]	94.6 (7.9)[b,c]	<0.001
Syntax comprehension (0–30)[j]	26.1 (3.6)	24.2 (5.0)[b]	25.4 (5.5)[c]	29.3 (1.5)[b,c]	0.005
Sentence repetition (0–100)[k]	81.2 (8.5)[e]	79.3 (12.1)[f]	62.9 (21.0)[c,e,f]	93.1 (4.4)[c]	<0.001

Note: Values are mean (standard deviation).

Abbreviations: lvPPA, logopenic variant primary progressive aphasia; MMSE, Mini-Mental State Examination; nfvPPA, non-fluent/agrammatic variant primary progressive aphasia; svPPA, semantic variant primary progressive aphasia.

[a]Significant between control and svPPA.
[b]Significant between control and nfvPPA.
[c]Significant between control and lvPPA.
[d]Significant between svPPA and nfvPPA.
[e]Significant between svPPA and lvPPA.
[f]Significant between nfvPPA and lvPPA.
[g]lvPPA ($n = 28$), nfvPPA ($n = 10$), svPPA ($n = 11$), control ($n = 19$).
[h]lvPPA ($n = 28$), nfvPPA ($n = 10$), svPPA ($n = 11$), control ($n = 19$).
[i]lvPPA ($n = 23$), nfvPPA ($n = 11$), svPPA ($n = 11$), control ($n = 18$).
[j]lvPPA ($n = 27$), nfvPPA ($n = 10$), svPPA ($n = 12$), control ($n = 21$).
[k]lvPPA ($n = 29$), nfvPPA ($n = 11$), svPPA ($n = 11$), control ($n = 21$).

3 | RESULTS

3.1 | Demographic characteristics and neuropsychological data

As detailed in Table 1, the study groups did not differ significantly in age of examination, sex, or handedness. However, participants with lvPPA had fewer years of formal education than control participants ($P = 0.002$). All PPA groups had significantly lower MMSE scores than healthy controls and lvPPA group scored lower in MMSE compared to participants with nfvPPA ($P < 0.001$). Concerning speech and language assessments, participants with svPPA performed significantly worse than control and other PPA groups in tests heavily dependent on semantic memory, including picture naming ($P < 0.001$), single-word comprehension ($P < 0.001$), and semantic association tests (word: $P < 0.001$; picture: $P < 0.001$). Conversely, nfvPPA participants scored significantly lower than control and other PPA participants when asked to repeat phrases that differ in place, manner, and tone of articulations

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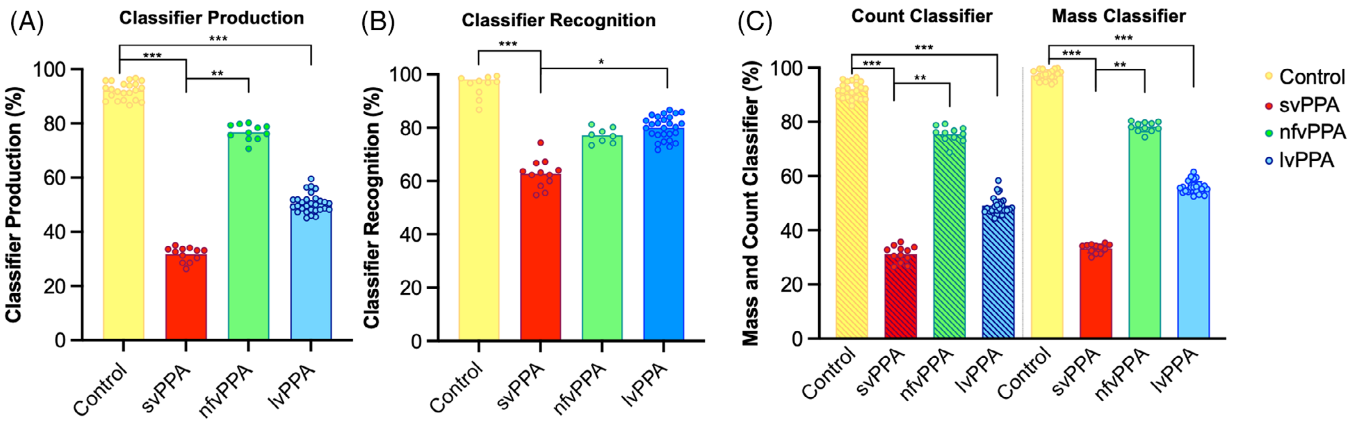

FIGURE 1 Classifier production and recognition scores across study groups. Depicted here are the scores of (A) classifier production, (B) classifier recognition, (C) count and mass classifier production after accounting for age and education level. lvPPA, logopenic variant primary progressive aphasia; nfvPPA, non-fluent/agrammatic variant primary progressive aphasia; svPPA, semantic variant primary progressive aphasia.

