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Webinar – 5. April 2022

‘The logopenic variant of primary progressive aphasia (lvPPA): language, cognitive, neuroradiological issues’

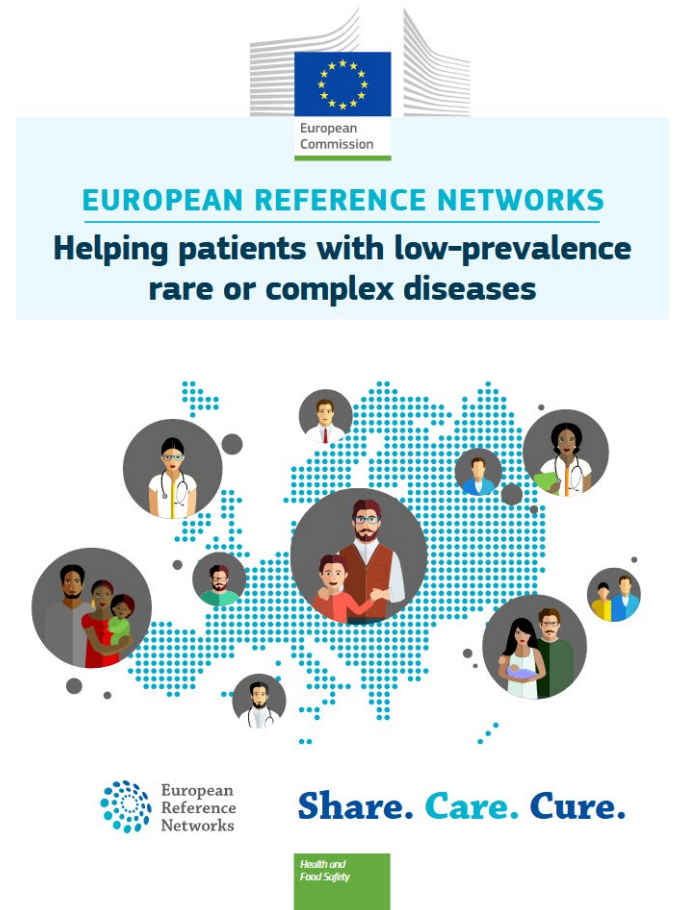
by Robert Rusina and Zsolt Cséfalvay

**Thomayer University Hospital, Prague, Czech Republic;
Comenius University, Bratislava, Slovakia**



European Reference Networks (ERNs)

- Networks of healthcare providers
- Established in 2017
- 24 different ERNs
- > 300 hospitals in 26 EU countries
- Goal: intensify collaboration and bundle expertise beyond borders to improve the quality of care for the patients.





European Reference Network for Rare Neurological Diseases (ERN-RND)

- Coordination: University Hospital Tübingen
- >100 clinicians
- 64 Full Members + 4 Affiliated Partners
- 10 patient representatives
- 1 secure telemedicine platform (CPMS)
- 6 Disease Groups:

1. Ataxia and HSP
2. Leukodystrophies
3. Dystonias /NBIA/Paroxysmal disorders
4. Chorea and Huntington's Disease
5. Frontotemporal Dementia
6. Atypical Parkinsonian Syndromes





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Learning objectives

- By the end of this webinar you will be able to:
 - discuss core associated features of the logopenic variant PPA
 - identify language impairments in patients with lvPPA
 - interpret of the clinical/formal language assessment results
 - assess focal atrophy on MR in lvPPA
 - discuss the neuropathological and genetic background of lvPPA



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Webinar outline

Neurologist's perspective

- definition
- hallmarks
- neuroimaging
- neuropathology
- anatomy & behavior

Language aspects

- anomia & circumlocutions
- impaired repetition
- low fluency
- early episodic amnesia

Case 1 – initial stage of lvPPA

Case 2 – early stage of lvPPA

Case 3 – advanced stage of svPPA



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IvPPA:

clinical, MRI and neuropathological aspects



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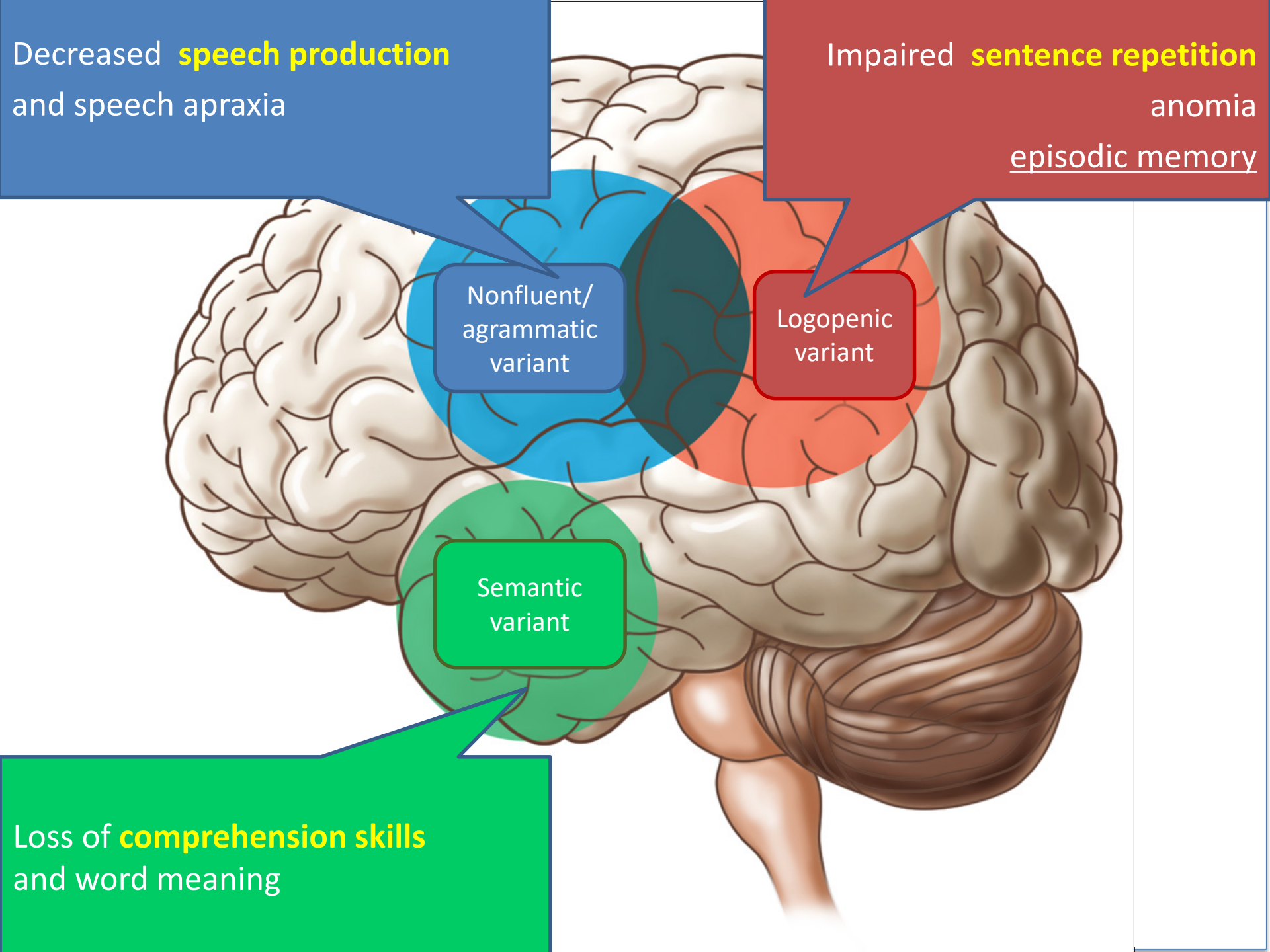


