Cyprus University of Technology
Faculty of Health Sciences

Doctoral Dissertation

PROFILING LANGUAGE AND COGNITION IN GREEK-SPEAKING PATIENTS WITH PRIMARY PROGRESSIVE APHASIA

Nomiki Karpathiou

Limassol, June 2020

Στους γονείς μου, Μαρία και Σακελλάρη,

στον Γιώργο, την Μαρία και τον Θανάση

CYPRUS UNIVERSITY OF TECHNOLOGY

FACULTY OF HEALTH SCIENCES

DEPARTMENT OF REHABILITATION SIENCES

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Approval Form

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Cyprus University of Technology

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ABSTRACT

Primary Progressive Aphasia (PPA) is a degenerative condition characterized by progressive loss of language function. Individuals with PPA are divided into three clinical variants based on distinct speech and language features and patterns of cognitive decline: the semantic variant of PPA (svPPA), the non-fluent/agrammatic variant of PPA (nfvPPA) and the logopenic variant of PPA (lvPPA). The most common types of neurodegeneration in PPA are frontotemporal lobar degeneration (FTD) and Alzheimer's disease (AD).

The main aim of the research was to describe the clinical presentation of PPA and provide a detailed cognitive-linguistic profile of PPA for the Greek-language. The vast majority of studies in PPA involve participants whose native language is English. Detailed reports of PPA in other languages are scarce.

To that end, 13 individuals with PPA, at the early and moderate stages of the disease, were evaluated. Nine demographically matched adults with AD have also completed the cognitive-linguistic battery. Fifteen neurotypical adults, matched for gender, age and education have served as controls. The assessment battery included neuropsychological tools for the evaluation of speech, language, other cognitive domains (attention, memory, executive and visuospatial functions) and mood. Linguistic assessment targeted auditory comprehension, motor speech, narrative production, naming, repetition, reading and writing. In addition, information about the level of functioning and the presence of neuropsychiatric symptoms was collected by each participant's primary caregiver.

Differences were documented in neuropsychological testing and connected speech production between Greek-speaking individuals with AD and PPA. PPA participants were less affected than AD participants in the delay conditions of episodic memory measures. However, they too were impaired in executive tasks, especially for working memory and phonemic verbal fluency. Naming, single word comprehension, auditory comprehension of complex material, repetition, reading and writing were all affected.

The most informative measures in differentiating svPPA and lvPPA from AD participants were repetition of long frequent sentences, frequency of phonological errors, mean sentence length and sentence elaboration index in connected speech.

Regarding narrative production, differences between a picture description and a story retell task were found for fluency, lexical selection, discourse and sentence productivity but not for grammatical accuracy measures. For the PPA group, measures of fluency, lexical selection, discourse and sentence productivity correlated with executive control, short-term memory and to a lesser degree with working memory. Fewer differences between the tasks were documented for the AD group.

Both tasks were able to capture connected speech deficits in PPA and AD and in that sense, both methods can be used interchangeably. However, story retell seems to be more sensitive in identifying deficits at the syntactic level of language production and may assist in the differential diagnosis between PPA and AD.

Inspection of individual profiles in individuals with PPA revealed heterogeneity in cognitive function, linguistic and narrative discourse abilities. Participants with svPPA presented with more typical phenotypes in comparison to the participants with lvPPA. Non-language cognitive deficits were common in lvPPA. Neuropsychiatric symptoms were reported for lvPPA participants, but to a lesser extent than for FTD participants. Participants with a prominent movement disorder manifested impairment in other areas, including speech, language and cognition.

Differences were also documented for 4 participants in cognitive, linguistic abilities and discourse production over time. The pattern of differences in performance of each participant was different. Despite, similar cognitive status at initial assessment, participants with lvPPA have shown greater decline than a participant with svPPA. All three were further affected in memory, writing and lexical retrieval. The lvPPA participants exhibited further difficulty with sentence repetition. One participant presented with a naming impairment. Naming was further affected, and a mild semantic deficit was documented in his second assessment.

Further studies with large PPA cohorts and balanced representation of each PPA variant, combining neuropsychological, linguistic and neuroimaging testing could better explore PPA subtyping.

Keywords: Primary progressive aphasia, Alzheimer disease, semantic variant, non-fluent agrammatic variant, logopenic variant

ΠΕΡΙΛΗΨΗ ΕΡΕΥΝΗΤΙΚΗΣ ΕΡΓΑΣΙΑΣ ΣΤΑ ΕΛΛΗΝΙΚΑ

Η Πρωτοπαθής Προοδευτική Αφασία (ΠΠΑ) είναι μία σπάνια μορφή Άνοιας η οποία χαρακτηρίζεται από μια αργά εξελισσόμενη γλωσσική διαταραχή. Τα άτομα με ΠΠΑ μπορούν να κατηγοριοποιηθούν σε τρεις κλινικές παραλλαγές (σημασιολογική, μη ρέουσα/αγραμματική και λογοπενική παραλλαγή) βάσει συγκεκριμένων γνωρισμάτων ομιλίας και λόγου.

Σκοπός της παρούσας ερευνητικής μελέτης είναι η λεπτομερής καταγραφή των γλωσσικών χαρακτηριστικών της ΠΠΑ και των παραλλαγών της στην Ελληνική γλώσσα, καθώς και η συσχέτισή τους με συνυπάρχοντα γνωστικά ελλείμματα. Οι περισσότερες έρευνες στο χώρο της ΠΠΑ έχουν διεξαχθεί στην Αγγλική γλώσσα και μόνο ένας πολύ μικρός αριθμός μελετών εστιάζεται σε μη αγγλόφωνους ασθενείς.

Για τον σκοπό αυτό εξετάστηκαν 13 άτομα με ΠΠΑ καθώς και 9 άτομα με νόσο Alzheimer (ΝΑ) με συμπτώματα ήπιας και μέτριας βαρύτητας. Δεκαπέντε υγιείς ενήλικες, εξισωμένοι ως προς το φύλο, την ηλικία και το επίπεδο εκπαίδευσης, αποτέλεσαν την ομάδα ελέγχου.

Η αξιολογητική διαδικασία περιλάμβανε νευροψυχολογικές δοκιμασίες για την εκτίμηση των γλωσσικών, των γνωστικών ικανοτήτων και της διάθεσης των συμμετεχόντων. Η γνωστική αξιολόγηση εστιάστηκε στους τομείς της προσοχής, της μνήμης, των επιτελικών και των οπτικοχωρικών ικανοτήτων. Επιπλέον, αξιολογήθηκε η λεκτική κατανόηση, ο κινητικός μηχανισμός της ομιλίας, ο αφηγηματικός λόγος, η ικανότητα κατονομασίας, επανάληψης, ανάγνωσης και γραφής. Πληροφορίες σχετικά με τη λειτουργικότητα και πιθανά συνοδά ψυχιατρικά συμπτώματα συλλέχθηκαν από τους φροντιστές τους με τη χρήση ερωτηματολογίων.

Καταγράφηκαν διαφορές στις γνωστικές και γλωσσικές λειτουργίες μεταξύ των συμμετεχόντων με ΠΠΑ και ΝΑ. Οι δοκιμασίες που βρέθηκε ότι μπορεί να βοηθήσουν στη διαφοροδιάγνωση είναι η επανάληψη προτάσεων με μεγάλο μήκος και αυξημένη συχνότητα εμφάνισης, ο αριθμός των φωνολογικών παραφασιών, το μέσο μήκος πρότασης και ο δείκτης ανάπτυξης πρότασης.

Συγκρίνοντας την παραγωγή αφηγηματικού λόγου κατά την περιγραφή μιας εικόνας και την αναδιήγηση μιας ιστορίας, βρέθηκε ότι και οι δύο δοκιμασίες μπορούν να

χρησιμοποιηθούν για την καταγραφή ελλειμμάτων. Η αναδιήγηση μιας ιστορίας φαίνεται ότι επιτρέπει επιπρόσθετα την διαφοροδιάγνωση των ατόμων με ΠΠΑ και ΝΑ.

Το γνωστικό και γλωσσικό προφίλ κάθε συμμετέχοντα συζητήθηκε σε σχέση με τα ισχύοντα κλινικά κριτίρια. Αναλύοντας τις γνωστικές και γλωσσικές τους δεξιότητες, διαπιστώθηκε ποικιλομορφία, ιδιαίτερα για τους συμμετέχοντες με τη λογοπενική παραλλαγή της νόσου.

Από τη μελέτη τεσσάρων περιπτώσεων που αξιολογήθηκαν ξανά μετά από διάστημα ενός έτους, βρέθηκε ότι οι δύο συμμετέχοντες με τη λογοπενική παραλλαγή παρουσίασαν γρηγορότερη έκπτωση, καθώς και έκπτωση σε περισσότερους τομείς, σε σχέση με τους άλλους δύο συμμετέχοντες.

Προοπτικές μελέτες με μεγαλύτερο αριθμό συμμετεχόντων και ισορροπημένη αντιπροσώπευση των 3 παραλλαγών της ΠΠΑ είναι απαραίτητες προκειμένου να διερευνηθούν περαιτέρω και να διευρυνθούν τα συμπεράσματα αυτής της μελέτης.

Keywords: Πρωτοπαθής προοδευτική αφασία, Νόσος Alzheimer, λογοπενική, αγραμματική, σημασιολογική παραλλαγή

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LIST OF ABBREVIATIONS

PPA:	Primary Progressive Aphasia
svPPA	Semantic variant of Primary Progressive Aphasia
nfvPPA	Non-fluent/agrammatic variant of Primary Progressive Aphasia
lvPPA	Logopenic variant of Primary Progressive Aphasia
AOS	Apraxia of Speech
PAOS	Progressive Apraxia of Speech
AD	Alzheimer's disease
FTD	Frontotemporal Dementia
FTLD	Frontotemporal Lobar Degeneration
bvFTD	Behavioral variant of Frontotemporal Dementia
ALS	Amyotraphic Lateral Sclerosis
MND	Motoro Neuron Disease
PSP	Progressive Supranuclear Palsy
CBD	Corticobasal Degeneration
CBS	Corticobasal Syndrome
PD	Parkinson's disease
CDR	Clinical Dementia Rating
FTLD-CDR	Frontotemporal Lobar Degeneration – Modified Clinical Dementia Rating
MMSE	Mini Mental State Examination
BDAE	Boston Diagnostic Aphasia Examination
BNT	Boston Naming Test
WAB	Western Aphasia Battery
DDK rates	Diadochokinetic rates

PPVT	Peabody Picture Vocabulary Test
PPTT	Pyramids and Palm Trees Test
CDT	Clock Drawing Test
TMT	Trail Making Test
GDS	Geriatric Depression Scale
BDI	Beck Depression Inventory
PASS	Progressive Aphasia Severity Scale
FRS	Frontotemporal Dementia Rating Scale
QPA	Quantitative Production Analysis
Syd-Bat	Sydney Language Battery
MRI	Magnetic Resonance Imaging
GDPR	General Data Protection Regulation
GRN	Progranulin gene
C9ORF72	Chromosome 9 open-reading-frame 72 gene
MCI	Mild Cognitive Impairment

1 Introduction

1.1 Overview

Primary Progressive Aphasia (PPA) is a degenerative condition characterized by gradual, progressive loss of language function. Cognitive abilities as well as activities of daily living are preserved during the first two years of the disease. Language symptoms remain predominant during much of the course of the disease (Gorno-Tempini et al., 2011; Mesulam, 2003; 2001).

Patients diagnosed with PPA, are divided into clinical variants based on specific speech and language features according to International Consensus Criteria (Gorno-Tempini et al., 2011). Investigators agree that the proposed classification is more applicable at the relatively early stages of the disease (Gorno-Tempini et al., 2011). The semantic variant (svPPA) is associated with difficulties in single word comprehension and naming. The non-fluent/agrammatic variant (nfvPPA) is characterized by apraxia of speech and production errors in syntax. The logopenic variant (lvPPA) is characterized by difficulties in repetition and word finding. Individuals with the latter variant often make phonological errors and their rate of speech is slow.

PPA results from a variety of underlying diseases, but the most common types of neurodegeneration are frontotemporal lobar degeneration (FTLD) and Alzheimer's disease (AD) (Spinelli et al., 2017). For the vast majority of patients with AD, the most prominent clinical symptom is memory loss rather than an impairment of language. However, the logopenic variant of PPA tends to be associated with AD pathology. The most typical pathology of svPPA and nfvPPA is FTLD.

The prevalence of PPA is estimated in the range of 1.1–6 per 100.000 (Grossman, 2014). PPA usually occurs before the age of 65, with approximately equal prevalence between the sexes (Mesulam et al., 2014). Survival is about 7 years (Grossman, 2014). Mean survival is longer in nfvPPA (8 years) and median survival in svPPA (12 years). Survival in FTD is comparable to AD survival with the exception of the amyotrophic lateral sclerosis-frontotemporal dementia complex FTD-ALS (Kansal et al., 2016).

The vast majority of studies involving individuals with PPA have been conducted with participants whose native language is English. Detailed analysis of language in PPA in

other languages are scarce (Auclair-Ouellet, 2015). Only a small number of studies have been conducted in Greek speakers with PPA. Most of the research is single-case studies or studies with few participants, and focus on isolated aspects of language, predominantly morphosyntax. More evidence is needed to understand the clinical presentation of PPA in Greek-speaking individuals in order to improve speech and language assessment and therapy provision for this under-researched population.

1.2 Aims and Research Questions

The main aim is to document the clinical presentation of PPA in Greek-speaking individuals with PPA at the early and moderate stages of the disease. This involves developing a detailed profile of the speech and language abilities in Greek-speaking individuals with PPA and investigating how speech and language characteristics correlate with other areas of cognitive functioning.

The main research questions that drive this research are four-fold:

1. What are the existing neuropsychological instruments, for Greek, that can be used in the evaluation of the speech, language, and other cognitive deficits in individuals with PPA?

2. What are the measures that differentiate Greek-speaking individuals with PPA from neurotypical controls?

3. What are the measures that differentiate Greek-speaking individuals with PPA from individuals with AD?

4. Which instruments are useful in diagnosing PPA and classifying individuals into the established variants of PPA?

Phase One: Development of the evaluation protocol

Literature review on the neuropsychological tests used in the evaluation of individuals with PPA

Aim: To identify the cognitive and linguistic domains of interest and specify the neuropsychological instruments in the Greek language that can be used in documenting the deficits encountered in PPA.

Pilot study one: Bilingualism in a case of the non-fluent/agrammatic variant of PPA

Aim: To compare the participant's connected speech production to that of Greek-speaking normal controls and determine whether Greek (first language) and French (second language) are differentially impaired.

Pilot study two: A case study of a Greek-speaking individual with the semantic variant of PPA

Aim: To evaluate the assessment battery and describe the clinical presentation of the disease in a Greek-speaking individual with the semantic variant of PPA.

Pilot study three: Comparing two Greek-speaking individuals with the non-fluent and semantic variant of primary progressive aphasia using neuropsychological, narrative, and acoustic measures.

Aim: The aim of this study was to evaluate the battery of neuropsychological tests, narrative analysis and acoustic measures and compare the clinical presentation of nfvPPA and svPPA, in two Greek-speaking individuals with PPA.

Phase Two: Research Studies: linguistic and cognitive profiles of Greek-speaking individuals with PPA

Study one: Comparing Greek-speaking individuals with PPA to individuals with AD and neurotypical controls

Aim: To establish which measures can differentiate Greek-speaking individuals with PPA from individuals with AD and neurotypical adults.

Study two: Comparing two narration tasks in PPA and AD: picture description and story retell.

Aim: To compare performance on two frequently used narration tasks and examine whether the two elicitation tasks placed different cognitive demands on individuals with PPA and AD.

Study three: Cognitive-linguistic profiles of Greek-speaking individuals with a degenerative disease: a case-control study

Aim: To explore the range of cognitive and language symptoms in PPA and FTD and document the challenges associated with the clinical diagnosis of PPA and classification of the PPA variants.

Study four: A case-series study of disease progression: how do cognitive-linguistic profiles of individuals with PPA change in one year as the disease evolves?

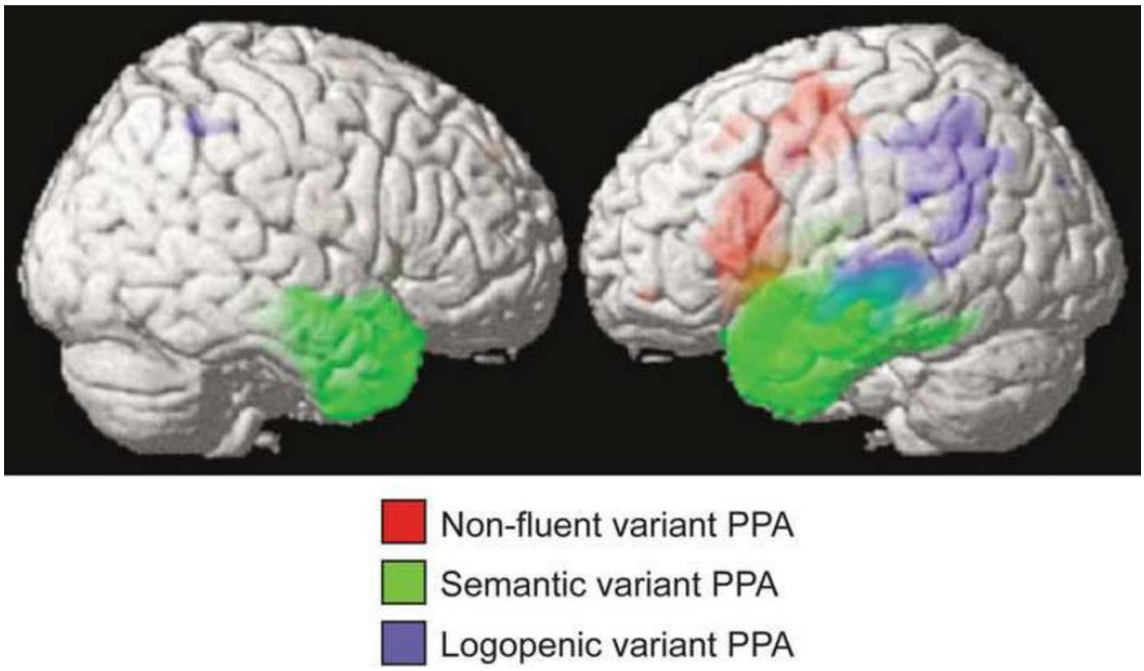
Aim: To gain an insight into how performance on the neuropsychological assessment battery changed after a one-year period, in relation to which language/cognitive abilities deteriorated, and which remained stable over time.

1.3 Literature Review

1.3.1 Historical Overview and Conceptual Framework

The first reports of patients with a progressive language disorder go back to the 1980's. Pick and Serieux (in Gorno-Tempini et al., 2011) were the first to describe language deterioration due to atrophy of the left frontal and temporal lobes. The term primary progressive aphasia (PPA) was first used by Marsel Mesulam in the 1980s (Mesulam, 1982) to described the distinct syndrome of a slowly progressive language impairment. For approximately two decades PPA was divided into semantic dementia and progressive non-fluent aphasia. However, not all cases could be classified into these two subtypes. A third subtype, logopenic primary progressive aphasia, was first described by Gorno-Tempini et al (2004). The current consensus criteria for PPA recognize three variants: the semantic variant of PPA (svPPA), the non-fluent/agrammatic variant of PPA (nfvPPA) and the logopenic variant of PPA (lvPPA) (Gorno-Tempini et al., 2011).

Each variant has a distinct profile of language impairment, a specific distribution of atrophy on neuroimaging, and a different likelihood of the exact underlying molecular pathology.



Source: (Wilson, Galantucci, Tartaglia, & Gorno-Tempini, 2012)

Figure 1: Characteristic patterns of brain atrophy in PPA variants affecting frontal, parietal and temporal lobes.

Each PPA variant shows a distinct pattern of underlying brain atrophy in the left hemisphere (Gorno-Tempini et al., 2011). Typically, nfvPPA is associated with fronto-insular atrophy, lvPPA with atrophy of temporo-parietal regions and svPPA with atrophy of the anterior and inferior temporal lobe, more pronounced in the left hemisphere.

PPA overlaps clinically and pathologically with Frontotemporal Dementia (FTD) and Alzheimer's disease AD). FTD is an umbrella term that encompasses degenerative disorders of the frontal and anterior temporal lobes that affect behavior and language. FTD typically includes the behavioral variant of FTD (bvFTD) and the two language variants of PPA, nfvPPA and svPPA (figure 1). Amyotrophic lateral sclerosis (ALS) (also known as Motor Neuron Disease, MND) and the atypical parkinsonian syndromes of Corticobasal syndrom (CBS) and Progressive supranuclear palsy (PSP) are also included in the FTD spectrum (Olney, Spina, & Miller, 2017). FTD is (together with AD) the most common cause of dementia in individuals with early-onset dementia, before the age of 65 (Bang, Spina, & Miller, 2015).

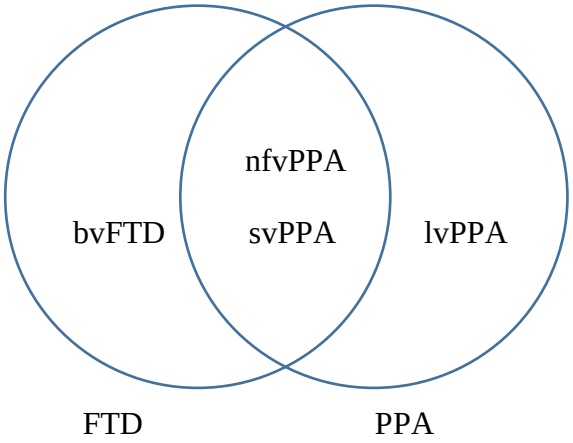
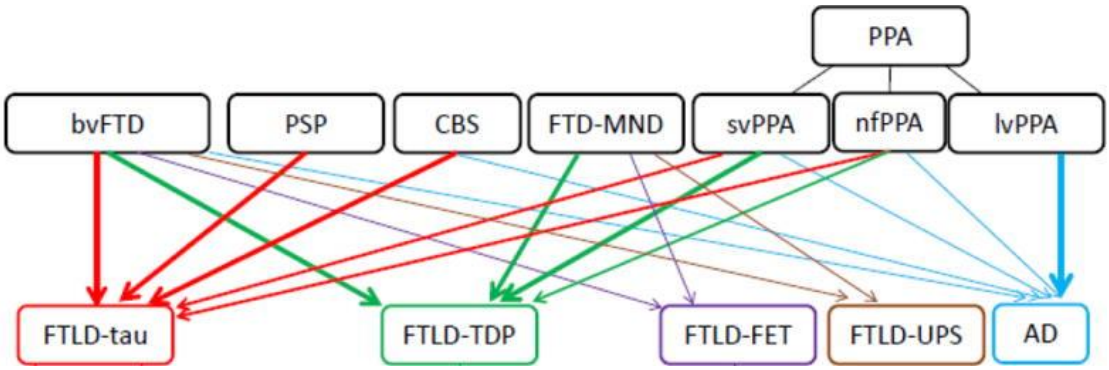


Figure 2: A schematic diagram of the diagnostic overlap between FTD and PPA

The term frontotemporal lobar degeneration (FTLD) is used from a neuropathological perspective. Three histopathological inclusions characterize FTLD: FTLD-Tau, FTLD-TDP and FTD-FET (Mackenzie & Neumann, 2016). SvPPA has been correlated with FTLD-TDP, while nfvPPA with FTLD-Tau (Josephs et al., 2011; Spinelli et al., 2017). Although strong associations exist, the relationship between clinical diagnoses and specific pathologies is not always clear cut (figure 3).



Source: (Olney et al., 2017)

Figure 3: Clinical and pathological correlations in FTD spectrum disorders

The logopenic variant of PPA is strongly associated with Alzheimer's disease pathology. AD which is the most frequent type of dementia (60–70%), is clinically characterized by memory deficits and pathologically by the presence of two proteins: amyloid, and tau (Reitz, Brayne, & Mayeux, 2011). Amyloid beta (β) peptides

accumulate to form extracellular plaques, while TAU proteins form intracellular neurofibrillary tangles.

Most cases of PPA are sporadic. However, around one third of the persons with PPA have a family history of PPA or another disorder within the FTD spectrum (Flanagan et al., 2015; Goldman et al., 2005; Rohrer, 2014). A gene mutation has been found in a small proportion of affected people. Two mutations, in the progranulin (GRN) and the chromosome 9 open-reading-frame 72 (C9ORF72) genes, are considered to be the major cause of familial cases of PPA (Flanagan et al., 2015; Rohrer, 2014) . Genetic predisposition varies among the different PPA variants. In particular, nfvPPA has been found to be more hereditary than the semantic and the logopenic variant (Rohrer, 2014).

Currently, there is no pharmacological treatment for FTD that can stop or alter the course of disease progression. Treatment of FTD is symptomatic. Medications that have been used to improve behavioral, cognitive, and motor symptoms include antidepressants, antipsychotics, antiepileptics, N-methyl D-aspartate glutamate (NMDA) receptor antagonists, acetylcholinesterase inhibitors and dopamine replacement (Tsai & Boxer, 2016). Acetylcholinesterase inhibitors, commonly used in AD, may worsen symptoms in FTD (Olney et al., 2017).

Individuals with FTD and their caregivers may benefit from non-pharmacological therapies. Physical exercise, caregiver education are among the treatments that have been found to have a positive effect (Shinagawa et al., 2015). Moreover, speech and language intervention can improve language outcomes in individuals with PPA (Cadório, Lousada, Martins, & Figueiredo, 2017; Carthery-Goulart et al., 2013; Tippett, Hillis, & Tsapkini, 2015).

1.3.2 **Diagnostic criteria of PPA variants**

According to the established criteria, the diagnosis of a PPA variant is made in two stages. First, a person must meet Mesulam's criteria for PPA (Gorno-Tempini et al., 2011; Mesulam, 2001). For a diagnosis of PPA to be established, the language deficits must be the most prominent deficit at symptom onset and for the early stages of the disease, as well as the principal cause of impaired activities of daily living. Furthermore, the existing deficits should not be better accounted for by other medical, neurodegenerative or psychiatric disorders. Finally, the prominent initial behavioral

disturbances, episodic memory, visual memory or visuoperceptual impairments should not be present at the time of diagnosis.

Once an individual is diagnosed with PPA, speech and language features guide the classification process into a PPA variant. The language domains that contribute to this process include the following: speech production, repetition, single-word comprehension, comprehension of syntax, naming, semantic knowledge, reading and spelling. The diagnosis is clinical and can be supported by neuroimaging such as MRI, SPECT or PET scan and/or supported by histopathology or genetic evidence of definite pathology. Histopathological confirmation can only be made at post-mortem. The diagnostic criteria of the three variants of PPA are presented in Table 1.

Table 1: Diagnostic criteria for the three PPA variants

nfvPPA	svPPA	lvPPA
	I. Clinical Diagnosis	
At least one of the following core features must be present:	Both of the following core features must be present	Both of the following core features must be present
1. Agrammatism in language production	1. Impaired confrontation naming	1. Impaired single-word retrieval in spontaneous speech and naming
2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)	2. Impaired single-word comprehension	2. Impaired repetition of sentences and phrases
At least 2 of 3 of the following other features must be present:	At least 3 of the following other features must be present:	At least 3 of the following other features must be present:
1. Impaired comprehension of syntactically complex sentences	1. Impaired object knowledge	1. Speech (phonologic) errors in spontaneous speech and naming

2. Spared single-word comprehension	2. Surface dyslexia or dysgraphia	2. Spared single-word comprehension and object knowledge
3. Spared object knowledge	3. Spared repetition	3. Spared motor speech
	4. Spared speech production	4. Absence of frank agrammatism

II. Neuroimaging-supported diagnosis

Both criteria must be present

1. Clinical diagnosis of the specific PPA variant
2. Neuroimaging must show one or more of the following results:

Predominant left posterior-fronto-insular atrophy on MRI or	Predominant anterior temporal lobe atrophy on MRI or	Predominant left posterior perisylvian or parietal atrophy on MRI or
Predominent left posterior frontoinsular hypoperfusion or hypometabolism on SPECT or PET	Predominent anterior temporal hypoperfusion or hypometabolism on SPECT or PET	Predominent left posterior perisylvian or parietal hypoperfusion or hypometabolism on SPECT or PET

III. Diagnosis of PPA variant with definite pathology

1. Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
2. Clinical diagnosis of the specific PPA variant
    a. Histopathologic evidence of a specific neurodegenerative pathology (e.g. FTLD-tau, FTLD-TDP, AD, other)
    b. Presence of a known pathogenic mutation

Source: Gorno-Tempini et al. (2011)

PPA can reliably be classified into 3 subtypes in around 75-80% of cases (Nickels & Croot, 2014). A patient may display a central feature of a specific variant, but not other supporting features at a particular time in the disease course (Sapolsky, Domoto-Reilly

& Dickerson, 2014). Sometimes, a patient may present with characteristics which comply with more than one subtype (e.g. Vandenberghe, 2016). To accommodate these inconsistencies, it has been suggested that classification should include other variants, such as primary progressive apraxia of speech (PPAOS) (Duffy et al., 2015; Josephs et al., 2012), anomic PPA (Vandenberghe, 2016) and mixed PPA (Mesulam et al., 2014). The classification of some patients remains challenging and this has important implications for clinical management, as well as scientific investigations.

1.3.3 The clinical characteristics of PPA variants

1.3.3.1 *Overview*

Within PPA, there is great heterogeneity with varying symptoms and trajectories. The characteristic profiles of PPA variants include linguistic, as well as non-linguistic features, namely apraxia in nfvPPA, behavioral changes in svPPA and working memory deficits in lvPPA. The profiles evolve with disease progression and this is one of the main reasons that renders the analysis of deficits in PPA complex (Leyton & Ballard, 2016). The distinctive features of the PPA variants can be more clearly identified in the early stages of the disease.

Aphasia is an impairment of language which affects the production and/or comprehension of speech, as well as the ability to read or write, and carry out arithmetic calculations. In PPA, aphasia is the most prominent deficit at onset, but there may be subtle evidence of deficits in other domains, reflecting a spread of the disease to areas adjacent in the language network. These may include ideomotor apraxia, dyscalculia, disinhibition (i.e. lack of restraint, impulsivity), and constructional deficits. Nevertheless, these types of non-language deficits do not restrict daily living activities to a significant degree.

As the disease progresses, other domains are increasingly affected, most notably executive functions and behavior. Memory deficits for recent events, face and object recognition deficits, mild pyramidal (e.g. spasticity, weakness, hyperactive reflexes) and extrapyramidal (e.g. bradykinesia, rigidity, tremor) deficits may arise. At the advanced stages, aphasia is characterized by severe comprehension deficits. Similarly, expressive language is significantly reduced to single words, palilalic repetitions of syllables or

grunts. All persons with PPA become mute at the end stage of the disease-complex (Harciarek, Sitek, & Kertesz, 2014).

The literature on linguistic, other cognitive and behavioral deficits in PPA is quite extensive. The following review will focus on the distinctive features of the PPA variants.

1.3.3.2 *Speech/language characteristics*

Speech and language can be evaluated using structured production and comprehension tasks, as well as connected speech analysis of spontaneous speech or discourse genres.

Motor speech

Motor speech disorders include two major entities: apraxia of speech (AOS) and dysarthria. Poole et al. (2017) reviewed the evidence on motor speech impairment in PPA. Motor speech disorders, usually AOS, occur frequently in nfvPPA. Dysarthria has also been reported although less commonly. Dysarthria, when present, is usually of the spastic or the hypokinetic type (Ogar et al., 2007). The most common perceptual features of AOS in nfvPPA include impaired prosody, slow speech rate and articulation errors, both phonemic and phonetic. In PPA, apraxia of speech (AOS) has been linked to pathology of the speech motor regions of the frontal cortex. Neither AOS, nor dysarthria has been documented in svPPA. Slow speech rate and the presence of hesitations in this variant may be attributed to anomic difficulties. Finally, there have been reports of motor speech deficits in lvPPA. It must be noted, however, that production errors in this variant are more likely to represent phonemic paraphasias (Poole, Brodtmann, Darby, & Vogel, 2017).

Connected speech production

The evaluation of connected speech enables a multi-level naturalistic assessment of language production (Marini, Andreetta, del Tin, & Carlomagno, 2011). All linguistic levels, phonetics, phonology, morphology, syntax, semantics, pragmatics, and discourse can be evaluated when analyzing connected speech samples.

Boschi et al. reviewed the evidence from studies focusing on connected speech deficits in neurodegenerative disorders (Boschi et al., 2017). People with the non-fluent/agrammatic variant of PPA typically speak at a slower speech rate than healthy

controls and make frequent speech sound errors (Ash et al., 2009; Wilson et al., 2010). At the lexical level, an increased number of errors in closed class words (less nouns with determiners) has been reported (Knibb, Woollams, Hodges, & Patterson, 2009; Sajjadi, Patterson, Tomek, & Nestor, 2012b). At the syntactic level, they make syntactic and inflectional errors (Graham, Patterson, & Hodges, 2004; Sajjadi et al., 2012b) and produce simplified sentences with lower number of words per utterance, clauses, verb phrases and coordinated sentences (Fraser et al., 2014; Knibb et al., 2009; Wilson et al., 2010). Concerning discourse abilities, individuals with nfvPPA produce a reduced number of words, limited relevant information and they have difficulty maintaining the topic (Graham et al., 2004; Wilson et al., 2010; Sajjadi et al., 2012; Ash et al., 2013; Fraser et al., 2014). It should be noted that agrammatic features may also be evident in writing (Bettcher & Sturm, 2014).

In svPPA speech rate is slower than in healthy controls and it is associated with false starts (Ash et al., 2006, 2013; Meteyard and Patterson, 2009; Wilson et al., 2010). At the lexical level, reduced proportion of open class words, use of high-frequency words and increased number of pronouns and semantic errors have been reported (Meteyard and Patterson, 2009; Sajjadi et al., 2012a Fraser et al., 2014a Wilson et al., 2010). At the syntactic level, compared to normal controls, reduced mean length of utterance, syntactic complexity and range of syntactic constructions have been verified (Sajjadi et al., 2012a; Meteyard et al., 2013 Wilson et al., 2010; Fraser et al., 2015b Ash and Grossman, 2015). Difficulties in discourse planning (impairment of local coherence) have been shown (Ash et al., 2006; Ash and Grossman, 2015).

LvPPA is characterized by the presence of phonological errors, slower speech rate and increased number of dysfluencies (pauses, false starts, filled pauses, repaired sequences) in comparison to controls (Ash & Grossman, 2015; Ash et al., 2013; Wilson et al., 2010). In the same studies, reduced proportion of well-formed sentences, reduced number of open class words but increased number of pronouns used was reported.

The presence of distortions has been found to be the most informative measure for distinguishing between nfvPPA and lvPPA (Wilson et al., 2010). Additional measures that may assist in differentially diagnosing these subtypes are proportion of verbs and number of embeddings used in spontaneous speech, which are higher in lvPPA. Faster speech rate, less distortions, higher proportion of pronoun and verb usage, and

production of nouns of higher frequency and or familiarity were found in svPPA compared to nfvPPA (Ash et al., 2013; Fraser et al., 2014; Wilson et al., 2010).

Inflectional morphology

Formal structured testing has yield inconsistent results regarding morphological difficulties in PPA (Auclair-Ouellet, 2015). At a group level, individuals with nfvPPA are impaired, whereas morphological processing is preserved in lvPPA. Individual patient data however indicate variable performance. In svPPA, morphology is spared, though difficulty inflecting irregular and low-frequency verbs has been displayed in some studies (Meteyard, Quain, & Patterson, 2014).

Sentence comprehension

Impaired comprehension of complex sentences attributed to morphosyntactic deficits is one of the hallmark features of nfvPPA that has been attested in several studies (eg. Thompson et al., 2013; Wilson, et al., 2010). Difficulty with complex sentences has also been found in lvPPA, but has been associated with verbal working memory deficits (Thompson & Mack, 2014). Sentence comprehension is relatively preserved in svPPA, but may be affected at later stages of the disease (Thompson & Mack, 2014).

Naming

Naming impairment and naming decline has been documented in all PPA variants (eg., Sebastian et al., 2018). Migliaccio et al. (2016) assessed picture naming in 30 patients with PPA. All svPPA, lvPPA and one fifth of the nfvPPA patients were impaired on confrontation picture naming. Naming was more impaired in svPPA than in lvPPA and least impaired in nfvPPA. Semantic paraphasias and no responses were more likely to occur in svPPA, whereas phonemic paraphasias were prominent errors in nfvPPA.

Anomia in svPPA has been linked to degraded semantic representations or impaired access to phonological representations from semantics, whereas in lvPPA and nfvPPA to impaired phonological representations (Meyer, Tippett, Turner, & Friedman, 2019).

Writing and Reading

Reading and writing impairments are common in PPA and different profiles of deficits have been reported in the different variants of PPA. Handwriting, although generally

preserved, can also be affected in PPA in the presence of a constructional, visuospatial or motor deficit in the later stages of the disease (Graham, 2014).

The semantic variant of PPA is characterized by surface dysgraphia (difficulty with exceptional and low-frequency words and regularization errors) (Faria et al., 2013; Henry, Beeson, Alexander, & Rapcsak, 2012). Non-phonologically plausible errors can be expected with disease progression (Graham, 2014).

Impairment patterns are more variable in the other variants. In the non-fluent/agrammatic variant, most commonly, there is phonological dysgraphia (impairment in lexical spelling and phoneme-to-grapheme conversion and production of non-phonologically plausible errors). Phonological dysgraphia is usually accompanied by the presence of phonologically plausible errors (Graham, 2014). Several cases of graphemic buffer disorder (difficulty with letter sequencing) have also been reported (Graham, 2014). Deep dysgraphia (characterized by the production of semantic errors) is rare, but has been reported in a small number of nfvPPA cases (Faria et al., 2013; Tree, Kay, & Perfect, 2005).

In the logopenic variant, dysgraphia can be the presenting symptom (Rapp & Glucroft, 2009). Similarly to nfvPPA, any type of writing disorder can be observed in this variant (Graham, 2014). Most studies have documented the presence of phonological dysgraphia. Surface dyslexia has also been reported. Finally, a graphemic buffer disorder is less likely to be found in lvPPA (Graham, 2014).

Recently, it has been proposed that spelling may assist classification. Neophytou et al. used words and pseudowords in a spelling task and employed automated classification to sybtype PPA variants (Neophytou, Wiley, Rapp, & Tsapkini, 2019). Classification accuracy was 70% for nfvPPA, 66% for svPPA and 59% for lvPPA.

Regarding reading abilities, surface dyslexia has been associated with svPPA, whereas phonological dyslexia with lvPPA (S. M. Brambati, Ogar, Neuhaus, Miller, & Gorno-Tempini, 2009; Matías-Guiu et al., 2017) and nfvPPA (Matías-Guiu et al., 2017).

1.3.3.3 *Language-specific characteristics*

A limited number of studies indicates that some symptoms are unique in different languages (Tee & Gorno-Tempini, 2019).

In Italian, stress assignment errors in reading aloud have been documented in a person with svPPA and have been interpreted as indications of surface dyslexia (Galante, Tralli, Zuffi, & Avanzi, 2000). Japanese individuals with svPPA, even with mild impairment, have been found to perform considerably better with alphabetic script (kana) than with logographic script (kanji) (Ikeda et al., 2011). The authors of this study recognize that the early discovery of Gogi aphasia/SD in Japan was related to the demanding nature of the Japanese written language. In Chinese, which is a logographic language, individuals with svPPA exhibit deep dyslexic errors (Ting, Chia, & Hameed, 2016).

Finally, Canu et al. directly compared Italian and English-speaking individuals with nfvPPA (Canu et al., 2020). They found that the Italian speakers were more impaired in measures of syntactic productivity and comprehension, whereas the English-speaking participants were more impaired in measures of motor speech ability, despite higher level of education.

These findings suggest that there may be language specific presentations of PPA, which depend on the specific characteristics of each language (Canu et al., 2020).

1.3.3.4 *Cognitive functions*

Neuropsychological testing may reveal additional areas of cognitive impairment in PPA variants. In this section, memory, executive, and visuospatial functions are reviewed.

Memory

Memory deficits have been reported in PPA. In a recent meta-analysis, effect sizes of memory deficits were estimated for each variant (Eikelboom et al., 2018). The largest effect size was for lvPPA. Memory deficits, both verbal and non-verbal, seem to be more pronounced in the logopenic than in the non-fluent/agrammatic variant. Impaired verbal memory is also found in the semantic variant. Progression of lvPPA to posterior temporal regions and involvement of the hippocampus may explain the memory deficits displayed by persons with lvPPA (Bettcher & Sturm, 2014).

Executive functioning

Individuals with nfvPPA have shown executive deficits on verbal tasks of working memory, verbal fluency, as well as on non-verbal tasks of mental flexibility and abstract

reasoning (Macoir, Lavoie, Laforce, Brambati, & Wilson, 2017). There are however reports of unimpaired non-verbal executive functioning (e.g., Butts et al., 2015). Executive functions seem to decline over the course of the disease (Libon et al., 2009).

In svPPA, a person may have difficulty comprehending instructions and/or stimuli due to the underlying semantic impairment. This difficulty affects performance on neuropsychological tests. Mixed results have been reported about the presence of executive deficits in the early stages of this variant and the progression of the decline (Macoir et al., 2017).

In lvPPA, executive deficits have been found on the Trail-Making Test (TMT) (Butts et al., 2015). Time to complete part B of the TMT test was significantly slower than in svPPA. Impairment has also been reported in a few other studies, but more research is needed to better describe executive decline in lvPPA (Macoir et al., 2017).

Visuospatial functioning

SvPPA is the variant in which visuospatial functioning is less affected in comparison to the other two variants (Butts et al., 2015). However, individuals with svPPA are more impaired in recalling visual information (Watson et al., 2018). Individuals with lvPPA may display deficits on visuospatial tasks (visual localization and construction) such as copying a complex figure at the early stages of the disease (Bettcher & Sturm, 2014). Persons with nfvPPA are also impaired in visuospatial functioning but perform better in delayed recall than persons with lvPPA. Both variants show decline in visuo-construction, namely figure copying, over time (Watson et al., 2018).

Mathematical calculations

Early in the course of the disease, individuals with lvPPA may display deficits on calculation tasks (e.g., multiplication or complex addition) (Stenclik et al., 2013). Individuals with nfvPPA may have trouble with complex mathematical calculations due to executive deficits (Bettcher & Sturm, 2014). In svPPA, some persons may have lost the knowledge of arithmetic facts (e.g. basic multiplications) and not remember the significance of an operation sign, but still be capable of performing mathematical calculations (Bettcher & Sturm, 2014).

In summary, executive deficits are more common in nfvPPA, followed by lvPPA. The logopenic variant is characterized by difficulty in calculation ability and visuospatial

functioning. Memory functions are more impaired in lvPPA. Individuals with the semantic variant may display a memory impairment which can be attributed to the loss of semantic knowledge.

1.3.3.5 *Behavioral symptoms*

Although marked behavioral changes are atypical at the initial stages of PPA, a variety of neuropsychiatric symptoms have been documented with disease progression. However, very few studies have directly compared the neuropsychiatric symptoms in the three PPA variants using different neuropsychiatric and behavioral scales.

In a review of the relevant literature, Modirrousta et al. noted that neuropsychiatric symptoms are relatively infrequent initially in the non-fluent/agrammatic and logopenic variant, whereas they are more common in early stages of svPPA (Modirrousta, Price, & Dickerson, 2013). Loss of empathy, changes in eating, compulsive behavior and disinhibition are typically found in svPPA. The nfvPPA variant is associated with apathy, depression and irritability. Finally, agitation, irritability and apathy have been found in cases of lvPPA (Modirrousta et al., 2013).

Singh et al. (2015) investigated the neuropsychiatric symptoms exhibited by persons with PPA and PPAOS from the perspective of the primary caregiver using a questionnaire. Significant differences between the PPA variants were found comparing the occurrence of neuropsychiatric symptoms. The most significant distinguishing features among the three variants were disinhibition and appetite. Disinhibition was more frequent in svPPA, whereas appetite changes were more likely to be found in svPPA and nfvPPA. Delusion and hallucination were found only in lvPPA. Although individuals with PPA presented initially with depression related symptomatology, probably as a response to their communication difficulties, with disease progression, disinhibition and aberrant motor behavior were more likely to be reported. Apathy was correlated with the diagnosis of PPAOS.

In a longitudinal investigation of behavioral changes in PPA variants (Van Langenhove, Leyton, Piguet, & Hodges, 2016) individuals with svPPA, in the mild stages of the disease, presented with more behavioral disturbances compared to the nfvPPA and lvPPA group. Stereotypical behavior, loss of empathy, and presence of apathy were the most prominent symptoms, followed by disinhibition and changes in eating. The

nfvPPA and the lvPPA groups did not differ at initial assessment. In both groups, manifesting of apathy was the most frequent symptom. When examined one year later, loss of empathy was greater in svPPA and nfvPPA than in lvPPA. Stereotypical behavior remained the most discriminating feature of svPPA.

Most behavioral symptoms in FTD are associated with right frontal and temporal areas. Rohrer and Warren (2010) proposed a similar neural finding in PPA for symptoms of anxiety, apathy, irritability, and appetite changes. Disinhibition has been correlated with reduced gray matter density in the left hemisphere. Individuals with PPA exhibit atrophy in the left hemisphere. However, a subtle atrophy in homologous regions of the right hemisphere which may explain initial behavioral symptoms, is not uncommon (Modirrousta et al., 2013). At later stages, right hemisphere involvement underlies behavioral disturbances (Gainotti, 2019).

1.3.3.6 *Functional ability*

Typically, an individual's functional ability is measured by performance in activities of daily living (ADL). Activities such as eating, dressing, and bathing are considered to be more basic than instrumental activities, like using the telephone, managing money and shopping, which are more complex. PPA impacts communication. As a consequence, all activities of daily living that depend on communication are compromised. Individuals with PPA may experience restrictions in participating in conversations and social events, making phone calls and accessing social support (O'Connor, Ahmed, & Mioshi, 2014; Taylor et al., 2014).

Preservation of activities of daily living that do not depend on language and communication at the early stages of the disease is considered to be a criterion for establishing a diagnosis of PPA. Functional abilities remain intact for the first five years from disease onset (O'Connor et al., 2016). However, with disease progression, generalized dementia affects multiple functional domains.

In lvPPA and svPPA, functional impairment is initially limited to instrumental ADLs. In the nfvPPA variant both basic and instrumental ADLs are affected, and changes are more pronounced compared to the other variants (Jang, Cushing, Clemson, Hodges, & Mioshi, 2012). Cognitive factors seem to underly the functional decline in svPPA, whereas baseline behavioral and functional scores seem to predict decline in nfvPPA

(O'Connor et al., 2016). Cognition and behavior are the main predictors of ADL decline in AD (O'Connor et al., 2016) .

1.3.3.7 *Summary and Implications*

Speech and language deficits may be the core features of PPA variants, but other cognitive and psychosocial domains are also affected, especially with disease progression. In order to develop an accurate profile of deficit patterns in PPA variants, linguistic and additional neuropsychological testing should cover manifestation of all symptoms. Neuropsychological evaluation should document functional status, as well as specific behavioral, speech, language and other cognitive symptoms which are integral to PPA. Moreover, it should identify the features that can assist in differential diagnosis of PPA variants.

1.3.4 **Studies of Greek-speaking individuals with PPA**

Studies of Greek-speaking individuals with PPA are limited and there is no overall description of the speech and language clinical presentation.

All group studies of Greek-speakers with PPA are non-linguistic in nature. Konstantinopoulou et al. (2011) included a group of 19 individuals with FTD in the Greek adaptation study of Addenbrooke's Cognitive Examination-Revised (ACE-R) screening test, but no further details are provided about the performance of the different FTD groups which comprise two out of three variants of PPA.

The largest study to date, involving 33 patients with PPA, was conducted in the context of investigating the role of cognitive reserve in FTD (Maiovis, Ioannidis, Gerasimou, Gotzamani-Psarrakou, & Karacostas, 2017; Maiovis, Ioannidis, Nucci, Gotzamani-Psarrakou, & Karacostas, 2016). The sample consisted of 25 participants with the nfvPPA variant and 8 participants with the svPPA variant. The two subgroups did not differ in any demographic or basic neuropsychological variable. Demographic and neuropsychological variables were reported for the PPA group as a whole. Half of the PPA group were males. The mean age was 68.06 years (*SD* = 8.21), mean duration of disease was 2.39 years (*SD* = 1.3) and mean duration of formal education was 10.18 years (*SD* = 4.21). PPA participants mean sum of boxes score on the Frontotemporal Lobar Degeneration-Modified Clinical Dementia Rating Scale (FTLD-CDR) was 8.03

(*SD* = 4.8) and mean score on the Frontotemporal Dementia Rating Scale (FRS) was 0.48 (*SD* = 1.35). It should be noted that the first score provides an indication of disease severity (max = 24), whereas the second an estimate of the functional impairment (max = 1). Maiovis et al. (2016) concluded that cognitive reserve may have a protective role in PPA, as in participants with the same level of temporal lobe perfusion, disease severity was correlated with cognitive reserve. Language was evaluated using the language composite score of the Addenbrooke's Cognitive Examination (ACE-R) (Konstantinopoulou et al., 2011). This test includes a written command and a 3-step verbal command, repetition of 4 words and 2 sentences, confrontation naming of 12 pictures and 2 objects, word-picture semantic association of 4 items (comprehension), reading of 5 words and written production of one sentence. Again, data about the language performance of their participants with PPA was not made available.

Linguistic studies on PPA in Greek have focused on isolated phenomena in a specific variant, such as, compound naming in nfvPPA (Kordouli et al., 2018) and verb retrieval, argument structure and inflection marking in svPPA (Koukoulioti, Stavrakaki, Konstantinopoulou, & Ioannidis, 2018).

Kordouli et al. (2018) examined compound naming in one agrammatic participant with stroke aphasia and two participants with the non-fluent/agrammatic variant of PPA. All participants were impaired in producing compound words compared to healthy controls, although with distinct error patterns. Different error patterns were attributed to the different nature of the two diseases and the different level of PPA severity.

Koukoulioti et al. (2018) evaluated the performance of 7 individuals with svPPA on two sentence elicitation tasks. The aim of this study was to investigate verb production in respect to the number and type of arguments required, as well as the interaction between verb retrieval and inflection marking. The findings suggested difficulty with verb retrieval, whereas inflection was affected in the more severe stages of the disease.

Kambanaros and Grohmann (2012) explored bilingualism in a case-study of a multilingual person with PPA. The authors provided a detail account of their participant’s performance on the Bilingual Aphasia Test (BAT) in 3 languages (Greek, English and Czech), consistent with the clinical diagnosis of lvPPA.

In addition to these studies, several unpublished reports have been presented at national and international conferences (e.g., Karpathiou, Kambanaros, Papatriantafyllou, Potamianou, Kartsaklis & Sakka, 2017; Stavrakaki, Manouilidou, Konstantinopoulou, & Ioannidis, 2012). They share the same limitations with the aforementioned studies: they have a single or a small number of participants and they examine an isolated aspect of language. These features hinder the generalization of their results and do not contribute to the description of the clinical presentation of the PPA variants.

1.3.5 **Conclusion**

The characteristic profiles of the PPA variants extend beyond language and include other cognitive and behavioral deficits. Profiling both language and non-language impairments plays an important role in diagnosing PPA and differentiating between PPA variants. The review of the available research on Greek-speaking individuals with PPA highlights the critical need for further research in this area. The available studies do not provide information about the specific speech and language features encountered in Greek-speaking individuals with PPA. The inherent assumption that the deficits established in the English-speaking population are experienced the same by speakers of other languages, does not take into account the linguistic characteristics of each language. Furthermore, lack of data on discourse abilities and performance on neuropsychological tests does not allow clinicians to determine whether an observed behavior or result is normal or deficient. Completing a detailed profile of strengths and weaknesses has clinical implications, as it forms the basis for effective language rehabilitation.

2 Development of the assessment battery and pilot studies

2.1 Overview

Two phases were planned for this research program. Phase one focused on developing an assessment battery for Greek-speaking individuals with PPA through a literature review of the available assessment tools, and three pilot studies. The first pilot study evaluated the use of a connected speech analysis protocol in a bilingual person with nfvPPA, whereas the second pilot study evaluated the use of a neuropsychological battery of tests in a person with svPPA. In the third pilot study these two individuals were compared across all cognitive and linguistic domains using the research battery. Phase two involved recruitment of participants and assessment of their speech, language, and other cognitive abilities. Analysis of the findings was completed in 4 separate studies in order to address the research questions.

2.2 Literature review on the neuropsychological tests used in the evaluation of individuals with PPA

2.2.1 Introduction

Diagnosing PPA is challenging. Different research groups employ different methodologies and several instruments have been used for the overall description of speech and language abilities in PPA, and the evaluation of individual cognitive domains. The strengths and limitations of the assessment measures are not always straightforward. A published review of the neuropsychological tests that have been developed for the assessment of speech and language disorders in PPA (Battista et al., 2017) has provided information about the available neuropsychological tools in English and the relevant methodological concerns. There is no agreement in the literature or in practice on how language assessment should be performed. This is more complex in languages like Greek where available tools for the assessment of speech and language are extremely limited. More research has been conducted regarding cognitive functioning. Current research has yet to explore which instruments or battery of tests can be used to evaluate language and cognitive performance in Greek-speaking

individuals with PPA. This review seeks to illustrate current practices and identify potential assessment tools.

2.2.2 **Aim**

To identify the cognitive and linguistic domains of interest and specify the neuropsychological tools in Greek that can be used in documenting the deficits encountered in PPA.

2.2.3 **Method**

For the first part of the review regarding the cognitive and linguistic domains of interest, a selection of published articles, previously identified and used in the description of the clinical characteristics of PPA variants, was reviewed.

For the second part, a more systematic search was performed from June 2017 until December 2017. The review focused on published validation studies of tests in Greek assessing behavior, mood, cognition, speech and language or specific domains of these functions in individuals with primary progressive aphasia, dementia or aphasia after stroke. The following key words were used for the literature search in several databases (e.g., PUBMED, CINAHL, PsycARTICLES) through the Cyprus University of Technology library service 'Pantognostis': (Greek) AND ((primary progressive aphasia OR logopenic OR non-fluent OR agrammatic OR semantic OR dementia OR aphasia) AND (cognition OR language OR speech OR memory OR executive OR visuospatial OR behavior* OR neuropsychiatric OR neuropsycholog* OR synta* OR phonolog* OR gramma*) AND (assessment OR evaluation OR testing OR validation OR battery OR test OR instrument)). Reference lists were checked manually to find additional studies. The search was limited to peer-reviewed academic journals and papers published in Greek or English. Studies using experimental tasks were excluded from the review. The final selection was made by inspecting the title and the abstract of all relevant papers. The methodological quality of the primary studies was not assessed.

2.2.4 **Results**

Areas of testing (table 2) were primarily recognized applying the diagnostic criteria of PPA variants (Gorno-Tempini et al., 2011). Additional domains have been identified

reviewing studies that sought to describe in detail the core features of PPA variants, as well as the associated deficits (e.g. Harris, Saxon, Jones, Snowden, & Thompson, 2018; Hoffman, Sajjadi, Patterson, & Nestor, 2017; Marshall et al., 2018; Mesulam, Wieneke, Thompson, Rogalski, & Weintraub, 2012).

Table 2: Areas of testing

Cognitive	Speech/Language
Executive function	Motor speech
Working memory	Connected speech production
Memory	Fluency
Visuospatial abilities	Repetition
Object semantics	Single word comprehension
Other domains	Complex sentence comprehension
Disease severity/Staging	Syntactic comprehension
Functional status	Confrontation naming
Neuropsychiatric symptoms (behavior/mood)	Reading
Praxis	Writing

Concerning validated tests in Greek, 35 studies and a total of 43 tests (table 3) were included in the review of the available neuropsychological instruments in Greek. The instruments are presented in table 3, organized in terms of the domain tested. They are heterogeneous in form and scope. They include general cognitive and language measures and domain-specific tools. Some tests can be used for screening, others for in-depth assessment and others for staging PPA. Most tests are performance-based. Other tests rely on an informant's feedback to determine level of functioning. The majority of the tests focus on cognitive functioning. As for the language instruments, one study evaluated a general aphasia battery (Tsapkini, Vlahou, & Potagas, 2009), three studies focused on confrontation naming (Patricacou, Psallida, Pring, & Dipper, 2007; Simos, Kasselimis, & Mouzaki, 2011a, 2011b) and three studies on verbal comprehension

(evaluating five tests) (Simos et al., 2011a, 2011b; Simos, Kasselimis, Potagas, & Evdokimidis, 2014). Only one paper was in Greek (Solias et al., 2014). No test has been validated in persons with PPA. Nevertheless, the Pyramid and Palm Trees Test (PPTT) was administered to a small sample of Greek-speaking individuals with PPA (n = 12) in a cross-cultural study to inform selection of culturally appropriate items for the PPTT (Breining, Lala, Martínez, & Manes, 2015).

