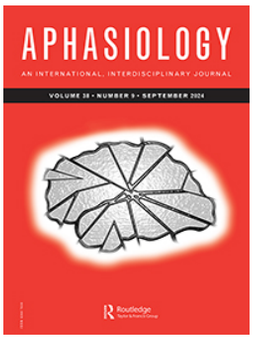

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The pattern of phonological, semantic, and circumlocution naming errors for nouns and verbs in primary progressive aphasia

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ABSTRACT

Background: In the diagnostic criteria for lvPPA (Gorno-Tempini et al. 2011), "speech (phonologic) errors in spontaneous speech and naming" is a secondary criterion, but studies of naming error patterns in PPA have not found evidence to support this criterion. Furthermore, only a few studies have examined naming error patterns in PPA.

Aims: In the current study, we examined the pattern of naming errors for nouns and verbs in all three subtypes of PPA, as well as unclassifiable PPA and typical (amnestic) Alzheimer's disease (AD). Statistical analyses focused on three common error types: phonological, semantic, and circumlocution errors.

Methods & Procedures: The final sample included 35 participants with PPA and four participants with typical AD. Participants were asked to name 284 noun pictures and 116 verb pictures. Separately for nouns and verbs, repeated-measures ANCOVA was used to examine the interaction between Error Type and Diagnostic Subtype.

Twenty of the participants also completed a structural MRI scan. For these participants, we examined the relationships between naming errors and brain volume within ten left hemisphere regions of interest (ROIs).

Outcomes & Results: In lvPPA, the proportion of phonological errors was significantly lower than the proportion of semantic errors for verbs. In svPPA, uPPA, and typical AD, semantic errors were significantly greater than phonological errors for both nouns and verbs. In between-subtype analyses, the proportion of semantic errors for nouns was significantly greater for participants with svPPA and uPPA, compared to those with nfvPPA.

For nouns, the MRI analyses revealed significant negative correlations between the proportion of circumlocution errors and volume in the left inferior temporal gyrus and the left fusiform gyrus. For verbs,

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there were significant negative correlations between circumlocution errors and volume in the left insula, and between semantic errors and volume in the left superior temporal pole.
Conclusions: The findings of this study indicate that semantic naming errors may be common for both nouns and verbs in typical AD and all subtypes of PPA, with the possible exception of nouns in nfvPPA. In contrast, phonological naming errors were not significantly more common than semantic errors in any diagnostic subtype. Furthermore, phonological naming errors were not significantly more common in lvPPA, compared to any other diagnostic subtype.

1. Introduction

In neurodegeneration, anomia is a common deficit, and it can be observed in disorders such as typical Alzheimer's disease (AD; Appell et al., 1982) and primary progressive aphasia (PPA; Westbury & Bub, 1997). PPA is a clinical syndrome that involves progressive language impairment (Gorno-Tempini et al., 2011; M. M. Mesulam, 1982). During the initial phases of the illness, behavior and other aspects of cognition, such as visuospatial skills and episodic memory, are relatively preserved. Three subtypes of PPA have been identified by the international diagnostic criteria (Gorno-Tempini et al., 2011): the logopenic variant (lvPPA), which has the core features of impaired single-word retrieval and impaired repetition of sentences and phrases; the nonfluent/agrammatic variant (nfvPPA), which has the core feature(s) of effortful, halting speech with apraxia and/or agrammatic language production; and the semantic variant (svPPA), which has the core features of impaired confrontation naming and single-word comprehension deficits. However, between 10% and 41% of PPA cases have been found to be unclassifiable according to these criteria (M. Mesulam et al., 2014; Botha et al., 2015; Harris et al., 2013; Sajjadi et al., 2012; Wicklund et al., 2014; see Teichmann, 2021, for a recent review).

In the diagnostic criteria for lvPPA (Gorno-Tempini et al., 2011), "speech (phonologic) errors in spontaneous speech and naming" is a secondary criterion, along with "spared single-word comprehension and object knowledge, spared motor speech, and absence of frank agrammatism". Three of these four features are required for a diagnosis of lvPPA. The inclusion of "spared single-word comprehension and object knowledge" suggests that semantic processing may be relatively unimpaired in lvPPA. However, the presence or absence of semantic errors is not specifically addressed in the criteria for lvPPA or any other variant.

Prominent areas of atrophy in lvPPA include the left inferior parietal lobe and the left posterior superior temporal lobe (Gorno-Tempini et al., 2004; Josephs et al., 2013; Rohrer et al., 2010). These areas have been associated with phonological processing and phonological short-term memory (Baldo & Dronkers, 2006; Baldo et al., 2012; Buchsbaum et al., 2011; Gorno-Tempini et al., 2008; Hickok & Poeppel, 2007; Leff et al., 2009). Therefore, anomia in lvPPA may be caused by impaired phonological processing and/or difficulty maintaining phonological representations, and phonological naming errors may be more common, compared to semantic naming errors (although semantic errors can also occur in the presence of intact semantic processing;

see Caramazza & Hillis, 1990). However, atrophy in lvPPA may spread to areas of the temporal lobe that are associated with lexical-semantic and conceptual processing (Leyton et al., 2016, 2019), and semantic impairment may appear in lvPPA (Leyton et al., 2013; Roncero et al., 2020). Consequently, both phonological and semantic errors could be common in lvPPA.

A core symptom of nfvPPA is "effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)". Although apraxia of speech and phonological speech errors have distinct underlying mechanisms, they can be difficult to distinguish from one another (Ash et al., 2013; Conca et al., 2022; Croot et al., 2012; Wilson et al., 2010). Furthermore, analysis of discourse samples has provided evidence of prominent phonological errors in nfvPPA (Ash et al., 2013; Dalton et al., 2018). Two of the secondary criteria for nfvPPA are "spared single-word comprehension" and "spared object knowledge", suggesting that semantic processing may be relatively unimpaired in nfvPPA.

There are several prominent left hemisphere areas of atrophy in nfvPPA, including the inferior frontal gyrus, insula, and premotor and supplementary motor areas (Grossman et al., 1996; Josephs et al., 2006; Nestor et al., 2003). These regions have been associated with phonological speech encoding (Indefrey, 2011) and articulation (Hickok & Poeppel, 2007; Indefrey, 2011). Therefore, anomia in nfvPPA may be caused by difficulty producing the correct phonological output, and phonological naming errors may be more common, compared to semantic naming errors. However, compared to noun naming, impaired verb naming has been found to emerge earlier in nfvPPA (Cotelli et al., 2006; Hillis et al., 2002, 2004; Thompson et al., 2012), suggesting that verb anomia in nfvPPA may be due in part to grammatical or conceptual-semantic impairment (Meyer et al., 2020, 2024). As a result, both phonological and semantic naming errors may be common for verbs in nfvPPA, while phonological errors may be common for nouns.