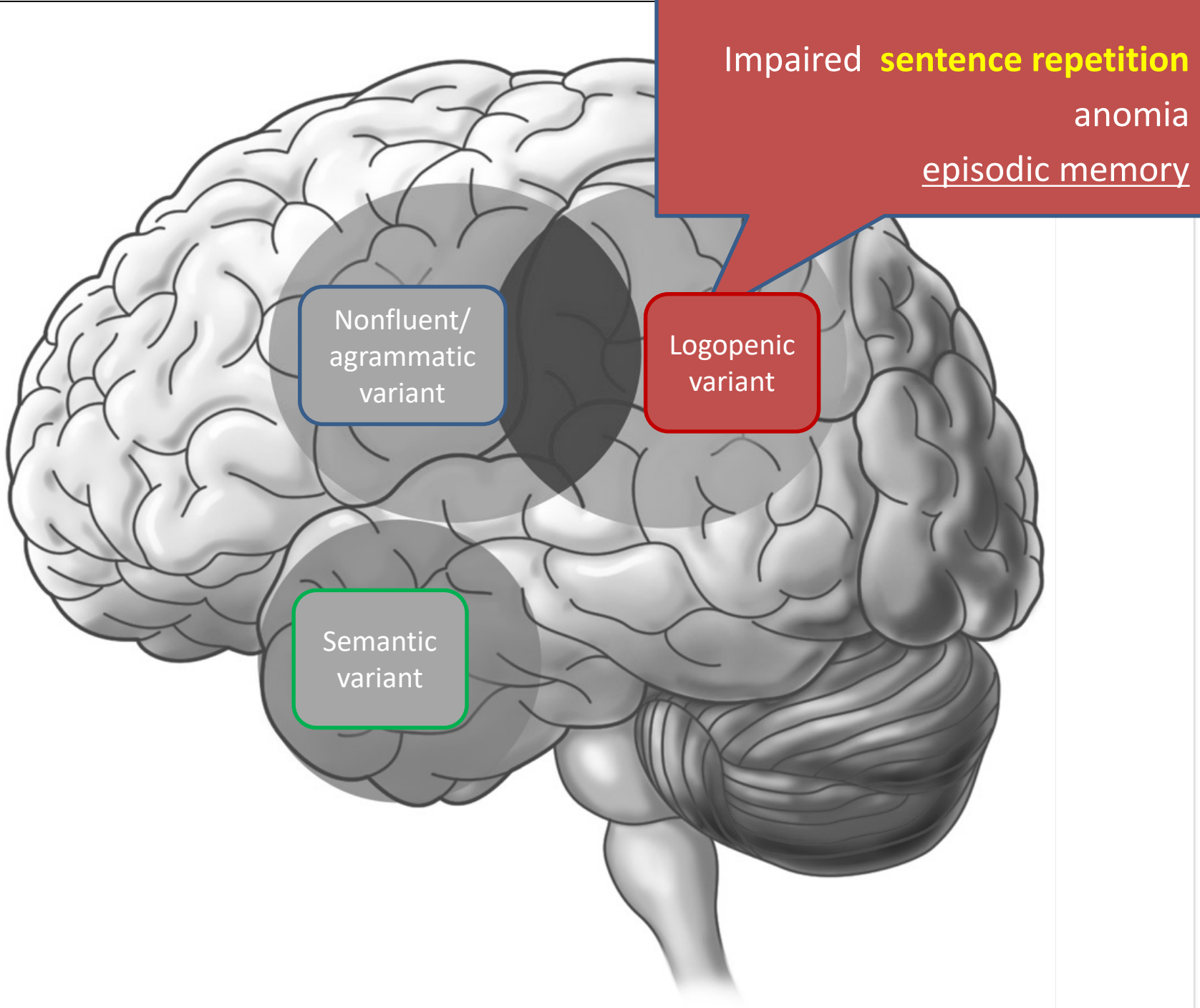
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PPA core criteria...

1. **Insidious onset** and **gradual progression** of **language impairment**
(speech production/comprehension, reading/spelling)
2. **Aphasia** is the initial and most salient cognitive deficit and the main cause of disability
3. All patients **develop** more widespread **cognitive impairment**
4. Diagnostic tests provide confirmation of an **underlying neurodegenerative** process (FTD, PSP, CBD, ALS, AD...)





Quizz ???...

Typical language feature of patients with lvPPA is:

- a. fluent speech production with impaired single word comprehension
- b. good repetition of sentences, but poor comprehension
- c. anomic pauses in speech production and poor sentence repetition
- d. agrammatism in speech production with slow speech rate



IvPPA – concept, terminology...

Important word finding difficulties

Anomia & **circumlocutions** (efforts describing the missing word)

Frequent anomic pauses and low cadence

Nonfluent speech (but less pronounced than in nfvPPA!)

Impaired repetition

Early loss of episodic memory

anomia
impaired repetition
and memory loss





IvPPA – neuropsychology...

Episodic memory loss

Impaired attention

Delayed visuospatial memory

Visual set-shifting

Acalculia....

....reflecting the posterior temporoparietal atrophy observed early in IvPPA

Quizz ???...

Typical MR findings in lvPPA include:

- a. posterior fronto-insular atrophy
- b. left perisylvian and bilateral symmetrical hippocampal atrophy
- c. atrophy of the left anterior temporal lobe
- d. atrophy of the inferior parietal lobe



IvPPA – neuroimaging...

Atrophy predominates in the left perisylvian area

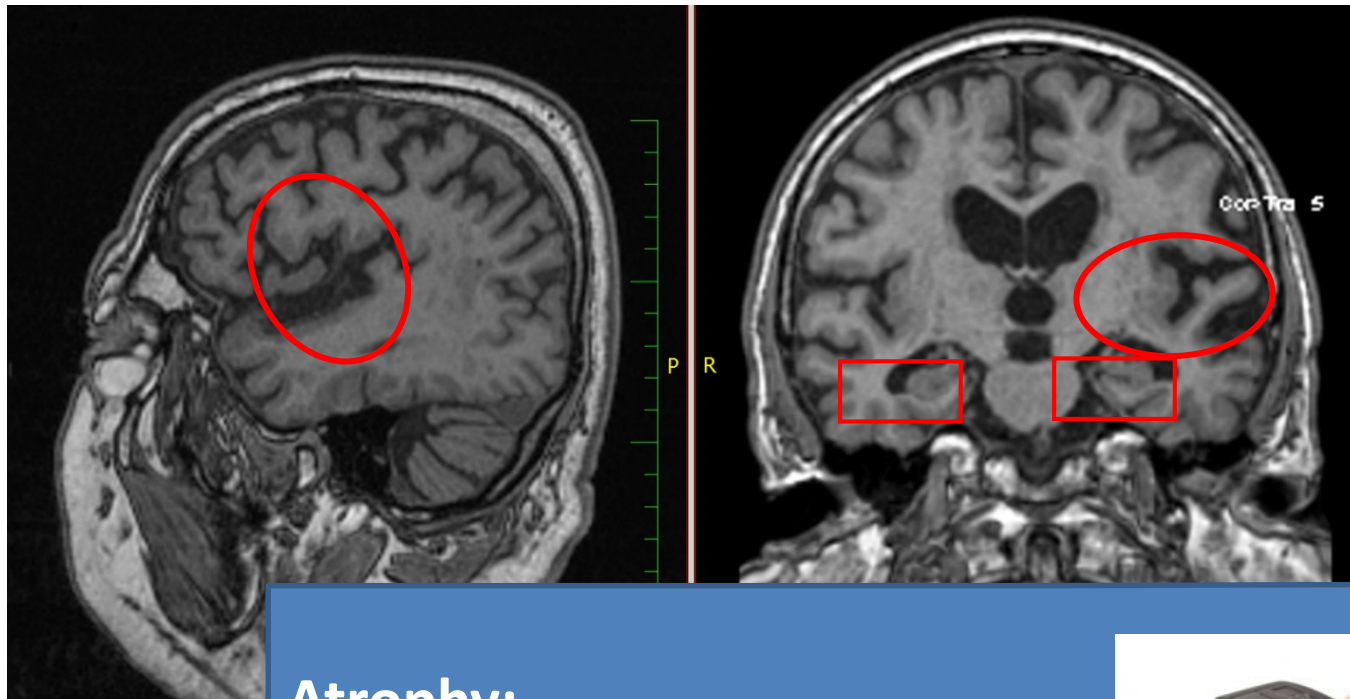
Early bilateral hippocampal atrophy

Late bilateral parietal and frontal atrophy



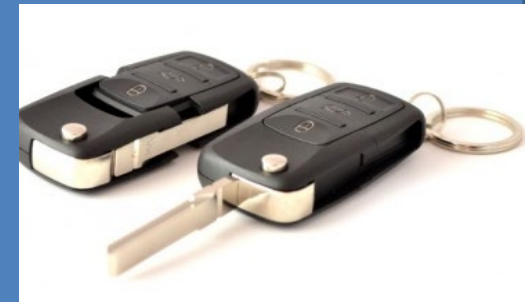


IvPPA – neuroimaging...