Table 3: Neuropsychological instruments available in Greek

General aphasia battery
Boston Diagnostic Aphasia Examination - Short Form (Tsapkini et al., 2009)
Confrontation naming
The Boston Naming Test (BNT) (Patricacou et al., 2007)
BNT-45 (Simos et al., 2011a)
BNT-20 (Simos et al., 2011b)
Single word comprehension (lexical semantics)
Peabody Picture Vocabulary test PPVT (Simos et al., 2011a)
Peabody Picture Vocabulary test PPVT-32 (Simos et al., 2011b)
Vocabulary subtest from the Wechsler Abbreviated Scale of Intelligence (WASI) (Simos et al., 2011a)
Vocabulary subtest from the Wechsler Abbreviated Scale of Intelligence (WASI)-15 (Simos et al., 2011b)
Sentence comprehension
Comprehension of Instructions in Greek (CIG) (Simos et al., 2014)
Reading
Reading fluency - Words & Non-words (Simos, Sideridis, Kasselimis, & Mouzaki, 2013)
Object semantics

Pyramid & Palm Trees Test (Breining et al., 2015)
Face recognition
The Hellenic famous face screening test (Proios, Malatra, & Farmakis, 2007)
Severity/Staging
Frontotemporal Lobar Degeneration-Modified Clinical Dementia Rating Scale (FTLD-CDR) (Maiovis et al., 2017)
Functional Status
Frontotemporal Dementia Rating Scale (FRS) (Maiovis et al., 2017)
Functional Cognitive Assessment Scale (FUCAS) (Kounti, Tsolaki, & Kiosseoglou, 2006)
Instrumental Activities of Daily Living (IADL) (Theotoka et al., 2007)
Composite cognitive measures
Mini Mental State Examination (MMSE) (Fountoulakis, Tsolaki, Chantzi, & Kazis, 2000; Solias et al., 2014)
Addenbrooke's Cognitive Examination-Revised (Konstantinopoulou et al., 2011)
Montreal Cognitive Assessment (MOCA) (Konstantopoulos, Vogazianos, & Doskas, 2016)
The Cambridge Cognitive Examination (CAMCOG) (Tsolaki, Fountoulakis, Chantzi, & Kazis, 2000)
Mattis Dementia Rating Scale (Katsarou et al., 2010)
Alzheimer's Disease Assessment Scale (ADAS) (Tsolaki, Fountoulakis, Nakopoulou, Kazis, & Mohs, 1997)
Greek severe impairment battery (SIB) (Konsta et al., 2014)
The Seven-Minute Screen (Tsolaki et al., 2002)
Executive function

Clock Drawing Test (Bozikas, Giazkoulidou, Hatzigeorgiadou, Karavatos, & Kosmidis, 2008)
The verbal fluency task (Kosmidis, Vlahou, Panagiotaki, & Kiosseoglou, 2004)
The Trail making test A and B (Zalonis et al., 2008)
Color Trails Test (Messinis, Malegiannaki, Christodoulou, Panagiotopoulos, & Papathanasopoulos, 2011)
Memory
The 5 word test (Economou, Routsis, & Papageorgiou, 2016)
The 5 Objects Test (Papageorgiou, Economou, & Routsis, 2014)
Rey's Auditory Verbal Learning Test (Messinis et al., 2016)
Greek Verbal Learning Test (GVLT) (Vlahou et al., 2013)
Test your memory (Iatraki et al., 2017, 2014)
Visuospatial abilities
Hooper Visual Organization Test (HVOT) (Kosmidis, Tsotsi, Karambela, Takou, & Vlahou, 2010)
Judgement of Line Orientation (JLO) (Kosmidis et al., 2010)
Group Embedded Figures Test (GEFT) (Kosmidis et al., 2010)
Rey Osterrieth Complex Figure Test (R-O) (Kosmidis et al., 2010)
Visuospatial Tasks (VOSPT) (Kosmidis et al., 2010)
Face Recognition (FR) (Kosmidis et al., 2010)
Neuropsychiatric symptoms
Geriatric Depression Scale -short (GDR) (Fountoulakis et al., 1999)
Hellenic Neuropsychiatric Inventory (H-NPI) (Politis, Mayer, Passa, Maillis, & Lyketsos, 2004)
Cognitive reserve
Cognitive Reserve Index Questionnaire (CRIq) (Maiovis et al., 2016)

Quality of life
Stroke and Aphasia Quality of Life Scale (SAQOL)-39 (Efstratiadou et al., 2012; Kartsona & Hilari, 2007)

2.2.5 **Conclusions**

Most of the tests used in the evaluation of speech and language abilities in PPA have been originally devised for assessing individuals with other conditions. Assessment tools that come from the stroke-induced aphasia tradition, like the BDAE or the WAB, are commonly used in assessing individuals with PPA. However, classification into traditional aphasia syndromes that reflects the vascular distribution of stroke is not relevant for PPA which is characterized by a more diffuse and progressive pattern of damage. The speech and language profiles in PPA variants are different from the profiles in stroke-induced aphasia. For example, agrammatism in nfvPPA may be milder than in Broca's aphasia and semantic loss in svPPA more severe than in stroke aphasia (Henry & Grasso, 2018). Moreover, these batteries may not be sensitive to the early, subtle deficits that characterize PPA.

Other tests used in the assessment of PPA have been specifically designed for this condition. Nine of the tests that assess speech and language abilities were included in a review by Battista et al. (2017); three were developed for the differentiation between the PPA variants, two for the assessment of language disorders in PPA and four for staging severity of speech and language deficits in PPA. An example of a test that has been developed for differentiating between the PPA variants is the Sydney Language Battery (Syd-Bat) (Savage et al., 2013). It comprises tasks for assessing picture naming, word comprehension, semantic association and repetition. Another example is the Make A Sentence Test (MAST) and the SEntence Comprehension Test (SECT) (Billette, Sajjadi, Patterson, & Nestor, 2015), which assess an isolated linguistic function (grammatical ability) at the sentence level.

These tests have important limitations. Methodological issues that have been brought to light include use of inappropriate reference tests, non-representative samples, lack of information about consecutive enrolment, diagnostic accuracy analysis, and blinding procedures (Battista et al., 2017).

There is evidence to suggest that connected speech analysis may be a valuable tool in profiling speech and language in PPA, as it is able to capture the distinctive features of the PPA variants (e.g., Ash et al., 2013; Boschi et al., 2017; Fraser et al., 2014; Wilson et al., 2010b). It is an ecologically valid measure, as connected speech production is the most representative form of an individual's everyday language production (Ash & Grossman, 2015). However, it is time-consuming and lacks normative data. Furthermore, different protocols have been employed for the elicitation of speech samples and the analysis of speech output. These disadvantages may limit its clinical application (Battista et al., 2017).

To conclude, there is general consensus in the research literature that comprehensive assessment of PPA should address both speech and language functions, as well as other cognitive and behavioral aspects of functioning. On the other hand, there is no agreement on which test, or battery of tests should be used in PPA for documenting linguistic and neuropsychological deficits and subtyping PPA variants. The available instruments should be used cautiously taking their limitations into careful consideration.

The outcome of this literature review was the informed selection of appropriate instruments for an assessment battery specifically designed to assess Greek-speaking individuals with PPA.

The battery can be divided into three sections. The first section assesses severity of aphasia and functional status using the Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2010) and the Frontotemporal Rating Scale (FRS) (Mioshi, et al., 2010), respectively. The second section comprises measures that assess speech and language abilities. The third section focuses on tools that measure neuropsychological domains (e.g., behavior/mood, executive skills, visuospatial perception, memory, object semantics and praxis). The tests that were selected are presented in tables 4 and 5. It should be noted that for the domains of motor speech, connected speech, repetition and morphosyntax, no validated tests were available in the Greek language. Moreover, the available instrument for the assessment of visuospatial abilities in Greek, was found to be too difficult for use with this population. For these domains, a non-validated test was selected. A brief description for each test and a rational for its selection is provided in the methodology section of the research studies.

Table 4: Speech and Language Assessment Battery

Domain	Test/Task
Motor Speech Assessment	Motor speech evaluation
	Phonation time
	DDK rates
	Repetition of polysyllabic words
	Repetition of words of increasing length
	Repetition of sentences
	Reading Grandfather passage
Language	Boston Diagnostic Aphasia Examination (BDAE)-Short
Connected Speech Analysis	*Picture description, Story retell, Spontaneous speech*
	QPA- measures
	Other Fluency measures
	Error analysis
	MAIN macrolinguistic measures
Repetition	WAB- words and phrases
	Bayles' Repetition of sentences
Naming	Boston Naming Test (BNT)
	BDAE - BNT-15
Single word comprehension	PPVT
	BDAE-words
Language comprehension	BDAE-commands
	BDAE-complex ideational material
Morphosyntax	BDAE-3 sentence-picture matching (syntax)
	Grammaticality judgment task

Reading	Reading Fluency - Words
	Reading Fluency - Non-words
	BDAE- reading sentences
	BDAE- comprehension of written words
	BDAE- comprehension of written sentences
Writing	Spelling - words
	Spelling - non-words
	BDAE - Picture description

Table 5: Cognitive Assessment Battery

Domain	Test/Task
Cognitive functioning (composite measure)	Mini Mental State Examination (MMSE)
Executive functioning	Trail Making Test - A
	Trail Making Test - B
	Digit Span
	Verbal Fluency Test
	Clock Drawing Test
Memory	5 Words Test
	5 Objects Test
	Benson Complex Figure Recall Condition
Visuospatial functioning	Pentagons copy (from MMSE)
	Benson Complex Figure Copy Condition
	Clock Drawing Test
Object Semantics	Pyramids and Palm Trees-52
	Pyramids and Palm Trees-14

Neuropsychiatric Symptoms	Neuropsychiatric Inventory (NPI)
	Geriatric Depression Scale
Praxis	Western Aphasia Battery – Apraxia subtest

The literature review of the available instruments for the assessment of PPA had contributed to the selection of tests and the development of an assessment battery that was evaluated in the following pilot studies.

2.3 Pilot Study 1

The study was published in Frontiers in Communication:

Karpathiou, N., Papatriantafyllou, J., & Kambanaros, M. (2018). Bilingualism in a case of the non-fluent/agrammatic variant of primary progressive aphasia. Frontiers in Communication, 3, 52. doi: 10.3389/fcomm.2018.00052

Part of this study was presented at a national conference:

Karpathiou, Nomiki, Maria Kambanaros, Dimitra Potamianou, John Papatriantafyllou, & Paraskevi Sakka (2018). Quantitative connected speech analysis in a case of non-fluent/agrammatic primary progressive aphasia. *1st National congress of Neuropsychology,* Athens, Greece. (April 27-29). *Dialogues in Clinical Neuroscience and Mental Health,* 1(3), 24.

The published paper and the poster can be found in Appendix 3.

2.3.1 **Overview**

The study examined fluency, lexical, discourse and grammatical abilities of a late bilingual (Greek-French) male with the non-fluent/agrammatic variant of primary progressive aphasia (nfvPPA). Speech samples derived from three different narrative tasks in both languages were analyzed using quantitative production analysis (QPA) and fluency measures.

2.3.2 **Aim**

The first aim of the study was to compare the participant's connected speech production to that of Greek-speaking normal controls. The second aim was to determine whether Greek (L1) and French (L2) were differentially impaired.

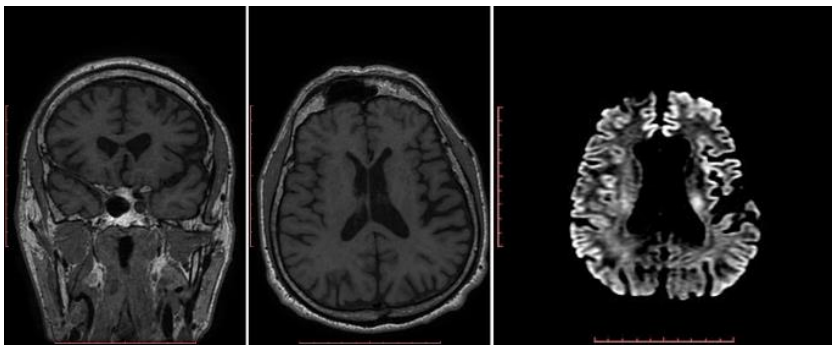
2.3.3 **Study design**

The study combined a case study and a case-control study design.

2.3.4 **Participant**

Participant L.J. is a chef in his early sixties, with 6 years of formal education. He is a right-handed late bilingual whose native language (L1) is Greek. At the age of 25, he moved to a French-speaking country and worked as a cook in a French-speaking environment for 7 years. On his return to Greece, he continued to use French (L2) both at work and at home with his wife who is a French native speaker.

LJ reported a progressive deterioration of speech and language functions. Language impairment was the primary impairment for at least the first two years. L.J. was initially assessed five years after symptom onset. He was diagnosed with PPA, as neuroimaging results ruled out other causes of focal brain damage and extensive white matter disease (figure 4) and was given a clinical diagnosis of non-fluent/agrammatic PPA according to current criteria (Gorno-Tempini et al., 2011).



A B C

Figure 4: Coronal T1-weighted (A), axial T1-weighted (B) and axial diffusion-weighted (C) brain imaging at initial assessment showing left perisylvian atrophy.

The present study was conducted 9 months after the initial evaluation (5 years and 9 months after the reported onset of the disease). At the time of the study, L.J. had a FTLD-modified Clinical Dementia Rating (CDR) sum of boxes score of 9 (MMSE = 17/30).

2.3.5 **Control group for QPA**

QPA measures for the picture description task in Greek were compared to the measures of a control group included in a previous study by Varkanitsa (2012). Varkanitsa used the QPA protocol in order to compare the connected speech of Greek-speaking persons with aphasia following stroke to that of neurologically healthy adults. The same picture description task was used in the present study to elicit speech samples. Taking into account the fact that in Greek isolated verbs may constitute grammatical utterances, Varkanitsa categorized utterances as 'utterances with verb', 'utterances without verb' and 'single-word utterances'. The QPA protocol was applied without other modifications. The control group consisted of six normal native Greek speakers (3 males and 3 females) with a mean age of 61.17 (*SD* = 5) years and a mean of 9 (*SD* = 4.15) years of education.

2.3.6 **Procedure**

2.3.6.1 ***Elicitation and transcription of speech samples***

Three different speech samples were collected in both Greek and French, under 3 conditions: a picture description task ('Cookie Theft', from Boston Diagnostic Aphasia Examination, BDAE), a story retell task, the dog story protocol from the Multilingual Assessment Instrument for Narratives, MAIN (Gagarina et al., 2012) and a semi-spontaneous speech task where L.J. was asked to talk about his job. Interruptions and questions by the examiner (first author) were kept to a minimum. The examiner is a monolingual Greek-speaking clinician who is also a proficient speaker of French. Samples were collected in 4 sessions, first for the Greek language and 2 weeks later for French. All samples were audio-recorded.

Speech samples were transcribed orthographically using ELAN (Sloetjes & Wittenburg, 2008). Phonological paraphasias unintelligible or incomprehensible words were transcribed phonetically using the International Phonetic Alphabet. Dysfluent variables, such as silent and filled pauses, sound errors, repetitions and false starts were also coded.

2.3.6.2 *Quantitative analysis of speech samples*

Speech samples were analyzed following the procedures described by Saffran et al. (1989) for quantitative production analysis (QPA) (Saffran et al., 1989; Berndt et al., 2000). The QPA procedures were followed for all samples with the exception of the direct discourse utterances produced in the story retell task, as these structures were modelled in story telling.

Narrative samples were formed by extracting comments on the narrative, direct responses to the examiner, repetitions of the examiner's utterances, stylistic and dysfluent repetitions, subsequently repaired utterances, and discourse markers. The narrative samples were then segmented into utterances based on semantic, syntactic, and prosodic information. Utterances and narrative words were used in subsequent analysis.

The QPA summary measures were classified into four categories: discourse productivity, sentence productivity, grammatical accuracy and lexical selection (Gordon, 2006). A set of additional measures were used to quantify dysfluent speech and narrative variables.

2.3.6.3 *Speech rate and other fluency variables*

Speech rate for each sample was calculated by dividing total completed words by sample duration in minutes. Samples were timed, and total time duration was computed by subtracting the examiner's interjections.

Pauses longer than 1 second were coded according to QPA instructions and counted for the calculation of the pause frequency measure. However, a threshold of 0.250 ms was used in the calculation of pause duration (de Jong & Bosker, 2013) and speaking time was calculated by subtracting silent pausing time from total time in order to control for the effect of pauses. Articulation rate was computed by dividing total completed words by speaking time.

Speech sound errors included distortions, which were defined as phonetic errors resulting in distorted phonemes, and phonological paraphasias defined as words with non-distorted phonemic insertions, deletions, or substitutions. Whole-word immediate repetitions were counted as dysfluent repetitions. Words or phrases repeated later in the

narratives were counted as speech repairs. Partially produced words were coded as false stars and small words, such as ‘eh’, as filled pauses.

Speech samples were of different duration and direct comparison of the aforementioned frequency measures was not possible. Thus, these measures were calculated as proportions of total words produced. They were also corrected for speaking length by dividing dysfluency counts by speaking time (de Jong, 2016).

2.3.6.4 *Discourse measures*

QPA discourse productivity measures included speech rate, number of narrative words, and proportion of narrative to total words produced, as a measure of discourse efficiency.

An additional discourse variable, Guiraud’s index (the square root variant of Type-Token Ratio, TTR) was also measured. Guiraud’s index is a measure of lexical richness that is less affected by sample size/length in comparison to TTR (Van Hout and Vermeer, 2007). This was derived by dividing the number of unique words (types) by the square root of narrative words (tokens). Number of unique words (types), lemmas and utterances are also reported.

2.3.6.5 *Lexical measures*

Grammatical category class (closed/open class, nouns, verbs, adjectives, adverbs, pronouns, prepositions, conjunctions) was coded for each narrative word. Their proportion was calculated by dividing the number of words in each category by the number of narrative words. Nouns, verbs, and adjectives were considered as open class. All other words were counted as closed class. Proportion of verbs to nouns and verbs was also computed. Proportion of pronouns was derived by dividing the number of pronouns by the total number of nouns and pronouns.

Finally, mean log word frequency of open class words was calculated for each narrative sample. Calculations were based on data about word frequencies per million taken from the ‘ILSP PsychoLinguistic Resource’ for the Greek language (Protopapas et al., 2012) and ‘Lexique’ for the French language (New et al., 2001).

2.3.6.6 ***Grammatical measures***

QPA sentence productivity measures encompass proportion of words in sentences, mean utterance length (in words), median utterance length (in words), sentence elaboration index (number of open class words per phrase for noun and verb phrases) and an embedding index (proportion of embeddings to sentences).

QPA grammatical accuracy measures consist of proportion of well-formed sentences, verb inflection index (proportion of inflectable verbs inflected) and determiner index (proportion of determiners produced in obligatory contexts). The auxiliary complexity index, a measure of morphological complexity of the main verb indicating change from its base form, was also calculated.

Table 6: QPA measures

Measures	Connected Speech Level
Total Time (min)	
Number of Complete Words (Total Words)	
Pause Duration (min)	
Speaking Time (min) (excluding pauses)	
Articulation Rate wpm	
	Dysfluencies per Total Words
Pauses >1sec	
Fillers	
Distortions	
Phonological errors	
False Starts	
Repetitions	
Total	
	Lexical Distribution per Narrative Words

Nouns

Verbs

Adjectives

Adverbs

Pronouns

Prepositions

Conjunctions

QPA Discourse Productivity Measures

Speech Rate wpm

Number of Narrative Words (Tokens)

Narrative / Complete Words

Other Discourse Measures

Number of Utterances

Number of Types (Unique words)

Number of Lemmas

Guiraud's index (Type Token Ratio square root variant)

QPA Lexical Selection Measures

Closed Class Words

Pronouns / Nouns & Pronouns

Verbs / Nouns & Verbs

*Mean Log Frequency (open class words)

QPA Grammatical Productivity Measures

Proportion of Words in Sentences

Mean Utterance Length

Median Utterance Length

Sentence Elaboration Index
Embedding Index
QPA Grammatical Accuracy Measures
Proportion of Well-formed Sentences
Auxiliary Complexity Index
Verb Inflection Index
Determiner Index
Key: * additional measures, not included in QPA

2.3.6.7 ***Macrolinguistic analysis (MAIN)***

Narrative assessment focused on the analysis of microlinguistic aspects of language production. Macrolinguistic aspects were addressed for the 'Dog story' retell task with the story structure score and the structural complexity measures proposed by MAIN (Gagarina et al., 2012). Although the MAIN was originally designed to assess narrative skills of bilingual children, it is controlled for macro-and microlinguistic features across Greek and French. As there is no other standardized procedure for adults, it was deemed appropriate for comparing story retell abilities in both languages.

The 'Dog story' starts with a setting statement and consists of three short episodes. Each episode consists of an initiation, a goal, an attempt, an outcome and a reaction statement. Credit is given for the production of each initiation, goal, outcome, reaction when computing the story structure score.

Five structural complexity measures are included in the MAIN: number of sequences where an attempt and outcome statement has been generated (but no goal), number of single goal statements, number of incomplete episodes which they include a goal and an attempt statement sequences, number of incomplete episodes which they include a goal and an outcome statement, and number of complete episodes which include all three goal-attempt-outcome components. Comprehension of the story structure was also assessed by means of questions targeting the main macrostructure components.

2.3.6.8 *Error Analysis*

The following type of errors were also identified and measured as a proportion of narrative words. Syntactic errors were recorded when L.J. produced ungrammatical sentences. Morphological errors, affecting articles, nouns, adjectives and verbs, were counted separately. Semantic errors included selections that were semantically inappropriate for the context. Code switching errors were defined as words produced in languages other than the target language (number of tokens not in the target language).

2.3.7 **Statistical analysis**

LJ's narrative scores for the picture description task in Greek were compared to the scores of a neurologically healthy control group (Varkanitsa, 2012). T-values were calculated using Crawford and Howell's method which enables the comparison of performance of a single subject with that of a small control sample (Crawford and Garthwaite, 2012). Differences between L.J. 's performance in Greek (L1) and French (L2) were calculated using the Wilcoxon signed-rank nonparametric test for related samples because of the small sample size. Finally, scores from both languages were collapsed and correlations between errors and fluency, lexical productivity, grammatical accuracy, and productivity measures were calculated using the nonparametric Kendall's tau-b correlation coefficient due to the limited number of samples used in the analysis.

2.3.8 **Ethical considerations**

The study was approved by the ethics committee of the Athens Alzheimer's Association. The research was conducted in accordance with the latest version of the Declaration of Helsinki. L.J. was informed about the purpose and procedures of the study and gave written consent for participating in the study, as well as for the recording, analysis, and publication of the study data.

2.3.9 **Results/Conclusions**

Compared to neurologically healthy controls, L.J. was impaired in lexical, discourse and grammatical productivity measures, but did not differ in measures of grammatical accuracy (see Appendix 1). The presence of dysfluencies, reduced speech rate and simplified syntax is consistent with the pattern of impairment reported for nfvPPA.

Results showed that narrative production measures did not differ significantly between languages. However, they suggest a slightly worse performance in his second, non-dominant, language despite a similar pattern of impairment in both languages. These findings indicate shared lexical and grammatical representations for both languages. Lengthier exposure to L2 and daily use of L2 at work and home may explain the preservation of discourse abilities in his non-dominant language. Connected speech analysis using QPA, fluency variables and error analysis has enabled the documentation of speech and language deficits present in this case of nfvPPA and the comparison of performance between the participant's languages.

2.4 Pilot Study 2

2.4.1 Overview

In this pilot study, a Greek-speaking participant with the semantic variant of PPA was evaluated using the language and cognitive assessment battery that was developed by reviewing the available literature. The main objective was to establish whether the proposed battery of tests can identify the distinctive features of this variant, namely anomia, single word comprehension deficit, surface dyslexia and dysgraphia, alongside with preserved repetition and syntactic comprehension.

2.4.2 Aim

The aim of this pilot study was first to evaluate the feasibility of the assessment procedure and the specificity of the proposed battery and second to describe the clinical presentation of the disease in a Greek-speaking individual with the semantic variant of PPA.

2.4.3 Study design

This pilot study employed a case study design.

2.4.4 Participant

The participant E.R. is a 73 years old retired handyman with 9 years of formal education. He was diagnosed with the semantic variant of PPA, 3 years post-onset. His

MRI scan showed the typical pattern of anterior temporal lobe atrophy, with left greater than right volume loss. He presented with mild disinhibition and logorrhea (i.e. excessive talking). His speech was fluent with word finding difficulties, circumlocutions and semantic paraphasias. E.R. was well oriented in time and place and able to drive and navigate around independently. He could recall autobiographical details and recent events. Cognitive testing established relatively preserved memory, attention, visuospatial skills, and executive function. Language assessment revealed a significant naming impairment and semantic difficulties. At the time of the study he was 5 years into the disease.

2.4.5 **Procedure**

ER was recruited from the memory clinic of the Dementia Day Care Center of the Athens Alzheimer Association. The assessment battery derived from the literature review was used for the linguistic and cognitive evaluation. Cognitive-linguistic testing was completed in six sessions of 45 minutes each.

2.4.6 **Data analysis**

The participant's scores were compared to the scores of neurologically healthy adults from the respective normative studies. The standard deviation method (z-scores) was used to provide estimates of impairment for each neuropsychological test. Estimated z-scores were calculated for raw scores taking into account, when available, the demographic predictors of gender, age and education. The criterion of 2 *SD*s below normative means (Hillis, 2015) was employed for determining the presence of impairment on a specific measure, indicating a significant change in scores. Crawford's t values were calculated in cases there was a control sample.

For two measures (GDS and TMT), test scores were transformed by multiplying by minus one, so that all tests have the same polarity, i.e. higher scores indicate better performance.

This type of analysis enables confirmation of the impairment in terms of severity (degree of impairment) and performance profile (number of domains impaired).

2.4.7 **Ethical Considerations**

The study was approved by the ethics committee of the Athens Alzheimer's Association. The research was conducted in accordance with the latest version of the Declaration of Helsinki. The participant was informed about the purpose and procedures of the study and gave written consent for participating in the study, as well as for the recording, analysis and publication of the study data.

2.4.8 **Results**

Results on neuropsychological tests are presented in Appendix 1. Based on the language measures, E.R. was found to be severely impaired in confrontation naming (z = -13.4) and single word comprehension (z = -5.25). Repetition and comprehension of syntax was preserved, as well as reading aloud and spelling. Comprehension of auditory complex material was affected (z = -2.41), although his ability to follow commands was within normal limits and performance for syntactic comprehension on the BDAE-3 was at ceiling. Comprehension of written sentences was 5.11*SD* below the mean of the normative sample.

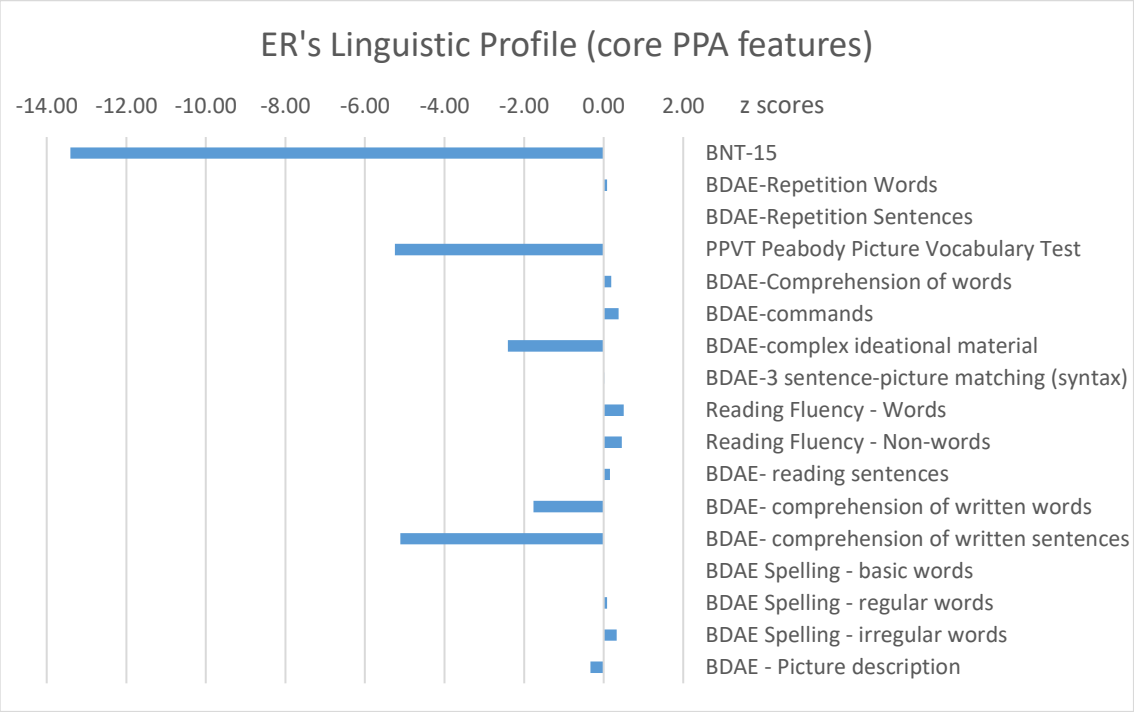


Figure 5: E.R.'s linguistic deficits profile.

Regarding neuropsychological functioning, E.R. was found to be impaired in object semantics (t = -2.982, p < .006, one-tailed on PPTT-14). The effect size (z_{cc}) (plus 95% *CI*) was -3.103 (-4.490 to -1.695). He was also impaired in semantic category fluency (z = -3.42). Non-verbal stimuli were better recalled (z = 0.39) than verbal (z = -1.76). This finding has previously been reported and attributed to loss of conceptual knowledge (Bettcher & Sturm, 2014). Performance on the Benson complex figure test – copy condition and the WAB-Apraxia subtest was at ceiling.

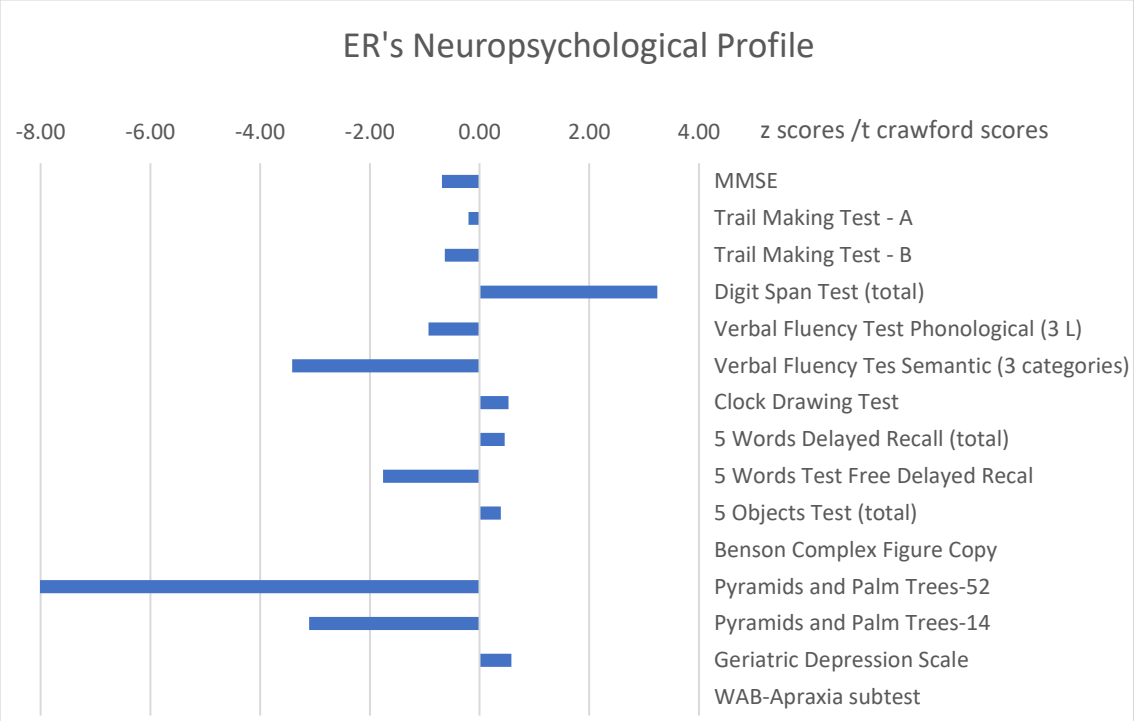


Figure 6: E.R.'s neuropsychological deficits profile.

2.4.9 **Conclusions**

E.R. was found to be impaired primarily in lexical and semantic knowledge. The assessment battery successfully identified impaired and preserved domains of functioning and degree of the impairment. This suggests that the selected tests can be used in profiling language and cognition in this participant with the semantic variant of PPA.

An important limitation of this study was the absence of control data. Only validated instruments were used in evaluating the participant's performance.

A conclusion that can be drawn from this pilot study is the worth of undertaking detailed testing in order to reveal deficits that cannot always be captured by screening tests. This was the case with single-word comprehension that was found to be intact when evaluated using the BDAE-short form but was found to be severely impaired upon administration of the Peabody Picture Vocabulary test (PPVT). E.R. has mild dementia, as suggested by his CDR sum of boxes score (CDR = 3) and at this stage, semantic deficits may be masked during neuropsychological testing. The same may be true for other linguistic domains, like spelling. This issue could be further explored once control data are available for all the selected instruments.

2.5 Pilot Study 3

Results from this study have been presented at two international conferences.

Nomiki Karpathiou & Maria Kambanaros (2019). Comparing two cases of the non-fluent and semantic variants of primary progressive aphasia using neuropsychological, narrative, and acoustic measures. *57th Annual Meeting of the Academy of Aphasia*, Macau, Hong Kong. (October 27–29) Front. Hum. Neurosci. Conference Abstract: doi: 10.3389/conf.fnhum.2019.01.00004

Nomiki Karpathiou & Maria Kambanaros (2019). Frontotemporal dementia: a comparative case study of Greek-speaking individuals with the non-fluent and semantic variants of Primary Progressive Aphasia. *Science of Aphasia XX*, Rome, Italy. (September 23–26)

The posters are available in Appendix 3

2.5.1 **Overview**

In this final pilot study, the two participants presented in the previous studies are compared with each other with reference to a control group.

2.5.2 **Aim**

The aim of this study was to compare the clinical presentation of nfvPPA and svPPA, in two Greek-speaking individuals with PPA, using a battery of neuropsychological tests, narrative analysis and acoustic measures.

2.5.3 **Study design**

This pilot study employed a case-control study design.

2.5.4 **Participants**

The first participant with nfvPPA was a 61-year-old male with 6 years of formal education. The second participant with the semantic variant of PPA was a 73-year-old male with 9 years of education. His MRI scan showed the typical pattern of asymmetric anterior temporal lobe atrophy. Both participants were assessed five years post-onset. The first participant had a sum of boxes score of 9 on the FTLD-modified Clinical Dementia Rating, whereas the second had a score of 6.

The control group consisted of 12 neurologically healthy adults, native Greek speakers, with a mean age of 68.08 (*SD* = 5.52) years and a mean of 13 (*SD* = 3.19) years of education.

2.5.5 **Procedure**

Participants were evaluated using a comprehensive battery of neuropsychological tests. Quantitative production analysis (QPA) (Saffran, Berndt, & Schwartz, 1989) was used for the analysis of a picture description and a story retell task. Acoustic analysis was performed in order to calculate temporal measures of the participants' speech.

2.5.6 **Statistical analysis**

The performance of each participant was compared to that of the control sample using the Crawford and Howell method (Crawford, Garthwaite, & Porter, 2010). T-values were also calculated to compare the scores of the two participants with reference to the control sample (Crawford, Garthwaite, & Wood, 2010).

2.5.7 **Results**

The participant with nfvPPA performed worse than the participant with svPPA on the Digit Span – reverse recall task ($p = .025$), Clock Drawing Test ($p < .001$), syntactic comprehension (Boston Diagnostic Aphasia Examination, BDAE-3, $p = .014$) and reading fluency for words ($p < .001$). Furthermore, he was slower in temporal measures of speech production (Table 7).

Table 7: Temporal measures for diadochokinetic rates, passage reading and sentence repetition for pilot study 3.

Temporal measures	Case 1 nfvPPA	Case 2 svPPA	*t* values	Control *n* = 12 Mean (*SD*)	
Diadochokinetic rates (rep/sec)					
/pa/	3.478**	8.349	-4.38	6.97	(0.74)
/ta/	3.765*	7.278	-3.029	6.93	(0.82)
/ka/	3.106**	7.145	-4.023	6.24	(0.71)
/pataka/	4.629*	7.697	-3.055	6.86	(0.71)
Passage Reading Duration	142.092**	63.701	8.386	49.44	(6.61)
Passage Reading Syll/sec	1.696*	3.783	-2.635	4.94	(0.56)
Repetition of Sentences (sylls/sec)					
S1 (15 syllables)	0.223	0.164	1.989	0.17	(0.02)
S2 (11 syllables)	0.881**	0.220	17.748	0.20	(0.03)
S3 (14 syllables)	0.343*	0.161	4.100	0.18	(0.03)
S4 (16 syllables)	0.339*	0.167	4.316	0.17	(0.03)
S5 (12 syllables)	0.263	0.192	1.632	0.19	(0.03)

*$p < .05$; **$p < .01$ level of statistical significance for differences between case 1 and 2.

The participant with svPPA was more impaired in confrontation naming (Boston Naming Test-15, $p < .001$), single word comprehension (Peabody Picture Vocabulary Test, $p < .001$) and object semantics (Pyramid and Palm Trees Test, $p = .001$). Comprehension of auditory complex material, written words and sentences were affected ($p = .022$, $p = .005$ and $p < .001$, respectively), although his ability to follow commands was within normal limits and performance for syntactic comprehension was at ceiling. Both participants were impaired in the Trail Making Test A and B, verbal fluency, spelling, and written picture description.

The narrative production measures that differed significantly between the two participants were speech rate (slower for the nfvPPA participant, $p = .007$), average pause duration (longer for the nfvPPA participant, $p < .001$), false starts per min (more for the nfvPPA participant, $p = .045$), proportion of nouns (lower for the svPPA participant, $p = .012$) and closed class words (lower for the nfvPPA participant, $p =$

.016). Compared to the control group, the nfvPPA participant produced shorter sentences (p = .023), fewer closed class words (p = .006), made longer pauses (p < .001) and spoke at a slower rate (p < .001). The svPPA participant used fewer nouns (p = .027), more pronouns (p = .02) and fewer narrative words as a proportion of the total words produced (p = .003).

2.5.8 **Conclusions**

The results confirm the distinctive features of both PPA variants, namely anomia, a single word comprehension deficit, preserved repetition and syntactic comprehension for the participant with svPPA, as well as motor speech and syntactic processing difficulties alongside with intact repetition, semantic knowledge and naming ability for the nfvPPA participant.

Taking into account the neuroimaging findings, these two cases illustrate the different distribution of atrophy in the language variants of FTD and highlight the role of the left anterior temporal lobe in naming and single word comprehension.

Neuropsychological testing combined with narrative and acoustic analysis have enabled the documentation of speech and language deficits present in these cases of PPA and the comparison of the two participants.

3 Methodology for research studies

3.1 Overview

Four research studies were completed in the second phase of the research program. Common methodological details are presented in this section, whereas information concerning individual studies are discussed in the respective chapters.

3.2 Research Studies

Study 1: Comparing Greek-speaking individuals with PPA to individuals with AD and neurotypical controls

Aim

To establish differences on neuropsychological testing and connected speech production and investigate whether specific measures or tasks can differentiate individuals with PPA from individuals with AD and neurotypical adults.

Study 2. Comparing two narration tasks in PPA and AD: picture description and story retell.

Aim

To compare performance on two frequently used narration tasks and examine whether the two elicitation tasks placed different cognitive demands on individuals with PPA and AD.

Study 3. Cognitive-linguistic profiles of Greek-speaking individuals with a degenerative disease: a case-control study

Aim

To explore the range of cognitive and language symptoms in PPA and FTD and document the challenges associated with the clinical diagnosis of PPA and classification of the PPA variants.

Study 4. A case-series study of disease progression: how do cognitive-linguistic profiles of individuals with PPA change in one year as the disease evolves?

Aim

To gain insight into how performance on the neuropsychological battery alters over time, specifically, in the course of 12 months in order to determine which abilities are more affected, and which remain stable.

3.3 Research Studies Design

Studies were prospective and followed a case-series-control study design. Case studies enable the detailed description of an observed phenomenon and have been found to be valuable in the study of rare disorders, when recruitment of large samples is problematic (Nock, Michel, & Photos, 2007). Moreover, case studies are useful for documenting the development of new assessment techniques and procedures which require considerable time and resources (Nock, Michel, & Photos, 2007). However, case studies have been criticized for lacking methodological rigor and the capacity to draw valid conclusions from the results (Kazdin, 2011). However, objective assessment, systematic data collection and analysis can be incorporated into case studies to increase their internal validity. Observational studies using a case-control design can be informative when employing appropriate methodological and statistical analysis techniques (Crawford & Garthwaite, 2012).

3.4 Participants

For the studies of the second phase of this research program, experimental data were collected from a total of 40 (25 female and 15 male) individuals. Their mean age was 68.55 (*SD* = 8.8) and they had a mean of 12.93 (*SD* = 3.78) years of formal education.

Thirteen individuals had a prominent speech and language deficit and met the basic PPA criteria. Nine individuals met criteria for one of the three PPA variants (7 logopenic, 2 semantic) whereas four did not meet the criteria for any of the PPA variants. Three participants with PPA were excluded from the first studies (study 1, study 2 and study 3) due to advanced dementia (MMSE < 12, BDAE severity ≤ 2, mean PASS sum of boxes score = 10.5, *SD* = 2.78). One of them was not able to complete the experimental assessment. Participants in the ‘early’ PPA group had a mean BDAE severity score of 3.40 (*SD* = 0.97) and their mean PASS sum of boxes score was 5.05 (*SD* = 1.67).

Fifteen demographically matched neurologically healthy adults served as controls.

Nine individuals were diagnosed with Alzheimer's disease, with a mean CDR sum of boxes score of 2.28 (*SD* = 1.99). One of them was diagnosed with amnestic mild cognitive impairment (MCI) one year before participating in the current study. She exhibited further decline in follow-up assessment and reported difficulty in managing her finances. A consensus clinical diagnosis of early Alzheimer disease was reached. However, her original CDR score was used in data analysis, as it has not been updated. All AD participants had been diagnosed in the memory clinic of the Dementia Day Care Center of Athens Alzheimer's Association, using a different neuropsychological battery of tests which included among others the Addenbrooke's Cognitive Examination (ACE), the Greek Verbal Learning Test (GVLT) and the Georgia Complex Figure Test.

Another three individuals were diagnosed with a non-language variant of FTD (FTD-ALS, PSP and CBS). The participants with FTD are included in the third case-control study.

Information about staging, severity of the communication disorder, cognitive, neuropsychiatric and functional status can be found in table 8.

Table 8: Communicative, cognitive, neuropsychiatric and functional status of the participants.

Group (Max. Score)	BDAE severity (/5)	MMSE (/30)	Years post-onset	NPI (/144)	NPI impact (/60)	FRS (/100)
Neurotypical Mean	5.00	28.87				
Median	5.00	29.00				
SD	.00	1.06				
AD Mean	4.78	24.89	3.22	13.60	8.00	77.84
Median	5.00	26.00	3.00	14.00	7.00	92.86
SD	.44	2.47	1.54	13.43	7.48	28.53
PPA early Mean	3.40	24.30	2.10	4.25	3.38	79.78
Median	3.50	25.00	2.00	4.50	2.00	80.00

SD	.97	3.65	.77	2.12	3.74	15.69
PPA moderate Mean	1.67	11.00	3.67	3.67	4.00	41.24
Median	2.00	11.00	4.00	3.00	3.00	36.00
SD	.58	1.00	1.53	4.04	4.58	9.08
FTD Mean	3.00	27.00	2.50	25.33	11.67	41.56
Median	3.00	27.00	3.00	19.00	15.00	21.11
SD	1.00	.00	.87	13.65	10.41	38.27
Total Mean	4.15	25.35	2.74	9.95	6.00	68.61
Median	5.00	27.00	2.00	5.00	3.00	69.62
SD	1.19	5.09	1.28	11.34	6.51	28.15

BDAE: Boston Diagnostic Aphasia Examination-Severity Scale: evaluates the severity of the communication problem; MMSE: Mini Mental State Examination: evaluates general cognitive status; NPI: Neuropsychiatric Inventory: evaluates the presence, severity and impact of neuropsychiatric symptoms; FRS: Frontotemporal dementia Rating Scale: evaluates functional status.

All participants were right-handed, apart from one neurotypical male who was ambidextrous. All individuals were native Greek speakers. They all reported to have normal or corrected-to-normal vision and hearing.

Demographic information of the sample is presented in figures 7 to 10.

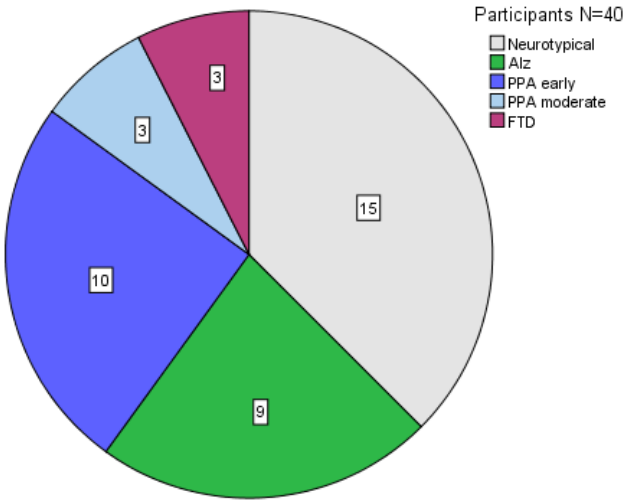


Figure 7: Number of participants in each diagnostic group.

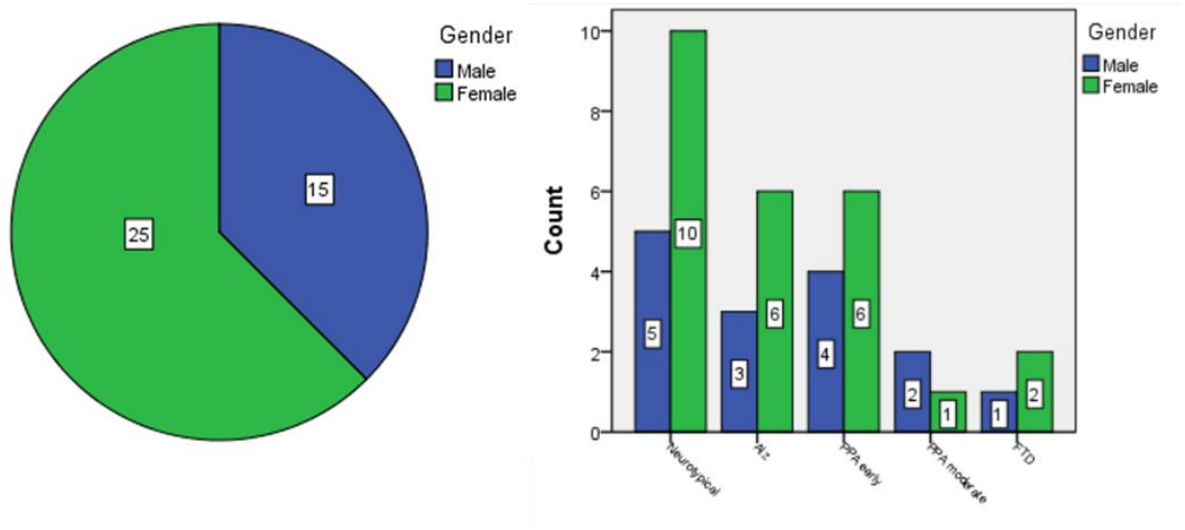


Figure 8: Participants gender and group membership based on gender.

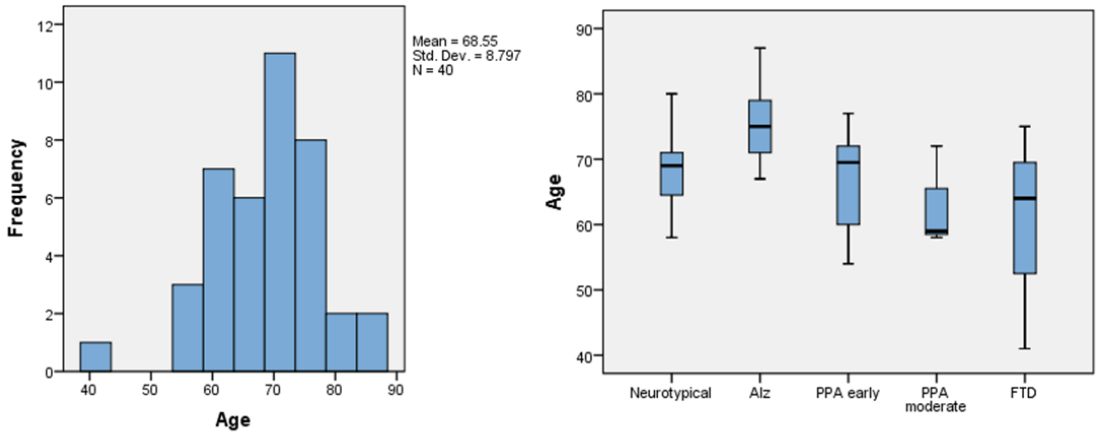


Figure 9: Age distribution and boxplots for each diagnostic group.

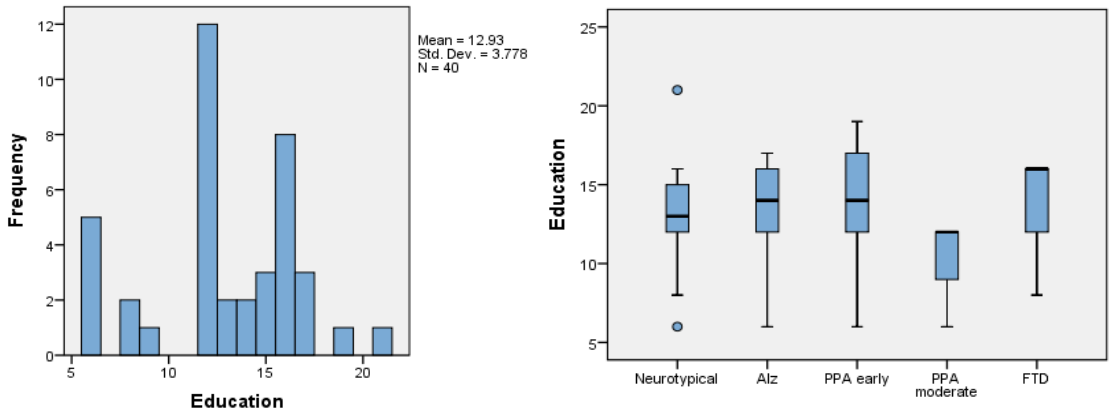


Figure 10: Distribution of the years of formal education and boxplot of years of education of each group of participants.

Four individuals with PPA were assessed one year after their first baseline assessment. Data from these follow up assessments are analyzed separately in the fourth case-study which evaluates progression of the disease.

3.4.1 Inclusion criteria

a. Participants should have a clinical diagnosis of PPA, based on Mesulam's criteria (2001), probable/possible AD or FTD, according to currently acceptable research criteria (Albert et al., 2013; Chare et al., 2014; McKhann, 2012). Clinical diagnosis was based on neurological examination and standard neuropsychological testing and was brain imaging-supported by MRI scan.

b. Participants should be in the mild or moderate stage of the disease, as specified by severity ratings (CDR and FTLD-CDR score < 3, BDAE aphasia severity scale >3)

c. Greek should be their native language

d. Participants should have at least 6 years of formal education.

3.4.2 Exclusion criteria

The following factors constituted reasons for exclusion from participating in the study:

a. other major systemic, psychiatric or neurological diseases

b. uncorrected visual and hearing impairment

c. difficulty completing the assessment procedure

3.5 Recruitment and enrollment

Participants were recruited through the memory clinic of the Dementia Day Care Center of the Athens Alzheimer's Association and referral from other memory clinics and specialists (neurologists and psychiatrists) working in the private sector. Referrals from multiple sources limit selection bias (more representative of the broader population).

Enrollment was consecutive. All individuals that were identified as eligible during the registration period (from January 2018 to January 2020), were included in the study. They were assessed in the order in which they were first identified.

3.6 Assessment

3.6.1 **Assessment procedure**

Eligible patients were identified upon reviewing referral information. In most cases, referral from a specialized center or specialist includes information about medical history, neurological examination, clinical staging, medication, as well as results from a brief neuropsychological assessment. The Clinical Dementia Rating (CDR) and the Frontotemporal Lobar Degeneration-Modified Clinical Dementia Rating (FTLD-CDR) (Knopman et al., 2009) are typically used for dementia clinical staging.

An initial session was conducted for screening. If the patient fulfilled the inclusion criteria subsequent sessions were scheduled. Assessment was completed over 3 or 4 hourly sessions depending on disease severity and practical issues, such as fatigue and time constraints. Assessment of the neurotypical individuals was completed in two 90-minutes-sessions.

3.6.2 **Initial evaluation - Screening**

Detailed case history information regarding cognition, communication, speech and language was collected from the participants and/or their primary caregiver with the aid of a clinical case history form, (see Appendix 2). The case history form was adapted from a generic case history form for adults with a neurogenic disease, to specifically address issues relevant to the clinical presentation of PPA.

The screening assessment consisted of a composite measure of cognitive function, the Mini Mental State Examination (MMSE; Folstein, Folstein and Hughes, 1975; Fountoulakis et al., 2000, Solias et al., 2014) and the short form of the Boston Diagnostic Aphasia Examination (BDAE; Goodglass and Kaplan, 1983; Messinis et al., 2013).

Additional information about severity of the disease, functional status and co-existing neuropsychiatric symptoms was gathered from the primary caregiver through the use of the following informant questionnaires.

- Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2010; Karpathiou et al., 2018) (see Appendix 2)

- Frontotemporal Dementia Rating Scale (FRS) (Mioshi et al., 2010; Maiovis et al., 2016)
- Neuropsychiatric Inventory (NPI) (Cummings et al., 1994; Politis et al., 2004)

Neuroimaging reports and/or scans were also gathered when available. Brain imaging was used to exclude other causes of focal brain damage (e.g. stroke, tumor).

3.6.3 **Neuropsychological Assessment Battery**

The assessment battery included the tests that have been selected in the first phase of the research program.

3.6.3.1 ***Severity / Staging / Functioning***

Two instruments have been specifically devised for measuring aphasia severity and tracking disease progression in PPA: the Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2010) and the Progressive Aphasia Language Scale (PALS) (Leyton et al., 2011). The PALS is based on formal testing. The **Progressive Aphasia Severity Scale (PASS)** was developed to rate severity of impairment in ten domains of language and monitor disease progression. A global PASS score is derived from scores on all domains (articulation, fluency, syntax and grammar, word retrieval – expression, repetition, auditory comprehension, single word comprehension, reading, writing and functional communication). The scoring system is similar to that of CDR. Ratings are based upon informant reports, standardized assessment and clinical judgment. Although the PASS scale has not been fully validated in Greek, it has been cross-culturally adapted, and PASS ratings were found to be reliable between raters, while the scale was proven to be valid against other established measures (Karpathiou et al., 2018).

Another tool that can been used for the same purposes is the **FTLD-modified CDR** (Knopman, Weintraub, & Pankratz, 2011; Maiovis et al., 2017) which, compared to the original CDR, includes two additional domains, one for language and one for behavior. A score of 0 denotes normal functioning, whereas 1, 2 and 3 mild, moderate and severe impairment. In the studies of this research, FTLD-CDR is provided at referral (usually scored by a neurologist) and is used as an indicator of disease severity.

The **Frontotemporal Dementia Rating Scale (FRS)** (Maiovis et al., 2016; Mioshi, et al., 2010) is an alternative scale used as a measure of severity and functional ability.

Scoring is based on the reported frequency of behaviors and daily activities explored by a 30-item informant questionnaire. Raw scores are converted into percentage scores and with the aid of a logit table to logit scores ranging from 5.39 (normal) to -6.66 (profound impairment). The FRS looks into activities such as going on outings and shopping, household chores and using the telephone, managing finances and correspondence, medications, meal preparation and eating, self-care and mobility. It also includes 7 items about behavioral changes. The scale was able to show different decline rates in the three variants of PPA and detect functional deterioration over one year (Hsieh, Hodges, Leyton, & Mioshi, 2012; Mioshi et al., 2010). This scale has been preferred over the IADL (Theotoka et al., 2007) as it has been developed specifically for FTD and used in PPA.

3.6.3.2 *Neuropsychiatric symptoms*

The **Neuropsychiatric Inventory (NPI)** (Cummings et al., 1994) has been widely used to measure the frequency and severity of neuropsychiatric symptoms in PPA (Modirrousta et al., 2013). The NPI assesses 12 domains: delusions, hallucinations, agitation-aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, sleep, and appetite. Each domain is scored for its frequency, its severity, and the distress that the symptom causes to the caregiver. Higher scores indicate more severe deficits and distress. The Frontal Behavioral Inventory (FBI) or the behavioral domain of the FTLD-modified CDR have also been utilized in studies of PPA. The Greek version of NPI will be used in this research. The Hellenic NPI was validated in a clinical sample of AD patients and was proven to detect neuropsychological changes (Politis et al., 2004). This is the third instrument of the assessment battery that is completed by interviewing the caregiver.

Mood was evaluated through the use of a 15-item questionnaire, the short form of the **Geriatric Depression Scale (GDS)** (Fountoulakis et al., 1999; Sheikh & Yesavage, 1986). For younger participants (< 65years of age), the **Beck Depression Inventory (BDI)** (Beck, Steer, & Brown, 1996; Giannakou et al., 2013) was administered. Lower scores on these scales are indicative of better mood. Depression can affect cognitive performance. In PPA, depression has been associated with the communication difficulties experienced, and may necessitate appropriate management (Medina &

Weintraub, 2007). For data analysis, scores on the BDI were rescaled to match the GDS scoring system. The new combined variable was labeled Mood-15.

3.6.3.3 *Cognitive Functioning*

The **Mini-Mental State Examination** (Folstein, Folstein, & McHugh, 1975) was used as a screening tool and measure of general cognitive status. In PPA, the MMSE may overestimate cognitive impairment, as it relies on language processing. The validation data from Solias et al. (2014) was used in the present studies.

Attention and executive functioning was assessed by the **Trail Making Test (TMT)** (Zalonis et al., 2008). The TMT-A is a test of scanning and visuomotor tracking and is considered to measure information processing speed. The TMT-B assesses divided attention and cognitive flexibility. For data analysis, the scores are reversed. Actual completion time was deducted from the maximum allowed time for completion, that is, 180s for TMA-A and 300 for TMA-B. In this way, higher scores reflect better performance.

The **Verbal Fluency Test** (Kosmidis et al., 2004) measures executive functions. Phonemic and semantic fluency was assessed using 3 letters and 3 categories. In each task, the participant needs to generate as many items as possible in 1 minute. A total score is calculated based on the number of responses for each verbal fluency category.

The **Clock Drawing Test** (Bozikas et al., 2008) measures both executive and visuospatial abilities. The scoring scheme of the original validation study was used in the research studies.

The **Digit span test** from the WAIS-IV was used as a measure of working memory. Individuals with lvPPA have been found to be more impaired on this measure compared to individuals with the other variants of PPA.

Both verbal and non-verbal episodic memory were evaluated through **the five words test** (Economou et al., 2016) and **the five objects test** (Papageorgiou et al., 2014) respectively. The first test uses written words which are encoded using explicit semantic information. Total scores are calculated for free and cued recall of the words. The second test is based on recalling the positioning of 5 objects. Finally, the recall condition of **the Benson Complex Figure** (Possin, et al., 2011) was used as a measure

of visuospatial memory. The copy condition of the Benson Complex Figure test is considered to assess perception and constructional praxis. The test has not been validated in Greek.

3.6.3.4 *Linguistic assessment*

The **Boston Diagnostic Aphasia Examination (BDAE)** (Goodglass and Kaplan, 1983) is a widely used tool that is used to document language abilities in stroke-induced aphasia and PPA. The version that was selected for use in this assessment battery is the commercially available Greek short version of the BDAE (Messinis et al., 2013). In the short form of the test, multiple language domains are assessed to document an individual's strengths and weaknesses, namely, auditory comprehension, automatic speech, naming, repetition, reading and writing. It also includes a 15-item naming test (BNT-short), an aphasia severity rating scale and the 'Cookie Theft' picture that has been extensively used in eliciting spontaneous speech samples. It takes approximately 40 to 60 minutes to administer. Some of the limitations of the test are the limited number of items used in the sentence repetition task, the limited range of psycholinguistic features evaluated in the spelling section, as well as the fact that it does not assess comprehension of syntactic structures. For this reason, a short sentence-picture matching task, the "**embedded sentences" from BDAE-3** which examines syntactic comprehension of 10 reversible sentences (subject object relative clauses) with 5 verbs (hit, kiss, call, kick, chase) and 5 agents/patients (boy, girl, mother, woman, man) was selected, even though this task has not been validated in Greek.

