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Sentence repetition span in primary progressive aphasia and Alzheimer's disease: Insights from preliminary results

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Primary Progressive Aphasia (PPA) is a neurocognitive disorder ascribed to cortical atrophy impacting language abilities. It is widely classified into three main variants, logopenic PPA (lvPPA), the semantic variant of PPA (svPPA), and the non-fluent PPA (nfvPPA), showing different impairment patterns across variants. However, in the early phases of PPA, it is not always easy to dissociate different PPA variants and distinguish PPA from other neurodegenerative disorders. One characteristic language symptom that seems to be a distinguishing factor of PPA, especially the logopenic variant, is impaired sentence repetition. Nonetheless, studies examining sentence repetition in PPA, and Alzheimer's disease (AD) more broadly, have resulted in mixed findings. To better understand the working memory-intensive nature of sentence repetition deficits, we designed a sentence repetition span task. We seek to understand (i) whether three diagnostic groups (lvPPA, svPPA, and AD) encounter greater sentence repetition difficulties than the controls, and (ii) whether using a span task design, in which the number of content words increases as the span length increases, would help dissociate PPA variants from AD type dementia. In this study, we administered a sentence repetition span task to four groups of French-speaking individuals with lvPPA (n = 14), svPPA (n = 5), and with AD (n = 13), and their age-matched healthy controls (n = 61). The results showed that all three diagnostic groups (lvPPA, svPPA, and AD) performed equally poorly compared to the controls on the repetition span task virtually in all measures (i.e., sentence span, the number of content words, and the number of omission and substitution errors). One intriguing finding was that the lvPPA group produced an exalted number of phonological errors during repeating sentences, while this type of error was somewhat moderate in the svPPA group and only minimal in the AD group. We conclude that the sentence repetition difficulty in PPA and AD should be modulated by working memory capacity, as our participants undoubtedly demonstrated greater difficulty as

the span length increased. However, we note that working memory-intensive sentence repetition deficits based on the number of content words might not reveal critical diagnostic differences between the neurodegenerative groups.

KEYWORDS

primary progressive aphasia, short-term memory, sentence repetition span task, Alzheimer's disease (AD), sentence repetition

Introduction

Primary Progressive Aphasia (PPA) is referred to as 'focal' dementia caused by progressive atrophy or neurodegeneration impacting language network areas of the brain (Mesulam, 2001, 2013). PPA is a progressive form of aphasia, meaning that it is mainly characterized by 'salient' language problems, and these problems become more severe as the disease progresses over time (Mesulam et al., 2014). PPA can be caused by different underlying pathologies such as *amyloidopathy* associated with Alzheimer's disease (AD), *tauopathy* associated with some frontotemporal lobar degeneration or *alpha-synucleinopathy* associated with some subcortical neurocognitive disorders like Parkinson's or Lewy bodies disease. Unlike in AD, rather isolated language problems surface in PPA. However, depending on the locus of brain neuropathology, individuals with PPA might show different language impairment profiles (Gorno-Tempini et al., 2011). According to the widely accepted (Gorno-Tempini et al., 2011) classification, three main variants of PPA have been described: the non-fluent variant of PPA (nfvPPA) with prominent non-fluent speech and wide range of grammatical errors; the logopenic variant of PPA (lvPPA) exhibiting moderate to severe word finding difficulties and impaired sentence repetition; and the semantic variant (svPPA) with often severely impaired naming and word comprehension difficulties. However, it is important to note that several PPA cases have then been reported to show mixed impairments, not fitting in well with a single variant classification (see e.g., Vandenberghe, 2016).

Certain language-related difficulties, including naming and word finding problems, are often common symptoms, especially in frontotemporal lobar degeneration; however, rather isolated and progressive language-related symptoms dissociate PPA from other degenerative syndromes (Neary et al., 1998). Individuals with nfvPPA are best characterized by the presence of simplified grammatical structure in speech output, and reduced complexity in grammatical processing. Single word comprehension and object naming are often relatively spared (Thompson et al., 1997; Rohrer et al., 2010b). Cortical atrophy is often found to be extensive in the left inferior frontal gyrus and in the insular lobe (Grossman, 2012). Symptoms in svPPA are often characterized by a settled pattern of anomia with associated atrophy in anterior sectors of middle and superior temporal gyri extending to other anterior parts of the perisylvian areas (Mesulam et al., 2009). Although salient deficits in all PPA phenotypes are often observed in the language, other cognitive difficulties involving executive functioning or working memory may arise as the severity of symptoms increases over time (see Macoir et al., 2017b). Reduced visual and semantic memory performances are more often found in svPPA as compared to different PPA variants, while verbal memory performance is rather more commonly impaired across all phenotypes (Gorno-Tempini et al., 2004). This is clinically quite relevant because verbal memory in the early stages of PPA is often found impaired compared to AD, dissociating the two syndromes, while either the reverse happens or no strong dissociations are found for visual memory (Gorno-Tempini et al., 2004; Foxe et al., 2013).

While having said that cognitive tasks can be informative clinical markers for PPA, it is often difficult to differentiate certain PPA symptoms from those found in AD or other neurocognitive disorders without salient language impairments. Although AD type neuropathology can be the underlying cause of most PPA variants, this type of pathology seems to be slightly more often associated with the logopenic variant (Leyton et al., 2011). Therefore, in the early stages of the disease, it is oftentimes hard to provide a clear lvPPA diagnosis since symptoms may commence with somewhat isolated word finding difficulties but then evolve into an AD type global neurocognitive disorder. As briefly mentioned, a characteristic symptom in lvPPA is an inability to repeat sentence stimulus. Henry and Gorno-Tempini (2010) report that people with lvPPA experience sentence repetition deficits especially when the compositional probability is low, and that semantically loaded content words are likely to be omitted or substituted. For instance, a person with lvPPA has been reported to repeat the sentence "*The valuable watch was missing*" as "*The watch was gone*" (Henry and Gorno-Tempini, 2010).