Atrophy:

posterior sylvian - left
hippocampal - bilateral



Quizz ???...

The background of lvPPA is mainly:

- a. Alzheimer's disease
- b. tauopathy
- c. protein TDP-43 deposits
- d. PSEN2 mutation



svPPA – neuropathology...

Most frequent finding are **amyloid beta and tau deposits**

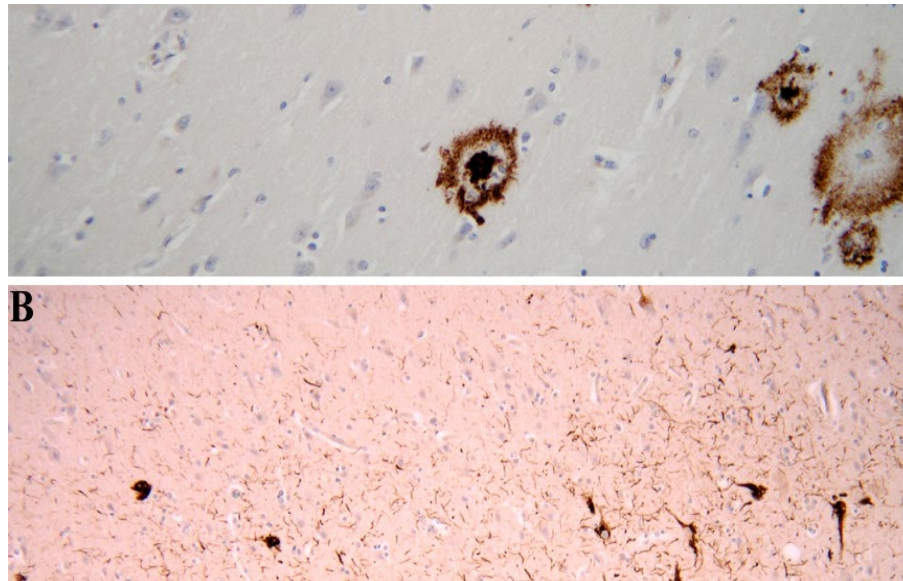
AD is the primary pathology of lvPPA

(tau, TDP-43, Lewy body dementia, and Creutzfeldt–Jakob disease have been identified as less common etiologies for lvPPA)

Genetic forms: *PGRN* (progranulin) gene and C9ORF72 mutations



IvPPA – neuropathology...



Amyloid beta deposits (A) and neurofibrillary tangles (B) corresponding to **Alzheimer disease**



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IvPPA – behavioral features...

- hallucinations and delusions may occur
- comorbid AD and Lewy body dementia...



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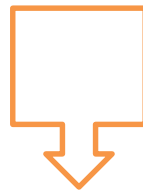
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Clinical features and language assessment of lvPPA



**The core deficit in lv PPA is thought to involve
word finding and repetition**

... and early impairment of episodic memory



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Language assessment:

1. Screening tests (SYDBAT, SAND...)
2. Formal aphasia batteries (WAB-R, CAT...)

Distinguishing subtypes in primary progressive aphasia: application of the Sydney language battery

Sharon Savage¹, Sharpley H

Affiliations + expand

PMID: 23467307 DOI: 10.11

Abstract

Background/aims: Primary progressive aphasia (PPA) is a clinical feature, patterns of brain activity, and is important for treatment and prognosis. It is lacking. This study introduces a new test to assist clinicians.

Methods: Fifty-seven PPA patients were compared on naming, repetition, and comprehension.

Results: Significant group differences were found for each group. Using discriminant analysis, three SYDBAT scores, from word

Conclusion: The SYDBAT is a promising tool for diagnosing PPA.

JSLHR

Research Article

The Diagnostic Value of Language Screening in Primary Progressive Aphasia: Validation and Application of the Sydney Language Battery

Nikki Janssen,^{a,b} Ardi Roelofs,^a Esther van den Berg,^c Willem S. Eikelboom,^c Meike A. Holleman,^d Dymphie M. J. M. in de Braek,^e Olivier Piguet,^{f,g} Vitória Piai,^{a,b} and Roy P. C. Kessels^{a,b,h}

Purpose: The three variants of primary progressive aphasia (PPA) differ in clinical presentation, underlying brain pathology, and clinical course, which stresses the need for early differentiation. However, brief cognitive tests that validly distinguish between all PPA variants are lacking. The Sydney Language Battery (SYDBAT) is a promising screening instrument that can be used as a first step in a comprehensive neuropsychological assessment to distinguish PPA subtypes, but evidence on its validity and reliability is to date limited. In the current study, the validation and diagnostic value of the SYDBAT are described for discriminating PPA subtypes as well as distinguishing PPA from mild cognitive impairment (MCI) or Alzheimer's dementia (AD).


Method: Forty-five patients with PPA (13 with semantic PPA, 20 with logopenic PPA, and 12 with nonfluent/agrammatic PPA), 25 MCI patients, 13 AD patients, and 50 cognitively unimpaired controls were included in this study. Both patients and controls completed the SYDBAT-NL (Dutch version). Performance on and predictive ability of the four subtests

(i.e., Naming, Word Comprehension, Repetition, and Semantic Association) were assessed. In addition, construct validity and internal consistency were examined.

Results: Different SYDBAT performance patterns were found across PPA and non-PPA patient groups. While a discriminant function analysis based on SYDBAT subtest scores could predict PPA subtype with 78% accuracy, it was more difficult to disentangle PPA from non-PPA patients based on SYDBAT scores alone. For assisting in clinical interpretation, simple rules were set up and translated into a diagnostic decision tree for subtyping PPA, which was capable of diagnosing a large proportion of the cases. Satisfying validity and reliability measures were found.

Conclusions: The SYDBAT is an easy-to-use and promising screen for assessing single-word language processes, which may contribute to the differential diagnostic process of PPA and the assessment of language impairment in MCI and AD. It can be easily implemented for initial screening of patients in a memory clinic.

SAND: a Screening for Aphasia in NeuroDegeneration. Development and normative data

Eleonora Catricalà¹  · Elena Gobbi² · Petronilla Battista^{1,3,4} · Antonio Miozzo⁵ ·
Cristina Polito⁶ · Veronica Boschi¹ · Valentina Esposito² · Sofia Cuoco⁷ · Paolo Barone⁷ ·
Sandro Sorbi⁴ · Stefano F. Cappa^{1,8} · Peter Garrard⁹

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© Springer-Verlag Italia 2017

Abstract Language assessment has a critical role in the clinical diagnosis of neurodegenerative diseases, in particular, in the case of Primary Progressive Aphasia (PPA). The current diagnostic criteria (Gorno-Tempini et al., 2011) identify three main variants on the basis of clinical features and patterns of brain atrophy. Widely accepted tools to diagnose, clinically classify, and follow up the heterogeneous language profiles of PPA are still lacking. In this study, we develop a screening battery, composed of nine tests (picture naming, word and sentence comprehension, word and sentence repetition, reading, semantic association, writing and picture description), following the recommendations of current diagnostic guidelines and taking into account recent research on the topic. All tasks were developed

with consideration of the psycholinguistic factors that can affect performance, with the aim of achieving sensitivity to the language deficit to which each task was relevant, and to allow identification of the selective characteristic impairments of each PPA variant. Normative data on 134 Italian subjects pooled across homogeneous subgroups for age, sex, and education are reported. Although further work is still needed, this battery represents a first step towards a concise multilingual standard language examination, a fast and simple tool to help clinicians and researchers in the diagnosis of PPA.