The **Boston Naming Test** is a picture confrontation naming test included in the full BDAE test that can be administered independently. A 45-item version of the test validated in Greek by Simos et al. (2011) was used in the battery, as there is normative data available stratified by gender, age and education level. A longer version of the naming test provided in the BDAE-short form, may prove useful in cases where there is a subtle naming deficit, as in early stages of PPA. This may also be the case for other linguistic domains. Aphasia tests that have been devised for stroke-induced aphasia are not always sensitive enough in early-stage PPA deficits (Henry & Grasso, 2018).

The **Western Aphasia Battery (WAB)** – Revised (Kertesz, 2006) has also been developed for stroke-induced aphasia. It has been used in PPA and has been found

useful in documenting language deterioration (Harciarek et al., 2014). The test has not been formally adapted in Greek. The **WAB fluency scale** incorporates lexical, grammatical and motor speech aspects to rate fluency on a scale from 0 (no speech) to 10 (fluent speech) and is more appropriate for use in PPA than the BDAE rating scale of speech characteristics that evaluates articulation, grammatical and word finding abilities individually. Fluency is affected in all PPA variants for different underlying reasons, phonological and lexical in lvPPA, grammatical/motor in nfvPPA and lexical in svPPA. Individuals with nfvPPA and lvPPA are less fluent than individuals with svPPA. The **WAB repetition** subtest also shows some advantages over the repetition tasks of the BDAE-short, mainly the inclusion of a larger number of items, the stepwise increase of word and phase length and the detailed scoring which is more sensitive to detect different levels of impairment. (see Appendix 2). The WAB also includes a **praxis subtest** that assesses face and limb ideomotor apraxia. All these subtests have been widely used, either individually or combined, in studies of PPA (e.g. Adeli, Whitwell, Duffy, Strand, & Josephs, 2013; Butts et al., 2015).

In order to be able to document a repetition deficit at an early stage (a core feature of lvPPA), more thorough testing may be needed. **The sentence repetition test** by Bayles et al. (1996) examines the effect of sentence frequency and length, as well as semantic content on repetition. It consists of 25 sentences organized in 5 sets: short meaningful, short non-meaningful, long meaningful, long non-meaningful and long frequent sentences. It has originally been used for language testing in AD, but has also been used in PPA (Henry et al., 2013; Lukic et al., 2019). This test was adapted to Greek in order to be used in the research studies (see Appendix 2).

Motor speech evaluation included oral motor assessment, maximum phonation time, diadochokinetic (DDK) rates, repetition of utterances of increasing articulatory complexity (two-syllable words, polysyllabic words, sentences) and passage reading. No validated instrument is available in Greek, thus, the motor speech evaluation by Wertz et al. (1984) was used. The test was adapted to Greek and can be found in Appendix 2.

A spoken word-picture matching test was used for assessing single word comprehension. The short form of the **Peabody Picture Vocabulary Test** (Simos et al., 2014) comprises of 32 items which are presented in graded difficulty. The test can be a

challenge for individuals with svPPA as they have to select the picture that corresponds to a spoken word among four semantically related pictures.

Object knowledge is another domain that is impaired in persons with svPPA. In order to assess picture semantics the **Pyramids and Palm Trees Test (PPTT)** (Howard & Patterson, 1992) was selected. In this test a person needs to identify two semantically related pictures in the presence of a third distractor. A **short form of the Pyramids and Palm Trees Test** (Breining et al., 2015) was previously administered to a small number of Greek-speaking individuals with svPPA and found to be culturally appropriate. The complete version was administered to the participants of the research studies, but scores were calculated for both tests and used as separate variables in analysis.

A **grammaticality judgment test** developed by Fyndanis (unpublished) was used to assess receptive ability and knowledge of tense, aspect and agreement. In this task, the participant has to decide on the grammatical status of sentences which are presented in written form.

Reading and writing can assist with the differentiation between PPA variants. Three psycholinguistic parameters are the most relevant in assessing written processing: word frequency, regularity and lexicality (words/non-words). These factors are controlled for in all the relevant tasks that have been selected. Twenty words (10 high frequency and 10 low frequency words) from Sideridis (2008) and 14 matched non-words from Simos et al. (2013) were selected for assessing **spelling of words and non-words**. The selected words and their linguistic properties are provided in Appendix 2. **Written description** was evaluated using the 'Cookie Theft' picture and scoring instructions from the BDAE.

Reading fluency (Simos et al., 2013) for words and non-words was assessed in two tasks, in which the participant has to read as quickly as possible a list of words and non-words. Performance is evaluated by counting the number of items that have been read correctly in 45 seconds.

3.6.4 Connected Speech Analysis

Concerning connected speech analysis the **Quantitative Production Analysis (QPA)** (Gordon, 2006; Saffran, Berndt, & Schwartz, 1989; Varkanitsa, 2012) was selected for

the quantification of fluency, discourse, lexical and grammatical production. The procedure was employed for the analysis of two narrative productions from a picture description task ('Cookie Theft' from the BDAE) and a story retell task (from the **Multilingual Assessment Instrument for Narratives (MAIN)** (Gagarina et al., 2012). These instruments are presented in pilot study 1. The stimuli can be found in Appendix 2.

3.7 Ethical considerations

The research was conducted in accordance with the latest version of the Declaration of Helsinki (JAVA, 2013). The study was approved by the ethics committee of the Athens Alzheimer's Association. Participants and, when appropriate, caregivers were informed about the purpose and procedures of the study and gave written consent for participating in the study, as well as for the recording, analysis and publication of the study data (see Appendix 2). Data were held and processed securely with an appropriate level of protection. The EU General Data Protection Regulations (GDPR) were followed.

3.8 Data Analysis

IBM SPSS Statistics version 21 for windows was used for statistical analysis. Both parametric and non-parametric procedures were applied for the analysis of the data after examining the appropriate statistical assumptions. Crawford and Howell's method was employed for comparing individuals with PPA, AD and FTD with the control group (Crawford & Garthwaite, 2012; Crawford, Garthwaite, & Porter, 2010). A p value of $< .05$ was adopted to determine statistical significance.

4 Study 1. Comparing Greek-speaking individuals with PPA to individuals with AD and neurotypical controls

4.1 Introduction

Alzheimer's disease (AD) is the most common cause of dementia in older people. In a recent epidemiological study in Greece, the prevalence of dementia in adults of 65 years old and above was estimated to be 5%. Out of all the dementia cases, 75% is attributed to AD (Kosmidis et al., 2018).

While memory problems are typically one of the first signs of AD, other cognitive domains such as orientation, visuospatial abilities, executive function, and language may be affected. Language problems in AD are linked to semantic and pragmatic processing deficits. People with AD may have word-finding difficulties or make semantic paraphasias. They may also have trouble participating in conversations and may repeat themselves. Lexical retrieval deficits have been reported both in formal testing and connected speech production (Kavé & Goral, 2018).

The phonological and syntactic level of language processing seems to be more resilient (Ferris & Farlow, 2013). However, reduced syntactic complexity, morphosyntactic impairment, as well as phonetic and phonological manifestations have been documented in AD (Ahmed, De Jager, Haigh, & Garrard, 2012; Cera, Ortiz, Bertolucci, & Minett, 2018; Fyndanis et al., 2018).

On the other hand, language deficits are the hallmark of Primary Progressive Aphasia. They may arise at any level of language processing. Aphasia is the most prominent deficit at onset even though there may be subtle deficits in additional cognitive domains. The two conditions resemble each other more in the later stages as the diseases evolve.

There is no consensus about which tests best capture impairment in PPA. Clinicians and research teams employ different tests, fact that may have contributed to the variability that exists between findings (Harris et al., 2019). Furthermore, there is limited research concerning tests that are used in the evaluation of PPA in the Greek-speaking population.

Although PPA is the primary syndrome under investigation in this research program, differentiation between PPA and AD is of clinical importance. Speech and language

therapists in Greece are increasingly involved in characterizing the deficits experienced by individuals with dementia and assisting differential diagnosis. Given the potential sources of confusion, diagnosis poses a common and challenging clinical problem. Information about typical performance on specific neuropsychological and linguistic tasks is valuable in informing selection of tests and documenting deficits in PPA and AD.

To this end, 10 individuals with PPA and 9 demographically and cognitively matched individuals with AD took part in a comprehensive cognitive-linguistic evaluation. In an attempt to identify optimal measures for documenting language and associated deficits, several tools were included in the assessment battery after reviewing the respective literature and analyzed separately.

The main aim of this study was to establish differences on neuropsychological testing and connected speech production between Greek-speaking individuals with AD and PPA. A secondary aim was to investigate whether specific measures or tasks can differentiate individuals with PPA from individuals with AD and neurotypical adults.

We hypothesized that individuals with AD in comparison to individuals with PPA would be more affected in cognitive measures tapping into memory, visuospatial and executive function, but less affected in linguistic measures. Lexical retrieval deficits and associated manifestations such as dysfluencies and reduced lexical diversity, were expected to be evident in participants with AD, but to a lesser degree compared to participants with PPA.

4.2 Method

4.2.1 **Participants**

A total of 34 individuals (12 male and 22 female) participated in this study. The control group consisted of 15 neurotypical adults with a mean age of 67.93 (*SD* = 6.17) years and a mean of 13.13 (*SD* = 3.482) years of education. The AD group consisted of 9 participants (mean age 76.22, *SD* = 6.833 and mean years of education 12.67, *SD* = 4.153). Ten individuals participated in the PPA group (mean age 66.80, *SD* = 7.525 with mean years of education 13.60, *SD* = 4.088). Additional information about the group can be found in section 3.4.

Two of the PPA participants met the criteria for svPPA and six for lvPPA. One participant did not meet the criteria for any of the three established variants. He presented with anomia and a lower score in the picture semantics task (PPTT), but with no other indication of a semantic deficit. The last participant with PPA, had a mixed PPA phenotype. All PPA participants were analyzed together as a group, as no further comparison between PPA variants would be reliable.

The three groups did not differ significantly in education and gender composition. General cognitive status, as indicated by scores on the MMSE, was similar for AD and PPA groups. There was a statistically significant difference in age between the groups ($H(2) = 7.943$, $p = .019$) with a median of 69 years for neurotypical controls, 69.5 for the PPA group and 75 for the AD group. Post-hoc analysis revealed that the AD group was significantly older than the control group ($U = 10.867$ ($z = 2.595$), $p = .028$), but not significantly older than the PPA group ($U = 10.900$ ($z = 2.389$), $p = .051$).

4.2.2 **Procedure**

Participants were evaluated using a comprehensive battery of neuropsychological tests. Quantitative production analysis (QPA) was used for the narrative analysis of a picture description and a story retell task. Connected speech analysis was complemented with additional fluency and lexical measures. Acoustic analysis was also performed in order to calculate temporal measures of participants' speech. Detailed information about the assessment battery and procedure can be found in sections 2.3. and 3.6.

4.2.3 **Statistical analysis**

As the number of participants in each group was small, the most appropriate statistical test was the non-parametric Kruskal-Wallis *H* test. In cases where the test was significant, a series of 3 Mann-Whitney *U* post hoc tests were conducted to compare pairs of groups. The corrected α value ($\alpha = .016$) was used to interpret the results. In order to determine whether the distributions in each group had the same variability (shape), the corresponding histograms were visually inspected. Median and mean ranks are reported accordingly.

For the measures that discriminated the PPA group, sensitivity and specificity, were calculated, and optimum cut-off values were selected using Youden's index in Receiver Operating Characteristic (ROC) Curve Analysis.

Correlations between cognitive and linguistic tests were performed using non-parametric Spearman correlation coefficients.

4.3 Results

Several differences were found among the three groups that participated in the study. Significant and non-significant differences identified by statistical analysis using the Kruskal-Wallis *H* test and Mann-Whitney *U* post-hoc test results are provided in table 17 in the Appendix 1.

Participants with PPA performed worse than participants in the other two groups on two repetition tasks, the BDAE sentence repetition and the long frequent sentences of the Bayles Sentence repetition test. They produced fewer narrative words, unique words (type) and lemmas in describing the 'Cookie Theft' picture from BDAE. In comparison to the other two groups, they produced less elaborated and shorter sentences, as measured by the sentence elaboration index, mean sentence length, mean and median utterance length in the MAIN story retell task. Finally, they made more phonological errors in both narrative tasks.

Table 9: Tasks and measures that differentiated participants with PPA from AD and Neurotypical controls.

Group /max. score	Control median	AD median	PPA median	Test statistic*	Adj. sig
BDAE sentence repetition /2	2	2	1	20.533	< .001
Bayles Long Frequent Sentences /80	80	80	55	16.724	< .001
PD phonological errors ptw	.000	.000	.032	25.475	< .001
MAIN phonological errors ptw	.000	.000	.010	9.589	.008
PD narrative words	90	97	56	11.470	.003
PD type words	62	63	40.5	12.711	.002

MAIN Mean Sentence Length	8.466	7.636	6.187	15.713	< .001
MAIN Sentence Elaboration Index	2.103	1.769	1.332	17.582	< .001

*Kruskal-Wallis *H* test. Abbreviations: PD: picture description; ptw: per total words.

Using ROC analysis, two measures were found to be reliable and useful in discriminating the PPA group: Mean Sentence Length (AUC = 0.925, 95% confidence interval: 0.834-1, $p < .001$) and Sentence Elaboration Index for the MAIN story retell task (AUC = 0.946, 95% confidence interval: 0.868-1, $p < .001$). Cut-off and related values are provided in Table 10.

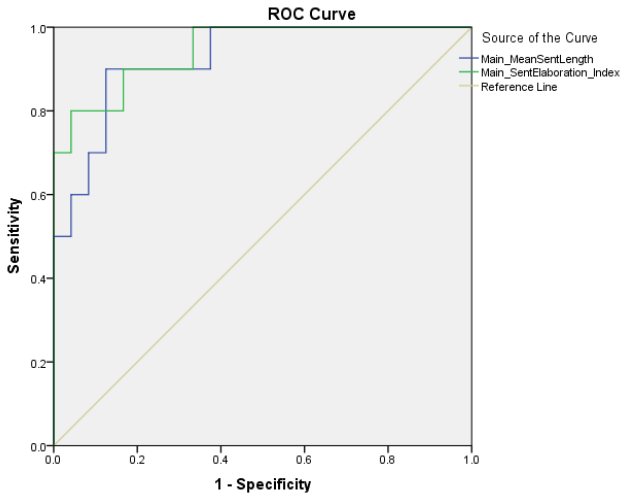


Figure 11: Receiver Operating Curves for Mean Sentence Length and Sentence Elaboration Index.

Table 10**:** Cut-off, sensitivity and specificity values for the two measures that differentiate the PPA group.

	Cut-off	Sensitivity	Specificity
Mean Sentence Length	< 7.07	90%	87.5%
Sentence Elaboration Index	< 1.6	80%	95.8%

Compared to neurotypical controls PPA participants recalled shorter digit sequences, produced less words in the phonemic condition of the verbal fluency task and were as a

group less reliable in identifying semantic relations in the PPTT. Significant differences were found for the WAB repetition test and 3 out of 5 subtests of the Bayles sentence repetition test (short meaningful, short non-meaningful and long meaningful sentences). Spoken language comprehension was found to be impaired at the word level, as suggested by scores on the PPVT (U = 13.555 (z = 3.347), p = .02) with a median of 24 correct compared to 30 for the neurotypical group. At the phrase level, the PPA group showed greater difficulty in following commands, processing complex ideational material and syntactically difficult sentences. Participants with PPA were impaired in understanding written sentences and spelling real words in comparison to the control group. Their articulation rate for passage reading was slower (mean rank = 9.44) compared to the neurotypical group (mean rank = 21.57), U = 11.917 (z = 4.064), p = .01).

Differences for fluency and narrative measures between the PPA and the control group that were found to be statistically significant are depicted in figures 12 and 13.

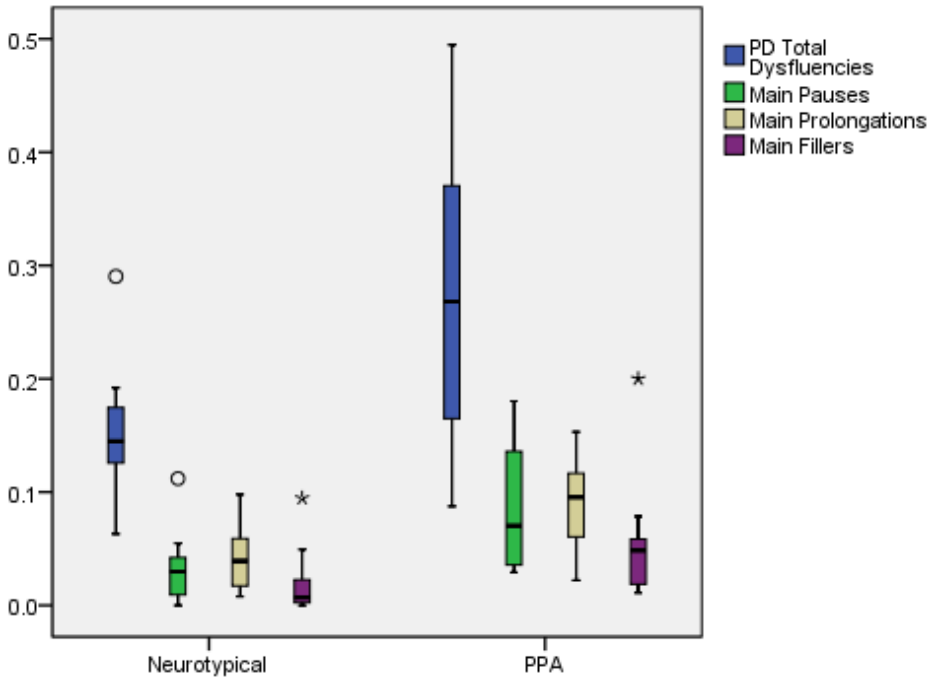


Figure 12. Fluency measures (per total words) that differed significantly between the PPA and control group.

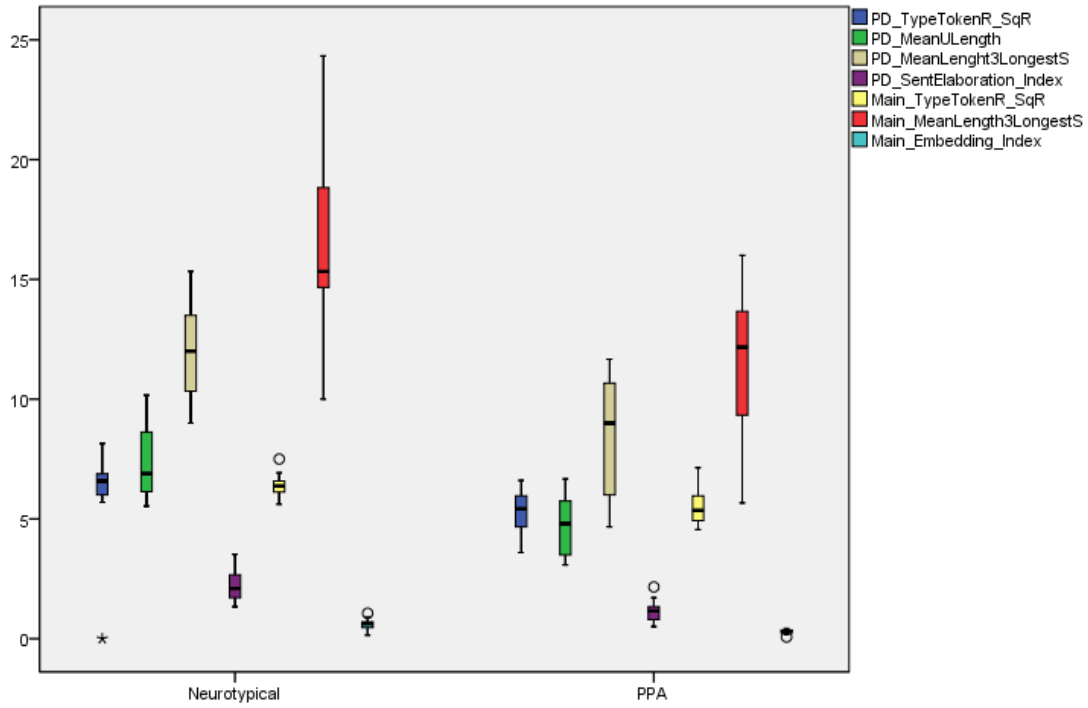


Figure 13. Narrative measures that differed significantly between the PPA and control group.

However, these measures did not differ significantly between the PPA and the AD group. In fact, no measure could differentiate on each one the AD group from the PPA and the control group. Participants with AD performed worse than controls on the Clock Drawing Test, 5-Objects Test and the delayed conditions of the 5-Words Test. They were impaired in the reading fluency test for non-words. Differences were also detected for articulation rate in story retell, and total time, median pause duration, semantic errors and proportion of words in sentences during picture description. There was finally a statistically significant difference in the temporal measures for the repetition of two sentences from the motor speech evaluation. Again, these measures did not differentiate the AD from the PPA group.

Finally, both groups performed significantly worse than the neurotypical control group on the MMSE, TMT-A, TMT-B, Verbal Fluency (category condition and total score), 5-Words Test, Benson Figure delayed recall, Bayles Sentence repetition (long non-meaningful sentences and total score), BNT, Grammaticality judgement, Reading fluency for words, WAB-apraxia and written picture description. Concerning fluency measures and narrative production analysis, AD and PPA participants differed from neurotypical controls in mean pause duration, pauses per total words and mean

logarithmic frequency of narrative words for picture description and total dysfluencies per total words, speech rate and proportion of narrative words for the story retell task.

4.4 Discussion

The presence of phonological errors, difficulty in repeating long frequent sentences, and the production of simple and short sentences has differentiated PPA participants not only from neurotypical controls but from participants with AD as well. No single measure could differentiate the AD group from the other two groups. For every measure, that the performance of the AD participants was worse than neurotypical participants', performance of the PPA participants was also impaired but not to the extent to be statistically different from controls. One possible explanation for this finding could be the fact that the assessment battery was specifically designed to measure language and other deficits encountered in PPA. Taken together, results of the AD group support the presence of memory, executive and lexical retrieval deficits.

The AD group was the only group that differed from controls on measures of episodic memory. Even though the PPA group scored lower than controls on the 5-Words Test, as did the AD group, on the delayed conditions, the group's performance was similar to controls. This may be due to reduced working memory capacity as suggested by low scores on the Digit Span Test and difficulties in almost all repetition tasks. These results are heavily influenced by the composition of the PPA group and more specifically by the larger proportion of individuals with the logopenic variant. Indeed, by inspecting individual profiles, one can note that the individuals with the semantic variant do not have repetition nor working memory deficits. This is consistent with previous studies which underly the differential nature of working memory deficits in PPA variants (Eikelboom et al., 2018). An opposite result can be observed for the semantic tasks. Difficulties with non-verbal semantic associations and single-word comprehension can be attributed to the inclusion of individuals with the semantic variant of PPA.

Several measures of language comprehension have been found to differ between the PPA and neurotypical group. In this study, the ability to follow commands, understand complex auditory material and process written sentences does not seem to be related to agrammatism. Other underlying deficits, such as single word comprehension deficits relevant to the svPPA participants or working memory difficulties pertinent to

participants with lvPPA provide a more likely explanation for the difficulties observed during evaluation. In the same way, difficulties in detecting grammatical violations, evident both in AD and PPA group, are most probably associated with reduced working memory capacity. Indeed, concerning the PPA group, performance on the grammatical judgement task was significantly correlated with the backward condition of the Digit Span test (r = .877, p = .001) and the B form of Trail Making Test (r = .854, p = .002).

In this study, repetition was evaluated using a number of different measures. All were informative, albeit in a different way. The PPA group was impaired on all repetition tasks compared to the control group. The sentence repetition subset from the BDAE-short form which differentiated participants with PPA, and AD, is an easy task comprising of just two sentences, one short and one long. As such, a ceiling effect is likely to be achieved. Although it may be useful for screening, it cannot be used to evaluate degree of deficit nor monitor change over time. AD participants could repeat words and most sentences reasonably well. However, increasing processing difficulty with very long sentences (e.g. last sentence in WAB) or long non-meaningful sentences (e.g. subset in Bayles) resulted in impaired performance compared to controls. The WAB repetition test combines in one score repetition performance for words, short phrases and sentences, even though sentence repetition is considered to be more useful for PPA diagnosis and classification (Clark et al., 2020). The WAB repetition test did not differentiate participants with PPA from participants with AD. The only repetition measure that achieved this was the long frequent sentences subset from the Bayles Sentence Repetition Test. Given the fact that the entire test is quite long and, in our experience, demanding for individuals with more pronounced deficits, the use of the long frequent sentences set seems to be preferable in the clinical setting.

The Bayles Sentence Repetition test was recently used to investigate differences in repetition among PPA variants (Lukic et al., 2019). Healthy controls, nvfPPA and svPPA participants had difficulty repeating long non-meaningful sentences, whereas lvPPA participants had difficulty with short non-meaningful and all long sentences. This suggests that inclusion of the short non-meaningful sentences in a test battery can assist PPA classification.

The inclusion of connected speech measures has also proven valuable. Concerning narrative production, the PPA group was impaired in discourse and sentence

productivity measures but did not differ from the neurotypical control group in measures of grammatical accuracy. The increased proportion of dysfluencies and more specifically of pauses, prolongations and fillers together with the lower number and proportion of unique words can be attributed to lexical difficulties.

The timed and temporal measures used in the battery suggest slower motor ability for the AD participants. This is more clearly reflected in slower articulation rate which does not include pauses and hesitations. The AD group was older than the control group and speech rate and articulatory movement have been found to decline as a function of age (Bilodeau-Mercure et al., 2015). Slower articulation rate was found for narrative production and may have contributed to lower scores on the two reading fluency tasks. However, articulation and speech rate for passage reading was within normal limits. This suggests an additional processing difficulty factor imposed by the maximum performance nature of the reading fluency task and discourse demands.

For the AD group, increased duration of pauses, proportion of pauses, semantic errors, use of higher frequency words and incomplete sentences in the picture description task are indicative of word-finding difficulties. This is also supported by lower scores on the naming test. These results are in line with the findings of a recent meta-analysis concerning connected speech in AD (Kavé & Goral, 2018).

The study has several limitations. Some limitations are inherent in the research design and methodology and are pertinent to the subsequent studies as well. One could argue that there may be some degree of circularity bias as diagnosis is based on impaired functioning which is detected through neuropsychological testing. However, all participants had already received a diagnosis before referral and were tested using different assessment batteries and tests, with the exception of a limited number of tasks. The primary areas of interest, namely memory and language were evaluated with tools that are not typically used in memory clinics.

The main limitation is the small sample size. This is particularly relevant to the extensive assessment battery. Statistical analysis was restricted by the fact that the number of variables was greater than the number of observations. Another limitation was that the non-fluent variant of PPA was not represented in the PPA group. This is mainly due to the consecutive recruitment method that was employed. Fluency and grammatical measures may have been more impaired with the inclusion of individuals

with nfvPPA. Furthermore, the composition of the PPA group was unbalanced in respect to the number of participants with the logopenic and the semantic variant. However, the same may also be true for the AD group. The group is not homogeneous and different single or multiple deficits were documented for AD participants. For example, one participant (P21) with a prominent memory deficit was also impaired in language measures at a similar degree to some of the PPA participants.

The assessment tools have been chosen by reviewing the PPA literature. Nevertheless, there are a number of domains that have not been evaluated, most notably, calculation and social cognition. Research for social cognition deficits, typically found in the behavioral variant of FTD, has been extended to the PPA variants and is increasingly receiving attention (Fittipaldi et al., 2019).

One limitation, specific to this study, is the fact that the AD group was older than the control group. PPA participants were also younger than the participants with AD, but the age difference did not reach statistical significance. This is due to the fact that the control group was matched demographically to the PPA group and age of onset of PPA is typically younger than AD.

4.5 Conclusions

Neuropsychological testing combined with narrative analysis has documented language and other cognitive deficits in participants with lvPPA, svPPA and AD. AD participants were, as expected, impaired in memory, speed of processing, visuospatial and executive functions. Moreover, they exhibited lexical retrieval difficulties, as well as difficulties in linguistic tasks with an increased processing load.

PPA participants were less affected in episodic memory measures. However, they too were impaired in executive tasks, especially for working memory and phonemic verbal fluency. Naming, single word comprehension, auditory comprehension of complex material, repetition, reading and writing were all affected.

The most informative measures in differentiating PPA from AD participants were sentence repetition, phonological errors, mean sentence length and sentence elaboration index in a connected speech sample. These findings should be interpreted with caution

taking into account the small sample size and the biased composition of the PPA group which did not include participants with nfvPPA.

5 Study 2. Comparing two narration tasks in PPA and AD: picture description and story retell

5.1 Introduction

Single word production deficits have been extensively examined in neurodegenerative diseases and PPA in particular. However, connected speech analysis has relatively recently begun to be systematically studied (Sajjadi, Patterson, Tomek, & Nestor, 2012a).

Boschi et al. (2017) reviewed the evidence from studies focusing on connected speech deficits in neurodegenerative disorders. The most commonly reported findings for individuals with AD, in comparison to neurologically healthy controls, are slower speech rate with frequent hesitations, greater number of closed class words produced, higher production of high-frequency words, greater number of semantic and inflectional errors, and production of fewer sentences and shorter utterances.

For individuals with svPPA, several studies have reported slower speech rate as a result of false starts, reduced mean length of utterances and syntactic complexity, production of fewer nouns but more pronouns, increased frequency of use of narrative words, and the presence of semantic errors, compared to healthy controls (Fraser et al., 2014; Sajjadi et al., 2012a; Wilson et al., 2010). With respect to the logopenic variant, the most consistent findings include slow speech rate, increased number of fillers, false starts and phonemic errors (Ash & Grossman, 2015; Ash et al., 2013; Wilson et al., 2010). A reduced proportion of well-formed sentences has also been reported. In the same studies, people with the non-fluent/agrammatic variant of PPA typically produced a reduced number of narrative words, spoke at a slower speech rate and made frequent speech sound errors. Reduced syntactic complexity and syntactic errors have been reported, at the syntactic level.

The evaluation of connected speech enables a multi-level naturalistic assessment of language production (Marini et al., 2011). All linguistic levels, phonetics, phonology, morphology, syntax, semantics, pragmatics, and discourse can be evaluated when analyzing connected speech samples.

Different tasks have been used to elicit speech samples and evidence suggests that they have different specificity for addressing different linguistic levels (Boschi et al., 2017). For example, a picture description task may be more useful in documenting lexical and semantic deficits, whereas story narration tasks favor the evaluation of discourse and syntactic abilities. Spontaneous speech production tasks are more sensitive to morphological, syntactic and discourse level deficits, as in unconstrained tasks it is easier for speakers to compensate for their word-finding difficulties.

Ash et al. (2013) compared speech and language production using a picture description task with the 'Cookie Theft' picture from BDAE, and a story from the picture book 'Frog Where Are You' (Mayer, 1969, as cited in Ash et al., 2013)They concluded that the performance of individuals with PPA was similar under the two conditions. In two other studies where a picture description and a semi-structured interview task were compared, a different performance was reported on the two tasks concerning individuals with PPA and AD (Sajjadi et al., 2012a, 2012b). The authors suggested that picture description is better at capturing lexico-semantic deficits, whereas interviews capture morphosyntactic deficits.

Moreover, it is recognized that different tasks place differential demands on cognitive abilities like auditory attention, executive control and memory (Duinmeijer, de Jong, & Scheper, 2012; Gonçalves et al., 2018). Neurodegenerative diseases like PPA provide an opportunity for investigating the relationship between narrative tasks and cognitive abilities, since cognitive deficits may also be present although language is the primary domain affected.

In study 1, both the AD and PPA group scored significantly worse than neurotypical controls on a number of cognitive and narrative measures. With respect to narrative measures, difficulties were found for both groups with discourse productivity, sentence productivity and lexical selection. However, findings did not show a clear pattern of deficits; different measures were affected in the two groups and it is not clear whether one of the two tasks favors narrative production in terms of lexical selection, discourse and sentence productivity and accuracy.

Thus, the first aim of the study was to elaborate on the findings of the previous study, by investigating whether there was a difference in the narratives produced by participants under two conditions: describing a picture and re-telling a story. A second

aim was to explore whether there was an interaction effect between group of participants and type of task, i.e., whether there was a differential performance under the two conditions for individuals with PPA, individuals with AD and neurotypical controls. A final aim was to examine whether the two elicitation tasks placed different cognitive demands on the participants.

5.2 Method

5.2.1 Participants

The same individuals from the previous study (study 1) were assigned to two experimental groups (PPA and AD) and one control group (neurotypical adults).

5.2.2 Procedure

Two connected speech samples were collected under 2 different conditions: a picture description task ('Cookie Theft' story, from the Boston Diagnostic Aphasia Examination, BDAE) and a pictured based story retell task, 'The Dog Story' from the Multilingual Assessment Instrument for Narratives, MAIN (Gagarina et al., 2012).

Samples were transcribed orthographically using ELAN software (Sloetjes & Wittenburg, 2008). Phonological paraphasias, unintelligible or incomprehensible words were transcribed phonetically using the International Phonetic Alphabet. Dysfluency variables, such as silent and filled pauses, sound errors, repetitions and false starts were also coded.

Narrative analysis of speech samples and extraction of summary measures was completed following the quantitative production analysis (QPA) procedures (Saffran et al., 1989). Segmentation of narratives into utterances was evaluated by a second investigator (M.K.). Differences were discussed and resolved by consensus. Inter-rater reliability for utterance segmentation was 91.5%. A set of additional measures was used to quantify speech dysfluent characteristics and narrative variables not addressed by the QPA protocol. Narrative measures were classified into four categories: discourse productivity, sentence productivity, grammatical accuracy and lexical selection (Gordon, 2006).

Details about the QPA methodology and the measures reported in this study can be found in pilot study 1.

Ten neuropsychological tasks were selected for evaluating interaction between cognitive functioning and narrative production. These included the TMT-A for evaluating visual attention and processing speed, the TMT-B for executive functioning, e.g. set shifting, mental flexibility, Verbal Fluency (phonemic and semantic) for executive control and verbal ability, the Forward and Backward Digit Span tasks as measures of short-term auditory memory and verbal working memory, the delayed conditions of 5-Words-Test, the 5-Objects-Test, the Benson Figure Test for auditory and visuospatial memory, the copy condition of Benson Figure Test as a measure of visuospatial processing and the picture version of the Pyramids and Palm Trees Test as a measure of semantic abilities.

5.2.3 **Statistical analysis**

Differences between the picture description and the story retell tasks were explored using paired sample T tests for each pair of narrative measures. In cases where assumptions for the dependent T test were not met, comparisons were performed using the non-parametric Wilcoxon Sign Rank Test. Significance values were adjusted for multiple comparisons (α =.016).

In order to examine the interaction effect between group and type of task, a series of Kruskal-Wallis *H* tests were performed with paired differences (Story retell – Picture description) for each measure. Post-hoc comparisons of pairs of groups were conducted with Mann-Whitney *U* tests with Bonferroni adjustment.

Correlations between neuropsychological tests and narrative measures were calculated by computing two-tailed Spearman's rank coefficients as several variables were not normally distributed.

5.3 Results

A number of statistically significant differences between the narratives produced using the two elicitation tasks was found (see Table 11).

All participants produced words of higher frequency in the picture description condition (Control *Mdn* = 2.649, AD *Mdn* = 2.783, PPA *Mdn* = 2.86) than in the story retell condition (Control *Mdn* = 2.512, AD *Mdn* = 2.535, PPA *Mdn* = 2.678). Differences in frequency were statistically significant ($T = 4$, $z = -3.045$, $p = .002$, $T = 0$, $z = -2.666$, $p = .008$, $T = 0$, $z = -2.803$, $p = .005$, respectively).

Table 11: Mean paired differences between the picture description and the story retell task per group.

	Control	Sig.	AD	Sig.	PPA	Sig.
Total Time (min) (np)	-0.104	*ns*	0.117	*ns*	-0.978	*
Total Words	-24.067	*ns*	17.667	*ns*	-79.700	*
Articulation Rate wpm	-3.595	*ns*	16.575	*	3.944	*ns*
Dysfluencies						
Pauses >1sec ptw	0.018	**	0.013	*ns*	0.034	*ns*
Fillers ptw (np)	0.009	*ns*	-0.022	*	-0.026	*ns*
False Starts ptw	-0.007	*	0.000	*ns*	-0.006	*ns*
Discourse Productivity						
Number of Narrative Words (np)	-42.467	**	-16.000	*ns*	-52.100	**
Narrative / Total Words	-0.157	***	-0.116	*ns*	-0.105	*
Number of Sentences (np)	-3.067	*	-1.333	*ns*	-6.900	**
Number of Utterances (np)	-2.467	*ns*	1.556	*ns*	-5.800	**
Number of Types (np)	-9.533	*	-2.000	*ns*	-18.200	**
Number of Lemmas	-6.667	*ns*	-0.222	*ns*	-12.200	**
Type Token Ratio (np)	0.113	*	0.067	*ns*	0.181	**
Lexical Distribution						
Number of Adjectives	0.027	**	0.022	*ns*	0.024	*
Number of Nouns	-0.010	*ns*	-0.038	**	-0.014	*ns*
Lexical Selection						
Mean Log Frequency (np)	0.230	**	0.276	**	0.364	**

Sentence Productivity						
Proportion of Words in Sentences	-0.050	*	-0.203	**	-0.027	*ns*
Mean Sentence Length	-1.429	*	-1.937	*	-0.955	*ns*
Mean Utterance Length	-1.488	*	-1.814	*ns*	-1.279	*
Median Sentence Length	-0.600	*ns*	-1.667	*ns*	-1.400	*
Mean Length 3 Longest	-4.756	***	-3.148	*ns*	-2.967	*
Embedding Index	-0.238	*	-0.022	*ns*	-0.096	*ns*
Auxiliary Complexity Index	-0.191	*ns*	-0.091	*ns*	-0.255	*

*$p < .05$; **$p < .01$; ***$p < .001$ level of statistical significance; ns: non-significant difference; np: non-parametric test used.

For the PPA group, significant differences between the two narrative tasks were found for variables of lexical selection (mean logarithmic frequency of open class words), discourse productivity (proportion of narrative to total words, number of narrative words, types, lemmas, sentences and utterances and type token ratio) and sentence productivity (median sentence length, mean length of the 3 longest sentences) and auxiliary complexity index, (figures 14 and 15). Finally, the PPA group produced significantly more adjectives in the picture description task ($M = 0.033$, $SD = 0.032$) than in story retell ($M = 0.009$, $SD = 0.01$); $t(9) = 0.024$, $p = .040$.

Performance of the AD group was statistically different under the two connected speech conditions in terms of fluency for articulation rate and fillers, as illustrated in figure 16, mean logarithmic frequency and sentence productivity for proportion of words in sentences and mean sentence length. The AD group produced significantly fewer nouns in the picture description ($M = 0.192$, $SD = 0.047$) than in the story retell task ($M = 0.23$, $SD = 0.035$); $t(8) = -0.038$, $p = .007$.

Concerning the control group, there was a statistically significant difference for fluency (pauses and false starts), lexical selection (mean logarithmic frequency of opened class words), discourse productivity (proportion of narrative to total words, number of narrative words, number of sentences and type token ratio) and sentence productivity (proportion of words in sentences, mean length of the 3 longest sentences and embedding index). Similar to the PPA group, neurotypical controls produced more

adjectives in picture description than in story retell (Mean difference = 0.027, *SD* = 0.033); $t(9) = 3.17$, $p = .007$.

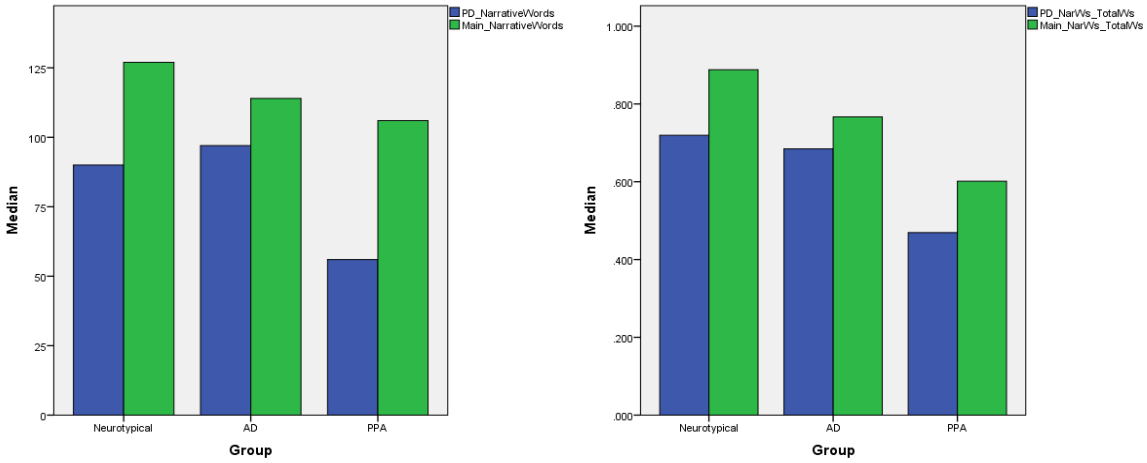


Figure 14. Discourse productivity measures: number of narrative words and proportion of narrative to total words produced in the two narrative tasks.

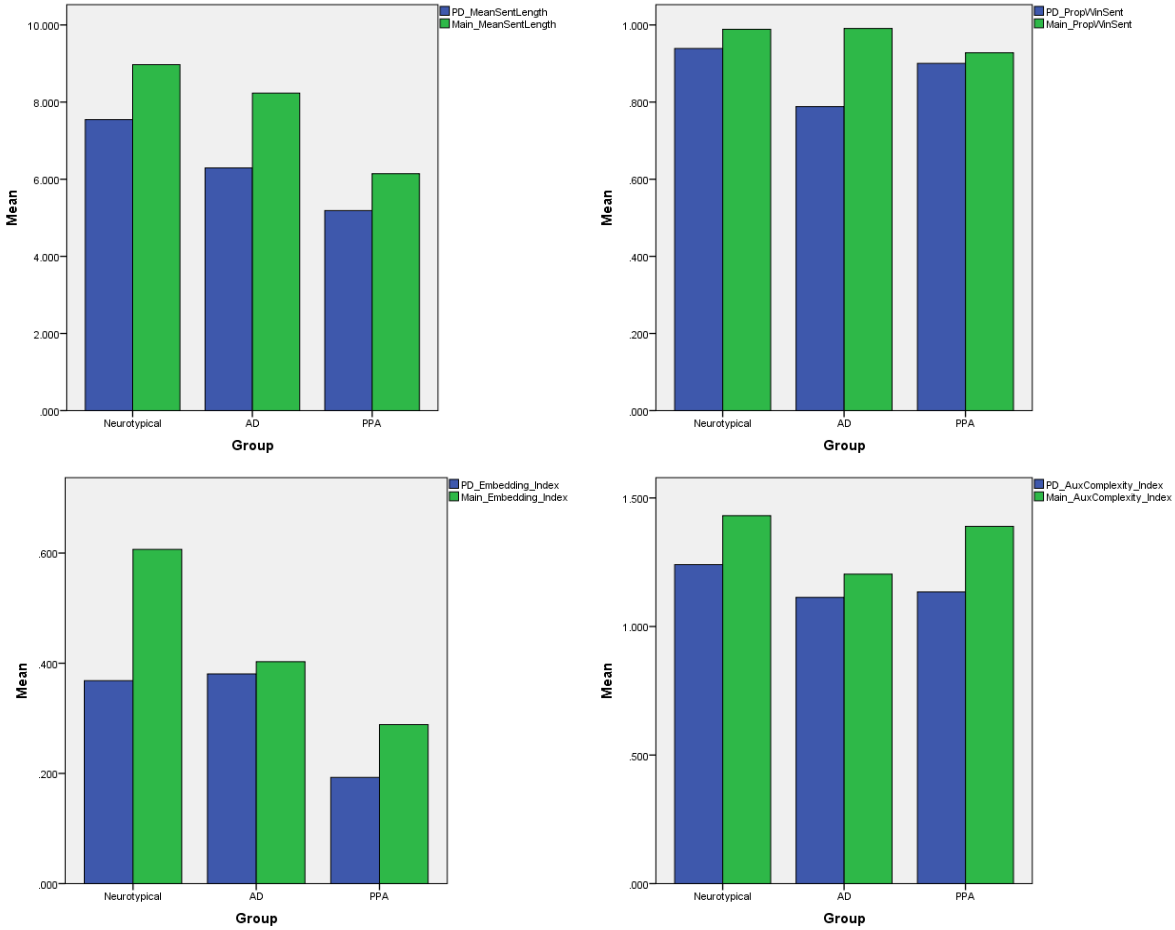


Figure 15. Sentence productivity (mean sentence length, embedding index, proportion of words in sentences) and auxiliary complexity index for picture description and story retell.

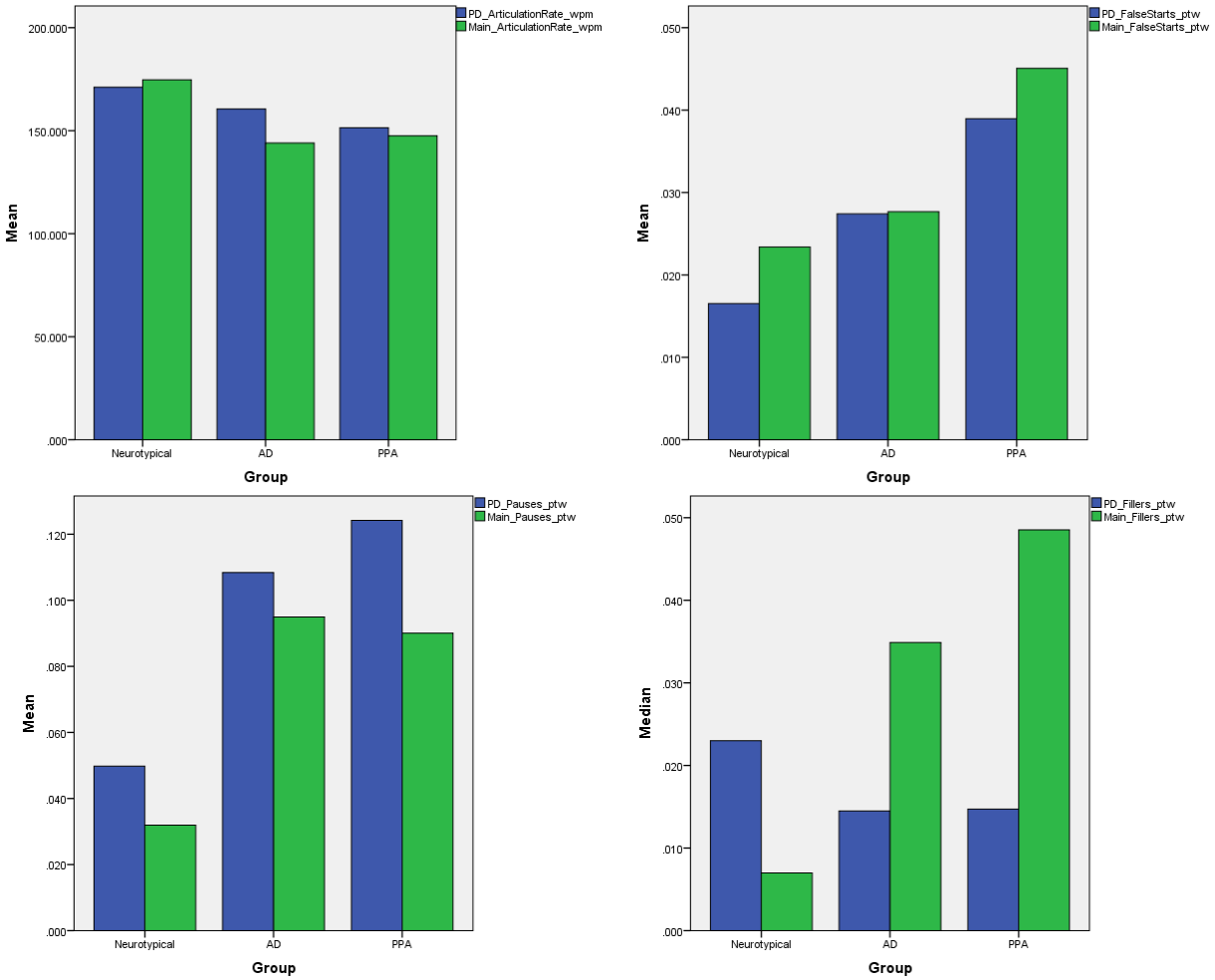


Figure 16. Fluency variables for picture description and story retell: articulatory rate, false starts, silent and filled pauses.

Significant differences in the performance under the two narration conditions between groups are reported in table 18 (see Appendix 1). Statistically significant interaction effects between group and type of narrative were found for discourse productivity measures (narrative words, total words, sentences, utterances, types and type-token ratio). Post- hoc comparisons with Mann-Whitney Tests revealed differences between the PPA and the AD group. Both groups produced more total words (PPA *Mdn* = 168.5; AD *Mdn* = 162) and narrative words (PPA *Mdn* = 106; AD *Mdn* = 114) in story retell than in picture description (PPA *Mdn* = 112.5, AD *Mdn* = 138 and PPA *Mdn* = 56, AD *Mdn* = 97), but for the PPA group the difference between the two narrative tasks was significantly greater than for the AD group; U = -12.078, z = -2.64, p = .025 and U = -12.15, z = -2.657, p = .024, respectively. Participants with PPA also produced more sentences (*Mdn* = 16) and utterances (*Mdn* = 17) in the story retell task than in the

picture description task (*Mdn* = 9.5; *Mdn* = 10.5). Participants with AD however, produced fewer sentences (*Mdn* = 12) and utterances (*Mdn* = 13) in story retell than in picture description (*Mdn* = 13; *Mdn* = 16). These differences were found to be significant (*U* = -11.478, *z* = -2.521, *p* = .035 and *U* = -14.039, *z* = -3.079, *p* = .006, respectively). Type token ratio was reduced in picture description in comparison to story retell for both groups, but even more so for the PPA group (*Mdn* = 0.715; *Mdn* = 0.534; *U* = 12.044, *z* = 2.632, *p* = .025).

A significant interaction between type of task and group was also found for semantic errors. The PPA group made significantly more semantic errors on the story retell task (*Mdn* = 0.009) than on the picture description task (*Mdn* = 0.003), whereas the opposite was evident for the AD group (*Mdn* = 0.005 for story retell, *Mdn* = 0.008 for picture description; *U* = -11.667, *z* = -2.666, *p* = .023)

A statistically significant interaction was also detected between type of narrative task and group for the production of fillers per total words (*H*(2) = 12.185, *p* = .002). Post-hoc comparisons revealed differential performance on the two narrative tasks between the control and the PPA group (*U* = -10.733, *z* = -2.64, *p* = .025), as well as between the control and the AD group (*U* = -13.133, *z* = -3.128, *p* = .005). The control group produced more fillers in describing the picture (*Mdn* = 0.023) than in re-telling the story (*Mdn* = 0.007). Both the PPA and the AD group produced more fillers in story retell (PPA *Mdn* = 0.049; AD *Mdn* = 0.035) than in picture description (PPA *Mdn* = 0.015; AD *Mdn* =0.014).

Finally, although the omnibus test was statistically significant for proportion of words in sentences (*H*(2) = 6.165, *p* = .046), post-hoc comparisons did not confirm differential performance under the two conditions for any pair of groups.

Correlational analyses revealed a significant positive correlation for AD participants between mean logarithmic frequency of narrative words for story retell and the delayed recall conditions of the 5-object-test (*r* = 0.807, *p* = .009) and Benson Figure test (*r* = .77, *p* = .005). For the PPA group, there was a significant negative correlation of the same measure in both tasks with TMT-B and the forward condition of the Digit Span test (*r* = -.681, *p* = .03; *r* = -.746, *p* = .013 for picture description; *r* = -.755, *p* = .002; *r* = -.703, *p* = .023 for story retell, respectively).

For AD participants, sentence elaboration, embedding index and mean length of the 3 longest sentences were positively correlated with TMT-B only for the story retell task (r = .749, p = .02; r = .785, p = .012; r = .715, p = .03, respectively). Articulation rate and pauses were correlated with backward digit span, as well as the delayed conditions of 5-words and 5-objects test, only for the picture description task.

For PPA participants, the sentence embedding index was correlated with TMT-A (r = .804, p = .005) and TMT-B (r = .702, p = .024), only for the picture description task, whereas sentence elaboration for the same task was positively correlated with TMT-B (r = .644, p = .044) and forward digit span (r = .801, p = .005). Sentence elaboration for story retell correlated only with forward digit span (r = .667, p = .035). Mean length of utterance was correlated with TMT-B (r = .839, p = .002) and forward digit span (r = .799, p = .006) for the picture description and backward digit span (r = .642, p = .045) and phonemic verbal fluency (r = .685, p = .029) for the story retell task. Speech rate was correlated with TMT-B (r = .693, p = .026) and forward digit span (r = .752, p = .012), only for story retell.

5.4 Discussion

In this study, a picture description task was compared to a story retell task in two groups of individuals with different neurodegenerative conditions (PPA and AD) and a neurotypical control group. In order to evaluate the cognitive demand of each task, correlations were computed between narrative discourse and cognitive measures.

Differences between the two connected speech tasks were found for fluency, lexical selection, discourse, and sentence productivity but not for grammatical accuracy measures. The only lexical selection measure that was significantly different between the two tasks, was mean logarithmic frequency of open class narrative words. All participants used higher frequency words in picture description, indicating reliance on ‘easier’, more common words for the completion of this task or even for masking of word retrieval difficulties. Another finding, which was common in all groups, was higher sentence productivity scores for the story retell task.

A finding worth considering is the increased morphological complexity of forms used by individuals with PPA in the story retell narrative, as suggested by the higher auxiliary complexity index in this task compared to the picture description. With respect

to discourse productivity, results indicate better performance in the story retell task for the PPA and the control group, but similar performance to the picture description task for the AD group. Speech rate did not differ between the two narrative tasks, but articulation rate was found to be faster in picture description than in story retell for individuals with AD who also did not differ in the number of silent pauses they made in the two tasks. However, they made more filled pauses in story retell. These findings may indicate that AD participants had an additional difficulty with recalling the story plot. Neurotypical participants made more pauses in the picture description task but produced more false starts in the story retell task. For the PPA group, fluency measures did not vary significantly between the two narrative tasks.

For the PPA and AD group, an interaction effect was found between group and method of elicitation for frequency of semantic errors, as well as discourse productivity measures. The PPA group made more semantic errors in the picture description task, whereas the AD group in the story retell task. Furthermore, the PPA group produced far more narrative words in the story retell task in comparison to the picture description task than the AD group. An explanation for this finding could be related to the cognitive load of each task and the additional recall component of the story retell task.

Results from the correlation analysis suggested a heavier involvement of memory capacity for fluency and word frequency measures for AD participants. Sentence productivity was correlated with executive function. For PPA participants, all fluency measures, as well as measures of lexical selection, discourse and sentence productivity correlated with executive control, short-term memory and to a lesser degree with working memory.

In picture description, fluency measures correlated both with episodic and working memory for participants with AD. In story retell, involvement of executive function was evident for sentence productivity measures. In PPA, there was no clear relationship between cognitive load and type of task.

Both picture description and story retell tasks involve inhibition of distractions, keeping important information in working memory, integrating semantic knowledge, planning, organization, and other executive skills. The presence of visual stimuli (pictures) lessens the memory load of the tasks. These capacities are recruited in order to produce complete and accurate narratives. Additional executive resources are needed to

compensate for a deficit in linguistic processing or memory. Task complexity and the presence of a linguistic or cognitive deficit seems to account for the increased involvement of multiple executive components in individuals with PPA and AD in comparison to the control group. This is a commonly reported conclusion in the research literature on the topic (Gonçalves et al., 2018; Mueller, Hermann, Mecollari, & Turkstra, 2018).

Individuals with PPA performed better in the story retell task in comparison to the picture description task; they produced words of lower frequency, more narrative words and utterances, longer sentences and used more complex morphosyntactic elements than they did when describing the 'Cookie Theft' picture.

This finding has clinical implications as it suggests that individuals with PPA could benefit from input in structured activities during therapy to maximize their verbal output. Story retell seems to have an advantage over picture description activities which are very popular in clinical settings. A possible use of such an activity in intervention could involve rehearsing personal relevant stories with visual prompts (Khayum, Wieneke, Rogalski, Robinson, & O'Hara, 2012).

Fewer differences between the tasks were documented for the AD group and they were not always in the same direction. A possible explanation could be that the AD group does not benefit from or cannot capitalize on the auditory input provided by the examiner in the retell task due to memory limitations. If this assumption is true, both tasks would be treated as picture description tasks and the story retell task would place more cognitive demands to the AD group, as a result of the need to convey information about a relatively complex story plot and not just about a static scene. Results from the previous study contradict this interpretation, as participants with AD differed from neurotypical controls in articulation and speech rate, total dysfluencies and proportion of narrative words under the story retell condition. It seems thus, that both tasks presented the same degree of difficulty for participants with AD and that the underlying deficit is executive in nature, as substantiated by the correlation analysis. We could thus conclude that in this group both elicitation methods could be used interchangeably.

Regarding ability to capture connected speech deficits, both tasks seem to perform equally well in participants with PPA. Recapitulating findings from study 1, PPA participants were found to be affected in fluency, lexical selection, discourse and

sentence productivity measures in both tasks: total dysfluencies, pauses, mean pause duration, phonological errors, square root variant of type token ratio, mean logarithmic frequency of open class words, number of narrative words, mean length of the 3 longest sentences and sentence elaboration index, in picture description; speech rate, total dysfluencies, pauses, prolongations, fillers, phonological errors, square root variant of type token ratio, proportion of narrative to total words, mean length of the 3 longest sentences, mean sentence length, sentence elaboration index and embedding index in story retell. In that sense, both methods can be used interchangeably, as suggested by Ash et al. in the only study, so far, that has directly compared picture description to story narratives in individuals with PPA (Ash et al., 2013).

On the other hand, if the purpose of the assessment is to assist differential diagnosis between degenerative conditions and more specifically between PPA and AD, which is by far the most frequent clinicopathological entity encountered in clinical settings, then we reach a different conclusion. In study 1, two measures were deemed appropriate for differentially diagnosing PPA and AD participants: mean sentence length and sentence elaboration index derived from the story retell elicitation procedure. Story retell thus seems to be more sensitive in identifying deficits at the syntactic level of language production. In that respect, the findings are in partial agreement with two studies which compared picture description and semi-structured interviews (Sajjadi et al., 2012a, 2012b). They concluded that picture descriptions are more suitable for detecting lexical deficits, whereas interviews are more suitable for detecting morphosyntactic and discourse deficits. It must be noted however, that these results originate from different tasks and sample composition. In this study, PPA participants were grouped together irrespective of variant categorization and there was no participant with the non-fluent/agrammatic variant of PPA.

The generalizability of the findings is limited by the fact that the PPA sample did not include participants with the non-fluent/agrammatic variant of PPA. Difficulty with sentence productivity, grammatical accuracy and dysfluencies have been consistently reported in this variant (Boschi et al., 2017).

A further limitation of this study is that discourse-pragmatic measures are not included in the current analysis. Cohesion and coherence have been studied both in AD (Mueller et al., 2018) and PPA (Ash & Grossman, 2015).

