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Doctoral Dissertation

Oral And Written Production in Healthy Subjects and Primary Progressive Aphasia: A Cross-Linguistic Comparison

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Abstract (English)

The present work aims to describe cross-linguistic similarities and differences, using different production tasks, in healthy participants and patients with Primary Progressive Aphasia (PPA). The characterization of healthy controls' production is a crucial preliminary step to further assess neurodegenerative patients, as it provides the identification of intrinsic constraints and features of each language. Accordingly, we firstly compared, using an oral picture description task, the production of English, Chinese, and Italian healthy subjects, revealing differences in the phonological, lexico-semantic, and morpho-syntactic domains, which can be ascribed to the specific organization of sound, words, and sentences, typical of the three languages. In the second study, using the same oral picture description task, we characterized the production of English, Chinese, and Italian PPA patients by comparing them with their respective healthy control (HC) groups. We identified both cross-linguistic-shared and language-specific features able to distinguish PPA from HC. Language-shared features well differentiated between PPA and controls for all three languages, despite differences in accuracy. The highest was reported for Italian. In addition, only for Italian, the language-specific features significantly ameliorated the classification obtained by the shared ones. In the third study, we characterized the written production of two patients with non-fluent variant of PPA (nfvPPA), whose first languages were English and Italian, respectively, via comparison with matched healthy controls. Both nfvPPA presented with a typical agrammatic profile but also revealed deficits in different features, only partially ascribable to differences between English and Italian orthographies. These studies support the relevance of cross-linguistic assessment in enhancing our understanding of language organization and promoting an adequate assessment of patients.

Abstract (Italiano)

Lo scopo del presente lavoro è quello di descrivere similitudini e differenze tra lingue diverse, usando diversi compiti di produzione, sia in soggetti sani che pazienti con Afasia Primaria Progressiva (PPA). La caratterizzazione del linguaggio di soggetti sani è un passaggio preliminare cruciale per la successiva valutazione dei pazienti con patologie neurodegenerative; consente infatti di indentificare le caratteristiche peculiari di ciascuna lingua di interesse. Nel primo studio abbiamo dunque confrontato, usando un compito di descrizione orale di figura, la produzione di soggetti sani inglesi, cinesi e italiani, che ha rivelato differenze a livello dei domini fonologico, lessico-semantico e morfo-sintattico. Tali differenze possono essere ascritte al diverso modo in cui, in ciascuna delle tre lingue, suoni, parole e frasi sono tipicamente prodotti. Nel secondo studio, abbiamo quindi caratterizzato la produzione orale, usando il medesimo task, di pazienti inglesi, cinesi e italiani con PPA, confrontandola con quella dei rispettivi gruppi di controllo. Tale confronto ci ha consentito di identificare sia variabili condivise che specifiche per ciascuna lingua in grado di distinguere significativamente tra PPA e controlli. Le variabili condivise hanno mostrato una buona capacità di differenziare i pazienti in tutte e tre le lingue, mostrando tuttavia diversi livelli di accuratezza, particolarmente elevati per la lingua italiana. Inoltre, per l'italiano, l'utilizzo delle variabili specifiche ha determinato un ulteriore incremento nell'accuratezza della classificazione di PPA e controlli. Nel terzo studio, abbiamo infine caratterizzato, utilizzando un compito di descrizione di figura scritta, la produzione scritta di due pazienti con diagnosi di Afasia Progressiva Primaria variante non fluente; il primo madrelingua inglese, il secondo italiana. Entrambi i pazienti hanno mostrato un profilo tipicamente agrammatico, rivelando deficit in domini diversi, solo parzialmente ascrivibili alle differenze di ortografia esistenti tra inglese e italiano. Questi studi sostengono l'importanza di condurre valutazioni cross-linguistiche, sia al fine di incrementare la conoscenza e comprensione del linguaggio e della sua organizzazione, sia al fine di favorire una valutazione adeguata dei pazienti.

General Introduction

The Need for Cross-Linguistic Studies

Nowadays, we count more than 7,000 living languages, excluding those that are not spoken anymore and those that have not yet been discovered. Interestingly only a minority of them, around a third, has been formally studied (Bakker, 2011), and an even smaller amount has been included in cognitive science research (Blasi et al., 2022; Evans and Levinson, 2009).

Across these idioms, an elevated level of variation and diversity is reported. Similarities and differences are related to the proximity of idioms, which are usually organized into language families, represented as trees, i.e., Indo-European, Sino-Tibetan (Bouckaert et al., 2012; LaPolla, 2019). Languages belonging to the same family share a higher degree of similarity. Differences across and within families, observable in phonology, phonetics, lexicon, semantics, syntax, morphology, and orthography, are the product of language development, and may also be influenced by direct contact with other linguistic groups (Moravcsik, 2012).

To provide a few examples of linguistic variability, we can consider the system we use to codify language in writing; some languages use an alphabet, in which one symbol corresponds to one sound, and others use a logographic system in which a character represents a word or a morpheme (Daniels, 2017). Syllables, defined as a pronounceable portion of speech, may vary in their order of presentation, with the majority of cases organized as consonant-vowel (CV) clusters and only in smaller proportion as vowel-consonant (VC) clusters. Generally, in Indo-European languages, speakers use tone, pitch, and prosody changes to highlight their intention or emotional state (Ladd and Arvaniti, 2023; Trott et al., 2023). In tonal languages, which are 70-80% of the total (Yip, 2002), changes in tone vehicle different meanings, and recognition of tone is crucial for content understanding (Ladd and Arvaniti, 2023; Peng et al., 2005). Differences at the morphological level range from the presence of rich inflectional morphology, i.e., Italian, to the very limited presence of inflections, i.e. Chinese (Pescuma et al., 2021; Pizzuto et al., 1994). Differences also involve syntactic rules and sentence generation. Word order generally follows the subject-verb-object (S-V-O) combination, however, languages that are context-dependent, such as Chinese, might allow S-O-V order. Some words might be omitted without compromising the grammaticality of the sentence; i.e., determiners and pronouns can be dropped in Chinese (Huang, 1999; Simpson et al., 2016), and in Italian, the elision of pronouns is possible (Russo et al., 2012).

Up today, an Anglocentric approach has characterized language research (Levisen, 2019), both in healthy and neurological participants (García et al., 2023), resulting in the tendency to use English as the main language on which cognitive models are based, underestimating the impact that this approach exerts on the whole scientific processes (Levisen, 2019), from hypothesis formulation to results interpretation through method selection (Konno et al., 2020). A significant and relative selective language impairment is central for the diagnosis of Primary Progressive Aphasia (PPA), a neurodegenerative condition in which language impairment is the hallmark of the disease insurgence and the main and relatively selective symptom in the first two years of the disease presentation (Gorno-Tempini et al., 2011). PPA is considered an excellent model for studying language functioning and organization. Again, however, current diagnostic criteria are tailored to English-speaking patients, and even if they are certainly valid, they might not fully account for the cross-linguistic diversity and peculiarity of non-English patients.

In the field of cognitive science and in general, in the scientific community, we are witnessing today the increase in awareness of cross-linguistic differences, and their implications, boosting the attention toward cross-linguistic studies (García et al., 2023; Hatahet et al., 2023). In this light, English subjects have been compared to participants speaking languages of the same family, i.e., Italian (Canu et al., 2020), or different families, i.e., Korean (Sung and Dede, 2016), Chinese (Yiu and Worrall, 1996), and Bengali (Bose et al., 2021), confirming a relevant effect of the linguistic specificity in language production. From a clinical perspective, studying language neurodegenerative diseases, such as PPA, from a cross-linguistic perspective is undoubtedly relevant, or rather essential, as it became increasingly evident that, the need for equitable, inclusive, and cross-linguistic assessment cannot be further ignored.

The possibility to study and compare languages adopting a cross-linguistic approach, namely accounting for each language specificity, including both similarities and differences across languages, is a powerful tool to enhance our understanding of language organization and its neural correlates. To fulfill this goal, however, it is vital to adopt and develop appropriate language tasks, that account for cultural and linguistic diversity (Bose et al., 2022), providing a real chance to develop an accurate and adequate language assessment of neurological patients who are not English native speakers.

Outline and aim of the thesis.

A cross-linguistic approach is the common thread of the present thesis. Accordingly, we aimed to identify shared and specific linguistic markers across different languages, not to characterize them at a typological level, but to provide an adequate and appropriate characterization of neurodegenerative patients' linguistic profile across languages. In particular, we focused on languages belonging to different families, Indo-European – including Germanic language (English), and

Romance language (Italian), and Sino-Tibetan – including Sinitic language (Chinese Mandarin and Chinese Cantonese) (http://elinguistics.net/).

We will assess the language production, via both an oral and written description task, of both healthy participants and patients with neurodegenerative diseases. The adoption of a picture description task allows to elicit contents that are similar across subjects, facilitating the comparison across different groups. In addition, this task provides a significant amount of information, regarding a wide range of linguistic domains, i.e., phonetic, phonological, lexico-semantic, morphological, and syntactic; namely a great number of factors that possibly, taken together, account for linguistic diversity. A further step is the use of the picture description via different output modalities, i.e., the written and the oral ones, to permit a more comprehensive assessment also of orthography and to overcome severe articulation impairments typical of some PPA patients.

In all cases, the characterization of healthy controls' production is a crucial step to provide the identification of the intrinsic constraints/features of each language, namely to account for each linguistic specificity. In the first chapter, we will investigate cross-linguistic differences in English, Chinese, and Italian healthy participants' production, aiming to reveal differences possibly ascribable to the specific organization of the three languages.

In the second chapter, we will move to the characterization of English, Chinese, and Italian patients with Primary Progressive Aphasia. The results of the second study will certainly be relevant in identifying cross-linguistic-shared and language-specific features able to adequately differentiate PPA from controls for each language.

In the third chapter, we will describe, using a single case approach, the writing profile of two nfvPPA patients, having as their first language English and Italian. We will compare their performance to matched groups of healthy participants, to identify typical features and to qualitatively describe cross-linguistic differences and similarities between the two languages.

This study aims to be a first step into the complexity of cross-linguistic world, and not be fully exhaustive, as cultural differences, in terms of education level, school system (i.e., years of mandatory schooling), economic and social background (i.e., access to higher education, public or private school system, low-middle-high income country, etc.), may have additional important impacts into the performance of participants.

Language Variability in Picture Description: Examining Speech Markers in Chinese, English, and Italian Cognitively Healthy Individuals

1. Introduction

There are over 7,000 living languages, excluding those that are no longer in use or are yet to be discovered (Bakker, 2010). Expanding cognitive research beyond frequently studied languages enables an exploration of possible differences in the manifestations of language disorders, and may contribute to the prevention of health inequities stemming from linguistic variations (García et al., 2023). Cross-linguistic studies are an ideal model to examine the possible differences in brain response to linguistic variations and have been increasingly adopted by cognitive researchers (Blasi et al., 2022; Evans and Levinson, 2009). They enable the disclosure of linguistic variability, elucidate similarities and differences, and significantly enhance our understanding of language and the symptoms, diagnosis, and treatment of aphasia. While cross-linguistic studies have investigated different cohorts (i.e., cognitively healthy (Ardila, 2020; Valaki et al., 2004), developmental (McLeod and Crowe, 2018), and participants with neurological diseases (Bates, 1991; Bates et al., 1987; Benedet et al., 1998; Canu et al., 2020; Mirman and Thye, 2018; Sung and Dede, 2016; Yiu and Worrall, 1996)) across various tasks, most of these studies have mostly included languages of the same family (i.e., Indo-European: English vs German (Bates et al., 1987), vs Italian (Bates et al., 1987; Canu et al., 2020), or vs Spanish (Benedet et al., 1998)).

Language differences can significantly affect the neural underpinnings of speech and language functions (Wei et al., 2023), as well as the manifestation of symptoms in neurological diseases (Canu et al., 2020).

In this study, we delve into the linguistic performance of cognitively healthy speakers of English, Italian, and Chinese (i.e., Cantonese and Mandarin) in describing the content of a complex picture. These languages exhibit varying degrees of language proximity: English and Italian, stem from distinct branches of the Indo-European family—Germanic and Roman, respectively, while the Chinese languages belong to the Sino-Tibetan language family (Bouckaert et al., 2012; LaPolla, 2019). According to eLinguistic (2023), which quantifies the temporal distance when two languages last shared a common ancestor (i.e., language genetic proximity), English and Italian languages exhibit a high language relatedness score of 49.9, implying a shared ancestor that likely emerged approximately from 2,000 to 4,000 years ago. In contrast, English, and Chinese, as well as Italian and Chinese, demonstrate no common linguistic ancestry, as indicated by their high language distances (i.e., genetic proximity of Italian - Chinese (Cantonese): 92.2; Italian - Chinese (Mandarin): 88.5; English - Chinese (Cantonese): 87.5; English - Chinese (Mandarin): 83.9). These language distance metrics partially reflect the degree of linguistic similarities across various linguistic domains, including but not limited to phonology, morphology, and syntax (Evans and Levinson, 2009). For instance, in terms of phonology, the English language is organized into consonant-vowel (CV) or CCV clusters; Italian predominantly presents CV cluster, and Chinese relies on V, CV, or CVC configurations (Bowen, 2023; Duanmu, 2011; Paoli, 2016). Furthermore, Chinese is a tonal language, which requires intricate control of oropharyngeal and vocal cord muscles to generate pitch variation that synchronizes with syllable production, whereas English and Italian rely on lexical stress that emphasizes specific syllables through increased voice intensity, vowel length, and changes in pitch. At the level of word morphology, Italian has richer inflectional morphology than English (Pizzuto et al., 1994) and Chinese, which is instead an analytic language lacking affixes and having only a few types of inflectional and derivational morphology. Moreover, unlike English and Italian, the Chinese language is a classifier language in which classifier use is mandatory when numbers or determiners precede nouns (Erbaugh, 2012). Syntactic differences, although understudied (Jaeger and Norcliffe, 2009), are present. For example, Italian and Chinese are pro-drop languages, thus elements such as pronouns, verbs, and/or determiners are not always obligatory to form grammatically coherent sentences (Li and Thompson, 1989; Russo et al., 2012). Variations across different linguistic features can significantly impact speech production and, consequently, its assessment.

It is increasingly crucial to gain a deeper understanding of how linguistic features manifest in cognitively healthy individuals and therefore to explore the possible role of intrinsic linguistic differences and/or the involvement of degenerative processes in the presentation of diverse linguistic characteristics. This knowledge can be instrumental in unraveling the intricacies of language organization and potentially contribute to the development of accurate language assessments, particularly in cases of neurological impairment (García et al., 2023). The present work had two aims: 1) to delineate the distinctive linguistic characteristics inherent to English, Chinese, and Italian speakers, and 2) to identify shared linguistic features among these languages for the potential development of language assessment tools with cross-linguistic applicability.

2. Materials and Methods

2.1 Participants

A cohort of 39 cognitively healthy participants (HP) was included. Within this cohort, 13 participants were recruited for each of the target languages, encompassing American English speakers from the University of California, San Francisco, Chinese speakers from the CLAP project from seven sites in Taiwan and Hong Kong, and Italian speakers through collaboration with the ICON Lab at the University of Advanced Studies – IUSS – Pavia. All included HP did not have a significant history of neurological and psychiatric disorders and had completed the oral picture description task from the Western Aphasia Battery (Kertesz, 1982). Participants were native speakers of one of the included languages and fulfilled the literacy requirement of having completed at least three years of school.

2.2 Oral Picture Description

Every participant completed the oral description of the Picnic Scene from the Western Aphasia Battery (Kertesz, 1982). The picture description task is a widely employed tool in cognitive research for its time efficiency and low technical demand while offering language data across different linguistic domains. Moreover, the possibility to prompt oral production using a picture scene facilitates access to conceptual knowledge in healthy and neurological subjects (Ralph, 1999; Vandenborre et al., 2018), and elicits contents that are similar across subjects. Performance data were audio recorded and stored in compliance with the ethical protocols established at each participating center. The examiners instructed HP to look at the picture and describe in sentences what they saw. The audio samples were then transcribed with English, Chinese, and Italian languages, and linguistic features of interest (detailed in Section 2.3) were coded in compliance with Computerized Language ANalysis program (CLAN; detailed in Section 2.4) instructions. In each language group, two raters independently transcribed and coded the speech samples, followed by a subsequent comparison of the results. For any coding discrepancy, a third rater was consulted, and researchers engaged in discussions for every single case until a consensus was reached.

2.3 Linguistic Features

A total of 28 features were chosen (listed in Table 1 with definitions), drawing upon existing literature (Boschi et al., 2017; Canu et al., 2020; Mueller et al., 2021; Wilson et al., 2010) and the authors' knowledge of each language. These features encompass various linguistic domains, including phonology, lexico-semantic, morpho-syntactic, and discourse and pragmatics. For each domain, we selected features that were considered relevant linguistic markers in at least one of the languages included in the study, and they were: 1) features that have been previously used to describe the linguistic performance of healthy participants (Mueller et al., 2021); 2) features that characterized the linguistic performance of clinical populations, i.e., stroke aphasia (Boucher et al., 2020; Vandenborre et al., 2018); and primary progressive aphasia patients; (Wilson et al., 2010). Accordingly, 25 features were common across speakers of different languages (i.e., words/minute, number of nouns, number of sentences, etc.,), while we included three features, namely the ratio of classifiers over the total number of words, the number of classifier generalization and the number or classifier omission that are specific for Chinese speakers.

Table 1 Speech and Language included features.