Conversely, in the diagnostic criteria for svPPA (Gorno-Tempini et al., 2011), "impaired single-word comprehension" is a core criterion, and "impaired object knowledge, particularly for low-frequency or low-familiarity items" is a secondary criterion, along with "spared speech production (grammar and motor speech)". In svPPA, there is bilateral atrophy of the anterior temporal lobe (Gorno-Tempini et al., 2004, 2011; Mummery et al., 2000), which has been associated with conceptual-semantic processing (Binney et al., 2010; Lambon Ralph et al., 2010; Migliaccio et al., 2016; Mummery et al., 2000; Rogalski et al., 2011; T. T. Rogers et al., 2006). In the left hemisphere, atrophy may extend to more posterior portions of the middle temporal gyrus and inferior temporal gyrus (Leyton et al., 2016; M. Mesulam et al., 2012), areas that have been associated with the interface between lexical and semantic information (Hickok & Poeppel, 2004, 2007; Indefrey, 2011; Indefrey & Levelt, 2004; Migliaccio et al., 2016). Thus, anomia in svPPA appears to be caused by degraded conceptual representations and/or degraded lexical-semantic connections, and semantic naming errors may be more common, compared to phonological naming errors.

Typical (amnestic) AD involves degeneration that originates within the medial temporal lobe (Braak & Braak, 1995; Delacourte et al., 1999). Anomia in typical AD may be due to impaired semantic processing (Caputi et al., 2016; Chertkow & Bub, 1990; Domoto-Reilly et al., 2012; Frings et al., 2011; Hodges & Patterson, 1995; Hodges et al., 1992), impaired lexical retrieval (Nebes et al., 1984), or a combination of the two (Joubert et al.,

2010; Reilly et al., 2011; S. L. Rogers & Friedman, 2008). Therefore, semantic naming errors may be more common than phonological naming errors in typical AD.

Only a few studies have examined naming error patterns in PPA, and most of these studies have only examined naming error patterns for nouns. In one study that focused on noun naming, Catricala et al. (2020) examined semantic, phonological, and visual errors in a large group of participants with neurodegenerative disorders. In within-subjects analyses, semantic errors were more common than phonological and visual errors in lvPPA, svPPA, and AD. In nfvPPA, semantic errors were more common than visual errors, while semantic and phonological errors were not significantly different.

In two additional studies that examined naming error patterns for nouns, the only significant differences in error patterns between PPA subtypes involved circumlocution errors (Budd et al., 2010; Bruffaerts et al., 2020). One of these studies found that the rate of circumlocutions was significantly higher in both lvPPA and svPPA, compared to nfvPPA, while semantic errors were common in all subtypes (Budd et al., 2010). The other study (Bruffaerts et al., 2020) found that the rate of circumlocutions was significantly higher in svPPA, compared to both nfvPPA and mixed PPA (cases with impaired comprehension and grammar; this is more restrictive than the unclassifiable subgroup from the current study). In contrast to these two studies, Migliaccio et al. (2016) found significant between-subtype differences for both phonological and semantic errors in a noun naming task. Phonological errors were more common in nfvPPA, compared to both lvPPA and svPPA. Semantic errors were more frequent in svPPA, compared to lvPPA and nfvPPA, and semantic errors were also more frequent in lvPPA, compared to nfvPPA.

To our knowledge, only one study has examined naming error patterns for verbs in PPA (Lukic et al., 2022). Unlike the studies cited above, which used a picture naming task, this study utilized an auditory noun to verb generation task (e.g., after hearing the word *bed*, participants were asked to generate an associated verb, such as *sleep*). In this task, Lukic et al. found that participants with lvPPA produced significantly more semantically-related noun errors (e.g., producing *baseball* in response to *ball*), compared to those with nfvPPA and svPPA.

A few studies have examined the relationships between naming errors in PPA and hypometabolism or reduced volume within specific brain areas. Areas associated with semantic errors for nouns include the left fusiform gyrus and left middle and inferior temporal gyri (Bruffaerts et al., 2020; Catricala et al., 2020), as well as the left temporal pole and left insula (Catricala et al., 2020). Areas associated with phonological errors for nouns include the left superior and middle temporal gyri (Catricala et al., 2020), as well as the left inferior parietal lobe and the left supramarginal gyrus (Petroi et al., 2020). No significant relationships were found between circumlocution errors and reduced cortical volume within specific brain areas (Bruffaerts et al., 2020).

In the current study, we examined the pattern of naming errors for nouns and verbs in all three variants of PPA, as well as individuals with unclassifiable PPA (uPPA) or typical (amnestic) AD. Individuals with uPPA were included because up to 41% of PPA cases may be unclassifiable (Sajjadi et al., 2012). If this estimate is correct, then uPPA may be the most common subtype of PPA. Therefore, it is important to understand the features of uPPA, including the types of naming errors that occur in this subtype. Individuals with typical AD were included because they have neurodegeneration and often have anomia, similar to individuals with PPA. While lvPPA has been connected with an atypical

presentation of AD (Leyton et al., 2016; M. Mesulam et al., 2014; Rabinovici et al., 2008), anomia in typical AD has been associated with semantic or lexical impairment (e.g., Reilly et al., 2011), rather than phonological impairment. Therefore, the pattern of naming errors in typical AD may be similar to svPPA, rather than lvPPA.

Analyses focused on three types of errors: phonological errors and semantic errors, because they are related to the hypotheses of the current study; and circumlocutions, which are a common type of error in studies of naming error patterns in PPA. We predicted that phonological errors would be significantly greater than semantic errors in lvPPA and nfvPPA. An alternative hypothesis for lvPPA was that both phonological and semantic errors would be common. For nfvPPA, an alternative hypothesis was that both phonological and semantic naming errors would be common for verbs, while phonological errors would be common for nouns.

In svPPA and typical AD, we predicted that semantic errors would be significantly greater than phonological errors. In uPPA, both types of errors were expected to be common.

For a subset of the participants, we also examined the relationships between naming errors and brain volume within ten left hemisphere regions of interest (ROIs). We predicted that phonological errors would be associated with lower volume in the superior temporal gyrus, middle temporal gyrus, and supramarginal gyrus (Catricala et al., 2020; Petroi et al., 2020). We predicted that semantic errors would be associated with lower volume in the temporal pole, middle temporal gyrus, inferior temporal gyrus, fusiform gyrus, and insula (Bruffaerts et al., 2020; Catricala et al., 2020).

2. Materials and methods

2.1. Participants

The participants completed a baseline evaluation for an anomia treatment study (Meyer et al., 2024). The inclusion criteria were a clinical diagnosis of PPA or typical (amnestic) AD, native English speaker (or learned English during childhood), at least 10 years of education, age of at least 40 years, and no history of other neurological or psychiatric disorders. Participants completed a battery of language and cognitive tests (see Table 1), including the MMSE (Folstein et al., 1975), the BNT (Kaplan et al., 2001), Auditory Word-Picture Matching (S. L. Rogers & Friedman, 2008), Pseudoword Repetition (five-syllable pseudowords; Meyer et al., 2015), Reading of Regular and Irregular Words (Meyer et al., 2018), the 3-picture version of Pyramids and Palm Trees (P&PT; Howard & Patterson, 1992), and the 3-picture version of Kissing and Dancing (K&D; Bak & Hodges, 2003). For the latter two tests, items that were missed by more than 20% of unimpaired control participants were removed, which resulted in a total of 50 items for P&PT and 48 items for K&D. Selected subtests from the BDAE (Goodglass et al., 2001) were also administered, including Picture Description, Embedded Sentences, and Sentence Repetition.