5.5 Conclusion

Different elicitation tasks for the assessment of connected speech can be used to document narrative abilities in individuals with degenerative disorders. However, clinicians should be aware that different methods may lead to a different outcome depending on the purpose of the assessment. Story retell seems to be more sensitive in capturing morphosyntactic deficits and may assist in the differential diagnosis between PPA and AD.

6 Study 3. Cognitive-linguistic profiles of Greek-speaking individuals with a degenerative disease: a case-control study

6.1 Introduction

In the last decade, language has been increasingly studied in the context of neurodegenerative diseases, not only in PPA, but also in various disorders with a predominant cognitive, movement or behavioral deficit (Mueller et al., 2018; Peterson, Patterson, & Rowe, 2019; Vinceti et al., 2019). Differences and similarities between individuals with PPA and AD were documented in the two previous studies. However, other diseases such as Frontotemporal dementia - Amyotrophic lateral sclerosis (FTD-ALS), Progressive supranuclear palsy (PSP), Corticobasal syndrome (CBS) have also clinical phenotypes which overlap with PPA and may manifest with language impairment amongst other cognitive symptoms.

In this study, the cognitive-linguistic and narrative discourse profiles of Greek-speaking individuals with a degenerative disease were analyzed. Thirteen individuals with a progressive speech and language impairment participated in this study: 10 with a diagnosis of PPA and 3 with an FTD associated diagnosis. Fifteen demographically matched neurotypical adults served as controls. Each clinical diagnosis was discussed with reference to the established criteria. The different phenotypes were compared, and key characteristics of each condition were identified.

The main aim of the study was to explore the range of cognitive and language symptoms that can occur in PPA and FTD related neurodegenerative diseases. A second aim was to document the challenges associated with the clinical diagnosis of PPA and classification of the PPA variants.

6.2 Method

6.2.1 Participants

Ten individuals with PPA (mean age 66.80, *SD* = 7.525 with mean years of education 13.60, *SD* = 4.088) and 3 individuals with an FTD associated diagnosis (mean age 60, *SD* = 17.3 with mean years of education 13.33, *SD* = 4.62) participated in the study.

FTD diagnoses included: FTD-Amyotrophic lateral sclerosis (FTD-ALS), Progressive supranuclear palsy (PSP) and Corticobasal syndrome (CBS).

Two of the PPA participants met the criteria for svPPA and six for lvPPA. One participant did not meet the criteria for any of the three established variants and another one presented with a mixed variant phenotype.

The control group consisted of 15 neurotypical individuals (mean age 67.93, *SD* = 6.17, mean years of education 13.13, *SD* = 3.482).

Additional information about the control group, PPA and FTD participants can be found in section 3.4. The same neurotypical controls and individuals with PPA participated in study 1 and study 2.

6.2.2 **Procedure.**

All participants were evaluated using the same comprehensive battery of tests. Details about recruitment, assessment and obtaining informed consent are described in detail in chapter 3.

6.2.3 **Statistical analysis**

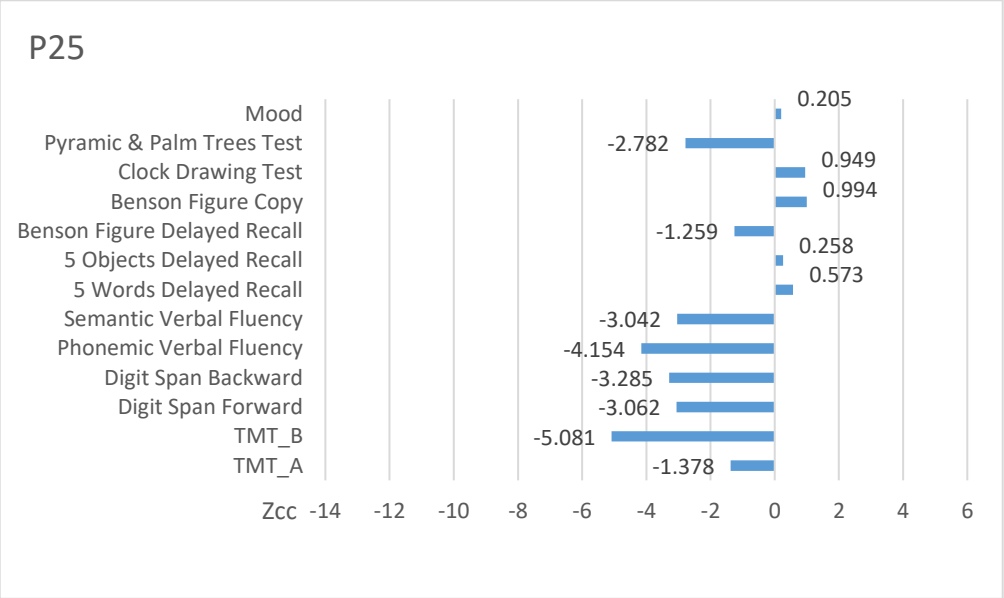
Each participant was compared to the control group using Crawford and Howell's method (Crawford & Howell, 1998) which enables the comparison of performance of a single participant with that of a small control sample. *T* values and effect sizes (z_{cc}), for case-control designs, have been computed (Crawford & Garthwaite, 2012).

6.3 Results

In the following sections, demographic information, as well as information about staging, communicative, functional, neuropsychiatric, and general cognitive status are provided in a tabular format for each participant. Linguistic assessment results are summarized and discussed in relation to classification criteria. Concerning cognitive function and narrative discourse abilities, results are presented in bar charts.

6.3.1 **Participant 25 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	2
Gender	female	BDAE Severity	2
Age	60	WAB Fluency	7
Education	12	Frontotemporal Rating Scale	63.333
MMSE	22	NPI	5
PASS sum of boxes	7	NPI Iimpact	4



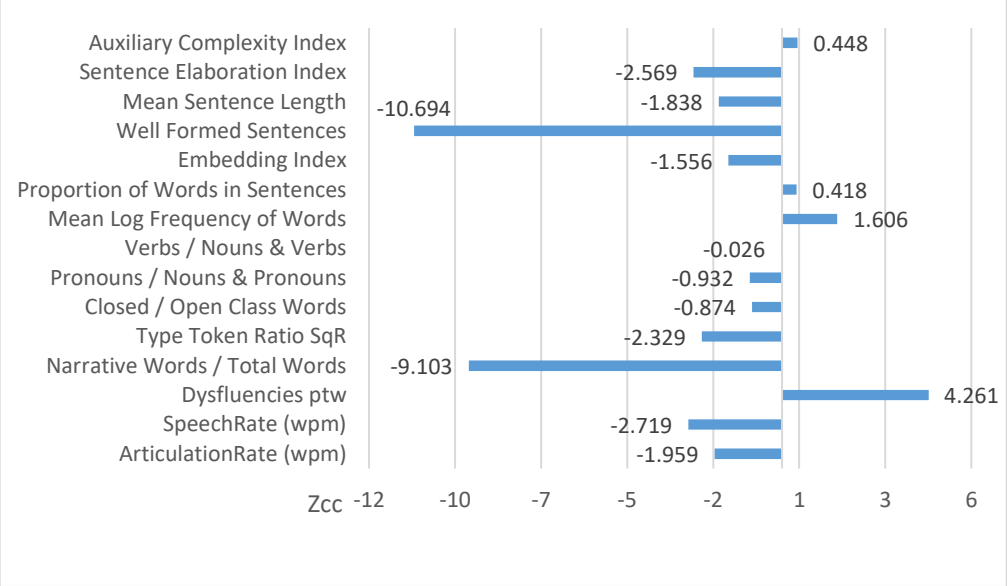


Figure 17: Participant 25: cognitive and narrative discourse profile.

For the first participant with PPA, both core criteria for lvPPA were met. A severe repetition deficit was documented (t = -24.590, p < .001, z_{cc} = -25.396, for the WAB test and t = -110.375, p < .001, z_{cc} = -113.995, for the long frequent sentences from Bayles repetition test). Moreover, single-word retrieval in spontaneous speech and naming was impaired. Performance on the BNT was significantly different than neurotypical controls' performance (t = -11.375, p < .001, z_{cc} = -11.748). In a recent meta-analysis of neuropsychological function in lvPPA (Kamath, Sutherland, & Chaney, 2020), naming was found to be significantly more impaired than repetition. However, when simple repetition tasks and tests which combined performance for repetition of words, short and long sentences together in one score were removed, severity of naming deficits was comparable to severity of repetition deficits.

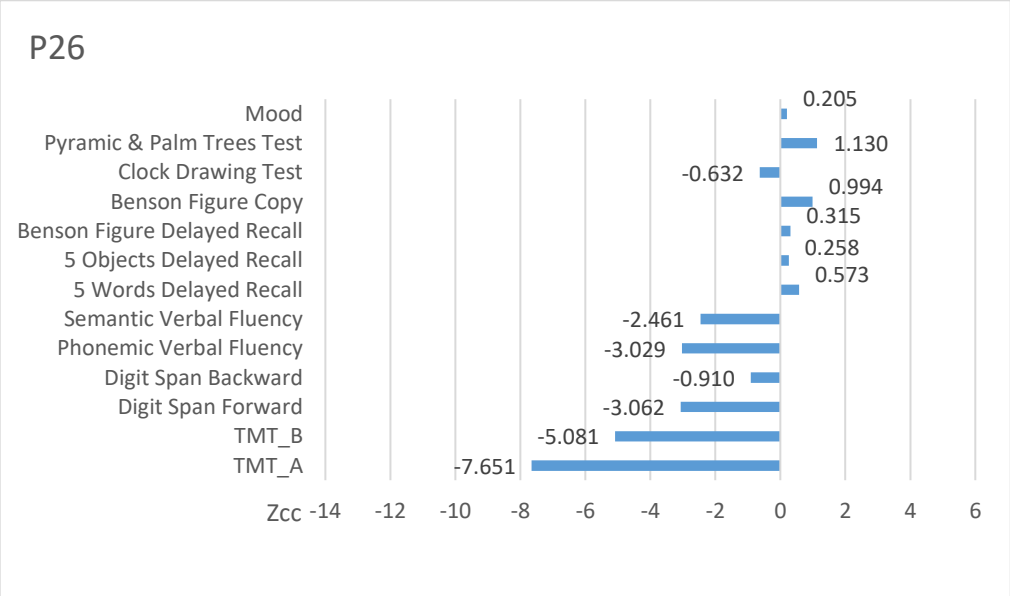
Additional criteria were also met. This participant made frequent phonological errors (t = 9.788, p< .001, z_{cc} = 10.109, for the picture description task), had spared single-word comprehension as indicated by scores on PPVT (t = -1.626, p = .063, z_{cc} = -1.679) and spared motor speech (even though repetition of multisyllabic words generated phonemic paraphasias). There was no evidence of frank agrammatism. Comprehension of complex syntactic structures was impaired (t = -10.012, p < .001, z_{cc} = -10.341), but to a lesser degree than other auditory comprehension tasks (t = -22.250, p < .001, z_{cc} = -22.980 for following commands). This finding could be attributed to underlying short-term and working memory deficits (see figure 17). The low proportion of well-formed sentences in the story retell task, depicted in figure 17, was associated with word finding problems and difficulties in retrieving the phonological form of words which resulted in pervasive phonological errors.

Reading and writing were also affected. Performance in reading fluency was better with non-words than real words (t = -1.542, p = .073, z_{cc} = 1.592; t = -4.219, p < .001, z_{cc} = -4.358, respectively), but spelling was better for words than non-words (t = -6.355, p < .001, z_{cc} = -6.563; t = -9.798, p < .001, z_{cc} = -10.119, respectively).

Neuropsychological testing documented executive impairment with relative sparing of memory and visuospatial abilities.

6.3.2 **Participant 26 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	2
Gender	female	BDAE Severity	2
Age	61	WAB Fluency	5
Education	12	Frontotemporal Rating Scale	93.333
MMSE	26	NPI	4
PASS sum of boxes	6	NPI Iimpact	2



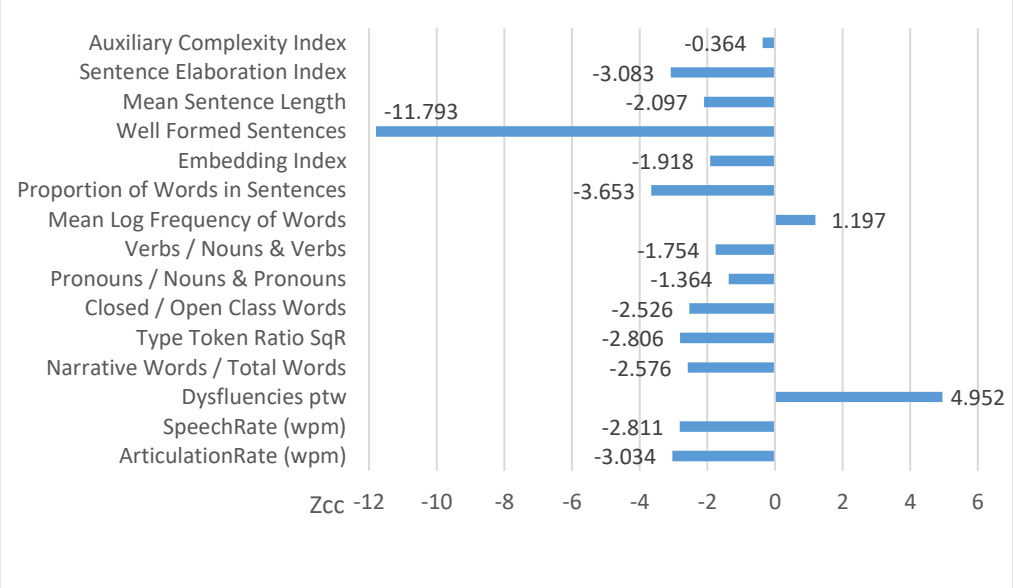


Figure 18: Participant 26: cognitive and narrative discourse profile.

The second participant with PPA was severely impaired in sentence repetition (t = -11.233, p < .001, z_{cc} = -11.602, for the WAB test and t = -69.125, p < .001, z_{cc} = -71.392 for the long frequent sentences from the Bayles repetition test) and in confrontation naming (t = -3.500, p = .002, z_{cc} = -3.615 for BNT). Concerning the additional criteria for the lvPPA classification, this participant made phonological errors in picture description (t = 15.861, p < .001, z_{cc} = 16.381). She had intact semantic knowledge for objects and pictures (t = 1.094, p = .146, z_{cc} = 1.130 for the PPT test), but single word comprehension was found affected (t = -2.981, p = .005, z_{cc} = 3.078). However, the same participant was tested one year later (see study 4) and her performance on the same test was normal (t = -0.610, p < .276, z_{cc} = -0.630) despite cognitive decline and deterioration in all other tests. A possible explanation for this finding may be test-retest variability or underlying performance anxiety alleviated by familiarizing with the setting. Motor speech was intact, but assessment revealed difficulty with sentences with increased articulatory complexity. It must be noted that this was a common finding in participants with co-existing severe repetition deficits. In these cases, repetition of single words with increasing length and articulatory complexity seems to be more reliable for evaluating motor speech function. Thus far, three out of the four additional criteria are fulfiled and this participant can be classified as logopenic.

Reading and writing were affected as in the first participant. Performance in reading fluency was better with non-words than real words (t = -1.402, p = .091, z_{cc} = 1.448; t = -3.134, p = .004, z_{cc} = -3.236, respectively) and spelling was better for words than non-words (t = -8.880, p < .001, z_{cc} = -9.171; t = -15.922, p < .001, z_{cc} = -16.444, respectively).

With respect to neuropsychiatric symptoms, only anxiety was reported to be present. An executive impairment was documented, as in the previous participant, with relative sparing of memory and visuospatial abilities. It must be noted that TMT-A and TMT-B were interrupted following the directions of the tasks protocol about timed administration. Thus, the corresponding effect size values do not reflect the magnitude of executive deficit. The same limitation applies to all participants.

Nonetheless, the final criterion of absence of frank agrammatism merits further discussion. For this participant, as well as for other participants in this study, the answer

as to whether her speech was agrammatic or not is not that straightforward. Her speech production was severely affected by lexical retrieval deficits. She used 25 unique words in picture description compared to 65.533 (*SD* = 19.416) of the control sample (*t* = -2.021, *p* = .031, z_{cc} =-2.088). Mean sentence length was 3.4 (*t* = -2.314, *p* = .018, z_{cc} = -2.390) and proportion of well-formed sentences was 0.8 (*t* = -3.006, *p* = .005, z_{cc} = -3.104).

Concerning receptive language, she was impaired in syntactic comprehension (*t* = -14.243, *p* < .001, z_{cc} = -14.710), but less so than in following commands (*t* = -18.500, *p* < .001, z_{cc} = -19.107). Sentence comprehension deficits in this variant are frequently reported and have been associated with short-term memory demands for sentence processing (Wilson et al., 2012).

The diagnosis of nfvPPA is based on either agrammatism in language production or apraxia of speech and at least two of the following features: spared single-word comprehension, spared object knowledge and impaired comprehension of syntactically complex structures. Even if the receptive deficit were dismissed for this participant, she could still be classified as nfvPPA, lvPPA or as a mixed case. As Ash et al. point out, impaired grammaticality with disease progression in lvPPA contributes to difficulty in distinguishing lvPPA from nfvPPA (Ash et al., 2019). Given the prominent nature of the repetition and word retrieval deficits, the diagnosis of lvPPA seems to be more appropriate for this participant.

Pertinent to the discussion is also the progression of cognitive and language features over time. PPA subtyping is easier at initial stages (Mesulam, 2016) and the timing of assessment is crucial for accurate diagnosis. Such dilemmas have been previously reported and have raised awareness about the limitations of clinical diagnosis and classification (Montembeault, Brambati, Gorno-Tempini, & Migliaccio, 2018; Tippett, 2020).

6.3.3 **Participant 27 (PPA group)**

Diagnosis	svPPA	Years Post Onset	4
Gender	male	BDAE Severity	4

Age	72	WAB Fluency	8
Education	9	Frontotemporal Rating Scale	-
MMSE	27	NPI	-
PASS sum of boxes	4	NPI Iimpact	-

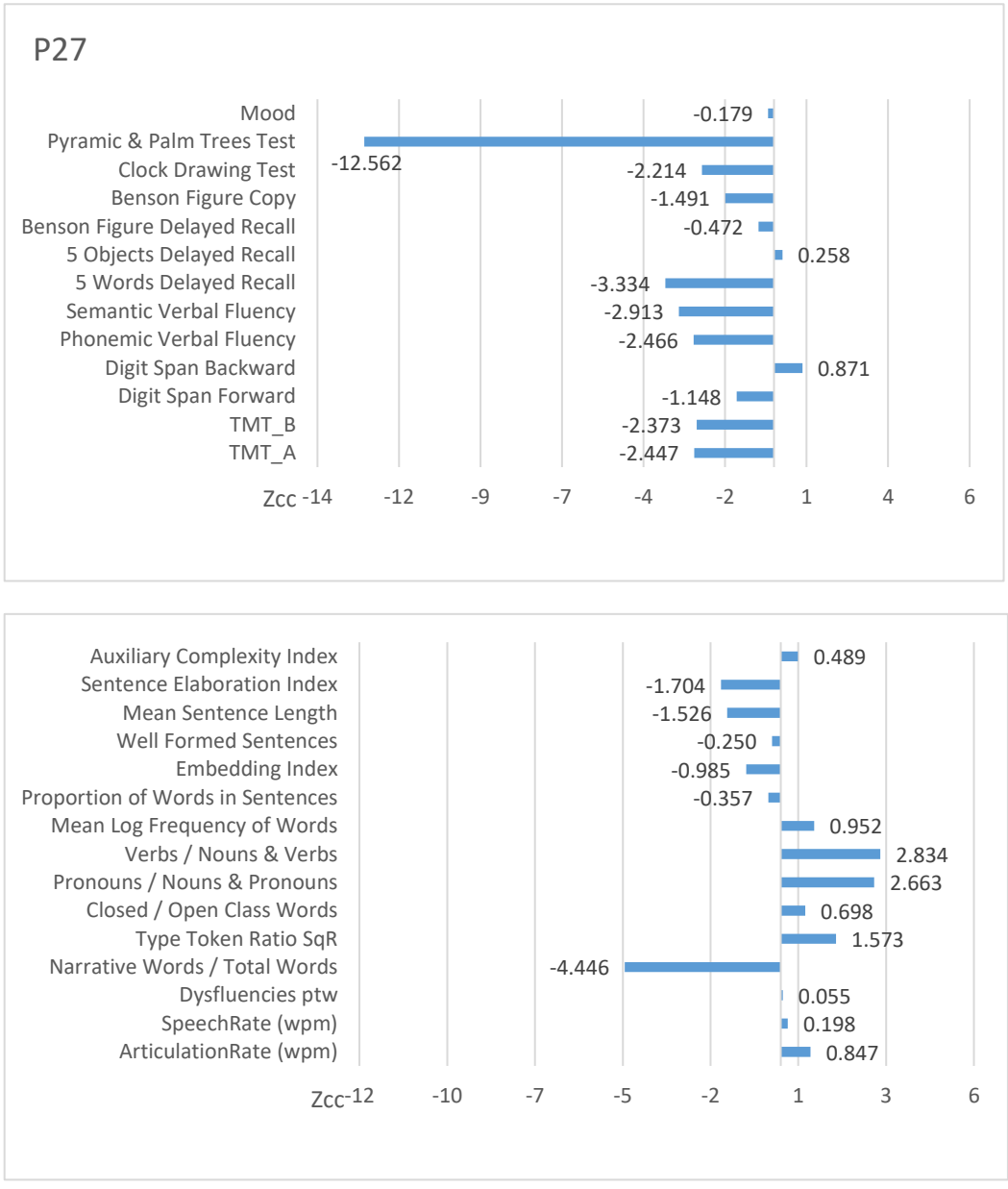


Figure 19: Participant 27: cognitive and narrative discourse profile.

In order to be classified as svPPA, a person must be impaired in confrontation naming and single-word comprehension. Additional features of this variant include impaired object knowledge, surface dyslexia or dysgraphia, spared repetition, grammaticality,

and motor speech abilities. At least three of these features must be present for the diagnosis of svPPA.

This participant was indeed severely impaired in naming (t = -13.625, p < .001, z_{cc} = -14.072), single-word comprehension (t = -8.061, p < .001, z_{cc} = -8.326) and object semantics (t = -12.163, p < .001, z_{cc} = -12.562). Comprehension of syntactically complex sentences was intact (t = 0.564, p = .291, z_{cc} = 0.583), as was production of sentences (see figure 19). He had difficulty repeating long non-meaningful sentences (t = -4.680, p < .001, z_{cc} = -4.834), but repetition of long frequent sentences was flawless (80/80) (t = 0.250, p = .403, z_{cc} = 0.258). Motor speech evaluation did not reveal any signs of dysarthria or apraxia of speech. Reading fluency was within normal limits (t = 0.014, p = .494, z_{cc} = 0.015 for words and t = 0, p = .5, z_{cc} = 0 for non-words). Spelling, on the other hand, was impaired for real words (t = -3.830, p = .001, z_{cc} = -3.955), but not for non-words (t = 0.919, p = .187, z_{cc} = 0.949).

On cognitive testing, he exhibited mild to moderate memory and executive impairment, but spared visuospatial functioning (see figure 19). This participant presented with disinhibition and logorrhea. Behavioral symptoms were reported by his primary caregiver one year later on re-assessment. At that time, he had a score of 25 on the Neuropsychiatric Inventory.

A finding worth commenting on, is the increased proportion of pronouns in story retell narrative production (t = 2.579, p = .011, z_{cc} = 2.663) and verbs (t = 2.744, p = .008, z_{cc} = 2.834), consistent with previous reports (Wilson et al., 2010), which reflects lexical retrieval deficits for nouns.

The semantic variant of PPA is the variant with the most salient characteristics and consistent clinical presentation (Hoffman et al., 2017) and this participant seems to represent the typical phenotype of svPPA.

6.3.4 **Participant 28 (PPA group)**

Diagnosis	Anomic PPA	Years Post Onset	2
Gender	male	BDAE Severity	4
Age	68	WAB Fluency	9

Education	16	Frontotemporal Rating Scale	92.590
MMSE	29	NPI	4
PASS sum of boxes	1.5	NPI Iimpact	2

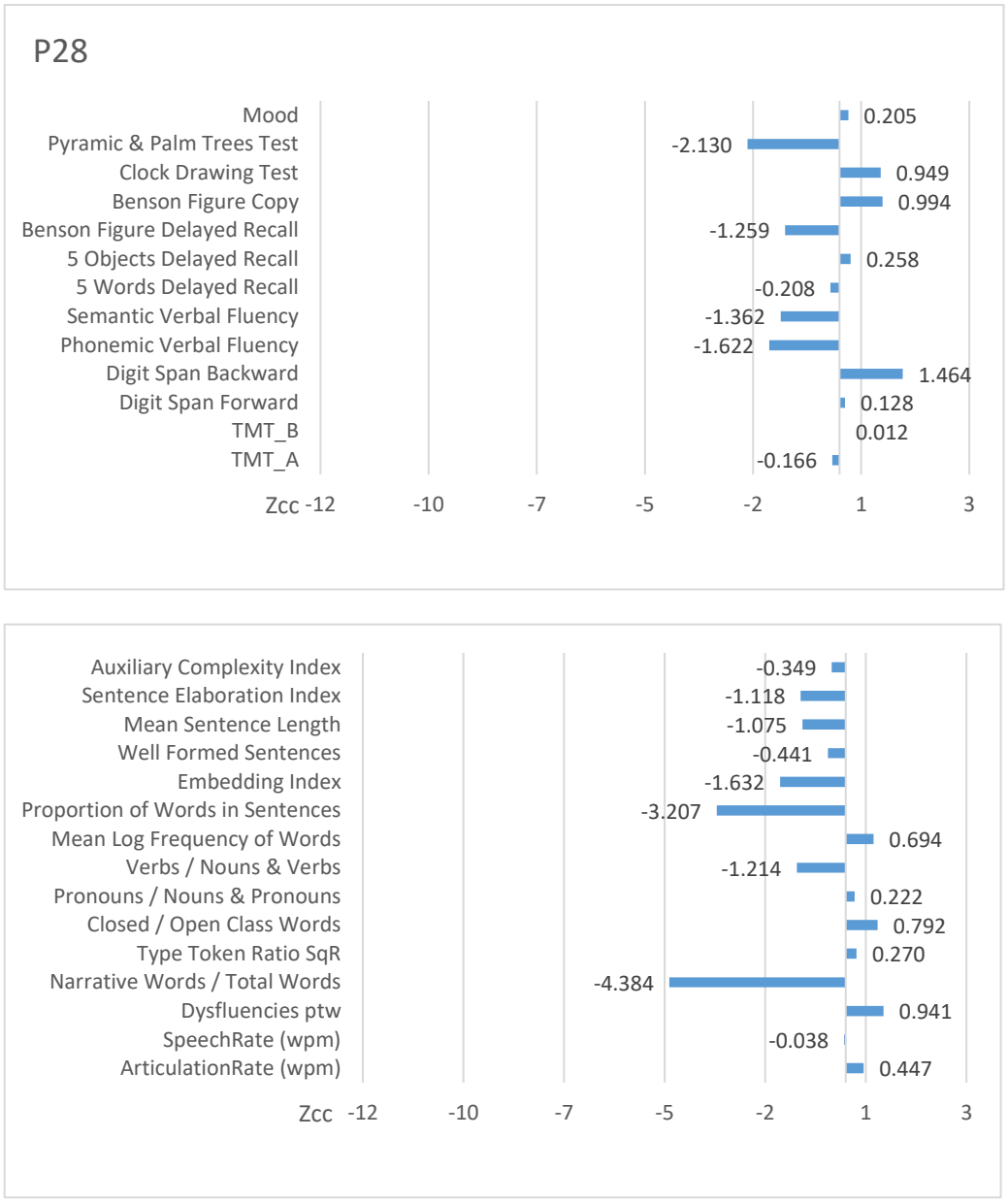


Figure 20: Participant 28: cognitive and narrative discourse profile.

This participant could not be classified in any of the established variants of PPA. He presented with a naming deficit (t = -6.5, p < .001, z_{cc} = -6.713) and a mild deficit in object semantics (t = -2.062, p = .029, z_{cc} = -2.13). However, single-word

comprehension, one of the two main criteria for the svPPA classification, was intact (t = -0.271, p < .395, z_{cc} = -0.280).

He also did not meet the lvPPA basic criteria, as sentence repetition was intact (t = 0.582, p = .285, z_{cc} = 0.601, for the WAB test and t = 0.25, p = .403, z_{cc} = 0.258 for the long frequent sentences from the Bayles repetition test).

Comprehension of syntactically complex sentences was unaffected (t = 0.564, p = .291, z_{cc} = 0.583), but impaired comprehension of sentences was documented in following commands (t = -3.5, p = .002, z_{cc} = -3.615). Reading, writing and motor speech abilities were spare. Cognitive testing revealed intact memory, executive and visuospatial functioning (see figure 20).

No phonological (t = 0.206, p = .42, z_{cc} = 0.213) and semantic errors (t = 1.688, p = .057, z_{cc} = 1.743) were evident in story retell, but he made significantly more errors than the control participants in describing the 'Cookie Theft' picture (t = 12.298, p < .001 , z_{cc} = 12.701 for phonological errors; t = 2.408, p = .015, z_{cc} = 2.487 for semantic errors).

Increased anxiety levels were documented on the NPI, but no other behavioral symptom was reported.

Similar phenotypes have been reported in various studies. Mesulam et al., for example, in a cohort of 25 individuals with PPA, identified as 'anomic' three participants (Mesulam et al., 2012). Two of them, at a later stage, fulfilled the criteria of svPPA. Taking into account the mild impairment in object semantics and the preserved executive and visuospatial abilities, which seem to be better preserved in the semantic than in the other variants of PPA (Kamath et al., 2020), further deterioration of semantic knowledge could be anticipated.

For this participant, results were available from two consecutive assessments. He was first evaluated as a candidate for the control group. As there were indications of a lexical retrieval deficit, he was disqualified and re-assessed one year later. A comparison of the two assessment results is presented in study 4.

6.3.5 **Participant 29 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	1

Gender	female	BDAE Severity	3
Age	60	WAB Fluency	6
Education	16	Frontotemporal Rating Scale	69.230
MMSE	19	NPI	3
PASS sum of boxes	6.5	NPI Iimpact	1

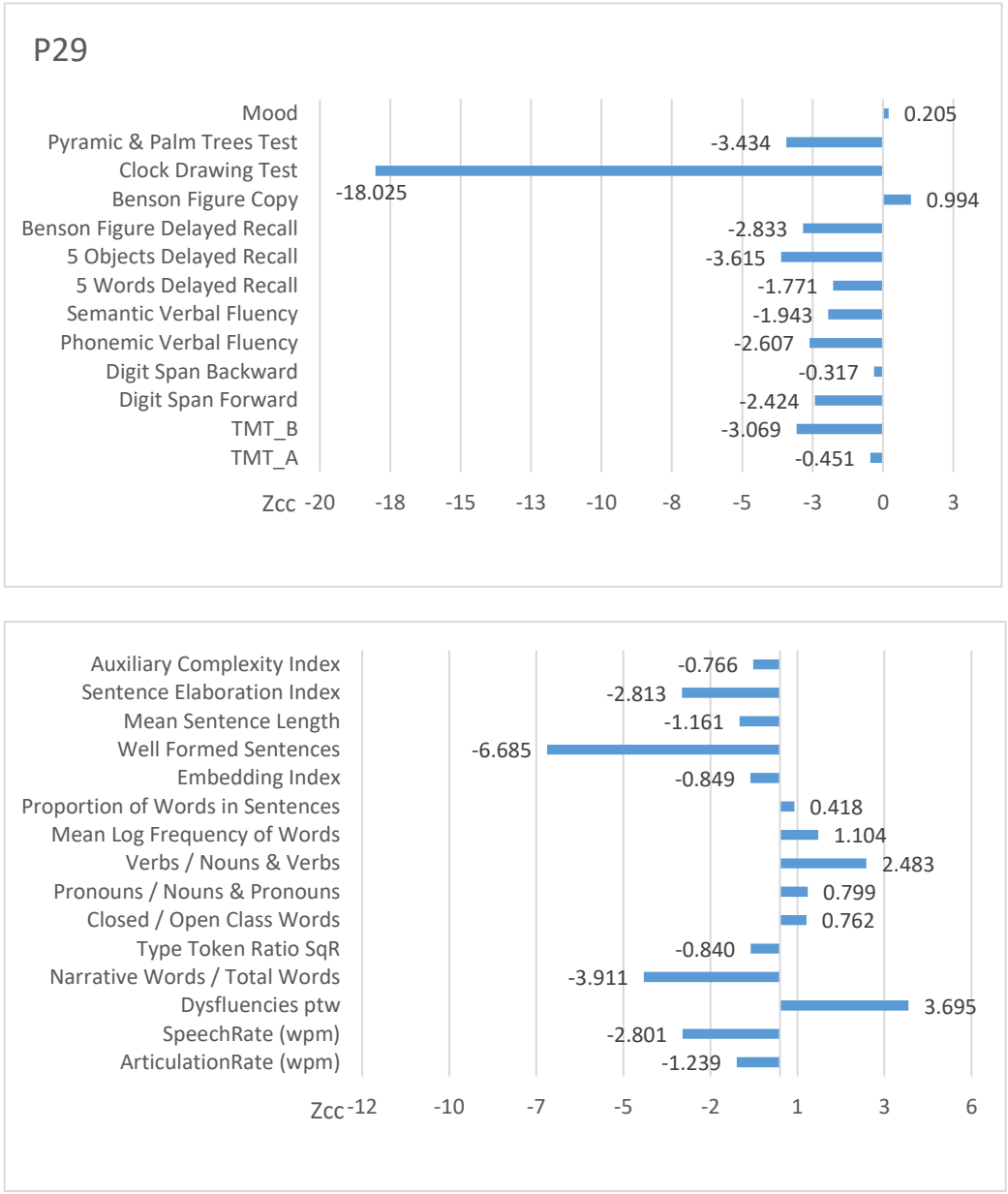


Figure 21: Participant 29: cognitive and narrative discourse profile.

This participant presented with a naming deficit (t = -2, p < .033, z_{cc} = -2.066 for BNT-45 and t = -13.392, p < .001, z_{cc} = -13.831 for BNT-15) and impaired sentence repetition

(t = -7.124, p < .001, z_{cc} = -7.386, for the WAB test and t = -63.5, p < .001, z_{cc} = -65.583 for the long frequent sentences from the Bayles repetition test). Lexical retrieval deficits were evident in speech production, as suggested by her connective speech profile in figure 21, and more specifically by the increased number of dysfluencies, the high proportion of verbs in comparison to nouns and the reduced sentence elaboration index (Emily Rogalski et al., 2011; Wilson et al., 2010).

Additional criteria for the lvPPA diagnosis were also met. She made phonological errors in both narration tasks (t = 7.165, p < .001, z_{cc} = 7.4, in picture description and t = 3.577, p = .002, z_{cc} = 3.695, in story retell). Single word comprehension (t = -0.948, p = .18, z_{cc} = -0.980) and comprehension of complex syntactic structures (t = -1.551, p = .072, z_{cc} = -1.602) were intact.

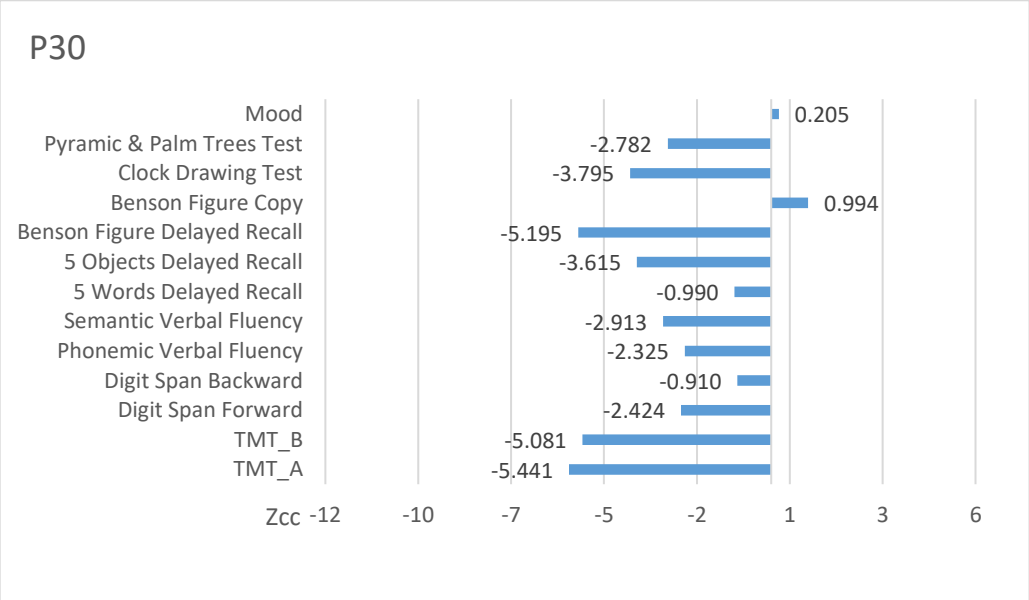
Motor speech evaluation revealed severe difficulty with sequential motion rate (puh-tuh-kuh) (t = 15.067, p < .001, z_{cc} = 15.561), but normal repetition of polysyllabic words and words with increasing length and articulatory complexity. She also had difficulty repeating sentences of increased articulatory complexity. As it has been aforementioned, these results might not be reliable given her sentence repetition deficit. There was no evidence of apraxic errors in spontaneous speech and passage reading (t = -1.371, p = .096, z_{cc} = -1.416, for speech rate and t =-1.712, p = .054, z_{cc} = -1.768, for articulation rate in reading).

Reading performance was impaired for real words (t = -2.374, p = .016, z_{cc} = -2.452). Reading fluency for non-words (t = 0.561, p = .292, z_{cc} = 0.579) and spelling was unaffected (t = -0.042, p = .484, z_{cc} = -0.043, for words and t = -0.612, p =.275, z_{cc} = -0.632, for non-words).

She showed a mild executive deficit. Verbal memory was within normal limits, but memory for positioning objects and delay recall of the Benson figure was impaired (see figure 21). Visuospatial abilities have been found to be more affected in the logopenic variant in comparison to the other two variants of PPA (Watson et al., 2018). Poor visuospatial abilities might also explain her score on the Clock drawing test, which was originally developed as a test of visuo-constructive abilities (Pinto & Peters, 2009). Her performance was significantly lower than neurotypical controls (t = -17.453, p < .001, z_{cc} = -18.025).

6.3.6 **Participant 30 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	2
Gender	female	BDAE Severity	3
Age	71	WAB Fluency	6
Education	19	Frontotemporal Rating Scale	60.000
MMSE	24	NPI	7
PASS sum of boxes	6	NPI Iimpact	4



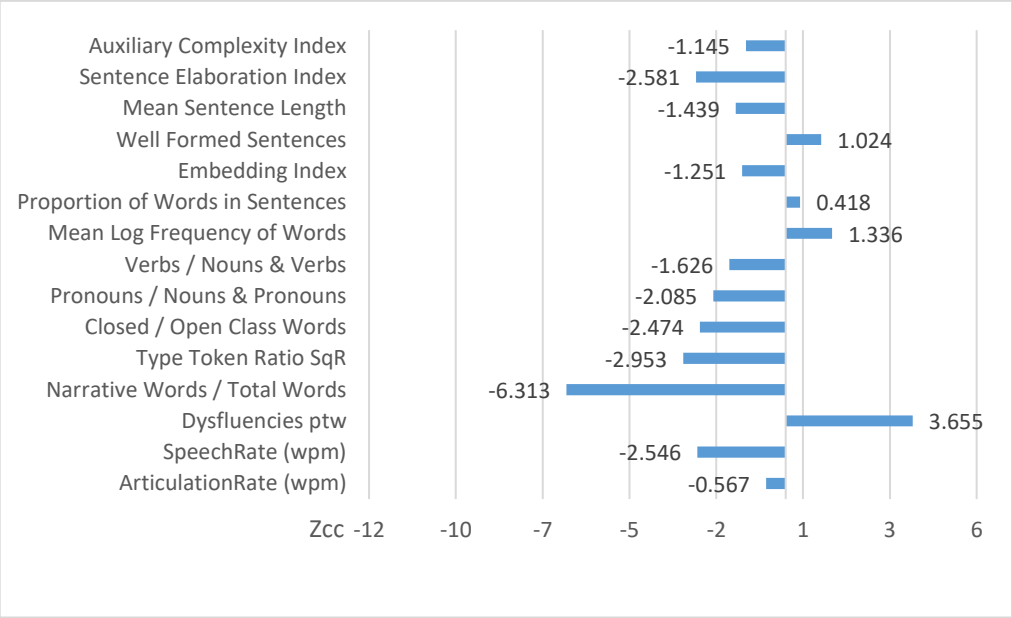


Figure 22: Participant 30: cognitive and narrative discourse profile.

This participant had a severe naming (t = -9.5, p < .001, z_{cc} = -9.812) and repetition deficit (t = -10.206, p < .001, z_{cc} = -10.541, for the WAB test and t = -76.625, p < .001, z_{cc} = -79.138 for the long frequent sentences from the Bayles repetition test).

Her speech was non-fluent, characterized by frequent word-finding associated prolongations and false starts, as reflected by increased proportion of dysfluencies in figure 22. Phonological errors were evident in her spontaneous speech (t = 15286, p < .001, z_{cc} = 15.787). Single word comprehension (t = -0.61, p = .276, z_{cc} = -0.63) and motor speech abilities were intact.

Comprehension of commands, complex ideational material and syntactic structures was impaired (t = -11, p < .001, z_{cc} = -11.361; t = -5.561, p < .001, z_{cc} = -5.941; t = -10.012, p < .001, z_{cc} = -10.341, respectively). Sentence comprehension was also impaired in participants P25 and P26.

Reading and writing performance was within normal limits apart from written picture description (t = -8.886, p < .001, z_{cc} = -9.178). All PPA participants were impaired in the latter task, apart from the unclassified participant with the anomic clinical presentation (P28), who was the participant with the best cognitive performance.

She had a similar cognitive profile to the previous participant (see figure 22). She had a mild executive deficit and difficulty with all visuospatial tasks (the 5-Objects test, the delay recall of the Benson figure, and the Clock drawing test).

6.3.7 **Participant 31 (PPA group)**

Diagnosis	svPPA	Years Post Onset	2
Gender	male	BDAE Severity	5
Age	74	WAB Fluency	10
Education	17	Frontotemporal Rating Scale	70.000
MMSE	27	NPI	5
PASS sum of boxes	4.5	NPI Iimpact	12

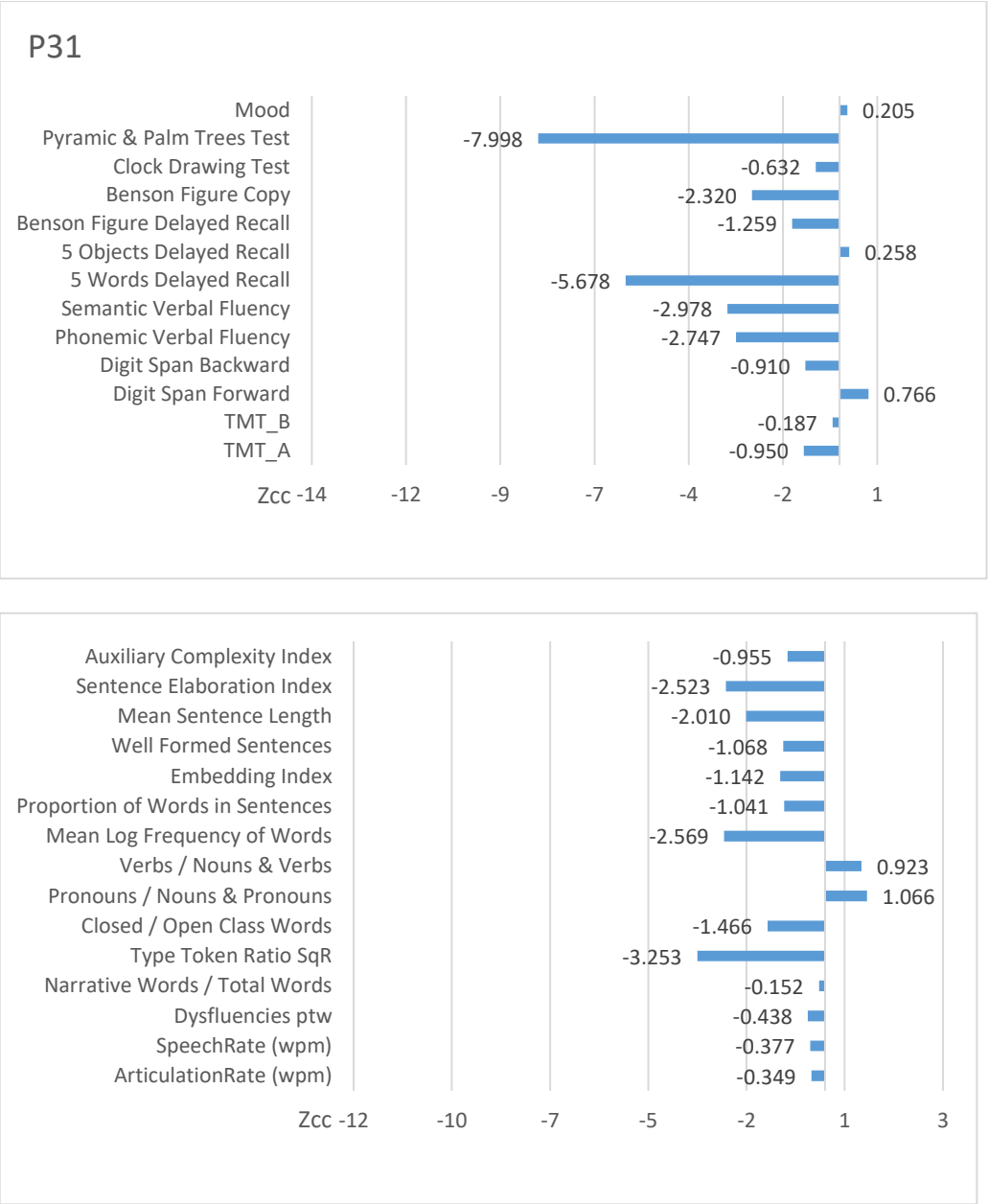


Figure 23: Participant 31: cognitive and narrative discourse profile.

The second participant with the semantic variant of PPA, exhibited a severe naming deficit (t = -14, p < .001, z_{cc} = -14.459, for BNT-45 and t = -29.902, p < .001, z_{cc} = -30.883, for BNT-15) and a single-word comprehension deficit (t = -3.658, p = .001, z_{cc} = -3.778). Moreover, he was impaired in object semantics (t = -7.744, p < .001, z_{cc} = -7.998). Sentence comprehension was impaired, as indicated by following commands, and responding to questions for complex auditory material (t = -14.750, p < .001, z_{cc} = -15.234; t = -8.890, p < .001, z_{cc} = -9.181, respectively). However, comprehension of syntactically complex sentences was similar to controls (t = 0.564, p = .291, z_{cc} =

0.583). In spontaneous speech, his sentences were relatively shorter, less elaborated than those produced by control participants, but there were grammatically correct (see figure 23).

Sentence repetition was intact (t = -0.445, p = .331, z_{cc} = -0.460, for the WAB test) even for the long non-meaningful sentences from the Bayles repetition test (t = -0.425, p = .338, z_{cc} = -0.439). His reading ability was within normal limits both with words (t = -0.963, p = .176, z_{cc} = -0.994) and non-words (t = -0.981, p = .172, z_{cc} = -1.013). Speech rate for passage reading was comparable to neurotypical controls (t = 0.039, p = .464, z_{cc} = 0.096). Spelling performance was superior for non-words (t = -0.612, p = .275, z_{cc} = -0.632) than for real words (t = -1.936, p = .037, z_{cc} = -1.999). Motor speech abilities were spared.

Regarding neuropsychological functioning (see figure 23), episodic memory was impaired only for verbal stimuli (t = -5.497, p < .001, z_{cc} = -5.678). Attention, processing speed and working memory were intact. Nevertheless, there was a mild executive impairment, as reflected by his category and letter fluency performance.

Behavioral problems for this participant were reported by his primary caregiver in NPI. These included delusions, irritability, euphoria, and apathy.

6.3.8 **Participant 32 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	1.5
Gender	female	BDAE Severity	4
Age	77	WAB Fluency	9
Education	17	Frontotemporal Rating Scale	100
MMSE	28	NPI	0
PASS sum of boxes	4.5	NPI Iimpact	0

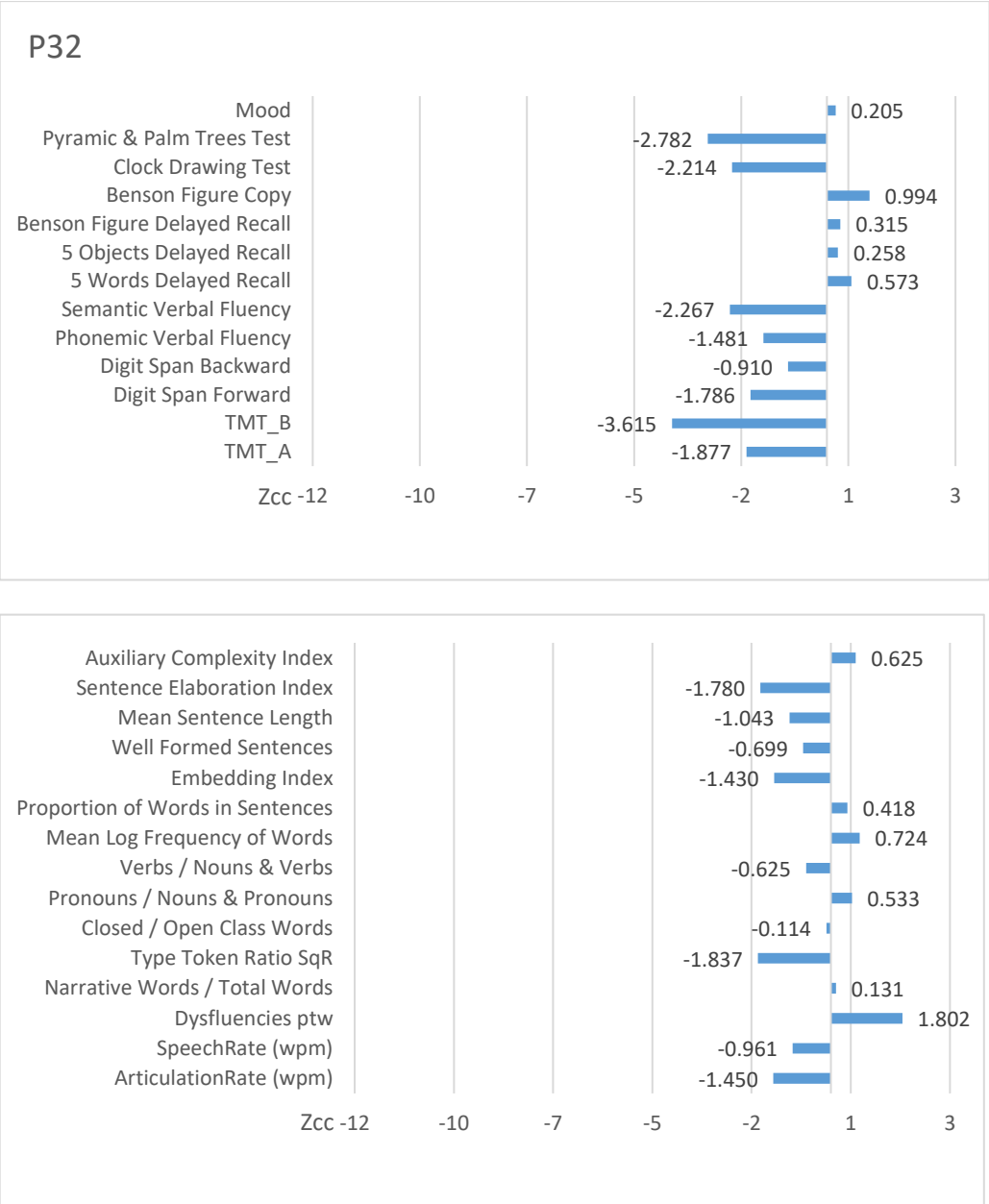


Figure 24: Participant 32: cognitive and narrative discourse profile.

Writing difficulties were reported by this participant as the leading cause of functional impairment. Although she was able to write words and construct written sentences to convey a message, she had given up writing altogether. Information about level of functioning and neuropsychiatric symptoms were gathered by a close relative who did not report any functional limitations or behavioral problems.

As depicted in figure 24, neuropsychological testing revealed a mild executive impairment, but memory and visuospatial functioning were spared.

She presented with a naming deficit (t = -2.750, p = .008, z_{cc} = -2.84) and impaired sentence repetition (t = -3.014, p = .005, z_{cc} = -3.113, for the WAB test and t = -33, p < .001, z_{cc} = -34.082, for the long sentences from the Bayles repetition test). Single-word comprehension was intact (t = -1.626, p = .063, z_{cc} = -1.679), even though there was a mild deficit in object semantics (t = -2.694, p = .009, z_{cc} = -2.782).

She did not make any phonological error in story retell, but increased proportion of phonological and semantic errors was evident in connected speech analysis of the picture description task (t = 4.411, p < .001, z_{cc} = *4*.555; t = 6.661, p < .001, z_{cc} = 6.879, respectively).

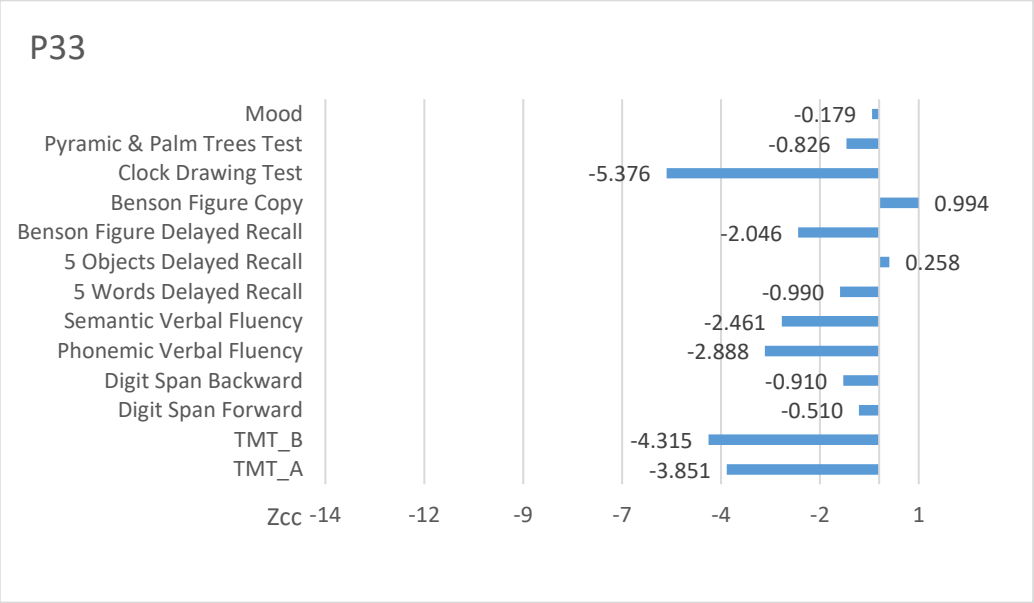
Comprehension of commands was impaired (t = -3.5, p = .002, z_{cc} = -3.615). On the other hand, comprehension of complex ideational material and sentences with complex syntactic structure was normal (t = -1.046, p = .157, z_{cc} = -1.080; t = -1.551, p = .072, z_{cc} = -1.602, respectively).

Reading performance was mildly impaired for real words (t = - 1.940, p = .036, z_{cc} = -2.003). However, speech rate for passage reading was within normal limits (t = 1.034, p = .159, z_{cc} = 1.068). Reading fluency and spelling for non-words were unaffected (t = -1.121, p = .14, z_{cc} = -1.158; t = -0.612, p = .275, z_{cc} = -0.632, respectively). She was impaired in spelling real words (t = -5.092, p < .001, z_{cc} = -5.259) and severity of spelling impairment was greater than severity of confrontation naming.

A word frequency effect was detected for words spelled correctly (mean frequency was 82.549, mean word letters = 8, mean syllables = 4, for correctly spelled words and mean frequency = 25.910, mean word letters =10, mean syllables = 4 for incorrect words). All errors were phonologically plausible letter substitutions. Given her intact spelling performance with non-words, which reflected spare phonology to orthography conversion, this participant probably relied on sub-lexical mechanisms to spell. This explanation also accommodates impaired performance with real words. The words that have been selected for spelling assessment were highly dependent on the ability to access stored orthographic representations (e.g. ‘αλλιώτικος’, ‘ματαιώνεται’, ‘διευθυντής’). Surface dysgraphia is one of the hallmarks of svPPA. Nevertheless, it is the second most common pattern of spelling impairment in the logopenic variant of PPA (Graham, 2014).

6.3.9 **Participant 33 (PPA group)**

Diagnosis	lvPPA	Years Post Onset	2.5
Gender	female	BDAE Severity	3
Age	54	WAB Fluency	6
Education	12	Frontotemporal Rating Scale	-
MMSE	19	NPI	-
PASS sum of boxes	4	NPI Iimpact	-



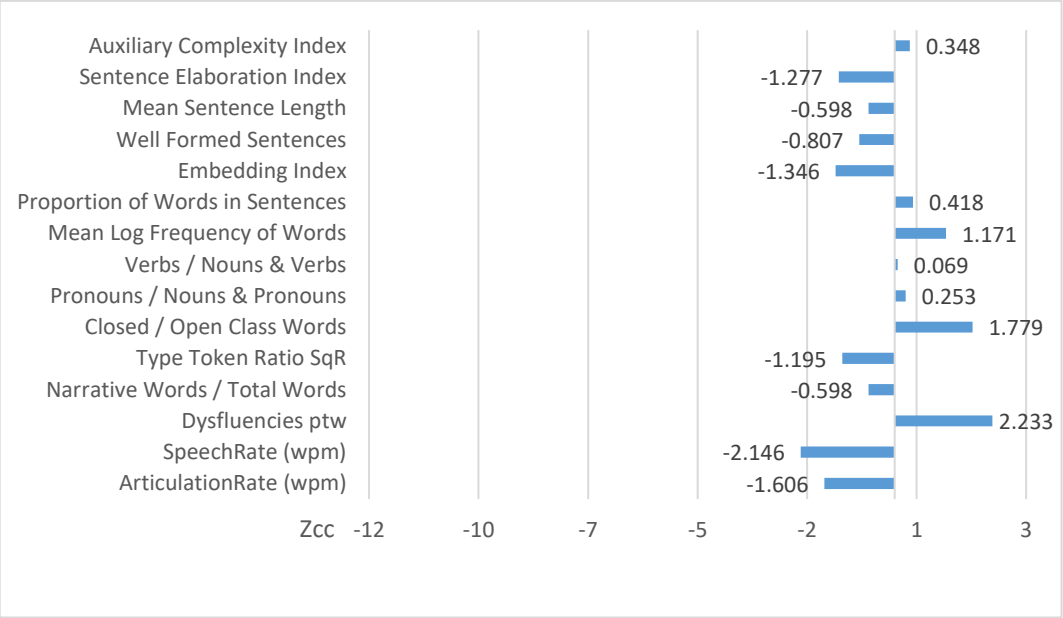


Figure 25: Participant 33: cognitive and narrative discourse profile.