(place: $P < 0.001$; manner: $P < 0.001$; tone: $P < 0.001$). On repetition test, lvPPA participants performed significantly worse compared to the other groups ($P < 0.001$). When tasked to match pictures and sentences based on syntactic structures, nfvPPA and lvPPA groups scored significantly lower than the control group ($P = 0.005$).

3.2 | Noun classifier production and recognition

When tasked to spontaneously produce specific classifiers, svPPA and lvPPA groups scored significantly lower than controls, with svPPA patients also scoring significantly lower than nfvPPA patients ($P < 0.001$; Figure 1). In contrast, our analysis revealed no statistically significant difference between control and nfvPPA groups. Similar patterns were noted in mass ($P < 0.001$) and count classifiers ($P < 0.001$; Figure 1), even after covarying for age and years of education (Tables S3 and S4 in supporting information). When provided with multiple choices, svPPA patients were significantly less able to accurately select the specific classifiers than control and lvPPA participants after correcting for age and education level ($P < 0.001$; Table 2). When studying the word/character frequency effect on noun classifier production scores, we found that the character frequency of classifiers significantly predicted accuracy of classifier production in the svPPA group ($F_{24,1} = 5.09$, $P = 0.034$, $\eta 2 = 0.19$), while classifier production accuracy was not related to the word frequency of noun stimuli in any group. This finding underscores the distinct nature of the association between a classifier's character frequency and classifier production accuracy, particularly with svPPA.

3.3 | Correlation between speech and language measures and noun classifier performance

The correlations of the noun classifier scores with semantic and lexical retrieval measures are depicted in Figure 2. Classifier production and recognition scores positively correlated with picture naming (production: $r = 0.872$, $P < 0.001$; recognition: $r = 0.711$, $P < 0.001$), single-word comprehension (production: $r = 0.718$, $P < 0.001$; recognition: $r = 0.505$, $P < 0.001$), picture-based semantic association (production: $r = 0.659$, $P < 0.001$; recognition: $r = 0.648$, $P < 0.001$), and word-based semantic association (production: $r = 0.584$, $P < 0.001$; recognition: $r = 0.539$, $P < 0.001$). These correlations remained significant when analyzing each PPA variant separately (Table S5 in supporting information).

3.4 | Neuroanatomical correlation of the classifier production scores

The atrophy patterns of svPPA, nfvPPA, and lvPPA groups are depicted in Figure S2 in supporting information. In the neural correlate analysis involving svPPA patients and controls, classifier production score correlated positively with GM volume over the left fusiform gyrus, bilateral inferior temporal gyrus, and left visual association cortex. Conversely, lvPPA patients and controls showed positive correlations over the left fusiform gyrus, left inferior temporal gyrus, bilateral inferior frontal gyri, left dorsolateral prefrontal cortex, left dorsal anterior cingulate gyri, and left visual association cortex (Figure 3, Table 2). Upon consolidating the findings of svPPA and lvPPA groups, overlapping GM regions were observed in the left fusiform gyrus, left visual association cortex, left anterior temporal, and inferior temporal gyri.

4 | DISCUSSION

About 22% to 35% of world languages are classifier languages, with ~ 70% found in Asia.[22,23] To our knowledge, this is the first study examining behavioral and neuroanatomical correlates of noun classifier processing in PPA patients. We found that both svPPA and lvPPA patients were impaired in producing specific classifiers. Compared to individuals with lvPPA, svPPA patients were less able to choose the accurate classifiers when given choices. The classifier production

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TABLE 2 Neuroanatomical correlates of the noun classifier production test.