PPA subtyping was based on the behavioral criteria (Gorno-Tempini et al., 2011) and each participant's assessment results (see Table 1). Participants were diagnosed with uPPA if they met the core criteria for PPA but either did not meet the criteria for any subtype or met the criteria for more than one subtype. Diagnoses for participants with typical (amnestic) AD were based on the McKhann et al. (2011) criteria. The final set of

Table 1. Demographic Information and Assessment Results

Subject	Age	Ed	Sex	R	Symptom Duration	MMSE/ 30	BNT /60 (50)	WPM /48 (47)	P&PT /50 (48)	K&D /48 (46)	BDAE AA/ 7	BDAE PL/ 7	BDAE GF/ 7	BDAE ES/10 (8)	BDAE SR/10 (9)	PR/ 10 (7)	Reading (-1)
LV1	75	20	M	W	62 mo.	27	25	48	49	45	6	7	7	10	9	10	-2
LV2	74	12	F	W	29 mo.	10	3	36	37	32	7	7	7	7	6	3	0
LV3	70	18	F	W	74 mo.	22	43	48	46	47	6	7	7	6	8	6	-2
LV4	57	13	F	W	68 mo.	20	24	48	46	44	7	7	7	4	1	3	-4
LV5	70	12	F	W	43 mo.	24	29	48	49	43	7	7	7	10	8	8	-2
LV6	73	16	M	W	13 mo.	29	34	47	45	45	7	7	6	7	7	8	-1
LV7	76	18	F	W	76 mo.	23	31	48	44	45	6	7	7	8	7	7	0
LV8	75	18	F	W	45 mo.	20	43	47	46	46	7	7	7	6	8	7	-1
LV9	75	16	M	W	33 mo.	18	23	47	41	41	7	6	7	9	9	6	-2
LV10	77	17	F	W	48 mo.	22	30	47	50	46	7	7	7	8	9	6	-2
SV1	76	16	F	W	20 mo.	20	23	39	43	45	7	7	7	4	10	10	-3
SV2	67	18	F	AA	112 mo.	23	6	46	41	45	7	7	7	10	9	8	-3
SV3	55	16	F	AA	19 mo.	6	29	45	32	31	7	6	7	8	6	6	-4
SV4	69	20	F	W	23 mo.	13	18	46	43	39	7	7	6	4	7	9	-2
SV5	70	16	F	W	40 mo.	25	23	46	45	44	7	7	7	7	5	2	-2
NFV1	79	18	F	W	57 mo.	26	47	48	48	46	7	6	6	9	9	4	0
NFV2	76	16	F	W	28 mo.	30	47	48	50	47	5	5	4	10	5	1	0
NFV3	74	12	M	W	34 mo.	18	32	47	47	45	6	6	5	8	6	NA	1
NFV4	63	20	F	AA	100 mo.	25	23	48	50	48	4	4	3	6	0	0	-3
NFV5	66	16	F	W	43 mo.	26	42	48	49	48	6	7	6	8	7	4	0
NFV6	67	20	M	W	16 mo.	26	57	48	49	45	5	7	6	9	10	9	-1
NFV7	72	16	M	W	35 mo.	29	45	48	50	48	4	4	5	6	5	2	-1
NFV8	76	13	F	W	31 mo.	10	11	48	38	31	2	2	2	5	1	0	1
UPPA1	78	16	M	W	74 mo.	26	13	46	43	40	7	7	7	9	3	3	-4
UPPA2	71	18	M	W	99 mo.	25	8	45	44	46	7	7	7	10	3	4	-3
UPPA3	55	16	F	W	92 mo.	12	33	45	44	44	7	7	7	4	2	2	-2
UPPA4	62	15	F	W	41 mo.	18	18	32	44	33	7	6	6	4	5	4	-5
UPPA5	80	18	M	W	36 mo.	18	20	35	34	36	3	4	4	9	3	4	5
UPPA6	76	16	F	W	29 mo.	14	37	46	43	32	7	7	6	6	6	9	0
UPPA7	80	16	F	W	35 mo.	25	48	40	43	36	6	7	6	5	9	9	1
UPPA8	72	19	M	W	35 mo.	21	56	48	44	42	6	7	6	10	7	5	0
UPPA9	62	16	F	W	50 mo.	8	7	44	41	36	4	4	4	NA	0	0	-2
UPPA10	75	18	M	W	50 mo.	27	52	48	50	46	7	7	7	10	10	NA	0
UPPA11	67	18	F	W	40 mo.	28	31	48	49	48	7	7	7	10	9	8	-1
UPPA12	68	18	F	W	38 mo.	27	44	48	46	42	4	6	6	9	7	5	-2

(*Continued*)

Table 1. (Continued).

Subject	Age	Ed	Sex	R	Symptom Duration	MMSE/ 30	BNT /60 (50)	WPM /48 (47)	P&PT /50 (48)	K&D /48 (46)	BDAE AA/ 7	BDAE PL/ 7	BDAE GF/ 7	BDAE ES/10 (8)	BDAE SR/10 (9)	PR/ 10 (7)	Reading (-1)
AD1	86	16	M	W	52 mo.	29	31	37	47	39	6	7	6	10	9	9	0
AD2	62	16	M	W	86 mo.	25	57	48	48	41	7	7	7	10	10	10	0
AD3	58	18	M	AA	96 mo.	1	2	31	29	24	5	5	6	4	0	0	-4
AD4	82	14	F	W	26 mo.	17	34	46	45	41	7	7	6	3	8	NA	-1

Note. Numbers in parentheses are cutoff scores. Scores below this threshold are more than 2 SDs below the control mean. LV: logopenic variant; SV: semantic variant; NFV: nonfluent/agrammatic variant; UPPA: unclassifiable primary progressive aphasia; AD: Alzheimer's disease; Ed: Education; mo: months; R: race and ethnicity; W: White, non-Hispanic; AA: African American, non-Hispanic; MMSE: Mini-Mental State Examination; BNT: Boston Naming Test; WPM: Word-Picture Matching; P&PT: 3-picture version of Pyramids and Palm Trees; K&D: 3-picture version of Kissing and Dancing; BDAE: Boston Diagnostic Aphasia Examination; AA: Articulatory Agility; PL: Phrase Length; GF: Grammatical Form; ES: Embedded Sentences; SR: Sentence Repetition; PR: Pseudoword Repetition; Reading: Low Frequency Irregular Words minus Low Frequency Regular Words (a more negative score indicates greater surface alexia); NA: not administered.

participants included 10 with lvPPA, 8 with nfvPPA, 5 with svPPA, 12 with uPPA, and 4 with typical AD (see Table 2). One additional participant with uPPA was excluded from the statistical analyses because many of her naming responses exceeded the response time limit (see Section 2.3).

Participants were considered to have impaired repetition if they were impaired on BDAE sentence repetition and/or 5-syllable pseudoword repetition (see Meyer et al., 2015). One participant (LV1) was above both cutoff scores but was classified as lvPPA, because he had unimpaired grammar, speech, word comprehension, and object knowledge, and he made phonological errors during picture description, suggesting that he had early-stage lvPPA. This subtype diagnosis was confirmed by subsequent testing (7 months later), which revealed impaired sentence repetition, along with unimpaired grammar, speech, word comprehension, and object knowledge.