Keywords Language assessment · Neurodegenerative diseases · Normative data · Primary progressive aphasia · Screening battery · Aphasia

„...this battery represents a first step towards a concise multilingual standard language examination, a fast and simple tool to help clinicians and researchers in the diagnosis of PPA.“

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American Journal of Speech-Language Pathology, Vol. 29, 498–510, **2020**

AJSLP

Research Article

Western Aphasia Battery–Revised Profiles in Primary Progressive Aphasia and Primary Progressive Apraxia of Speech

**Heather M. Clark,^a Rene L. Utianski,^a Joseph R. Duffy,^a Edythe A. Strand,^a
Hugo Botha,^a Keith A. Josephs,^a and Jennifer L. Whitwell^b**



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American Journal of Speech-Language Pathology,
Vol. 29, 498–510, **2020**

Conclusions:

- 1) AQ underestimated the presence of PPA and WAB-R classification did not distinguish among PPA classification determined by consensus.
- 2) Performance on individual subtests and relative performance across subtests demonstrated inconsistent alignment with PPA classification.
- 3) the WAB-R in isolation is inadequate to detect or characterize PPA.
- 4) Utilizing the WAB-R as 1 component of a comprehensive language and motor speech assessment when PPA is suspected

Is single word-word
comprehension impaired?

Task: word/picture matching
ask high and low frequency word

Is single word-word
comprehension impaired?

Task: word/picture matching
ask high and low frequency word

3. Word Comprehension Task

"Now, I would like you to point to the picture that matches the word I say [show picture]. Where is the... [Word]?"

Discontinue test if patient has failed more than 6 consecutive items and appears distressed.

Item	Pointing Response	Repetition Response
PRACTICE :kangaroo		
PRACTICE: strawberry		
1. banana		
2. butterfly		
3. computer		
4. potato		
5. bicycle		
6. cigarette		
7. elephant		
8. radio		
9. envelope		
10. battery		
	Subtotal = ____ / 10	Subtotal = ____ / 10
11. catenillar		



Is single word-word
comprehension impaired?

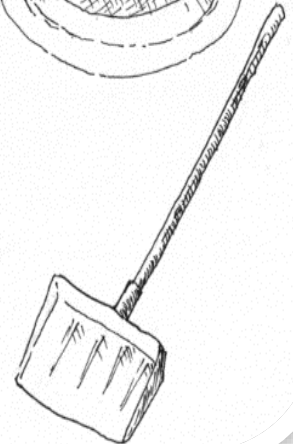
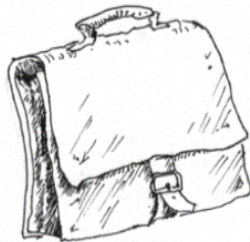
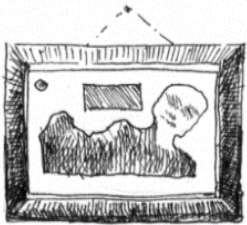
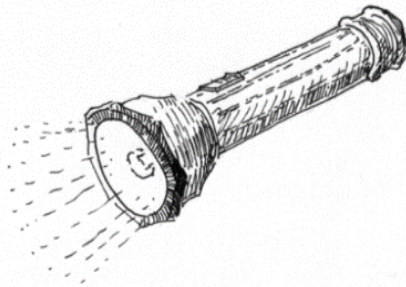
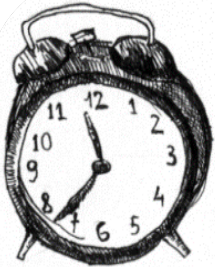
Task: word/picture matching
ask high and low frequency word



Is single word-word
comprehension impaired?

Task: word/picture matching

pointing to objects
(ask high and low frequency word)



Task:
picture description, story telling

Is single word-w
comprehension imp

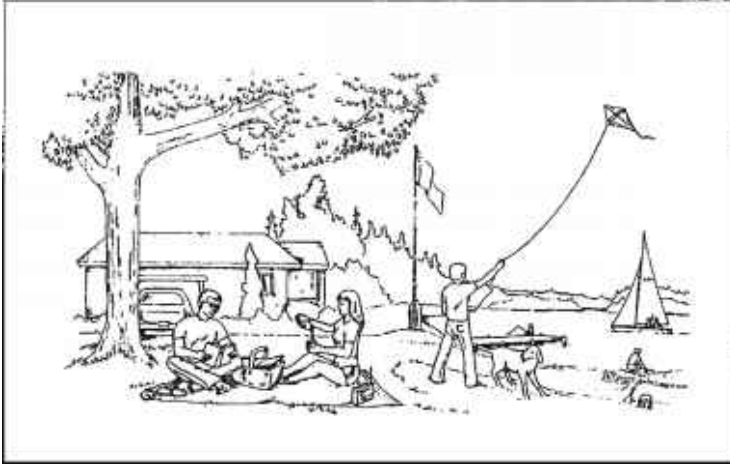
Ask patients to produce sentences, not only
naming object on the picture...

NO

Is agrammatism with/without
AOS present?

Assessment of speech production

(picture description, spont.speech)



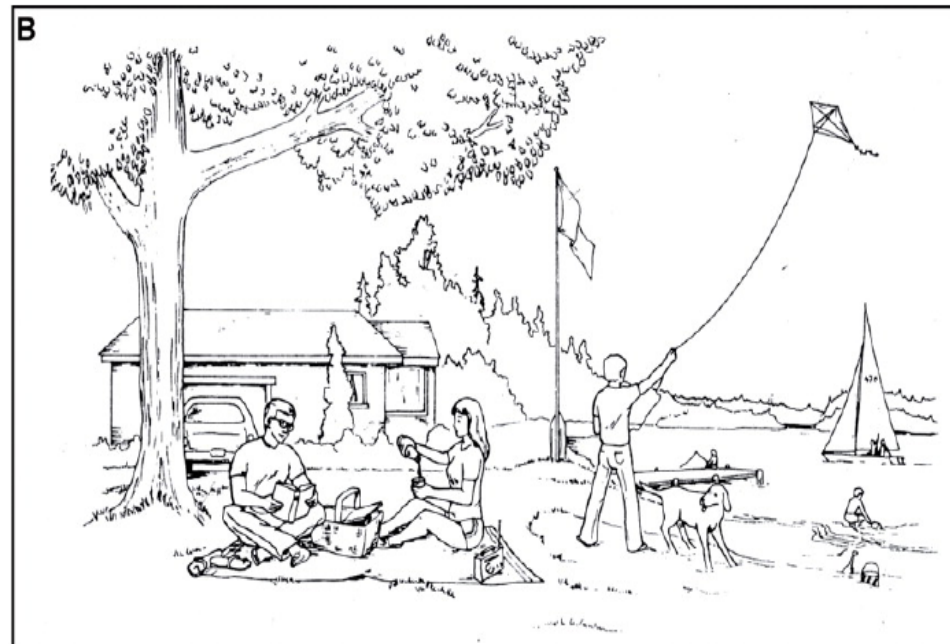
- Western Aphasia Battery (WAB)



- Boston Diagnostic Aphasia Examination (BDAE)

Logopenic Variant PPA

Beeson, Rapcsak, (2015)