Regions	Extent	*t* value	MNI coordinates		
			x	y	z
Noun classifier production: svPPA					
Left fusiform gyrus	35764	11.27	−50	−62	−21
Left fusiform gyrus		9.56	−33	−36	−20
Left fusiform gyrus		8.86	−24	−44	−12
Left angular gyrus	1177	6.52	−33	−74	36
Left visual association cortex		5.46	−34	−84	30
Left visual association cortex		5.29	−45	−72	24
Right inferior temporal gyrus	539	4.81	16	−6	−40
Right parahippocampal gyrus		4.40	14	3	−38
Right temporal pole		4.04	19	9	−44
Noun classifier production: lvPPA					
Left visual association cortex	14649	6.59	−48	−68	10
Left secondary visual cortex		5.84	−40	−84	3
Left inferior temporal gyrus		5.82	−44	−3	−36
Right inferior frontal gyrus	3571	5.24	46	20	−2
Right inferior frontal gyrus		4.93	52	18	16
Right insula		4.92	46	8	−2
Left fusiform gyrus	1189	4.84	−57	−44	−24
Left fusiform gyrus		4.06	−50	−56	−20
Left fusiform gyrus		3.77	−50	−62	−14
Right orbitofrontal gyrus	362	4.78	14	16	−15
Left supramarginal gyrus	463	4.64	−50	−27	45
Left supramarginal gyrus		4.63	−45	−36	45
Right fusiform gyrus	404	4.59	48	−56	6
Right fusiform gyrus		4.31	58	−46	8
Left dorsolateral prefrontal cortex	502	4.45	−18	44	34
Left dorsolateral prefrontal cortex		4.13	−22	40	40
Left anterior prefrontal cortex		4.11	−20	56	32
Left dorsal anterior cingulate cortex	307	4.22	−2	48	14
Left dorsal anterior cingulate cortex		4.12	−10	45	0
Left dorsal anterior cingulate cortex		3.80	−4	48	4
Right parahippocampal gyrus	782	3.99	15	−18	−21
Right parahippocampal gyrus		3.97	24	−22	−22
Right hippocampus		3.80	27	−12	−15

Abbreviations: lvPPA, logopenic variant primary progressive aphasia; MNI, Montreal Neurological Institute; svPPA, semantic variant primary progressive aphasia.

scores positively correlated with GM volume in the left fusiform, bilateral inferior temporal, and left visual association cortices in svPPA patients and controls. Conversely, individuals with lvPPA and controls showed additional correlations over the bilateral frontal cortices. Through researching Chinese-speaking PPA patients, we identified the potential diagnostic role of noun classifiers in PPA patients and offered further neuroanatomical understanding to classifier production function, which is critical information for speakers of classifier languages.

Word production, including noun classifier production, is a complex process which involves semantic formulation, retrieval of lexical–syntactic attributes, phonological/orthographical word form access, and motor speech planning and execution.[24–28] The lexical–syntactic attributes of nouns vary across languages and can include grammatical gender (e.g., feminine, masculine, neutral), number (e.g., singular, dual, plural), countability (e.g., mass, count), and specific classifier.[29] Wilson et al. showed that French and English svPPA patients had

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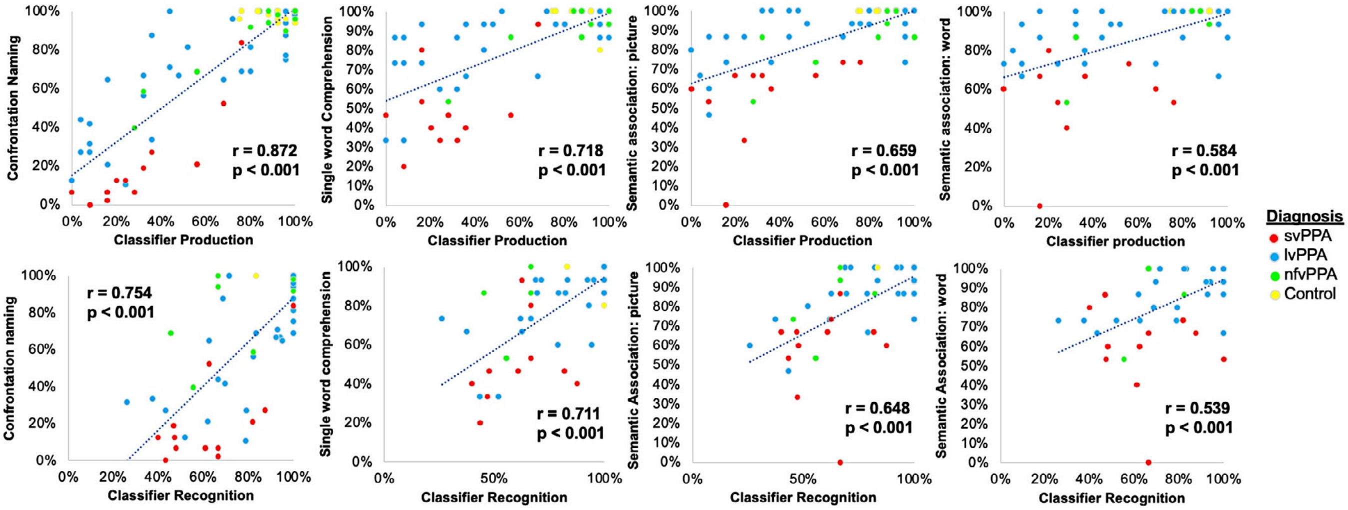