Linguistic testing revealed a naming deficit (t = -2.375, p = .016, z_{cc} = -2.453) and impaired sentence repetition (t = -6.096, p < .001, z_{cc} = -6.296, for the WAB test and t = -27.875, p < .001, z_{cc} = -28.789, for the long frequent sentences from the Bayles repetition test). Single-word comprehension (t = -0.948, p = .18, z_{cc} = -0.98) and object knowledge (t = -0.8, p = .219, z_{cc} = -0.826) were intact.

She made phonological errors both in picture description (t = 3.184, p = .003, z_{cc} = 3.289) and in story retell (t = 2.453, p = .014, z_{cc} = 2.533). She also made semantic errors in the latter task (t = 5.462, p < .001, z_{cc} = 5.641). Her spontaneous speech was characterized by frequent word-finding dysfluencies. She made significantly more silent and filled pauses, as well as false starts than neurotypical controls, as reflected by total dysfluencies in figure 25. In picture description, she produced even more dysfluencies (t = 6.306, p < .001, z_{cc} = 6.513). Nevertheless, motor speech was spared.

Comprehension of commands and syntactically complex structures was impaired (t = -11, p < .001, z_{cc} = -11.361; t = -7.897, p < .001, z_{cc} = -8.156, respectively), but sentence comprehension for complex ideational material was normal (t = -1.046, p = .157, z_{cc} = -1.08).

Reading performance was impaired for real words (t = -2.917, p = .006, z_{cc} = -3.012). Reading fluency for non-words (t = -0.981, p = .172, z_{cc} = -1.013) and spelling was unaffected (t = -1.305, p = .107, z_{cc} = -1.347, for words and t = 0.919, p = .187, z_{cc} = -0.949, for non-words).

Concerning neuropsychological functioning, performance on episodic memory measures with verbal and object stimuli was intact. Visuospatial memory and visuo-constructional abilities were affected, like in previous cases. Moreover, she manifested an executive impairment on the verbal fluency and the trail making tests (see figure 25).

6.3.10 **Participant 34 (PPA group)**

Diagnosis	mixed PPA	Years Post Onset	2
Gender	male	BDAE Severity	4
Age	71	WAB Fluency	9

Education	6	Frontotemporal Rating Scale	90.000
MMSE	22	NPI	6
PASS sum of boxes	6.5	NPI Iimpact	2

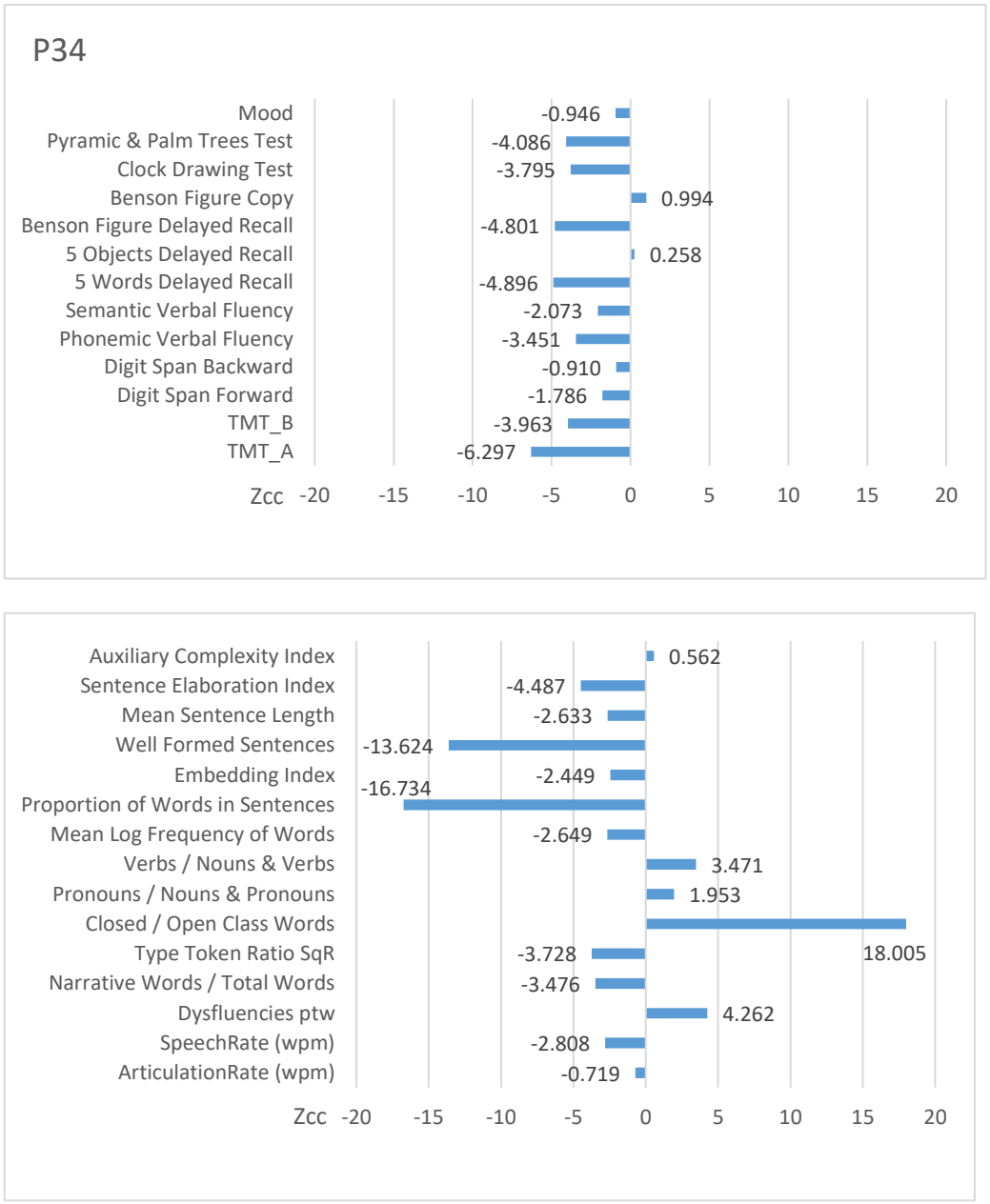


Figure 26: Participant 34: cognitive and narrative discourse profile.

The last participant of the PPA group was diagnosed with mixed PPA. Predominant features were compatible with the diagnosis of logopenic PPA. However, there were additional findings that did fit this diagnostic category.

He had a severe naming deficit (t = -11, p < .001, z_{cc} = -11.361). He also had a severe sentence repetition deficit (t = -15.857, p < .001, z_{cc} = -16.377, for the WAB test and t = -95.375, p < .001, z_{cc} = -98.503, for the long frequent sentences from the Bayles repetition test).

Phonological errors were detected both in picture description (t = 16.062, p < .001, z_{cc} = 16.589) and in story retell (t = 14.815, p < .001, z_{cc} = 15.301) and similarly to the previous participant, he also made semantic errors in the latter task (t = 2.361, p = .017, z_{cc} = 2.439). Lexical selection, discourse and sentence productivity measures were all affected in narrative production (see figure 26). Taken together, connected speech analysis reflected lexical retrieval deficits, as well as difficulty in formulating sentences. However, it should be noted that production of syntactic structures depends on the availability of information at the level of the lexicon (Meteyard et al., 2014). Moreover, on several occasions, this participant had interrupted his utterances and attempted to rephrase his productions. This type of 'retracing', in the presence of impaired working memory, may lead to increased syntactic errors (Wilson et al., 2012).

Comprehension of commands and syntactically complex structures was impaired (t = -11, p < .001, z_{cc} = -11.361; t = -3.666, p = .001, z_{cc} = -3.787, respectively), but sentence comprehension for complex ideational material was normal (t = -1.046, p = .157, z_{cc} = -1.08). A similar pattern of sentence comprehension was also found for the previous participant (P33) who was diagnosed with lvPPA.

He was impaired in single-word comprehension (t = -3.997, p = .001, z_{cc} = -4.128) and object semantics (t = -3.958, p = .001, z_{cc} = -4.086). However, this finding should be interpreted in relation to his educational level; he had completed only 6 years of formal education.

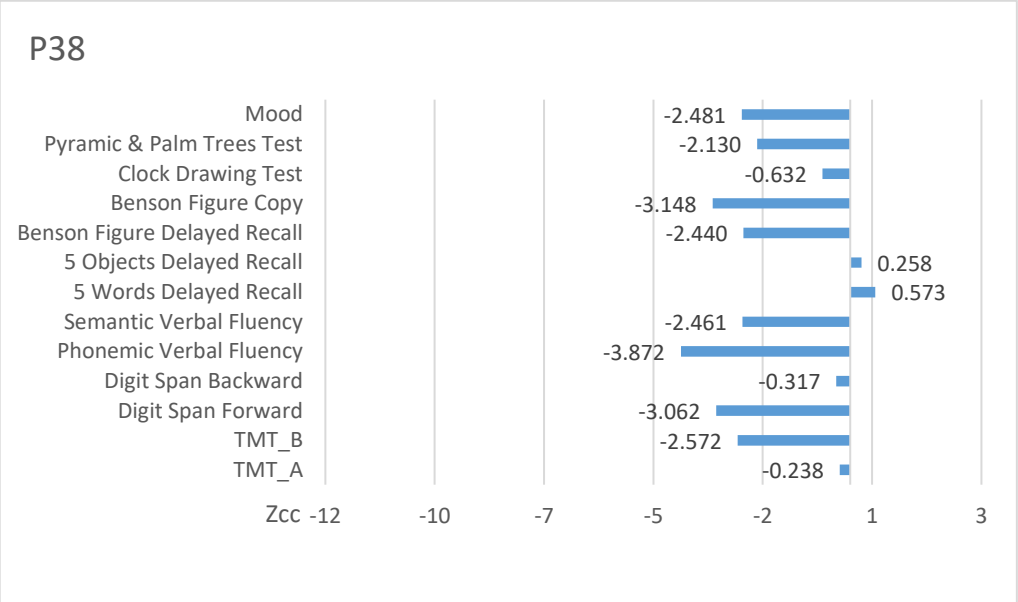
Reading performance was impaired both for real words (t = -4.002, p = .001, z_{cc} = -4.133) and non-words (t = -2.523, p = .012, z_{cc} = -2.606), and his speech and articulation rate during passage reading was slow (t = -2.145, p = .025, z_{cc} = -2.215; t = -3.34, p = .002, z_{cc} = -3.45, respectively), even though his spontaneous articulation rate was much faster (see figure 26). Motor speech evaluation revealed mild dysphonia, normal maximum phonation time (t = 0.987, p = .17, z_{cc} = 1.020) and diadochokinetic rates and no evidence of apraxia of speech.

Spelling was affected only for words (t = -11.405, p < .001, z_{cc} = -11.779), but not for non-words (t = -0.612, p = .275, z_{cc} = -0.632). However, it should be noted that schooling might have contributed to this finding, as all errors were phonologically plausible and correct target-word production depended on orthographic knowledge.

This participant manifested deficits in almost all the cognitive domains that were evaluated. However, language was reported as the only factor that limited daily functioning and participation in activities.

6.3.11 **Participant 38 (FTD-ALS)**

Diagnosis	FTD-ALS	Years Post Onset	3
Gender	male	BDAE Severity	2
Age	41	WAB Fluency	5
Education	16	Frontotemporal Rating Scale	17.857
MMSE	27	NPI	19
Motor Speech Score	5/7	NPI Iimpact	15



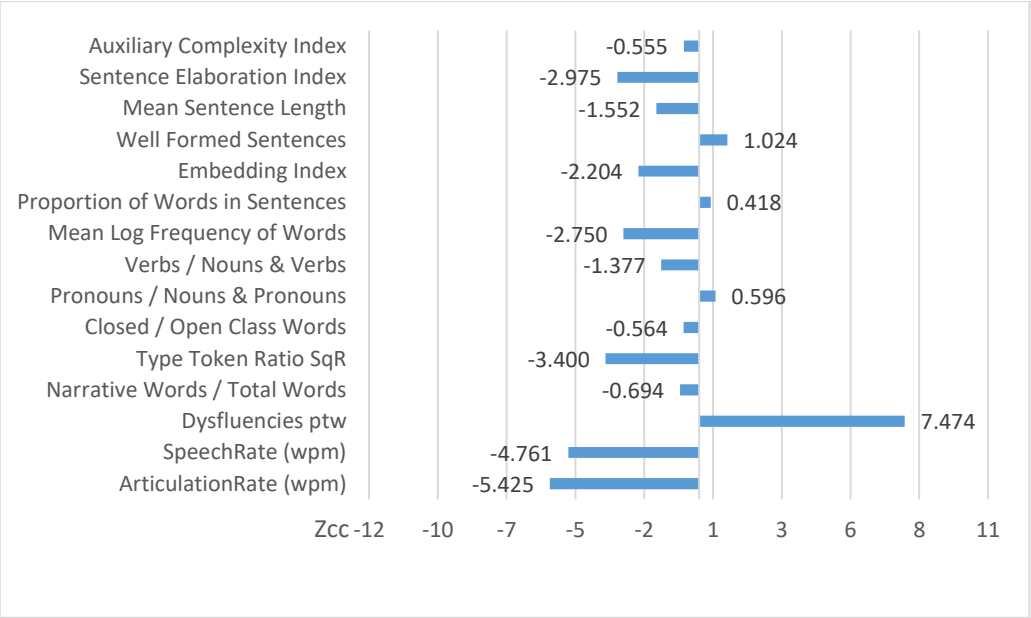


Figure 27: Participant 38: cognitive and narrative discourse profile.

Frontotemporal dementia (FTD) encompasses a group of neurodegenerative dementias which primarily affect behavior (behavioral variant of FTD, bvFTD) and language (nfvPPA and svPPA). These presentations may overlap with movement disorders, such as Amyotrophic lateral sclerosis (ALS), Progressive supranuclear palsy (PSP) and Corticobasal syndrome (CBS).

The first participant of the FTD group was diagnosed with FTD-ALS/MND. The presenting symptom was a behavioral disorder with obsessive and stereotyped behaviors, followed by motor, cognitive and neuropsychiatric symptoms. Motor onset involved the bulbar muscles, resulting in pseudobulbar palsy, dysarthria, and dysphagia. He was evaluated approximately 3 years after disease onset.

His confrontation naming (t = -1.625, p = .063, z_{cc} = - 1.678) and single-word comprehension (t = -0.61, p = .276, z_{cc} = -0.63) were intact. Sentence repetition was relatively preserved (t = -1.473, p = .081, z_{cc} = -1.521 for the WAB test; t = -5.375, p < .001, z_{cc} = -5.561, for the long frequent sentences; but t = -0.638, p = .267, z_{cc} = -0.659 for the long non-meaningful sentences from the Bayles repetition test).

Comprehension of commands was impaired (t = -3.5, p = .002, z_{cc} = -3.615). However, comprehension of complex ideational material and syntactically complex structures was unaffected (t = -0.523, p < .305, z_{cc} = -0.54; t = -1.551, p = .072, z_{cc} = -1.602, respectively).

Reading fluency for words and non-words was affected by his slow speech/articulation rate. Nevertheless, he read correctly all target words. His articulation rate during passage reading was significantly slower than controls' rate (t = -10.559, p < .001, z_{cc} = -10.905) and slower than his rate in discourse production (see figure 27).

Spelling was impaired for real words (t = -3.830, p = .001, z_{cc} = -3.955), but spared for non-words (t = -0.612, p = .275, z_{cc} = -0.632).

Regarding neuropsychological functioning (see figure 27), episodic memory was intact. Visuospatial functioning was affected, but delayed copy recall was better than immediate copy. There was a mild deficit in object semantics (t = -2.062, p = .029, z_{cc} = -2.13) and short-term memory. Finally, he manifested an executive impairment. His performance in letter fluency was worse than in category fluency, a typical finding in ALS with cognitive involvement (Strong et al., 2017).

Conclusively, the main domains that were affected in this case of FTD-ALS included behavior, movement, and executive functioning. Even though speech and language deficits were not predominant at disease onset nor at the time of assessment, one year after his initial cognitive-linguistic evaluation, this participant became completely unintelligible and was relying on text messages to communicate.

6.3.12 **Participant 39 (PSP)**

Diagnosis	PSP	Years Post Onset	1.5
Gender	female	BDAE Severity	3
Age	75	WAB_Fluency	6
Education	16	Frontotemporal Rating Scale	21.111
MMSE	27	NPI	16
Motor Speech Score	6/7	NPI Iimpact	-

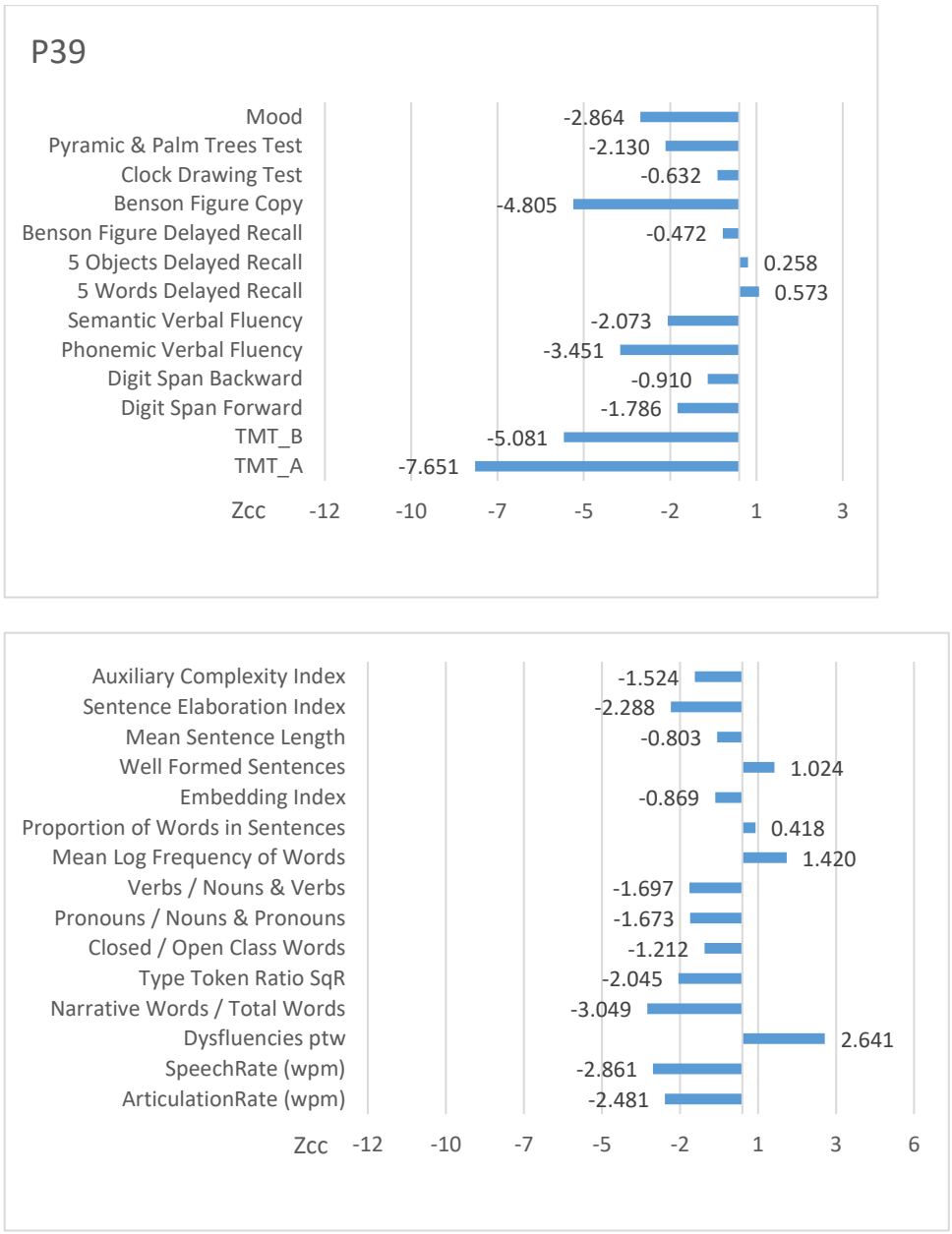


Figure 28: Participant 39: cognitive and narrative discourse profile.

This participant exhibited typical motor symptoms of PSP: bradykinesia, supranuclear gaze palsy (impaired vertical ocular movement), mixed spastic-hypokinetic dysarthria, dysphagia as well as neuropsychiatric symptoms (apathy and depression).

Linguistic assessment revealed a naming deficit (t = -5, p < .001, z_{cc} = -5.164) and impaired comprehension of commands and syntactically complex sentences (t = -3.5, p = .002, z_{cc} = -3.615; t = -3.666, p = .001, z_{cc} = -3.787, respectively). However, comprehension of complex ideational material was unaffected (t = -0.523, p < .305, z_{cc} = -0.54). Her performance on the word comprehension task (t = -1.287, p = .109, z_{cc} = -

1.329) and the sentence repetition test from WAB (t = -0.959, p = .177, z_{cc} = -0.99) was within normal limits. She manifested a difficulty repeating the long frequent sentences from the Bayles repetition test (t = -5.375, p < .001, z_{cc} = -5.561). A mild deficit was also detected in object semantics (t = -2.062, p = .029, z_{cc} = -2.13).

Phonological errors were found in picture description (t = 8.568, p < .001, z_{cc} = 8.849) and semantic errors in story retell (t = 3.885, p = .001, z_{cc} = 4.012). In discourse, she produced relatively simple sentences and used a limited number (and range) of words (see figure 39).

Reading performance was impaired for real words (t = - 6.390, p < .001, z_{cc} = -6.6) and non-words (t = -4.205, p <.001, z_{cc} = -4.343). It should be noted however, that reading fluency was affected by dysarthria and visual scanning deficits. Spelling was better for words than non-words (t = -0.673, p = .256, z_{cc} = -0.695; t = -3.674, p = .001, z_{cc} = -3.795, respectively). This spelling pattern has been frequently reported in nfvPPA (Graham, 2014; Neophytou et al., 2019).

With respect to neuropsychological functioning, episodic and working memory was spared (see figure 28). Processing speed and executive functions were impaired. Letter fluency was worse than category fluency. Severe letter fluency and moderate category fluency deficits are typically detected in PSP and CBS (Peterson et al., 2019). Visuospatial construction (figure copy) was affected, but delayed figure recall was intact.

The latest Movement Disorders Society PSP criteria (Höglinger et al., 2017) include a clinical phenotype that presents with the distinctive features of nfvPPA before the appearance of motor symptoms. Participant P39 seems to fall into the PSP-Richardson's syndrome phenotype which is the typical syndrome of PSP that was originally described as a movement disorder (Boxer et al., 2017).

6.3.13 **Participant 40 (CBS)**

Diagnosis	CBS	Years Post Onset	3
Gender	female	BDAE Severity	4
Age	64	WAB_Fluency	9

Education	8	Frontotemporal Rating Scale	85.714
MMSE	27	NPI	41
Motor Speech Score	7/7	NPI Iimpact	20

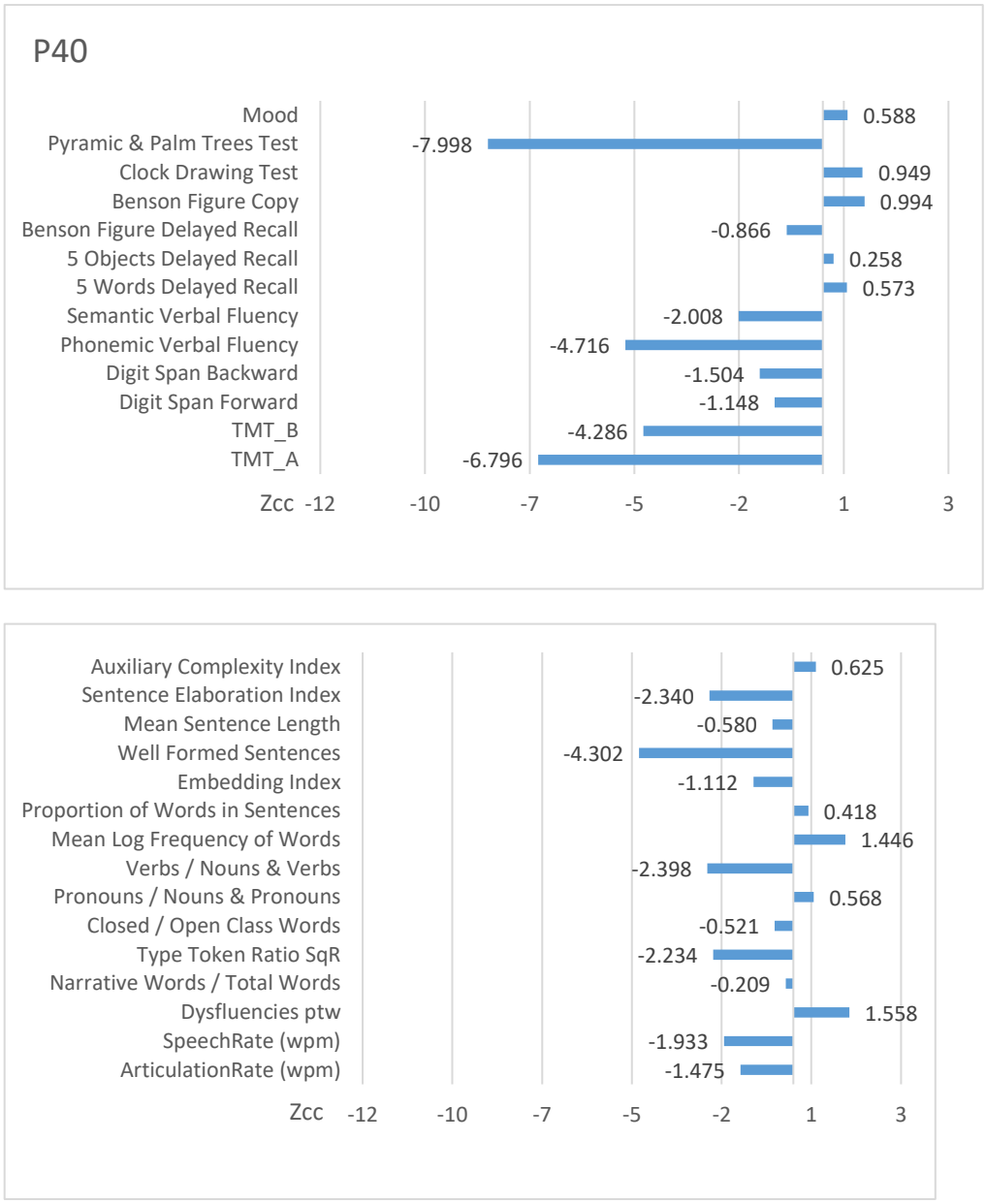


Figure 29: Participant 40: cognitive and narrative discourse profile.

This participant was diagnosed with CBS. She presented with behavioral and motor symptoms (asymmetrical rigidity, bradykinesia, and alien limb). Her speech was dysarthric, characterized by slow rate, prolonged duration of phonemes and limited pitch and loudness variation.

Language assessment revealed a naming (t = -3.875, p = .001, z_{cc} = -4.002), word comprehension (t = -2.981, p = .005, z_{cc} = -3.078) and object semantics deficit (t = -7.744, p < .001, z_{cc} = -7.998). Comprehension of complex ideational material and syntactically complex structures was impaired (t = -4.183, p < .001, z_{cc} = -4.32; t = -3.666, p = .001, z_{cc} = -3.787, respectively). However, comprehension of commands was intact (t = 0.25, p = .403, z_{cc} = 0.258). Phonological and semantic errors were detected both in picture description (t = 4.411, p < .001, z_{cc} = 4.555; t = 3.571, p < .001, z_{cc} = 14.017) and in story retell (t = 4.042, p = .001, z_{cc} = 4.175; t = 2.529, p = .012, z_{cc} = 2.612).

Word comprehension deficits have been reported in CBS, but reports about sentence processing difficulties, phonological and semantic errors are more consistent (Peterson et al., 2019).

Sentence repetition was intact on the WAB repetition test (t = -0.445, p = .331, z_{cc} = -0.46) and all conditions of the Bayles repetition test but the long frequent sentences (t = -3.5, p = .002, z_{cc} = -3.615). Reading performance was impaired both for real words (t = -2.808, p = .007, z_{cc} = -2.9) and non-words (t = -3.084, p = .004, z_{cc} = -3.185). Spelling was better for non-words than real words (t = -0.612, p = .275, z_{cc} = -0.0.632; t = -2.567, p =.011, z_{cc} = -2.651, respectively).

Narrative measures (see figure 29) suggested lexical retrieval deficits, especially for verbs (low proportion of verbs relative to nouns and verbs), simplified sentences and syntactic errors, even though determiners and inflected forms were used correctly. A selective action/verb impairment has been described in cases of CBS and linked to the movement impairment (Silveri & Ciccarelli, 2007)

Cognitive symptoms including memory, executive functioning and visuospatial abilities are common in persons with CBS (Peterson et al., 2019). In this case, memory and visuospatial abilities were preserved. However, an executive deficit was documented on verbal fluency tasks. Phonemic fluency was disproportionally affected in comparison to semantic fluency.

Clinical phenotypes of CBS with non-fluent, agrammatic features, as well as with frontal behavioral features have been proposed among other phenotypes (Armstrong et al., 2013) reflecting shared pathology with nfvPPA and bvPPA. On several occasions,

diagnostic categorization depends on decisions about which features are more salient. Moreover, motor, behavioral and language features change over time. The question as to whether a diagnostic label should change or be complemented by a second one remains open (Murley et al., 2019).

6.4 Conclusions

Inspection of individual profiles in individuals with PPA revealed heterogeneity in cognitive function, linguistic and narrative discourse abilities. Non-language cognitive deficits are common in lvPPA affecting performance on language testing (Owens et al., 2018). Kamath et al in a meta-analysis of neuropsychological function in lvPPA have found that dyscalculia, attention and executive deficits were as prominent as language deficits (Kamath et al., 2020). Neuropsychiatric symptoms were reported for lvPPA participants, but to a lesser extent than for FTD participants, with svPPA, FTD-ALS, PSP and CBS.

Neuropsychological evaluation revealed mild to moderate memory and executive impairment for both svPPA participants but spared visuospatial functioning. Regarding linguistic abilities, they were more impaired in naming, single-word comprehension, and semantic knowledge. Word-finding difficulties were the principal cause of communication impairment.

Participants with a prominent movement disorder, have manifested impairment on language assessment. Non-motor symptoms, especially language deficits, were until recently underestimated in conditions such as PSP, CBS, and FTD-ALS. However, language involvement has been increasingly recognized and considered in revised clinical diagnostic criteria (Gazzina et al., 2019; Strong et al., 2017).

Clinical evaluation of neurodegenerative diseases should include neuropsychological assessment targeting different cognitive domains, including language, behavior, neuropsychiatric symptoms, and daily functioning, in order to assist differential diagnosis and subtyping. Clinical presentations and pathologies overlap and information from multiple sources (e.g. patient and caregiver reports, clinical assessment, neuroimaging, biomarkers) and specializations (e.g. neurologists, neuropsychologists, speech and language therapists/pathologists, etc.) is needed to reach an accurate

diagnosis. This step is essential for managing symptoms and planning therapeutic strategies.

7 Study 4. A case-series study of disease progression: how do cognitive-linguistic profiles of individuals with PPA change in one year as the disease evolves?

7.1 Introduction

One of the first studies on the pattern of decline in PPA has documented substantial progression of clinical deficits and cortical atrophy in an interval of 2 years (Rogalski et al., 2011). Brambati et al reported different patterns of neuroanatomical contraction and clinical progression in nfvPPA, svPPA and lvPPA over 1 year following diagnosis (Brambati et al., 2015). Atrophy progression involved lateral/posterior temporal and medial parietal regions in lvPPA and the medial and lateral temporal lobe in svPPA. Individuals with svPPA presented decline in semantic memory abilities, whereas individuals with lvPPA decline in memory, sentence repetition and calculations.

Ash et al. investigated decline in connected speech production and language over a period of 18 months in the 3 variants of PPA and the behavioral variant of FTD (bvFTD) (Ash et al., 2019). Individuals with svPPA manifested a decline in sentence complexity and individuals with lvPPA in fluency and grammaticality of utterances (Ash et al., 2019). Interestingly, they found that decline in language performance did not correlate with change in neuropsychological functioning.

In general, a more rapid and generalized cognitive decline has been found in lvPPA in comparison to svPPA (Hsieh et al., 2012; Macoir et al., 2017). It has been suggested that individuals with lvPPA follow the pattern of AD, with language and episodic memory impairment, whereas behavioral dysfunction in individuals with svPPA simulates deficits found in bvFTD (Harciarek et al., 2014).

Studies concerning the course of PPA in the later stages are limited.

The reported rates of clinical decline in PPA suggest that a clinician should not only be informed about the presenting features of the disease, but also about the evolution of these features and the additional features that may develop with disease progression.

In the previous study (study 3), the cognitive-linguistic profiles of Greek-speaking PPA participants in relatively ‘early’ stages of the disease were documented. In this study,

results from two consecutive assessments, one year apart, are compared for 4 PPA participants: 2 with lvPPA, one with svPPA and one with unclassified-anomic PPA. The aim of the study was to gain an insight of how performance on the neuropsychological battery and narrative discourse abilities can change in the course of one year.

We hypothesized that the 2 participants with lvPPA will show a greater and more generalized decline than the participant with svPPA and the participant with progressive anomia.

Single assessment data for 3 additional individuals with PPA are also reported. These participants were not included in previous studies for methodological reasons (i.e. presence of moderate deficits). However, inclusion of their assessment results can be informative, and strengthen the discussion about disease progression.

7.2 Method

7.2.1 Participants

Four individuals with PPA participated in the study. All four (P25, P26, P27 and P28) were included in the previous studies. They were re-assessed one year after their baseline assessment. P25 and P26 were diagnosed with lvPPA, P27 with svPPA and P28 with anomic PPA, or a probable prodromal phase of svPPA (see previous study for details). Their first assessment results were analyzed in the previous studies, apart from P28; his second set of results was included in previous data analyses.

Three additional participants, at a later stage of PPA, were included in this study (see table 12). They were assessed only once.

Table 12: Demographic information and neuropsychological status of moderately impaired participants with PPA.

Participants	P35	P36	P37
Gender	male	female	male
Age	59	58	72
Education	6	12	12
Years post onset	2	5	4

Boston Diagnostic Aphasia Examination (BDAE) severity	2	2	1
Progressive Aphasia Severity Scale (PASS) (sum of boxes)	10	8	13.5
Frontotemporal Rating Scale	51.73	36	36
Nneuropsychiatric Inventory (NPI)	0	8	3
NPI impact	0	9	3
Mini Mental State Examination (MMSE)	11	12	10

The control group consisted of 15 neurotypical individuals (mean age 67.93, *SD* = 6.17, mean years of education 13.13, *SD* = 3.482).

Additional information about the control group and PPA participants can be found in the general methodology section (chapter 3) and study 3 (chapter 6), respectively.

7.2.2 Procedure

Participants were evaluated using the same comprehensive battery of tests at baseline and one year after their initial evaluation. The 3 participants with more advanced PPA were evaluated once using the same tests. Details about recruitment, assessment and obtaining informed consent are described in detail in chapter 3.

7.2.3 Statistical analysis

Each participant was compared to the control group at two time points, one year apart, using Crawford and Howell's method (Crawford & Howell, 1998) which enables the comparison of performance of a single participant with that of a small control sample. *T* values and effect sizes (z_{cc}), for case-control designs, have been computed (Crawford & Garthwaite, 2012). Effect sizes were used to evaluate change in performance. Descriptive statistics are reported for differences in effect size.

7.3 Results

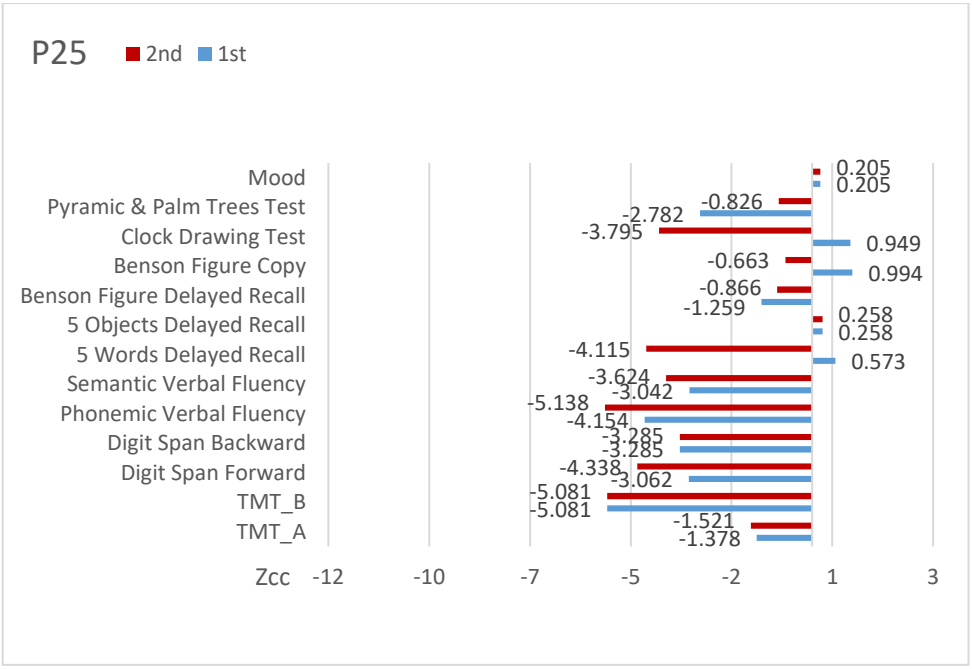
7.3.1 Participant 25

Assessment	1st	2nd		1st	2nd

Diagnosis	lvPPA		Years Post Onset	2	3
Gender	female		BDAE Severity	2	1
Age	60	61	WAB Fluency	7	7
Education	12		Frontotemporal Rating Scale	63.333	-
MMSE	22	6	NPI	5	-
PASS sum of boxes	7	12	NPI Iimpact	4	-

Mean z difference for cognitive measures was -0.902 (*SD* = 1.906). Further deterioration was detected on the Clock drawing test, the 5-Words test, whereas performance was better on the Pyramid and Palm Trees test, results were within normal limits on the second assessment (t = -0.8, p = .219, z_{cc} = -0.826). Concerning linguistic testing, mean difference of effect sizes between the two assessment results was -4.241, with *SD* = 11.436. Spelling of non-words, reading passage speech and articulation rate and comprehension of syntactically complex structures were more affected. The domain which showed the greatest decline was sentence repetition (the difference in effect sizes was -15.386 for WAB and -40.666 for the long frequent sentences from the Bayles Sentence repetition test). For discourse summary measures, mean difference was -0.099 (*SD* = 2.529). However, she was more impaired in lexical selection measures, as indicated by differences in the proportion of closed class words, verbs and pronouns she used in the story retell task and sentence productivity, as indicated by sentence elaboration index. She also used simpler morphological forms (z difference for auxiliary complexity index was -6.31).

Conclusively, this participant manifested further decline in memory, repetition, writing, word retrieval and grammatical productivity.


P25
2nd
1st
Mood
Pyramic & Palm Trees Test
Clock Drawing Test
Benson Figure Copy
Benson Figure Delayed Recall
5 Objects Delayed Recall
5 Words Delayed Recall
Semantic Verbal Fluency
Phonemic Verbal Fluency
Digit Span Backward
Digit Span Forward
TMT_B
TMT_A
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-2.782
-3.795
0.949
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0.994
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-4.115
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-3.624
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-5.138
-4.154
-3.285
-3.285
-4.338
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1
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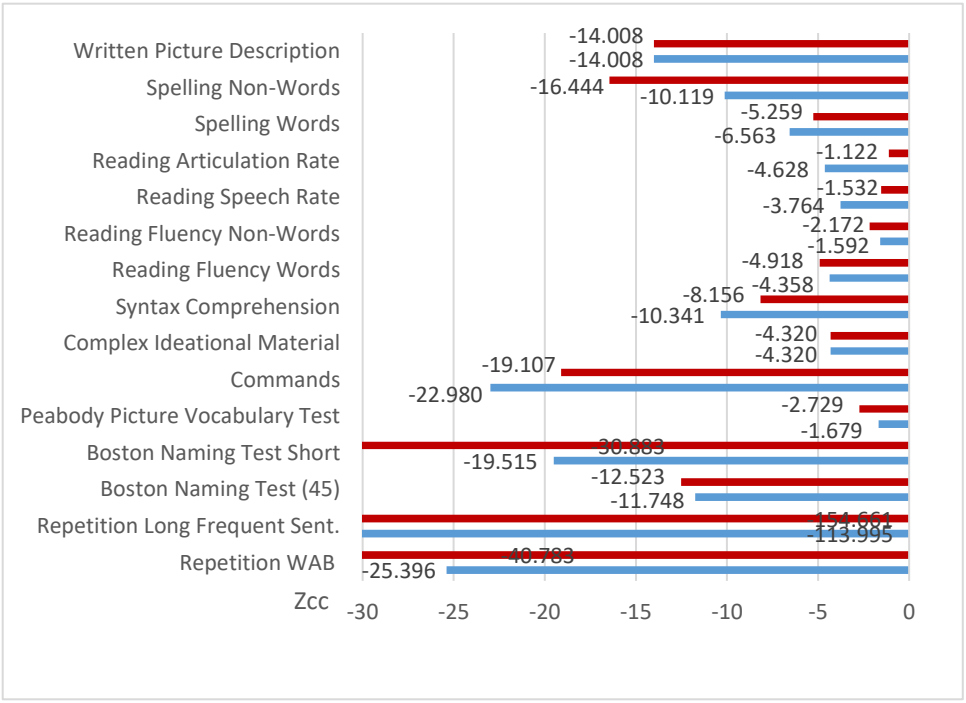
Written Picture Description
Spelling Non-Words
Spelling Words
Reading Articulation Rate
Reading Speech Rate
Reading Fluency Non-Words
Reading Fluency Words
Syntax Comprehension
Complex Ideational Material
Commands
Peabody Picture Vocabulary Test
Boston Naming Test Short
Boston Naming Test (45)
Repetition Long Frequent Sent.
Repetition WAB
Zcc
-14.008
-14.008
-16.444
-10.119
-5.259
-6.563
-1.122
-4.628
-1.532
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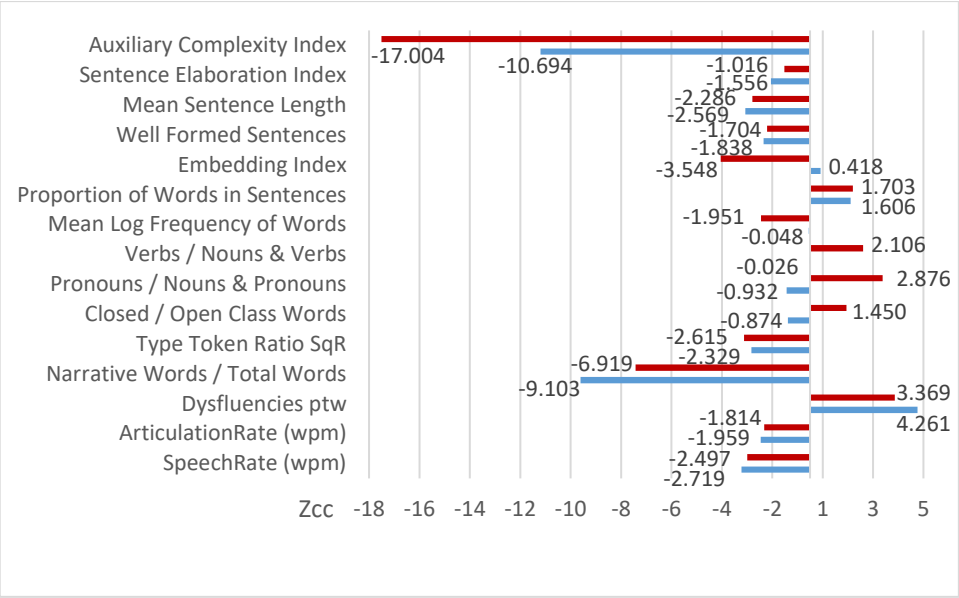


Figure 30: Participant 25: changes in cognitive, linguistic and discourse abilities in 1 year.

7.3.2 **Participant 26**

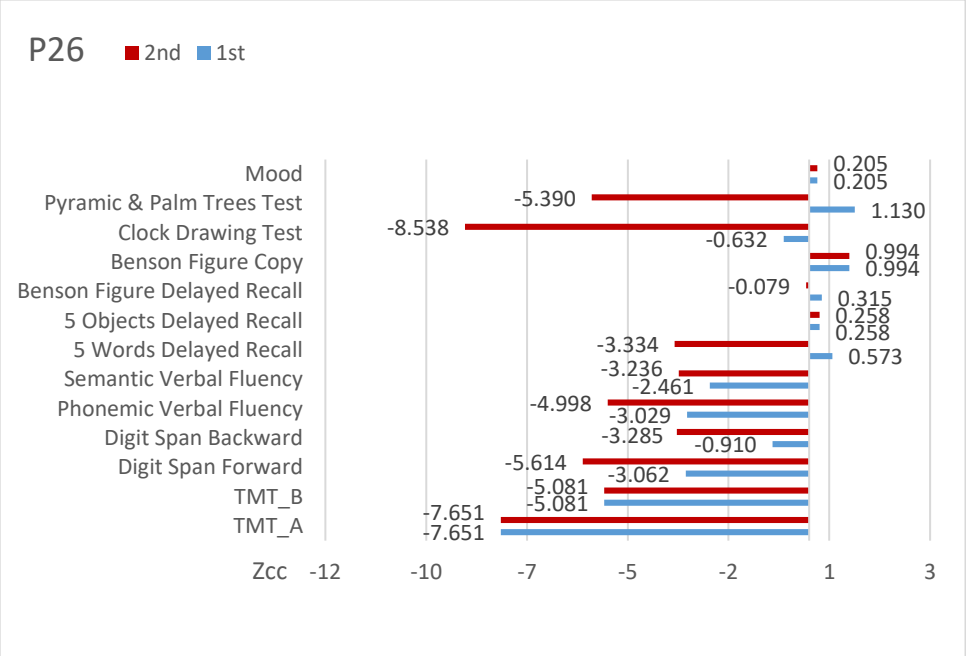
Assessment	1st	2nd		1st	2nd
Diagnosis	lvPPA		Years Post Onset	2	3
Gender	female		BDAE Severity	2	1
Age	61	62	WAB Fluency	5	4
Education	12		Frontotemporal Rating Scale	93.33	63.3
MMSE	26	9	NPI	4	27
PASS sum of boxes	6	14	NPI Iimpact	2	22

For this participant, mean difference between baseline and follow-up assessment in z scores for cognitive measures was -2.031 (*SD* = 2.637), for linguistic measures -7.593 (*SD* = 21.479) and discourse summary measures -2.259 (*SD* = 5.987).

Further deterioration was detected on the 5-Words test, the Digit span test, the Clock drawing test and the Pyramid and palm trees test. With respect to language measures,

greatest decline was found for repetition (the difference in effect sizes was -13.795 for WAB and -83.269 for the long frequent sentences from the Bayles Sentence repetition test), as well as writing (difference in effect sizes for written picture description was -12.076). Naming, reading and comprehension of syntactically complex structures were also more affected (difference in effect size z >2). Single word comprehension had improved (as it has been discussed in study 3). Several discourse measures were more affected in follow-up assessment. The greatest differences concerned embedding index, auxiliary complexity index, proportion of narrative to total words, proportion of words in sentences, type token ratio and number of dysfluencies. These results reflect increased difficulty in word retrieval and sentence formation.

Memory, executive functioning, repetition, and writing are the areas that seem to show a further decline in this participant with lvPPA.



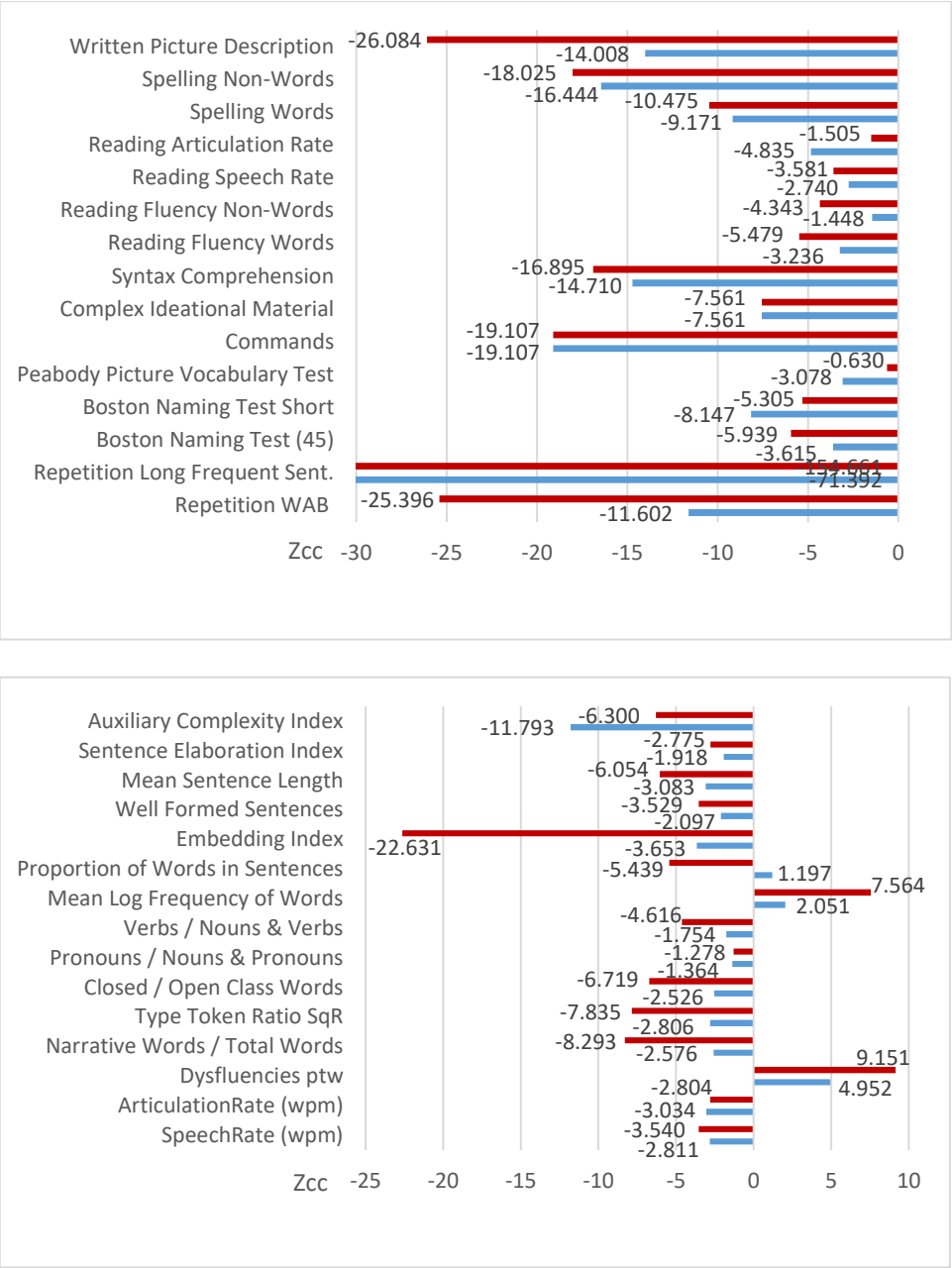


Figure 31: Participant 26: changes in cognitive, linguistic and discourse abilities in 1 year.

7.3.3 **Participant 27**

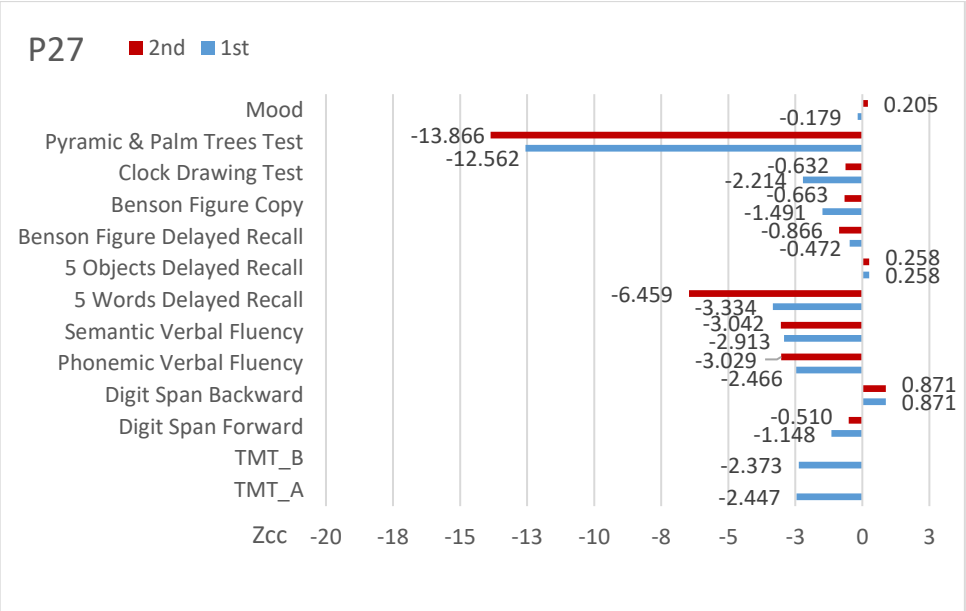
Assessment	1st	2nd		1st	2nd
Diagnosis	svPPA		Years Post Onset	4	5
Gender	male		BDAE Severity	4	4

Age	72	73	WAB Fluency	8	8
Education	9		Frontotemporal Rating Scale	-	36
MMSE	27	27	NPI	-	25
PASS sum of boxes	4	4.5	NPI Iimpact	-	13

Mean difference of z scores between baseline and follow-up assessment for cognitive measures was -0.189 (*SD* = 1.237), for linguistic measures -0.742 (*SD* = 1.827) and discourse summary measures -0.034 (*SD* = 1.988).

The only cognitive domain that showed further decline in this participant with svPPA was episodic memory. The difference in effect sizes for performance on the 5-Words test was -3.125). Concerning language, he performed better (15/32 in comparison to 5/32) on the Peabody picture vocabulary test, although his score was still significantly different from the control group (t = -4.676, p < .001, z = -4.828). Reading and writing showed a further deterioration, with a difference in effect sizes of -2.461 for non-word reading fluency and -4.830 for written picture description. With respect to discourse production, greater differences of effect sizes were found for lexical selection measures (-3.533 for Type token ratio, 3.055 for proportion of pronouns, 2.843 for proportion of verbs), as well as for auxiliary complexity index (-4.306).

Taken together, these results suggest further decline in memory, reading, writing and word retrieval, although differences for this participant were more confined than for the previous participants.


P27
2nd
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Mood
Pyramic & Palm Trees Test
Clock Drawing Test
Benson Figure Copy
Benson Figure Delayed Recall
5 Objects Delayed Recall
5 Words Delayed Recall
Semantic Verbal Fluency
Phonemic Verbal Fluency
Digit Span Backward
Digit Span Forward
TMT_B
TMT_A
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-0.179
-13.866
-12.562
-0.632
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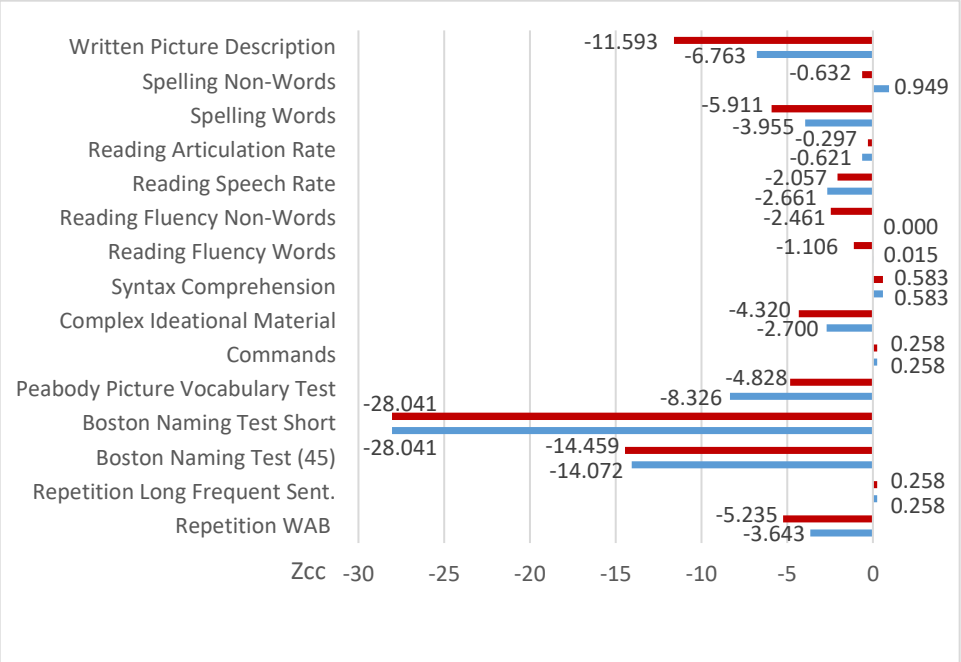
3


Written Picture Description
Spelling Non-Words
Spelling Words
Reading Articulation Rate
Reading Speech Rate
Reading Fluency Non-Words
Reading Fluency Words
Syntax Comprehension
Complex Ideational Material
Commands
Peabody Picture Vocabulary Test
Boston Naming Test Short
Boston Naming Test (45)
Repetition Long Frequent Sent.
Repetition WAB
-11.593
-6.763
-0.632
0.949
-5.911
-3.955
-0.297
-0.621
-2.057
-2.661
-2.461
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-1.106
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-28.041
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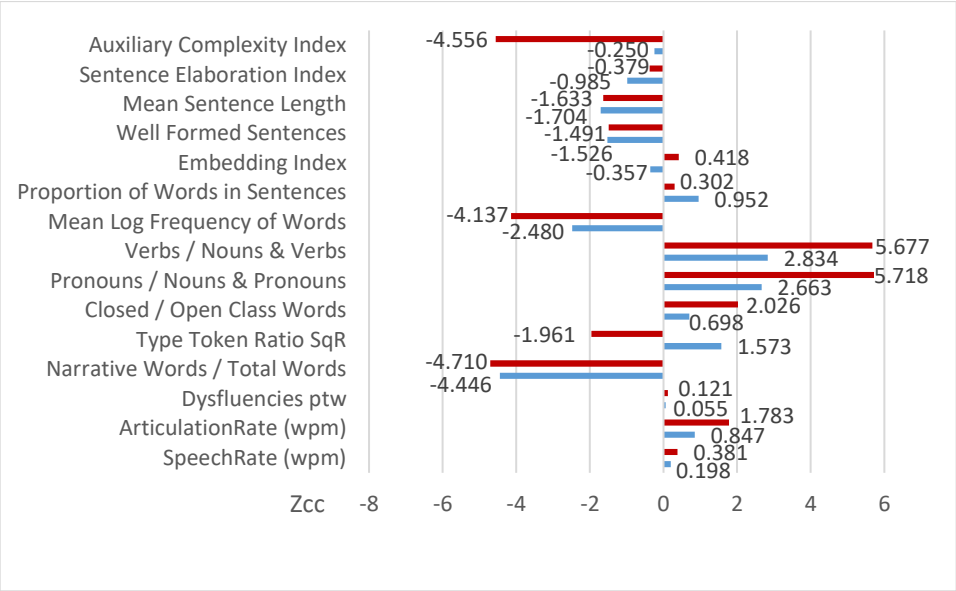


Figure 32: Participant 27: changes in cognitive, linguistic, and discourse abilities in 1 year.