None of the diagnostic subgroups were significantly different in terms of mean Age, Education, or Symptom Duration (all p's $> .10$). Fisher's exact test indicated that the svPPA and AD subgroups were significantly different on the variable of Sex ($p = .048$). No other between-subgroup differences were significant for this variable.

Twenty of the participants also had a 3T brain MRI. The participants who were scanned included LV1-LV5, LV7-LV10, SV1, NFV4, NFV5, NFV7, NFV8, UPPA1, UPPA2, UPPA10-UPPA12, and AD1. The participants who were not scanned were ineligible for scanning due to incompatible implants, unable to travel to the scanning site, or they were not scanned because the scanner was unavailable during the COVID-19 pandemic.

For the MRI analyses, an unimpaired control group included 37 participants with a mean age of 62.4 (SD = 7.6). The control group included 18 males and 19 females.

2.2. Stimuli

Participants were asked to name 284 noun pictures and 116 verb pictures. The picture stimuli were black and white line drawings that were selected from Snodgrass and Vanderwart (1980) and online clipart collections.

In norming conducted with unimpaired controls, the selected pictures had high name agreement. For the noun pictures, the unimpaired group consisted of 24 individuals with a mean age of 52.3 (SD = 7.0) and mean education of 15.4 years (SD = 2.4). Mean naming accuracy for the noun pictures was 96.3% (SD = 2.2%). For the verb pictures, the unimpaired group consisted of 24 individuals with a mean age of 67.4 (SD = 9.3) and mean education of 17.3 years (SD = 2.1). Mean naming accuracy for the verb pictures was 92.0% (SD = 4.1%). The testing procedure was the same as the procedure described in Section 2.3, except that different groups of subjects were tested on the noun stimuli and the verb stimuli.

Semantic categories included in the noun images consisted of Animals (e.g., cow), Appliances (e.g., toaster), Body Parts (e.g., arm), Clothing (e.g., shoe), Food (e.g., banana), Furniture (e.g., desk), Musical Instruments (e.g., guitar), Items from Nature (e.g., cloud), Common Objects (e.g., candle), People (e.g., doctor), Structures

Table 2. Mean demographic information, naming accuracy percentages, and naming error percentages by diagnostic subtype.

	N	Age	Education	Sex	Noun Accuracy	Noun Phon. Errors	Noun Semantic Errors	Noun Circ. Errors	Verb Accuracy	Verb Phon. Errors	Verb Semantic Errors	Verb Circ. Errors
lvPPA	10	72.2 (5.8)	16.0 (2.8)	7 F	67.9 (17.4)	2.8 (2.6)	5.4	3.3	61.1	1.2	7.1	4.4
		57–77	12–20	3 M			(3.5)	(3.8)	(19.2)	(0.7)	(1.8)	(6.9)
svPPA	5	67.4 (7.7)	17.2 (1.8)	5 F	55.4 (10.8)	1.0 (0.5)	7.1	8.5	48.3	0.7	7.9	9.0
		55–76	16–20				(1.9)	(7.8)	(20.3)	(0.7)	(3.5)	(7.7)
nfvPPA	8	71.6 (5.7)	16.4 (2.9)	5 F	78.3 (24.5)	8.8 (13.3)	2.1	0.7	69.8	3.0	5.5	0.2
		63–79	12–20	3 M			(1.3)	(0.7)	(26.5)	(3.1)	(3.1)	(0.7)
uPPA	12	70.5 (7.9)	17.0 (1.3)	7 F	63.0 (25.4)	4.2 (5.4)	6.9	2.5	50.7	2.4	7.4	2.9
		55–80	15–19	5 M			(4.3)	(5.6)	(28.6)	(3.1)	(4.2)	(3.8)
AD	4	72.0 (14.0)	16.0 (1.6)	1 F	61.3 (38.3)	1.0 (0.4)	7.4	1.1	60.1	0	6.3	0.6
		58–86	14–18	3 M			(3.8)	(0.8)	(40.0)	(0)	(5.3)	(1.3)

Numbers in parentheses are standard deviations. The range is also included for Age and Education. lvPPA: logopenic variant.
svPPA: semantic variant; nfvPPA: nonfluent/agrammatic variant; uPPA: unclassifiable primary progressive aphasia.
AD: Alzheimer's disease; Phon.: Phonological; Circ.: Circumlocution.

(e.g., bridge), Tools (e.g., hammer), and Vehicles (e.g., truck). Verb categories included Object Action (e.g., *lifting*), Body Action (e.g., *clapping*), Body Action Motion (e.g., *marching*), and Mental State (e.g., *thinking*).

The target nouns had a mean CELEX frequency per million of 27.23 (SD = 46.29; Baayen et al., 1995), a mean syllable length of 1.76 (SD = 0.80), a mean phoneme length of 4.79 (SD = 1.79), and a mean letter length of 5.74 (SD = 1.90). The target verbs had a mean CELEX frequency per million of 27.93 (SD = 40.34), a mean syllable length of 2.13 (SD = 0.36), a mean phoneme length of 5.59 (SD = 0.95), and a mean letter length of 7.36 (SD = 0.91). The target verbs included 46 that were intransitive and 70 that were transitive. The frequencies of the target nouns and verbs were not significantly different, $t(398) = 0.14$, $p = .887$, while the target verbs (in inflected form) were significantly longer than the target nouns in terms of syllables, phonemes, and letters (all p's $< .001$).

2.3. Procedure

Using E-Prime 3, each picture was presented on a computer screen for 10 seconds. Participants were instructed to name each picture while it appeared on the screen. There were three practice trials for both nouns and verbs. The items were presented in the same order for each participant. Not counting breaks, the total experiment time was 48 minutes for nouns and 20 minutes for verbs.

Nouns and verbs were tested in separate assessment sessions, which were between 1.5 and 3 weeks apart. Nouns were tested in the first session, and the same examiner conducted both sessions.

2.4. Naming error coding

The naming responses were transcribed in IPA and then independently coded by two raters. Any coding discrepancies between the two raters were resolved by a third rater. A distorted phoneme that was still recognizable as the target phoneme was considered correct.

For verbs, the root and inflected forms of the verb were accepted as correct responses. One participant with nfvPPA was excluded from the verb analyses because her most frequent type of response was a correct root combined with an incomplete suffix (e.g., *eating*: "/iti/").

If the participant's final response was incorrect, it was coded as one of the following eleven error codes: semantic (e.g., *fan*: "cooler"; *dog*: "animal"); circumlocution (e.g., *binoculars*: "something to see long distance"); phonological (including both word and nonword responses that included at least 50% of the phonemes in the target word; e.g., *razor*: "raisin"; *frog*: "/flug/"); semantic/phonological real word (e.g., *cat*: "rat"); semantic/phonological nonword (e.g., *tomato*: "/kjukəm/"); inflectional (e.g., *table*: "tables"); derivational (e.g., *calculator*: "calculate"); part of object (e.g., *finger*: "nail"); part of scene (e.g., *kitchen*: "cabinet"); visual (e.g., *film*: "paper towels"); other. The "other" code included seven types of responses: empty speech (e.g., "here I go again"); no response; "I don't know"; unrelated word (e.g., *chair*: "shoe"); phonologically-unrelated nonword (e.g., *lighthouse*: "/ɛmaɪ/"); negation of correct response (e.g., *rake*: "that's not a rake"); ambiguous response (e.g., *goat*: "goat or cow").