Domains	Features	Definition
Phonological	N° words repetition	Begin to say something, stop, and repeat without changes
	N° prolonged sound	Sounds that are abnormally prolonged
	N° broken words	Pause within word
	N° Abandoned words/tot words	Changes from one word to another
	N° Empty pauses/tot words	Number of silent (no sound produced) pauses
	N° filled pauses/ tot words	Number of filled pauses (i.e., uhm, ehm)
Lexico-Semantic	Open class words/total words	Total number of content words (verbs, nouns, adjectives, adverbs)/total number of words
	Close class words/total words	Total number of function words (determiners, classifiers§, pronouns, prepositions…)/total number of words
Morpho-syntactic	N° utterances	Utterances require subject and main verb
	Mean Length of utterances	Ratio of morphemes to utterances
	N° utterances without verb/n° utterances *	Elision (drop) of the main verb
	Determiner elision/substitution	Elision (drop) or substitution of article
	Prepositions elision/substitution	Elision (drop) or substitution of preposition
	Classifier elision §/generalization §	Elision (drop) or generalization of classifier
Discourse and Pragmatic	Words/min	Total number of words/minutes
	N° irrelevant words/tot words	N° words syntactically correct but do not convey relevant meaning/ total number of words
	N° tangential word/ tot word	N° words not related to the task/total number of words

List of included features and their definition.
** Features manually coded.*
§ *specific features for the Chinese language.*
N° number.

2.4 Computerized Language ANalysis program

Speech samples were manually transcribed and coded using CLAN and instructions provided in its manual. CLAN has been designed to analyze speech data and has been extensively used in studies involving healthy participants, children, and neurological populations. For comprehensive information on CLAN and its applications, please refer to the Aphasia Bank project at https://aphasia.talkbank.org/. Additionally, CLAN is accessible in multiple languages, encompassing English, Chinese, and Italian, thereby allowing us the opportunity to operate within a unified analytical framework.

It is essential to acknowledge that definitions and coding procedures may vary with the studied language. For instance, the omission of pronouns is deemed an error in English, rendering agrammatic sentences, whereas in Italian, such omissions are both acceptable and common, thus not considered inaccurate grammatically. Additionally, certain features may be described and coded exclusively in one language, as they are linguistically inapplicable to others; for example, classifier generalization and omission are specific to the Chinese language. Analysis of speech production was performed using the CLAN pipeline, which allowed us to automatically derive the features of interest. For the features that were not configured in the CLAN software, they were manually coded first and processed via the CLAN command interface.

2.5 Statistic Analysis

Demographic and CLAN data were compared across groups using chi-square tests for categorical variables and parametric ANOVA for continuous variables with Bonferroni's correction applied for post hoc analysis.

3. Results

3.1 Demographic Data

Demographic information for the healthy participants is presented in Table 2. Gender, age, and education levels were carefully matched across the three language groups (English, Chinese, and Italian), with all p-values being higher than 0.05.

Table 2 - Demographic Data of healthy participants

	English (n=13)	**Chinese (n=13)**	**Italian (n=13)**	**P value**
Age (years)	70.5 (3.2)	67.53 (5.9)	64.9 (8.2)	0.080
Education (years)	16.6 (1.5)	15.07 (1.6)	14.7 (3.0)	0.068
Gender (Female/Male)	4/9	4/9	5/8	0.749

Mean and standard deviation, between brackets, are reported for each group.

3.2 Speech Sample Analysis: Language Features

The results of the speech sample analysis are summarized in Table 3 and Figure 1. Among the 28 examined features, six manifested in significantly different (survived Bonferroni's correction) proportions across the language groups, three were uniquely produced by one or two groups, and the remaining nineteen showed similar proportions or amounts of production across all groups.

Figure 1 presents the six features that varied significantly across languages. Specifically, within the phonological domain, Italian speakers exhibited a higher proportion of empty pauses to total words than their English and Chinese counterparts ($F(2,28)=11.98$, $p<0.001$). In the lexico-semantic domain, the Chinese group showed a lower proportion of prepositions, determiners, and pronouns to total words compared to both English and Italian groups (F(2,28)=34.32, p<0.001; F(2,28)=307.26, p<0.001; F(2,28)=16.508, p<0.001, respectively). Italian group produced a lower proportion of prepositions compared to English speakers. In contrast, the Chinese group produced a higher proportion of adverbs than the speakers of the other two language groups (F2,28)=12.491, p<0.001). Although Italian speakers exhibited fewer prepositions than the English group, they generated a higher proportion of conjunctions than the English and Chinese groups (F(2,28)=18.31, p<0.001). Furthermore, the Chinese group used a higher proportion of adverbs compared to the English and Italian groups (F(2,28)=12.491, p<0.001).

Three features were exclusively produced by one or two of the study groups. In the phonological domain, we found that only English and Italian speakers produced broken words, meanwhile, such in-word interruption was not observed among Chinese speakers. In the morpho-syntactic domain, English speakers produced agrammatical sentences due to the omission of verbs. Conversely, Italian, and Chinese speakers produced sentences without verbs that were considered grammatically correct in their respective languages, such as in Italian: "Vedo una coppia (.) un albero con tante foglie" (I see a couple (.) a tree with many leaves), and in Chinese: "這棵樹很高" (literal English translation: "This (+classifier) tree very high"). Similarly, English and Italian omitted determiners in therefore agrammatic sentences, however, Cantonese speakers omitted determiners but produced grammatically valid sentences, as in the example: "~~（這）~~個男仔 側邊有隻 狗" // ~~(Determiner)~~ <Classifier> Boy side has <Classifier> Dog // "Ragazzo con il cane a fianco" (Boy with the dog next to him).

Finally, the remaining nineteen features, spanning various linguistic domains examined, were universally expressed across the three languages, with no significant differences after post-hoc correction. These attributes were manifested in comparable proportions or amounts across the linguistic groups, indicating a shared linguistic functionality.

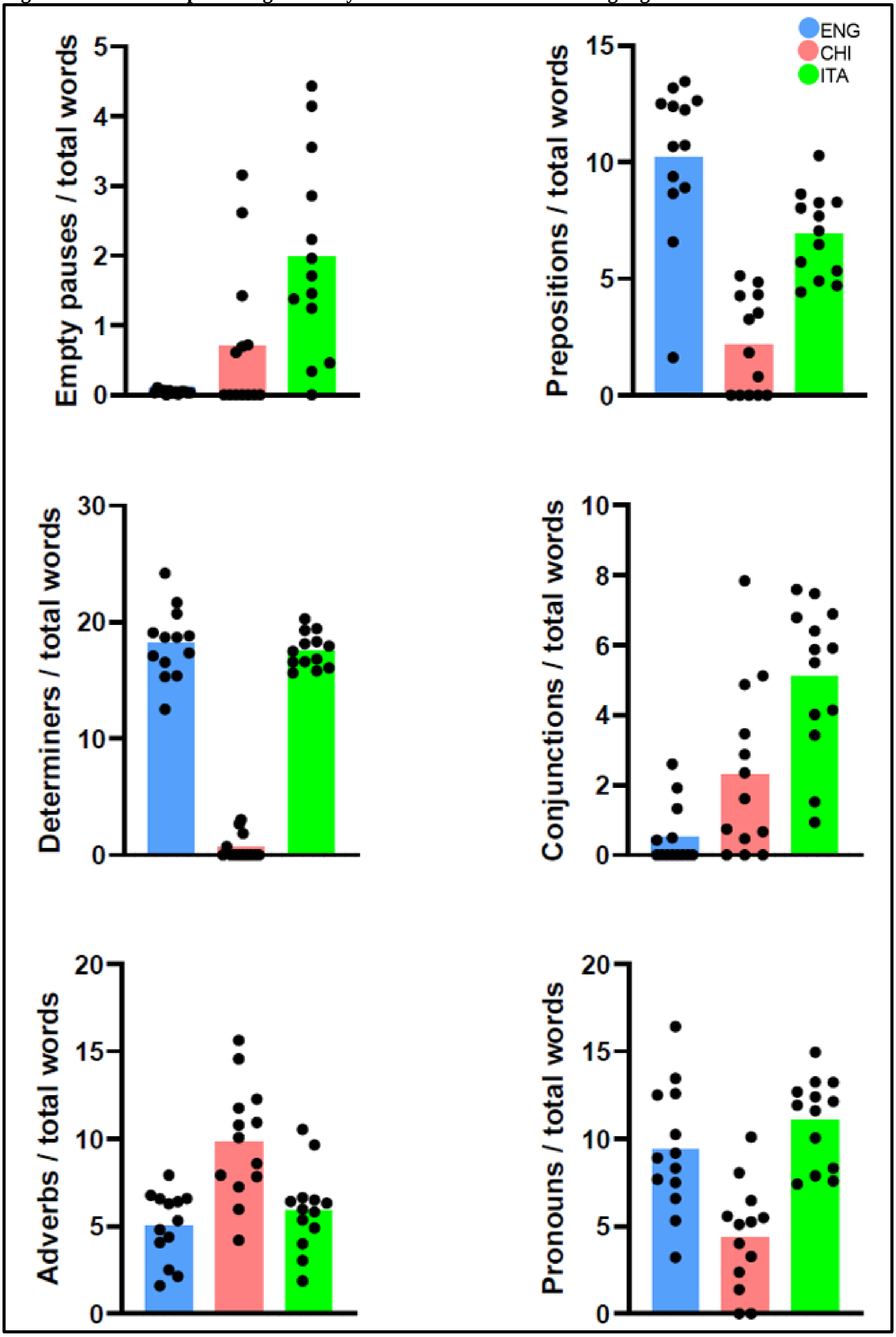
We also identified interindividual variability in the speech production of speakers of similar language, considering individual performances that deviate by two standard deviations from the group mean. For instance, preposition elision and substitution were produced only by one subject in English and one in the Italian group, respectively; meanwhile only three Chinese speakers produced noun classifier generalization. Lastly, at the discourse level, one English speaker produced tangential speech, meaning he/she produced grammatically corrected sentences that were not related in terms of content to the picture.

Table 3 Cross-linguistic comparisons

Domain	Features	ENG	CHI	ITA	P value
Phonological	N° word repetition/tot words	0.512 (0.718)	1.125 (0.893)	0.976 (0.873)	0.161
	N° prolonged sounds	2.077 (2.326)	0.769 (1.423)	1.308 (1.494)	0.189
	N° broken words/tot words	0.103 (0.37)	0 (0)	0.033 (0.119)	0.499
	N° abandoned words/tot words	0.306 (0.463)	0.341 (0.526)	0.261 (0.452)	0.914
	N° empty pauses/tot words	0.044 (0.028)	0.709 (1.067)	1.982 (1.419)[ab]	<0.001
	N° filled pauses/tot words	0.041 (0.027)	0.056 (0.049)	0.018 (0.013)[b]	0.024*
Lexico-Semantic	Nouns/tot words	24.528 (2.098)	22.403 (5.542)	24.72 (2.633)	0.229
	Verbs/tot words	21.789 (6.388)	18.353 (4.458)	18.431 (2.359)	0.118
	Preposition/tot words	10.226 (3.314)	2.154 (2.113)[ac]	6.906 (1.804)[a]	**<0.001***
	Adjectives/tot words	2.548 (1.529)	3.33 (1.777)	1.876 (1.544)	0.087
	Adverbs/tot words	5.034 (1.992)	9.836 (3.296)[ac]	5.929 (2.351)	**<0.001***
	Conjunctions/tot words	0.522 (0.873)	2.312 (2.447)	5.118 (2.164)[ab]	**<0.001***
	Determiners/tot words	18.152 (3.019)	0.639 (1.121)[ac]	17.563 (1.478)	**<0.001***
	Pronouns/tot words	9.386 (3.617)	4.394 (2.99)[ac]	11.042 (2.504)	**<0.001***
	N° classifiers/tot words[§]		9.448 (3.703)		
Morpho-syntactic	N° total utterances	17.077 (6.02)	16.462 (3.526)[c]	21.538 (4.612)	0.021*
	Mean Length of utterances	8.153 (2.126)	9.847 (2.745)	9.308 (2.126)	0.186
	N° utterances without verb/ tot utterances	0.154 (0.376)	0 (0)	0 (0)	0.128
	N° classifier substitution[§]		0 (0)		
	N° classifier generalization[§]		0.231 (0.832)		
	Determiner elision	0.385 (0.65)	0 (0)	0.385 (0.87)	
	Prepositions elision	0.077 (0.277)	0 (0)	0 (0)	
	Determiner substitution	0 (0)	0 (0)	0 (0)	
	Preposition substitution	0 (0)	0 (0)	0.077 (0.277)	
Discourse and Pragmatic	Words/min	178.031 (76.165)	125.543 (38.249)	116.898 (19.157)[a]	0.008*
	N° tangential Words/tot words	1.619 (5.839)	0 (0)	0 (0)	0.378
	N° words empty speech/tot words	15.66 (13.868)	4.062 (9.821)[c]	16.909 (11.989)	0.018*

Mean and standard deviation, between brackets, for each group.
[a] Different from English.
[b] Different from Chinese.
[c] Different from Italian.
In grey: not applicable results.
N° number.
[§] *specific features for the Chinese language.*
**P* < 0.05. In bold statistically significant values after Bonferroni's correction (p<0.001).

Figure 1 Scatter dox plot of significantly different features across languages.



4. Discussion

To the best of our knowledge, this is the first study that compared the speech production of healthy individuals across English, Chinese, and Italian languages. Most existing crosslinguistic studies involve languages belonging to the same family, thus offering a more limited perspective due to the inherent similarities among these languages (Canu et al., 2020; Levisen, 2019). In the few existing studies that included a direct comparison of languages belonging to different families, such as English vs Chinese (Yiu and Worrall, 1996) or English vs Korean (Sung and Dede, 2016), the results suggest the verbal descriptions of the same pictures differ linguistically among cognitively normal individuals. These cross-linguistic variations are crucial for understanding the aphasia symptoms observed in individuals with neurodegenerative diseases.

Our primary objective was to identify both shared and distinctive linguistic features that pertain to each language during the picture description task, thus providing valuable insights into the task's cross-linguistic applicability. Our result underlined several cross-linguistic variations that manifest in cognitively healthy individuals, even within small sample size groups matched for age, education, and gender. Differences involved mainly phonological and lexico-semantic domains and they likely stemmed from the fundamental linguistic characteristics of each language, see for a summary Table 4. These findings hold significant importance in the development of speech markers for identifying various neurological diseases across diverse linguistic contexts.

Our results indicated that Italian speakers produced a higher proportion of empty pauses. Empty pauses in speech production serve numerous roles; they may act as a strategic pause for speakers to gather their thoughts and structure their speech, especially with more complicated morphosyntactic structures, or aid in the demarcation of discourse (Esposito et al., 2007; Fon et al., 2011). While the Italian language generally adopts a more complex word morphology and syntactical structures, English morphology presents lower levels of inflection, and Chinese languages are analytic languages that have limited forms of nouns and verbs, thus potentially having different demands for pauses. Additionally, pauses carry varying linguistic inferences across languages. While speakers of Indo-European languages use pauses to highlight discourse boundaries and hierarchy, Chinese speakers may rely on other markers (i.e., sound prolongation) to indicate boundaries in sentences (Fon et al., 2011; Peng et al., 2005). These factors could potentially contribute to the differences in empty pauses across Chinese, English, and Italian speakers.

Pausing differences were not relevant only when considering between words silence, but also within words. We noted that English and Italian speakers produced a similar proportion of pauses within words, meanwhile Chinese ones did not produce any. This event might be explained by looking at the structure of the Chinese language, which is primarily monosyllabic (Duanmu, 2011) meanwhile the two Indo-European languages follow a multisyllabic structure, which might increase the complexity of phonological processing.

Numerous cross-linguistic variations have also been identified in the lexico-semantic domain, particularly concerning the proportion and type of tokens that speakers predominantly utilize in their speech. Specifically, speakers of Chinese produced a notably lower proportion of function words, such as prepositions, determiners, and conjunctions, compared to speakers of English and Italian. This pattern is consistent with the fact that the Chinese language allows a significant amount of ellipsis in sentences, especially in spoken language, thereby omitting function words such as prepositions and conjunctions (Li and Wei, 2014). If verbatim translated into English or Italian, similar structures would often appear agrammatic or telegraphic. Conversely, the role of prepositions is highly significant in the English language, which accounts for the notably greater production of this class of words (see Table 4). Studies reported that approximately one in every ten words in English is a preposition (Fang, 2000), with the language containing over 100 prepositions, a number that is higher than other languages (Koffi, 2010), for example, Italian has only nine simple prepositions.

Additionally, both Chinese and English speakers used fewer conjunctions compared to their Italian counterparts. Conjunctions occupy various roles in Italian grammar across different communicative contexts. Furthermore, the multifaceted roles of conjunctions in the Italian language complicate their categorization. For example, the GRADIT dictionary lists over 50 Italian adverbs that can also function as conjunctions (Tamburini, 2014). This significantly elevates the usage frequency of this word class, particularly in spoken language (D'Agostino, 1998). Experimental data based on translation studies showed that the Italian language relies more heavily on conjunctions and subordination than English to maintain speech coherence and organization (Palumbo, 2010). Furthermore, studies on second language acquisition highlighted that Chinese native speakers tend to omit conjunctions that precede subordinate clauses when speaking English, which is grammatically inaccurate and uncommon among native English speakers (Kong et al., 2023). While Indo-European languages rely on cohesive components such as conjunctions to maintain cohesion, the Chinese language achieves discourse coherence primarily using word meanings and repetition. As a result, Chinese discourse features fewer conjunctions compared to English, significantly reducing the presence of this linguistic element in verbal production (Chao, 1968; Yang, 2014). We speculate a continuum across the three language groups, where the reliance on explicit markers of cohesion and organization progressively declines from Italian to Chinese.

In terms of open-class words, the Chinese group produced more adverbs than the English and Italian participants. This finding aligns with the characteristics of Chinese morphology. Unlike Italian and English, which use verb tenses, and plural and gender forms (the latter only in Italian), Chinese does not convey chronological and numerical information through inflectional morphology or suffixes. Instead, this information is typically indicated by adverbs or aspect markers (Lin, 2006).