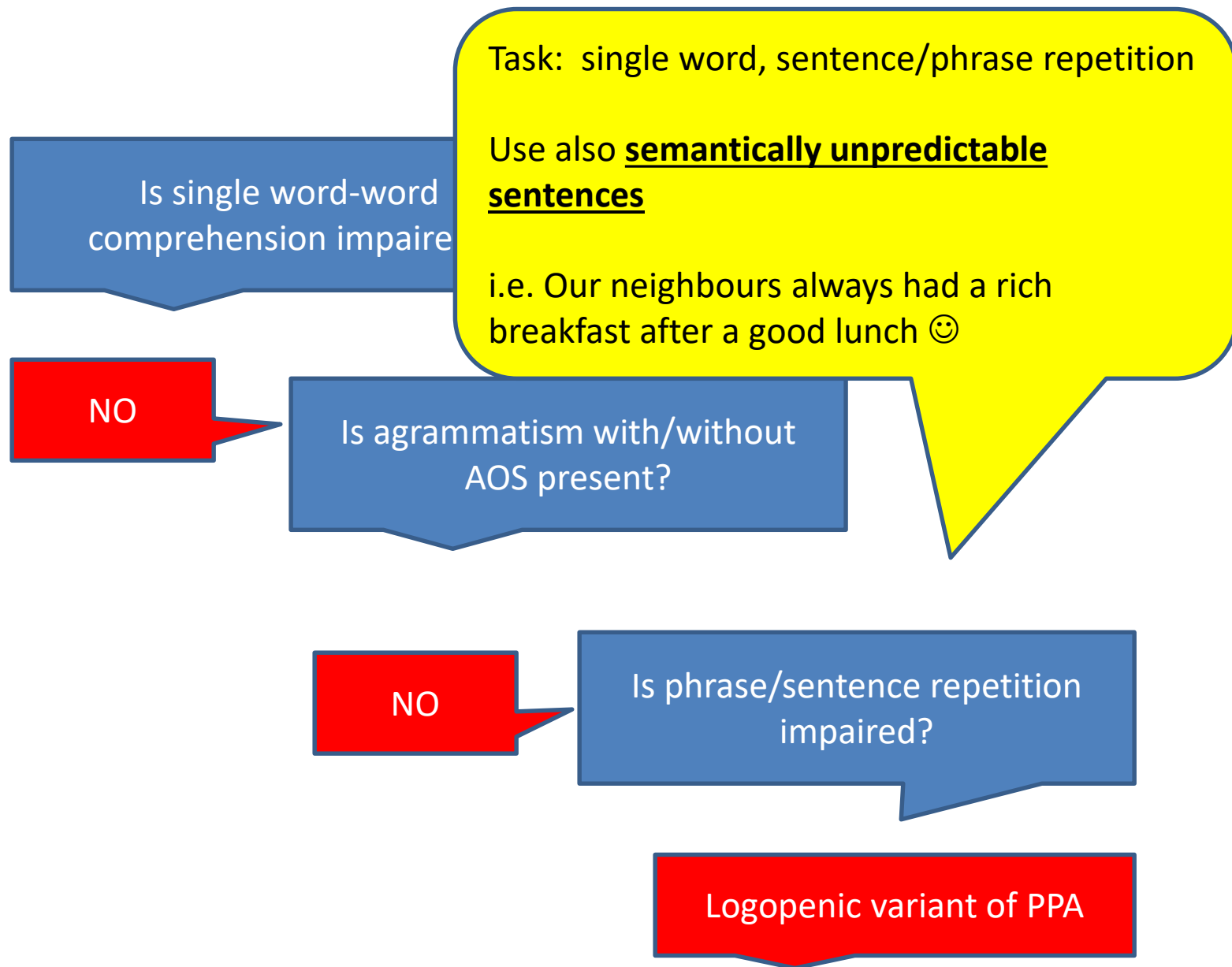
Uhm..., I see three people, no I see four people who are at a house or somewhere that has a... beautiful trees..., and there's a car in the... (I don't know) ...uhm. And...uhm... people are...one man is reading a book and the woman, I don't know what she is doing.

A man is fluh..make..is..has a...fl..has a...oh shoot... Well, I'm going to go to over here and then I'll try to find..think about that is, ok, so, uhm... there is uhm... a ...boy who it looks like in the water and there is a boat and there is a dog under what look likes a table, and that man has a....I'll go around that...say... that... there is... you can take this up in the air and children have fun with it, and then there is a flag here....

Assessment of speech production



- Picture description subtest from the Czech language battery (Cséfalvay et al., 2018)



Predictability, sentence length, and grammatical complexity are the main factors affecting performance on this task.

Three lvPPA patients with different language profile



Patient 1: mild lvPPA



Patient 2: moderate lvPPA



Patient 3: severe lvPPA



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Case 1

71-year-old musician

one year word finding difficulties

often irritable, stressed in unfamiliar environment

GP is neglecting the patient's symptoms, the family asked for neurological assessment



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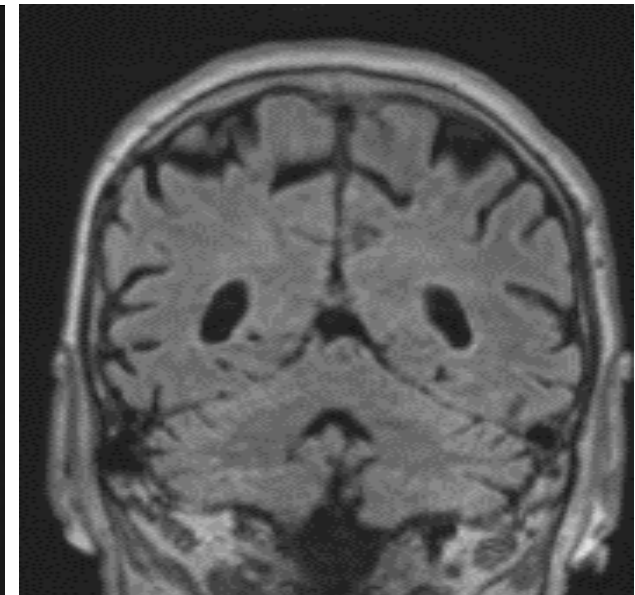
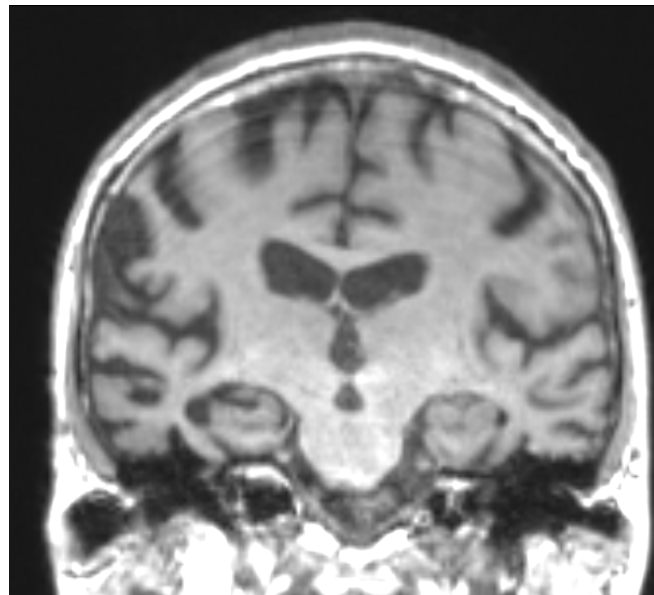
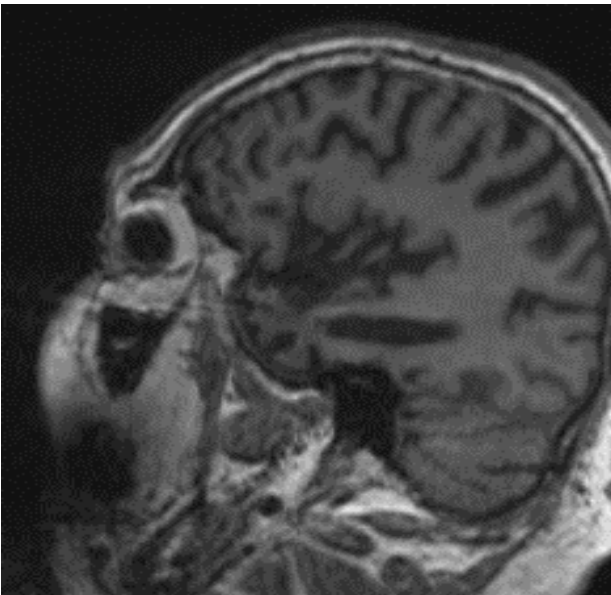
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Case 1



Patient with mild lvPPA

Core features		Associated characteristics	
Impaired naming in spontaneous speech or picture description	mild	phonological errors in speech production	paraphasias
Impaired repetition of sentences and phrases	very mild		
		spared single word comprehension/ spared object knowledge	yes mildly impaired
		preserved grammar	yes
		intact motor speech	yes



No signs of agrammatism, no AOS, fluent connected speech with short pauses, difficulties retrieving words while speaking:

P: Somewhere in the apartment in the kitchen, where the wife... Did... yes here she has on the table.... she's already done something to eat, she's made a cup of coffee, or something like that... and that ... will pour it there... there is one girl, one big boy, and a husband and a little boy...