2.5. Naming error statistical analysis

SPSS 28 was utilized for statistical analyses. For each participant, each type of naming error was calculated as a proportion of all naming trials, and the proportions were arcsin transformed to control for possible violations of the normality assumption. Following arcsin transformation, normality was verified through inspection of Normal Q-Q plots for each diagnostic subtype.

Statistical analyses focused on three error types: phonological, semantic, and circumlocution errors. Separately for nouns and verbs, repeated-measures ANCOVA was used to examine the interaction between Error Type and Diagnostic Subtype. The Greenhouse-Geisser correction was utilized when Mauchly's Test indicated that sphericity was not present. Age, Education, Sex, Symptom Duration, and BDAE Severity Rating were entered as covariates. The Šidák correction for multiple comparisons was utilized for follow-up analyses.

Using Cohen's *f*, power for the Error Type x Diagnostic Subtype interaction was 85% for nouns and 79% for verbs. For the smallest diagnostic subgroup (AD), using Cohen's d_z, power for the most important comparison (phonological errors vs. semantic errors) was 97% for nouns and 74% for verbs (before correction for multiple comparisons).

2.6. Image acquisition and processing

Twenty of the participants had a brain MRI in a 3T scanner, including T1 high- resolution-weighted images (T1-WI). The image parameters were: sagittal orientation, original matrix 170×170, 256 slices, voxel size $1 \times 1 \times 1.2$ mm, TR/TE 6700/3.1 ms. Associated focal lesions and visually detectable artifacts were excluded by visual inspection. The images were automatically segmented and post-processed in a public web-based service for multi-contrast imaging segmentation and quantification, the MRICloud (http://www.MRICloud.org; Mori et al., 2016). Briefly, in MRICloud, the process for segmenting the T1-WI, used for volumetric analysis, involves orientation and homogeneity correction; two-level brain segmentation (skull-stripping, then whole brain); image mapping based on a sequence of linear, non-linear algorithms, and Large Deformation Diffeomorphic Mapping (LDDMM); and a final step of multi-atlas labeling fusion (MALF), adjusted by PICSL (Tang et al., 2013). The multi-atlas set used, developed at Johns Hopkins University, in MNI space, is a set of 26 adult brains, age ranging from 50 to 90 years old, in which a parcellation map (PM) of 283 structures was defined and manually adjusted in 3D. The automatically measured volumes within the 283 structures provide information about each subject's anatomical status.

2.7. MRI statistical analysis

The MRI analyses focused on ten grey matter ROIs in the left hemisphere. The ROIs included the following areas: inferior frontal gyrus, insula, supramarginal gyrus, angular gyrus, superior temporal pole, middle temporal pole, superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, and the fusiform gyrus. Nine of these ROIs were selected because they have been associated with semantic or phonological naming errors in PPA (Bruffaerts et al., 2020; Catricala et al., 2020; Petroi et al., 2020). While the inferior

frontal gyrus has not been associated with semantic or phonological naming errors in PPA, it was also included because it is a prominent area of atrophy in nfvPPA (Grossman et al., 1996). These ten areas have also been implicated in language processing in studies of stroke and unimpaired control participants (Binder et al., 1997; Binney et al., 2010; Hickok & Poeppel, 2004, 2007; Indefrey, 2011; Indefrey & Levelt, 2004; T. T. Rogers et al., 2006). The ROIs were normalized for brain size by dividing each ROI volume by the participant's intracranial volume.

The volume of each ROI was transformed into a z-score based on data from the control participants. Separately for nouns and verbs, Pearson correlations were then computed between the z-score for each ROI and the proportion of phonological, semantic, and circumlocution errors. For each type of error, we corrected for multiple comparisons, using Bonferroni correction for 10 comparisons and an alpha level of .05. The corrected alpha was .005.

3. Results

3.1. Noun naming errors

For nouns, the only covariate that interacted with Error Type was BDAE Severity, $F(2, 58) = 11.76$, $p < .001$; all other p's > .10.

The Error Type x Diagnostic Subtype interaction was significant, $F(8, 58) = 3.89$, $p = .001$. Follow-up analyses compared the three types of errors in two ways: within each diagnostic subtype and between diagnostic subtypes. Within svPPA, semantic errors were significantly greater than phonological errors, while circumlocution errors were not significantly different from phonological or semantic errors (see Figure 1). Within both uPPA and AD, semantic errors were significantly greater than both phonological and circumlocution errors, while phonological and circumlocution errors were not significantly different. Within nfvPPA, phonological errors were significantly greater than circumlocution errors, while semantic errors were not significantly different from phonological or circumlocution errors. Within lvPPA, there were no significant differences between error types (all p's > .05).

In between-subtype analyses, the proportion of semantic errors was significantly greater for participants with svPPA and uPPA, compared to those with nfvPPA (see Figure 2), and the proportion of circumlocution errors was significantly greater in svPPA, compared to nfvPPA. There were no significant differences across subtypes in the proportion of phonological errors, and there were no significant differences involving the lvPPA or AD subgroups (all p's > .05).

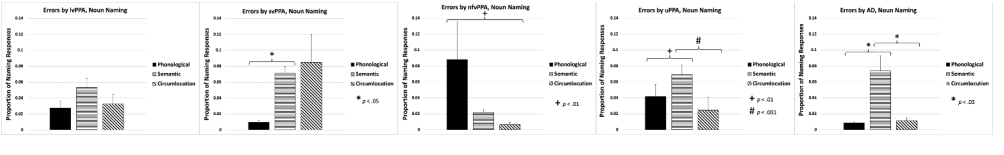

Figure 1. Comparison of noun naming errors within each diagnostic subtype. For this figure and those that follow, the means and standard errors are the original untransformed values, rather than the arcsin transformations.

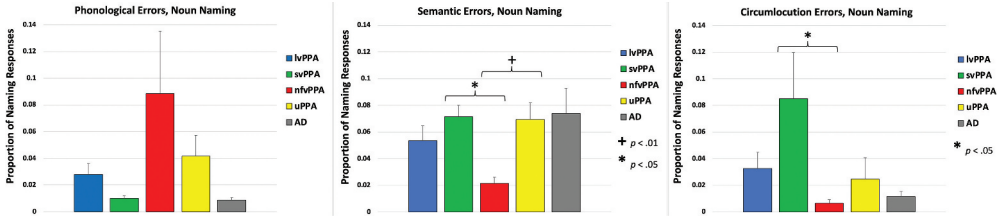

Figure 2. Comparison of noun naming errors between each diagnostic subtype.

3.2. Verb naming errors

For verbs, none of the covariates interacted with Error Type (all *p*'s > .10).

The Error Type x Diagnostic Subtype interaction was significant, $F(8, 56) = 3.70$, $p = .004$. Within lvPPA, semantic errors were significantly greater than phonological errors, while circumlocution errors were not significantly different from phonological or semantic errors (see Figure 3). Within svPPA, both semantic and circumlocution errors were significantly greater than phonological errors, while semantic and circumlocution errors were not significantly different. Within uPPA and AD, semantic errors were significantly greater than phonological and circumlocution errors, while phonological and circumlocution errors were not significantly different. Within nfvPPA, semantic and phonological errors were significantly greater than circumlocution errors, while semantic and phonological errors were not significantly different.