7.3.4 **Participant 28**

Assessment	1st	2nd		1st	2nd
Diagnosis	Anomic PPA		Years Post Onset	1	2
Gender	male		BDAE Severity	5	4
Age	67	68	WAB Fluency	10	9
Education	16		Frontotemporal Rating Scale	-	92.59
MMSE	27	29	NPI	-	4
PASS sum of boxes	0.5	1.5	NPI Iimpact	-	2

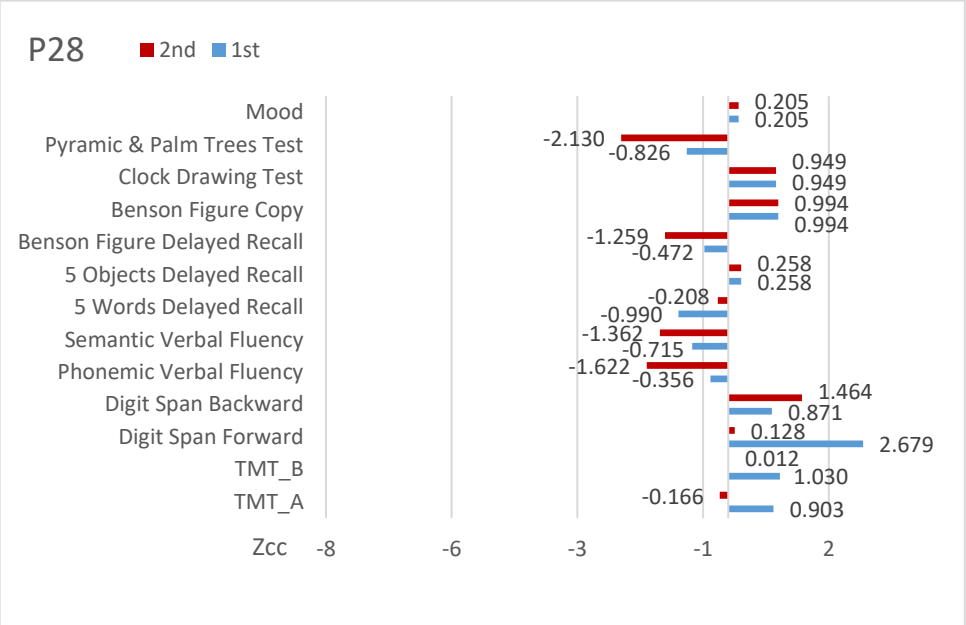
Mean difference of z scores between baseline and follow-up assessment for cognitive measures was -0.559 (*SD* = 0.91), for linguistic measures -0.725 (*SD* = 1.615) and discourse summary measures -0.025 (*SD* = 1.94).

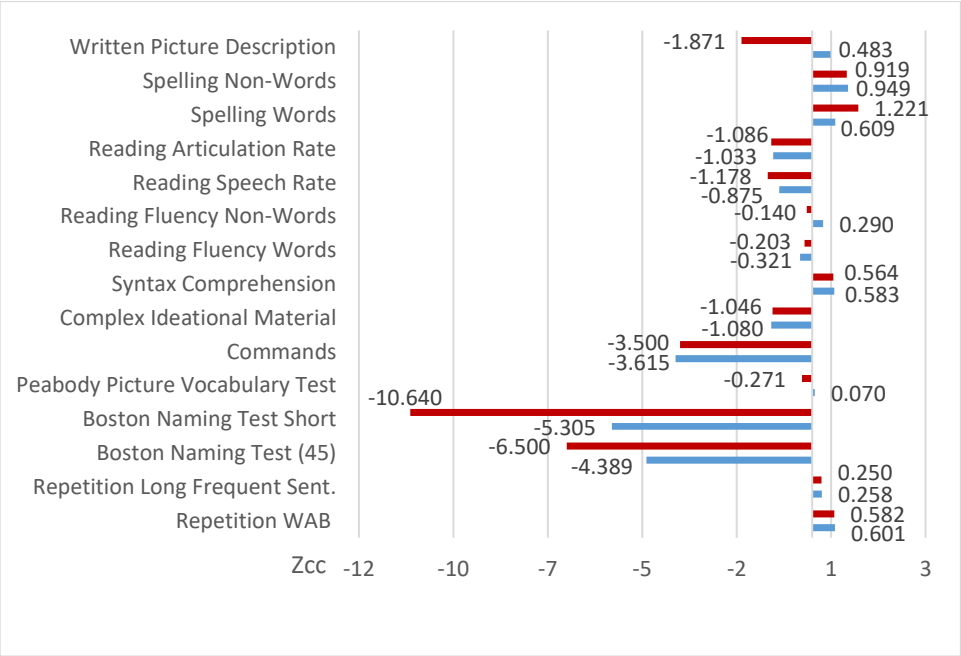
Performance on cognitive measures at the follow-up assessment revealed a mild deficit in object semantics (t =-2.062, p = .029, z_{cc} = -2.130). The difference in effect sizes for

performance on the Pyramid and Palm trees test was -1.304. There was a difference of -2.552 in effect size for the forward Digit Span test, but his score was still above the control group mean (t = 0.124, p = .452, z_{cc} = 0.128). Concerning linguistic testing, the domains that showed the greater change was naming and writing, with a difference in effect sizes of -2.324 for BNT and -2.415 for written picture description. Performance in the latter test was just below normal limits (t = -1.871, p = .041, z_{cc} = -1.932).

Regarding discourse production, performance was similar on the two assessment. There was a difference of -3.625 in effect sizes for embedding index. The auxiliary complexity index was found to be greater in follow-up (effect size difference = 5.51).

Conclusively, memory, executive and visuospatial functioning seem to remain intact in this case. The only domains that have shown a decline are naming and object semantics.





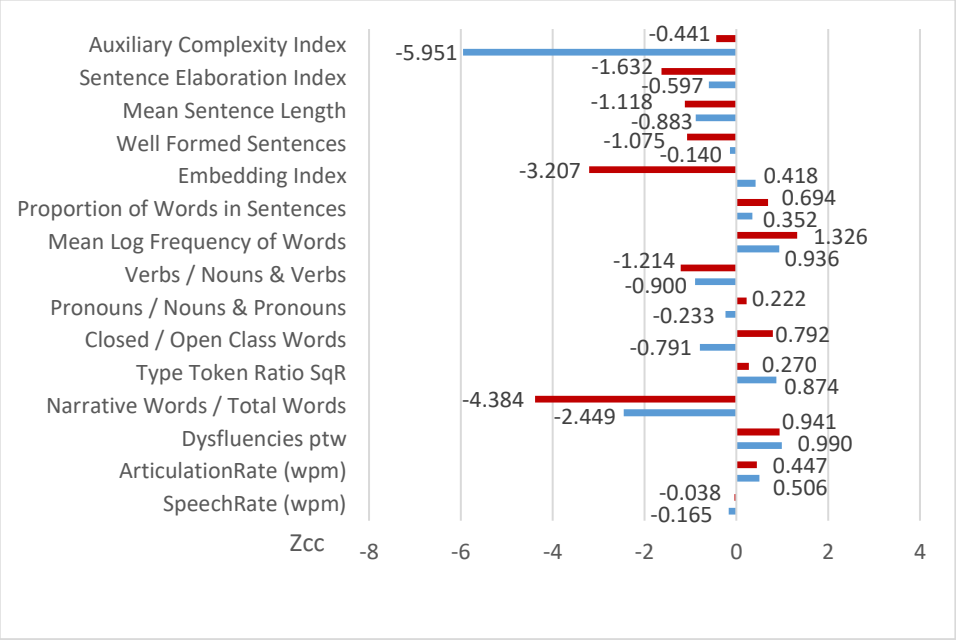


Figure 33: Participant 28: changes in cognitive, linguistic and discourse abilities in 1 year.

7.3.5 **Participants P35, P36, P37**

Results for participant P35, P36, P37 are presented in table 13. Participant P37 had limited spontaneous speech. He was able to read words and paragraphs. His articulation rate for passage reading was normal (t = -0.379, p = .355, z_{cc} = -0.392), but speech rate, on the same task, was slower than control participants' (t = -3.239, p = .003, z_{cc} = -3.345) indicating difficulty in reading. He produced only 3 words in story recall, even

though he correctly answered all relevant questions (MAIN comprehension score = 10/10). Maximum phonation time and diadochokinetic rates for /pa/, /ta/, /ka/ and /pataka/, were within normal limits (t = -0.985, p = .171, z_{cc} = -1.017; t = -1.516, p = .076, z_{cc} = -1.565; t = -1.304, p = .107, z_{cc} = -1.347; t = -1.061, p = .153, z_{cc} = -1.096, respectively).

Table 13: Cognitive-linguistic functioning and discourse production of moderately impaired participants with PPA.

Test/Measure /Max. Score	Score	*t*	*p*	z_{cc}	Score	*t*	*p*	z_{cc}	Score	*t*	*p*	z_{cc}
TMT_A /180	0	-7.41	0.00	-7.65	0	-7.41	0.00	-7.65	0	-7.41	0.00	-7.65
TMT_B /300	0	-4.92	0.00	-5.08	0	-4.92	0.00	-5.08	0	-4.92	0.00	-5.08
5-Words Del. Recall /10	0	-7.01	0.00	-7.24	0	-7.01	0.00	-7.24	0	-7.01	0.00	-7.24
5 Objects Del. Recall /5	2	-11.0	0.00	-11.36	0	-18.50	0.00	-19.11	5	0.25	0.40	0.26
Benson Figure Del. Recall /17	2	-4.27	0.00	-4.41	0	-5.03	0.00	-5.19	-			
Benson Figure Copy /17	4	-9.46	0.00	-9.78	3	-10.27	0.00	-10.60	-			
PPTT /52	37	-8.38	0.00	-8.65	40	-6.48	0.00	-6.69	-			
Mood /15	15	0.57	0.29	0.59	12	-0.54	0.30	-0.56	8	-2.03	0.03	-2.10
Repetition WAB /100	73	-13.29	0.00	-13.72	86	-6.61	0.00	-6.83	82	-8.66	0.00	-8.95
BNT /45	14	-10.25	0.00	-10.59	24	-6.50	0.00	-6.71	-			
BNT /15									3	-32.65	-33.72	0.00
PPVT /32	18	-3.66	0.00	-3.78	18	-3.66	0.00	-3.78	22	-2.30	0.02	-2.38
BDAE Syntax /10	2	-16.36	0.00	-16.89	1	-18.47	0.00	-19.08	8	-3.67	0.00	-3.79

Read Fluency Words	31	-5.52	0.00	-5.70	31	-5.52	0.00	-5.70	-			
Read Fluency Non-Words	11	-4.35	0.00	-4.49	22	-2.80	0.01	-2.90	-			
Spelling Words /20	1	-10.77	0.00	-11.13	8	-6.36	0.00	-6.56	2	-10.14	0.00	-10.48
Spelling Non-Words /12	3	-12.86	0.00	-13.28	3	-12.86	0.00	-13.28	0	-17.45	0.00	-18.02
Phonological Errors ptw	0.05	16.34	0.00	16.87	0.02	7.81	0.00	8.06				
ArticulationRate (wpm)	133.78	-1.40	0.09	-1.45	163.65	-0.38	0.36	-0.39				
SpeechRate (wpm)	45.49	-3.44	0.00	-3.55	50.61	-3.24	0.00	-3.34				
Dysfluencies ptw	0.42	4.57	0.00	4.72	0.45	4.96	0.00	5.12				
Narrative / Total Words	0.66	-2.72	0.01	-2.81	0.69	-2.43	0.01	-2.51				
Embedding Index	0.04	-2.49	0.01	-2.58	0.00	-2.69	0.01	-2.78				
Well Formed Sentences	0.78	-5.17	0.00	-5.34	0.5	-13.19	0.00	-13.62				
Mean Sent. Length	4.3	-2.46	0.01	-2.54	4.5	-2.36	0.02	-2.44				
Elaboration Index	0.73	-4.36	0.00	-4.51	0.5	-5.08	0.00	-5.24				
Auxiliary Complexity Index	1.17	-0.68	0.25	-0.70	1.5	0.18	0.43	0.18				

These results indicate decline in all cognitive and linguistic domains. Performance reflects the pattern of impairment observed in lvPPA with more severe deficits in

sentence repetition and word retrieval, but subtyping in later stages is challenging, as other areas are additionally involved (in this case, grammaticality and semantics).

7.4 Conclusions

In this study, four participants with PPA were re-assessed one year after their initial evaluation. Differences were documented for all participants in cognitive, linguistic abilities and discourse production over time. However, the pattern of differences in performance of each participant was different. Despite, similar cognitive status, as indicated by MMSE scores at initial assessment, the participants with the logopenic variant of PPA have shown greater decline than the participant with the semantic variant of PPA. All three were further affected in memory, writing and lexical retrieval. The lvPPA participants exhibited further difficulty with sentence repetition. The anomic participant presented with a naming impairment. Naming was further affected, and a mild semantic deficit was documented in his follow-up assessment.

These results are consistent with reports of a different rate of decline in svPPA and lvPPA (Macoir et al., 2017). Results from connected speech analysis, are in partial agreement with the study by Ash et al. (Ash et al., 2019) who found a decline in sentence complexity in svPPA and in fluency and grammaticality in lvPPA. The participant with svPPA exhibited decline both in lexical selection and sentence complexity. The two participants with lvPPA showed decline in sentence productivity measures. Only the second lvPPA showed further decline in fluency and to a lesser extent in grammaticality. However, it should be noted that their results derive from a group study and that great heterogeneity has been consistently reported in cases of lvPPA (Leyton et al., 2015).

This study employed a case-series design and, as such carries inherent limitations. Results of this study cannot be generalized to the Greek-speaking PPA population and require prospective investigations. Larger cohorts of individuals with PPA are needed to document clinical features of disease progression. Despite the limitations, the detailed clinical profiles of the PPA participants enable some tentative conclusions.

The follow-up assessment results of the two lvPPA participants and the additional data of the PPA participants who were at a later disease stage in initial assessment, demonstrate that as disease progresses, more domains are affected. Even though some

characteristic variant features can be identified, diagnostic accuracy is compromised (Rogalski et al., 2011).

Given the progressive nature of PPA, the timing of assessment has several implications. First, it plays a crucial role in accurate diagnosis, as the distinctive features of each variant are best captured early in the course of the disease. Second, it determines practical issues, such as choice of psychometric tools and tasks, length of assessment procedures, etc. Finally, it influences management decisions, such as type and format of intervention.

8 Discussion and conclusions

8.1 Summary of findings

8.1.1 Study 1

The main aim of the first study was to establish differences on neuropsychological testing and connected speech production between Greek-speaking individuals with AD and PPA. A secondary aim was to investigate whether specific measures or tasks can differentiate individuals with PPA from individuals with AD and neurotypical adults.

AD participants were impaired in memory, speed of processing, visuospatial and executive functions. Moreover, they exhibited lexical retrieval difficulties, as well as difficulties in linguistic tasks with an increased processing load such as repetition of long non-meaningful sentences.

PPA participants were less affected in the delay conditions of episodic memory measures. However, they too were impaired in executive tasks, especially for working memory and phonemic verbal fluency. Naming, single word comprehension, auditory comprehension of complex material, repetition, reading, and writing were all affected.

The most informative measures in differentiating svPPA and lvPPA from AD participants were repetition of long frequent sentences, frequency of phonological errors, mean sentence length and sentence elaboration index in a connected speech sample. For mean sentence length a cut-off value of 7.07 has been found to differentiate the PPA participants from AD participants with a sensitivity of 90% and specificity of 87.5%. For sentence elaboration index the optimal cut-off value for identifying PPA participants was 1.6 with a sensitivity of 80% and specificity of 95.8%.

8.1.2 Study 2

In this study, a picture description task was compared to a story retell task in two groups of individuals with different neurodegenerative conditions (PPA and AD) and a neurotypical control group.

The first aim of the second study was to investigate whether there was a difference in the narratives produced by participants using two different tasks. A second aim was to

explore whether there was a differential performance under the two conditions for individuals with PPA, individuals with AD and neurotypical controls. A final aim was to examine whether the two elicitation tasks placed different cognitive demands on the participants.

Differences between the two connected speech tasks were found for fluency, lexical selection, discourse, and sentence productivity but not for grammatical accuracy measures. The only lexical selection measure that was significantly different between the two tasks, was mean logarithmic frequency of open class narrative words. All participants used higher frequency words in picture description, indicating reliance on 'easier', more common words for the completion of this task or even for masking of word retrieval difficulties. Another finding, which was common in all groups, was higher sentence productivity scores for the story retell task.

Individuals with PPA performed better in the story retell task in comparison to the picture description task; they produced words of lower frequency, more narrative words and utterances, longer sentences and used more complex morphosyntactic elements. Fewer differences between the tasks were documented for the AD group.

Both tasks were able to capture connected speech deficits in PPA and AD and in that sense, both methods can be used interchangeably.

However, with respect to differential diagnosis between the two degenerative conditions (PPA and AD) a different conclusion may be reached. In study 1, two sentence productivity measures were deemed appropriate for differentially diagnosing PPA and AD participants: mean sentence length and sentence elaboration index derived from the story retell elicitation procedure. Story retell thus seems to be more sensitive in identifying deficits at the syntactic level of language production.

The generalizability of the findings is however limited by the fact that the PPA sample did not include participants with the non-fluent/agrammatic variant of PPA.

Results from the correlation analysis suggested a heavier involvement of memory capacity for fluency and word frequency measures for AD participants. Sentence productivity was correlated with executive function. For participants with AD, fluency measures correlated both with episodic and working memory in picture description. In story retell, involvement of executive function was evident for sentence productivity

measures. For PPA participants, all fluency measures, as well as measures of lexical selection, discourse and sentence productivity correlated with executive control, short-term memory and to a lesser degree with working memory. In PPA, there was no clear relationship between cognitive load and type of task.

Task complexity and the presence of a linguistic or cognitive deficit seems to account for the increased involvement of multiple executive components in individuals with PPA and AD in comparison to the control group.

To conclude, different elicitation tasks for the assessment of connected speech can be used to document narrative abilities in individuals with degenerative disorders. However, clinicians should be aware that different methods may lead to a different outcome depending on the purpose of the assessment. Story retell seems to be more sensitive in capturing morphosyntactic deficits and may assist in the differential diagnosis between PPA and AD.

8.1.3 **Study 3**

In the third study, the cognitive-linguistic and narrative discourse profiles of 13 Greek-speaking individuals with a degenerative disease were analyzed. Ten out of them had a root diagnosis of PPA and 3 with an FTD associated diagnosis, namely, Frontotemporal dementia - Amyotrophic lateral sclerosis (FTD-ALS), Progressive supranuclear palsy (PSP) and Corticobasal syndrome (CBS). These conditions have clinical phenotypes which overlap with PPA and may manifest with language impairment amongst other cognitive symptoms.

The main aim of the study was to explore the range of cognitive and language symptoms that can occur in PPA and FTD-related neurodegenerative diseases. A second aim was to document the challenges associated with the clinical diagnosis of PPA and classification of the PPA variants.

Inspection of individual profiles in individuals with PPA revealed heterogeneity in cognitive function, linguistic and narrative discourse abilities. Non-language cognitive deficits were common in lvPPA. Neuropsychiatric symptoms were reported for lvPPA participants, but to a lesser extent than for FTD participants, with svPPA, FTD-ALS, PSP and CBS.

Participants with svPPA presented with more typical phenotypes in comparison to the participants with lvPPA. Neuropsychological evaluation revealed mild to moderate memory and executive impairment for the svPPA participants but spared visuospatial functioning. Regarding linguistic abilities, they were more impaired in naming, single-word comprehension, and semantic knowledge.

Participants with a prominent movement disorder manifested, as expected, impairment in other areas, including speech, language, and cognition.

Each clinical diagnosis was discussed with reference to the established criteria. The different phenotypes were compared, and key characteristics of each condition were identified. Moreover, typical sources of confusion, including grammaticality and sentence comprehension, were discussed.

Analysis of individual profiles highlighted the need for using instruments targeting different cognitive domains, including language, behavior, and neuropsychiatric symptoms, in clinical assessment, in order to assist differential diagnosis and subtyping.

8.1.4 **Study 4**

In this study, results from two consecutive assessments, one year apart, were compared for four PPA participants: 2 with lvPPA, one with svPPA and one with unclassified-anomic PPA. The aim of the study was to gain an insight of how performance on the neuropsychological battery and narrative discourse abilities can change in the course of one year.

Single assessment data for 3 additional individuals with PPA were also reported.

Differences were documented for all participants in cognitive, linguistic abilities and discourse production over time. However, the pattern of differences in performance of each participant was different. Despite, similar cognitive status at initial assessment, the participants with the logopenic variant of PPA have shown greater decline than the participant with the semantic variant of PPA. All three were further affected in memory, writing and lexical retrieval. The lvPPA participants exhibited further difficulty with sentence repetition. The anomic participant presented with a naming impairment. Naming was further affected, and a mild semantic deficit was documented in his follow-up assessment.

The follow-up assessment results of the two lvPPA participants and the additional data of the PPA participants who were at a later disease stage in initial assessment, demonstrate that as disease progresses, more domains are affected. Even though some characteristic variant features can be identified, diagnostic accuracy is compromised.

8.2 Implications for clinical knowledge and practice

In this research program, an assessment battery was specifically designed to assess Greek-speaking individuals with PPA. Areas of testing were primarily recognized applying the diagnostic criteria of PPA variants. Additional domains have been identified reviewing studies that sought to describe in detail the core features of PPA variants, as well as the associated deficits. Selection of appropriate instruments was informed by reviewing the corresponding literature.

The research studies inform clinicians about the assessment instruments that can be used for the assessment of discourse production, language, and other cognitive functions in individuals with PPA and other neurodegenerative diseases. Information about typical performance on specific neuropsychological and linguistic tasks is valuable in informing selection of tests and documenting deficits in PPA and AD.

As it has been aforementioned, speech and language therapists/pathologists in Greece are increasingly involved in characterizing the deficits experienced by individuals with dementia and assisting differential diagnosis. Given the potential sources of confusion, the detailed description of cognitive-linguistic profiles of individuals with a neurodegenerative disease, exemplifies clinical thinking in challenging cases.

Finally, the outcome of the diagnostic process is not limited to the identification of deficits; it also includes identification of competencies. Using a comprehensive battery of tests, like the battery that has been administered in these studies, enables clinicians to build a profile of strengths and weaknesses. It has been suggested that in order to maximize therapeutic effects an individual with PPA can capitalize on spared language abilities (Croot, 2018; Henry et al., 2013). For example, individuals with svPPA can build on phonological and autobiographical memory and individuals with lvPPA on semantic abilities.

8.3 Future directions

The results of these studies can inform several lines of research. One area that needs to be further investigated is grammaticality. Lexical retrieval deficits could probably account for the decrease in the production of well-formed sentences evident in the connected speech of several participants. However, the use of determiners and inflected forms proved resilient to degeneration. Whether this finding can be extended to Greek-speaking individuals with nfvPPA and generalized to all individuals with PPA needs to be examined.

Extensive data were collected for these studies and full analysis was restricted by time and resource constraints. This extensive data provides a solid basis for conducting an in-depth analysis of different linguistic phenomena in future studies. Examples of these analyses include, morphosyntactic analysis of written paragraph description, error analysis of the reading and spelling tasks, analysis of response times and types of errors on BNT, on sentence repetition test, etc.

Further studies with large PPA cohorts and balanced representation of each PPA variant, combining neuropsychological, linguistic and neuroimaging testing could better explore PPA subtyping. It should be stressed that in clinical studies an indication of underlying pathologies is immensely expedient. Use of supplemental biomarker assessments can increase diagnostic power in future studies.

8.4 Concluding Remarks

The overarching theme of this thesis was the clinical diagnosis of Primary Progressive Aphasia.

Although the PPA classification captures the full range of progressive aphasia, there are cases where subtyping is difficult. Individuals with PPA may fulfill criteria for more than one variant. In this thesis, some participants exhibited shared logopenic and non-fluent/agrammatic variant or logopenic and semantic variant features. Moreover, there are individuals who cannot be classified in any PPA variant, like the participant with the progressive anomia.

Speech and language deficits may be the core features of PPA variants, but other cognitive and psychosocial domains are also affected, especially with disease

progression. Profiling both language and non-language impairments plays an important role in diagnosing PPA and differentiating between PPA variants.

Furthermore, other neurodegenerative diseases may present with speech and language deficits. In the studies of this research program, individuals with Alzheimer's disease, Corticobasal syndrome, Progressive supranuclear palsy and FTD-Amyotrophic lateral sclerosis, exhibited cognitive and linguistic profiles which had common features with those of individuals with PPA.

Understanding the theoretical and factual cognitive-linguistic correlates of PPA, as well as the progression of the associated deficits, is essential, not only for clinical diagnosis, but also for providing individualized treatment. Completing a detailed profile of strengths and weaknesses, as it has been substantiated in this thesis, forms the basis for effective language rehabilitation.

Given the growing ageing population, the improved diagnostic characterization of different dementia types and the availability of evidence-based speech and language treatments, the need to provide appropriate speech therapy services for people with PPA will grow. Speech and language assessment and therapy provision should be available to ensure equity of access for people with PPA and their families.

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APPENDIX I

Table 14: Neuropsychological Assessment Results for Pilot studies 1 and 2.

Task	Domain	L.J.'s Score	E.R.'s Score
	Composite Measure		
MMSE		17/30*	22/30
	Executive functioning		
Trail Making Test - A		150sec**	77sec
Trail Making Test - B		300sec**	191sec
			1 mistake
Digit Span Test (total)		8/30	14/30
Forward (3)		6/16 [a]	7/16 [a]
Backward (0)		2/16 [a]	7/16 [a]
Verbal Fluency Test			
Phonological (3 letters)		6*	16
Semantic (3 categories)		12**	13**
Clock Drawing Test		8/15**	14/15
	Memory		
5 Words Test (total)		19/20	13/20
Delayed Recall (total)		10/10	5/10
Free Delayed Recal		5/5	2/5*
5 Objects Test (total)		23/25	25/25
Delayed Recall		5/5	5/5
Benson Complex Figure Delayed Recall Condition		10/17 [a]	13/17 [a]
Benson Complex Figure Delayed Recognition		Yes [a]	Yes [a]

Visuospatial functioning		
Benson Complex Figure Copy Condition	11/17 [a]	17/17 [a]
Object Semantics		
Pyramids and Palm Trees-52	41/52**	31/52**
Pyramids and Palm Trees-14	13/14	12/14**
Mood		
Geriatric Depression Scale	10/15**	2/15
Praxis		
Western Aphasia Battery – Apraxia subtest	58/60 [a]	58/60 [a]

Key: *1.5*SD*, **2*SD* below the normative mean. [a] no control/normative data

Table 15: Speech and language Assessment Results for Pilot studies 1 and 2.

Task	Domain	L.J.'s Score	E.R.'s Score
	Severity/Staging		
BDAE severity		3/5	4/5
PASS		7/30	4/30
	Motor Speech Assessment		
Motor speech evaluation			
Apraxia Severity		3/7	0/7
Dysarthria Severity		1/7	0/7
	Fluency		
WAB Fluency Scale		*4/10*	*8/10*
	Discourse		
MAIN Retell score		7/17 [a]	
	Repetition		

WAB- words and phrases	95/100 [a]	92/100 [a]
Repetition of Sentences	302/340 [a]	323/340 [a]
Short meaningful	50/50 [a]	50/50 [a]
Short non-meaningful	50/50 [a]	49/50 [a]
Long meaningful	70/80 [a]	74/80 [a]
Long non-meaningful	65/80 [a]	70/80 [a]
Long frequent	77/80 [a]	80/80 [a]
Naming		
Boston Naming Test (BNT)	34/45	-
BNT-15	13/15**	5/15**
Single word comprehension		
PPVT	25/32	5/32**
BDAE-words	16/16	16/16
Language comprehension		
BDAE-commands	10/10	10/10
BDAE-complex ideational material	5/6	4/6**
Morphosyntax		
BDAE-3 sentence-picture matching (syntax)	8/10 [a]	10/10 [a]
Grammaticality judgment (tense, aspect, agreement)	60/80 [a]	73/80 [a]
Reading		
Reading Fluency - Words	14 (45')**	82 (45')
Reading Fluency - Non-words	12 (45')*	42 (45')
BDAE- reading sentences	4/5*	5/5
BDAE- comprehension of written words	4/4	3/4*
BDAE- comprehension of written sentences	4/4	2/4**

Writing		
Spelling - words	11/20[a]	11/20[a]
Spelling - non-words	11/12[a]	12/12[a]
BDAE - Picture description	4/11**	8/11

Key: *1.5*SD*, **2*SD* below the normative mean

Table 16**.** Group results for the cognitive-linguistic battery.

	Neurotypical control		AD		PPA	
Task (Max. Score)	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Composite Measure						
MMSE (/30)	28.87	1.06	24.89	2.47	24.30	3.65
Executive functioning						
Trail Making Test – A (180)	107.33	14.03	46.44	46.00	64.53	36.84
Trail Making Test – B (300)	204.53	40.26	34.00	44.79	72.68	76.67
Digit Span Test (total)(/32)	14.33	2.41	11.44	2.70	10.80	3.65
Forward (/16)	8.80	1.57	7.44	1.59	6.40	2.07
Backward (/16)	5.53	1.68	4.00	1.50	4.40	2.12
Verbal Fluency Test	94.60	18.41	54.56	11.90	37.80	12.09
Phonological (3 letters)	36.53	7.11	26.00	8.93	17.50	5.64
Semantic (3 categories)	58.07	15.47	28.56	11.01	20.30	8.43
Memory						
5 Words Test (total) (/20)	19.07	1.39	11.33	4.64	14.90	5.07
Delayed Recall (total) (/10)	9.27	1.28	4.33	2.96	7.20	2.94
Free Delayed Recall (/5)	4.40	.99	1.44	1.33	3.10	1.91
Cued Delayed Recall (/5)	4.87	.35	2.89	1.83	4.10	1.10
5 Objects Test (total) (/25)	24.87	.52	20.11	5.97	22.50	3.89
Delayed Recall (/5)	4.93	.26	3.89	1.69	4.80	.42

Benson Complex Figure Delayed Recall Condition (/17)	13.20	2.54	6.44	3.28	8.50	4.88
Visuospatial functioning						
Benson Complex Figure Copy Condition (/17)	15.80	1.21	15.11	1.69	16.30	1.49
Clock Drawing Test (/15)	14.40	.63	11.67	2.74	12.20	3.49
Mood						
Mood Scale (/15)	13.47	2.67	10.89	3.48	13.50	.97
Object Semantics						
Pyramids and Palm Trees-52	50.27	1.53	48.78	2.85	44.4	5.91
Pyramids and Palm Trees-14	14	0	13.33	0.87	12.7	1.16
Praxis						
WAB – Apraxia subtest (/60)	59.93	.26	58.11	1.83	55.90	2.42

Table 17. Kruskal-Wallis test with Mann-Whitney post-hoc test results for study 1.

Group	Control	AD	PPA	Chi-Square	Asymp. Sig.	Post-hoc
MMSE	29.00	26.00	25.00	19.139	.000	N>AD**=PPA**
TMT_A	111.00	40.00	77.00	16.311	.000	N>AD**=PPA**
TMT_B	209.00	.00	52.00	22.122	.000	N>AD***=PPA**
DigitSpanTotal	14.00	12.00	10.00	8.839	.012	AD=PPA AD=N PPA*<N
DigitSpanForward	8.00	8.00	6.00	7.694	.021	AD=PPA AD=N PPA*<N
DigitSpanBackward	5.00	4.00	4.00	4.850	.088	
VFluencyTotal	95.00	55.00	35.50	25.549	.000	N>AD**=PPA***
VFluency3Letters	37.00	27.00	17.50	19.529	.000	AD=PPA AD=N PPA***<N

VFluency3Cat	58.00	29.00	20.00	23.569	.000	N>AD**=PPA***
CDT	14.00	13.00	13.00	10.252	.006	AD=PPA N=PPA AD*<N
Words5Test	20.00	11.00	16.00	16.153	.000	N>AD***=PPA*
Words5DelRecall	10.00	4.00	8.00	15.370	.000	AD=PPA N=PPA AD***<N
Words5FreeRecall	5.00	1.00	3.50	15.002	.001	AD=PPA N=PPA AD***<N
Words5CuedRecall	5.00	2.00	4.50	9.788	.007	AD=PPA N=PPA AD**<N
Objects5Test	25.00	22.00	24.50	10.499	.005	AD=PPA N=PPA AD**<N
Objects5DelRecall	5.00	5.00	5.00	3.393	.183	
BensonFigureDelRecall	13.00	6.00	10.00	16.247	.000	N>AD***=PPA*
BensonFigureDelRecogn	1.00	1.00	1.00	1.009	.604	
BensonFigureCopy	15.00	15.00	17.00	3.136	.208	
PPTT_52	50.00	50.00	46.00	10.475	.005	AD=PPA AD=N PPA**<N
PPTT_14	14.00	14.00	13.00	13.661	.001	AD=PPA AD=N PPA**<N
Mood_15	15.00	12.00	14.00	5.707	.058	
BDAEs_RepetitionS	2.00	2.00	1.00	20.533	.000	N***=AD**>PPA
WAB_RepetitionWPh	100.00	97.00	86.00	13.336	.001	AD=PPA AD=N PPA**<N
Bayles_RepetitionS	339.00	332.00	206.50	19.367	.000	N>AD*=PPA***
ShortMeaningful	50.00	50.00	44.50	14.951	.001	AD=PPA AD=N PPA***<N
ShortNMeaningful	50.00	50.00	46.00	14.017	.001	AD=PPA AD=N PPA**<N

LongMeaningful	80.00	75.00	36.50	15.964	.000	AD=PPA AD=N PPA***<N
LongNMeaningful	80.00	74.00	28.50	17.439	.000	N>AD*=PPA***
LongFrequent	80.00	80.00	55.50	16.724	.000	N***=AD*>PPA
BNT_45	42.00	33.00	20.00	23.425	.000	N>AD**=PPA***
BNT_15	15.00	14.00	9.00	23.037	.000	N>AD*=PPA***
BDAEs_WrNaming	4.00	4.00	3.50	6.133	.047	
PPVT_32	30.00	27.00	24.00	11.232	.004	AD=PPA AD=N PPA**<N
BDAEs_WCompr	16.00	16.00	16.00	2.400	.301	
BDAEs_Commands	10.00	9.00	7.50	20.763	.000	AD=PPA AD=N PPA***<N
BDAEs_ComIdMat	6.00	5.00	3.50	15.330	.000	AD=PPA AD=N PPA***<N
MAIN_Compr	10.00	10.00	10.00	3.459	.177	
BDAE3_SyntCompr	10.00	9.00	8.50	8.706	.013	AD=PPA AD=N PPA*<N
FGramJudgment	79.00	72.00	70.00	17.771	.000	N>AD*=PPA***
BDAEs_WrWCompr	4.00	4.00	4.00	4.231	.121	
BDAEs_WrSCompr	4.00	4.00	4.00	6.692	.035	AD=PPA AD=N PPA*<N
ReadFluency_W	83.00	57.00	62.00	15.177	.001	N>AD**=PPA**
ReadFluency_NW	43.00	25.00	35.00	12.303	.002	AD=PPA N=PPA AD**<N
ReadPassDuration	47.00	53.99	55.44	4.403	.111	
ReadPassPhonT	39.62	46.22	48.06	5.250	.072	
ReadPassSpeechR	4.12	4.04	3.52	2.860	.239	
ReadPassArtR	5.05	5.05	4.66	9.067	.011	AD=PPA AD=N PPA*<N

BDAEs_Spelling	9.00	9.00	9.00	5.144	.076	
SpellingW	18.00	16.00	13.50	8.038	.018	AD=PPA AD=N PPA*<N
SpellingNW	11.00	12.00	11.00	1.016	.602	
BDAE_WrPictDescr	11.00	8.00	7.50	25.296	.000	N>AD**=PPA***
WAB_Apraxia	60.00	58.00	55.50	22.470	.000	N>AD*=PPA***
MaxPhonTime_mean	16.26	17.30	12.25	.524	.769	
MaxPhonTime_longest	19.19	19.17	13.14	.659	.719	
DDK_pa_Reps	6.92	6.54	6.59	1.790	.409	
DDK_ta_Reps	6.86	6.57	6.87	3.661	.160	
DDK_ka_Reps	6.51	5.63	6.26	4.688	.096	
DDK_pataka_Reps	6.94	6.59	7.42	2.120	.346	
S2Dur_11_psyll	.20	.30	.23	10.546	.005	AD=PPA N=PPA AD**<N
S5Dur_12_psyll	.18	.24	.19	8.259	.016	AD=PPA N=PPA AD*<N
S3Dur_14_psyll	.16	.20	.18	3.891	.143	
S1Dur_15_psyll	.16	.18	.16	.644	.725	
S4Dur_16_psyll	.16	.20	.17	3.974	.137	
PD_TotalPauseDuration	16.59	49.90	38.39	13.167	.001	N>AD**=PPA*
PD_MeanPauseDuration	.85	1.40	1.32	18.371	.000	N>AD***=PPA**
PD_MedianPauseDuration	.66	1.02	.87	11.539	.003	AD=PPA N=PPA AD**<N
PD_PauseDurationPerc	28.11	41.13	44.64	15.297	.000	N>AD**=PPA**
PD_SpeakingTime_min	.77	.96	.86	3.114	.211	
PD_ArticulationRate_wpm	170.66	162.27	138.47	4.105	.128	
PD_Pauses_ptw	.05	.09	.13	12.327	.002	N>AD*=PPA**
PD_Prolongations_ptw	.06	.05	.09	2.589	.274	

PD_Fillers_ptw	.02	.01	.01	.672	.715	
PD_FalseStarts_ptw	.01	.02	.02	2.236	.327	
PD_Distortions_ptw	.00	.00	.00	5.355	.069	
PD_Unintelligible_ptw	.00	.00	.00	1.569	.456	
PD_TotalDysfl_ptw	.14	.18	.27	7.492	.024	AD=PPA AD=N PPA*<N
PD_Repetitions_ptw	.00	.00	.00	2.844	.241	
PD_PhonologicalEr_ptw	.00	.00	.03	25.475	.000	N***=AD***>PPA
PD_MorphEr_ptw	.00	.01	.00	4.645	.098	
PD_SemEr_ptw	.00	.01	.00	8.424	.015	AD=PPA N=PPA AD*<N
PD_TotalTime_min	1.01	1.84	1.38	6.588	.037	AD=PPA N=PPA AD*<N
PD_TotalWords	130.00	138.00	112.50	2.072	.355	
PD_NarrativeWords	90.00	97.00	56.00	11.470	.003	N**=AD*>PPA
PD_NoTypeW	62.00	63.00	40.50	12.711	.002	N**=AD*>PPA
PD_NoLemmas	52.00	54.00	35.50	11.552	.003	N**=AD*>PPA
PD_NoUtterances	13.00	16.00	10.50	2.926	.232	
PD_NoSentences	13.00	13.00	9.50	2.148	.342	
PD_SpeechRate_wpm	121.44	87.25	74.68	10.865	.004	AD=PPA AD=N PPA**<N
PD_NarWs_TotalWs	.72	.68	.47	5.936	.051	
PD_TypeToken_Ratio	.70	.66	.71	4.748	.093	
PD_TypeTokenR_SqR	6.59	6.11	5.43	9.306	.010	AD=PPA AD=N PPA**<N
PD_Closed_ClassWs	.51	.53	.52	3.387	.184	
PD_Pron_NsPron	.19	.27	.24	.746	.689	
PD_Vs_NsVs	.51	.56	.51	1.536	.464	

PD_Ns_Vs	.94	.80	.97	1.536	.464	
PD_MeanLogFNWs	2.65	2.78	2.86	14.707	.001	N>AD*=PPA**
PD_Prepositions	.06	.07	.06	.799	.671	
PD_Adverbs	.05	.08	.07	5.514	.063	
PD_Adjectives	.04	.04	.03	1.652	.438	
PD_Articles	.19	.16	.22	1.626	.444	
PD_Conjuctions	.09	.07	.04	4.890	.087	
PD_Nouns	.22	.19	.21	2.265	.322	
PD_Pronouns	.05	.05	.05	.308	.857	
PD_Verbs	.23	.23	.24	1.701	.427	
PD_PropWinSent	.96	.77	.93	6.580	.037	AD=PPA N=PPA AD*<N
PD_MeanSentLength	6.89	5.67	5.16	13.101	.001	AD=PPA AD=N PPA**<N
PD_MeanULength	6.89	6.00	4.80	13.225	.001	AD=PPA AD=N PPA**<N
PD_MedianULength	6.00	5.00	3.50	15.717	.000	AD=PPA AD=N PPA***<N
PD_MeanLenght3LongestS	12.00	10.00	9.00	9.533	.009	AD=PPA AD=N PPA**<N
PD_SentElaboration_Index	2.09	1.52	1.15	13.873	.001	AD=PPA AD=N PPA**<N
PD_Embedding_Index	.31	.38	.19	4.645	.098	
PD_WellFormedSent	1.00	.93	.87	5.114	.078	
PD_AuxComplexity_Index	1.20	1.20	1.06	1.098	.578	
PD_VerbInflection_Index	1.00	1.00	1.00	.000	1.000	
PD_Determiner_Index	1.00	1.00	1.00	2.451	.294	

Main_TotalPauseDuration	14.40	21.35	39.94	9.686	.008	AD=PPA AD=N PPA*<N
Main_MeanPauseDuration	.75	1.07	1.18	4.871	.088	
Main_MedianPauseDuration	.60	.74	.84	5.291	.071	
Main_PauseDurationPerc	22.44	27.66	33.94	6.876	.032	AD=PPA AD=N PPA*<N
Main_SpeakingTime_min	.92	1.07	1.26	6.236	.044	AD=PPA AD=N PPA*<N
Main_ArticulationRate_wpm	167.43	140.82	147.06	7.676	.022	AD=PPA N=PPA AD*<N
Main_Pauses_ptw	.03	.06	.07	7.504	.023	AD=PPA AD=N PPA*<N
Main_Prolongations_ptw	.04	.06	.10	7.403	.025	AD=PPA AD=N PPA*<N
Main_Fillers_ptw	.01	.03	.05	8.724	.013	AD=PPA AD=N PPA*<N
Main_FalseStarts_ptw	.02	.02	.04	1.685	.431	
Main_Distortions_ptw	.00	.00	.00	1.757	.415	
Main_Unintelligible_ptw	.00	.00	.00	4.945	.084	
Main_TotalDysfl_ptw	.11	.18	.31	12.636	.002	N>AD*=PPA**
Main_Repetitions_ptw	.00	.01	.01	12.750	.002	N>AD*=PPA**
Main_PhonolEr_ptw	.00	.00	.01	9.589	.008	N*=AD*>PPA
Main_MorphEr_ptw	.00	.00	.00	5.330	.070	
Main_SemEr_ptw	.00	.01	.01	12.858	.002	AD=PPA AD=N PPA**<N
Main_TotalTime_min	1.18	1.54	2.01	12.072	.002	AD=PPA AD=N PPA**<N
Main_TotalWords	159.00	162.00	168.50	.845	.655	
Main_NarrativeWords	127.00	114.00	106.00	5.817	.055	

Main_NoTypeW	73.00	60.00	54.00	8.923	.012	AD=PPA AD=N PPA*<N
Main_NoLemmas	61.00	49.00	42.50	8.434	.015	AD=PPA AD=N PPA*<N
Main_NoUtterances	16.00	13.00	17.00	5.472	.065	
Main_NoSentences	15.00	12.00	16.00	3.452	.178	
Main_SpeechRate_wpm	132.33	92.27	75.49	11.001	.004	N>AD*=PPA*
Main_NarWs_TotalWs	.89	.77	.60	14.002	.001	N>AD*=PPA**
Main_TypeTokenRatio	.56	.58	.53	.930	.628	
Main_TypeTokenR_SqR	6.37	5.70	5.36	9.514	.009	AD=PPA AD=N PPA*<N
Main_Closed_ClassWs	.53	.52	.54	.245	.885	
Main_Pron_NsPron	.18	.23	.22	.891	.641	
Main_Vs_NsVs	.48	.48	.49	.140	.933	
Main_Ns_Vs	1.10	1.07	1.04	.140	.933	
Main_MeanLogFNWs	2.51	2.54	2.68	2.884	.236	
Main_Prepositions	.06	.06	.04	2.879	.237	
Main_Adverbs	.05	.05	.04	2.188	.335	
Main_Adjectives	.01	.02	.01	4.553	.103	
Main_Articles	.23	.22	.23	.467	.792	
Main_Conjuctions	.07	.06	.05	5.305	.070	
Main_Nouns	.24	.23	.25	.131	.937	
Main_Pronouns	.05	.08	.06	1.429	.489	
Main_Verbs	.22	.22	.23	4.848	.089	
Main_PropWinSent	1.00	1.00	.99	3.613	.164	
Main_MeanSentLength	8.47	7.64	6.25	15.713	.000	N***=AD*>PPA
Main_MeanULength	8.47	7.64	6.19	14.418	.001	N**=AD*>PPA
Main_MedianULength	7.00	7.00	5.00	11.303	.004	N**=AD*>PPA

Main_MeanLength3LongestS	15.33	14.33	12.17	9.570	.008	AD=PPA AD=NPPA**<N
Main_SentElaboration_Index	2.10	1.77	1.33	17.582	.000	N**=AD*>PPA
Main_Embedding_Index	.63	.42	.30	15.848	.000	AD=PPA AD=NPPA***<N
Main_WellFormedSent	.94	.95	.93	4.279	.118	
Main_AuxComplexity_Index	1.47	1.09	1.43	2.470	.291	
Main_VerbInflection_Index	1.00	1.00	1.00	2.778	.249	
Main_Determiner_Index	1.00	1.00	1.00	.531	.767	

Table 18. Kruskal-Wallis *H* Test (*df*=2) with Mann-Whitney *U* test for post-hoc comparisons for paired differences of narrative measures for Main and Picture description (Study 2).

Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Asymptotic Sig.(2-sided)	Adj. Sig.
Narrative Words	7.59			.022	
AD-Neurotypical	8.9	4.197	2.121	.034	.102
AD-PPA	-12.15	4.573	-2.657	.008	.024
Neurotypical-PPA	-3.25	4.063	-0.8	.424	1
Total Words	7.118			.028	
AD-Neurotypical	5.044	4.197	1.202	.229	.688
AD-PPA	-12.078	4.574	-2.64	.008	.025
Neurotypical-PPA	-7.033	4.064	-1.731	.084	.251
Sentences	7.054			.029	
AD-Neurotypical	3.178	4.179	0.761	.447	1
AD-PPA	-11.478	4.553	-2.521	.012	.035
Neurotypical-PPA	-8.3	4.046	-2.051	.040	.121
Semantic Errors	7.56			.023	

AD-Neurotypical	3.933	4.015	0.98	.327	.982
AD-PPA	-11.667	4.375	-2.666	.008	.023
Neurotypical-PPA	-7.733	3.888	-1.989	.047	.140
Repetitions	7.898			.019	
Neurotypical-PPA	-7.517	3.848	-1.953	.051	.152
Neurotypical-AD	-10.411	3.975	-2.619	.009	.026
PPA-AD	2.894	4.331	0.668	.504	1
Fillers	12.185			.002	
Neurotypical-PPA	-10.733	4.065	-2.64	.008	.025
Neurotypical-AD	-13.133	4.199	-3.128	.002	.005
PPA-AD	2.4	4.575	0.525	.600	1
Type of Words	7.068			.029	
AD-Neurotypical	6.633	4.195	1.581	.114	.342
AD-PPA	-12.15	4.572	-2.658	.008	.024
Neurotypical-PPA	-5.517	4.062	-1.358	.174	.523
Utterances	9.481			.009	
AD-Neurotypical	7.389	4.184	1.766	.077	.232
AD-PPA	-14.039	4.559	-3.079	.002	.006
Neurotypical-PPA	-6.65	4.051	-1.642	.101	.302
TypeToken Ratio	7.089			.029	
PPA-Neurotypical	4.333	4.065	1.066	.286	.859
PPA-AD	12.044	4.575	2.632	.008	.025
Neurotypical-AD	-7.711	4.199	-1.837	.066	.199
Proportion of Ws in Sentences	6.165			.046	
PPA-Neurotypical	0.1	4.059	0.025	.980	1
PPA-AD	9.656	4.568	2.114	.035	.104
Neurotypical-AD	-9.556	4.192	-2.279	.023	.068

APPENDIX II

Τμήμα Επιστημών Αποκατάστασης

Τεχνολογικό Πανεπιστήμιο Κύπρου

Βραγαδίνου 15, 3041 Λεμεσός

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ΕΝΤΥΠΟ ΕΝΗΜΕΡΩΣΗΣ ΓΙΑ ΣΥΜΜΕΤΟΧΗ ΣΕ ΔΙΔΑΚΤΟΡΙΚΗ ΕΡΕΥΝΗΤΙΚΗ ΜΕΛΕΤΗ

Υπεύθυνη Διδακτορικού Προγράμματος*: Δρ. Μαρία Καμπανάρου, Τεχνολογικό Πανεπιστήμιο Κύπρου - Τμήμα Επιστημών Αποκατάστασης*

Διδακτορική φοιτήτρια*: Καρπαθίου Νομική*

Ποιος είναι ο σκοπός αυτής της μελέτης;

Ο σκοπός αυτής της μελέτης είναι η αξιολόγηση των γνωστικών και γλωσσικών ικανοτήτων ατόμων με επίκτητη προοδευτική διαταραχή λόγου και ομιλίας.

Γιατί επιλέχθηκα να συμμετέχω;

Σας ζητήθηκε να συμμετάσχετε γιατί ο γιατρός σας έκρινε πως αντιμετωπίζετε κάποιου βαθμού δυσκολία στην ομιλία, τη γραφή ή την ανάγνωση.

Είναι υποχρεωτική η συμμετοχή μου;

Η συμμετοχή σας στη μελέτη δεν είναι υποχρεωτική. Ακόμα κι αν αποφασίσετε να συμμετάσχετε, μπορείτε να αποσυρθείτε οποιαδήποτε στιγμή, χωρίς να αναφέρετε το λόγο. Η απόφασή σας να αποσυρθείτε ή η απόφασή σας να μην συμμετάσχετε στη μελέτη δεν θα έχει καμία συνέπεια για εσάς.

Η συμμετοχή μου στη μελέτη θα είναι εμπιστευτική;

Κάθε πληροφορία που σας αφορά είναι αυστηρά εμπιστευτική. Τα στοιχεία που θα συλλεχθούν θα φυλαχτούν σε ασφαλές μέρος, με περιορισμένη πρόσβαση. Σε περίπτωση που τα αποτελέσματα της έρευνας δημοσιευτούν ή παρουσιαστούν σε συνέδρια δεν θα χρησιμοποιηθούν προσωπικά δεδομένα.

Θα έχω προσωπικό όφελος από την συμμετοχή μου;

Θα ενημερωθείτε σχετικά με τα αποτελέσματα των δοκιμασιών στις οποίες θα υποβληθείτε. Θα λάβετε πληροφορίες σχετικά με τις δυσκολίες τις οποίες αντιμετωπίζετε. Η εκτίμηση θα είναι δωρεάν.

Τι θα συμβεί αν συμμετάσχω;

Πριν την έναρξη της αξιολόγησης θα ενημερωθείτε αναλυτικά για τη μελέτη και θα σας ζητηθεί να υπογράψετε το έντυπο συναίνεσης. Η αξιολογητική διαδικασία περιλαμβάνει σταθμισμένες και άτυπες δοκιμασίες για την εκτίμηση των γνωστικών και γλωσσικών σας ικανοτήτων. Οι απαντήσεις σας θα καταγραφούν, θα μαγνητοφωνηθούν και θα αναλυθούν σε δεύτερο χρόνο. Ακόμη, θα ληφθούν σχετικές πληροφορίες και από ένα δικό σας πρόσωπο αναφοράς. Ο τόπος και ο χρόνος των συνεδριών θα συμφωνηθεί από κοινού. Η συμμετοχή στην μελέτη δεν ενέχει κινδύνους.

Τμήμα Επιστημών Αποκατάστασης
Τεχνολογικό Πανεπιστήμιο Κύπρου
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ΕΝΤΥΠΟ ΣΥΓΚΑΤΑΘΕΣΗΣ

Υπεύθυνη Διδακτορικού Προγράμματος: Δρ. Μαρία Καμπανάρου, Τεχνολογικό Πανεπιστήμιο Κύπρου - Τμήμα Επιστημών Αποκατάστασης

Διδακτορική φοιτήτρια: Καρπαθίου Νομική

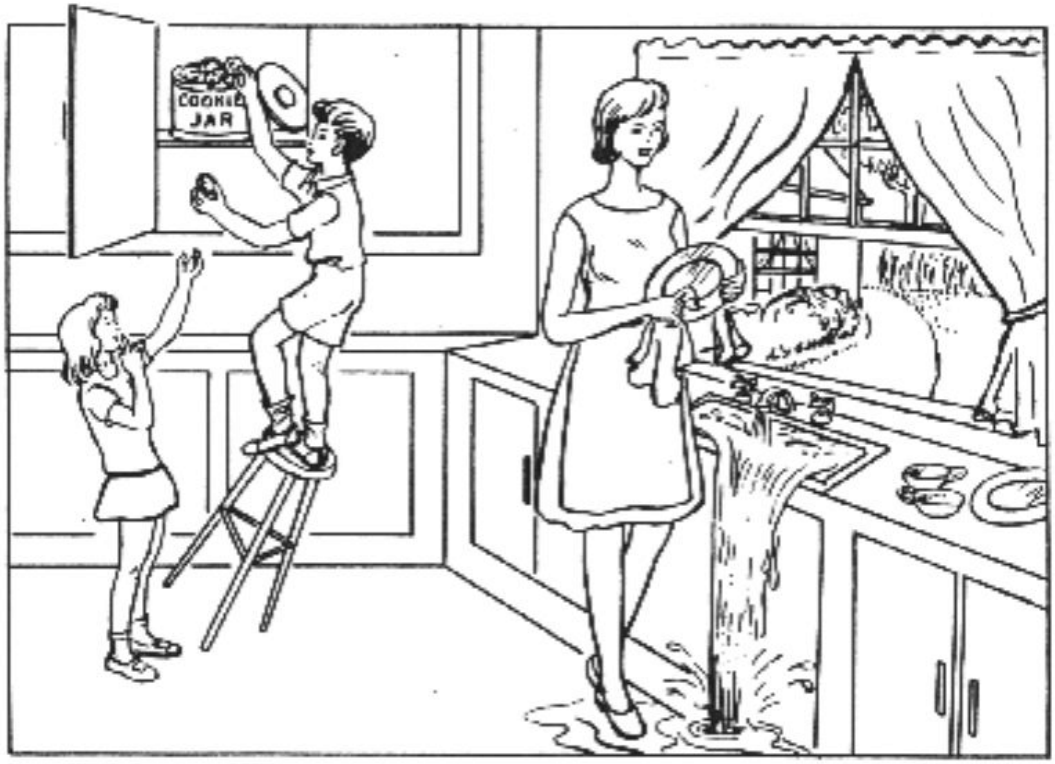
Έχω ενημερωθεί για την έρευνα αυτή και συμφωνώ να συμμετάσχω σε δοκιμασίες για την αξιολόγηση των γνωστικών και γλωσσικών μου ικανοτήτων.
Έχω επίσης ενημερωθεί ότι οι απαντήσεις μου θα καταγραφούν, θα μαγνητοφωνηθούν και θα αναλυθούν για τους σκοπούς της παρούσας έρευνας. Τα προσωπικά μου στοιχεία (όνομα, διεύθυνση κτλ.) δεν θα χρησιμοποιηθούν.
Σε περίπτωση που τα αποτελέσματα των αξιολογήσεων και της έρευνας δημοσιευτούν ή παρουσιαστούν σε συνέδρια θα διασφαλιστεί το απόρρητο των προσωπικών δεδομένων.

Ονοματεπώνυμο: ……

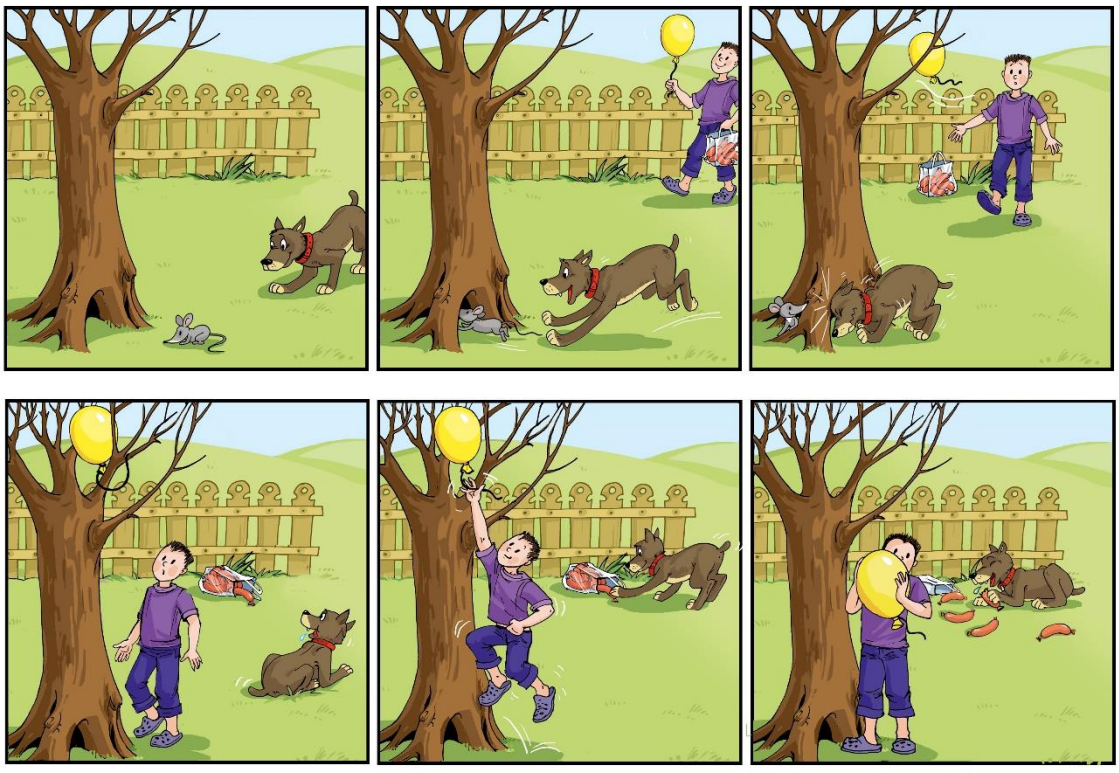
Ημερομηνία Υπογραφή

....