No signs of agrammatism, no AOS, fluent connected speech with short pauses, difficulties retrieving words while speaking:

P: Somewhere in the apartment in the kitchen, where the wife... Did... yes here she has on the table.... she's already done something to eat, she's made a cup of coffee, or something like that... and that ... will pour it there... there is one girl, one big boy, and a husband and a little boy...

Quizz ???...

What were the most obvious symptoms in this patient's speech production?

- a. agrammatism
- b. word-finding difficulties
- c. phonological errors
- d. apraxia of speech

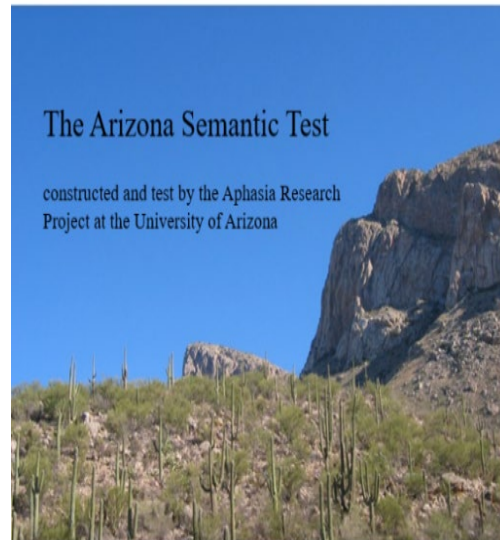


Naming test: 43/60

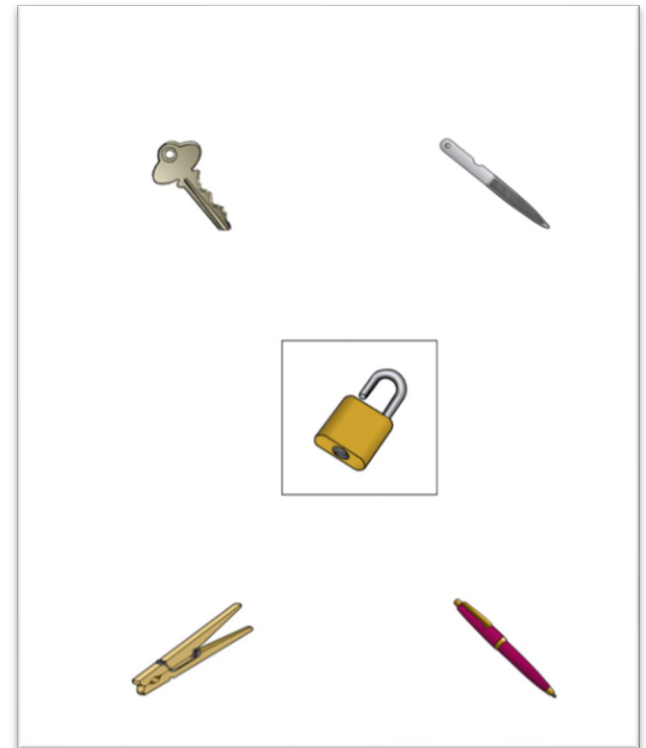
23 out of 30 objects

20 out of 30 actions

- delayed naming after 20 seconds
- no improvement with semantic cueing
- effective with phonemic cueing



Manuscript with normative data in preparation. Cite as
Beeson, P.M. (unpublished). The Arizona Semantic Test.



Object knowledge (Arizona Semantic Test):
mild impairment



singe word repetition:

repeated without problems even low-frequency,
longer, phonologically more complex words
only one phonological paraphasia

0:12 *SLT: snop*

P: snok

sentence repetition:

correct repetition of even longer sentences,
the only problem was with semantically
unpredictable sentence

0:43 *SLT: Maybe we'll have a house fall
before the tree.*

*P: maybe... that... in front of a tree... us... cut
down house houses*

Quizz ???...

Which sentence would be the hardest to repeat for this patient?

- a. We have a big dog at home.
- b. There was a car in front of the house.
- c. They always had breakfast late in the evening.
- d. Mom kissed her little daughter.



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Case 2

59-year-old botanist

More than two-years word finding and verbal expression difficulties

Almost unable to describe and refer his problems

Agitation, unrest, forgetfulness, the family for neurological examination



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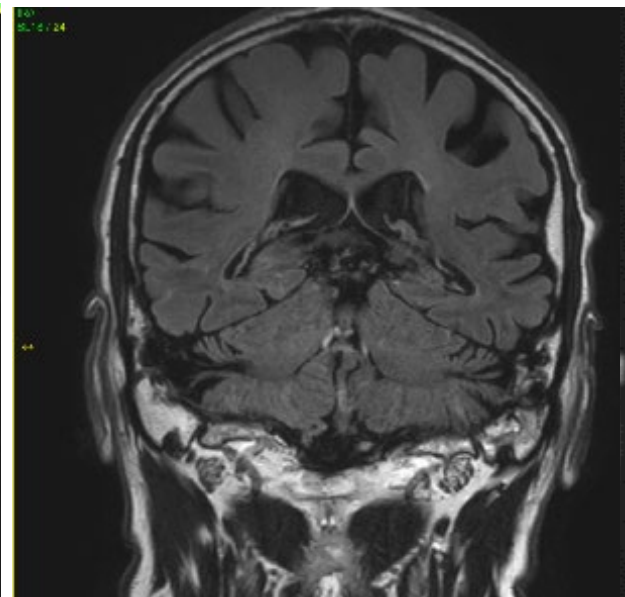
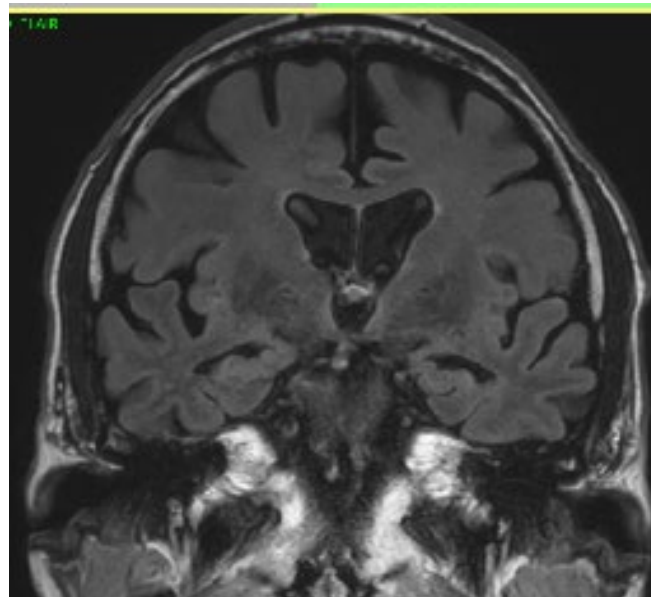
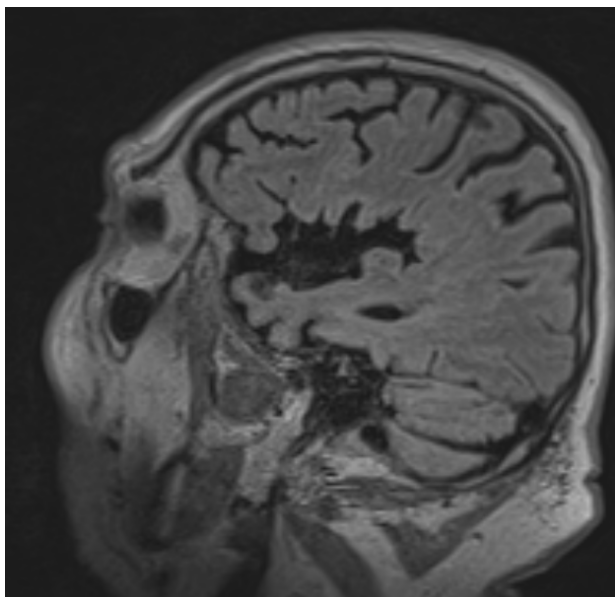
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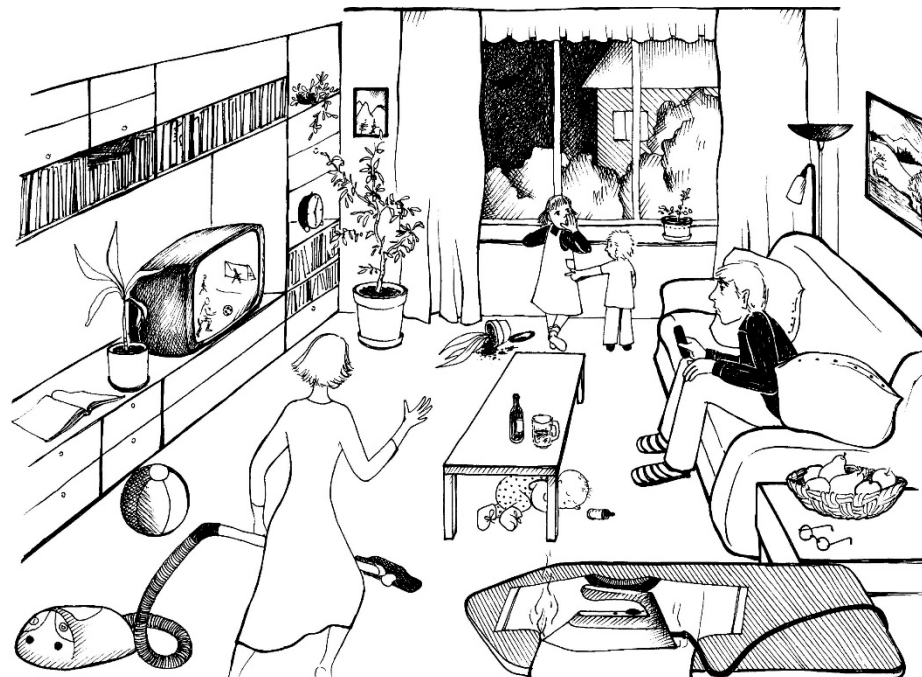
Case 2