FIGURE 2 Correlation between speech and language measures and noun classifier performance. Depicted here are scatter plots showcasing the Pearson correlations analyses of the noun classifier scores with semantic and lexical retrieval measures from the CLAP battery, namely confrontation naming, single word comprehension, semantic association: picture, and semantic association: word tests. CLAP, Chinese Language Assessment for PPA; lvPPA, logopenic variant primary progressive aphasia; nfvPPA, non-fluent/agrammatic variant primary progressive aphasia; svPPA, semantic variant primary progressive aphasia.

impaired access to these lexical–semantic properties, resulting in inaccurate inflection of irregular English nouns.[8,10] Chinese nouns lack gender category and have limited inflectional morphology based on plurality and countability. Hence, lexical–syntactic attributes are mainly represented by Chinese classifiers.[11,30] Given the arbitrariness and multifariousness of noun-classifier pairings, accessing word-level lexical–syntactic information and retrieving the contextually matched classifiers to generate appropriate noun-classifier phrases are highly dependent on semantic knowledge and lexical retrieval functions,[31] which are known to be degraded in svPPA and lvPPA.[2] It is thus unsurprising that Chinese-speaking patients with svPPA and lvPPA struggled with spontaneously generating accurate classifiers. Interestingly, individuals with svPPA and lvPPA differed in their ability to select classifiers when presented with choices. Hence, we speculate that while both study groups rely on semantic and lexical retrieval skills for noun classifier processing, Chinese svPPA patients struggle with classifier production more predominantly due to frequency-modulated degraded access to lexical–syntactic information whereas the classifier processing performance of lvPPA patients is more dominantly associated with lexical retrieval ability.

In Indo-European languages, mass and count nouns can vary semantically, syntactically, and morphologically.[29,32–35] However, Chinese nouns do not differ morphologically or carry grammatical inferences based on countability. Consequently, there have been speculations that all Chinese nouns are mass nouns or that there is no mass/count distinction in Chinese languages.[36–39] Given the comparable performance of mass and count classifiers in Chinese PPA patients, we infer a common cognitive process between mass and count classifiers in Chinese languages.

The neural basis of Chinese classifiers has been explored using tasked-based functional MRI with a semantic distance comparison task, in which participants were presented with three classifiers and asked to identify the two most semantically related.[16,17] Cui et al. found that classifiers elicited greater activation over left inferior frontal and middle temporal gyri, whereas Her et al. reported higher activation over bilateral inferior parietal lobules.[16,17] The former study presented solely classifier stimuli (e.g., a section/chapter/sentence of) while the latter presented noun-classifier phrases and judged classifier distance based on quantity inference (e.g., one earring vs. one pair of earrings vs. one dozen earrings). Therefore, the neuroanatomical findings of both studies reflected different cognitive processes: semantic judgement and magnitude interpretation of classifiers, respectively. The CLAP classifier test predominantly assesses the ability to accurately produce noun classifier lexicon. Both variant-specific VBM analyses conducted in svPPA and lvPPA identified common regions, including the left visual association cortex, left fusiform, anterior and inferior temporal gyri. These regions are responsible for semantic knowledge, lexical retrieval, and visual interpretation of picture stimuli. The overlapping regions identified imply there exist shared neural mechanisms contributing to classifier processing impairments in Chinese PPA patients. Conversely, the partially distinct neuroanatomical patterns between the svPPA and lvPPA groups signify a certain degree of nuanced variation in the neural underpinning of classifier production in both groups. Previous research has indicated that the left anterior temporal region is relatively specific to lexical knowledge whereas the right anterior temporal region represents semantic information of visual inputs.[40] The involvement of bilateral temporal and left visual cortices in svPPA may reflect the combined need for word and pictorial interpretation of noun stimuli to generate specific classifiers (e.g., liquid or solid chocolate to determine a bar/cup of chocolate). Additionally, the involvement of left frontal regions found in the lvPPA group might be related to the