An associated reason for impaired repetition ability in PPA is thought to be disrupted verbal short-term memory (Rohrer et al., 2010a). This is not surprising at all since a large portion of lvPPA diagnosed cases demonstrate poor short-term memory performances accompanied by atrophy in the left temporo-parietal regions (Gorno-Tempini et al., 2004; Rohrer et al., 2010a; Leyton et al., 2012; Foxe et al., 2016). These findings seem

compatible with Baddeley's working memory model (Baddeley and Hitch, 1974; Baddeley, 2003), which holds that verbal and visual information are separately stored for a temporary duration in the "phonological loop" and "visual sketchpad" and that a central-executive component subserves the memory system with a shared pool of executive functions during processing information. These memory components have been conventionally examined using "span tasks", which is based on the idea that increasing complexity in stimulus manipulation reaches a maximum span at which individuals cannot retain stimulus accurately in memory anymore. There have been several different adaptations of span tasks but for our purpose the most relevant ones would be "sentence span" (see Just and Carpenter, 1992) or digit span tasks (Wechsler, 2008) in which individuals read or repeat increasing length of sentences or digits, respectively. Scholars often distinguish tasks that require forward repetition as "short-term memory" while backward modality would tap into "working memory". Phonological short-term memory tasks have in fact been associated with several regions at the junction of the posterior part of the temporal lobe and the parietal lobe including the supramarginal gyrus, the planum temporale, and the posterior part of the superior temporal sulcus (see Jacquemot and Scott, 2006; Hickok and Poeppel, 2007; Miller et al., 2021). It is therefore logical to assume that in lvPPA, these regions might be affected due to ongoing atrophy, leading to difficulties in processes following the perception of speech input that enable the retainment of verbal information in memory. This is compatible with Foxe et al.'s (2020) findings, who using a set of forward spatial and digit span tasks, examined three variants of PPA in comparison to AD and healthy controls. The authors found that lvPPA and AD groups showed impaired recall in spatial span while all groups except for svPPA showed impaired performance in digit span tasks. The authors found strong correlations between impaired recall and gray matter intensity decrease in temporo-parietal regions extending into occipital regions.

It is quite remarkable that PPA is a very heterogeneous syndrome, and some cases have been reported to exhibit blended language symptoms fitting in with more than one PPA variant criteria. There have been volumes of research attempting to identify relevant clinical markers of PPA dissociating different phenotypes from each other, and/or distinguishing PPA from other neurocognitive disorders (see Grossman, 2014 for a review). One highlighted clinical marker proposed for the classification of lvPPA from other phenotypes seems to be the presence of repetition impairments (Mesulam and Weintraub, 2014; Wicklund et al., 2014). However, there seem to be some inconsistencies in results from studies that looked at sentence repetition in PPA and AD. Leyton et al. (2014) report that both groups of PPA and AD patients they tested with diagnostic sentence repetition tasks failed to perform at control participant norms, while the authors found no significant differences between groups, suggesting that repetition errors in PPA and AD do not necessarily dissociate these syndromes from each other. However, results from Meyer et al. (2015) showed a pattern in which, unlike in AD, their lvPPA patients performed less accurately in repeating both meaningful sentences/words and pseudowords as compared to healthy controls. Lukic et al. (2019) examined the repetition of meaningful and non-meaningful phrases in a variety of length in groups of English-speaking individuals suffering from lvPPA, nfvPPA, and svPPA as compared to a control group. The authors' findings have demonstrated that their people with lvPPA were impaired in the repetition of all types of phrases disregarding length and meaningfulness, while people with nfvPPA and svPPA were shown to have difficulty in repeating long and meaningless phrases.

Hohlbaum et al. (2018) conducted a longitudinal investigation on the dissolution of sentence repetition ability in a German-speaking group of people with lvPPA. A large portion of the individuals tested showed worsening phonological errors and the omission of words in time over re-test intervals. The authors used sentences with different syntactic structures including word order variation, yes/no questions, and different forms of tense marking. The authors conclude that the omission of words leads to syntactic problems. Beales et al. (2019) studied groups of lvPPA, svPPA, and AD patients speaking English with a sentence repetition task adapted from Hohlbaum et al. (2018) and a number of complementary digit span tasks. The authors report that people with svPPA performed better than lvPPA and AD in their response accuracy on sentence repetition; however, the authors found no significant differences between people with lvPPA and AD. Beales et al. (2019) found significant correlations between their participants' group performances on sentence repetition and digit span tasks, contemplating that a relationship between sentence repletion and working memory indeed exists. Seckin et al. (2022), using word reading and repetition tasks (the Repeat and Point Test), studied groups of German-speaking people with three variants of PPA. Their findings have shown that repetition task outcomes might be useful in dissociating people with svPPA from lvPPA and nfvPPA, as people with svPPA performed more accurately in repeating words over people with lvPPA and nfvPPA. The latter two groups performed poorly and showed no group differences.

Research on sentence repetition deficits in PPA has shown mixed results, which is more likely due to different stimulus materials, varying numbers of individuals with PPA, a varying severity of symptoms, and different task designs used across different studies. One certain commonality is that people with lvPPA are likely to experience relatively severe sentence repetition difficulty. However, whether this profound deficit in repetition dissociates lvPPA from other neurocognitive disorders requires further understanding. While a number of authors found worse performance in lvPPA as compared to AD (Meyer et al., 2015), or compared to semantic dementia (Beales et al., 2019; Seckin et al., 2022), suggesting that sentence

repetition deficits constitute a reliable clinical marker, others found equally affecated repetition ability in both AD and PPA populations (e.g., see Leyton et al., 2014). Interestingly a number of authors have underlined the impact of stimulus length linking this impairment with diminished phonological short-term capacity in PPA (Hohlbaum et al., 2018; Beales et al., 2019; Lukic et al., 2019). Since a majority of sentence repetition tasks manipulated syntactic variables (see for intance, Hohlbaum et al., 2018), further understanding on the limits of sentence repetition capacity in PPA is warranted. The most viable way to test this would be assessing sentence repetition ability within a span task in which sentence length and number of semantically loaded content words systematically vary.

The current study

In the current study we explore how French-speaking individuals with PPA, both the semantic and logopenic variants, experience sentence repetition difficulties as compared to broader neurocognitive disorders in AD when sentences are presented within a span task design. The available research on French-speaking PPA and AD individuals' sentence repetition ability is scant. Epelbaum et al. (2021) developed a rapid language test to dissociate PPA from other Alzheimer's type neurocognitive disorders, which includes word and sentence repetition subtasks containing five items each. These authors reported that sentence repetition performance distinguishes lvPPA from semantic variants, as the lvPPA perform more poorly on this task. Macoir et al. (2021), using the French sentence repetition subtask initially developed for post-stroke aphasia by Bourgeois-Marcotte et al. (2015), tested four cases of French speaking PPA as compared to a group of healthy controls. The authors found that all four lvPPA cases performed poorly in comparison to their controls, and that involvement of semantic reversibility of verb used and syntactic constructions used (i.e., active passive) only influenced performance in one or two participants. Building upon the aforementioned literature, we aim to understand:

(i) Whether three diagnostic groups (lvPPA, svPPA, and AD) experience sentence repetition difficulties to a larger extent than healthy aging adults.
(ii) Whether testing sentence repetition with a span task would dissociate the logopenic variant of PPA from other types of neurocognitive disorders (svPPA and AD type).