Lastly, the Chinese group produced fewer pronouns compared to both Italian and English speakers. Chinese is recognized as a pro-drop language, characterized by the minimal use of pronouns, possibly influenced by the prevalent use of elliptical sentences (Li and Thompson, 1989; Yang, 2014; Yiu and Worrall, 1996). Although the use of pronouns is relevant in Chinese speech production (Simpson et al., 2016), the proportion of this token might be reduced when compared to English and Italian. Similarly, Italian and Chinese speakers produce sentences in which the main verb is omitted, a typical phenomenon in pro-drop languages, described especially in cases of oral production (Marello, 1989). This tendency is common in coordinate or subordinate sentences, in which the verb could be omitted if it was already introduced in the main utterance (Mandelli, 2011). The extreme tendency to drop words is reported in the Chinese group in which also determiners are omitted, without compromising the grammaticality of the sentence or its meaning. This tendency is also consistent in second language acquisition studies, in which Chinese speakers erroneously omit determiners when speaking in English (Robertson, 2000).

Table 4 Linguistic markers with cross-linguistic variabilities across English, Chinese, and Italian languages.

Domain	Features with cross-linguistic variabilities	Data Pattern	SPECULATION		
			ENG	CHI	ITA
Phonological	Broken words*	ENG = ITA > CHI	CV or CCV cluster; multisyllabic	V, CV, CVC cluster; mono or by-syllabic	CV cluster; multisyllabic
	N° empty pauses/tot words	ITA > ENG = CHI	Sentence organization; pragmatic role	Prosody, rhythm, and sentence demarcation related to tone	Sentence organization; morphological complexity; pragmatic role
Lexico-semantic	Prepositions/tot words	ENG > ITA > CHI	Highly represented; high frequency; polysemic and multifunctional	Pro-drop language; different semantic representation of world/space	Different available semantic structures and semantic representation of world/space
	Adverbs/tot words	CHI > ENG = ITA	Specify the meaning of other word class	Carry verbal information (tense, number)	Specify the meaning of other word class
	Conjunctions/tot words	ITA > ENG = CHI	Subordination; coherence and cohesion markers;	Low frequency; not needed for subordination; no cohesion markers	High frequency; subordination; coherence and cohesion markers;
	Determiners/tot words	ENG = ITA > CHI	Mandatory	Pro-drop language	Mandatory

	Pronouns/tot words	ENG = ITA > CHI	Mandatory	Pro-drop language	Pro-drop language
Morpho-syntactic	N° utterances without verb/tot utterances*	ENG > CHI = ITA	Verb elision is not acceptable	Verb can be dropped when it was already presented or was contextually available to speakers	Verb can be dropped when it was already presented in previous coordinate and/or in principal utterances
	Determiner elision*	CHI > ENG = ITA	Not acceptable	Pro-drop language	Not acceptable

Characterization of linguistic markers that are represented across languages in different frequency, or that are unique for one or two languages.
*Unique markers for one or two languages.

We also identified a set of features that reflected the presence of individual heterogeneity in our sample and individual variability within each language. The presence of such features, namely classifier generalization, preposition omission or substitution, and tangential speech, is extremely rare. Heterogeneity might be related to different specific lifetime experiences, such as education level, personality, and individual factors of the included participants. Since the low frequency of such features, we believe their careful assessment might be useful in detecting abnormal performance in neurological patients.

Lastly, our findings showed a set of features consistently distributed across all groups, spanning various linguistic domains. Specifically, in the phonological domain, the proportion of abandoned words, repeated words, and filled pauses showed no significant differences between groups. Similarly, in the lexico-semantic domain, the distribution of nouns, verbs, and adjectives remained consistent across groups. In the morpho-syntactic domain, no significant differences were found in the number of utterances and their length after applying Bonferroni's correction. Likewise, at the discourse level, no characteristics significantly varied across the groups. We propose that these features might serve as universal markers for speech and language impairment, suggesting that their cross-linguistic assessment should focus on neurological patients.

We acknowledge the limitations posed by the small sample size in our study, a common issue in cross-linguistic research due to the need to match participants across various languages. Furthermore, to examine multiple linguistic domains and markers, we incorporated a broad set of features, despite the potential effect on statistical power. Future studies should aim for larger datasets and include more languages, selecting a priori features that have already been identified as significant in the cross-linguistic field. Although the Picnic Scene is regarded as a valid cross-cultural tool among the experts who collaborated in this study, the depiction may be more familiar to speakers of Western cultures (Bose et al., 2022).

To conclude, we identified a set of linguistic markers that are distinctive across the three studied languages. Conversely, we also described a set of shared linguistic features that could potentially be universal speech and language markers to distinguish between cognitively normal individuals and those living with neurological conditions. Taken together, our findings affirm that cross-linguistic differences are discernible even among healthy participants. This highlights the necessity for a cross-linguistic framework that acknowledges the similarities, differences, and unique aspects of each language. Cross-linguistic research is vital for comprehensively understanding language organization and ensuring equitable and tailored assessment of language symptoms.

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Using a picture description task in cross-linguistic studies: insights from Primary Progressive Aphasia

1. Introduction

Primary Progressive Aphasia (PPA) is an umbrella term that encompasses different clinical conditions, or variants, united by a significant and peculiar impairment of language and speech, which selectively characterize the insurgence and the first two years of the disease presentation. According to the current guidelines (Gorno-Tempini et al., 2011), diagnosis of PPA is based on the clinical assessment of speech and language performance, and additional imaging and biomarkers to provide a full description of the patient's profile. Three are the main variants of PPA. The semantic variant (svPPA) is characterized by a loss of semantic knowledge, anomia, and single-word comprehension deficit, associated with left anterior temporal cortex atrophy or hypometabolism. The logopenic variant of PPA (lvPPA) is characterized by anomic production, verbal working memory, and repetition deficits, in association with atrophic or hypometabolic patterns in the left temporo-parietal regions. The non fluent variant of PPA (nfvPPA) is characterized by agrammatic and effortful speech and difficulties in comprehension of syntactically complex sentences, and it is associated with marked atrophy or hypometabolic pattern in the left posterior fronto-insular regions.

PPA is considered a relevant model for studying language brain organization, as well as its vulnerability to aging, genetic risk factors, and therapeutic interventions (Mesulam et al., 2021; Tee and Gorno-Tempini, 2019).

Most of the studies, which characterized deeply the language PPA's profile, enrolled large cohorts of English-speaking patients; accordingly, current diagnostic criteria are mainly based on the English language. However, nowadays, we assist in the global raising of awareness towards linguistic diversity (see also Chapter 1), and therefore to the possible implications that linguistic variation might have on language presentation in neurological patients (Adolfo M García et al., 2023).

Language diversity spans all the different linguistic domains, including phonetic and phonology, lexico-semantic, morpho-syntactic, and discourse organization (Blasi et al., 2022; Evans and Levinson, 2009), namely related to the variation in the way sounds, words, sentences and their meaning are produced and organized (Moravcsik, 2012). Language performance in PPA patients speaking non-English languages has been described in the past few years, including Chinese (Tee, Deleon, et al., 2022), Italian (Catricalà et al., 2020, 2022; Polito et al., 2023), German (Hohlbaum et al., 2018), French (Lavoie et al., 2021; Macoir et al., 2021), and Spanish (Matias-Guiu et al., 2022), however, only one study directly performed cross-linguistic comparisons on PPA population; i.e. Italian vs. English (Canu et al., 2020).

The present work aims to explore similarities and differences in the speech and language production of 3 groups of PPA patients, speaking respectively English, Chinese (Cantonese and Mandarin), and Italian, using a picture description task, enabling to prompt access to similar content (Vandenborre et al., 2018). Picture description is a commonly used task in clinical settings, and it allows one to obtain, in a short amount of time, information on different domains of impairment (Boschi et al., 2017).

The three languages share various levels of similarities and differences, belonging to different language families, i.e., English and Italian to Indo-European, while Chinese to Sino-Tibetan, or different branches of the same family, i.e., Germanic, and Roman for English and Italian, respectively. Such linguistic differences might be extrapolated by the production of patients, showing different areas of impairment. In this study, we aimed to characterize the speech and language profile of patients with PPA across several linguistic domains.

We hypothesized the existence of features equally impaired across languages as well as specifically impaired for each language. Some specific language features may be hypothesized to be identified, for example, a higher number of phonetic and phonological errors in the English sample (Wilson et al., 2010), morphological difficulties in the Italian one (Canu et al., 2020), or tonal abnormalities in the Chinese sample. Language-specific features could enhance the accuracy of the diagnostic process in clinical practice, bringing the attention of clinicians to language-specific aspects that might not be included or specified in the current diagnostic criteria (Gorno-Tempini et al., 2011).

2. *Methods*

2.1 Participants

A total of 129 participants, including PPA patients and healthy controls, was retrospectively enrolled. American English speakers were enrolled at the Memory and Aging Center, University of California, San Francisco; Chinese speakers were recruited from the CLAP project from seven sites in Taiwan and Hong Kong, Italian PPA patients were enrolled at San Raffaele Hospital of Milan and University Vita-Salute San Raffaele, and Italian healthy controls were enrolled through the ICON Lab at the University of Advanced Studies of Pavia.

A total of 90 PPA patients was included in the study, 30 for each language of interest, i.e., English, Chinese, and Italian. In each language group, variants were equally represented, namely, we included 10 svPPA, 10 lvPPA, and 10 nfvPPA. All the clinical diagnoses were made according to current diagnostic guidelines (Gorno-Tempini et al., 2011) by expert neurologists. Different biomarkers were adopted according to the local availability. To be included in the study, PPA patients had completed the oral picture description task from the Western Aphasia Battery (Kertesz, 1982); did not have any other psychiatric or neurological disorder, were native speakers of one of the included languages; and were right-handed. Lastly, PPA patients need to fulfill a literacy requirement, having completed at least three years of school.

A total of 39 healthy participants (HC) was also included, 13 speakers for each language, see also Chapter 1. Inclusion criteria were do not have a significative history of neurological and psychiatric disorders; had completed the oral picture description task from the Western Aphasia Battery (Kertesz, 1982); being right-handed, being a native speaker of one of the included languages, and fulfilled, as PPA, the literacy requirement of three years of school.

2.2 Neuropsychological Assessment

All PPA patients underwent a complete neuropsychological evaluation, assessing verbal and visuo-spatial episodic memory, short-term memory, attentional and executive functions, visuo-constructional abilities, praxis, and language. Different tasks were used across centers for each domain.

2.3. Oral picture description

All participants completed the oral description task of the Picnic Scene from the Western Aphasia Battery (Kertesz, 1982). Performances were audio recorded and stored in compliance with the ethical protocols established at each participating center. The examiners instructed participants to look at the picture and describe it, using sentences. The audio samples were then transcribed in the respective languages, namely English, Chinese, and Italian, and linguistic features of interest (see 2.4) were coded in compliance with Computerized Language ANalysis program (CLAN; see 2.5) instructions. If examiners prompted more than two times the production, the following patient's production was not transcribed. In each language group, two raters independently transcribed and coded the speech samples, followed by a subsequent comparison of the results. For any coding discrepancy, a third rater was consulted, and researchers engaged in discussions for every single case until a consensus was reached.

2.4 Linguistic Features

A total of 37 features were chosen (listed and defined in Table 1), based on existing literature (Boschi et al., 2017; Canu et al., 2020; Mueller et al., 2021; Wilson et al., 2010), as well as authors' linguistic knowledge of the respective language. Features encompass various linguistic domains, including phonetic and phonology, lexico-semantic, morpho-syntactic, and discourse and pragmatics. For each domain, we selected: 1) features that have been previously used to describe the linguistic performance of healthy participants (Mueller et al., 2021); 2) features that characterized the linguistic performance of clinical populations, i.e., stroke aphasia (Boucher et al., 2020; Vandenborre et al., 2018), and primary progressive aphasia patients (Wilson et al., 2010). Thirty-four features were common across the three languages, and only three features, namely the ratio of classifiers over the total number of words, the number of classifier generalizations, and tone errors, were specific to Chinese.

Table 1 Speech and Language included features.

Domains	Features	Definition
Phonetic and Phonological	Number of phonological errors	Words with at least one deletion, insertion, or transposition of phonemes; or 50% modified compounds
	Number of distortions	Insertion of not recognizable sounds
	Number of tone errors§	Mispronunciation of words affecting their meaning
	Number of prolonged sounds	Sounds that are abnormally prolonged
	Number of broken words	Pause within word
	Number of abandoned words/tot words	Changes from one word to another
	Number of empty pauses/tot words	Number of silent (no sound produced) pauses
	Number of filled pauses/ tot words	Number of filled pauses (i.e., uhm, ehm)
Lexico-Semantic	Open class words/total words	Total number of content words (verbs, nouns, adjectives, adverbs)/total number of words
	Close class words/total words	Total number of function words (determiners, classifiers§, pronouns, prepositions…)/total number of words
	Number of semantic errors	Paraphasia, circumlocutions, anomia
	Number of words repetition	Begin to say something, stop, and repeat without changes
Morpho-syntactic	Number of utterances	Utterances require subject and main verb
	Mean length of utterances	Ratio of morphemes to utterances
	Number of utterances without verb/ number of utterances *	Elision (drop) of the main verb
	Number of sentences with broken syntax	Agrammatic utterances/tot utterances
	Number of morphological errors	Errors in conjugation, agreement (gender/number), declination of words
	Determiner elision/substitution	Elision (drop) or substitution of article
	Prepositions elision/substitution	Elision (drop) or substitution of preposition
	Classifier elision§/generalization§	Elision (drop) or generalization of classifier
Discourse and Pragmatic	Total words	Total number of words
	Words/min	Total number of words/minutes

Number of irrelevant words/tot words	Number of words syntactically correct but not convey relevant meaning/ total number of words
Number of tangential words/ tot word	Number of words not related to the task/total number of words
Idea density	Ratio of adverbs, adjectives, adverbs, prepositions, and conjunctions to the total number of words

List of included features and their definition.
** features manually coded.*
§ specific features for the Chinese language.

2.5 Computerized Language ANalysis program

Speech samples were manually transcribed and coded using CLAN. CLAN has been designed to analyze speech data and has been extensively used in studies involving healthy participants, children, and neurological populations. For comprehensive information on CLAN and its applications, please refer to the Aphasia Bank project at https://aphasia.talkbank.org/. CLAN is accessible in multiple languages, encompassing English, Chinese, and Italian, thereby allowing researchers the opportunity to operate within a unified analytical framework. It is essential to acknowledge that definitions and coding procedures may vary with the studied language. For instance, the omission of pronouns is deemed an error in English, rendering agrammatic sentences, whereas in Italian, such omissions are both acceptable and common, thus not considered grammatically inaccurate. Additionally, certain features may be described and coded exclusively in one language, as they are linguistically inapplicable to others; for example, classifier generalization, or tone errors are unique to Chinese. Analysis of speech production was first performed using the CLAN pipeline, which allowed us to automatically derive the features of interest. If the features were not included in the CLAN program, they were manually coded.

2.6 Statistical Analysis

Demographic data, including age, gender, and education level, were compared between healthy controls and PPA within the same language, i.e., English, Chinese, and Italian. Language scores were converted into z scores, based on the whole sample.

Within language comparisons. To assess differences separately for each language, for each feature we compared PPA and HC groups using the Mann-Whitney test. If a comparison was significant, Bonferroni's correction was adopted for post-hoc analysis. To further characterize the linguistic profile of PPA within each language, we performed comparisons between groups, namely svPPA, lvPPA, nfvPPA, and HC, using the Kruskal-Wallis test; results are reported in Supplementary Materials.

Identifying relevant features. We then examined the resulting significant features to investigate which were the most relevant features able to distinguish PPA from controls. In particular, we assessed whether features significantly able to distinguish PPA patients from controls in all languages were sufficient, or whether distinctive language features (those features distinguishing PPA from controls not in all languages) significantly improve the identification of PPA patients. With this aim, we split the features into those shared across languages and those specific to two or one language only.

To this aim, we adopted two steps for each language:

1) A regression model using only shared features as predictors.
2) Hierarchical regression model including in the first step the significant shared features and in the second one the distinctive features.

1) To have the right number of predictors (i.e., n=4) for 43 observations, we first performed a correlation analysis between all shared linguistic features for each language. When a correlation between two variables was > |0.8|, we considered the one with higher R^2, based on the following single regression analyses. We performed a series of single logistic regressions, one for each shared feature, and each language separately, to identify which shared features were most relevant in predicting the diagnosis of PPA compared to HC. The R^2 Cox and Snell values were used to quantify the variance explained by each linguistic feature, selecting the 4 with the higher R^2 (Catricalà et al., 2014). We then performed a final model in terms of logistic regression for each language separately, to identify the accuracy of cross-linguistic features supporting the classification of PPA vs HC.
2) shared features were collapsed into a shared composite measure, which was calculated as the mean score of significant shared features for each language. When features represented an impaired performance (i.e., phonological errors, proportion of empty pauses, and word repetition), we multiply the z scores by -1. We then selected markers that are language-tailored for the distinction of PPA vs HC. In particular, based on the results of the previous comparisons (within language comparison), we selected features (features after mentioned as "specific") that were specifically valid in distinguishing PPA vs HC in each language. We performed a correlation analysis between all specific linguistic features for each language. When a correlation between two variables was > |0.8|, we considered the one with higher R^2 obtained from the following logistic regression analyses. We performed a series of single logistic regressions for each language separately, to identify the ability of each language-specific feature to significantly predict the diagnosis of PPA compared to HC. R^2 Cox and Snell values were used to quantify the variance explained by each linguistic feature. When more than 3 features were significant, we computed

composite scores (average score of significant features) for each linguistic domain (Catricalà et al., 2014). For the final model, a hierarchical logistic regression model was adopted to assess whether the addition to the shared features of language-specific features significantly improves the ability to distinguish PPA from controls. As for each language, 43 observations were available for each language, only 4 features could be included. The first step involved the shared features as derived from the previous analysis, namely the shared composite score. The second step included language-specific features, or if they were more than 3, composite scores for each domain were calculated, as the mean of significant features for phonetic and phonological, lexico-semantic, morpho-syntactic and discourse and pragmatic domain. The increase in fit of the model when adding the second step was assessed in terms of $\Delta\chi^2$ as described in a previous study (Ye, 2006).