In between-subtype analyses, the proportion of phonological errors was significantly greater in nfvPPA, compared to AD (see Figure 4). Furthermore, the proportion of circumlocution errors was significantly greater in svPPA, compared to nfvPPA. There were no significant differences across subtypes in the proportion of semantic errors, and there were no significant differences involving the lvPPA or uPPA subgroups (all *p*'s > .05).

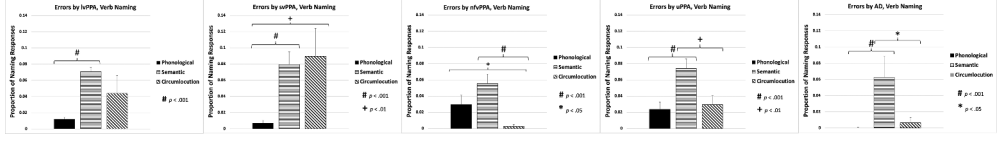

Figure 3. Comparison of verb naming errors within each diagnostic subtype.

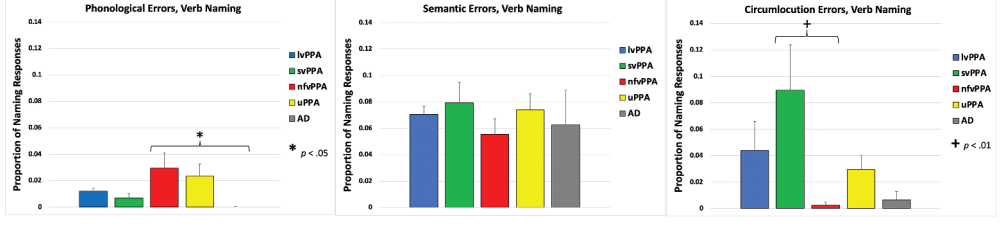

Figure 4. Comparison of verb naming errors between each diagnostic subtype.

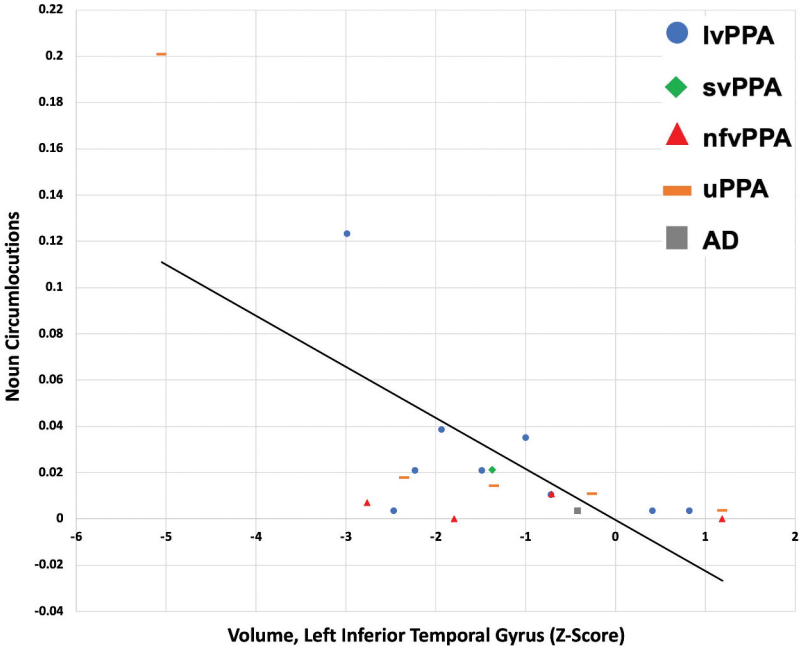

Figure 5. Correlation between the proportion of noun circumlocution errors and volume of the left inferior temporal gyrus.

3.3. Correlations between brain volume and naming errors

For nouns, there were significant correlations between the proportion of circumlocution errors and volume in the left inferior temporal gyrus [$r(18) = -.722$, $p < .001$; see Figure 5] and volume in the left fusiform gyrus, $r(18) = -.641$, $p = .002$ (see Figure 6). For nouns, there were no significant correlations between brain volume and phonological or semantic errors (all p's $> .005$).

For verbs, there were significant correlations between semantic errors and volume in the left superior temporal pole, [$r(17) = -.623$, $p = .004$; see Figure 7], and between circumlocution errors and volume in the left insula, $r(17) = -.673$, $p = .002$ (see Figure 8). For verbs, there were no significant correlations between brain volume and phonological errors (all p's $> .005$).

3.4. Low MMSE scores

A few participants had MMSE scores lower than 10 (SV3, UPPA9, AD3). None of these participants were scanned. When these participants were removed from the behavioral analyses, the overall pattern of results was similar, with only a few changes in the significant effects. For nouns, within svPPA circumlocution errors were significantly greater than phonological errors after SV3 was removed ($p = .04$). Within AD, after AD3 was removed the reduction of statistical power resulted in only one remaining significant effect for this subgroup: for verbs, semantic errors were significantly greater than phonological errors ($p < .001$).

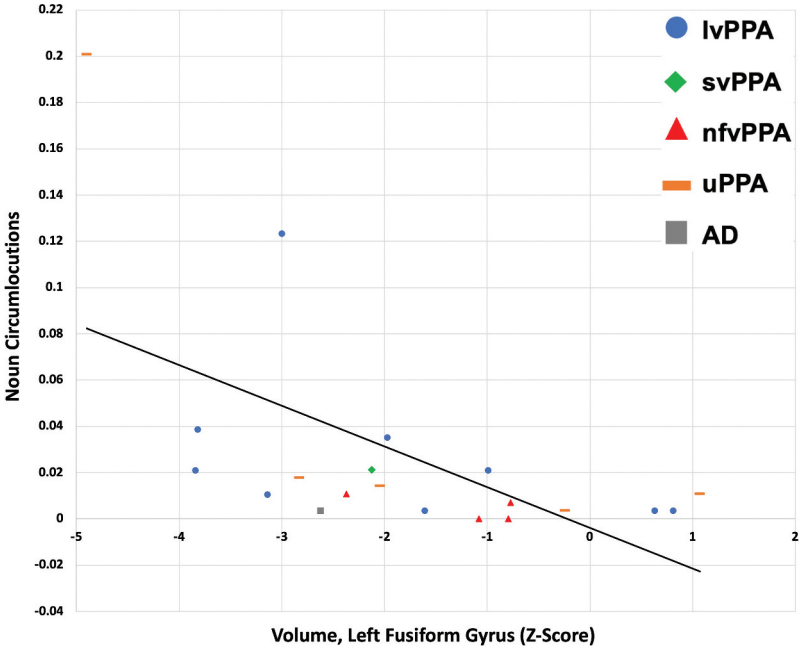

Figure 6. Correlation between the proportion of noun circumlocution errors and volume of the left fusiform gyrus.