In the current study we administered a sentence repetition span task to groups of French-speaking individuals with PPA (lvPPA = 14; svPPA = 5), and with Alzheimer's disease (n = 13) and their age-matched healthy controls (n = 61). Given the results from previous research implying that sentence repetition difficulties in PPA might be associated with the working memory-intensive nature of the processing, which seems affected especially in the logopenic variant, we aimed to test sentence repetition deficits employing a sentence span task. The rationale behind this was that as the span of content words increases, PPA patients would encounter greater difficulty potentially dissociating them from individuals with other neurocognitive disorders.

Methods

Participants

For this study, we recruited three groups of participants. Our PPA group included a total of 19 individuals suffering from progressive aphasia symptoms, 14 of which were classified as logopenic variant with atrophy patterns in anterior temporal regions at the junction of parietal areas (8 females and 6 males; *Age mean* = 75.07, SD = 9.48) and 5 of which had a semantic PPA variant and were typically diagnosed with frontotemporal lobar degeneration (2 females and 3 males; *Age mean* = 69, SD = 11.66). The second group included 13 individuals suffering from Alzheimer's disease most of whom had a diagnosis with either rather global atrophies overall or bilateral atrophy in hippocampal regions (7 females, 6 males; *Age mean* = 79.15, SD = 8.17). See Table 1 for further demographic and etiological details of these participants.

These two diagnostic groups of participants were recruited at the Nice University Hospital's Resources and Research Memory Center and Cognition and Behavior and Technology (CoBTeK) facilities located at the Institute Claude Pompidou in Nice, France. All these diagnostic group participants have been selected from the Nice University Hospital's neurology follow-up patient database. The patient groups had been initially diagnosed with the presence of neurodegeneration by a neurologist according to the diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychological Association). Trained speech and language pathologists had documented their aphasiological assessment using the GREMOTs battery (Bézy et al., 2016).

In order for us to detail cognitive profiles, the diagnostic patient groups were screened with the Detection Test for Language Impairments in Adults and the Aged (Macoir et al., 2017a), which is a quick language screening for aging individuals to determine potential neurodegenerative language problems developed for French-speaking regions, and *La Batterie Rapide d'Efficience Frontale* (BREF; Dartinet and Martinaud, 2005) which is a French adaptation of the Frontal Assessment Battery at Bedside (Dubois et al., 2000). The BREF is a short screening task for cognitive abilities including mental flexibility, motor programming, interference, and inhibitory control. Finally, the diagnostic participants were screened with the French version

TABLE 1 Demographic and neuropsychological details of the participants.

Participant	Diagnosis	Gender	Age	Education (years)	MMSE	BREF	DTLA	Etiology and affected areas
Logopenic PPA group ($n = 14$)								
1014GR	lvPPA	F	87	8	19	11	53	
1018DD	lvPPA	F	73	12	25	18	86	
1019NT	lvPPA	M	80	15	-	-	70	
1024AY	lvPPA	F	83	7	26	15	78	Moderate cortical and subcortical atrophy
1042CG	lvPPA	M	80	7	22	17	90	
10049SM	lvPPA	F	75	17	29	17	90	Moderate atrophy in the left perisylvian region including postcentral sulcus and medial frontal areas.
10051CA	lvPPA	F	71	7	25	14	86	Hypometabolism in the left planum temporal posterior temporal areas.
10056DJ	lvPPA	M	69	17	24	9	94	Lobar degeneration left posterior part of the parietal areas.
10064IN	lvPPA	M	52	7	28	15	78	fistula occlusion
10065VN	lvPPA	F	77	7	-	-	68	
10074GJ	lvPPA	M	88	13	27	16	92	Microangiopathy. Atrophy in sub arachnoid areas and the Ventricular System. No hippocampal anomaly.
10139PM	lvPPA	M	75	12	-	-	75	
10161GJ	lvPPA	F	78	7	20	-	57	Dilatation in the Ventricular System. Atrophy associated with Bilateral atrophy in hippocampal and connected areas.
10163AV	lvPPA	F	63	9	28	17	85	
Semantic PPA group ($n = 5$)								
01002SE	svPPA	M	55	15	27	15	62	Frontal-temporal degeneration
10040LJ	svPPA	F	79		22	15	77	Frontal-temporal degeneration
10077SM	svPPA	M	81	13	30	10	83	Frontal-temporal degeneration extending to insular regions
10146RY	svPPA	F	59	17	-	-	74	
10159MN	svPPA	M	71	12	5	-	40	Frontal-temporal degeneration. Hypometabolism in left temporo-parietal
Alzheimer's disease group ($n = 13$)								
1013CV	AD	F	82	<4	-	7	55	Hypometabolism in bilateral frontal areas, global cortical atrophy predominantly in frontal areas
1015JO	AD	F	59	8	18	11	87	Bilateral hippocampal atrophy
1016NCA	AD	M	80	15	18	14	91	
1017CD	AD	M	83	9	29	14	88	Bilateral hippocampal atrophy
1039GD	AD	M	80	17	-	-	56	
1041MN	AD	F	88	9	22	10	71	
10068NJ	AD	M	74	13	24	15	94	Global sub-cortical atrophy
10070BL	AD	F	82	7	5	5	51	
10071RP	AD	M	67	17	20	16	93	

(Continued)

TABLE 1 (Continued)

Participant	Diagnosis	Gender	Age	Education (years)	MMSE	BREF	DTLA	Etiology and affected areas
10072AJ	AD	F	87	9	21	8	96	Global dilation observed in ventricular system and strong white matter atrophy in bilateral frontal cortices
10091OM	AD	F	85	7	-	-	98	
10160PL	AD	F	83	15	21	12	89	
10162SG	AD	M	79	9	17	13	85	Bilateral hippocampal atrophy. Hypometabolism in left parietal lobe. Global cortical and subcortical atrophy. Leukoaraiosis in periventricular region.

of the Mini Mental State Examination to verify their cognitive abilities (MMSE; Folstein et al., 1975).

Our third group included a total of 63 healthy aging individuals without any neurological and/or psychiatric impairments, who acted as control participants. The control group contained 47 females and 16 males, and their ages ranged between 40 and 91 with a mean of 60.03 (sd = 11.5). The control participants were screened with the MMSE before being admitted to the study, and individuals who scored below 27 out of 30 on this task were removed from our participant pool.