3. Results

3.1 Demographic Data

Demographic data are reported in Table 2. Italian PPA and HC did not differ for age, gender, and education (all p>0.339), meanwhile English and Chinese PPA showed lower levels of education than their HC. No differences were found between English and Chinese PPA and HC for age and gender (all p>0.173). All PPA across languages did not differ for age, education, gender, and MMSE (raw score) (all p values>0.143).

Table 2 Demographic data of participants

Whitin' languages

	ENGLISH (n=43)				**CHINESE (n=43)**				**ITALIAN (n=43)**			
	Age	**Education**	**Gender**	**MMSE raw score**	**Age**	**Education**	**Gender**	**MMSE raw score**	**Age**	**Education**	**Gender**	**MMSE raw score**
All PPA	67.6 (7.0)	15.3 (1.7)	16|14	24.83 (4.1)	67.7 (6.4)	12.3 (4.3)	16|14	22.26 (5.4)	68.2 (7.0)	13.23 (4.4)	13|17	24.98 (3.7)
HC	70.5 (3.2)	16.6 (1.50)	4|9		67.53 (5.9)	15.07 (1.6)	4|9		64.9 (8.2)	14.7 (3.0)	5|8	
P value	0.244	0.042	0.173		0.865	0.028	0.173		0.313	0.339	0.766	

Mean and standard deviation, between brackets for each group

Between language

	Age p-value	**Education p-value**	**Gender p-value**	**MMSE raw score p-value**
All PPA	0.434	0.994	0.177	0.143
HC	0.080	0.068	0.749	

3.2 Differences Between PPA And Controls Within Language

English sample

Considering the English sample, comparisons between PPA and HC revealed a set of significant differences, see Table 3.

Phonetic and phonological domain. PPA produced more phonological errors, distortions, a higher proportion of abandoned words, and empty pauses compared to HC.

Lexico-semantic domain. PPA produced a lower proportion of prepositions and more proportion of repeated words than HC.

Morpho-syntactic domain. PPA produced shorter sentences than HC and a higher amount of agrammatic utterances.

Discourse and pragmatic domain. PPA produced fewer words per minute compared to HC.

Table 3 – Quantitative analysis of speech and language production of the English sample

Domains	Features	PPA	HC	P value
		Mean (SD)	mean (SD)	
Phonetic and Phonological	**Phonological errors**	0.933 (1.639)	0.154 (0.555)	**0.033**
	Distortion	1.167 (2.705)	0 (0)	**0.030**
	Prolongation	2.1 (3.22)	2.077 (2.326)	0.428
	Tone errors			
	Broken words/tot words	0.505 (1.479)	0.103 (0.37)	0.430
	Abandoned words/ tot words	1.971 (2.653)	0.306 (0.463)	**0.014**
	Empty pauses/ tot words	0.119 (0.12)	0.306 (0.463)	**0.006**
	Filled pauses/ tot words	0.09 (0.08)	0.041 (0.027)	0.086
Lexico-semantic	Open class/tot words	58.167 (38.245)	66.846 (26.984)	0.234
	Close class/tot word	64.7 (40.701)	69.385 (26.387)	0.348
	Open/closed	1.059 (0.944)	0.959 (0.098)	0.139
	Nouns/tot words	24.422 (12.973)	24.528 (2.098)	0.062
	Verbs/ tot words	20.276 (5.877)	21.789 (6.388)	0.334
	Prepositions/tot words	7.509 (3.279)	10.226 (3.314)	**0.005**
	Adjectives/tot words	2.092 (2.12)	2.548 (1.529)	0.208
	Adverbs/tot words	5.285 (3.567)	5.034 (1.992)	0.947
	Conjunctions/tot words	0.818 (1.111)	0.522 (0.873)	0.405
	Determiners/tot words	17.223 (6.606)	18.152 (3.019)	0.428

	Pro/tot words	10.283 (5.91)	9.386 (3.617)	0.711
	Classifiers/tot words			
	Semantic errors	2.805 (3.169)	0.231 (0.439)	0.237
	Word repetition/tot words	0.6 (0.968)	0.512 (0.718)	**0.008**
Morpho-syntactic	N° utterances tot	19.9 (10.905)	17.077 (6.02)	0.491
	Mean Length of utterance	6.292 (2.229)	8.153 (2.126)	**0.015**
	N° utterances without verb/N° tot utterances	11.4 (22.74)	1.01 (2.52)	0.109
	N° morphological errors	1.2 (1.518)	1.077 (1.038)	0.624
	N° Classifier generalization			
	Determiner omission	0.897 (1.423)	0.385 (0.65)	0.493
	Determiner substitution	0 (0)	0 (0)	0.129
	Preposition omission	0 (0)	0.077 (0.277)	
	Preposition substitution	0.167 (0.379)	0 (0)	0.122
	N° sentences with flawed syntax	11.715 (12.285)	2.793 (5.654)	**0.005**
Discourse and Pragmatic	Total words	123.4 (78.809)	136.846 (52.838)	0.255
	Words/min	102.285 (59.633)	178.031 (76.165)	**0.003**
	N° Irrelevant words/tot words	0.243 (0.275)	0.192 (0.172)	0.853
	N° tangential words/ tot words	0.004 (0.014)	0.02 (0.059)	0.264
	Idea Density	0.404 (0.108)	0.405 (0.068)	0.812

*Different from HC; In bold significant results; In red differences survived Bonferroni's correction; In grey not applicable features

Chinese sample

Considering the Chinese sample, comparisons between PPA and HC, revealed a set of significant differences, see Table 4.

Phonetic and phonological domain. PPA produced more distortions and tone errors compared to HC. Similarly, patients produced a higher proportion of empty and filled pauses compared to HC.

Lexico-semantic domain. PPA produced a lower proportion of open and close class words compared to HC, a lower proportion of adverbs and conjunctions. Finally, they produced a higher proportion of word repetition compared to HC.

Morpho-syntactic domain. PPA patients produced fewer utterances, shorter and generally more agrammatic utterances, or without verbs compared to HC.

Discourse and pragmatic domain. PPA produced fewer words and words per minute compared to HC.

Table 4 - Quantitative analysis of speech and language production of the Chinese sample

Domains	Features	PPA	HC	p-value
		Mean (SD)	Mean (SD)	
Phonetic and Phonological	Phonological errors	1.033 (1.629)	0.154 (0.376)	0.107
	Distortion	1.033 (2.593)	0 (0)	**0.043**
	Prolongation	1.033 (2.414)	0.769 (1.423)	0.988
	Tone errors	2.033 (4.453)	0 (0)	**0.030**
	Broken words/tot words	0.095 (0.522)	0 (0)	0.510
	Abandoned words/ tot words	1.127 (2.434)	0.341 (0.526)	0.732
	Empty pauses/ tot words	6.262 (8.62)	0.709 (1.067)	**0.006**
	Filled pauses/ tot words	5.303 (13.871)	5.558 (4.935)	**0.005**
Lexico-semantic	**Open class/tot words**	44.667 (26.719)	92.077 (33.738)	**<0.001**
	Close class/tot word	29.3 (21.657)	68.077 (35.013)	**<0.001**
	Open/closed	2.206 (2.181)	1.722 (1.324)	0.302
	Nouns/tot words	22.714 (11.723)	22.403 (5.542)	0.588
	Verbs/ tot words	21.746 (7.867)	18.353 (4.458)	0.209
	Prepositions/tot words	2.187 (2.379)	2.154 (2.113)	0.978
	Adjectives/tot words	2.027 (2.132)	3.33 (1.777)	**0.034**
	Adverbs/tot words	10.337 (6.336)	9.836 (3.296)	0.853
	Conjunctions/tot words	0.805 (1.628)	2.312 (2.447)	**0.007**
	Determiners/tot words	2.454 (2.527)	1.49 (1.229)	0.424
	Pronouns/tot words	4.852 (4.768)	4.394 (2.99)	0.770
	Classifiers/tot words	8.463 (4.701)	9.448 (3.703)	0.242
	Semantic errors	0.067 (0.254)	0.077 (0.277)	0.905
	Word repetition/tot words	4.505 (4.91)	1.125 (0.893)	**0.024**
Morpho-syntactic	**N° utterances tot**	13.233 (7.238)	16.462 (3.526)	**0.020**
	Mean length of utterance	5.83 (2.104)	9.847 (2.745)	**<0.001**
	N° utterances without verb/N° tot utterances	7.402 (15.332)	0 (0)	**0.020**
	N° morphological errors	0 (0)	0 (0)	\
	N° Classifier generalization	0.133 (0.346)	0.231 (0.832)	0.669
	Determiner omission	0 (0)	0 (0)	\
	Determiner substitution	0 (0)	0 (0)	\
	Preposition omission	0 (0)	0 (0)	\
	Preposition substitution	0.033 (0.183)	0 (0)	0.510
	N° sentences with broken syntax	1.867 (2.3)	0.077 (0.277)	**0.003**

Discourse and Pragmatic	**Total words**	74.867 (46.438)	164.154 (63.922)	**<0.001**
	words/min	90.925 (56.961)	125.543 (38.249)	**<0.001**
	N° Irrelevant words/tot words	6.06 (8.172)	1.867 (3.913)	0.108
	N° tangential words/ tot words	0 (0)	0 (0)	\
	Idea Density	0.372 (0.098)	0.363 (0.68)	0.531

*Different from HC; In bold significant results; In red differences survived Bonferroni's correction.

Italian sample

Considering the Italian sample comparisons between each PPA variant and HC, revealed a set of significant differences, see Table 5.

Phonetic and phonological domain. PPA patients produced more phonological errors and sound prolongation than HC. They also produced a higher proportion of empty and filled paused and abandoned words compared to HC.

Lexico-semantic domain. PPA variants produced a lower proportion of nouns and prepositions than HC. However, they produced a higher proportion of adverbs, pronouns, and word repetition than HC. PPA patients also produced more semantic errors than HC.

Morpho-syntactic domain. PPA patients produced shorter utterances than HC and more utterances without verbs than HC.

Discourse and pragmatic domain. PPA produced fewer words per minute compared to HC, and higher idea density than HC.

Table 5 - Quantitative analysis of speech and language production of the Italian sample

Domains	features	PPA	HC	p-value
		Mean (SD)	Mean (SD)	
Phonetic and Phonological	**Phonological errors**	1.467 (1.592)	0.077 (0.277)	**0.001**
	Distortions	0.033 (0.183)	0 (0)	0.510
	Prolongations	6.467 (7.147)	1.308 (1.494)	**0.011**
	Tone errors			
	Broken words/tot words	0.974 (4.075)	0.033 (0.119)	0.185
	Abandoned words/	1.749 (1.798)	0.261 (0.452)	**0.001**
	Empty pauses/ tot words	12.994 (14.672)	1.982 (1.419)	**<0.001**
	Filled pauses/ tot words	0.086 (0.077)	0.018 (0.013)	**<0.001**
Lexico-semantic	Open class/tot words	84.267 (49.782)	101.308 (26.241)	0.070

	Close class/tot word	87.3 (50.601)	96.385 (22.522)	0.104
	Open/closed	0.997 (0.249)	1.046 (0.118)	0.296
	Nouns/tot words	18.612 (5.473)	24.72 (2.633)	**0.001**
	Verbs/ tot words	19.514 (4.233)	18.431 (2.359)	0.135
	Preposition/tot words	4.713 (2.371)	6.906 (1.804)	**0.011**
	Adjective/tot words	1.563 (1.847)	1.876 (1.544)	0.345
	Adverb/tot words	9.425 (5.62)	5.929 (2.351)	**0.023**
	Conjunction/tot words	5.182 (2.887)	5.118 (2.164)	0.916
	Determiner/tot words	19.598 (8.692)	17.563 (1.478)	0.492
	Pronoun/tot words	15.49 (5.461)	11.042 (2.504)	**0.003**
	Classifiers/tot words			
	Semantic errors	1.967 (1.712)	0.692 (1.182)	**0.013**
	Word repetition/tot words	4.94 (4.003)	0.976 (0.873)	**<0.001**
Morpho-syntactic	N° utterances tot	26.467 (12.057)	21.538 (4.612)	0.334
	Mean length of utterance	6.402 (2.301)	9.308 (2.126)	**0.001**
	N° utterances without verb/ n° tot utterances	7.029 (17.966)	0 (0)	**0.029**
	Morphological errors	0.866 (1.33)	0.615 (0.869)	0.748
	Classifier generalizations			
	Determiner omission	0.4 (0.968)	0.385 (0.87)	0.867
	Determiner substitution	0 (0)	0 (0)	\
	Preposition omission	0 (0)	0 (0)	\
	Preposition substitution	0 (0)	0.077 (0.277)	\
	Number of sentences with flawed syntax	2.633 (4.476)	0.769 (0.927)	0.319
Discourse and Pragmatic	Total words	172 (99.364)	197.846 (47.956)	0.072
	Words/min	75.9 (35.874)	116.898 (19.157)	**0.001**
	N° Irrelevant words/tot words	23.972 (23.09)	16.909 (11.989)	0.354
	N° Tangential words/ tot words	3.232 (9.333)	0 (0)	0.138
	Idea density	0.447 (0.093)	0.407 (0.043)	**0.024**

*Different from HC; In bold significant results; In red differences survived Bonferroni's correction; In grey not applicable features

3.3 Selection of Shared and Specific Features

Shared features. Based on previous comparisons, we identified 4 shared features, which were able to distinguish PPA from HC in all three languages, namely:

1) proportion of empty pauses
2) proportion of word repetition on total words,
3) mean length of utterances,
4) words per minute.

English-Italian specific features. Three specific features differentiated both English and Italian PPA from HC, including the number of phonological errors, the proportion of abandoned words, and prepositions.

Chinese-Italian specific features. Two features differentiated both Chinese and Italian PPA from the respective controls including the proportion of filled pauses, and sentences without verbs.

English Chinese specific features. Two features differentiated both English and Chinese PPA from HC, namely the number of distortions and sentences with flawed syntax.

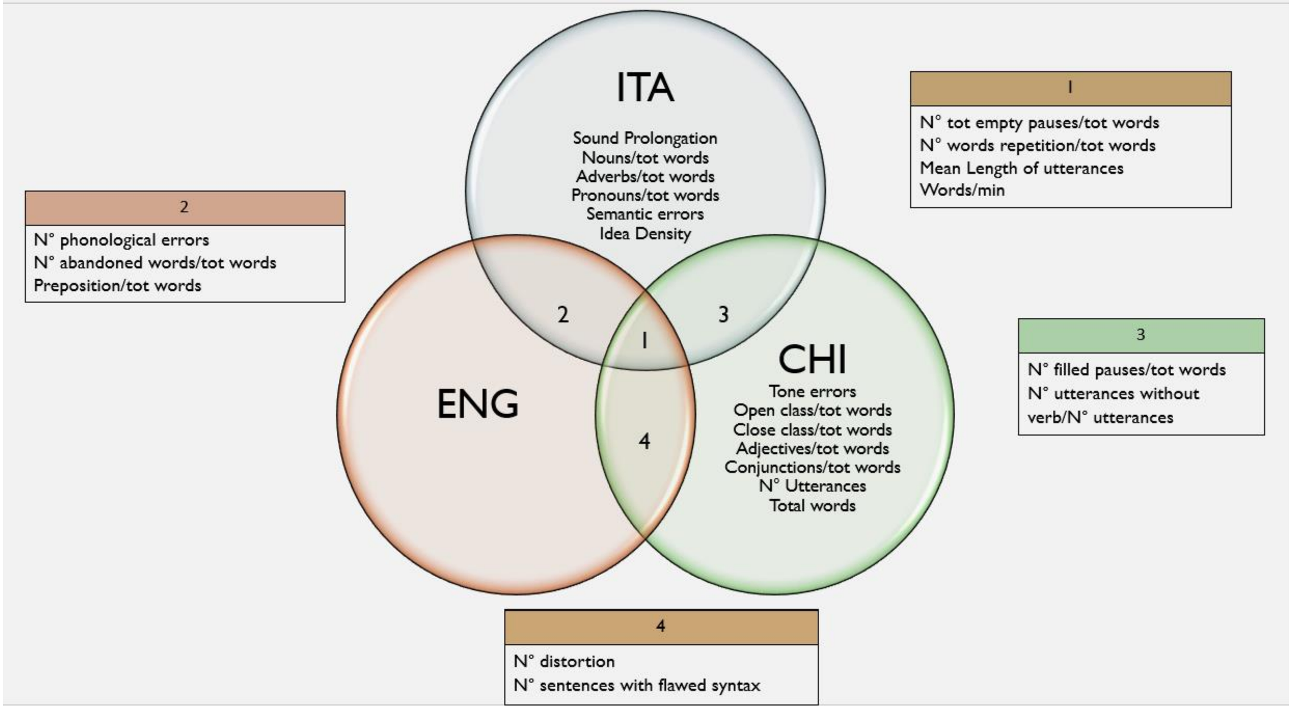
English specific features. No specific features resulted significant in any comparison.

Chinese specific features. Seven features were able to differentiate only Chinese PPA from controls, namely tone errors, open and closed class ratio, the proportion of adjectives and conjunctions, the number of utterances, and the total number of words.