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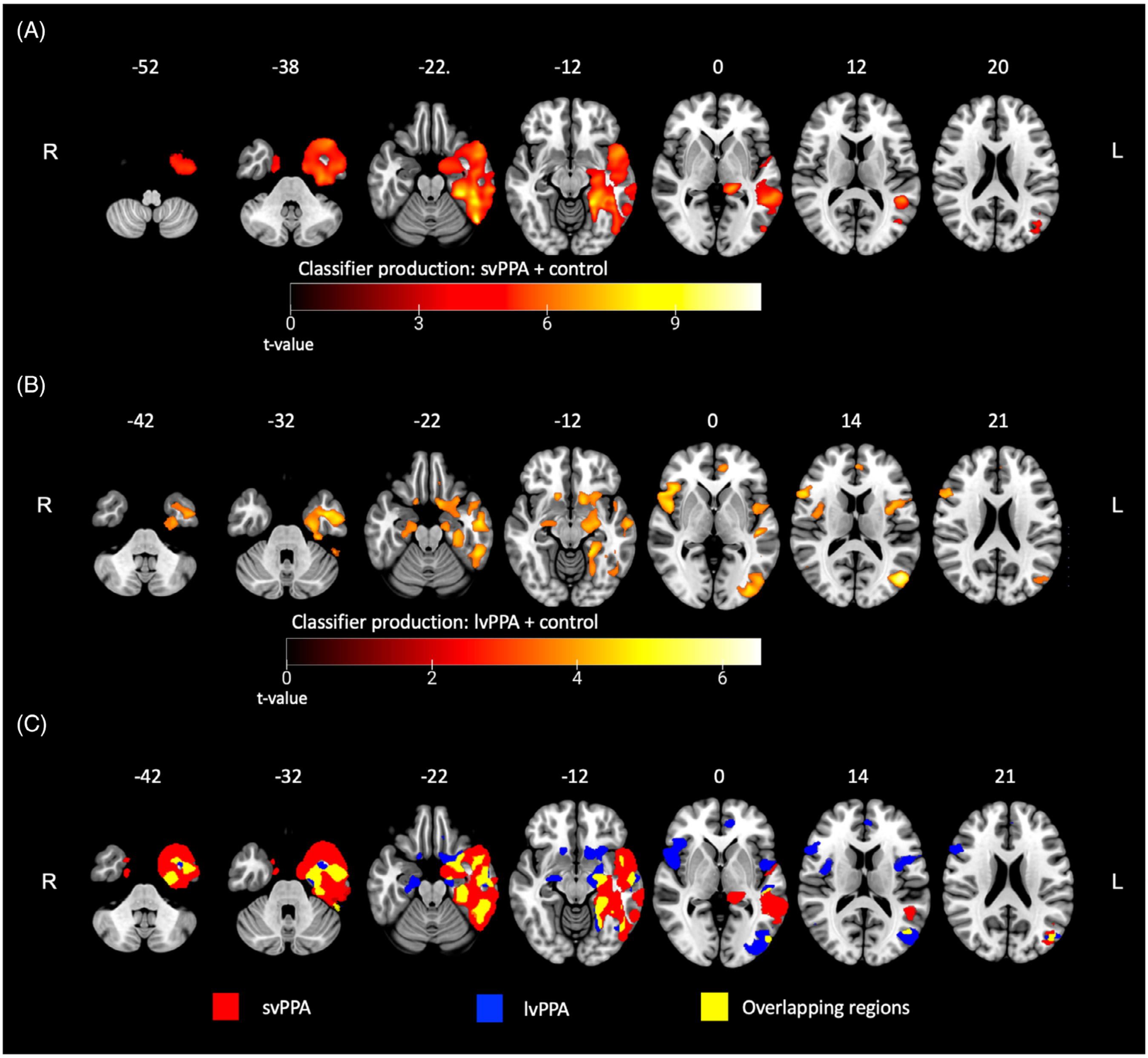