All the participants in this study were reported to be native French speakers without a significant effect of bilingualism. None reported to be bilingual from birth or having learned French as a second language. None of the participants had extended stays in a foreign country. They all were residents in the Côte d'Azur region including the metropolitan Nice and its surroundings.

Materials and procedures

We designed a sentence repetition span task in French to measure potential sentence repetition difficulty in PPA. The task contained 14 sentence stimuli in total with two items per span. We arranged "span" according to the number of content words, following a similar logic to the Sentence Repetition subtest of the Comprehensive Aphasia Test (Howard et al., 2010), which showed that sentence repetition span is a useful measure in aphasia assessment. The spans used in the current task ranged from simple sentences containing three content words (i.e., *Un étudiant fait ses devoirs.* "A student does his homework.") to complex sentences with nine content words (*Les chercheurs en archéologie ont découvert une grande tombe romaine dont des squelettes et des outils tranchants.* "Researchers in archaeology have discovered a large Roman tomb including skeletons and sharp tools."). The total number of words in those sentences ranged between 5 and 18. We particularly took the number of semantically loaded content words as sentential complexity, rather than manipulation of syntactic variables. This is because syntactic complexity is already known to pose processing challenges in PPA (Wilson et al., 2012). Therefore, we tried to reduce the impact of syntactic complexity while profiling sentence repetition deficits and we deliberately avoided using syntactically demanding structures as much as possible, such as embedded clauses, inversion, or passive structures. All the sentences used in this task were grammatically correct and semantically coherent. See Appendix 1 for a full list of materials used in the sentence repetition span task. Psychometric properties of the content words used in materials including word frequencies and syllable length were extracted from the LEXIQUE-2 French database (New et al., 2004). The content words had a mean number of 1.94 syllables (SD = 0.84, min = 1, max = 5). These content words had a mean surface frequency of 241.19 per million (SD = 564.25). Those psychometric properties are given per content word in Appendix 2.

Each participant was examined in a single session. For the diagnostic patient group, sessions took place at the Institute Claude Pompidou or at their home when this was more convenient. For control participants, sessions took place in diverse places including the individuals' home or at the lab facilities of University of Cote d'Azur. Before administration of the sentence span task, participants were given the complementary cognitive screening tasks and their demographic information was collected with a short questionnaire. During the sentence repetition tasks, participants were instructed that the experimenter would read aloud a sentence, they should listen carefully and repeat the sentence as much as they can remember. The experimenter recorded sessions with an audio recorder and then transcribed the responses. Each sentence was only presented once, on-demand presentation repeat was not permitted. The participants' sentence repetition duration was timed based on their voice onset and offset in order for us to be able to keep track of duration across participants. However, we did not impose a time off. We quantified the following variables:

(a) *Sentence Span* measured the maximum span length in reference to content words presented in sentences. Participants were read aloud two sentences for each span length in an increasing linear order (i.e., the order of items was not random). When a participant made one mistake in a single sentence from a span, they were allowed to continue to the next span, but their mistakes were recorded and were given half a score. If they made mistakes in both sentences while repeating, the task was terminated, we recorded the last span length in which at least one sentence was correctly repeated.
(b) *Number of Content Words* was the measure of the total number of correctly repeated consent words (i.e., disregarding function words such as pronouns, auxiliaries, etc.) including all sentences across all span length conditions.
(c) *Total Number of Words* contained all words accurately repeated including both content words and function words.
(d) *Number of Omissions* included all types of words that are omitted in the participants' responses.
(e) *Number of Substitutions* were the instances in which participants produced an alternative word during repeating sentences. We quantified substitution errors for all words not only for content words, but this type of error occurred virtually exclusively for the latter type of words. Self-corrections were accepted, which happened occasionally.
(f) *Number of Phonological Errors* represents the total number of errors in which the participants produced forms of phonological paraphasias (e.g., *l'évier* vs. *lavier*, 'the sink').

The procedures reported here were piloted with a smaller portion of the participants in this study to understand general trends (Arslan et al., 2020). Following an initial evaluation, data collection was carried out with a larger number of participants. While piloting we had aimed to include all variants of PPA including the nfvPPA variant, however, during the entire data collection process (2018-2022), we were not able to recruit more than one single case of a non-fluent individual with PPA. Given the issues of generalizing outcomes from single cases, we opted for removing this individual from further analyses. Participation in this study was voluntary and all the participants gave their consent that the data can be used for scientific purposes. One session with healthy controls took about 20–25 min, and sessions with the diagnostic group took a maximum of 45 min. The participants received no monetary remuneration. Experimental procedures reported in this study adhere to the Helsinki Declaration and its associated statements for ethical principles for medical research involving human subjects. The procedures of the overall project were approved by the University of Groningen, Faculty of Arts Research Ethics Committee (CETO, Decision No. 76006271), and locally by the Research Ethics Committee of the University of Côte d'Azur (CERNI, dossier no. 2019-2).

Data analysis

The experimental data collected with the above reported procedures were analyzed using linear mixed-effects regression models for within group comparisons with the *lme4* package (Bates et al., 2015) using R (R Core Team, 2022). As suggested by Baayen et al. (2008), we fit these mixed-effect models with subjects as random intercepts and slopes where applicable. We built a separate model for each of the above-mentioned measures as dependent variables (*Sentence Span*, *Number of Content Words, Total Number of Words, Number of Omissions, Number of Substitutions,* and *Number of Phonological Error*). The Fixed Effect of the Variant (AD × lvPPA × svPPA × Control) was added as an independent variable, which was treatment coded (i.e., 1–0) with the Control group set as 'base' so that each patient group can be compared against the controls. The fitting of the models was evaluated with the Akaike Information Criterion (AIC). Individual case-control comparisons[1] were conducted using the Crawford-Howell *t*-test (Crawford and Howell, 1998) computed in R with Dan Mirman's function script.[2] Please note that for a minimal error rate around 5%, relatively larger normative sample sizes, such as around 50, are recommended for the Crawford-Howell *t*-test to return reliable outcomes (see Crawford et al., 2009). Finally, we conducted a complementary error analysis for phonological errors, which were few in number with no observation in some participants, and this variable was not normally distributed. We therefore used the Kruskal-Wallis sum rank test with the *ruskal.test* function in R to calculate group differences.