Italian specific features. Six features were able to differentiate Italian PPA only, namely, the number of sound prolongations, the proportion of nouns, adverbs, and pronouns, the number of semantic errors, and idea density.

See Figure 1.

Figure 1 Shared and specific features for English, Chinese, and Italian



3.4 Identifying Relevant Features

English

In the English sample, we did not find shared features with a correlation higher than |0.8|. Out of the 4 shared features, all 4 features resulted significant predictors in distinguishing PPA patients from controls in single regression analyses, namely the proportion of empty pauses (R^2=0.193, p=0.041), of words repetition (R^2=0.204, p=0.036), the mean length of utterances (R^2=0.134, p=0.025) and the number of words per minute (R^2=0.2018, p=0.009). The final shared model then included the proportion of empty pauses, word repetition, the mean length of utterances, and the number of words per minute as possible predictors, and the group membership (HC vs PPA) as the dependent variable. Education was entered as a further possible predictor, as the two groups were not matched, however, it was not significant (p>0.05). The model was significant (χ^2 (3)=21.20, p<0.001), when compared to the null model, and correctly predicted 79.1% of cases (specificity: 0.86; sensitivity: 0.61).

We then collapsed the four significant shared features into one composite measure, the English shared-features component, namely we calculated the mean of the z scores of the proportion of empty pauses, of the word repetitions, the mean length of utterances, and the words per minute. When features represented an impaired performance (i.e., the proportion of empty pauses and word repetition), we multiply the z scores by -1. While considering specific features, five were specific to the English language, namely 3 shared only with Italian (phonological errors, proportion of abandoned words and prepositions) and 2 only with Chinese (number of distortions and sentences with flawed syntax). No specific feature had a correlation higher than |0.8|. Single logistic regressions showed that the proportion of prepositions (R^2=0.143, p=0.027) and the number of sentences with flawed syntax (R^2=0.179, p=0.026) significantly distinguished PPA from HC. See Table 6 for details. In the final model, we included in the first step the English shared component and in the second one the 2 significant specific features (the proportion of prepositions, and the number of sentences with flawed syntax). After entering both shared and specific features, the model was significant overall (χ^2 (3)=23.99, p<0.001), and reported an accuracy of 81.4% (specificity: 0.86, sensitivity: 0.69). However, the model did not demonstrate a significantly better fit when compared with the shared model only ($\Delta\chi^2$ = 2.79, df=2, p=0.25).

Chinese

In the Chinese sample, we found that no shared features had a correlation higher than |0.8|. Out of the 4 shared features, only the mean length of utterances (R^2=0.419, p=0.004) and words per minute (R^2 =0.316, p=0.003) significantly distinguished PPA from HC. The final shared model then included words per minute and the mean length of utterances as possible predictors, and the group membership (HC vs PPA) as the dependent variable. Education was entered as a further possible predictor as the two groups were not matched, however it was not significant (p>0.05). The model was significant (χ^2(1)=25.61, p<0.001), when compared to the null model, and correctly predicted 86% (specificity: 0.93, sensitivity: 0.69).

While considering unique features, eleven were specific to the Chinese language, namely 2 shared only with Italian (proportion of filled pauses, and sentences without verbs), 2 only with English (number of distortions and sentences with flawed syntax), and 7 presented only in Chinese (tone errors, open and close class ratio, the proportion of adjectives and conjunctions, the number of utterances and the total number of words). Between specific-language features, we identified three couples of features that had a correlation higher than |0.8|, namely open and close class words (r=0.806, p<0.001), total words, and open class (r=0.959, p<0.001), total words and closed class (r=0.940, p<0.001). Single logistic regression on specific features showed that the proportion of open class (R^2=0.336; p=0.002), closed class (R^2=0.303; p=0.006), conjunction (R^2=0.108; p=0.036), and total words (R^2=0.108; p=0.036) significantly distinguished PPA from HC. To avoid collinearity, we included the number of total words (and not the proportion of open and closed class words) since it showed a higher R^2. In the final model, we included in the first step the Chinese shared feature, the mean length of utterances and words per minute, and in the second one the 2 significant specific features (the proportion of conjunctions, and the number of total words). Words per minute were then excluded since it has a high level of collinearity with total words (tolerance limit <0.001, r=1.00). After entering shared (mean length of utterances) and specific features, the model was significantly overall (χ^2 (3)=27.26, p<0.001), reporting an accuracy of 88.4% (specificity: 0.93, sensitivity: 0.77) in distinguishing groups. However, it did not demonstrate a significantly better fit than the shared model only ($\Delta\chi^2$ = 1.65, df=2, p=0.56).

Italian

In the Italian sample, we found that no shared features had a correlation higher than |0.8|. Out of the 4 shared features, all 4 features resulted significant predictors in distinguishing all PPA patients from controls in single regression analyses, namely the proportion of empty pauses (R^2=0.448; p=0.004). words repetition (R^2=0.373; p=0.008), mean length of utterances (R^2=0.263; p=0.003) and words per minute (R^2=0.265; p=0.003). The final shared model then included the proportion of empty pauses, word repetition, the mean length of utterances, and the number of words per minute as possible predictors, and the group membership (HC vs PPA) as the dependent variable. The model was significant (χ^2 (4)=33.94, p<0.001), when compared to the null model, and correctly predicted 88.4% of cases (specificity: 0.90, sensitivity: 0.84).

We then collapsed the four significant features into one composite measure, the Italian shared-features component, namely we calculated the z scores mean of the proportion of empty pauses, word repetitions, the mean length of utterances, and words per minute. When features represented an impaired performance (i.e., the proportion of empty pauses and word repetition), we multiply the z scores by -1. While considering unique features, eleven were specific features for the Italian language, namely the 3 shared only with English (phonological errors, proportion of abandoned words and prepositions), 2 shared only with Chinese (proportion of filled pauses, and number of utterances without verb), and 6 presented only in Italian (number of sound prolongation, proportion of nouns, adverbs, pronouns, number of semantic errors and idea density). Between specific-language features, we identified one couple of features that had a correlation higher than |0.8|, namely nouns and idea density (r=-0.809, p<0.001). Single logistic regression showed that the number of phonological errors (R^2=0.286, p=0.033), the proportion of abandoned words (R^2=0.252, p=0.021), sound prolongation (R^2=0.214, p=0.025), filled pauses (R^2=0.396, p=0.007), nouns (R^2=0.260, p=0.003), prepositions R^2=0.185, p=0.012), adverbs (R^2=0.109, p=0.048), pronouns (p=0.017), and semantic errors (R^2=0.144, p=0.030) were significantly able to distinguish PPA from HC. See Table 6 for details. Due to the high number of significant features, we combined the specific language features into phonetic and phonological scores and lexico-semantic scores. The phonetic and phonological composite score was calculated from the mean score of the number of phonological errors, sound prolongation, abandoned words, and proportion of filled pauses. The lexico-semantic component was calculated from the mean score of the proportion of nouns, prepositions, pronouns, adverbs, and semantic errors. In the final model, we included in the first step the Italian shared component and in the second one the 2 composite measures. After entering shared and specific features, the model was significantly overall (χ^2 (3)=47.75, p<0.001), and reported an accuracy of 95% (specificity: 0.96, sensitivity: 0.92) in distinguishing groups. The model was significantly better than the shared model only ($\Delta\chi^2$ = 13.81, df=2, p0.001).

Table 6 Single logistic regression models for shared and specific features

		ENG		CHI		ITA	
Domains	**Features**	**R^2 Cox & Snell**	**p**	**R^2 Cox & Snell**	**P**	**R^2 Cox & Snell**	**p**
Phonetic and Phonological	Phonological errors	0.099	0.150			**0.286**	**0.033**
	Distortions	0.159	0.997	0.141	0.997		
	Prolongations					**0.214**	**0.025**
	Tone errors			0.159	0.997		
	Broken words/tot words						
	Abandoned words/tot words	0.189	0.053			0.252	0.021
	Empty pauses/ tot words	**0.193**	**0.041**	0.222	0.058	**0.448**	**0.004**
	Filled pauses/ tot words			1.022	0.948	0.396	0.007
Lexico-semantic	Open class/tot words			**0.336**	**0.002**		
	Closed class/tot word			**0.303**	**0.006**		
	Open/closed						
	Nouns/tot words					**0.260**	**0.003**
	Verbs/ tot words						
	Preposition/tot words	**0.143**	**0.027**			**0.185**	**0.012**
	Adjective/tot words			0.079	0.067		
	Adverb/tot words					**0.109**	**0.048**
	Conjunction/tot words			**0.108**	**0.036**		
	Determiner/tot words						
	pronoun/tot words					**0.169**	**0.017**
	Classifiers/tot words						
	Semantic errors					**0.144**	**0.03**
	Word repetition/tot words	**0.204**	**0.036**	0.181	0.059	**0.373**	**0.008**
Morpho-syntactic	N° utterances tot			0.051	0.144		
	Mean length of utterance	**0.134**	**0.025**	0.419	0.004	**0.263**	**0.003**
	N° of utterances without verb/ number of tot utterances			0.178	0.997	0.159	0.996
	Morphological errors						
	Classifier generalizations						
	Determiner omission						
	Determiner substitution						
	Preposition omission						
	Preposition substitution						
	N° sentences with flawed syntax	**0.179**	**0.026**	0.252	0.081		
Disc	Total words			**0.361**	**0.012**		

Words/min	**0.218**	**0.009**	**0.361**	**0.003**	**0.265**	**0.003**
N° irrelevant words/tot words						
N° tangential words/ tot words						
Idea density					0.046	0.169

In bold significant results included in the models; in grey non applicable features to the language; in red shared features across English, Chinese, and Italian.

4. *Discussion*

This work aimed to develop a relevant language-tailored approach to neurodegenerative patients' characterization. To the best of our knowledge, it is the first attempt to compare the speech and language profiles of PPA patients belonging to three different language groups, namely English, Chinese, and Italian. The inclusion of three healthy control groups, matched with their respective PPA cases, permitted the detection of connected speech differences across English, Chinese, and Italian PPA.

We identified markers that are cross-linguistically shared for English, Chinese, and Italian, in distinguishing PPA patients from controls, and only in the case of Italian also valid language-specific features for ameliorating the distinction between PPA and HC.

Differences between PPA and controls within each language. In all three languages, several features were significantly relevant in distinguishing PPA from controls. Looking at differences within each language, we noted that different linguistic domains might play a different role in differentiating PPA from HC. The phonetic and phonological features were the most represented in distinguishing PPA from controls in all three languages (57% for English, 50% for Chinese, and 71% for Italian). In the lexico-semantic domain, Italian PPA were characterized by the largest number of variables (46%), followed by Chinese (35%), and lastly by English (15%). In the morpho-syntactic domain, Chinese showed a higher number of features (40%), followed by English (22%) and Italian (22%). Lastly, in the discourse and pragmatic domain, differences across the three languages were less marked, with Chinese and Italian being characterized by the largest number of variables (40%), followed by English (20%).

Differences across languages were also present according to the different types of features within each domain.

Shared features significantly relevant in distinguishing PPA from controls across all three languages, namely empty pauses for the phonetic-phonological domain, the proportion of word repetition for the lexico-semantic domain, the production of shorter utterances for the syntactic domain, the ratio of words per minute for the discourse and pragmatic domain, may be related to a general aphasic presentation common to the three PPA variants, as they can be differently ascribed to word retrieval, or working memory, or syntactic, or fluency impairment (Ash et al., 2013; Matias-Guiu et al., 2022; Wilson et al., 2010).

At the phonetic and phonological domain, some features were shared only across some languages, but not all, reflecting the level of phonological complexity of each language, as suggested in previous studies (Canu et al., 2020). In addition, specific features represent peculiarities of a specific language, as in the case of tonal languages, such as Chinese. Accordingly, the number of abandoned words and the number of phonological errors were significant for both English (Dalton et al., 2018; Henry et al., 2016) and Italian (Catricalà et al., 2022), but not for Chinese, possibly reflecting the different syllabic structure of the first two languages, that generally implies multisyllabic words, while Chinese relies on monosyllabic ones. Distortions were instead significant only for English (Haley et al., 2021) and Chinese (Tee, Deleon, et al., 2022), and not for Italian, possibly due to the simple phonological structure of the Italian language, and lack of complex articulatory accommodations needed in tonal languages. Only in the Italian group was sound prolongation significant, possibly related to the phonotactic and syllabic structure (consonant-vowel) of Italian, which facilitates the prolongation not only of the last vowel but also others (Schettino and Cataldo, 2006). Language-specific features were identified for the Chinese in terms of the number of tone errors (Tee, Deleon, et al., 2022).

In the lexico-semantic domain, both English and Italian PPA presented a significant reduction in the proportion of prepositions, which was significantly different across PPA and HC. This result confirms the finding on healthy subjects (see Chapter 1), suggesting that the tendency of healthy Chinese speakers to produce a lower proportion of prepositions makes this feature less reliable in identifying impaired performances. In the Chinese group, we observed a generally reduced production of both open and closed-class words, with a particular impairment in adjectives and conjunctions. In the Chinese language, adjectives can be used to form compounds, in combination with nouns and verbs, becoming then more syntactically complex to be produced, especially in case of language impairment (Ma et al., 2021). In the Italian group, the PPA profile was characterized by a reduced production of nouns, and an increase of pronouns, adverbs, and semantic errors. This might be an attempt to compensate for the lexico-semantic deficit, using words that do not require morphological inflection (i.e., adverbs) or adopting a simple form of generally inflected tokens (i.e., first-person pronoun).

Summarizing, the comparison between PPA patients and their respective healthy controls suggests the existence of a partial overlap in terms of features, suggesting that both common and language-specific features may be important for the best characterization of the PPA profile in each language.

Identifying relevant features in distinguishing PPA from controls. We identified, independently for each language, 4 shared features able to distinguish PPA from controls in all three languages. They included the 4 different domains, namely, phonetic and phonological with the proportion of empty pauses, the lexico-semantic domain with the proportion of word repetition, the morpho-syntactic domain with the mean length of utterances, and the discourse and pragmatic domain with the ratio of words per minute. For all languages, regression models reached a significant accuracy in discriminating PPA from controls. The English shared model reached an accuracy of 79.1%, the Chinese of 86%, and the Italian of 88.4%. Interestingly, the majority of these features, such as pausing, repetitions, and reduced production in terms of words and sentences, are considered general markers of dysfluency and a clear hallmark of impaired speech production in neurodegenerative patients (Coppieters et al., 2024; García et al., 2022). Different studies also confirmed the relevance of morpho-syntactic impairment in the discrimination of pathological performance and generally reduced syntactic complexity was described in PPA cases (Cupit et al., 2017; Lukic et al., 2024). These markers also reflect the typical presentation of PPA variants as originally described by Mesulam (Mesulam, 2001) and as reported in the current diagnostic criteria (Gorno-Tempini et al., 2011), namely lexical retrieval deficit, effortful, slow, reduced, and simplified production. We can hypothesize that the impairment in such features may generally mirror the idea of a common language network across different languages, as supported by imaging studies (Malik-Moraleda et al., 2022).

However, supporting the relevance of language diversity assessment, we tried to identify a set of language-specific features able to characterize PPA patients for each language and to significantly increase the accuracy in distinguishing PPA patients from healthy controls. Despite an increase in the variance explained, specific English and Chinese features did not determine a significant increase in the distinction between PPA and healthy controls, while this was the case only for the Italian group. Language-specific features significantly increased the accuracy from 79.1% to 81.4% for the English group, from 86% to 88.4% for the Chinese group, and from 88.4% to 95% for the Italian group.

Very interestingly, the sensitivity in discriminating PPA is quite different between languages, with Italian having the highest (96%) and English and Chinese a lower one (69% and 79%, respectively).

According to the fact that diagnostic criteria were English language based, it is possible that all the relevant features were already present, and some of these are shared with other languages, as in all the other countries PPA diagnosis is based on the same criteria. However, this is not in line with the low sensitivity of the model, namely reflecting the difficulty of identifying nearly 30% of PPA. We can also note that probably other classical tests are necessary to detect all the English PPA, namely articulatory, and morpho-syntactic tasks.

Different is the case of research on Chinese speech and language characterization, which is still very scarce. It is possible that for a mere identification of PPA form controls, independently from the specific variant, common features are sufficient. In future studies in which specific variants will be the focus of the characterization, it will be possible to include and characterize further language-specific features, as recently proposed in Mandarin and Cantonese (Tee, Lorinda Kwan-Chen, et al., 2022).

Lastly, in the Italian group, language-specific features significantly increased the accuracy of the diagnostic process, with a remarkably high sensitivity. Specific features reflect mainly phonological and lexico-retrieval deficits. In particular, phonological errors reflect the general paucity of phonological errors in healthy speakers, who take advantage of the relative regularity of the syllabic structure of the Italian language (Paoli, 2016). Also, it is important to note that in Italian articulatory difficulties are less frequent than in English (Canu et al., 2020), reducing the possibility of a confounding score. The lexico-semantic domain is also particularly relevant in the characterization of the PPA profile; possibly this pattern reflects the over-reliance of the Italian language on inflectional morphology; therefore extended lexico-semantic deficit reflects the strong vulnerability of open and closed class words, which are inflected for gender, number, and tense, to abnormalities (Volterra and Bates, 1989). This hypothesis should be verified, including languages with similar or higher requests in terms of morphology, i.e., Spanish and German.

Finally, it is important to note that further detailed features should be included for the English and Chinese groups. For example, the assessment of connectives might require further investigation, considering their impact on non-English languages (Matias-Guiu et al., 2022).

We acknowledge that these results support the need for an extended language assessment, which might be time-consuming for clinicians; however, we believe that specific features and error patterns may better characterize eventual peculiarities in different languages.