Patient with moderate lvPPA

Core features		Associated characteristics	
Impaired naming in spontaneous speech or picture description	++	phonological errors in speech production	mild
Impaired repetition of sentences and phrases	+++		
		spared single word comprehension/object knowledge	yes
		preserved grammar	yes
		intact motor speech	yes

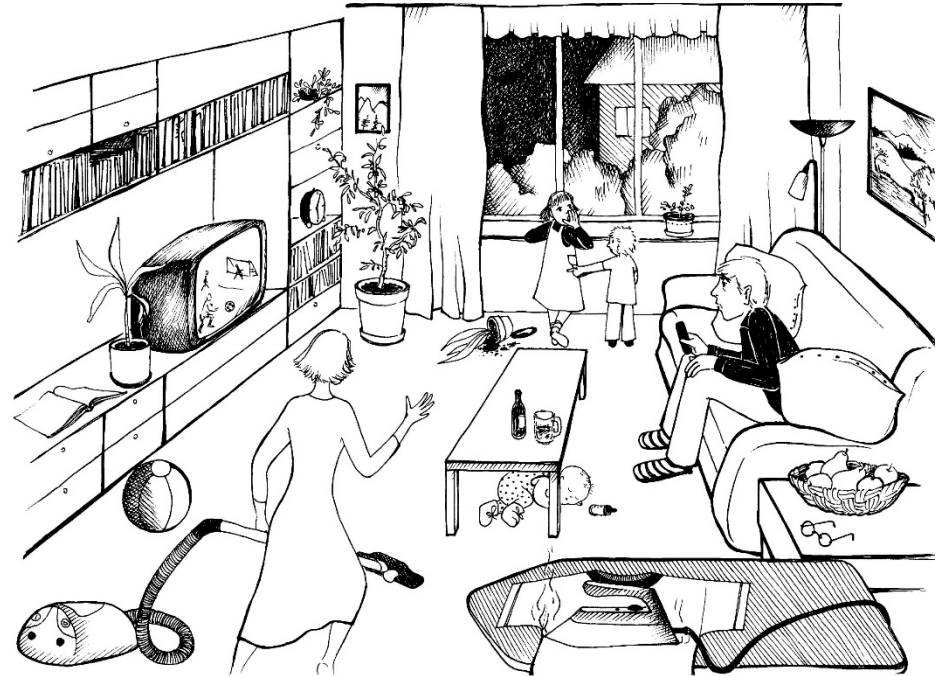
Connected speech



P: Pictured here?...

SLT: what happens in the picture?

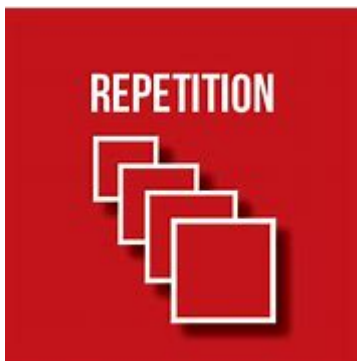
P: Ahaaa, here? Come on, the kids are playing.... the next one that is playing.... a ssss.... Um... but those, those.... Higher... Um... Um.... they play with the ball... Daddy has a beer.... on the table.. that's good (laughter).. I'd like that (laughing)... here he shines a lamp.... and here he has... here he has.... Um... Um.... Um... well... no Jesus..... Books... here are books, books... here.. Here's the picture.. here's the bouquet...



P: Pictured here?...

SLT: what happens in the picture?

P: Ahaaa, here? Come on, the kids are playing.... the next one that is playing.... a ssss.... Um... but those, those.... Higher... Um... Um.... they play with the ball... Daddy has a beer.... on the table.. that's good (laughter).. I'd like that (laughing)... here he shines a lamp.... and here he has... here he has.... Um... Um.... Um... well... no Jesus..... Books... here are books, books... here.. Here's the picture.. here's the bouquet...



Singe word repetition:

*SLT (0:7): you will repeat after
me the words I say*

*All words repeated correctly,
only minor phonological coding
errors in two words*

Sentence repetition

0:45

SLT: it's not raining outside today

P: it's not raining, not raining outside today

0:48

SLT: the water sailed away from me

P: the water saisailed away from me.

0:55

SLT: I forgot my keys at home

P: I for..for..got, forgot my keys at home

1:01

SLT: he politely apologized to me for that.

*P: pos..pol..politely...you... well... well.....
well already.... I don't know that*

1:14

*SLT: Maybe we'll have a house fall before the
tree.*

P: I don't know this.



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well already.... I don't know that*

1:14

SLT: Maybe we'll have a house fall before the tree.

P: I don't know this.

Singe word repetition:

*SLT (0:7): you will repeat after
me the words I say*

*All words repeated correctly,
only minor phonological coding
errors in two words*

Quizz ???...

Which statement describes the best the patient's problem?