Results

Table 2 demonstrates the mean performances of participant groups during our sentence repetition task. The control

1 As it might seem that the number of participants is relatively low, aphasiology has constantly dealt with a small number of participants as PPA in particular is a relatively rare condition of this syndrome. Even in small groups of participants, people with PPA show quite heterogeneous symptoms of the condition. Therefore, we used case-control tests computed per case of PPA/AD participants in addition to group statistics. We additionally ran a clinical trial sample size estimator for our smallest diagnostic group (svPPA $n = 5$). This group span task performance was 4.9 by average in comparison to controls who performed with a mean of 7 +/- 0.7. Assuming the alpha p value 0.05 and power at 0.80, we would need a minimum of 2 participants per group of comparison.

2 https://www.r-bloggers.com/2012/08/crawford-howell-1998-t-test-for-case-control-comparisons/

participants performed with a mean span of 7 ranging between 5.5 and 8, which corresponded above most individuals with PPA and AD. Results from an initial linear mixed effects regression model on sentence span data have shown that all diagnostic patient groups performed lower than the healthy controls, including lvPPA ($ß = -1.64$, SE $= 0.26$, $t = -6.22$, $p < 0.001$), svPPA ($ß = -2.09$, SE $= 0.40$, $t = -5.21$, $p < 0.001$), and AD groups ($ß = -1.42$, SE $= 0.25$, $t = -5.53$, $p < 0.001$). Comparisons between diagnostic groups did not show any reliable differences, however. The lvPPA group performance was comparable to the AD group ($ß = 0.22$, SE $= 0.33$, $z = 0.67$, $p = 0.90$) and the svPPA group ($ß = -0.67$, SE $= 0.45$, $z = -1.48$, $p = 0.42$). There were no reliable differences between the svPPA and AD group performances either ($ß = -0.44$, SE $= 0.45$, $z = -0.98$, $p = 0.74$).[3]

Regarding the number of content words correctly produced, the picture was somewhat mixed as svPPA variant ($ß = -13.77$, SE $= 5.88$, $t = -2.43$, $p = 0.02$) and the AD groups ($ß = -8.31$, SE $= 3.86$, $t = -2.15$, $p = 0.03$) performed significantly lower than the control ranges. However, the lvPPA group showed a slight trend but did not differ from the controls in the number of content words produced ($ß = -6.42$, SE $= 3.75$, $t = -1.71$, $p = 0.09$). In terms of total number of correctly repeated words, only the AD group performed less accurately than the control group ($ß = -16.66$, SE $= 7.35$, $t = -2.26$, $p = 0.02$), whilst neither the lvPPA ($ß = -11.17$, SE $= 7.13$, $t = -1.56$, $p = 0.12$) nor the svPPA variant groups ($ß = -16.14$, SE $= 11.19$, $t = -1.44$, $p = 0.15$) showed reliable differences from the control group level. We found no significant differences between the three diagnostic groups in their repetition of both content words and total number of words (all $ps > 0.31$).

In the three diagnostic groups, we have observed an elevated number of errors during repetition as compared to the control groups. These errors included two different types: omissions where a word was completely omitted during repetition, and substitution errors in which a word was replaced (mostly with a semantically associated word). Both kinds of errors were only minimal in the control group's repetition outcomes. Outputs from a series of mixed effects regression models have shown that all three groups produced greater number of substitution errors as compared to controls (lvPPA: $ß = 3.52$, SE $= 0.66$, $t = 5.26$, $p < 0.001$; svPPA: $ß = 2.62$, SE $= 1.04$, $t = 2.50$, $p = 0.014$; and AD: $ß = 0.97$, SE $= 0.29$, $t = 3.32$, $p = 0.001$). The diagnostic groups were shown to commit a greater number of omission errors in their repetitions as compared to the control groups, who seldomly did one or two omissions. The greater number of omissions in the three diagnostic groups than in the control group norms were also shown to be reliable by our statistical outputs (lvPPA: $ß = 21.85$, SE $= 2.36$, $t = 8.98$, $p < 0.001$; svPPA: $ß = 20.65$, SE $= 3.70$, $t = 5.58$, $p < 0.001$; and AD: $ß = 21.85$, SE $= 2.51$, $t = 8.68$, $p < 0.001$). Pairwise comparisons revealed no significant differences across the three diagnostic groups in their amount of substitution and omission errors, however (all $ps > 0.82$).

It is indispensable to mention that our analysis has signaled large individual differences, even in the svPPA group of five individuals. See Figure 1B for an illustration of individual variability within each group.[4] Table 3 demonstrates individual sentence span scores per individual across the three diagnostic groups. In the lvPPA group 6 out of 14 individuals, in the svPPA group one individual, and in the AD group 5 out of 13 individuals proved intact in their sentence span scores as compared to the control group norms. What predicts this individual variability? One possibility is that their language abilities might be interfering with their sentence repetition performance. To be able to test whether potential language impairments are interfering with sentence repetition span, we ran a complementary analysis exploring the diagnostic groups' sentence span and their language assessment outcomes as measured with the DTLA. Figure 1B exhibits the linear relationship between language outcomes and sentence span scores across the three diagnostic groups. Our regression analysis indicated that in all groups, language assessment outcomes largely predicted sentence span scores (lvPPA: $ß = 0.06$, SE $= 0.008$, $t = 7.65$, $p < 0.001$; svPPA: $ß = 0.06$, SE $= 0.01$, $t = 3.27$, $p = 04$; and AD $ß = 0.05$, SE $= 0.01$, $t = 4.26$, $p = 0.001$). This suggest that individuals who have better retained language abilities are more likely to perform well on the sentence repetition span task.

We did a complementary analysis to quantify phonological errors in our diagnostic groups' sentence repetition outputs. Phonological errors in the control group were virtually unobserved except for a few cases where the participant self-corrected immediately. However, in the diagnostic groups, these errors were quantified to a much larger extent. The participants with lvPPA committed a total of 19 instances of phonological error, with a mean error rate of 1.3 per individual, while the AD group had only 12, and svPPA group had 6 instances of

3 We ran a second model with the inclusion of per-million averaged frequencies per item to check whether the frequency is impacting the span scores. Our subsequent mixed-effect regression model returned that surface frequency is not a significant predictor of span scores (ß < 0.001, SE = 1.52, $t = 0.02$, $p = 0.98$).

4 An interesting point was raised by an anonymous reviewer regarding variability in our data in reference to unbalanced male-to-female ratio in our diagnostic groups. We ran a set of nested models with gender as a fixed effect and as a random nested factor. The outputs yielded that there are no critical gender differences in sentence span scores (Intercept ß= 6.99; Gender ß = 0.42, SE = 0.31, $t = 1.36$, $p = 0.17$), number of substitution errors (Intercept ß= 0.97; Gender ß = −0.53, SE = 0.82, $t = -0.64$, $p = 0.52$), and number of omission errors (Intercept ß= 1.14; Gender ß = 1.88, SE = 2.94, $t = 0.64$, $p = 0.52$). In all three models, the three diagnostic variants have showed reliable differences compared to the control group, all $ps < 0.01$.