FIGURE 3 Neuroanatomical correlates of classifier production in semantic variant primary progressive aphasia (svPPA) and logopenic variant primary progressive aphasia (lvPPA). The figure shows the neuroanatomical correlation analysis of classifier production scores using voxel-based morphometry (VBM) method for (A) svPPA and control, (B) lvPPA and control. We included age at assessment, years of education, total gray matter volume, sex, diagnosis, and testing language (Mandarin or Cantonese) as covariates in these regression models. The cluster threshold was set at $P < 0.05$, with family-wise error (FWE) correction and an extent threshold of $P < 0.001$, uncorrected, with $k > 100$. Additionally, (C) demonstrates the overlapping and variant-specific regions derived from the neuroanatomical analyses of (A) and (B).

integration and selection of semantic information, as illustrated in Cui et al.'s work.[17]

This study has several limitations. First, the sample size is rather modest as PPA is not the most common dementia syndrome. Consequently, the potential to conduct brain–behavioral analyses of classifier recognition for each PPA variant is constrained, impeding the clarification of their distinct neural mechanisms. Nonetheless, the CLAP study has one of the largest Chinese-speaking PPA cohorts worldwide with comprehensive speech, language, and imaging data. Moreover, the nfvPPA and lvPPA groups differ in their MMSE scores. Albeit the association between MMSE and PPA severity remains debatable, this discrepancy raises questions about potential variations in disease severity between nfvPPA and lvPPA groups. Additionally, the CLAP classifier test only included noun stimuli with high frequency. This may offer limited variability to examine the word frequency effect of nouns on classifier production. We solely included concrete nouns and noun classifiers; thus, these findings may not adequately capture processing of classifiers with abstract nouns (e.g., "a sliver of hope"), verbal

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classifiers (e.g., 哭 一 場), or classifier use in naturalistic speech. Moreover, among the 25 classifier stimuli assessed, only 5 were mass classifiers. Consequently, it may be prudent to undertake future investigations that specifically address different types of mass classifiers (e.g., "two grams of salt" and "a herd of sheep"). Although our findings offer valuable insights into classifier processing, these results must be further validated in other languages, especially when classifiers hold varying semantic and morphosyntactic significance.

This study underscores classifier processing as a promising marker in Chinese-speaking PPA patients. Our findings reinforce the view that syndromic distinctions in PPA can be best captured by targeting language-specific lexical–syntactic phenomena. Specifically, English-speaking PPA patients present with impairment in noun inflection morphology,[8] Spanish-speaking PPA patients show inaccurate pairing of noun articles,[9] while Chinese-speaking PPA patients have degraded classifier production ability. This study informs the diagnostic approach to Chinese-speaking PPA patients, addresses current calls for culturally and linguistically appropriate tests, and contributes to a better understanding of the neural basis of language by enhancing language diversity in cognitive research.

AUTHOR CONTRIBUTIONS

Dr. Tee had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Tee, Gorno-Tempini, Kwan-Chen, Lo. Acquisition of data: Tee, Kwan-Chen, Chen, Yan., Tsoh, Chan, Wong, Lo, Lu, Sun, Wang, Lee, Chuang, and Chiu. Analysis and interpretation of data: Tee, Gorno-Tempini, Kwan-Chen, Garcia, Bak, Battistella. Drafting of the manuscript: Tee, Gorno-Tempini. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Tee, Allen. Obtained funding: Tee, Gorno-Tempini. Administrative, technical, or material support: Tee, Gorno-Tempini, Kwan-Chen. Study supervision: Tee, Gorno-Tempini, Kwan-Chen, Chen, Lo.

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CONFLICT OF INTEREST STATEMENT

The authors report no disclosures or competing interests. Author disclosures are available in the supporting information.

CONSENT STATEMENTS

All participants or their medical proxies provided written informed consent consistent with the Declaration of Helsinki guidelines.

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