4.1 Conclusions

Our study showed the importance of cross-linguistic comparison for several aspects. Shared features across languages sustain the consistency of Primary Progressive Aphasia presentation across different linguistic groups, despite differences in terms of accuracy and sensitivity. Moreover, the addition of specific features supported a better characterization and higher accuracy only for the

Italian PPA, suggesting the need to identify further language-specific markers to improve the detection of English and Chinese PPA patients. It is also possible that classical language tests are optimal for identifying PPA patients, while more specific language features will be necessary for the discrimination of the three PPA variants. Notably, the assessment of connected speech demonstrated to be a remarkable tool to support variant diagnostic processes across languages (Matias-Guiu et al., 2022; Wilson et al., 2010).

We recognize some limitations in the presented work, mainly related to its small sample size. It is extremely important to develop tools that allow an automatic transcription and coding of speech and language production; progress has been made in recent years (Adolfo M. García et al., 2023), however great input should be provided to include different languages and specifically code for abnormality markers (i.e., distortions, tone errors, repetition, pauses). In this way, speech and language assessment could become an equitable marker for neurodegeneration across communities and groups.

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6. *Supplementary Materials*

For each language, we assessed the difference between each group, namely svPPA, lvPPA, nfvPPA, and HC using the Kruskal-Wallis test, for each speech and language feature.

Table 1 – Quantitative analysis of speech and language production of the English sample

Domains	features	svPPA	lvPPA	nfvPPA	HC	p-value
		mean (SD)	**mean (SD)**	**mean (SD)**	**mean (SD)**	
Phonetic and Phonological	Phonological errors	0.1 (0.316)	0.7 (0.675)*[a]	2 (2.449)*[a]	0.154 (0.555)	**0.006**
	Distortions	0.1 (0.316)	0 (0)	3.4 (3.893)*[ab]	0 (0)	**<0.001**
	Prolongations	0 (0)*	3 (2.449)[a]	3.3 (4.473)[a]	2.077 (2.326)	**0.001**
	Tone errors					
	Broken words/tot words	0.058 (0.183)	0 (0)	1.458 (2.346)[b]	0.103 (0.37)	**0.04**
	Abandoned words/ tot words	0.957 (1.282)	2.096 (2.455)*	2.859 (3.602)	0.306 (0.463)	**0.048**
	Empty pauses/ tot words	0.957 (1.282)	2.096 (2.455)*	2.859 (3.602)*	0.306 (0.463)	**0.012**
	Filled pauses/ tot words	0.061 (0.066)	0.116 (0.087)	0.093 (0.083)	0.041 (0.027)	0.081
Lexico-semantic	Open class/tot words	57.4 (29.636)	63.4 (49.717)	53.7 (36.191)	66.846 (26.984)	0.63
	Closed class/tot word	64.6 (30.87)	72.2 (50.435)	57.3 (41.446)	69.385 (26.387)	0.63
	Open/closed	0.875 (0.116)	0.85 (0.154)	1.453 (1.604)	0.959 (0.098)	0.09
	Nouns/tot words	20.905 (6.398)*[c]	20.174 (5.39)*[c]	32.187 (19.275)	24.528 (2.098)	**0.002**
	Verbs/ tot words	21.633 (5.388)	21.283 (4.409)	17.912 (7.31)	21.789 (6.388)	0.25
	Preposition/tot words	6.933 (2.938)*	7.172 (3.738)*	8.422 (3.258)	10.226 (3.314)	**0.014**
	Adjective/tot words	1.81 (1.574)	3.241 (2.871)	1.225 (1.173)	2.548 (1.529)	0.17
	Adverb/tot words	6.425 (3.241)	5.453 (4.068)	3.976 (3.251)	5.034 (1.992)	0.2
	Conjunction/tot words	0.905 (1.085)	0.869 (0.972)	0.68 (1.349)	0.522 (0.873)	0.49
	Determiner/tot words	15.559 (7.411)	15.626 (6.339)	20.485 (5.27)	18.152 (3.019)	0.1
	Pronoun/tot words	13.401 (3.877)*	11.371 (6.686)	6.078 (4.588)*[ab]	9.386 (3.617)	**0.006**
	Classifiers/tot words					
	Semantic errors	0.8 (1.033)	0.7 (1.252)	0.3 (0.483)	0.231 (0.439)	0.43
	Word repetition/tot words	2.072 (2.494)*	3.913 (2.934)*	2.429 (3.927)	0.512 (0.718)	**0.012**
Morpho-syntactic	N° of utterances tot	16.9 (5.953)	23.4 (11.721)	19.4 (13.656)	17.077 (6.02)	0.55
	Mean length of utterance	7.291 (2.457)	5.57 (1.893)*	6.016 (2.148)*	8.153 (2.126)	**0.013**
	N° of utterances without verb/ number of tot utterances	7.12 (13.24)	3.93 (4.52)	23.09 (35.12)*	1.01 (2.52)	**0.037**
	number of Morphological errors	1.1 (1.101)	1.2 (2.201)	1.3 (1.16)	1.077 (1.038)	0.309
	Classifier generalizations					
	Determiner omission	0.6 (1.075)	0.7 (1.059)	1 (1.491)	0.385 (0.65)	0.840
	Determiner substitution	0 (0)	0 (0)	0 (0)	0 (0)	\
	Preposition omission	0 (0)	0 (0)	0 (0)	0.077 (0.277)	0.510
	Preposition substitution	0.3 (0.483)	0.1 (0.316)	0.1 (0.316)	0 (0)	0.170
	N° sentences with flawed syntax	9.704 (15.457)	10.866 (8.737)*	14.574 (12.517)*	2.793 (5.654)	**0.019**
Discourse and Pragmatic	Total words	122.6 (59.889)	136.7 (99.741)	110.9 (78.146)	136.846 (52.838)	0.660
	Words/min	134.208 (72.447)	103.803 (52.749)*	68.845 (32.406)*	178.031 (76.165)	**0.002**
	N° irrelevant words/tot words	0.344 (0.263)	0.317 (0.347)	0.079 (0.079)	0.192 (0.172)	0.059

	N° tangential words/ tot words	0.006 (0.019)	0.005 (0.016)	0 (0)	0.02 (0.059)	0.65
	Idea density	0.43 (0.105)	0.422 (0.065)	0.361 (0.138)	0.405 (0.068)	0.14

*Different from HC; [a]Different from svPPA; [b]Different from lvPPA; [c]Different from nfvPPA; In bold significant results; In red differences survived Bonferroni's correction; In grey not applicable feature.

Table 2 - Quantitative analysis of speech and language production of the Chinese sample

Domains	Features	svPPA	lvPPA	nfvPPA	HC	p-value
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Phonetic and Phonological	Phonological errors	0 (0)	0.7 (1.252)[a]	2.4 (1.897)*[a]	0.154 (0.376)	**0.001**
	Distortion	0 (0)	1.5 (2.838)*	1.6 (3.438)*a	0 (0)	**0.012**
	Prolongation	0.2 (0.422)	0.5 (0.85)	2.4 (3.836)	0.769 (1.423)	0.174
	Tone errors	0 (0)	0.5 (1.581)	5.6 (6.328)*[ab]	0 (0)	**<0.001**
	Broken words/tot words	0 (0)	0 (0)	0.1 (0.316)	0 (0)	0.348
	Abandoned words/ tot words	0.2 (0.632)	0.7 (0.823)	0.8 (1.229)	0.538 (0.776)	0.273
	Empty pauses/ tot words	2.925 (4.172)	6.365 (7.238)*	9.494 (12.068)*	0.709 (1.067)	**0.028**
	Filled pauses/ tot words	2.742 (5.291)*	1.947 (2.964)*	11.22 (22.901)	5.558 (4.935)	**0.043**
Lexico-semantic	Open class/tot words	36.5 (15.357)*	50.5 (36.882)*	47 (24.212)*	92.077 (33.738)	**0.001**
	Closed class/tot word	34.5 (14.269)	32.6 (31.106)*	20.8 (14.756)*	68.077 (35.013)	**<0.001**
	Open/closed	1.124 (0.361)[bc]	1.955 (0.882)	3.541 (3.327)*	1.722 (1.324)	**0.001**
	Nouns/tot words	16.557 (6.616)*[c]	20.113 (7.888)[c]	31.473 (14.21)	22.403 (5.542)	**0.006**
	Verbs/ tot words	18.398 (6.487)	21.031 (5.598)	25.809 (9.728)	18.353 (4.458)	0.152
	Prepositions/tot words	2.565 (2.94)	3.09 (2.167)	0.908 (1.42)	2.154 (2.113)	0.136
	Adjectives/tot words	2.1 (2.099)	2.125 (2.264)	1.856 (2.251)	3.33 (1.777)	0.198
	Adverbs/tot words	9.296 (3.572)	13.261 (8.207)	8.454 (5.883)	9.836 (3.296)	0.424
	Conjunctions/tot words	0.81 (1.733)	0.721 (1.315)	0.884 (1.948)	2.312 (2.447)	0.056
	Determiners/tot words	2.747 (2.812)	3.841 (2.38)*	0.773 (1.279)[ab]	1.49 (1.229)	**0.012**
	Pronouns/tot words	5.772 (4.324)	6.894 (5.84)	1.891 (2.264)ab	4.394 (2.99)	0.060
	Classifiers/tot words	11.095 (4.649)	7.209 (3.808)	7.085 (4.852)	9.448 (3.703)	0.162
	Semantic errors	0.1 (0.316)	0 (0)	0.1 (0.316)	0.077 (0.277)	0.797
	Word repetition/tot words	6.01 (5.255)*	5.095 (5.957)	2.41 (2.606)	1.125 (0.893)	**0.050**
Morpho-syntactic	N° utterances tot	9.9 (3.479)*	13.5 (8.276)	16.3 (8.084)	16.462 (3.526)	**0.016**
	Mean length of utterance	7.264 (1.877)*	5.818 (1.526)*	4.408 (1.97)*[a]	9.847 (2.745)	**<0.001**
	N° utterances without verb/N°tot utterances	6.556 (11.903)*	2.167 (4.717)	13.485 (22.828)*	0 (0)	**0.045**
	Morphological errors	0 (0)	0 (0)	0 (0)	0 (0)	\
	Classifier generalization	0.2 (0.422)	0.2 (0.422)	0 (0)	0.231 (0.832)	0.458
	Determiner omission	0 (0)	0 (0)	0 (0)	0 (0)	
	Determiner substitution	0 (0)	0 (0)	0 (0)	0 (0)	
	Preposition omission	0 (0)	0 (0)	0 (0)	0 (0)	
	Preposition substitution	0 (0)	0.1 (0.316)	0 (0)	0 (0)	0.348
	N° sentences with broken syntax	1.8 (1.932)*	1 (1.491)	2.8 (3.048)*	0.077 (0.277)	**0.011**
Discourse and Pragmatic	Total words	71.8 (29.032)*	83.6 (66.805)*	69.2 (38.884)*	164.154 (63.922)	**0.001**
	Words/min	98.761 (64.672)*	99.505 (52.836)*	74.51 (55.055)*	125.543 (38.249)	**0.001**
	N° Irrelevant words/tot words	3.975 (6.854)	8.969 (10.308)	5.234 (6.853)	1.867 (3.913)	0.261
	N° tangential words/ tot words	0 (0)	0 (0)	0 (0)	0 (0)	\

Idea Density	0.336 (0.089)	0.401 (0.098)	0.382 (0.106)	0.363 (0.068)	0.396

*Different from HC; [a]Different from svPPA; [b]Different from lvPPA; [c]Different from nfvPPA; In bold significant results; In red differences survived Bonferroni's correction; In grey not applicable feature.

Table 3 - Quantitative analysis of speech and language production of the Italian sample

Domains	**features**	**svPPA**	**lvPPA**	**nfvPPA**	**HC**	**p-value**
		mean (SD)	mean (SD)	mean (SD)	mean (SD)	
Phonetic and Phonological	Phonological errors	0.7 (1.059)	1.8 (1.549)*	1.9 (1.912)*	0.077 (0.277)	**0.002**
	Distortions	0 (0)	0 (0)	0.1 (0.316)	0 (0)	0.35
	Prolongations	4.3 (3.164)*	9.7 (9.19)*	5.4 (7.214)	1.308 (1.494)	**0.029**
	Tone errors					
	Broken words/tot words	0 (0)	0.252 (0.426)	2.671 (6.964)*	0.033 (0.119)	**0.048**
	Abandoned words/ tot words	1.359 (1.493)*	2.834 (2.158)*	1.054 (1.232)	0.261 (0.452)	**0.002**
	Empty pauses/ tot words	9.673 (6.156)*	8.229 (6.24)*	21.08 (22.508)*	1.982 (1.419)	**<0.001**
	Filled pauses/ tot words	0.066 (0.046)*	0.068 (0.037)*	0.123 (0.114)*	0.018 (0.013)	**<0.001**
Lexico-semantic	Open class/tot words	115.9 (45.936)	91.1 (52.208)	45.8 (18.486)*[ab]	101.308 (26.241)	**<0.001**
	Closed class/tot word	116.6 (49.419)	95.1 (52.437)	50.2 (22.528)*[ab]	96.385 (22.522)	**0.002**
	Open/closed	1.023 (0.196)	0.965 (0.145)	1.003 (0.372)	1.046 (0.118)	0.63
	Nouns/tot words	13.839 (2.685)*[bc]	17.592 (2.73)*[c]	24.404 (4.257)	24.72 (2.633)	**<0.001**
	Verbs/ tot words	20.578 (2.976)	20.568 (2.365)	17.395 (5.984)	18.431 (2.359)	0.15
	Preposition/tot words	4.915 (2.386)	5.702 (1.751)	3.523 (2.578)*	6.906 (1.804)	**0.02**
	Adjective/tot words	1.482 (1.169)	1.571 (1.885)	1.637 (2.462)	1.876 (1.544)	0.73
	Adverb/tot words	14.196 (4.553)*[bc]	8.935 (3.511)*	5.143 (4.773)	5.929 (2.351)	**<0.001**
	Conjunction/tot words	6.417 (3.502)	4.551 (1.62)	4.579 (3.07)	5.118 (2.164)	0.61
	Determiner/tot words	14.126 (4.604)[bc]	18.944 (2.483)	25.722 (11.861)*	17.563 (1.478)	**0.003**
	Pronoun/tot words	18.395 (4.994)*	14.983 (4.932)*	13.093 (5.547)	11.042 (2.504)	**0.006**
	Classifiers/tot words					
	Semantic errors	3.2 (1.874)*[bc]	1.5 (1.434)	1.2 (1.135)	0.692 (1.182)	**0.007**
	Word repetition/tot words	3.847 (3.101)*	5.586 (3.026)*	5.387 (5.555)*	0.976 (0.873)	**<0.001**
Morpho-syntactic	N° of utterances tot	32.6 (12.276)*	26.1 (14.977)	20.7 (3.802)a	21.538 (4.612)	**0.03**
	Mean length of utterance	7.201 (2.232)*	7.283 (1.95)*	4.722 (1.887)*[ab]	9.308 (2.126)	**<0.001**
	N° of utterances without verb/ number of tot utterances	0.25 (0.810)	1.70 (3.90)	19.2 (27.11)*[ab]	0 (0)	**0.003**
	number of Morphological errors	1.2 (1.549)	0.5 (0.707)	0.9 (1.595)	0.615 (0.87)	0.680
	Classifier generalizations					
	Determiner omission	0.3 (0.675)	0.1 (0.316)	0.8 (1.476)	0.385 (0.87)	0.67
	Determiner substitution	0 (0)	0 (0)	0 (0)	0 (0)	
	Preposition omission	0 (0)	0 (0)	0 (0)	0 (0)	
	Preposition substitution	0 (0)	0 (0)	0 (0)	0.077 (0.277)	0.51
	N° sentences with flawed syntax	0.9 (1.853)	0.9 (0.876)	6.1 (6.35)	0.769 (0.927)	0.052
Discourse and Pragmatic	Total words	232.7 (93.786)	187.1 (103.697)	96.2 (39.16)*[ab]	197.846 (47.956)	**0.001**
	Words/min	106.11 (37.839)	70.362 (21.816)*[a]	51.23 (22.687)*[a]	116.898 (19.157)	**0.001**
	N° irrelevant words/tot words	38.684 (28.034)*[c]	21.509 (15.936)[c]	11.724 (16.255)	16.909 (11.989)	**0.02**

N° tangential words/ tot words	3.472 (5.74)	6.224 (15.038)	0 (0)	0 (0)	0.09
Idea density	0.515 (0.051)*[bc]	0.457 (0.046)*	0.368 (0.105)[b]	0.407 (0.043)	**<0.001**

*Different from HC; [a]Different from svPPA; [b]Different from lvPPA; [c]Different from nfvPPA; In bold significant results; In red differences survived Bonferroni's correction; In grey not applicable feature.

Cross-linguistic assessment of a written production: a study of two single cases of nfvPPA.

1. *Introduction*

Writing ability is a relatively recently developed competence, however, its relevance is pivotal in nowadays society, fostering everyday communication and activities. Writing is generally conceptualized as a competence that relies on specific but interacting processes, differently involved based on the task of interest, going from the analysis of input, the access, through the lexical or sub-lexical route, to the orthographic representation of the words, the maintenance of information in the graphemic buffer, the selection of symbol shape at the allographic level and the production of correct motor sequence for handwriting (Planton et al., 2017; Purcell et al., 2011).

Despite being a crucial competence for communication in daily life activities, and for possible rehabilitation strategies (Behrns et al., 2009), writing abilities have been scarcely investigated. Most of our knowledge about writing and its neural substrates derives from studies on healthy speakers (Beeson et al., 2003), or from neurological patients, such as cases of acquired dysgraphia after focal brain lesions (Planton et al., 2013).