TABLE 2 Participants' sentence repetition span task performance outcomes in means; standard deviations are given in parenthesis.

Group	Sentence span	Number of content words	Total number of words	Number of substitution errors	Number of omission errors	Number of phonological errors (total count)
lvPPA ($n = 14$)	5.57 (0.93)	53.35 (15.35)	99.57 (25.65)	4.33 (2.79)	22.35 (11.83)	1.35 (19)
svPPA ($n = 5$)	4.90 (1.14)	46.00 (19.91)	94.60 (44.68)	3.60 (3.13)	21.80 (14.16)	1.20 (6)
AD ($n = 13$)	5.34 (1.31)	51.46 (17.43)	94.07 (32.12)	4.53 (2.81)	23.00 (14.14)	0.92 (12)
Control	7.00 (0.70)	59.97 (10.09)	110.98 (19.79)	0.91 (1.74)	1.29 (3.37)	–

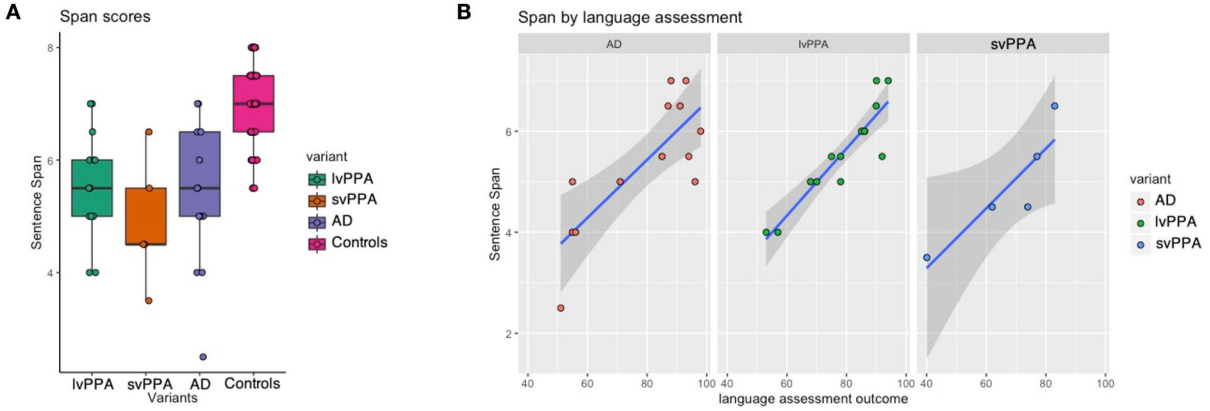

FIGURE 1
(A) Boxplot showing group performance across the three diagnostic groups points show individual performance; **(B)** Scatter plots demonstrating the relationship between span scores and language assessment outcomes.

phonological errors. Except for one participant with svPPA (i.e., 10077SM) and two participants with lvPPA (10056DJ, 10064IN) all participants with PPA had phonological errors ranging from one up to three. This type of error was rather more isolated in the AD group where only four out of 13 individuals made phonological errors. The number of phonological errors in the lvPPA group was statistically greater than in the AD group (Kruskal-Wallis $X^2 = 4.938$, df $= 1$, $p = 0.02$). There were no statistical differences between the svPPA and the lvPPA (Kruskal-Wallis $X^2 = 0.297$, df $= 1$, $p = 0.58$), or between the svPPA and the AD groups (Kruskal-Wallis $X^2 = 1.665$, df $= 1$, $p = 0.19$).

Discussion

The aim of this study was twofold: (i) understanding whether our three diagnostic groups (lvPPA, svPPA, and AD) demonstrate greater sentence repetition difficulties than healthy aging adults and (ii) understanding whether the span task design would be useful in dissociating the lvPPA from other types of neurodegenerative conditions under scrutiny here (svPPA and AD type). To this end, we administered a sentence repetition task within a span task in which content words to be repeated increased as the span condition increased from three to nine content words. We have recruited groups of PPA (lvPPA = 14; svPPA = 5), AD ($n = 13$) and a control group ($n = 61$). Following the idea that sentence repetition difficulties in PPA might be associated with the working memory-intensive nature of verbal processing, which seems affected especially in the logopenic variant, we have explored the possibility of whether individuals with lvPPA would perform more poorly than patients with svPPA or Alzheimer's disease. Our results showed that all three diagnostic groups (lvPPA, svPPA, and AD) performed more poorly in all repetition span measures than the control group without showing critical pairwise group differences between those diagnostic groups. One differential impairment pattern that signaled for particular attention was found in the lvPPA group which made a relatively larger number of phonological errors than the AD group did, while no differences were observed for the svPPA group. Our expectations are therefore only partially met. It is possible to conceive that the span task is sensitive enough to distinguish impaired sentence repetition ability in neurodegenerative conditions investigated

TABLE 3 Case-control comparisons computed per individual in the diagnostic group of participants.

Logopenic PPA group			Semantic PPA group			Alzheimer's disease group		
Participant	**Sentence span**	**Test statistics**	**Participant**	**Sentence span**	**Test Statistics**	**Participant**	**Sentence span**	**Test statistics**
1014GR	**4**	$t = -4.24, p < 0.001$	01002SE	**4.5**	$t = -3.53, p < 0.001$	1013CV	**5**	$t = -2.82, p = 0.006$
1018DD	6	$t = -1.41, p = 0.16$	10040LJ	**5.5**	$t = -2.12, p = 0.037$	1015JO	6.5	$t = -0.71$, p =0.48
1019NT	**5**	$t = -2.82, p = 0.006$	10077SM	6.5	$t = -0.71, p = 0.48$	1016NCA	6.5	$t = -0.71$, p = 0.48
1024AY	**5.5**	$t = -2.12, p = 0.037$	10146RY	**4.5**	$t = -3.53, p < 0.001$	1017CD	7	t = null
1042CG	6.5	$t = -0.71, p = 0.48$	10159MN	**3.5**	$t = -4.95, p < 0.001$	1039GD	**4**	$t = -4.24, p < 0.001$
10049SM	7	t = null				1041MN	**5**	$t = -2.82, p = 0.006$
10051CA	6	$t = -1.41, p = 0.16$				10068NJ	**5.5**	$t = -2.12, p = 0.037$
10056DJ	7	t = null				10070BL	**2.5**	$t = -6.36, p < 0.001$
10064IN	**5**	$t = -2.82, p = 0.006$				10071RP	7	t = null
10065VN	**5**	$t = -2.82, p = 0.006$				10072AJ	**5**	$t = -2.82, p = 0.006$
10074GJ	**5.5**	$t = -2.12, p = 0.037$				10091OM	6	$t = -1.41, p = 0.16$
10139PM	**5.5**	$t = -2.12, p = 0.037$				10160PL	**4**	$t = -4.24, p < 0.001$
10161GJ	**4**	$t = -4.24, p < 0.001$				10162SG	**5.5**	$t = -2.12, p = 0.037$
10163AV	6	$t = -1.41, p = 0.16$						