The ‘Cookie Theft’ picture



‘The dog story’ from MAIN: stimuli for story retell



Motor Speech Evaluation **ΗΧΟΓΡΑΦΗΣΗ**

		Απραξία			Δυσαρθρία		
1	'Πες α για όσο περισσότερο χρόνο μπορείς.'	1___	2___	3___	1___	2___	3___
	'Τώρα, θέλω να μου πεις τις συλλαβές όσο πιο γρήγορα και για όσο περισσότερο χρόνο μπορείς.'						
α	Πες *πα-πα-πα-πα-πα*	1___	2___	3___	1___	2___	3___
β	Πες *τα-τα-τα-τα-τα*	1___	2___	3___	1___	2___	3___
γ	Πες *κα-κα-κα-κα-κα*	1___	2___	3___	1___	2___	3___
	'Τώρα, θα πούμε και τις τρεις συλλαβές μαζί: πα-τα-κα.'						
δ	Πες *πα-τα-κα-πα-τα-κα-πα-τα-κα*	1___	2___	3___	1___	2___	3___
2	'Τώρα, θέλω να πεις ορισμένες λέξεις μετά από μένα.'						
α	Πες *τσαμπατζής*	1___	2___	3___	1___	2___	3___
β	Πες ***μεμονωμένη***	1___	2___	3___	1___	2___	3___
γ	Πες ***κολοκυθόπιτα***	1___	2___	3___	1___	2___	3___
3	'Τώρα, θέλω να πεις τις λέξεις μετά από μένα 5 φορές.'						
α	Πες *μοιρολατρία*	_ _ _ _ _			_ _ _ _ _		
β	Πες ***καταπληκτικός***	_ _ _ _ _			_ _ _ _ _		
γ	Πες ***παραστατικός***	_ _ _ _ _			_ _ _ _ _		
4	'Πες τις λέξεις μετά από μένα.'						
α	Πες *μαμά*	1___	2___	3___	1___	2___	3___
β	Πες *Βιβή*	1___	2___	3___	1___	2___	3___
γ	Πες *παπί*	1___	2___	3___	1___	2___	3___
δ	Πες *μπαμπά*	1___	2___	3___	1___	2___	3___
ε	Πες *νονά*	1___	2___	3___	1___	2___	3___
ζ	Πες ***τότε***	1___	2___	3___	1___	2___	3___
η	Πες *νταντά*	1___	2___	3___	1___	2___	3___
θ	Πες *Γωγώ*	1___	2___	3___	1___	2___	3___
ι	Πες ***κακό***	1___	2___	3___	1___	2___	3___
κ	Πες *όάσα*	1___	2___	3___	1___	2___	3___
λ	Πες *Φωφώ*	1___	2___	3___	1___	2___	3___
μ	Πες *σαισί*	1___	2___	3___	1___	2___	3___
ν	Πες *Ζωζώ*	1___	2___	3___	1___	2___	3___
ξ	Πες *γιαγιά*	1___	2___	3___	1___	2___	3___
ο	Πες *Λίλα*	1___	2___	3___	1___	2___	3___
5	'Πες τις λέξεις μετά από μένα.'						
α	Πες *πάντα*	1___	2___	3___	1___	2___	3___
	Πες ***πάντοτε***	1___	2___	3___	1___	2___	3___
	Πες *παντοτινά*	1___	2___	3___	1___	2___	3___
β	Πες *τρόμος*	1___	2___	3___	1___	2___	3___
	Πες *τρομάζω*	1___	2___	3___	1___	2___	3___
	Πες *τρομαγμένος*	1___	2___	3___	1___	2___	3___
γ	Πες *σπάς(σπάστε σπαστή)*	1___	2___	3___	1___	2___	3___
	Πες *σπαστικός*	1___	2___	3___	1___	2___	3___
	Πες ***σπαστικότητα***	1___	2___	3___	1___	2___	3___
δ	Πες *κορίτσι*	1___	2___	3___	1___	2___	3___
	Πες *κοριτσάκι*	1___	2___	3___	1___	2___	3___
	Πες *κοριτσίστικο*	1___	2___	3___	1___	2___	3___
6	'Επανέλαβε τις προτάσεις μετά από μένα.' 3η προσπάθεια: κάθε λέξη ξεχωριστά						
α	*Βάλε σε παρακαλώ τα πράγματα στο ψυγείο.*	1___	2___	3___	1___	2___	3___
β	*Ένα ζεστό **φρεσκοψημένο** ψωμί.*	1___	2___	3___	1___	2___	3___
γ	*Το καλοκαίρι φοράμε ελαφριά ρούχα*	1___	2___	3___	1___	2___	3___
δ	*Το πανάκριβο ρολόι του είχε εξαφανιστεί.*	1___	2___	3___	1___	2___	3___
ε	*Το ναυάγιο ξεβράστηκε στην ακτή.*	1___	2___	3___	1___	2___	3___
7	Περιγραφή Εικόνας (BDAE)						
	Τουλάχιστον 1 λεπτό συζήτησης (max 2 λεπτά). 'Πες μου τι γίνεται σε αυτήν την εικόνα.' (BDAE)	___			___		
8	Ανάγνωση Κειμένου						
	Σε περίπτωση σοβαρής διαταραχής max 2 λεπτά.	___			___		

Κείμενο για ανάγνωση

Νομίζω πως θα θέλατε να μάθετε για τον παππού μου. Λοιπόν, είναι σχεδόν ενενήντα τριών χρονών, αλλά το μυαλό του είναι ξυράφι. Φοράει συνήθως ένα γκρι πανωφόρι με τεράστιες τσέπες και τέσσερα στρογγυλά μπρούτζινα κουμπιά. Τα μαλλιά του και τα γένια του είναι άσπρα. Είναι ψηλός και η παρουσία του προκαλεί ένα αίσθημα βαθύτατου σεβασμού. Όταν μιλά, η φωνή του τρέμει. Δύο φορές την ημέρα πιάνει το βιολί του και παίζει με μεγάλη δεξιοτεχνία. Κάθε μέρα, εκτός κι αν βρέχει ή χιονίζει, βγαίνει βόλτα και περπατά περίπου για μισή ώρα. Πολλές φορές προσπαθήσαμε να τον πείσουμε να περπατά περισσότερο και να καπνίζει λιγότερο, αλλά εκείνος πάντα απαντά: ‘Τέτοια ώρα, τέτοια λόγια…’ Στον παππού μου αρέσουν οι παροιμίες.

Word Count	117				
Syllable Count	239				
Character Count	600				
Mean syllables per word	2.04				
Mean characters per word	5.12				
no 1syll	41 (41)	no 2syll	44 (88)	no 3syll	22 (66)
no 4syll	7 (28)	no 5syll	2 (10)	no 6syll	1 (6)

Επανάληψη WAB

Οδηγίες: Ζητήστε από τον ασθενή να επαναλάβει τις παρακάτω λέξεις με τη σειρά που δίνονται.

Επαναλάβατε τις λέξεις που θα σας πω. Πείτε _____.

Επανάληψη: Επαναλάβετε ολόκληρη την εντολή μία φορά αν φαίνεται να μην έχει ακούσει, ή αν σας το ζητήσει.

Βαθμολόγηση: Βαθμολογήστε με το μέγιστο βαθμό αν επαναλαμβάνει σωστά τη λέξη ή τη φράση.

Βαθμολογήστε με 2 κάθε αναγνωρίσιμη λέξη.

Αφαιρέστε 1 βαθμό για κάθε φωνημική παραφασία και κάθε αλλαγή στη σειρά παρουσίασης των λέξεων.

Θεωρήστε σωστές επαναλήψεις που διαφέρουν λόγω δυσαρθρίας, διαλέκτου και συντμήσεων.

1. **Φως** (2)
2. **Μύτη** (2)
3. **Κήπος** (2)
4. **Χόρτα** (2)
5. **Μπανάνα** (2)
6. **Σταφιδόψωμο** (4)
7. **Πενήντα πέντε** (4)
8. **Δώδεκα και δέκα.** (6)
9. **Ένας χρόνος και εννέα μήνες.** (10)
10. **Βγήκαν για βόλτα στην παραλία.** (10)
11. **Χτυπάει το τηλέφωνό σου.** (8)
12. **Δε θα ταξιδέψει ποτέ ξανά.** (10)
13. **Καλοψημένο φαγητό.** (8)
14. **Σαν να μην πέρασε ούτε μέρα.** (10)
15. **Ο Άγγελος κάθε βράδυ παίζει μόνος στο χιόνι φορώντας γάντια και μπότες.** (20)

Επανάληψη: ☐ (100)

Επανάληψη Προτάσεων (Bayles)

1.SM	Μικρά απομακρυσμένα χωριά.	_____ /10
2.LF	Μήπως θα μπορούσα να κάνω κάτι ακόμα για σας;	_____ /16
3.SNM	Ανίκανα πλαστικά κουτάλια.	_____ /10
4.LM	Οι σκεπτόμενοι συγγραφείς γράφουν αξιοσημείωτα.	_____ /16
5.LNM	Το χαμόγελό της ρουφά χρυσά μολύβια γραφείου.	_____ /16
6.LNM	Οι δυνατοί πρεσβευτές παγώνουν σταθερά κύματα.	_____ /16
7.LF	Θα πρέπει να κόστισε ολόκληρη περιουσία.	_____ /16
8.SNM	Ζεστά παραδοσιακά κλαρίνα.	_____ /10
9.SM	Λοξή γυάλινη επιφάνεια.	_____ /10
10.LM	Οι μασκαρεμένοι άντρες έφαγαν μαλλί της γριάς.	_____ /16
11.SM	Άσπρο τραυματισμένο πρόβατο.	_____ /10
12.SNM	Σιωπηλό μοντέρνο παντελόνι.	_____ /10
13.LF	Πραγματικά δεν ξέρω τίποτα για το θέμα αυτό.	_____ /16
14.LNM	Οι ψηλότερες κορυφές ψιθυρίζουν γλυκά πάθη.	_____ /16
15.LM	Τα κομψά κορίτσια δοκιμάζουν καλλυντικά συχνά.	_____ /16
16.LNM	Οι φουρκέτες ζητούν ζωηρά παιχνίδια μυστηρίου.	_____ /16
17.LM	Τα παλιά έπιπλα προσελκύουν τους εμπόρους αντικών.	_____ /16
18.SM	Σπανιότατο τροπικό φρούτο.	_____ /10
19.LF	Φοβάμαι ότι έχω πολύ άσχημα νέα για σας.	_____ /16

20.SNM Κινητό ιδιωτικό νησί. _____ /10

21.LM Τα ενεργά ηφαίστεια εκτοξεύουν καυτή λάβα. _____ /16

22.SM Νέος ικανός ιδιοκτήτης. _____ /10

23.SNM Σπασμένη μεταλλική αρρώστια. _____ /10

24.LF Θα μπορούσα να σας απασχολήσω για ένα λεπτό; _____ /16

25.LNM Οι τυφώνες δικάζουν παλιά βιβλία μελιτζάνας. _____ /16

SM: _____

SNM: _____

LM: _____

LNM: _____

LF: _____

Συνολικά: _____ /340

Ορθογραφική Δοκιμασία (Sideridis et al., 2008)

ILSP PsychoLinguistic Resource Spelling

Protopapas, A., Tzakosta, M., Chalamandaris, A., & Tsiakoulis, P. (2012).
IPLR: An online resource for Greek word-level and sublexical information. *Language resources and evaluation*, *46* (3), 449-459.

Word Order	Spelling	Phonetic	Frequency	N letters	N phonemes	N syllables	Mean syllable token frequency, spelling	Mean syllable type frequency, spelling	N orthographic neighbors (standard: replace only)
High Frequency									
5	δωρεάν	Doreán	38,772	6	6	3	0.913	1.460	2
16	ηθοποιός	iTopiós	43,746	8	7	4	3.103	2.218	0
8	αυτοκίνητο	aftocínito	84,210	10	10	5	13.944	12.145	3
18	αντικείμενο	adicímeno	97,202	11	9	5	15.637	16.000	4
11	άδεια	áDia	100,281	5	4	3	19.271	17.694	3
14	χαρακτηριστικό	xaraktiristikó	106,269	14	14	6	4.133	5.251	3
17	διευθυντής	DiefTidís	109,077	10	9	4	8.859	9.624	1
3	χρήματα	xrímata	135,331	7	7	3	7.325	7.637	4
9	παράδειγμα	paráDiJma	236,694	10	9	4	2.993	3.840	1
1	ξέρω	kséro	132,997	4	5	2	0.968	1.264	3
Low Frequency			108,458	8.500	8.000	3.900	7.715	7.713	2.400
13	δανείζω	Danízo	0.034	7	6	3	0.756	1.077	1
2	ποτίζω	potízo	0.101	6	6	3	4.253	4.943	0
19	αποχαιρέτησα	apoxerétisa	0.372	12	11	6	12.252	1.217	2
10	φωτισμένος	fotizménos	0.507	10	10	4	3.368	4.438	4
7	χώρισα	xórisa	0.541	6	6	3	3.727	5.320	5
12	αλλιώτικος	aLótikos	0.609	10	8	4	15.745	14.693	4
4	μεγαλώνω	meJalóno	0.643	8	8	4	5.143	5.755	1
6	παιχτών	pextón	0.677	7	6	2	0.455	0.390	1
20	ματαιώνεται	mateónete	0.71	11	9	5	4.732	5.373	0
15	ξεφυλλίζοντας	ksefilízodas	0.88	13	12	5	0.856	2.143	1
			0.507	9.000	8.200	3.900	5.615	4.535	1.900

Non-Words	Spelling	Phonetic	Stressed syllable	N letters	N phonemes	N syllables	Mean syllable token frequency, spelling	Mean syllable type frequency, spelling	N orthographic neighbors (standard: replace only)
	δέψος	Dépsos	2	5	6	2	0.286	0.310	0
	τρόσωμο	trósomo	3	7	7	3	1.709	2.361	0
	αραμωλώ	aramoló	1	7	7	4	14.704	14.398	0
	ρέναια	rénea	3	6	5	3	18.831	16.420	0
	γώχησε	JóXise	3	6	6	3	3.226	2.522	0
	άβρεια	ávria	3	6	5	3	19.091	17.496	0
	υφοχοραμός	ifoxoramós	1	10	10	5	3.125	3.597	0
	δαχονεφώντας	Daxonefódas	2	12	11	5	1.558	2.968	0
	πιευλυκτής	pievliktís	1	10	10	4	7.984	8.605	0
	εντόκειμο	edócimo	3	9	7	4	7.604	8.430	0
	ασοταιλέμησα	asotelémisa	3	12	11	6	10.661	10.298	0
	σαλαιώγκεται	saleóGete	3	12	9	5	1.777	2.271	0
			2.333	8.5	7.833	3.917	7.546	7.473	0.000

ΙΣΤΟΡΙΚΟ ΔΙΑΤΑΡΑΧΩΝ ΛΟΓΟΥ/ΟΜΙΛΙΑΣ ΕΝΗΛΙΚΑ

Όνομα: _____ Επίθετο: _____

Διεύθυνση: _____ Νομός: _____

Τηλέφωνο: _____ Κινητό_____ Email:_____

Ημερομηνία Γεννήσεως: _____Ηλικία: _____

Τόπος γεννήσεως: _____

Μορφωτικό επίπεδο (Δημοτικό, Γυμνάσιο, Λύκειο, Ανωτάτη Σχολή κλπ): Έτη: _____

Επάγγελμα: _____

Μητρική γλώσσα: _____ Άλλες γλώσσες: _____

Δεξιόχειρας◯ Αριστερόχειρας◯ Επικρατέστερο χέρι για την πλειοψηφία της οικογένειας: _____

Παραπέμπεται από: _____

Λόγος παραπομπής: _____

ΙΑΤΡΙΚΟ ΙΣΤΟΡΙΚΟ:

Ιατρική Διάγνωση: _____

Σημειώστε όπως αρμόζει:

o Υπέρταση o Διαβήτης o Υπερχολιστεραιμία

o Έλλειψη Β12 o Αλλεργίες o Πάθηση Θυρεοειδούς

o Καρδιακή ανακοπή o Αρρυθμίες o Bypass/stent/αγγειοπλαστική

o Επιληπτικές κρίσεις o Κατάθλιψη o Ψυχιατρικό ιστορικό

o Ακράτεια o Βαρηκοΐα / Κώφωση o Βρογχίτιδα / Άσθμα

o Χρόνια Αποφρακτική Πνευμονοπάθεια (ΧΑΠ)

o Γαστρο-οισοφαγική παλινδρόμηση (ΓΟΠ)

o Αγγειακό εγκεφαλικό επεισόδιο o Κρανιοεγκεφαλική Κάκωση

o Νεοπλασματική νόσος

o ALS o Νόσος του Huntington o Πολλαπλή Σκλήρυνση

o Νόσος του Parkinson o Άνοια o Άλλη νευρολογική πάθηση

Υπάρχουν άλλα προβλήματα πέραν όσων αναφέρονται πιο πάνω;

_____

Ποιο είναι το προεξάρχον σύμπτωμα (μνήμη, προσοχή, λόγος, συμπεριφορά, κίνηση, άλλο) _____

Ήταν και το αρχικό; Ναι ___ Όχι ___ Πότε πρωτοεμφανίστηκε; _____

ΝΕΥΡΟΛΟΓΙΚΗ ΕΞΕΤΑΣΗ: Εξετάσεις που έχουν γίνει στον ασθενή: (σημειώστε με √ ότι αρμόζει)

◯ Μαγνητική Τομογραφία - Διάγνωση / Αποτελέσματα:

_____

_____

◯ Αξονική Τομογραφία – Διάγνωση / Αποτελέσματα:

_____

◯ Ηλεκτροεγκεφαλογράφημα – Διάγνωση / Αποτελέσματα:

_____

◯ SPECT – Διάγνωση / Αποτελέσματα:

_____

◯ Άλλες Εξετάσεις:

_____

_____

Νευρολογική Διάγνωση:

_____

Πληροφορίες για τυχόν εγχειρήσεις που έγιναν:

_____

_____

Ακολουθεί κάποια φαρμακευτική αγωγή; Ναι___ Όχι___

Εάν Ναι, παρακαλώ σημειώστε όνομα και δοσολογία φαρμάκου:

ο _____

ο _____

ο _____

Κινητικές Δυσκολίες: (σημειώστε με ότι αρμόζει)

Έχει αστάθεια; Ναι ___ Όχι ___ Πτώσεις; Ναι ___ Όχι ___

Τρόμο; Ναι ___ Όχι ___ Βραδύτητα; Ναι ___ Όχι ___

Μπορεί να ανεβοκατεβαίνει σκαλιά ή σκάλες; Ναι ___ Όχι ___

◯ Ημιπληγία - Δεξιά ___ Αριστερά ___

◯ Διπληγία – Άνω άκρα ___ Κάτω άκρα ___

◯ Τετραπληγία, είδος _____

Χρησιμοποιεί κάποιο από τα ακόλουθα βοηθήματα;

ο Δε χρησιμοποιεί ο Μπαστούνι ο Τροχοκάθισμαο

ο Βοήθημα βάδισης (π.χ. πι, rollator) ο Άλλο βοήθημα _____

Συμπεριφορικά Συμπτώματα: (σημειώστε με ότι αρμόζει)

Απάθεια Ναι ___ Όχι ___ Κατάθλιψη Ναι ___ Όχι ___

Άρση αναστολών Ναι ___ Όχι ___ Ευερεθιστότητα Ναι ___ Όχι ___

Ανησυχία Ναι ___ Όχι ___ Ψευδαισθήσεις Ναι ___ Όχι ___

Αλλαγή προσωπικότητας Ναι ___ Όχι ___

Περιγραφή του παρόντος προβλήματος στο λόγο, ομιλία, επικοινωνία:

_____

_____

Εμφάνιση προβλήματος Σταδιακή □ Αιφνίδια □ Πότε πρωτοεμφανίστηκε; _

Πορεία προβλήματος Σταθερότητα □ Βελτίωση □ Επιδείνωση □

ΙΣΤΟΡΙΚΟ ΛΟΓΟΥ / ΟΜΙΛΙΑΣ (σημειώστε με √)

Σύμπτωμα Ποτέ Μερικές φορές Συχνά Από πότε;

Δυσκολία έκφρασης σκέψεων

Δυσκολία στην εξεύρεση λέξεων

Δυσκολία να παραμείνει σε ένα θέμα κατά τη διάρκεια συζήτησης

Δυσκολία να γίνει κατανοητός/η από άλλους

Δυσκολία να καταλάβει τι του/της λένε οι άλλοι

Δυσκολία στο να ακολουθεί οδηγίες

Δυσκολία Μνήμης

Δυσκολία Προσανατολισμού

Δυσκολία στην Επίλυση προβλημάτων

Δυσκολία στην Συγκέντρωση /Προσοχή

Δυσκολίες Ανάγνωσης/Γραφής

Δυσκολία στη ροή της ομιλίας (τραυλισμός)

Δυσκολίες φώνησης

Δυσκολία κατάποσης

Εάν παρουσιάζει προβλήματα σίτισης/κατάποσης, σημειώστε:

ο Σιελόρροια ο Δυσκολία στη μάσηση ο Δυσκολία στη κατάποση

ο Ιστορικό πνευμονίας ο Τρέφεται από το στόμα

ο Δυσκολία με: υγρά _ στερεά _ πολτοποιημένα _

ο Τρέφεται με ρινογαστρικό σωλήνα ο Τρέφεται με γαστροστομία

Τρόπος επικοινωνίας: Προφορικά __ Νοήματα /χειρονομίες __ Γραφή __

Άλλο __

Εναλλακτικός τρόπος επικοινωνίας (π.χ. ηλεκτρονική συσκευή) ____

- Άλλες δυσκολίες: _____

Άλλα θέματα:

- Παρουσιάζει προβλήματα όρασης; Ναι ___ Όχι ___, εάν Ναι, πότε άρχισαν;

_____

- Φοράει γυαλιά; Ναι ___ Όχι ___
- Εάν έχει βαρηκοΐα, φέρει ακουστικό βοήθημα; Ναι ___ Όχι ___,

εάν Ναι, σε ποιο αυτί; _____

- Υπάρχει κάποιος άλλος στην οικογένεια με παρόμοια ή τα ίδια προβλήματα;

Εξηγήστε: _____

- Παρουσιάζει προβλήματα με τον ύπνο; Ναι ___ Όχι ___
- Κάπνισμα: _____
- Αλκοόλ: _____

Για περιπτώσεις επίκτητων νευρολογικών διαταραχών (π.χ. αγγειακά εγκεφαλικά επεισόδια, άνοια, κρανιοεγκεφαλικές κακώσεις, κλπ) παρακαλώ σημειώστε:

- Προβλήματα υγείας πριν τη νευρολογική διαταραχή:

_____

- Προβλήματα λόγου και ομιλίας πριν τη διαταραχή:

_____

Παρακολουθείται από κάποιον ειδικό; Ναι ___ Όχι ___

Εάν Ναι, παρακαλώ αναφέρατε τη χρονική διάρκεια και τα αποτελέσματα της παρέμβασης: _____

Γενική Συμπεριφορά Ασθενή:

- Πριν τη διαταραχή: _____
- Μετά τη διαταραχή: _____
- Γενικές παρατηρήσεις: _____

Ανάγνωση

Δυσκολία κατανόησης □

Διαβάζει: καθημερινά □ σπάνια □ ποτέ □

Τι διαβάζει: βιβλία □ εφημερίδα □ περιοδικά □ λογαριασμούς □ μηνύματα □ άλλα □

Γραφή

Δυσκολία γραφής □

Γράφει: καθημερινά □ σπάνια □ ποτέ □

Τι γράφει:

_____

Συζήτηση

Δυσκολία με: Έναρξη □ Συμμετοχή □ Διατήρηση θέματος □

Πρόσωπα που προτιμά: _____

Θέματα που προτιμά: ___ _____

Διακύμανση Οι δυσκολίες είναι σταθερές ____ ή μεταβάλλονται ανάλογα με:

Καταστάσεις □ _____

Πρόσωπα □ _____

Χρόνος □ _____

ΟΙΚΟΓΕΝΕΙΑΚΟ/ ΚΟΙΝΩΝΙΚΟ ΙΣΤΟΡΙΚΟ

- Οικογενειακή κατάσταση:

o Άγαμος/η ○ Παντρεμένος/η

o Χωρισμένος/η ○ Χήρος/χήρα

- Όνομα Συζύγου: _____
- Τόπος παρούσης διαμονής: _____

- Παιδιά :

ΟΝΟΜΑΤΑ ΗΛΙΚΙΕΣ

- Τωρινή επαγγελματική απασχόληση: _____
- Συνεχίζει να εργάζεται; Ναι___ Όχι___

Εάν Ναι: ο Τίτλος εργασίας: _____

- Ακολουθεί ένα εβδομαδιαίο πρόγραμμα θεραπειών ή/και δραστηριοτήτων όπως:

_____

_____

- Αγαπημένες ασχολίες (χόμπι):

_____

_____

- Σωματική άσκηση:

_____

_____

- Αριθμός κοινωνικών επαφών / εβδομάδα:

_____

_____

Παρακαλώ σημειώστε οποιεσδήποτε άλλες πληροφορίες πιστεύετε ότι θα είναι χρήσιμες:

_____

_____

_____

_____

Το ερωτηματολόγιο αυτό συμπληρώθηκε από:

Όνομα : _____ (σχέση με το άτομο: _____)

Υπογραφή :_____ Ημερομηνία : _____

Ερωτηματολόγιο – Αξιολόγηση Δυσκολιών Λόγου

Κλίμακα Βαρύτητας Προοδευτικής Αφασίας

Το ερωτηματολόγιο συμπληρώνεται από ένα άτομο που γνωρίζει καλά τον εξεταζόμενο.

Όνομα Εξεταζόμενου: _____ Ημερομηνία: _____

Συμπληρώθηκε από (όνομα και σχέση με εξεταζόμενο): _____

Οι παρακάτω ερωτήσεις διερευνούν την λειτουργικότητα του εξεταζόμενου ως προς διάφορους τομείς της ομιλίας, του λόγου και της καθημερινής επικοινωνίας.

Κυκλώστε την απάντηση που περιγράφει καλύτερα το πώς λειτουργεί σήμερα, συγκριτικά με πέντε ή δέκα χρόνια πριν (πριν την έναρξη των προβλημάτων).

A. <u>Άρθρωση</u> (προφορά)

1. Έχει δυσκολία να προφέρει τους φθόγγους/ήχους που αποτελούν τις λέξεις; Για παράδειγμα, μιλάει σαν να τρώει τους φθόγγους/ήχους μέσα στις λέξεις; (Η ερώτηση αναφέρεται στη λάθος προφορά ενός φθόγγου και όχι σε αντικατάσταση ενός φθόγγου από έναν άλλο, όπως 'τρέχει' αντί 'βρέχει'.)

[Σε περίπτωση που η απάντηση είναι 'όχι' παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Β.]

α) Ναι β) Όχι

2. Πόσο συχνά έχει αυτήν τη δυσκολία στην προφορά;

α) Προφέρει περιστασιακά λάθος τις λέξεις.

β) Προφέρει πολλές λέξεις λάθος, όμως οι λέξεις γίνονται κατανοητές.

γ) Προφέρει πολλές ή τις περισσότερες λέξεις λάθος και οι λέξεις δύσκολα γίνονται κατανοητές.

δ) Δεν μιλά ή δεν λέει καμία κατανοητή λέξη.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

Β. <u>Εύρεση λέξεων και έκφραση</u>

1. Έχει δυσκολία να βρει τις κατάλληλες λέξεις, να τις παράγει και/ή να βρει πώς ονομάζονται τα αντικείμενα όταν μιλάει ή γράφει;

[Σε περίπτωση που η απάντηση είναι 'όχι', παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Γ.]

α) Ναι β) Όχι

2. Πόσο συχνά έχει αυτήν τη δυσκολία με τις λέξεις;

α) Λίγες φορές την εβδομάδα

β) Πολλές φορές την εβδομάδα

γ) Καθημερινά, αλλά όχι σε κάθε συζήτηση

δ) Σε κάθε συζήτηση

3. Παρά τη δυσκολία που αντιμετωπίζει, πόσο καλά μπορεί να εκφράσει ένα μήνυμα που να βγάζει νόημα;

α) Δεν έχει δυσκολία να εκφράσει ένα μήνυμα που να βγάζει νόημα.

β) Περνάει το μήνυμα με πολλές λεπτομέρειες.

γ) Περνάει το μήνυμα με λίγες λεπτομέρειες.

δ) Εκφράζει ένα γενικό μήνυμα με λίγες ή καθόλου λεπτομέρειες.

ε) Σπάνια ή ποτέ δεν εκφάζει ένα μήνυμα.

4. Τι συμβαίνει όταν προσπαθεί να βρει μια λέξη; *[Κυκλώστε όσα ισχύουν]*

α) Λέει μια λάθος λέξη.

β) Λέει τη σωστή λέξη, αλλά την προφέρει με λάθος τρόπο.

γ) Κάνει παύσεις.

δ) Συμπληρώνει τα κενά με παρατεταμένους φθόγγους/γεμίσματα (π.χ. 'εεε' ή 'ααα').

ε) Περιγράφει τη λέξη αρκετά καλά ώστε να μπορείτε να τη μαντέψετε.

στ) Προσπαθεί να περιγράψει τη λέξη, αλλά δεν μπορείτε να τη μαντέψετε.

5. Ποιες αλλαγές έχετε παρατηρήσει στο λεξιλόγιό του/της ή στον τύπο των λέξεων που χρησιμοποιεί; *[Κυκλώστε όσα ισχύουν]*

α) Καμία αλλαγή στο λεξιλόγιο

β) Το λεξιλόγιο του/της είναι περιορισμένο ή μειωμένο.

γ) Το λεξιλόγιο του/της είναι αόριστο και χρησιμοποιεί γενικούς όρους, όπως ‘το τέτοιο’, ‘πράγμα’, ‘εδώ’.

δ) Δεν προφέρει σωστά τις λέξεις, π.χ. λέει ‘κλαράβι’ αντί για καράβι.

ε) Αντικαθιστά τις λέξεις που θέλει να πει με άλλες, π.χ. λέει ‘μπλούζα’ αντί για παλτό.

στ) Λέει λέξεις που δεν αντιστοιχούν σε πραγματικές λέξεις, όπως ‘φαγέρι’ ή ‘καρτίο’.

6. Πόσο συχνά δυσκολεύεται να ονομάσει κοινά αντικείμενα, όπως οικιακά σκεύη, φαγώσιμα και ζώα;

α) Δεν δυσκολεύεται εμφανώς.

β) Δυσκολεύεται περιστασιακά, έως και κάποιες φορές την εβδομάδα, αλλά όχι καθημερινά.

γ) Δυσκολεύεται τακτικά, περίπου 1-2 φορές την ημέρα.

δ) Δυσκολεύεται συχνά, αρκετές φορές την ημέρα.

ε) Δυσκολεύεται τόσο συχνά που δεν μπορεί να ονομάσει τα περισσότερα αντικείμενα.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

_____

Γ. <u>Κατανόηση συζητήσεων και οδηγιών</u>

1. Δυσκολεύεται να καταλάβει τι λένε οι άλλοι;
[Σε περίπτωση που η απάντηση είναι ‘όχι’, παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Δ.]

α) Ναι β) Όχι

2. Ποιες αλλαγές έχετε παρατηρήσει στην κατανόηση του λόγου; *[Κυκλώστε όσα ισχύουν]*

α) Αναφέρει ότι οι άλλοι μιλάνε πολύ γρήγορα.

β) Καταλαβαίνει τα περισσότερα, αλλά χρειάζεται διευκρινήσεις ή επανάληψη.

γ) Αναγκάζεστε να μιλάτε πιο απλά και με μικρότερες φράσεις, αλλά όταν το κάνετε αυτό σας καταλαβαίνει.

δ) Καταλαβαίνει μόνο τα μισά από αυτά που του/της λέτε.

ε) Καταλαβαίνει μόνο οικείες φράσεις/φράσεις ρουτίνας (‘κάθησε κάτω’).

στ) Καταλαβαίνει πολύ λίγα από αυτά που του/της λέτε.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

Δ. <u>Κατανόηση μεμονομένων λέξεων</u>

1. Δυσκολεύεται να καταλάβει λέξεις που θα έπρεπε να γνωρίζει;
[Σε περίπτωση που η απάντηση είναι ‘όχι’, παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Ε.]

α) Ναι β) Όχι

2. Πόσο συχνά σας ρωτάει για τη σημασία μιας λέξης ή δείχνει να μη γνωρίζει μια λέξη;

α) Δυσκολεύεται περιστασιακά και κυρίως με λέξεις που δε χρησιμοποιούμε συχνά.

β) Δυσκολεύεται συχνά, αλλά όχι σε κάθε συζήτηση.

γ) Δυσκολεύεται σε κάθε συζήτηση, αλλά υπάρχουν ακόμη λέξεις που καταλαβαίνει.

δ) Δυσκολεύεται συνέχεια και με τις περισσότερες λέξεις.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

Ε. <u>Γραμματική και συντακτικό</u> (σωστή χρήση γραμματικών κανόνων και συνδυασμός λέξεων μέσα σε προτάσεις)

1. **Δυσκολεύεται να σχηματίσει ολοκληρωμένες και γραμματικά σωστές φράσεις και προτάσεις όταν μιλάει και/ή όταν γράφει;**
   [Σε περίπτωση που η απάντηση είναι 'όχι', παραλείψτε τις ερωτήσεις προχωρήστε στο μέρος ΣΤ.]

   α) Ναι β) Όχι

2. **Ποιες αλλαγές έχετε παρατηρήσει στην ικανότητά του/της να χρησιμοποιεί σωστά τη γραμματική και το συντακτικό;** *[Κυκλώστε όσα ισχύουν]*

   α) Αναφέρει ότι δυσκολεύεται να συνδυάζει λέξεις ή να εκφραστεί.

   β) Μιλάει κυρίως με απλές/μικρές προτάσεις.

   γ) Κάνει λάθη όπως τα παρακάτω:

   - βάζει τις λέξεις σε λάθος σειρά ή παραλείπει κάποιες λέξεις
   - χρησιμοποιεί λέξεις με λάθος τρόπο, όπως έφαγα' αντί για έφαγες
   - μπερδεύει μικρές λέξεις (π.χ. για, θα , το, από, σε, δεν, μην, αν)

   δ) Μπορεί να συνδυάσει μόνο δύο ή τρεις λέξεις, αντί να κάνει μεγαλύτερες φράσεις ή προτάσεις.

   ε) Μπορεί να πει ή να γράψει μόνο μία λέξη τη φορά.

3. **Πόσο συχνά δυσκολεύεται να χρησιμοποιήσει σωστή γραμματική και σύνταξη;**

   α) Δυσκολεύεται περιστασιακά, έως και κάποιες φορές την εβδομάδα, αλλά όχι καθημερινά.

   β) Δυσκολεύεται καθημερινά, αλλά όχι σε κάθε συζήτηση.

   γ) Δυσκολεύεται σε κάθε συζήτηση, αλλά μπορεί να σχηματίσει φράσεις μερικές φορές.

   δ) Σχεδόν ποτέ δεν μπορεί να σχηματίσει φράσεις.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

Στ. <u>Ροή ομιλίας</u> (ευχέρεια)

1. **Παρατηρούνται παύσεις, δισταγμοί ή άλλες δυσκολίες που επηρεάζουν τη ροή της ομιλίας;**
   [Σε περίπτωση που η απάντηση είναι 'όχι' παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Ζ.]

   α) Ναι β) Όχι

2. **Ποιες αλλαγές έχετε παρατηρήσει στην ροή της ομιλίας;** *[Κυκλώστε όσα ισχύουν]*

   α) Χρησιμοποιεί παρατεταμένους φθόγγους-γεμίσματα, όπως 'ααα' ή 'εεε'.

   β) Κάνει παύσεις καθώς μιλάει.

   γ) Διστάζει καθώς μιλάει.

   δ) Προσπαθεί επανειλημμένα να εκφέρει μια λέξη.

   ε) Ξεκινάει να πει μια λέξη ή φράση, αλλά στη συνέχεια την αλλάζει.

   στ) Λέει μόνο λίγες λέξεις κάθε φορά.

3. **Πόσες λέξεις λέει κατά μέσο όρο πριν διακοπεί η ομιλία του/της;**

   α) 7 ή περισσότερες λέξεις

   β) 4-6 λέξεις

   γ) 2-3 λέξεις

   δ) 1 λέξη

4. **Πόσο συχνά υπάρχει δυσκολία στη ροή της ομιλίας;**

   α) Δυσκολεύεται περιστασιακά, έως μερικές φορές την εβδομάδα, αλλά όχι καθημερινά.

   β) Δυσκολεύεται καθημερινά, αλλά όχι σε κάθε συζήτηση.

γ) Δυσκολεύεται σε κάθε συζήτηση, αλλά υπάρχουν φορές όπου η ομιλία του κυλάει στρωτά.

δ) Σχεδόν ποτέ η ομιλία του δεν κυλάει στρωτά.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

Ζ. <u>Ανάγνωση</u>

1. **Δυσκολεύεται να διαβάσει, ή διαβάζει λιγότερο από πριν;**
   [Σε περίπτωση που η απάντηση είναι 'όχι' παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Η.]

   α) Ναι β) Όχι

2. **Ποιες αλλαγές έχετε παρατηρήσει στις συνήθειες και στην ικανότητα ανάγνωσης;**
   [Κυκλώστε όσα ισχύουν]

   α) Αναφέρει πως δυσκολεύεται ή του/της παίρνει περισσότερο χρόνο να διαβάσει.

   β) Διαβάζει λιγότερο συχνά από πριν.

   γ) Έχει σταματήσει να διαβάζει πράγματα που τον/την ευχαριστούσαν, όπως βιβλία και εφημερίδες.

   δ) Διαβάζει μόνο απλό υλικό.

   ε) Δε φαίνεται να καταλαβαίνει αυτά που διαβάζει.

   στ) Δε διαβάζει καθόλου.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

Η. <u>Γραφή</u>

1. **Δυσκολεύεται να γράψει ή γράφει λιγότερο από πριν;**
   [Σε περίπτωση που η απάντηση είναι 'όχι' παραλείψτε τις ερωτήσεις και προχωρήστε στο μέρος Θ.]

   α) Ναι β) Όχι

2. **Ποιες αλλαγές έχετε παρατηρήσει στις συνήθειες και στην ικανότητα γραφής;**
   [Κυκλώστε όσα ισχύουν]

   α) Αναφέρει ότι δυσκολεύεται ή χρειάζεται περισσότερο χρόνο για να γράψει.

   β) Γράφει λιγότερο συχνά από πριν.

   γ) Σταμάτησε να γράφει συγκεκριμένα πράγματα, όπως e-mails, κάρτες και γράμματα.

   δ) Κάνει ορθογραφικά λάθη που δεν έκανε παλιά.

3. **Τι γράφει;**

   α) Γράφει προτάσεις με νόημα, παρόλο που μπορεί να κάνει κάποια λάθη.

   β) Γράφει λέξεις ή/και φράσεις με νόημα, παρόλο που μπορεί να κάνει κάποια λάθη.

   γ) Γράφει λέξεις, αλλά είναι δύσκολο για κάποιον να καταλάβει τι θέλει να πει.

   δ) Γράφει μόνο το όνομά του/της ή την υπογραφή του/της.

   ε) Δε γράφει.

4. **Ποιες αλλαγές έχετε διαπιστώσει στο γραφικό του/της χαρακτήρα;**

   α) Καμία αλλαγή

   β) Πιο ακατάστατα γράμματα

   γ) Μικρότερα γράμματα

5. **Γράφει σε υπολογιστή ή άλλη συσκευή προκειμένου να επικοινωνήσει; Περιγράψτε τις δραστηριότητες για τις οποίες στηρίζεται (εξαρτάται από) στον υπολογιστή ή τη συσκευή επικοινωνίας.**

_____

_____

_____

_____

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

Θ. <u>Λειτουργική επικοινωνία</u> (επιτυχία στην επικοινωνία παρά τα προβλήματα λόγου)

1. **Μπορεί να εκφράσει τις σκέψεις του/της με τρόπο κατανοητό, παρά τη δυσκολία που αντιμετωπίζει στην ομιλία;**

   α) Πάντοτε

   β) Συνήθως

   γ) Περιστασιακά

   δ) Σπάνια

   ε) Ποτέ

2. **Ποιες είναι οι αλλαγές στην καθημερινότητά του - στις καθημερινές του/της ρουτίνες και δραστηριότητες;**
   (Η ερώτηση αφορά σε αλλαγές που αποδίδονται στα προβλήματα λόγου/ομιλίας και όχι σε άλλους παράγοντες)

   α) Δεν έχει αλλάξει η καθημερινή του/της ρουτίνα, εργασία ή δραστηριότητες.

   β) Έχει αλλάξει ο τρόπος που εργάζεται ή συμμετέχει σε δραστηριότητες.

   γ) Έχει περιορίσει την εργασία ή/και τη συμμετοχή του/της σε δραστηριότητες.

   δ) Σταμάτησε να εργάζεται ή/και να συμμετέχει σε δραστηριότητες.

3. **Πώς επικοινωνεί με τους άλλους;**

   α) Συμμετέχει σε συζητήσεις για ποικίλα θέματα, απλά και σύνθετα.

   β) Συμμετέχει σε συζητήσεις για απλά θέματα.

   γ) Επικοινωνεί κυρίως για να εκφράσει τις ανάγκες και τις επιθυμίες του/της

δ) Επικοινωνεί κυρίως μέσω σωματικής επαφής, όπως με το να σας οδηγήσει στο αντικείμενο που θέλει ή αγγίζοντας το χέρι σας.

ε) Επικοινωνεί ελάχιστα.

4. **Πόσο συχνά αποφεύγει κοινωνικές περιστάσεις εξαιτίας των δυσκολιών με τον λόγο και την ομιλία;**
   (Η ερώτηση αφορά σε αλλαγές που αποδίδονται στα προβλήματα λόγου/ομιλίας και όχι σε άλλους παράγοντες)

   α) Σπάνια ή ποτέ δεν αποφεύγει κοινωνικές περιστάσεις.

   β) Περιστασιακά αποφεύγει κοινωνικές περιστάσεις.

   γ) Συχνά αποφεύγει κοινωνικές περιστάσεις.

   δ) Πάντοτε αποφεύγει κοινωνικές περιστάσεις.

5. **Ποιες αλλαγές έχετε παρατηρήσει στη διάθεση/κίνητρο για επικοινωνία;**

   α) Καμία αλλαγή.

   β) Ελαφρά χαμηλότερο κίνητρο για επικοινωνία.

   γ) Σχετικά χαμηλότερο κίνητρο για επικοινωνία.

   δ) Σημαντικά χαμηλότερο κίνητρο για επικοινωνία.

6. **Φαίνεται να αντιλαμβάνεται τα προβλήματα που περιγράφηκαν;**

   α) Ναι, αντιλαμβάνεται πλήρως το πρόβλημα.

   β) Αντιλαμβάνεται σε κάποιο βαθμό το πρόβλημα.

   γ) Όχι, δε φαίνεται να αντιλαμβάνεται το πρόβλημα.

7. **Επιμένει να εκφράζει αυτό που θέλει να πει (το μήνυμά του/της), ακόμη και στις περιπτώσεις που οι προσπάθειες είναι αποτυχημένες (ακόμη και όταν δεν τον/την καταλαβαίνετε);**

   α) Ναι, επιμένει για πολλή ώρα, ακόμη και αν δεν έχει επιτυχία.

   β) Ναι, επιμένει για λογικό χρονικό διάστημα και μετά σταματά.

   γ) Όχι, δεν επιμένει όταν οι πρώτες του/της προσπάθειες δεν έχουν επιτυχία.

8. **Αναστατώνεται ή θυμώνει όταν δεν τον/την καταλαβαίνετε;**

   α) Συνήθως δεν αναστατώνεται και δε θυμώνει.

   β) Αναστατώνεται ή/και θυμώνει λίγο.

γ) Αναστατώνεται ή/και θυμώνει αρκετά.

δ) Αναστατώνεται ή/και θυμώνει πολύ.

ε) Όταν δεν τον/την καταλαβαίνετε, δεν ενοχλείται όπως θα ήταν αναμενόμενο.

9. Μιλάει στο τηλέφωνο με συγγενείς/φίλους;

α) Όσο και πριν

β) Λιγότερο από πριν

γ) Όχι πλέον

10. Γράφει γράμματα και/ή ηλεκτρονικά μηνύματα (emails) σε συγγενείς/φίλους?

α) Όσο και πριν

β) Λιγότερο από πριν

γ) Όχι πλέον

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

_____

_____

_____

_____

_____

I. <u>Επικοινωνία - Κοινωνική αλληλεπίδραση</u> (Επιλέξτε το 'δεν ισχύει' αν δεν είναι ικανός/η να επικοινωνήσει εξαιτίας του προβλήματος λόγου/ομιλίας, και είναι δύσκολο να επιλέξετε μία από τις απαντήσεις.)

1. Ξεκινάει μια συζήτηση κάνοντας ένα σχόλιο, ή μια ερώτηση, είτε μιλώντας, είτε γράφοντας, είτε με κάποιο άλλο τρόπο επικοινωνίας (σε αντιδιαστολή με το να επικοινωνεί μόνο δίνοντας απάντηση σε μία ερώτηση);

α) Ξεκινάει μια συζήτηση τόσο συχνά όσο και πριν.

β) Ξεκινάει μια συζήτηση λιγότερο συχνά από πριν.

γ) Ξεκινάει μια συζήτηση περιστασιακά, αλλά συνήθως απλά απαντά σε άλλους.

δ) Σπάνια ή ποτέ δεν ξεκινάει μια συζήτηση.

ε) Δεν ισχύει.

2. **Περιμένει τη σειρά του σε μία συζήτηση ή έχει την τάση να μιλάει/γράφει την ώρα που μιλάει κάποιος άλλος;**

α) Περιμένει τη σειρά του όπως πριν.

β) Περιμένει τη σειρά του λιγότερο από πριν και διακόπτει τους άλλους πιο συχνά.

γ) Περιμένει τη σειρά του πολύ λιγότερο από πριν και διακόπτει τους άλλους συχνότερα.

δ) Σπάνια ή ποτέ δε περιμένει τη σειρά του και διακόπτει τους άλλους τις περισσότερες φορές.

ε) Δεν ισχύει.

3. **Εκφράζεται χρησιμοποιώντας ποικιλία λέξεων και φράσεων ή έχει την τάση να χρησιμοποιεί τις ίδιες λέξεις και φράσεις ή να λέει τις ίδιες ιστορίες ξανά και ξανά, σαν να είναι μαγνητοφωνημένες;**

α) Χρησιμοποιεί ποικιλία λέξεων και φράσεων για να εκφραστεί, όπως πριν.

β) Χρησιμοποιεί τις ίδες λέξεις και φράσεις ή λέει τις ίδιες ιστορίες πιο συχνά από πριν.

γ) Χρησιμοποιεί τις ίδες λέξεις και φράσεις ή λέει τις ίδιες ιστορίες πολύ πιο συχνά από πριν, αλλά συνεχίζει να εκφράζεται με ποικιλία λέξεων/φράσεων στις περισσότερες συζητήσεις.

δ) Επαναλαμβάνει σχεδόν πάντα την ίδια ιστορία ή χρησιμοποιεί τις ίδιες λέξεις και φράσεις. Σπάνια ή ποτέ δε χρησιμοποιεί ποικιλία λέξεων/φράσεων.

ε) Δεν ισχύει.

Παρακαλούμε προσθέστε επιπλέον πληροφορίες ή παραδείγματα:

APPENDIX III

Cyprus University of Technology

QUANTITATIVE CONNECTED SPEECH ANALYSIS IN A CASE OF NON-FLUENT/AGRAMMATIC PRIMARY PROGRESSIVE APHASIA

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Introduction

Primary progressive aphasia (PPA) is a neurodegenerative syndrome which is characterized by a relatively selective loss of language functions. In the nonfluent/agrammatic variant (nfvPPA), speech is slow, effortful and hesitant. Utterances are shorter, less complex and contain grammatical errors.

Single word production deficits in PPA have been extensively examined. However, connected speech analysis has only recently begun to be systematically studied. The evaluation of connected speech enables a multi-level naturalistic assessment of language production (Marini et al., 2011).

Objective

The aim of the present study was to investigate the connected speech deficits in a Greek-speaking person with the nfvPPA. To our knowledge, this is the first report of connected speech deficits in a Greek-speaking patient with PPA.

Participant

Participant LJ is a 60-year-old right-handed man, with 6 years of formal education. His native language is Greek. He was given a clinical diagnosis of non-fluent/agrammatic PPA according to the current criteria (Gorno-Tempini et al., 2011). His speech was slow with word finding problems, pauses and distortions. He had spared knowledge of objects and word recognition. A mild difficulty comprehending syntactically complex sentences was revealed in formal testing.

At the time of the study, he had a FTLD-modified CDR sum of boxes score of 9 (MMSE=17/30).

Material – Method

A narrative sample was collected using the 'cookie theft' picture from the Boston Diagnostic Aphasia Examination. Orthographic transcription and segmentation of the sample was made using ELAN. Dysfluent variables, such as silent and filled pauses, sound errors, repetitions and false starts were also coded. The sample was analyzed following the procedures described by Saffran et al. (1989) for quantitative production analysis (QPA).

A set of measures were used to quantify speech variables, discourse productivity, lexical content, grammatial productivity and accuracy. These included counts of dysfluencies and errors (morphological, syntactic and semantic), Guiraud's index of lexical richness, word frequency of open class words and QPA summary measures.

LJ's scores were compared to healthy neurologically controls included in a previous study by Varkanitsa (2012). T-values were calculated using the Crawford and Howell's method (Crawford and Garthwaite, 2012). The reported p-values are one-tailed.

Results

Speech rate was 40.37 words per minute.

LJ produced less nouns ($t_{(5)}$= -2.468, $p < .05$) and adverbs ($t_{(5)}$= -3.240, $p < .025$) compared to controls. On the other hand, he produced more pronouns ($t_{(5)}$= 7.406, $p < .0005$) and verbs ($t_{(5)}$= 2.546, $p < .05$). LJ used less narrative words ($t_{(5)}$= -2.089, $p < .05$) and more single word utterances ($t_{(5)}$= 7.869, $p < .0005$) to describe the picture compared to healthy subjects. Sentence productivity measures (mean length of utterance, elaboration index and embedding index) did not differ from controls (Table 1).

LJ made syntactic and speech sound errors. Syntactic errors included incomplete sentences. Dysfluencies included silent pauses, filled pauses, false starts, sound distortions and repetitions (23%, 20%, 3%, 2% and 1% of total words produced).

Table 1. Quantitative Production Analysis (QPA) measures

QPA measures	LJ	Controls (n=6) Median (SD)
Proportion of closed class words	0.52	0.53 (0.04)
Proportion of nouns	0.17*	0.25 (0.03)
Proportion of adjectives	0.04	0.02 (0.01)
Proportion of prepositions	0.02	0.06 (0.02)
Proportion of adverbs	0*	0.07 (0.02)
Proportion of pronouns	0.14**	0.06 (0.01)
Proportion of verbs	0.31*	0.20 (0.04)
MLU	4	5.41 (1.08)
Elaboration index	1	2.43 (1.43)
Embedding index	0.36	0.36 (0.17)
Number of narrative words	48*	127 (35)
Proportion of sentences	0.92	0.79 (0.11)
Proportion of utterances without verbs	0.08	0.19 (0.11)
Proportion of single-word utterances	0.17**	0.00 (0.02)
Proportion of well-formed utterances	0.75	0.96 (0.65)
Auxiliary complexity index	0.64	0.30 (0.27)

Conclusions

This case study reports differences between an individual with nfvPPA and healthy controls in lexical selection and discourse productivity measures. LJ's scores fit into the pattern of impairment reported for the nfvPPA. Connected speech analysis confirmed the presence of deficits at the phonetic/phonological and lexical level.

The study serves as an example of how connected speech analysis may be used for the evaluation of multiple linguistic levels not captured by traditional aphasia tests.

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Frontotemporal dementia: a comparative case study of Greek-speaking individuals with the non-fluent and semantic variants of primary progressive aphasia

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INTRODUCTION

Frontotemporal Dementia (FTD) is an umbrella term that encompasses degenerative disorders of the frontal and anterior temporal lobes that affect behavior and language. FTD overlaps clinically and pathologically with Primary Progressive Aphasia (PPA). PPA is a degenerative syndrome characterized by progressive loss of language function. The consensus criteria for PPA recognize three variants: the non-fluent/agrammatic variant of PPA (nfvPPA), the semantic variant of PPA (svPPA) and the logopenic variant of PPA (lvPPA) (Gorno-Tempini et al., 2011). Each PPA variant has a specific profile of language impairment, different distribution of atrophy on neuroimaging and different likelihood of underlying molecular pathology. Typically, nfvPPA is associated with fronto-insular atrophy, svPPA with atrophy of the anterior and inferior temporal lobe and lvPPA with atrophy of temporo-parietal regions. The most common types of neurodegeneration in PPA are frontotemporal lobar degeneration and Alzheimer's disease (Spinelli et al., 2017). FTD includes two out of three PPA variants, the nfvPPA and svPPA, as the most typical pathology of these variants is frontotemporal lobar degeneration.

PPA is characterized by a more partial and progressive pattern of damage than stroke-induced aphasia and targets areas such as the anterior temporal lobe that are rarely affected by stroke (Mesulam, 2016). Clinical and neuroimaging research on PPA has advanced our understanding of the language network. It has shown, for example, that the left anterior temporal lobe plays a critical role in single word comprehension and object naming and that the traditional 'Wernicke's area' is important for language repetition and sentence comprehension but not single word comprehension (Mesulam et al., 2019).

OBJECTIVE

The aim of this study is to compare the clinical presentation of the language variants of FTD, nfvPPA and svPPA, in two Greek-speaking individuals with PPA, using a comprehensive battery of neuropsychological tests and narrative analysis. Greek is a highly inflected and stem-based language, underrepresented in the literature on PPA research.

METHODS

Two individuals diagnosed with PPA and 12 neurologically healthy adults participated in this study. All participants were right-handed. The control group consisted of 2 male and 10 female native Greek speakers with a mean age of 68.08 (SD = 5.52) years and a mean of 13 (SD = 3.19) years of formal education.

Participants' Characteristics	1st Participant	2nd Participant
PPA variant:	non-fluent	semantic
Gender:	male	male
Age:	61	73
Years of education:	6	9
Years after symptom onset:	5	5
FTLD-modified Clinical Dementia Rating:	9	6
MRI atrophy:	Left perisylvian	Anterior temporal lobe (asymmetric)

Neuropsychological assessment was completed in four 45-minutes-sessions for the participants with PPA and three sessions for the control participants. MRI scans and reports were made available for the two individuals with PPA.

Areas of assessment included: executive function, memory, visuo-spatial abilities, object semantics, mood, praxis, motor speech abilities, single word and sentence comprehension, repetition, confrontation naming, reading, writing and connected speech production. Quantitative production analysis (QPA) (Saffran et al., 1989) was used for the narrative analysis of a story retell task.

Crawford and Howell's method was used to compare performance of each subject with that of the control sample (Crawford, Garthwaite & Porter, 2010). T values were also calculated to compare the scores of the two subjects with reference to the control sample (Crawford, Garthwaite & Wood, 2010).

RESULTS

Neuropsychological tasks that differed significantly between the two participants:

1st Participant (nfvPPA)*	2nd Participant (svPPA)*
Digit Span – reverse recall task (p=0.025)	Boston Naming Test-15 (p<0.001)
Clock Drawing Test (p<0.001)	Peabody Picture Vocabulary Test (p<0.001)
BDAE-3 syntactic comprehension (p=0.014)	Pyramid and Palm Trees Test (p=0.001)
Reading fluency for words (p<0.001)	*More affected

Comprehension of auditory complex material, written words and sentences was affected in the case of the 2nd participant (p=0.022, p=0.005 and p<0.001, respectively), although his ability to follow commands was within normal limits and performance for syntactic comprehension was at ceiling.

Narrative production measures that differed significantly between the participants:

- speech rate (slower for the nfvPPA participant, p=0.007)
- average pause duration (longer for the nfvPPA participant, p<0.001)
- false starts per min (more for the nfvPPA participant, p=0.045)
- proportion of nouns (lower for the svPPA participant, p=0.012)
- closed class words (lower for the nfvPPA participant, p=0.016)

Compared to the control group, the nfvPPA participant produced shorter sentences (p=0.023), fewer closed class words (p=0.006), made longer pauses (p<0.001) and spoke at a slower rate (p<0.001). The svPPA participant used fewer nouns (p=0.027), more pronouns (p=0.02) and fewer narrative words as a proportion of the total words produced (p=0.003).

DISCUSSION

The results confirm the distinctive features of both PPA variants, namely anomia, a single word comprehension deficit, preserved repetition and syntactic comprehension for the participant with the svPPA, as well as motor speech and syntactic processing difficulties alongside with intact repetition, semantic knowledge and naming ability for the nfvPPA participant.

Taking into account the neuroimaging findings, these two cases illustrate the different distribution of atrophy in the language variants of FTD and highlight the role of the left anterior temporal lobe in naming and single word comprehension.

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Comparing two cases of the non-fluent and semantic variants of primary progressive aphasia using neuropsychological, narrative and acoustic measures

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INTRODUCTION

Primary Progressive Aphasia (PPA) is a degenerative syndrome characterized by progressive loss of language function. The consensus criteria for PPA recognize three variants: the non-fluent/agrammatic variant of PPA (nfvPPA), the semantic variant of PPA (svPPA) and the logopenic variant of PPA (lvPPA) (Gorno-Tempini et al., 2011). Each PPA variant has a specific profile of language impairment, different distribution of atrophy on neuroimaging and different likelihood of underlying molecular pathology. Typically, nfvPPA is associated with fronto-insular atrophy, svPPA with atrophy of the anterior and inferior temporal lobe and lvPPA with atrophy of temporo-parietal regions. The most common types of neurodegeneration in PPA are frontotemporal lobar degeneration and Alzheimer's disease.

OBJECTIVE

The aim of this study is to compare the clinical presentation of the non-fluent/agrammatic and semantic variants of PPA, in two Greek-speaking individuals with PPA, using a battery of neuropsychological tests, narrative analysis and acoustic measures. Greek is a highly inflected and stem-based language, underrepresented in the literature on PPA research.

METHODS

Participants

Two individuals diagnosed with PPA participated in this study.

Participants' Characteristics	Case 1	Case 2
PPA variant:	non-fluent	semantic
Gender:	male	male
Age:	61	73
Years of education:	6	9
Years after symptom onset:	5	5
FTLD-modified Clinical Dementia Rating:	9	6
MRI atrophy:	Left perisylvian	Anterior temporal lobe (asymmetric)

The control group (n=12) consisted of 2 male and 10 female native Greek speakers with a mean age of 68.08 (SD = 5.52) years and a mean of 13 (SD = 3.19) years of formal education. All participants were right-handed.