In particular, the observation of English patients, assessed using a variety of tasks, including the spelling of regular, irregular, and non-words, has allowed the development of the dual route model, a widely accepted writing model (Ellis, 1982; Patterson, 1986; Rapp and Caramazza, 2002).

This model consequently accounts for the peculiarities of the English language, namely being an opaque language with no clear phoneme-to-grapheme correspondence. Despite being extremely valid in explaining and predicting English patients' performance, such models might underestimate the impairment in languages with different orthographic systems. One example is Italian, a transparent language, characterized by a high rate of regularity in phoneme-to-grapheme conversion. In this case, the adoption of spelling tasks, and dissociation between regular and irregular word patterns, might reduce the accuracy of profile characterization (Luzzi et al., 2010). In Italian, indeed, irregular words are mainly characterized by atypical stress positioning and loss of lexical knowledge might determine errors in language production (Cappa et al., 1997),

A cross-linguistic valid conceptualization of writing should be developed, to account for linguistic diversity, and ensure a full characterization of neurological patients and healthy participants profile (García et al., 2023).

A significant model that could enhance our understanding of writing abilities and its brain organization is Primary Progressive Aphasia (PPA), a neurodegenerative condition in which language deficit is pivotal and relatively focal at least in the early stage of the disease (Mesulam et al., 2021; Tee and Gorno-Tempini, 2019). As for stroke patients, also in the field of PPA, the majority of studies exploring writing abilities involved English patients, assessed using writing to dictation tasks (Graham, 2014). However, tasks like the written picture description could provide a more general and comprehensive characterization of the language impairment, namely permitting to assess simultaneously different linguistic domains, i.e., orthographic, script, lexico-semantic, morpho-syntactic and discourse and pragmatic. Additionally, assessment of written production might enlarge our knowledge of language organization and point out different patterns of impairment related to cross-linguistic variation, i.e., differences in orthographic systems.

Different studies suggested that writing assessment elicited by a written picture description task might be extremely useful in the characterization of the nfvPPA profile, especially in those patients with severe articulatory impairments (Graham et al., 2004; Josephy-Hernandez et al., 2023).

As reported in Chapter 2, nfvPPA (Gorno-Tempini et al., 2011) listed as core criteria the presence of effortful speech production with distortions and halting sounds and/or agrammatism, described as the production of short sentences, deficit in morphology, and reduced production of function words (i.e., prepositions). This profile is also associated with difficulties in comprehension of syntactically complex sentences and preserved semantic knowledge. Left posterior fronto-insular regions are mainly impaired in this variant, described in terms of atrophic and hypometabolic impairment (Agosta et al., 2015; Mandelli et al., 2018; Nuvoli et al., 2020). Recently, to explain the heterogenous presentation of the nfvPPA phenotype, this variant has been conceptualized as a spectrum, according to the presence of main apraxia, main agrammatic deficit, and a graded combination of the two symptoms (Illán-Gala et al., 2023).

Generally, nfvPPA patients are characterized by a deficit in the spelling of non-words, the generation of sentences and written texts, which are typically characterized by agrammatism, reduced number of sentences, and reduced syntactic complexity (Graham, 2014; Graham et al., 2004). Using a written description task, nfvPPA patients, compared to healthy controls, produced fewer words and informative units, and more grammatical errors (Code et al., 2006; Graham et al., 2004).

In this study, we aimed to describe the writing abilities of two nfvPPA patients, being native speakers and writers of English and Italian, respectively. Using a written picture description task, we want to characterize patients' impairment in terms of difficulties across multiple linguistic domains, highlighting similarities and differences across the two languages according to their intrinsic characteristics (see Chapters 1 and 2). We expect that both patients will present an agrammatic production, i.e., by simplifying syntactic structures; but some degree of cross-linguistic variation. In particular, we hypothesize that while the English patient will present a higher number of orthographic errors (i.e., graphemic paraphasia) due to the irregular phoneme-to-grapheme conversion pattern, the Italian patient might show higher levels of morphological difficulties, related to the richer inflectional morphology of Italian (Canu et al., 2020). To our knowledge, no study has compared the performance of nfvPPA patients in a written picture description task across different languages, such as English and Italian.

2. *Materials and methods*

2.1 Participants

English Case

One English patient was evaluated, ENG01. At the time of investigation, ENG01 was a 69-year-old, right-handed man with 16 years of education. His first language was English. His medical history did not include any pre-existing condition. No other neurological or psychiatric disorder was reported. His family history was negative for dementia.

ENG01 started developing language difficulties around three years before the present examination, at the age of 66, after work retirement. Language was described as non-fluent, somewhat effortful, and grammatically poor. No changes in personality, behavior, emotional expression, or empathy toward others were found.

ENG01 was assessed at the University of California San Francisco, Memory and Aging Center, San Francisco (USA), and received a diagnosis of nfvPPA according to consensus criteria (Gorno-Tempini et al., 2011). The diagnosis was based on neurological, neuropsychological, and imaging data. The neurological assessment reported the patient to be "awake, alert, appropriate, and pleasant". Imaging data from MRI reported atrophy in biparietal regions, dorsolateral and mesial frontal areas, and widened Sylvian fissures. Results from the amyloid PET scan were interpreted as positive while the tau tracer PET scan was interpreted as negative. The score on a global cognitive screener (MMSE) was below expectations, 24 out of 30, with points lost for orientation and sentence repetition. Neuropsychological assessment also highlighted weaknesses in language, echoic recall, and executive functioning.

ENG01 underwent an extended language assessment that included the administration of the Western Aphasia Battery (WAB) (Kertesz, 1982), and the Arizona Battery of Reading and Spelling (ABRS) Language (Beeson et al., 2010), revealing a profile characterized by word-finding difficulties, phonemic and grammatical errors, and impaired naming and repetition. There were also mild speech comprehension difficulties, such as complex commands or understanding jokes and sarcasm, as well as impairments in reading, writing, and spelling.

Italian Case

One Italian patient was evaluated, ITA01. At the time of the present investigation, ITA01 was a 69-year-old, right-handed man with 11 years of education. His first language was Italian, and he did not speak any other language. His medical history included dyslipidemia. No other neurological or psychiatric disorder was reported. His family history was negative for dementia.

ITA01 started developing language difficulties around one year before the present examination, at the age of 68. Language impairment was characterized by anomic and simplified oral production, difficulties in understanding complex sentences, and dysarthrophony. Additionally, ITA01 presented behavioral changes, in terms of apathy, social withdrawal, hyperphagia, especially for sweet food, and fixed ideas. Relatives of the patient reported an increase in irritability and verbal hostility. One month before the present investigation, ITA01 also reported the insurgence of dysphagia for solid food.

ITA01 was assessed at IRCCS Mondino Foundation, Pavia (Italy), and received a diagnosis of nfvPPA according to consensus criteria (Gorno-Tempini et al., 2011), associated with motor neuropathy. The diagnosis was based on neurological, neuropsychological, and imaging data. The neurological assessment reported ideo-motor slowing, reduced and simplified speech production, paratonic muscle rigidity, absence of strength deficit, great degree of autonomy in standing and walking. Imaging data, including MRI and FDG-PET, reported atrophy and hypometabolism in the fronto-temporal regions, and posterior parietal regions, with predominantly left impairment. The neuropsychological assessment highlighted the presence of spatial disorientation, a deficit in short and long-term visuo-spatial memory, and episodic memory. Deficits were also reported for executive functions, verbal fluency, and visuo-spatial abilities. Mini-Mental State Examination score was 18 out of 30.

ITA01 underwent an extended language assessment and showed a moderate deficit in the Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2014). In the SAND battery (Catricalà et al., 2017) he presented deficit in sentence comprehension, sentence repetition, and reading of non-words, in written production (reduced fluency and semantic errors). For a full characterization of the oral picture description, see Supplementary Materials. Naming and word reading from the SAND battery were normal. Additionally, ITA01 presented a normal performance in the naming task from

CaGi (Catricala et al., 2013), and an impaired performance in the Esame Neuropsicologico per l'Afasia, (ENPA) (Capasso and Miceli, 2001) comprehension and repetition tasks, and in the syntactic comprehension task assessed by the Nord Western Anagram Test-Italiano (NAT-I) (Canu et al., 2019). He showed also bucco-facial apraxia (De Renzi et al., 1966).

2.2 Written Picture Description

To assess written production, ENG01 and ITA01 completed a written picture description task, using the Urban Scene, developed at the University of California San Francisco. Six English healthy controls and six Italian healthy controls participants without any cognitive complaints and history of neurological or psychiatric diseases completed the task.

Participants were presented with a full-screen version of the picture, and they were asked to describe everything they saw, using sentences. They had two minutes to complete the task, during this period the picture was always available, to reduce attentional and memory burden.

The written samples were then transcribed, and linguistic features of interest (see 2.3) were coded in compliance with the Computerized Language ANalysis program (CLAN; see 2.4) instructions. In each case, two raters independently transcribed and coded the speech samples, followed by a subsequent comparison of the results. For any coding discrepancy, a third rater was consulted, and researchers engaged in discussions for every single case until a consensus was reached.

2.3 Linguistic Features

A total of 23 features were chosen for the written picture description (listed and defined in Table 1), encompassing different linguistic domains, including orthographic, script, lexico-semantic, morpho-syntactic, and discourse and pragmatics. Features were selected upon existing literature, including the linguistic performance of clinical populations, i.e., stroke aphasia, and primary progressive aphasia patients (Boschi et al., 2017; Boucher et al., 2020; Canu et al., 2020; Code et al., 2006; Graham et al., 2004; Mueller et al., 2021; Vandenborre et al., 2018; Wilson et al., 2010).

Table 1 – Written Language included features.

Domains	Features Written Production	Definition
Orthographic	Number of graphemic paragraphia	Total number of words with omitted, inserted, substituted, and transposed letters
Script	Allography	Switch between writing code

Lexico-semantic	Open class words/total words	Total number of content words (verbs, nouns, adjectives, adverbs)/total number of words
	Close class words/total words	Total number of function words (determiners, pronouns, prepositions…)/total number of words
	Number of semantic errors	Paraphasia, circumlocutions, anomia
	Number of words repetition/total words	Begin to write something, stop, and rewrite without changes
Morpho-syntactic	Number of utterances	Utterances require subject and main verb
	Mean length of utterances	Ratio of morphemes to utterances
	Number of utterances without verb/ number of utterances	Elision (drop) of the main verb
	Number of sentences with broken syntax	Agrammatic utterances/tot utterances
	Number of morphological errors	Errors in conjugation, agreement (gender/number), declination of words
Discourse and Pragmatic	Total words	Total number of words
	Words/min	Total number of words/minutes
	Idea density	Ratio of adverbs, adjectives, adverbs, prepositions, and conjunctions to the total number of words

2.4 Computerized Language ANalysis program

Samples were manually transcribed and coded using CLAN. CLAN has been designed to analyze language data and has been extensively used in studies involving healthy participants, children, and neurological populations. For comprehensive information on CLAN and its applications, please refer to the Aphasia Bank project at https://aphasia.talkbank.org/. Analysis of the written production was first performed using the CLAN pipeline, which allowed us to automatically derive the features of interest. If the features were not included in the CLAN program, they were manually coded.

2.5 Statistical Analysis

Demographic data of patients, ENG01 and ITA01, and of the two control groups were compared using the Crawford test for single cases (Crawford and Garthwaite, 2002). Scores obtained from written picture descriptions of each nfvPPA patient were compared with the performance of the respective healthy controls, using the same methodology. Cross-linguistic differences were analyzed at a qualitative level.

3. Results

3.1 Demographic Data

Demographic data are reported in Table 2. ENG01 and ITA01 and their respective healthy control groups did not differ for age, and education (all p values> 0.231).

Table 2 – Demographic data of participants

	ENGLISH			ITALIAN		
	Age	**Education**	**Gender (M|F)**	**Age**	**Education**	**Gender (M|F)**
nfvPPA	69	17	Male	69	11	Male
HC	64.66 (2.94)	15 (2.91)	2|4	65 (5.51)	13.83 (3.31)	4|2
P value	0.231	0.763		0.531	0.464	

Mean and standard deviation, between brackets, of participants.

3.2 Written Production

English case

We compared the written production in the picture description task and significant differences were reported for each linguistic domain, see Table 3 for the details and Figure 1a.

Orthographic domain. ENG01 produced significantly more graphemic paragraphia than HC.

Script domain. ENG01 showed a switch from letters to numbers, The last letter of the word 'three' was canceled and replaced with the corresponding number ('*thre~~e~~-3*').

Lexico-semantic domain. ENG01 produced a lower proportion of determiners and open-to-closed class words ratio than HC.

Morpho-syntactic domain. ENG01 produced an agrammatic sentence and morphological errors.

Discourse and pragmatic domain. No significant differences were reported between ENG01 and HC.

Table 3 – Quantitative and qualitative analysis of written production of ENG01 and English HC.

Domains	Features Written Production	ENG01	HC	P value
Orthographic	Graphemic paragraphia	3	0.16 (0.40)	**0.001**
Script	Allography	Switch from letters to number	Absent	-

Lexico-Semantic	Open class/tot words	17	30.5 (5.46)	0.071
	Closed class/tot word	7	26.66 (9.26)	0.107
	Open/closed	2.42	1.20 (0.22)	**0.004**
	Nouns/tot words	41.66	30.97 (6.15)	0.169
	Verbs/ tot words	26.08	18.94 (8.60)	0.499
	Prepositions/tot words	4.16	11.50 (3.42)	0.103
	Adjectives/tot words	4.16	3.35 (1.41)	0.618
	Adverbs/tot words	0	5.24 (2.92)	0.158
	Conjunctions/tot words	0	0.85 (1.01)	0.473
	Determiners/tot words	12.5	18.66 (2.04)	**0.038**
	Pronouns/tot words	4.16	3.78 (3.29)	0.919
	Semantic errors	Absent	Absent	-
	Words repetition/ tot words	Absent	Absent	-
Morpho-syntactic	N° of utterances	5	4.83 (0.98)	0.88
	Mean length of utterances	4.8	12.04 (3.73)	0.219
	N° utterances without main verb/number of utterances	Absent	Absent	-
	N° sentences with flawed syntax	**1 (20%)**	Absent	-
	Morphological errors	**7**	Absent	-
Discourse and Pragmatic	Total words	23	57 (14.40)	0.081
	Words/min	11.5	26.51 (7.16)	0.11
	Idea density	0.45	0.41 (0.06)	0.494

In bold significant features.

Italian case

We compared the written production in the picture description task and significant differences were reported in each domain, see Table 4 for the details and Figure 1b.

Orthographic domain. No significant differences were reported between ITA01 and HC.

Script domain. No significant differences were reported between ITA01 and HC.

Lexico-semantic domain. ITA01 produced a lower proportion of nouns, verbs, and open-to-close class words ratio than HC. ITA01 produced a higher proportion of adjectives than HC. ITA01 produced one semantic error.

Morpho-syntactic domain. ITA01 produced more agrammatic sentences than HC and a higher number of sentences without the main verb.

Discourse and pragmatic domain. ITA01 presented lower idea density compared to HC.

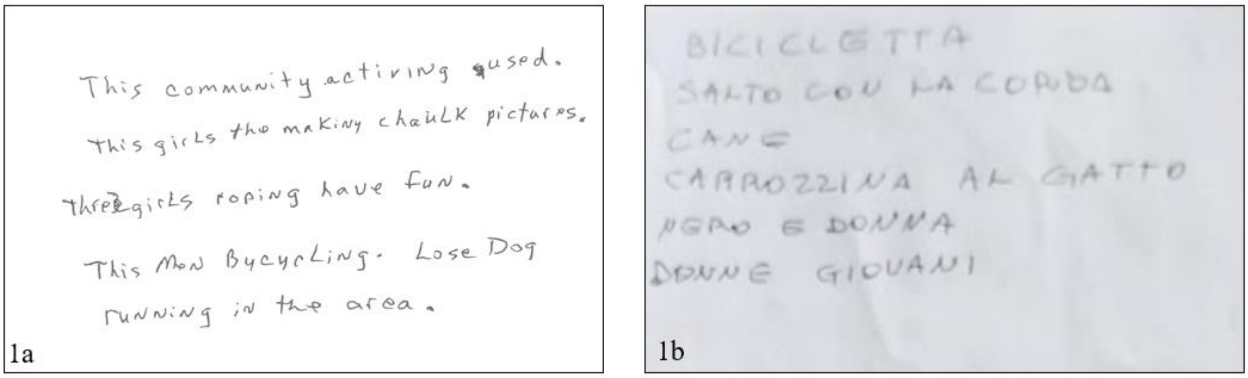
Table 4 – Quantitative and qualitative analysis of written production of ITA01 and Italian HC.

Domains	Features Written Production	ITA01	HC	P value
Orthographic	Graphemic paragraphia	Absent	Absent	-
Script	Allography	Absent	Absent	-
Lexico-Semantic	Open class/tot words	10	19.66 (4.96)	0.131
	Closed class/tot word	4	16.83 (5.56)	0.086
	Open/closed	2.5	1.20 (0.20)	**0.002**
	Nouns/tot words	57.14	32.65 (8.47)	**0.044**
	Verbs/ tot words	0	16.87 (3.48)	**0.006**
	Prepositions/tot words	7.14	12.48 (4.86)	0.356
	Adjectives/tot words	14.28	3.84 (3.67)	**0.046**
	Adverbs/tot words	0	1 (1.61)	0.590
	Conjunctions/tot words	7.14	3.68 (3.04)	0.340
	Determiners/tot words	7.14	10.47 (5.54)	0.602
	Pronouns/tot words	0	10.59	0.102
	Semantic errors	**1**	Absent	-
	Words repetition/ tot words	0	0.16 (0.40)	0.726
Morpho-syntactic	N° of utterances	6	3.83 (1.32)	0.198
	Mean length of utterances	2.33	10.09 (3.12)	0.070
	N° utterances without main verb/number of utterances	6 (100%)	13.88 (26.70)	**0.031**
	N° sentences with flawed syntax	6 (100%)	1 (1.09)	**0.008**
	Morphological errors	Absent	Absent	-
Discourse and Pragmatic	Total words	14	36.5	0.097
	Words/min	7	18.25 (5.10)	0.097

Idea density	0.28	0.48 (0.04)	**0.011**

In bold significant features.