Control group mean sentence span is 7 (ranging between 5.5 and 8). Significant comparisons are bolded.

in this study. However, the picture for working memory-intensive sentence repetition impairments as measured with sentence span being a reliable clinical marker for lvPPA seems far from being clear.

The control participants performed with a mean span of 7 content words on the sentence repetition span task. Immediate recall of 7 items is quite in line with Miller's *magical number seven* account for short-term memory capacity (Miller, 1956), although modern psychologists analyze those seven spans to be comparable to 3-4 chunks of information (see Mathy and Feldman, 2012; Cowan, 2015). It is therefore conceivable that the control participants reported in this study performed quite typically given these norms in the working memory literature. These results show that the selected sentences are able to assess short-term memory capacity in relation to the number of content words. The diagnostic groups' performances were clearly below the control norms on average. The svPPA group had a mean span of 4.90 while the lvPPA group had 5.57 and the AD group had 5.34. This suggests that the sentence span task was sensitive enough to dissociate the three neurodegenerative conditions as compared to healthy controls. These diagnostic groups however did not differ among themselves with regard to the sentence span outcomes. Our findings are not consistent with Foxe et al. (2013); they found greater impairments in lvPPA than AD during sentence repetition while our findings fully support Leyton et al. (2014) who found their diagnostic groups showed affected sentence repetition but no significant group differences. We partly support Beales et al. (2019) who found both their AD and lvPPA groups to perform poorly as compared to healthy controls without a critical pairwise difference between the two groups. However, Beales et al. (2019) found people with svPPA to be performing more poorly than lvPPA and AD, which our results do not reconcile with. Recall that lvPPA is often associated with an underlying AD pathology during the initial phases of the disease and that selective impairments in phonological short-term memory might be observed in both lvPPA and AD (Gorno-Tempini et al., 2008). Therefore, finding no critical working memory-intensive sentence repetition differences in both groups comes as no surprise. The finding of no significant difference between the svPPA and lvPPA groups' sentence repetition span is at odds with some studies (see e.g. Beales et al., 2019; Seckin et al., 2022). However, this might be due to a small number of people with svPPA recruited under the current study, and we should note that there was a large heterogeneity even in such a small number as five people with svPPA. However, it is important to mention that there were large individual differences. Eight individuals in both the lvPPA and AD groups and four individuals in the svPPA group performed more poorly, showing clear dissociation compared to the controls. The other six individuals in lvPPA, one in svPPA, and five in the AD group were intact in repeating sentences performing within the control norms. How can this extent of individual variability be explained?

One possibility is that the participant groups may be sensitive to certain psycholinguistic features such as familiarity and typicality of stimulus characteristics. Such features have been shown to influence object naming in neurodegenerative conditions (Brambati et al., 2006). In semantic variants of frontotemporal degeneration, object naming ability is better preserved for typical and familiar items (Woollams et al., 2008).

Therefore, it is a possibility that familiarity with the nouns utilized in our sentences may have resulted in such a variable pattern of sentence repetition performance. However, if our participants were influenced by an item level effect, we would have observed a greater variability across items. Particularly, in both the lvPPA and svPPA groups, individuals were able to repeat sentence stimuli up until around the span of four to five content words without much trouble (see Table 3). Furthermore, these content words used within these sentences included highly frequent and common everyday nouns (e.g., girl, teacher, door, cake, etc.) and simple transitive verbs (e.g., eat, do, close, chase). It is therefore unlikely to contemplate that the variability in our diagnostic groups' performances was due to a sheer set of psycholinguistic characteristics including familiarity, typicality, and/or frequency. A second possibility we cannot rule out is that semantic characteristics of content words may have resulted in differential performances. In svPPA, the ability to recognize certain semantic categories is only selectively impaired, suggesting that sentence repetition difficulty in the svPPA group might be related to alterations in semantic memory. For instance, animate objects are often found to be better preserved than inanimate ones, and interestingly this impairment pattern is not influenced by psycholinguistic factors such as familiarity or frequency (Henderson et al., 2021). Although recognition of objects in a picture matching task does not directly warrant verbatim impairments in the repetition modality in aphasic syndromes, there is still a possibility that particularly the svPPA individuals tested under the current study might have difficulty recognizing certain objects in auditory sentence stimulus presented to them to repeat. While it would be speculative to argue that our participants might have blended agnostic impairments[5], it is clearly demonstrated that the severity of language impairments predicted the scaled sentence repetition span scores (see Figure 1B). Another limitation under the current study is that we have not measured how far the severity of object naming and semantic category impairments in PPA influenced their sentence repetition ability. Indeed, this could have enabled us to verify whether the scores obtained, particularly by svPPA, related to an underlying impairment with the semantic content of words used as opposed to difficulty in repeating them without accessing the semantic system. Nonetheless, the data so far seem to suggest that the individuals with severely impaired language abilities overall tend to experience greater difficulty repeating sentences.

5 In fact, agnostic word deafness impairments are not completely unheard of in PPA, especially when cortical atrophy strongly extends to the left superior temporal regions (Otsuki et al., 1998). Slowly progressive pure word deafness. *European Neurology* 39, 135–140. In the absence of millimetric cortical atrophy data or further object recognition and comprehension data, however, it is impossible to contemplate whether some of our participants showed variability in sentence repetition due to impaired content word comprehension or a form of agnosia.