Procedure

Neuropsychological battery	Narrative analysis	Acoustic analysis
• Executive function • Memory • Visuo-spatial abilities • Object semantics • Mood • Praxis • Motor speech • Single word comprehension • Sentence comprehension • Repetition • Confrontation naming • Reading • Writing	Quantitative production analysis (QPA) (Saffran, Berndt, & Schwartz, 1989)	Temporal measures

Participants with PPA: 4×45-minutes sessions

Control participants: 3×45-minutes sessions

MRI scans and reports were made available for the individuals with PPA

Statistical Analysis

- Crawford and Howell's method: comparison of each subject with the control sample (Crawford, Garthwaite, & Porter, 2010)
- T values: comparison of the two subjects with reference to the control sample (Crawford, Garthwaite, & Wood, 2010)

RESULTS

- nfvPPA participant: more impaired in working memory (p=0.025), syntactic comprehension (p=0.014) and reading fluency for words (p<0.001), slower in temporal measures of speech production (Table 1)
- svPPA participant: more impaired in confrontation naming (p<0.001), single word comprehension (p<0.001) and object semantics (p=0.001)

Table 1. Temporal measures for diadochokinetic rates, passage reading and sentence repetition

Temporal measures	Case 1 nfvPPA	Case 2 svPPA	t values	Control (n=12) Mean	(SD)
Diadochokinetic rates (repetitions/sec)					
/pa/	3.478**	8.349	-4.380	6.97	(0.74)
/ta/	3.765*	7.278	-3.029	6.93	(0.82)
/ka/	3.106**	7.145	-4.023	6.24	(0.71)
/pataka/	4.629*	7.697	-3.055	6.86	(0.71)
Passage Reading					
Passage Reading Duration	142.092**	63.701	8.386	49.44	(6.61)
Passage Reading Syll/sec	1.696*	3.783	-2.635	4.94	(0.56)
Repetition of Sentences (syll/sec)					
S1 (15 syllables)	0.223	0.164	1.989	0.17	(0.02)
S2 (11 syllables)	0.881**	0.220	17.748	0.20	(0.03)
S3 (14 syllables)	0.343*	0.161	4.100	0.18	(0.03)
S4 (16 syllables)	0.339*	0.167	4.316	0.17	(0.03)
S5 (12 syllables)	0.263	0.192	1.632	0.19	(0.03)

*p < 0.05; **p < 0.01 level of statistical significance for differences between case 1 and case 2.

Narrative production measures that differed significantly between the participants:

- speech rate (slower for the nfvPPA participant, p=0.007)
- average pause duration (longer for the nfvPPA participant, p<0.001)
- false starts per min (more for the nfvPPA participant, p=0.045)
- proportion of nouns (lower for the svPPA participant, p=0.012)
- closed class words (lower for the nfvPPA participant, p=0.016)

Compared to the control group, the nfvPPA participant produced shorter sentences (p=0.023), fewer closed class words (p=0.006), made longer pauses (p<0.001) and spoke at a slower rate (p<0.001). The svPPA participant used fewer nouns (p=0.027), more pronouns (p=0.02) and fewer narrative words as a proportion of the total words produced (p=0.003).

DISCUSSION

The results confirm the distinctive features of both PPA variants: motor speech and syntactic processing difficulties in the case of the participant with the nfvPPA, anomia and a single word comprehension deficit in the case of the participant with the svPPA. Neuropsychological testing combined with narrative and acoustic analysis have enabled the documentation of speech and language deficits present in these cases of PPA and the comparison of the two participants.

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Bilingualism in a case of the non-fluent/agrammatic variant of primary progressive aphasia

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Abstract

There is a growing body of research on language impairment in bilingual speakers with neurodegenerative diseases. Evidence as to which language is better preserved is rather inconclusive. Various factors seem to influence language performance, most notably age of acquisition, level of proficiency, immersion and degree of exposure to each language.

The present study examined fluency, lexical, discourse and grammatical abilities of a Greek-French late bilingual man with the non-fluent/agrammatic variant of primary progressive aphasia (nfvPPA). Speech samples derived from three different narrative tasks in both languages were analyzed using quantitative production analysis (QPA) and fluency measures.

The first aim of the study was to compare the participant's connected speech production to that of Greek-speaking normal controls. The second aim was to determine whether Greek (L1) and French (L2) were differentially impaired. To our knowledge, this is the first report of connected speech deficits in a Greek-speaking patient with PPA and the first study which uses QPA to compare L1 and L2 narratives in a bilingual speaker with PPA.

Compared to neurologically healthy controls, our participant was impaired in lexical, discourse and grammatical productivity measures, but did not differ in measures of grammatical accuracy. The presence of dysfluencies, reduced speech rate and simplified syntax is consistent with the pattern of impairment reported for the nfvPPA. Results showed that narrative production measures did not differ significantly between languages. However, they suggest a slightly worse performance in his second, non-

dominant, language despite a similar pattern of impairment in both languages. Lengthy exposure to L2 and regular activation of L2 through daily use may explain the preservation of discourse abilities in his non-dominant language.

This study calls attention to factors such as language dominance, proficiency, patterns of use and exposure to a language. These factors play a key role in assessing bilingual individuals with PPA and making clinical decisions.

1 Introduction

The notion of bilingualism refers to the use of two or more languages by an individual in daily life (Grosjean, 1994). First language (L1) and second language (L2) are typically the terms used to characterize languages in respect to their order of acquisition. The terms early and late bilingual classify a person according to the age at which the second language is acquired. Finally, the terms dominant and non-dominant language refer to differences in processing abilities between the two languages and/or in language use. Most researchers agree that both proficiency and use are key contributors to the bilingual experience (Treffers-Daller, 2015).

Bilingualism is a complex construct. Various factors seem to influence language performance in bilingual individuals. Factors related to L2, include age of acquisition, method of acquisition, level of proficiency in the second language and in different modalities (listening, speaking, reading, and writing), similarity to the first language and patterns of language use (e.g., Lorenzen and Murray, 2008; Goral and Conner, 2013; Kambanaros, 2016). In bilingual speakers with an acquired language disorder, language performance in L1 and L2 also depends on the underlying pathophysiology including traumatic brain injury, stroke and neurodegeneration.

Different hypotheses have been put forward to account for language representation in the brain. Evidence comes from electrophysiological investigations and neuroimaging studies of impaired and unimpaired bilingual persons, as well as clinical studies examining the effect of brain damage on language processing in bilingual speakers.

In terms of lexical processing, clinical studies support nonselective lexical access to a multilingual lexicon with shared lexical-semantic representations (e.g., Abutalebi, 2008; Kambanaros, 2016). Parallel lexical-semantic decline in cases of neurodegeneration (Hernandez et al., 2008; Costa et al., 2012) or impairment in post-stroke aphasia (Kambanaros and Van Steenbrugge, 2006; Kambanaros, 2009; Faroqi-Shah and Waked, 2010; Kambanaros, 2010; Kambanaros, 2016) are in favor of a common underlying neural network. Neuroimaging studies indicate both shared and separated brain regions for the two languages (Khachatryan et al., 2016).

As for grammar processing, researchers (Ullman, 2001; Paradis, 1994, 2008) have proposed that L1 and L2 are differentially processed as they rely on different cognitive mechanisms: L1 is acquired implicitly through immersion, whereas L2, when it is acquired later in life, explicitly through tuition. Syntactic processes are served by different brain areas, more left anterior (frontal) and subcortical (basal ganglia) regions for L1 and more posterior (temporo-parietal) cortical regions for L2. Others support

shared L1 and L2 grammatical representations which are located in common regions (Hartsuiker et al., 2004; Weber and Indefrey, 2009). Evidence from functional neuroimaging studies suggest that L2 processing may become more automatic and converge to the same neural representations of L1 through long exposure to L2 (Abutalebi, 2008). However, differences between first and second language processing have been attributed to cognitive control mechanisms, as the functional demand placed on these regions is higher for speakers of multiple languages and influenced by factors such as age of acquisition, level of proficiency and exposure to a language (Abutalebi and Green, 2007; Green and Abutalebi, 2013; Weber et al., 2016).

Evidence from brain imaging studies emphasize the role of L2 proficiency and age of acquisition in interpreting results. In studies where the level of proficiency has been controlled for, there is a higher degree of L1 and L2 overlapping activation for high-proficient than for low-proficient participants (Higby et al., 2013). The dorsolateral prefrontal cortex, anterior cingulate cortex and right inferior frontal gyrus have been associated with L2 processing in lower proficient bilinguals in a meta-analysis by Sebastian, Laird and Kiran (2011). In another meta-analysis examining the role of age of acquisition in L1 and L2 processing, Liu and Cao (2016) concluded that language networks are more divergent for late bilinguals than for early bilinguals. Regions that were found to be more involved in L2 than in L1 processing were left insula and left middle frontal, inferior frontal and precentral gyri. The left superior frontal gyrus was more recruited by late bilinguals. This result suggests reliance on wider neural resources in the case of late bilinguals.

Primary progressive aphasia (PPA) is a neurodegenerative disease in which language is selectively impaired, at least in the initial stages, providing thus a unique opportunity to study bilingual aphasia and brain representations of language (Filley et al., 2006, Machado et al., 2010). The present study sought to investigate the connected speech deficits in a Greek-French late bilingual person with the non-fluent/agrammatic variant of PPA (nfvPPA). The nfvPPA is characterized by agrammatic production and/or apraxia of speech. Object knowledge and single-word comprehension are usually spared, whereas syntactic comprehension may be impaired. According to the 2011 consensus criteria (Gorno-Tempini et.al., 2011), PPA also comprises the semantic (svPPA) and the logopenic (lvPPA) variant. Recently, primary progressive apraxia of speech (PPAOS) has been recognized as a distinct clinical entity (e.g. Duffy et al., 2014). Individuals with PPAOS present with apraxia of speech as their primary deficit and have little or no evidence of aphasia.

Single word production deficits have been extensively examined in PPA and studies of bilingualism. However, connected speech analysis has only recently begun to be systematically studied and has been used only in one study to compare performance in bilingual speakers with PPA (Zanini et al., 2011). The evaluation of connected speech enables a multi-level naturalistic assessment of language production (Marini et al., 2011). All linguistic levels, phonetics, phonology, morphology, syntax, semantics, pragmatics and discourse can be evaluated when analyzing connected speech samples. Different tasks have been used to elicit speech samples and evidence suggests that they have different specificity for addressing different linguistic levels (Boschi et al, 2017). For example, a picture description task may be more useful in documenting lexico-semantic deficits, whereas story narration tasks favor the evaluation of discourse and

syntactic abilities. Spontaneous speech production tasks are more sensitive to morphological, syntactic and discourse level deficits, as in unconstrained tasks it is easier for speakers to compensate for their word-finding difficulties.

Deficits in the nfvPPA can arise at the phonetic-phonological level and manifest as a motor speech impairment and/or at the lexical-semantic, morphosyntactic, syntactic or discourse level and present as agrammatism. Boschi et al. (2017) reviewed the evidence from studies focusing on connected speech deficits in neurodegenerative disorders. People with the non-fluent/agrammatic variant of PPA typically speak at a slower speech rate than healthy controls and make frequent speech sound errors (Ash et al., 2009; Wilson et al., 2010; Rogalski et al., 2011). At the lexical level, an increased number of errors in closed class words has been reported (Knibb et al., 2009; Meteyard and Patterson, 2009; Sajjadi et al., 2012). At the syntactic level, they make grammatical errors (Graham et al., 2004; Sajjadi et al., 2012) and produce simplified sentences with lower number of words per utterance, clauses, verb phrases and coordinated sentences (Knibb et al., 2009; Wilson et al., 2010; Fraser et al., 2014). Concerning discourse abilities, individuals with the nfvPPA produce a reduced number of words, limited relevant information and they have difficulty maintaining the topic (Graham et al., 2004; Wilson et al., 2010; Sajjadi et al., 2012; Ash et al., 2013; Fraser et al., 2014).

Apart from allowing a multi-level evaluation of the speech and language deficits observed in PPA, connected speech measures enable comparison of patterns of impairment in different languages. For these reasons connected speech analysis has been deemed appropriate for the evaluation of narrative production in our bilingual subject with the nfvPPA. For the structural analysis of connected speech, we used the Quantitative Production Analysis (QPA) (Saffran et al., 1989). QPA was first used to describe agrammatic speech but has been found useful in identifying differences between fluent and non-fluent types of aphasia (e.g. Varkanitsa, 2012) and has been successfully applied in distinguishing normal from aphasic production and differentially diagnosing PPA variants (Wilson et al., 2010). An additional set of fluency measures, error analysis and macrolinguistic measures were also used to allow for a more thorough documentation of the deficits observed in nfvPPA.

A small number of case studies on bilingual speakers with PPA have been published in recent years (Filley et al., 2006; Hernandez et al., 2008; Machado et al., 2010; Zanini et al, 2011; Larner, 2012; Druks and Weekes, 2013). Kambanaros and Grohmann (2012) published a case study of a multilingual man with fluent PPA, highly proficient in three languages, Greek, English, and Czech. He was more impaired in L3 than L2 and L1, and more impaired in L2 than in L1. In other words, the extent of impairment in each language was correlated with the order of acquisition. In a short report Machado et al. (2010) presented a Portuguese-French bilingual speaker with PPA. He was impaired in both languages. Performance was overwhelmingly better in his L1 which was also his dominant language. Larner (2012) in another short report, described a Welsh-English speaker who used her L1 in daily communication although L2 was her dominant language. In a more detailed study, Hernandez et al. (2008) presented a Spanish-Catalan early bilingual individual with nfvPPA. They found a naming deficit which was more pronounced for L2 than for L1 at first assessment, but a parallel pattern of decline in both languages, even though L2 deteriorated more rapidly. A grammatical category-specific deficit was present in both languages with an advantage in noun naming over

verb naming. A Hungarian-English late bilingual speaker with nfvPPA was reported by Druks and Weekes (2013). Their participant was more impaired in L2 which was his dominant language. A parallel deterioration was found for lexical and grammatical knowledge in L1 and L2. Zanini et al. (2011) described a case of an early Friulian-Italian bilingual woman with nfvPPA. They analyzed her spontaneous speech production and found more phonemic paraphasias, morphological and syntactic errors in L2 than in L1. They reported similar scores for number of dysfluencies, discourse productivity, grammatical productivity and lexical selection measures (i.e., total words, utterances, subordinate clauses and open-class words) in both languages. Only Filley et al. (2006), who presented a Chinese–English-speaking woman with the logopenic variant of PPA, have reported a non-significant better performance for repetition, naming and conversation tasks, but more phonemic paraphasias, in L2 which was her dominant premorbid language. A parallel pattern of deterioration was observed in both languages. To conclude, most of these studies have found evidence of greater impairment in L2, irrespectively of language dominance and age of acquisition, indicating that L2 may be more vulnerable to degeneration than L1.

In the context of neurodegenerative diseases, there is also a growing body of group studies on language impairment in bilingual speakers with Alzheimer's Disease (AD). The available evidence is mixed. Some studies report parallel deterioration (Salvatierra et al., 2007; Costa et al., 2012; Manchon et al., 2015; Nanchen et al. 2017), while others report differential deterioration of the two languages (Mendez et al. 1999; Gollan et al., 2010). In the study by Gollan et al. (2010), bilingual persons with AD exhibited greater decline in the dominant than the non-dominant language. An opposite pattern was found by Mendez et al. (1999). Based on caregivers' reports, they concluded that the non-dominant language was more affected than the dominant language. Ivanova et al. (2014) found different longitudinal and cross-sectional patterns of decline. The non-dominant language declined more than the dominant language, but differences between patients and controls were greater for the dominant than for the non-dominant language. The authors concluded that both languages are affected by AD with different trajectories of decline over time.

The aim of the present study was twofold. First, to provide an account of connected speech deficits in the non-fluent variant of PPA in Greek. The participant's speech and language deficits in his native language were examined by comparing performance on connected speech elicited from a picture description task with speech samples obtained from a healthy control group on the same task. Second, to compare performance in Greek and French and evaluate impairment patterns in both languages connected speech samples from three different narrative tasks in each language were elicited. To our knowledge, this is the first report of connected speech deficits in a Greek-speaking patient with PPA and the first study which uses QPA to compare L1 and L2 narratives in a bilingual speaker with PPA.

The two languages differ in several respects. Greek is classified as an independent branch within the family of Indo-European languages, whereas French belongs to the Romance branch of the Indo-European family. The components of morphology and syntax are especially relevant to our study. Subject-verb-object (SVO) order is the basic word order in both languages. Word order is flexible in Greek, whereas French has a relatively strict word order. Moreover, Greek is a null subject language, i.e. subjects are

not typically expressed when they can be inferred from the context (Roberts and Holmberg, 2010). On the other hand, French is a non-null subject language which requires an explicit subject in a sentence. Regarding morphology, Greek is a highly inflected language, whereas French is considered to be a moderately inflected language. The main difference between the two languages is that in Greek nouns, pronouns and adjectives are inflected not only for number and gender but also for case. Case in French is expressed using mainly word order and prepositions (Prévost, 2009), although there is a morphological case marking system for weak object pronouns (clitics).

Despite the different linguistic properties of Greek and French, which may result in differences in the narrative measures (e.g. higher proportion of pronouns in French than in Greek because of the mandatory inclusion of subjects in sentences), we predict a similar pattern of impairment in both languages. We also predict that L2, the participant's non-dominant and less proficient language, will be affected to a greater degree compared to L1.

2 Materials and methods

2.1 Participant

Participant LJ is a chef in his early sixties, with 6 years of formal education. He is a right-handed late bilingual whose native language (L1) is Greek. At the age of 25, he moved to a French-speaking country and worked as a cook in a French-speaking environment for 7 years. On his return to Greece, he continued to use French (L2) both at work and at home with his wife who is a French native speaker. Details about his language history and proficiency were collected from his wife upon completion of the French version of the Language Experience and Proficiency Questionnaire (Marian et al., 2007) (table 1). Language dominance was determined based on the reported proficiency and extent of language exposure. Task specific measures of proficiency (for understanding, speaking and reading), across settings measures of language exposure (to family, friend, reading and television) and global measures of these two dimensions were all taken into account in order to ascertain language dominance.

Insert Table 1 here

LJ reported a progressive deterioration of speech and language functions. Language impairment was the primary impairment for at least the first two years. LJ was initially assessed five years after symptom onset. He received a comprehensive evaluation including case history, neurological examination and neuropsychological testing coordinated by the second author who is a psychiatrist specialized in memory disorders with extensive experience working with patients with degenerative diseases. He was referred for speech and language evaluation and completed an initial language assessment performed by the first author in Greek. He was diagnosed with PPA, as neuroimaging results ruled out other causes of focal brain damage and extensive white matter disease (see figure 1) and was given a clinical diagnosis of non-fluent/agrammatic PPA according to current criteria (Gorno-Tempini et al., 2011). There were no signs of limb apraxia, tremor, dystonia and myoclonus. There was a very mild hypertonicity on the right side, as well as reports of becoming more suspicious of

others. His speech was slow with word finding problems, hesitations, pauses and sound errors. Motor speech evaluation determined the presence of apraxia of speech with slow overall rate, deliberate, slowly sequenced speech sequential motion rates in comparison to speech alternate motion rates, imprecise articulation with sound distortions, a tendency to equalize stress across syllables, false starts and restarts and sound and syllable repetitions. Dysarthria, most probably spastic, was present, but less severe than apraxia of speech. LJ had spared knowledge of objects and word recognition. A mild difficulty comprehending syntactically complex sentences was revealed in formal testing. His consensus score on the Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2010) was 7 (see table 2). Background linguistic and neuropsychological evaluation results are presented in Table 3.

Insert Figure 1 here

Insert Table 2 here

Insert Table 3 here

Prior to testing for the present study, LJ had received speech and language therapy for approximately 4 months. Intervention included partner education, script training (Youmans et al., 2005) of telephone conversations with clients and techniques based on the 'Oral Reading for Language in Aphasia' treatment program (Cherney, 2010) that addressed production of multisyllabic words, as well as reading and auditory comprehension. Treatment was delivered in Greek.

The present study was conducted 9 months after the initial evaluation (5 years and 9 months after the reported onset of the disease) and 3 months after the last therapy session. At the time of the study, LJ had a FTLD-modified CDR sum of boxes score of 9 (MMSE=17/30). The Montreal Cognitive Assessment (MOCA) was administered both in Greek and French. He received a score of 18/30 in Greek and 20/30 in French (one additional point in visuospatial/executive function and one in memory). He generated 2 words in the phonemic verbal fluency task and 5 words in the semantic task (animals) and obtained a score of 3 on the forward digit span and 0 on the backward digit span. There was also a parallel deterioration of motor skills. These results suggest a deterioration in cognitive function, especially in the domain of executive function and progression of the nfvPPA to a corticobasal syndrome. Corticobasal syndrome can overlap clinically and pathologically with PPA and many cases initially classified as nfvPPA, meet the criteria for corticobasal syndrome at a later stage (Grossman, 2010; Duffy et al., 2014; Leyton and Ballard, 2016; Santos-Santos et al., 2016).

The study was approved by the ethics committee of the Athens Alzheimer's Association. The research was conducted in accordance with the latest version of the Declaration of Helsinki. LJ was informed about the purpose and procedures of the study and gave written consent for participating in the study, as well as for the recording and publication of his clinical data. Both LJ and his wife gave written informed consent for the publication of this manuscript. The initials LJ are fictional.

2.2 Elicitation and transcription of speech samples in L1 (Greek) and L2 (French)

Three different speech samples were collected in both Greek and French, under 3 conditions: a picture description task ('cookie theft', from Boston Diagnostic Aphasia Examination, BDAE), a story retell task (the dog story protocol from the Multilingual Assessment Instrument for Narratives, MAIN, Gagarina et al., 2012; 2015) and a semi-spontaneous speech task where LJ was asked to talk about his job. Interruptions and questions by the examiner (first author) were kept to a minimum. The examiner is a monolingual Greek-speaking clinician who is also a proficient speaker of French. Samples were collected in 4 sessions, first for the Greek language and 2 weeks later for French. All samples were audio-recorded.

Speech samples were transcribed orthographically using ELAN (Sloetjes and Wittenburg, 2008). Phonological paraphasias unintelligible or incomprehensible words were transcribed phonetically using the International Phonetic Alphabet. Dysfluent variables, such as silent and filled pauses, sound errors, repetitions and false starts were also coded.

2.3 Quantitative analysis of speech samples

Speech samples were analyzed following the procedures described by Saffran et al. (1989) for quantitative production analysis (QPA) (Saffran et al., 1989; Berndt et al., 2000, Rochon et al., 2000). The QPA procedures were followed for all samples, with the exception of the direct discourse utterances produced in the story retell task, which contrary to the QPA instructions were not excluded, as these structures were modelled in story-telling. Narrative samples were formed by extracting comments on the narrative, direct responses to the examiner, repetitions of the examiner's utterances, stylistic and dysfluent repetitions, subsequently repaired utterances and discourse markers. The narrative samples were then segmented into utterances based on semantic, syntactic and prosodic information. Utterances and narrative words were used in subsequent analysis.

The QPA summary measures were classified into four categories: discourse productivity, sentence productivity, grammatical accuracy and lexical selection (Gordon, 2006). A set of additional measures were used to quantify dysfluent speech and narrative variables.

2.3.1 Speech rate and other fluency variables

Speech rate for each sample was calculated by dividing total completed words by sample duration in minutes. Samples were timed, and total time duration was computed by subtracting the examiner's interjections.

Pauses longer than 1 second were coded according to QPA instructions and counted for the calculation of the pause frequency measure. However, a threshold of 0.250 ms was used in the calculation of pause duration (De Jong and Bosker, 2013) and speaking time was calculated by subtracting silent pausing time from total time in order to control for the effect of pauses. Articulation rate was computed by dividing total completed words by speaking time.

Speech sound errors included distortions, which were defined as phonetic errors resulting in distorted phonemes, and phonological paraphasias defined as words with non-distorted phonemic insertions, deletions or substitutions. Whole-word immediate repetitions were counted as dysfluent repetitions. Words or phrases repeated later in the narratives were counted as speech repairs. Partially produced words were coded as false stars and small words, such as 'eh', as filled pauses.

Speech samples were of different duration and direct comparison of the aforementioned frequency measures was not possible. Thus, these measures were calculated as proportions of total words produced. They were also corrected for speaking length by dividing dysfluency counts by speaking time (De Jong, 2016).

2.3.2 Discourse measures

QPA discourse productivity measures included speech rate, number of narrative words, and proportion of narrative to total words produced, as a measure of discourse efficiency.

An additional discourse variable, Guiraud's index (the square root variant of Type-Token Ratio, TTR) was also measured. Guiraud's index is a measure of lexical richness that is less affected by sample size/length in comparison to TTR (Van Hout and Vermeer, 2007). This was derived by dividing the number of unique words (types) by the square root of narrative words (tokens). Number of unique words (types), lemmas and utterances are also reported.

2.3.3 Lexical measures

Grammatical category class (closed/open class, nouns, verbs, adjectives, adverbs, pronouns, prepositions, conjunctions) was coded for each narrative word. Their proportion was calculated by dividing the number of words in each category by the number of narrative words. Nouns, verbs and adjectives were considered as open class. All other words were counted as closed class. Proportion of verbs to nouns and verbs was also computed. Proportion of pronouns was derived by dividing the number of pronouns by the total number of nouns and pronouns.

Finally, mean log word frequency of open class words was calculated for each narrative sample. Calculations were based on data about word frequencies per million taken from the 'ILSP PsychoLinguistic Resource' for the Greek language (Protopapas et al., 2012) and 'Lexique' for the French language (New et al., 2001).

2.3.4 Grammatical measures

QPA sentence productivity measures encompass proportion of words in sentences, mean utterance length (in words), median utterance length (in words), sentence elaboration index (number of open class words per phrase for noun and verb phrases) and an embedding index (proportion of embeddings to sentences).

QPA grammatical accuracy measures consist of proportion of well-formed sentences, verb inflection index (proportion of inflectable verbs inflected) and determiner index (proportion of determiners produced in obligatory contexts). The auxiliary complexity index, a measure of morphological complexity of the main verb indicating change from its base form, was also calculated.

2.4 Macrolinguistic analysis (MAIN)

Narrative assessment focused on the analysis of microlinguistic aspects of language production. Macrolinguistic aspects were addressed for the 'Dog story' retell task with the story structure score and the structural complexity measures proposed by MAIN (Gagarina et al., 2012; 2015). Although the MAIN was originally designed to assess narrative skills of bilingual children, it is controlled for macro-and microlinguistic features across Greek and French. As there is no other standardized procedure for adults, it was deemed appropriate for comparing story retell abilities in both languages.

The 'Dog story' starts with a setting statement and consists of three short episodes. Each episode consists of an initiation, a goal, an attempt, an outcome and a reaction statement. Credit is given for the production of each initiation, goal, outcome, reaction when computing the story structure score.

Five measures of structural complexity, included in the MAIN, were calculated: number of sequences where an attempt and outcome statement has been generated (but no goal), number of single goal statements, number of incomplete episodes which they include a goal and an attempt statement sequences, number of incomplete episodes which they include a goal and an outcome statement, and number of complete episodes which include all three goal-attempt-outcome components. Comprehension of the story structure was also assessed by means of questions targeting the main macrostructure components.

2.5 Error Analysis

The following type of errors were also identified and measured as a proportion of narrative words.

- Syntactic errors were recorded when LJ produced ungrammatical sentences.
- Morphological errors, affecting articles, nouns, adjectives and verbs, were counted separately.
- Semantic errors included selections that were semantically inappropriate for the context.
- Code switching errors were defined as words produced in languages other than the target language (number of tokens not in the target language).

Some morphological errors in L2 (article-noun gender agreement) occurred with the same nouns. These persistent errors were not included in individual error counts but contributed to the calculation of the total number of errors.

2.6 Inter-rater reliability

Analysis of 30% of the Greek speech samples was completed by 2 additional raters both native speakers of Greek with some linguistic training. Spoken word interrater reliability ranged from 90% to 95%. A consensus for each point of disagreement was reached through a discussion between the raters.

2.7 Control group for QPA

QPA measures for the picture description task in Greek were compared to the measures of a control group included in a previous study by Varkanitsa (2012). Varkanitsa used the QPA protocol in order to compare the connected speech of Greek-speaking persons with aphasia following stroke to that of neurologically healthy adults. The same picture description task was used in the present study to elicit speech samples. Taking into account the fact that in Greek isolated verbs may constitute grammatical utterances, Varkanitsa categorized utterances as 'utterances with verb', 'utterances without verb' and 'single-word utterances'. The QPA protocol was applied without other modifications. The control group consisted of six normal native Greek speakers (3 males and 3 females) with a mean age of 61.17 (SD = 5) years and a mean of 9 (SD = 4.15) years of education.

There was no control group for QPA measures in French, as we did not have access to a French-speaking population and published studies, which have applied QPA in French-speaking individuals, have not used the same methodology. For this reason, our analysis focused on the pattern of deficits observed in the two languages. Moreover, careful consideration was given to cross-linguistic differences.

2.8 Statistical analysis

LJ's narrative scores for the picture description task in Greek were compared to the scores of a neurologically healthy control group (Varkanitsa, 2012). T-values were calculated using Crawford and Howell's method which enables the comparison of performance of a single subject with that of a small control sample (Crawford and Garthwaite, 2012). Differences between LJ's performance in Greek (L1) and French (L2) were calculated using the Wilcoxon signed-rank nonparametric test for related samples because of the small sample size. Finally, scores from both languages were collapsed and correlations between errors and fluency, lexical productivity, grammatical accuracy and productivity measures were calculated using the nonparametric Kendall's tau-b correlation coefficient due to the limited number of samples used in the analysis.

3 Results

3.1 QPA measures for the picture description task in Greek – comparison to healthy subjects

LJ's scores for the picture description narrative in Greek are presented in table 4. His speech rate was slow, 40.37 words per minute. In the picture description task, he made two syntactic errors. Both errors involved the omission of obligatory post-verbal arguments. He also made speech errors. Dysfluencies included silent pauses, filled

pauses, false starts, sound distortions and repetitions (23%, 20%, 3%, 2% and 1% respectively of total words produced). Compared to the control group, LJ used less narrative words ($t_{(5)}$= -2.089, $p < .05$) and more single word utterances ($t_{(5)}$= 7.869, $p < .0005$) to describe the picture. Sentence productivity measures (mean length of utterance, elaboration index and embedding index) did not differ from controls. LJ produced less nouns ($t_{(5)}$= -2.468, $p < .05$) and adverbs ($t_{(5)}$= -3.240, $p < .025$). On the other hand, he produced more pronouns ($t_{(5)}$= 7.406, $p < .0005$) and verbs ($t_{(5)}$= 2.546, $p < .05$) than the control speakers.

Insert Table 4 here

3.2 Comparison of L1 and L2

Statistical analysis using the Wilcoxon signed-rank test revealed that the connected speech measures used to quantify speech production in L1 and L2 did not differ significantly across languages.

3.2.1 Fluency measures

The mean duration of narratives was 2.24 (SD = 0.09) minutes for L1 and 3.76 (SD = 1.86) for L2. Pause duration, for pauses >0.250ms, was 0.74 (SD = 0.11) minutes for L1 and 1.27 (SD = 0.36) for L2. Speaking time was 1.5 (SD = 0.08) minutes for L1 and 2.49 (SD = 1.58) for L2. Speech rate was faster for L2 than for L1, 44.10 (SD = 5.96) and 38.24 (SD = 2.52) words per minute (wpm), respectively. Similar results were noted for articulation rate: 73.00 (SD = 19.09) wpm for L2 and 57.43 (SD = 6.93) wpm for L1. However, these differences were not statistically significant.

Dysfluencies included silent pauses, fillers, false starts, distortions and immediate repetitions of whole words and in particular closed class words. The different types of dysfluencies are presented in figure 2.

Insert Figure 2 here

Although differences between languages did not reach statistical significance, there is a trend towards making more repetitions in L2, 0.040 (SD = 0.012) than in L1, 0.004 (SD = 0.007).

3.2.2 Discourse measures

LJ produced longer narratives in L2 than in L1, 94.67 (SD = 68.06) words and 16.33 (SD = 10.12) utterances versus 53.00 (SD = 8.66) words and 11.00 (SD = 3.61) utterances, respectively. Differences were not significant. From the narrative words, 47.00 (SD = 11.36) words in French and 34.33 (SD = 3.22) words in Greek were unique. Proportion of narrative to total words produced was 0.61 (SD = 0.07) in L1 and 0.55 (SD = 0.21) in L2.

3.2.3 Lexical measures

Regarding word class production, significant differences between L1 and L2 were not found. However, LJ produced more closed class words and pronouns in L2 compared to L1 narratives. In French, the proportion of closed class words was 0.56 (SD = 0.01), while in Greek, it was 0.49 (SD = 0.03). The proportion of pronouns was 0.22 (SD = 0.04) in L2, as opposed to 0.12 (SD = 0.04) in L1. LJ produced personal, demonstrative, indefinite and interrogative pronouns. In L1, all demonstrative pronouns (37.5%) were used as subjects, whereas all the rest, including personal pronouns (50%) in their weak form, were produced as object pronouns (62.5%). Of all the pronouns produced in L2, 87.7% were personal pronouns and 8.78% demonstrative. 94% of the personal pronouns were used in their strong form and the remaining 6% in their weak form. In L2, 87.7% of the pronouns produced were subject pronouns and 12.3% object pronouns.

LJ used more nouns per narrative words in Greek, ranging from 0.17 to 0.31 with a mean of 0.26 (SD = 0.08), in comparison to his L2 in which the proportion of nouns was 0.17 (SD = 0.04), ranging from 0.12 to 0.20. The proportion of verbs produced did not differ across languages (see Table 5).

Insert Table 5 here

LJ used more high frequency words in French than in Greek narratives. The mean logarithmic frequency of French open class words was 1.71 (SD = 0.17), as opposed to 1.392 (SD = 0.15) for Greek words. This difference was not statistically significant.

3.2.4 Grammatical Productivity and Accuracy measures

With regard to measures associated with grammatical production, no statistically significant differences were found between L1 and L2. Mean and median length of utterance in words was 5.12 (SD = 1.53) and 4.17 (SD = 1.04) for Greek and 5.58 (SD = 0.59) and 5.00 (SD = 1.00) for French respectively. LJ performed more poorly in L2 than in L1 as far as the proportion of embedded clauses is concerned (0.19 (SD = 0.08) for L2 and 0.34 (SD = 0.17) for L1).

3.2.5 Macrolinguistic measures for MAIN

The MAIN story structure and comprehension scores were 7/17 and 10/10 in L1 and 9/17 and 7/10 in L2, respectively. LJ produced one single goal statement in both languages. In French, he also used a sequence with an attempt and outcome statement. Neither incomplete episodes with a goal and an attempt/outcome statement nor complete episodes (with all three components) were present in his narratives.

3.2.6 Error analysis

Systematic errors involving article gender agreement in L2 were excluded from analysis.

LJ made more morphological and semantic errors per narrative words in L2, 0.031 (SD = 0.025) and 0.022 (SD = 0.006), respectively, than in L1, 0.014 (SD = 0.024) and

0.005 (SD = 0.009), respectively. These differences were not statistically significant. Syntactic errors were stable across languages, 0.026 (SD = 0.016) for L1 and 0.023 (SD = 0.008) for L2.

Code switching was evident in one speech sample (spontaneous narrative) in French. LJ produced 11 out of the 166 complete words in Greek.

3.3 Correlational Analysis

We undertook correlational analyses between errors and connected speech measures. Syntactic errors were significantly correlated with the total number of dysfluencies per total words ($\tau b = 0.733$, $p = 0.039$), whereas morphological errors with the distortions produced per articulation minute ($\tau b = 0.966$, $p = 0.007$). Finally, there was a positive correlation between semantic errors and number of complete words ($\tau b = 0.867$, $p = 0.015$).

4 Discussion

The present study examined fluency, lexical content, discourse and the grammatical abilities of a Greek-French late bilingual man with non-fluent/agrammatic PPA by analyzing speech samples derived from three different discourse tasks in both languages.

The first aim of the study was to compare the participant's performance to normal controls in L1. Compared to Greek-speaking neurologically healthy individuals, LJ was impaired in discourse and grammatical productivity measures, but did not differ in measures of grammatical accuracy. At the lexical level, there were some significant differences in the proportion of grammatical class words produced. In particular, LJ produced more verbs and pronouns, but less nouns and adverbs. However, proportion of closed class words was normal.

The second aim of the study was to determine whether or not L1 and L2 were differentially impaired. Results showed that discourse production measures did not differ significantly between languages. These findings indicate that both languages were similarly affected.

4.1 Comparison with healthy controls in L1 (Greek)

LJ produced a smaller number of narrative words, shorter utterances and simplified sentences compared to controls, as indicated by the MLU, proportion of single-word utterances and elaboration index measures. Production of embedded clauses was at the same level with the control group. The auxiliary complexity index, a measure of verb morphological complexity, was slightly higher for LJ than controls. However, the proportion of single-word utterances is the only grammatical productivity measure that reached statistical significance. Grammatical accuracy did not differ between LJ and neurologically healthy individuals, even though he produced a lower proportion of well-formed utterances. In the picture description task in Greek, LJ made two errors. Both

errors were syntactic in nature and involved the omission of obligatory post-verbal arguments. Taken together, these results indicate an impairment at the discourse and grammatical productivity levels.

Fluency, as measured by speech rate and frequency of dysfluent errors, is another area that was affected. Although we had no control data for the fluency variables, slow speech rate and high proportion of pauses and fillers corroborate reduced fluency. Indicatively, a normal speech rate of 143.70 (SD = 23.40) wpm has been reported for the 'cookie theft' description task in a study by Fyndanis, Varlokosta and Tsapkini (2013). The measure was based on three neurotypical Greek-speakers with a mean age of 58 (SD = 9.64) years. The presence of distortions and false starts indicate an underlying motor speech problem, apraxia of speech in particular (Ogar et al., 2007; Wilson et al., 2010).

Differential impairment of nouns and verbs has been reported in aphasia resulting from stroke and PPA. In particular, disproportionate impairment of naming actions is commonly associated with non-fluent types of aphasia (Kambanaros, 2010) and greater verb naming impairment has been found in nfvPPA (Hillis et al., 2006; Ash et al., 2009; Thompson et al., 2012). Even though LJ used more verbs than nouns during the picture description task in Greek, indicating an opposite pattern of noun-verb dissociation, mean noun-verb ratio from all three Greek speech samples was within normal limits. In fact, higher proportion of verbs seems to be task-related, as disproportionate production of verbs was evident in both languages for the picture description task only. Normal ratios of nouns to verbs in connected speech of individuals with the nfvPPA have been reported in several studies (Graham et al., 2004; Meteyard and Patterson, 2009; Knibb et al., 2009; Fraser et al., 2013; Marcotte et al., 2017).

LJ also used more pronouns in Greek (0.14 per narrative words, 80% demonstrative, 20% personal) than the control group in the picture description task. Increased proportion of pronouns has been found in svPPA and it has been suggested that it may indicate lexical retrieval deficits, vague, or non-specific speech (Kavé et al., 2007; Meteyard and Patterson, 2009; Wilson et al. 2010; Fraser et al., 2014). Nevertheless, all the pronouns used by LJ had clear referents. Furthermore, all the demonstrative pronouns were used in the subject position of sentences. In a null subject language like Greek, demonstrative pronouns may be used as subjects to place additional emphasis on the referent. The production of overt subjects in Greek could reflect the influence of the syntactic properties of the participant's L2 on his L1. Syntactic attrition effects have been reported in the production of preverbal subjects in a group of Greek (L1) speakers, highly proficient in English (L2) (Tsimpli et al., 2004). However, in the personal monologue LJ produced a substantially lower proportion of pronouns (0.08 per narrative words) than in the two picture-based tasks. This most probably suggests that LJ was using demonstrative pronouns to direct the attentional focus to the referent in the depicted scenes. It must be noted that, although the examiner's instruction for the picture description task was "tell me everything you see going on in this picture", for the story retell task, the instructions focused on the story itself, not the pictures ("Can you tell me the story?", "Tell me more."). Picture-based tasks have been reported to result in the production of descriptions of the depicted items, rather than narrative samples (Bryant et al., 2016).

Wilson et al. (2010) used a similar methodology to ours by combining QPA and fluency measures to analyze narrative production of 50 English-speaking individuals with PPA. Speech samples were elicited through a picture description task. They found that their nfvPPA group compared to normal controls spoke slower, produced less words and their samples were of longer duration. All nfvPPA participants made distortions and more filled pauses than controls. Their mean length of utterances and number of embeddings were significantly reduced. In respect to the other variants of PPA, the authors concluded that the presence of distortions was the most informative measure for distinguishing between the nfvPPA and lvPPA. Additional measures that may assist in differentially diagnosing these subtypes are proportion of verbs and number of embeddings, which are higher in the lvPPA. Faster speech rate, less distortions, higher proportion of pronouns and verbs and nouns of higher frequency were found in the svPPA compared to the nfvPPA.

LJ's scores support the pattern of impairment reported for the nfvPPA variety. In comparison to neurotypical controls, he made distortions, spoke slower, produced less words and more single word utterances. Although agrammatism has been described as a core characteristic of this variant (Ash et al., 2009; Thompson et al., 2012), grammatical deficits may not be the primary feature of nfvPPA (Graham et al., 2004; Patterson et al., 2006; Wilson et al., 2010). In a recent study, Graham et al. (2016) evaluated fluency and grammatical production in nine individuals with nfvPPA. They reported that frank agrammatism was not always present and reviewing the literature they pointed out that grammatical abilities in persons with the nfvPPA show a high degree of variability. Nevertheless, researchers have consistently reported reduced speech rate, as well as simplified syntax and shorter utterances in connected speech in comparison to healthy controls (Ash et al. 2009, 2010, 2013; Knibb et al., 2009; Wilson et al., 2010; Marcotte et al., 2017).

4.2 Comparison of L1 and L2

The observed differences between L1 and L2 did not reach statistical significance, contrary to our hypothesis. This may be due to the small sample size of linguistic data or the between-task variability. Alternatively, findings may be interpreted as indicating a similar degree of impairment in both languages. Before commenting on this finding, there are some trends in the results that are worth mentioning.

The total number of dysfluencies was similar across languages. However, LJ produced more immediate repetitions in L2 than in L1. He repeated mostly personal pronouns at the beginning of utterances, or after silent pauses. In French, personal pronouns are short monosyllabic words, like 'je' /ʒə/ (I), 'il' /il/ (he), 'elle' /ɛl/ (she). In this case, repetitions seem to be a manifestation of speech initiation difficulty and may be considered as false starts. They were counted separately, though, because of the definition we used; only partially repeated words were counted as false starts. Had they been clustered together, we would not have found a differential pattern of impairment in L1 and L2 for repetitions nor false starts.

LJ produced more filled pauses in L1 than in L2. Pauses are considered to be indicative of cognitive or linguistic processing difficulties (Krivokapi, 2007; Davis and Maclagan,

2009). In PPA, pauses have been associated with discourse, syntactic and motor speech planning, as well as word retrieval difficulties (Wilson et al., 2010; Mack et al., 2015). Given the fact that the underlying conceptualization process is the same in both languages, this finding cannot be attributed to different level of discourse processing abilities in L1 and L2. Results from the MAIN support a similar pattern of structural discourse deficits in both languages. Similarly, it cannot be attributed to differences in motor speech planning or articulation difficulties. In fact, distortions, which have been linked to apraxia of speech (Ogar et al., 2007; Duffy, 2013), were present to the same extent in both languages. The higher proportion of filled pauses in L1 could suggest a greater word finding problem in L1 compared to L2. However, LJ produced more nouns (as a proportion of narrative words) in L1 than in L2, while proportion of verbs was the same in L1 and L2. Furthermore, LJ used words of higher frequency in L2. This may indicate different levels of proficiency in L1 and L2. It must be noted here that lexical diversity was similar in both languages and that LJ made more semantic errors in L2. Greater number of filled pauses in L1 than in L2 may thus be explained with respect to the use of low frequency words and complex syntactic structures (Levelt, 1983; Ferreira et al., 1996), which is the case for the L1 narratives.

LJ produced a higher proportion of closed class words in L2 than in his L1 narratives. Nevertheless, this result must be interpreted by taking into account the increased rate of pronouns in L2. The proportion of pronouns was almost double in L2, but this can be explained by the underlying differences between French and Greek. As previously mentioned, Greek is a null subject language, whereas in French the inclusion of a subject is obligatory, and pronouns are commonly used to denote the subject in a sentence. Moreover, in the story retell task in L2, LJ was repeatedly using a double subject (both a noun and a pronoun as a subject), e.g., ‘The boy he was...’, ‘the mouse it went...’. The frequent use of subject doubling (double subject marking) may have inflated this measure.

In terms of discourse productivity, LJ produced longer narratives in L2 than in L1. However, proportion of narrative to total words was higher in L1 than in L2. This suggests that he was more efficient in getting his message across in L1 than in L2. Grammatical productivity was also better in L1. His sentences in Greek were more elaborate and complex, as indicated by the higher elaboration and embedding indexes in L1.

4.3 General discussion

Summarizing the information in respect to language acquisition and use, LJ is a late bilingual speaker who acquired French in adulthood through formal instruction and a 7-year-long day-to-day exposure in a French language environment. He has been using both Greek and French on a daily basis ever since, residing in a Greek-speaking country. Taking into account his wife’s evaluation of level of proficiency in L1 and L2, and current exposure to both languages, Greek, LJ’s first language, is his dominant language. Greek was designated as his more proficient language on the global measure of language proficiency and received a higher total score on task specific measures (11/30 in comparison to 10/30 for French). LJ has never attained fluency in reading and does not write in French. However, LJ was evaluated as being equally proficient in

speaking in both languages. Language exposure to the two languages was rated as equal on the respective global measure, whilst, across different settings, language exposure to Greek (28/60) was higher than to French (21/60). Yet, the same extent of exposure to L1 and L2 was reported for interaction with his family. Even though there are skills in which LJ is equally competent in both languages and settings in which both languages are used at the same extent, taken together these results suggest that Greek is his dominant language. These results underly the complexity of the bilingual experience and illustrate the difficulty in determining language dominance that has been attested by several researchers (Treffers-Daller, 2015).

In the present study, we predicted a similar pattern of impairment in both languages and a greater impairment in L2. Altogether, results suggest a slightly worse performance in LJ's second, non-dominant language for lexical and grammatical production and the presence of a similar pattern of impairment in both languages. Our predictions are therefore only partially supported.

According to Ullman (2001), L1 lexical processing is based on declarative memory, whereas syntactic and morphological processing on procedural memory. This is also the case for L2 when it is acquired at an early age. Given the fact that LJ is a late bilingual speaker, we would expect him to rely more on declarative memory for complex syntactic and morphological processing in L2 and on procedural memory processes for grammatical processing in L1. Increasing reliance on explicit processing for L2 could also be expected because French was learned formally (Paradis, 1994). Ullman (2001) has proposed that with extended practice and higher proficiency, L2 grammatical processing may increasingly rely on procedural memory.

However, a similar pattern of performance in L1 and L2 indicates that the same organizational principles underlie the two languages (Filley et al., 2006; Hernandez et al., 2008; Druks and Weekes, 2013). In a late bilingual person with different levels of proficiency in L1 and L2, like LJ, similar patterns of impairment in both languages seem to indicate shared neural representations for the two languages. This conclusion is in line with the convergence hypothesis (Abutalebi and Green, 2007; Abutalebi, 2008) which posits that L1 and L2 depend on the same neural mechanisms and that L2 lexical and grammatical representations converge to L1 representations.

This model also predicts differences between L1 and L2, as late bilingual speakers need to recruit additional cognitive control resources to process their L2. Under this theoretical account, increased processing demands exist for LJ because French is his non-dominant language. Differences between L1 and L2 may also be attributed to impaired control processes due to the underlying pathology of the nfvPPA. The executive deficit reported on neuropsychological assessment may account for the differences between the two languages. The cross-switching errors which were evident in the L2 personal narrative task support impairment in control functions. Cognitive control of L2 processing has been associated with the prefrontal cortex, the anterior cingulate cortex and the basal ganglia. (Abutalebi and Green, 2007). Atrophy in the nfvPPA extends with disease progression into these regions, prefrontal cortex and anterior cingulate regions in particular (Grossman, 2010; Mesulam et al., 2014).

The fact that no significant differences were found between L1 and L2 seems to contradict our hypothesis. It must be noted however that long exposure to L2 and daily use of L2 at work and home may have played a role in preserving discourse abilities in L2. LJ uses and is exposed to French now for 36 years. Such a degree of exposure and use may play a determining role in L2 preservation. In fact, Abutalebi et al. (2015) found that differences between L1 and L2 suggesting an age of L2 acquisition effect are not present in elderly individuals. Nanchen et al. (2017) examining preservation of L1 and L2 in an immigrant population of late bilingual speakers with dementia, found that languages were equally preserved. They concluded that for elderly individuals, exposure and immersion are the main determinants of language preservation.

Our findings are consistent with a previous report (Zanini et al., 2011) of an early bilingual speaker with nfvPPA, where a decline in connected speech was found in both languages (Friulian and Italian), with the second language being impaired to a greater, but not to a significant degree. A qualitative similar pattern of deficits in L1 and L2 has been reported by Hernandez et al. (2008) in an early, highly proficient Spanish-Catalan bilingual speaker with nfvPPA and Filley et al. (2006) in an early, proficient Chinese-English bilingual person with lvPPA. The only study which has investigated language abilities in a late bilingual speaker with nfvPPA was the study by Druks and Weekes (2013). Although grammatical production was not assessed, a parallel deterioration of lexical retrieval and grammatical knowledge in L1 (Hungarian) and L2 (English) was reported. This finding across two languages from different language families (Uralic and Indo-European, respectively) is similar to ours in that LJ was impaired, compared to controls, on both lexical and grammatical measures in his native language (Greek) and a parallel pattern of impairment was found in L2 (French), two structurally different languages albeit within the same family of languages.

In conclusion, we have found that LJ was impaired in lexical, discourse and grammatical productivity measures in his native language, Greek. A similar pattern of impairment was evident in his second language, French. Both L1 and L2 were affected to a similar degree. Lengthy exposure to L2 and regular activation of L2 through daily use may explain the preservation of discourse abilities in this non-dominant language. Connected speech analysis using QPA, fluency variables and error analysis has enabled the documentation of speech and language deficits present in this case of the nfvPPA and the comparison of performance between the participant's languages.

A growing body of literature indicates that behavioral interventions in PPA can result in improvement of the targeted language function, although there are generalization and maintenance issues (Cadório et al., 2017). Research on bilingual aphasia rehabilitation after stroke has yielded inconsistent results regarding the pattern of cross-linguistic therapy effects (Goral and Conner, 2013). Evidence suggests that cross-language transfer of treatment gains is easier between two highly proficient languages, and from a less-proficient language to a more-proficient language (Ansaldo and Saidi, 2014). However, cross-language transfer also depends on factors such as postmorbid proficiency levels and linguistic similarity between languages (Goral et al., 2012). These data underline the clinical importance of determining language dominance and performance in both languages in bilinguals with PPA.

One limitation of the present study is the size of the speech samples. A minimum of 150 words has been suggested for QPA (Berndt et al., 2000). However, it was difficult to obtain samples of this size without extensive prompting. A second methodological limitation was the lack of control subjects. Ideally, neurotypical Greek-French bilingual individuals should have served as controls for this study. Furthermore, performance was assessed at one time point for both languages. Although we have data that show cognitive decline, we have not evaluated language performance at two time points. Thus, no conclusions can be drawn about the pattern of decline in each language and across languages. Finally, a factor that may have influenced results in L2 is the fact that LJ was assessed in both languages by the same Greek-speaking clinician proficient in French. We know that healthy bilingual speakers' language choice is influenced by the social context and the linguistic background of the interlocutor (Blanco-Elorrieta and Pylkkänen, 2017). Nevertheless, code-switching was observed only during the personal narrative in French. It could be a task related effect explained by LJ's difficulty in accessing the relevant words in French when talking about his daily job routine.

This study calls attention to factors such as language dominance, proficiency, patterns of use and exposure to a language. These factors play a key role in assessing bilingual individuals with PPA and making clinical decisions based on the underlying linguistic and cognitive features.

Author Contributions

NK and MK designed the study. JP conducted the initial and follow-up assessments of the participant. Speech and language evaluation and QPA analysis was completed by NK. MK reviewed the QPA analysis. The manuscript was drafted by NK. Co-authors contributed to the final version of the manuscript.

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Conflict of Interest Statement

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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Table 1. Reported language history and proficiency for participant LJ based on the Language Experience and Proficiency Questionnaire (LEAR-Q, Marian et al., 2007).

Language history measures Languages	L1 history Greek	L2 history French	L3 history English	Range
Order of proficiency	1	2	3	
Order of acquisition	1	3	2	
Identification with culture[a]	10	6	1	0-10
Current exposure	46%	46%	8%	
Preference for reading	80%	20%		
Preference for conversing	40%	40%	20%	
Reported proficiency[b]				
Understanding	4	5		0-10
Speaking	5	5		0-10
Reading	2	0		0-10
Age milestones (years)				
Started learning		25		
Attained fluency		29		
Started reading	6	25		
Became fluent reading		n/a		
Immersion duration (years)				
Country	53	7		
Family	53	36		
School/Job	53	36		
Contribution to language learning[c]				
From family	10	10		0-10
From friends	0	8		0-10
From reading	0	0		0-10
From TV	2	5		0-10
From radio	0	0		0-10
From self -instruction	0	1		0-10
Extent of language exposure[d]				
To family	10	10		0-10
To friends	10	7		0-10
To reading	1	1		0-10
To TV	7	3		0-10
To radio	0	0		0-10
Self -instruction	0	0		0-10
Self -reported foreign accent[e]				
Perceived by informant	2	5		0-10
Identified by others	5	5		0-10

[a]Range: 0 (none) to 10 (complete). [b]Range: 0 (none) to 10 (perfect). [c]Range: 0 (not a contributor) to 10 (most important contributor). [d]Range: 1 (never) to 10 (always). [e]Range: 0 (none) to 10 (pervasive).

Table 2. Consensus score on the Progressive Aphasia Severity Scale (PASS) at initial evaluation.

PASS Domains	Normal	Quest/ble Very mild	Mild	Moderate	Severe
	0	0.5	1	2	3
Articulation			1		
Fluency			1		
Syntax and grammar			1		
Word retrieval - expression			1		
Repetition	0				
Auditory comprehension		0.5			
Single word comprehension	0				
Reading		0.5			
Writing			1		
Functional communication			1		
					Severity (Sum of boxes): 7

Table 3. Background neuropsychological assessment results.

Area of testing and tests	Score (correct)
General Cognitive Measures	
MMSE	28/30
ACE-R	86/100
Attention	18/18
Memory	26/26
Fluency	5/14 *
Language	25/26
Visuospatial abilities	12/16 *
Executive functioning	
Frontal Assessment Battery (FAB)	12/18
Visuospatial perception	
Benson Figure Test – Copy condition	15/17
Visual Memory	
Benson Figure Test – Delayed recall condition	17/17
Mood	
GDS-SF	3/15
Ideomotor Apraxia	
WAB	58/60
Repetition	
Informal (based on WAB)	95/100
Naming	
Boston Naming Test, BNT-SF	11/15 *

Language Comprehension	
Vocabulary (PPVT-32)	19/32
Auditory comprehension-words (BDAE-SF)	16/16
Sequential commands (BDAE-SF)	10/10
Written sentences/passages (BDAE-SF)	4/4
Written story (BDAE-SF)	3/3
Grammaticality judgment - morphology	77/80
Syntactic comprehension (BDAE-3)	8/10
Object Semantics	
Pictures (PPTT-SF)	14/14
Reading Efficiency (Simos et al., 2013)	
Real words	16 in 45s *
Pseudowords	13 in 45s
Writing	
Words (Informal)	7/20
Non-words (Informal)	14/14
Words (BDAE-SF)	8/9
Written Picture Description (BDAE-SF)	4/11 *
Motor Speech Evaluation (Wertz et al., 1984)	
Apraxia of speech rating	3/7
Dysarthria rating	1/7

Key: *= significant impairment (>2 standard deviations below the normative mean); MMSE = Mini Mental State Examination (Fountoulakis et al., 2000); ACE-R = Addenbrooke's Cognitive Examination – Revised (Konstantinopoulou et al., 2011); GDS-SF = Geriatric Depression Scale – Short Form (Fountoulakis et al., 1999); WAB = Western Aphasia Battery; BDAE-SF = Boston Diagnostic Aphasia Examination Short form (Goodglass et al. 2013); PPVT = Peabody Picture Vocabulary Test (Simos et al., 2011); PPTT-SF = Pyramid and Palm Trees Test-Short Form (Breining et al., 2015).

Table 4. LJ's scores, control group median and standard deviation values and Crawford-t values.

Spoken language measures	LJ	Controls[1] (n=6) Median (SD)	t-values[2]
Proportion of closed class words	0.52	0.53 (0.04)	-0.23
Proportion of nouns	0.17*	0.25 (0.03)	-2.47
Proportion of adjectives	0.04	0.02 (0.01)	1.85
Proportion of prepositions	0.02	0.06 (0.02)	-1.85
Proportion of adverbs	0*	0.07 (0.02)	-3.24
Proportion of pronouns	0.14**	0.06 (0.01)	7.41
Proportion of verbs	0.31*	0.20 (0.04)	2.55
MLU	4	5.41 (1.08)	-1.21
Elaboration index	1	2.43 (1.43)	-0.93
Embedding index	0.36	0.36 (0.17)	0.00

Number of narrative words	48*	127 (35)	-2.09
Proportion of sentences	0.92	0.79 (0.11)	1.09
Proportion of utterances without verbs	0.08	0.19 (0.11)	-0.93
Proportion of single-word utterances	0.17**	0.00 (0.02)	7.87
Proportion of well-formed utterances	0.75	0.96 (0.65)	-0.30
Auxiliary complexity index	0.64	0.30 (0.27)	1.17

[1]Control group values are taken from Varkanitsa (2012). [2]One-tailed (*p<0.05; **p<0.01).

Table 5. Proportion of nouns, verbs and pronouns per narrative words (NW) produced in personal narrative (task1), picture description (task 2) and story retell (task 3) in L1 and L2.

				L1				L2
Proportion per NW	Task 1	Task2	Task 3	Total Mean (SD)	Task1	Task 2	Task 3	Total Mean (SD)
Nouns	0.31	0.17	0.29	0.26 (0.08)	0.18	0.12	0.20	0.17 (0.04)
Verbs	0.21	0.31	0.24	0.25 (0.05)	0.20	0.30	0.18	0.23 (0.07)
Pronouns	0.08	0.15	0.14	0.12 (0.04)	0.20	0.26	0.19	0.22 (0.04)

Figure 1. Coronal T1-weighted (A), axial T1-weighted (B) and axial diffusion-weighted (C) brain imaging at initial assessment showing left perisylvian atrophy.

Figure 2. Dysfluencies per total words (TW) in L1 and L2.