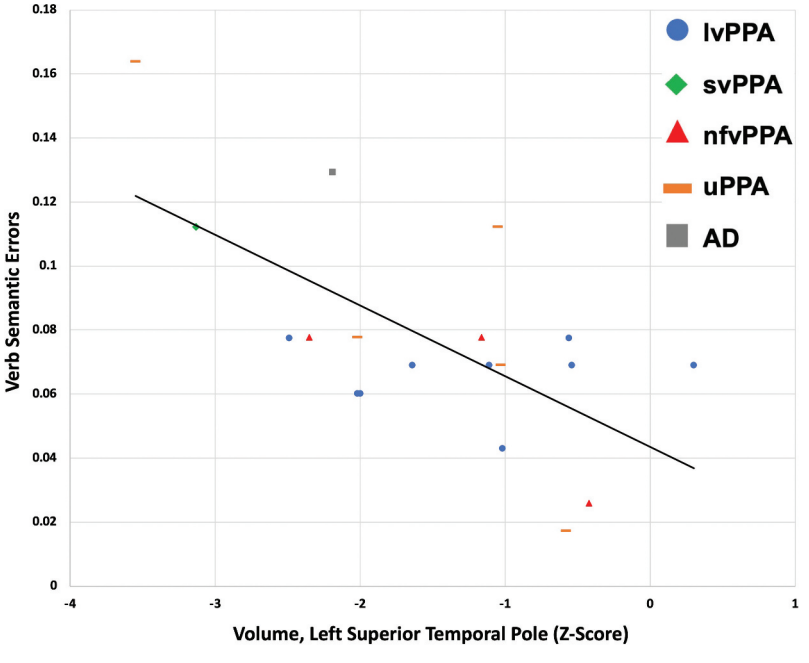

Figure 7. Correlation between the proportion of verb semantic errors and volume of the left superior temporal pole.

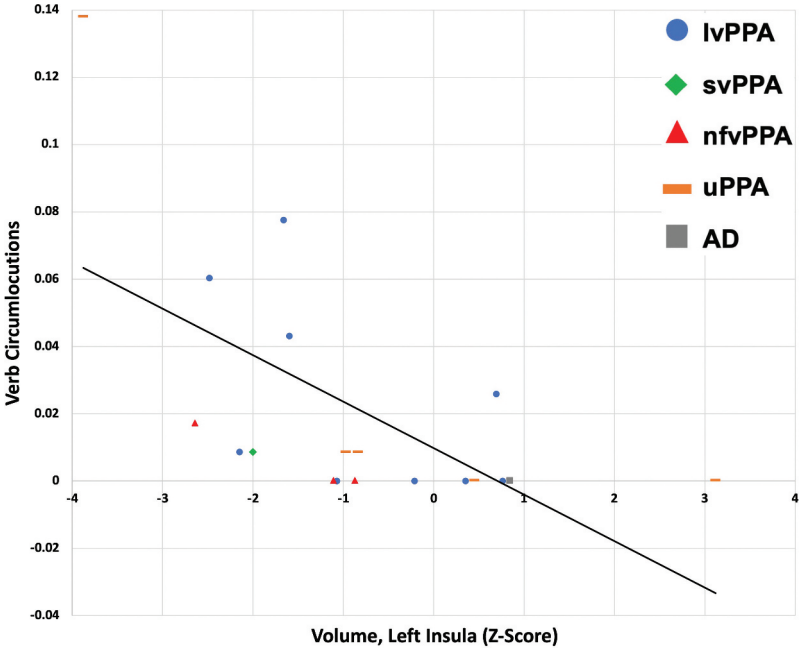

Figure 8. Correlation between the proportion of verb circumlocution errors and volume of the left insula.

4. Discussion

In the current study, we examined the pattern of naming errors for nouns and verbs in all three subtypes of PPA, as well as unclassifiable PPA and typical AD. Statistical analyses focused on three common error types: phonological, semantic, and circumlocution errors. We predicted that phonological errors would be significantly greater than semantic errors in lvPPA and nfvPPA; an alternative hypothesis for lvPPA was that both phonological and semantic errors would be common in this subtype. For nfvPPA, an alternative hypothesis was that both phonological and semantic naming errors would be common for verbs, while phonological errors would be common for nouns.

In svPPA and typical AD, we predicted that semantic errors would be significantly greater than phonological errors. In uPPA, both types of errors were expected to be common.

In the three subtypes of PPA, only svPPA was completely consistent with our predictions, with the proportion of semantic errors being significantly greater than the proportion of phonological errors for both nouns and verbs in this subtype. This pattern also occurred in uPPA and typical AD.

In lvPPA, we predicted that phonological errors would be more common than semantic errors, or, alternatively, that phonological and semantic errors would both be common in this subtype. While the pattern of errors for nouns was consistent with the alternative prediction, for verbs the proportion of phonological errors was significantly lower than the proportion of semantic errors. This pattern could be related to the presence of grammatical impairment or conceptual-semantic impairment for actions in some participants with lvPPA (see Meyer et al., 2020, 2024). While no participants with lvPPA had

substantial impairment of grammatical production, 7 had conceptual-semantic impairment for actions, as indicated by their impaired performance on the 3-picture version of K&D (see Table 1). However, there were also 7 participants with lvPPA who had conceptual-semantic impairment for objects, as indicated by their impaired performance on the 3-picture version of P&PT (see Table 1), and 5 lvPPA participants were impaired on both tasks. Furthermore, mean accuracy on these tasks was similar in lvPPA (P&PT: $M = 0.91$, $SD = 0.08$; K&D: $M = 0.90$, $SD = 0.09$). Thus, the source of the different naming error patterns for nouns and verbs in lvPPA remains unclear.

In nfvPPA, we predicted that phonological errors would be more common than semantic errors for nouns. The numerical pattern was consistent with this prediction, but there was a large amount of variability for phonological errors in nfvPPA, and the difference between error types was not significant. For verbs, the pattern of errors was consistent with the alternative prediction that both error types would be common for verbs.

In between-subtype analyses, the proportion of semantic errors for nouns was significantly greater for participants with uPPA and svPPA, compared to those with nfvPPA; the latter finding is consistent with Migliaccio et al. (2016). On the other hand, the noun findings are also somewhat inconsistent with Migliaccio et al. (2016), who found that phonological errors were significantly greater in nfvPPA, compared to both svPPA and lvPPA. This effect was not significant in the current study, but the numerical pattern was similar, with a large amount of variability in the noun naming responses of the nfvPPA subgroup. This variability may be related to the heterogeneity of the nfvPPA subtype (see Gorno-Tempini et al., 2011; Josephs et al., 2006; M. Mesulam et al., 2014; Meyer et al., 2020).

For verbs, the proportion of phonological errors was significantly greater in nfvPPA, compared to AD. In addition, the proportion of circumlocution errors for verbs was significantly greater in svPPA, compared to nfvPPA. The latter finding is consistent with previous findings of a greater proportion of circumlocution errors for nouns in svPPA, compared to nfvPPA (Budd et al., 2010; Bruffaerts et al., 2020).

We also examined the relationships between naming errors and brain volume within ten left hemisphere ROIs. We predicted that phonological errors would be associated with lower volume in areas such as the superior temporal gyrus, middle temporal gyrus, and supramarginal gyrus (Catricala et al., 2020; Petroi et al., 2020). Furthermore, we predicted that semantic errors would be associated with lower volume in areas such as the temporal pole, inferior temporal gyrus, middle temporal gyrus, fusiform gyrus, and insula (Bruffaerts et al., 2020; Catricala et al., 2020).