It is highly possible that sentence repetition difficulty in PPA and AD is modulated with extensive short-term memory deficits that might be picked up by a span task. Note that Beales et al. (2019) found a significant correlation with forward digit span task outcomes, but not with the backward digit task, and their diagnostic groups' performances on sentence repetition. The authors argued that sentence repetition and digit span might be requiring equivalent demands on the working memory capacity. Although the authors do not report whether this correlation holds in each subvariant of PPA, it is obvious that our findings are reconcilable with the idea that repetition deficits might be predicted by memory spans. We tested this claim using a sentence span task in which the increasing number of content words were manipulated as spans. We found that a reduced sentence span is a common characteristic of the three neurodegenerative conditions alike. We therefore support Beales et al. (2019) claim that sentence repetition deficits may be modulated with working memory demands; nonetheless, our data champion the idea that those working memory-intensive sentence repetition deficits reveal critical diagnostic differences between the neurodegenerative groups.

Two final critical issues need further attention. First, it is practicable to assume that sentence stimuli used in this study are somewhat different from previous studies, which may have resulted in certain disparities. While we used content words as critical span length, other sets of studies used sentences with meaningful words vs. pseudowords (Bayles et al., 1996; Meyer et al., 2015; Lukic et al., 2019), different lengths of syllables (Leyton et al., 2014), and sentences with different syntactic constructions (Hohlbaum et al., 2018; Beales et al., 2019). An important possibility that cannot be ruled out is that stimulus characteristics influence sentence repetition ability. It is obvious that working memory capacity is influenced by stimulus type and characteristics in visual span tasks (see Alvarez and Cavanagh, 2004). If we follow this logic, our finding that there were no critical group differences between the diagnostic groups with regard to sentence span, the mean numbers of words and the total number of content words produced may be due to the fact that repetition span length based on content words is not sensitive enough to distinguish different neurodegenerative conditions. In span length of up to five content words, our sentences involved simple transitive verbs (catch, eat, close, etc.), animate subjects (e.g., a girl or a cat), and either inanimate objects such as 'cake' and 'door', or animate objects such as a 'mouse' (see Appendix 1). However, from the span length of six content words, stimulus materials began to be complex encompassing syntactic coordination with more than one matrix clause connected with 'but' or 'so'. This is suggestive that syntactic complexity seems to play a role, although we deliberately aimed to keep it low by excluding notoriously complex constrictions such as embedded clauses, inversion, and passive voice. There is good evidence that different syntactically complex constructions might add

additional processing difficulties during the task of repeating sentence material (see Hohlbaum et al., 2018 for German; Macoir et al., 2021 for French PPA; and Small et al., 2000 for AD patients). A further point was raised by an anonymous reviewer, who posited that a potential syntactic effect here is that certain items might be susceptible to attraction errors with regard to subject-verb agreement. This is based on the idea that in sentences with extended prepositional phrases (see, for instance, Item 13: *Les chercheurs en archéologie ont découvert* 'The researchers in archaeology have discovered') listeners might tend to illicitly license the verb in singular form (see e.g., Franck et al., 2006). This is not what we observed, however. Four individuals with lvPPA (1024AY, 10049SM, 10056DJ, 10068NJ) who made it until this item fully produced the verb in plural form, and many other individuals had to terminate the task before this item. We should note that illicit licensing often happens in French due to the complexity of plural verb forms, nonetheless, it does not seem to us as a significant error pattern that characterized our diagnostic groups' sentence repetition performance. Notwithstanding the lack of attraction errors, we are unable to ultimately rule out potential syntactic complexity effects on sentence repetition in our diagnostic groups. It is not feasible to tease apart whether sentence repetition ability in PPA is independent of syntactic complexity since it is very difficult to banish the impact of syntactic complexity effects while designing meaningful sentences after a considerable number of words. However, a future study might have the courage to investigate this issue within a recall task using random word strings as stimulus items to be memorized.

The second issue that needs highlighting here is that the logopenic variant of PPA might be characterized with more phonological short-term memory impairments than semantic ones. We have observed similar cases of semantic renditions reported in Henry and Gorno-Tempini (2010). Two participants (1019NT and 1042CG) produced semantically appropriate alternations, such as for the phrase *Le lapin s'est échappé très vite* 'The rabbit has escaped very quickly' these participants repeated *Le lapin a fui (rapidement)* 'The rabbit has run away (rapidly)'. Although, we may have expected such a strategy to reduce semantic load while repeating an increased number of content words in the sentence materials to be a global issue in lvPPA, no other people with lvPPA except for the two individuals demonstrated such a rendition strategy. Complete omissions of words were much more common. However, the number of both types of substitution and omission errors did not differ across the lvPPA, svPPA, and AD groups. While the current study showed no clear diagnostic usability of sentence span with varying numbers of content words to distinguish lvPPA from AD and svPPA, it undoubtedly showed that the people with lvPPA produced an elevated number of phonological errors while repeating sentences. This finding is fully compatible with studies that characterized this disorder with a form of phonological loop deficiency (Gorno-Tempini et al., 2008, 2011). Very typical phonetical errors included adding an initial consonant to a word (e.g., '*attraper*' to '*rattraper*') or alternated voicing of vowels ('*l'évier*' to '*lavier*'). A strong possibility yet to be tested has to do with the vocal and acoustic features of stimulus to be repeated, including voice reaction time, silent pauses, and prosodic parameters. These features acting as sensitive markers dissociating lvPPA have been, in fact, shown to be affected (see Da Cunha et al., 2022).

In conclusion, we showed that all patient groups with a neurocognitive disorder under this study (lvPPA, svPPA, and AD) exhibit a sentence repetition difficulty as compared to the healthy controls; but within the diagnostic groups, they had sentence repetition span outcomes that are indistinguishable from each other. This suggests that sentence repetition span is in general reduced in neurocognitive disorders, which is modulated by a reduced working memory capacity. In other words, our diagnostic group participants had more severe impairments in sentence repetition as the span length increased. Nonetheless, working memory-intensive sentence repetition impairment as measured with our sentence span tasks built upon number of content words does not seem to be a clear sensitive marker of lvPPA distinguishing this variant from other neurocognitive disorders with a neurodegenerative pathology. We further conclude that sentence repetition difficulty in lvPPA is associated with a large number of phonological errors, which warrants more in-detail investigation regarding the nature of sentence repetition ability and capacity for phonological memory.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the University of Groningen, Faculty of Arts Research Ethics Committee (CETO, Decision No. 76006271), Research Ethics Committee of the University of Côte d'Azur (CERNI, Dossier No. 2019-2). The patients/participants provided their written informed consent to participate in this study.

Author contributions

SA, FM, VM, and AG conceived the study. SA and FM conceptualized and prepared the task materials. AP, MC, VM, AG, AM, JL, and GS supervised the data collection process. SA analyzed data and drafted the article. All authors revised the

draft. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcomm.2022.934487/full#supplementary-material

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