Figure 1 – Written sample from ENG01 (a) and ITA01 (b).



3.3 Qualitative Cross-linguistic Comparison

Based on the only qualitative assessment of ENG01 and ITA01 performance, we identified 2 features in which both patients performed significantly differently from their respective healthy controls, namely:

1) open to closed class ratio.

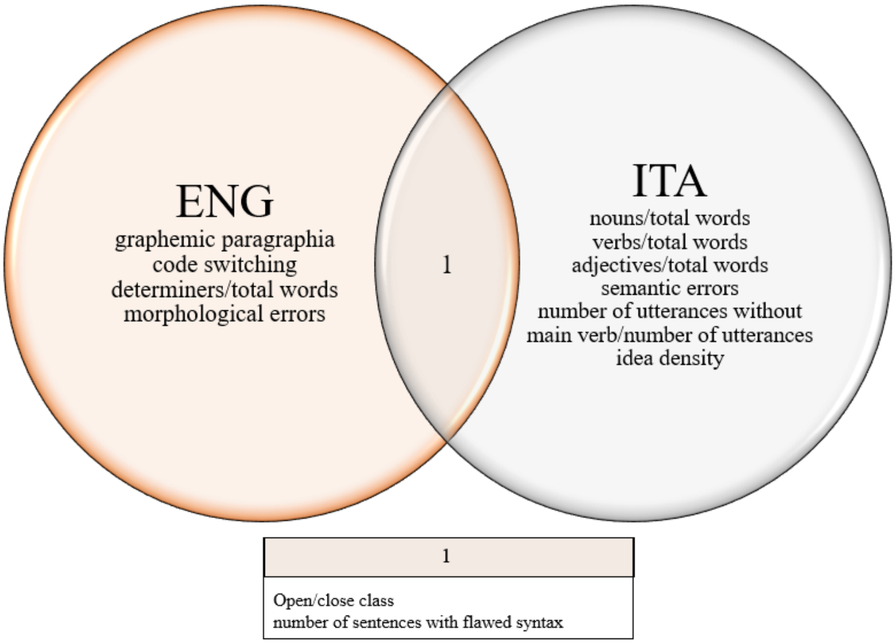
2) the number of sentences with flawed syntax.

English patient specific features. Four features differentiated ENG01 from the English HC group. One belonged to the orthographic domain and included graphemic paragraphia and one to the script domain: the patient presented a code switch (from letters to number). One feature belonged to the lexico-semantic domain, the proportion of determiners. One feature belonged to the morpho-syntactic domain, the number of morphological errors.

Italian patient specific features. Six features differentiated ITA01 from the Italian HC group. Four belonged to the lexico-semantic domain and included the proportion of nouns, verbs, and adjectives and the number of semantic errors. One belonged to the morpho-syntactic domain and included the omission of the main verb. One belonged to the discourse and pragmatic domain and included idea density.

See Figure 2.

Figure 2 - Qualitative cross-linguistic assessment of ENG01 and ITA01 written production.



4. *Discussion*

In this study, we describe the pattern of impairment in a written picture description task of two nfvPPA patients. We compared their performance with a respective group of matched healthy participants, to identify pathological features shared and/or language-specific across English and Italian. Generally, we observed a significant impairment in the written production of patients, involving the orthographic, lexico-semantic, and morpho-syntactic domains.

English Case

The English subject presented a relatively typical written profile, as, although he did not show a telegraphic production (Graham et al., 2004), morpho-syntactic and orthographic deficits were recognizable. Interestingly, the patient presented a switch from letters to numbers, in addition to a self-correction. A possible interpretation of this data is the attempt of the patient to maintain an adequate level of informativeness, despite uncertainty in the correct spelling.

Also, deficits reported at the lexico-semantic domain by ENG01 may be attributed to a syntactic nature. When compared to HC, he produced a significantly different ratio of open to closed-class words, with the former being more frequently produced than the latter. This difference was already described in previous studies (Code et al., 2006), with reduced production of conjunctions and prepositions, and a higher proportion of nouns. ENG01 also produced a reduced proportion of determiners, which might be a sign of reduced sentence complexity and agrammatism. No differences were instead found between the patient and controls in terms of the proportion of nouns and verbs production, as in previous studies (Graham et al., 2004). Although the proportion of verbs is similar to healthy participants, a qualitative observation again supports the presence of an agrammatic profile. ENG01 showed a consistent tendency of dropping the auxiliary (to be), to wrongly inflect words, generally nouns (‘activing’, ‘roping’, bycycling’) showing a peculiar deficit related to verb production and inflection, as previously described in cases of oral production (Thompson et al., 2012; Wilson et al., 2014). Verbs produced tend to be less specific and frequent (i.e., have, make, run in ENG01 vs skip, stroke, collide in controls) and to be used in an improper or simplified way. These data are in contrast with recent findings on syntax-lexicon tradeoff, which suggest that non-fluent PPA production is characterized by low-frequency words that convey relevant information, using simplified syntactic structures (Rezaii, 2022). Possibly, individual variability and frequency of exposure to different words/syntactic rules might explain these results. Globally, the written production of ENG01 supports the common loss of grammatical competence in nfvPPA, with resulting agrammatical production (Leyton and Hodges, 2014). In addition to inflection errors on verbs, ENG01 committed two agreement errors, in terms of number, in the use of demonstrative ‘this’. Morphological errors have already been reported using different tasks, such as verb/noun production or connected speech, in nfvPPA patients (Lukic et al., 2024; Thompson et al., 2013; Wilson et al., 2014) and they generally reflect deficits in syntactic processing, associated with left frontal regions disruption. Word-order impairment was also present, with a relatively low incidence on the performance. These results suggest the importance of in-depth characterization of morpho-syntactic deficits, including inflectional morphology, as a crucial tool to detect and describe English nfvPPA presentation.

Italian Case

The Italian nfvPPA participant presented a highly telegraphic and agrammatic production. Interestingly, this pattern mirrored his oral production, as clinically described, and as derived from our assessment (see Supplementary Material).

The agrammatic pattern becomes evident by observing the performance in different linguistic domains. In the lexico-semantic one, ITA01 showed a significantly increased production of nouns, combined with the total absence of verbs. Dissociation between nouns and verbs was already described in different tasks, such as picture naming (Beber et al., 2019; Hillis et al., 2004) or connected speech (Wilson et al., 2010) suggesting that reduced production of verbs is related to grammatical deficit and difficulties in accessing/adopting correct morpho-syntactic rules. Looking at the other types of tokens, we noticed an increase in adjective production. It should also be noted that the only adjective ITA01 produced was used as a circumlocution: instead of saying ‘bambine’ (young girls), he said ‘donne giovani’ (young women). Semantic errors, including circumlocutions, may be present even in cases of nfvPPA (Catricalà et al., 2022). A significant reduction of closed-class words, with no production of adverbs and pronouns, was observed. Only a few studies explored the number of adverbs and pronouns produced in written samples, and existing data suggested that pronouns are not frequent in nfvPPA texts (Josephy-Hernandez et al., 2023). The Italian nfvPPA patient did not produce any morphological errors: this could be explained by the highly telegraphic production with the absence of tokens, i.e., verbs, determiners, pronouns, that require adequate morphological inflection, i.e., number, gender, and tense.

Qualitative cross-linguistic comparison

English and Italian nfvPPA, compared to their respective healthy controls, shared a higher ratio of open to closed-class words, and the number of sentences with flawed syntax. These findings reflect the typical deficit of non fluent patients, i.e., difficulties in accessing and processing grammatical and syntactical rules. This data, consistent with the current diagnostic criteria, suggests that written production might be considered a useful cross-linguistic tool to identify language impairment (Graham et al., 2004); furthermore, this modality could overcome limitations related to severely impaired oral production.

It is important to note that the presence of agrammatism should be based on specific language characteristics and error assessment, accounting for linguistic diversity, to guarantee an equitable evaluation.

The English patient produced, differently from the Italian one, graphemic paragraphia, possibly related to the greater syllabic complexity of English words. Other differences between the two patients regarded the lexico-semantic domain and in particular the type of produced tokens, with ITA01 showing a particular involvement of closed class words, while he did not produce any morphological errors. The English patient produced morphological errors instead.

These results confirmed only partially our expectations, as several factors could explain such variability. Only some differences seem linked to the intrinsic characteristics of the languages, i.e., the presence of graphemic errors in the English patient. Lexico-semantic features are extremely relevant for Italian PPA diagnosis and are related to cross-linguistic variability (see Chapter 2). In the oral production, lexico-semantic features contributed to a better characterization of Italian PPA from healthy controls and resulted in the second domain in order of number of impaired features, suggesting the great relevance of these features in Italian. Other factors, such as the different disease severity of the two patients, might have played a role in the performance; indeed ITA01, who has a lower MMSE score, showed a higher level of impairment and reduced production.

This study presents some limitations; it is a multiple single case study and the differences in terms of disease duration, around three years for ENG01 and one year for ITA01, and in terms of global cognitive abilities, MMSE is equal to 24/30 for ENG01 and to 18/30 and ITA01, do not allow a generalization of our results and conclusions. Further studies with larger sample size should be conducted to better understand and characterize the written impairment of PPA patients and its possible cross-linguistic implications. Moreover, the assessment of different languages, with higher degrees of variation, i.e., logographic languages, should be included to increase our understanding of language organization and possibly identify written linguistic markers that are cross-linguistically valid and tailored to PPA diagnosis.

To conclude, in this study, we described the written profile of two nfvPPA patients, assessed in two different languages. Our results suggest the importance of written assessments, particularly in those cases where oral production is particularly effortful due to motor impairment. Cross-linguistic differences are already visible when comparing at the qualitative level patients' performance, strengthening the need for tailored language assessment.

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6. Supplementary Materials

ITA01 also performed the oral picture description from the SAND battery, namely the Summer Scene. Following the same procedure for written production and adopted in Chapter 1 and 2 for speech and language assessment, we identified, coded, and extracted a set of speech and language features. See Table 1.

Table 1 – Speech and language included features.

Domains	Features Oral Production	Definition
Phonetic and Phonological	Number of phonological errors	Words with at least one deletion, insertion, or transposition of phonemes; or 50% modified compounds
	Number of distortions	Insertion of not recognizable sounds
	Number of broken words	Pause within word
	Number of abandoned words/tot words	Changes from one word to another
	Number of empty pauses/tot words	Number of silent (no sound produced) pauses
	Number of filled pauses/ tot words	Number of filled pauses (i.e., uhm, ehm)
Lexico-semantic	Open class words/total words	Total number of content words (verbs, nouns, adjectives, adverbs)/total number of words
	Closed class words/total words	Total number of function words (determiners, pronouns, prepositions…)/total number of words
	Number of semantic errors	Paraphasia, circumlocutions, anomia
	Number of words repetition	Begin to say something, stop, and repeat without changes
Morpho-syntactic	Number of utterances	Utterances require subject and main verb
	Mean length of utterances	Ratio of morphemes to utterances
	Number of utterances without verb/ number of utterances	Elision (drop) of the main verb
	Number of sentences with broken syntax	Agrammatic utterances/tot utterances
	Number of morphological errors	Errors in conjugation, agreement (gender/number), declination of words
Discourse and Pragmatic	Total words	Total number of words
	Words/min	Total number of words/minutes
	Idea density	Ratio of adverbs, adjectives, adverbs, prepositions, and conjunctions to the total number of words

We compared the oral production in the picture description task of ITA01 with a group of 6 healthy controls, matched for age and education level. Using the Crawford method described before (Crawford and Garthwaite, 2002) we compared the performance of ITA01 with the HC across the different linguistic domains. Significant differences were reported in different linguistic domains, see Table 2 for the details.

Phonetic and phonological domain. ITA01 produced phonological error and distortion and a significantly higher proportion of empty pauses compared to HC.

Lexico-semantic domain. ITA01 produced less proportion of close class words, nouns, and open to close class words ratio than HC.

Morpho-syntactic domain. ITA01 produced more utterances (noun phrases), however they were shorter sentences and more agrammatic than HC. Also, he produced a higher number of sentences without the main verb.

Discourse and pragmatic domain. ITA01 presented lower idea density compared to HC.

Table 2 - Quantitative and qualitative analysis of speech and language production of ITA01 and Italian HC.

Domains	Features	ITA01	HC	P value
Phonetic and Phonological	Phonological errors	1	Absent	-
	Distortions	1	Absent	-
	Broken words/tot words	0	0.147 (0.361)	0.722
	Abandoned words/ tot words	0	0.408 (0.645)	0.584
	Empty pauses/ tot words	66.667	5.294 (3.849)	**0.000**
	Filled pauses/ tot words	4.762	2.672 (3.191)	0.571
Lexico-semantic	Open class/tot words	18.000	42.833 (12.624)	0.128
	Closed class/tot word	3.000	38.333 (12.596)	**0.048**
	Open/closed	6.000	1.147 (0.244)	**0.000**
	Nouns/tot words	71.429	26.126 (3.425)	**0.000**
	Verbs/ tot words	14.286	20.183 (3.851)	0.215
	Prepositions/tot words	0.000	5.878 (2.688)	0.098
	Adjectives/tot words	0.000	1.451 (2.01)	0.534
	Adverbs/tot words	0.000	5.154 (3.006)	0.173
	Conjunctions/tot words	0.000	2.19 (1.565)	0.250
	Determiners/tot words	9.524	16.911 (6.544)	0.343
	Pronouns/tot words	0.000	13.025 (5.071)	0.063
	Semantic errors	0.000	0.333 (0.516)	0.580
	Word repetition/tot words	0.000	0.996 (1.228)	0.484

Morpho-syntactic	N° utterances tot	19.000	10 (1.549)	**0.003**
	Mean Length of utterance	1.105	7.919 (1.524)	**0.009**
	N° utterances without verb/N°tot utterances	0.789	Absent	-
	Morphological errors	0.000	0.333 (0.516)	0.580
	N° sentences with flawed syntax	19	0.167 (0.408)	**0.000**
Discourse and Pragmatic	Total words	21.000	81.167 (23.928)	0.067
	Words/min	17.797	131.157 (68.585)	0.187
	Idea Density	0.143	0.388 (0.046)	**0.004**

In bold significant results.

General Conclusions

In the present work, we assessed and compared cross-linguistic similarities and differences in the oral and written production of healthy individuals and neurological patients.

We believe that cross-linguistic comparisons are pivotal to increase our understanding of language organization and to develop more equitable and comprehensive clinical guidelines, specifically tailored to assess language deficits in different groups. The universality of the current diagnostic criteria for PPA based on the English language has so far been tacitly assumed, possibly compromising an accurate diagnosis of non-English-speaking patients. Our study can be considered very innovative as it tries to shed light on this issue.

Our work identified differences in oral production across English, Chinese, and Italian healthy participants. Language-specific profiles involved phonological, lexico-semantic, and morpho-syntactic domains, according to the diverse ways in which sound, words, and sentences are built and organized in the respective language. Differences in healthy controls' speech and language production should be considered mandatory in improving our understanding and framing the language impairment in Primary Progressive Aphasia across different languages. Results on PPA patients permitted indeed to define language impairments in the three different groups, namely English, Chinese, and Italian, providing useful insight and directions for clinicians on which features should be assessed and possibly used as targets for rehabilitation, or compensation strategies.

Cross-linguistic comparisons increased the awareness of differences in the clinical presentation of patients, which are obviously linked to a specific language. Our results suggest a role of core features in the identification of PPA patients. These core features were equally impaired in patients speaking very distant languages, and they are consistent with the description of the PPA condition, involving phonological, lexico-semantic, and morpho-syntactic processes. It is important to note, however, that these features showed different levels of accuracy in distinguishing PPA from HC across languages and reported a relatively lower sensitivity for English and Chinese samples. Interestingly, but not expectedly, the addition of specific features allowed for better discrimination only for the Italian PPA. The low accuracy for English and Chinese models might suggest that other tasks (i.e., articulatory, morpho-syntactic) or other language-specific features (i.e., noun classifier production) should be considered since they might be more specific in English and Chinese PPA characterization. On the contrary, we believe that connected speech greatly characterizes the impairment of Italian PPA patients. This task indeed targets the production of abnormal patterns (i.e., lexico-semantic impairment) that are strongly related to Italian language structure (i.e., low phonological complexity, high reliance on inflectional morphology) and that therefore constitute areas in which an impairment may be more detectable. Moreover, a greater role of the language-specific features can be expected when considering the single PPA variants instead of the entire PPA group.

The assessment of written production could be considered a relatively new, and useful instrument to explore and describe the language profile of patients, but also of healthy controls, and neurological populations in general. Written production allowed the assessment of patients with marked deficits in oral production and also permitted the evaluation of differences in a linguistic domain, the orthographic, which received less attention, despite showing a high level of variability.

We want to highlight the importance of including under-represented populations, therefore, in the future, different language tasks should be included or developed to capture the full cultural and linguistic complexity. This study represents a first attempt to characterize cross-linguistic differences, and further exploration should be performed on bigger samples and a wider range of tasks.

To conclude, we believe this work pinpointed the relevance of cross-linguistic studies, as they give the possibility to gain a deeper understanding of language organization and provide insight into the different phenotypes in which linguistic deficits may manifest across clinical populations.

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