For nouns, the proportion of circumlocution errors was negatively correlated with volume in the left inferior temporal gyrus and the left fusiform gyrus. Atrophy in these areas has previously been associated with naming impairment (Amici et al., 2007; Migliaccio et al., 2016; Race et al., 2013). Catricala et al. (2020), who classified circumlocutions as a type of semantic error, found that hypometabolism in these areas was associated with semantic errors for nouns. In the current study, participants with svPPA had the highest proportion of circumlocution errors (see Figure 2). However, as can be seen in Figures 5 and 6, one participant with lvPPA (LV1) and one participant with uPPA (UPPA2) had high proportions of circumlocution errors and low volume in both of these areas, indicating that the relationship between these variables is not limited to individuals with svPPA. These two participants were outliers in terms of their proportion of noun circumlocution errors, and the correlations were not significant

when the two participants were removed from the analyses. However, neither participant was an outlier in terms of their volume in these two areas or their demographic characteristics, including age, education, symptom duration, and BDAE Severity. Therefore, there is no strong evidence that these participants are not representative of the population of individuals with PPA.

For verbs, there was a significant negative correlation between semantic errors and volume in the left superior temporal pole (LSTP). The temporal pole has been associated with conceptual-semantic processing (Binney et al., 2010; Lambon Ralph et al., 2010; Migliaccio et al., 2016; Mummery et al., 2000; Rogalski et al., 2011; T. T. Rogers et al., 2006), and it becomes atrophied in svPPA (Gorno-Tempini et al., 2004, 2011; Mummery et al., 2000). As the syndrome progresses, individuals who have lvPPA or nfvPPA may also develop atrophy in the temporal pole (Leyton et al., 2019). In the current study, 3 out of 9 participants with lvPPA and 1 out of 3 participants with nfvPPA who were scanned had LSTP volume that was at least 2 SDs below the control mean (see Figure 7), suggesting that these 4 participants may have been developing conceptual-semantic impairment. In terms of their behavioral performance on tests of object knowledge (P&PT) and action knowledge (K&D), 2 of these 4 participants (LV10 and NFV5) were unimpaired on both tasks (see Table 1), while LV1 was impaired on K&D but not P&PT, and LV7 was impaired on both tasks.

In addition, for verbs there was a significant negative correlation between the proportion of circumlocution errors and volume in the left insula. Catricala et al. (2020) found that the left insula was associated with semantic errors (including circumlocutions) for nouns. In the current study, there was a negative correlation between circumlocution errors for nouns and volume in the left insula that approached significance ($p = .012$). Thus, reduced volume in the left insula may contribute to circumlocution errors for both nouns and verbs.

The findings of this study suggest that semantic naming errors may be common for both nouns and verbs in all three variants of PPA. The verb findings are novel, as the current study is the first to examine phonological and semantic picture-naming error patterns for verbs in PPA, while the noun findings are consistent with previous studies of noun naming errors in PPA (Budd et al., 2010; Catricala et al., 2020). In lvPPA and nfvPPA, semantic naming errors may be due to atrophy that has spread to brain areas that are associated with conceptual-semantic processing (Leyton et al., 2019), resulting in semantic impairment (Leyton et al., 2013; Roncero et al., 2020). Another possibility is that semantic naming errors in these variants are due to impairment of the phonological output lexicon (Caramazza & Hillis, 1990). The findings of the current study suggest that the former cause of semantic errors may be more common in lvPPA than in nfvPPA. In lvPPA, 9 out of 10 participants were impaired on at least one test of conceptual-semantic processing (the 3-Picture version of P&PT and/or the 3-Picture version of K&D). In contrast, only 3 out of 8 participants with nfvPPA were impaired on either of these tasks, and symptom duration in months was similar in these two variants (lvPPA: $M = 49.1$; $SD = 20.8$; nfvPPA: $M = 43.0$; $SD = 25.9$).

The findings of the current study also indicate that phonological naming errors for nouns and verbs in lvPPA are not more common than semantic naming errors, which are not specifically addressed in the criteria for lvPPA. Furthermore, phonological naming errors are not significantly more common in lvPPA, compared to svPPA, nfvPPA, uPPA, or typical AD. However, the proportion of phonological errors in lvPPA may be task-

dependent (Croot et al., 2012; Petroi et al., 2014, 2021). For example, Croot et al. reported that only one participant out of 14 made phonological errors during a clinical assessment, but five of these participants made phonological errors during a clinical interview, and 10 of these participants made phonological errors during a polysyllabic word repetition task. Petroi et al. (2021) argued that the proportion of phonological errors is task-dependent because individuals with lvPPA can suppress phonological errors by reducing output on some types of tasks, including naming and picture description. In a naming task, a participant could choose not to respond if he or she is uncertain regarding the accuracy of a potential response. However, this type of response strategy could presumably be used to reduce additional error types besides phonological errors, including semantic errors. In the current study, we found that participants with lvPPA made significantly more semantic errors than phonological errors for verbs. Therefore, a reduced output explanation does not appear to account for the lvPPA participants' relatively low proportion of phonological naming errors. Another possibility is that these participants have an impaired phonological output lexicon, which results in semantic naming errors (Caramazza & Hillis, 1990).

While the criterion of "speech (phonologic) errors in spontaneous speech and naming" is not required for the diagnosis of all lvPPA cases, it does play a role in the diagnosis of many lvPPA cases. For example, in the current study, 7 out of 10 participants with lvPPA were impaired on the 3-Picture version of P&PT, indicating impaired object knowledge. As a result, these participants did not meet the criterion of "spared single-word comprehension and object knowledge". Therefore, these participants had to meet the criteria of "speech (phonologic) errors in spontaneous speech and naming, spared motor speech, and absence of frank agrammatism" in order to be diagnosed with lvPPA.

Limitations of the current study include the relatively small sample size for some subgroups (e.g., 5 with svPPA and 4 with AD). Another limitation is that only 20 participants were scanned, which prevented a comparison of error-volume relationships across diagnostic subtypes from being feasible. In addition, the 10-second time limit that was utilized for naming may have affected the types of errors that were measured. For example, the proportion of circumlocution errors was low in nfvPPA. Given that these individuals typically have a reduced speech rate, the proportion of circumlocution errors may have been higher in this variant if they had been given more time to respond. Finally, the majority of the participants in the current study were White and native speakers of English.

In conclusion, the results of the current study suggest that phonological errors during a picture-naming task are not preferentially associated with the logopenic variant. While the number of participants with lvPPA was only 10 in the current study, this finding is consistent with all previous studies of naming error patterns in PPA (Budd et al., 2010, Bruffaerts et al., 2020; Catricala et al., 2020; Migliaccio et al., 2016). A different possibility is that phonological errors during word repetition and reading tasks are associated with lvPPA (Croot et al., 2012; Petroi et al., 2014, 2021). However, the proportions of phonological and semantic errors on these tasks have not been compared in lvPPA, and phonological and semantic error patterns on these tasks have not been compared across lvPPA, svPPA, and nfvPPA. Thus, additional research will be needed to evaluate this hypothesis. If the hypothesis is confirmed, then the criteria for lvPPA could be modified, with the criterion of "speech (phonologic) errors in spontaneous speech and naming" being revised to specify the appropriate tasks.

Disclosure statement

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