- a. severe impairment of single word comprehension
- b. mild anomia in repetition
- c. mildly impaired sentence repetition
- d. severely impaired sentence repetition



**European
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complex diseases



Network
Neurological Diseases
(ERN-RND)



ean
european academy of neurology



**European
Reference
Network**

for rare or low prevalence
complex diseases



Network
Neuromuscular
Diseases (ERN EURO-NMD)



Case 3

74-year-old craftsman

Five years speech difficulties

Three years increasing forgetfulness, repeated asking for the same information

Unable to find the correct way outside his home

Anosognosia

Depressive mood



**European
Reference
Network**

for rare or low prevalence
complex diseases

 **Network**

Neurological Diseases
(ERN-RND)



**European
Reference
Network**

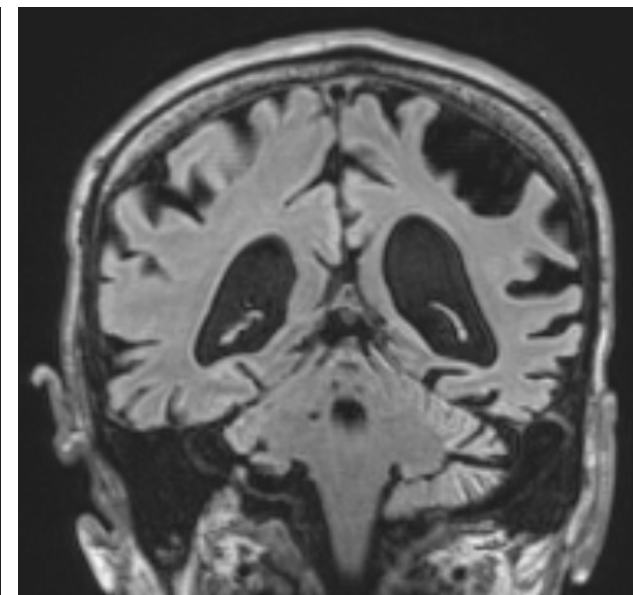
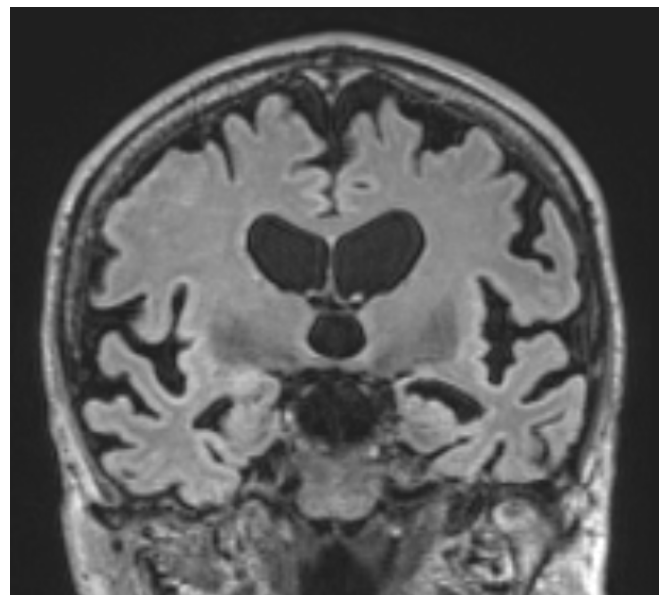
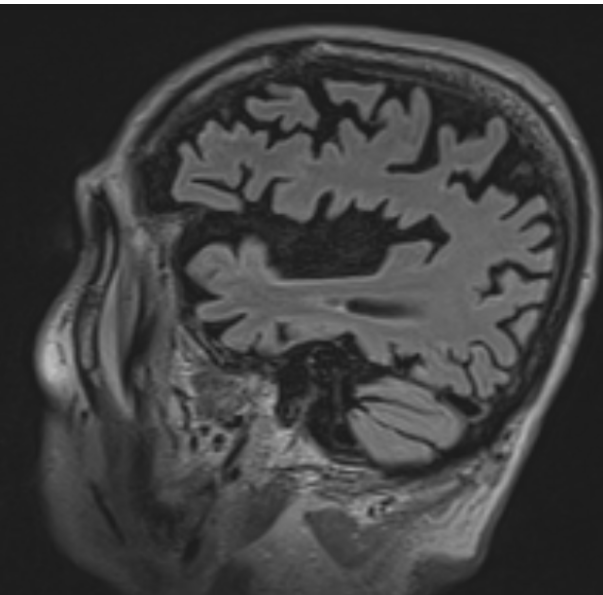
for rare or low prevalence
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Case 3



Patient with severe lvPPA

Core features		Associated characteristics	
Impaired naming in spontaneous speech or picture description	+++	phonological errors in speech production	severe
Impaired repetition of sentences and phrases	+++		
		spared single word comprehension/object knowledge	impaired
		preserved grammar	yes
		intact motor speech	yes



SLT Try to say what you see in that picture.... well.. well.. well.. here's the family...
Just here.. Just here.. dog.... dog... There's the kids.. Here's some flower.. well...
What else am I supposed to say.?....no
SLT anything that's out there ... probably dad or something... That's about.. here's
some... I just see some of this.. some...
SLT and how many people are there? ... four...
SLT so try to count ... one...two ... and there was another one...



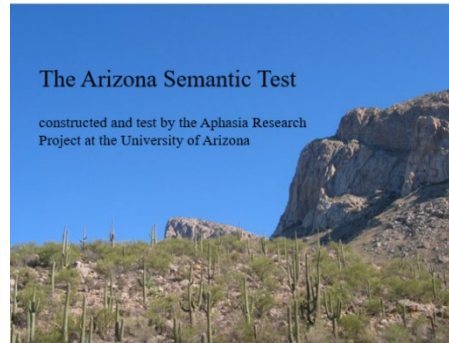
11 out of 30 actions

- delayed naming after 10 seconds
- failed to retrieve words
- no improvement with semantic cueing
- very effective with phonemic cueing

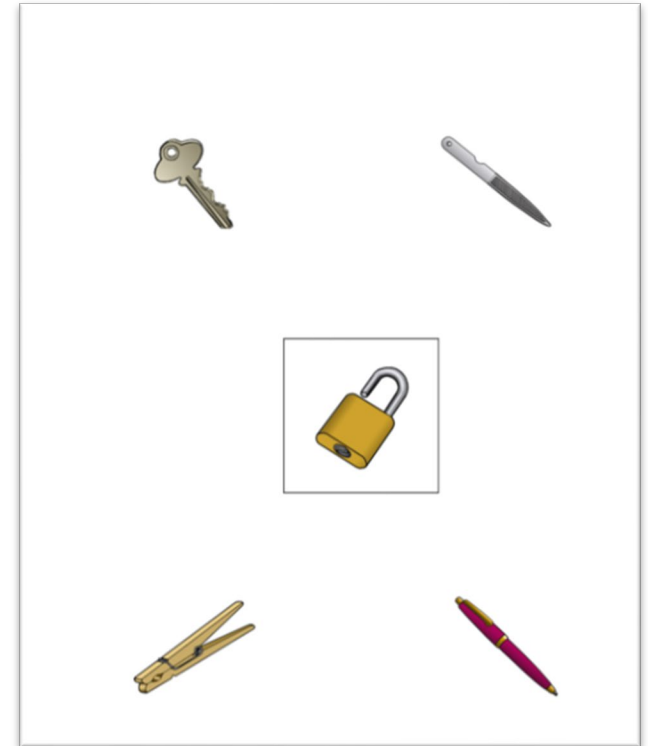
Quizz ???...

Which prompt helped the most for this patients in naming the pictures?

- a. semantic cueing („*this is an animal*“)
- b. phonemic cueing („*This word starts with a C*“)
- c. orthographic cueing („*This word starts with this letter...*“)
- d. no cueing was effective for him in naming task



Manuscript with normative data in preparation. Cite as
Beeson, P.M. (unpublished). The Arizona Semantic Test.



Object knowledge (Arizona Semantic Test):
mild impairment (31/40)

REPETITION



sing word repetition:

(0:4) *snop* - *snop*

(0:7) *prales* - *prales*

(0:10) *aktovka* - *af...af...av..aktov... ehm..
aktovka*

(0:21) *sloučenina* - *slou..ni...ni (laughter) ...
snou...ne...ne...nedeli...*



sing word repetition:

(0:4) *snop* - *snop*

(0:7) *prales* - *prales*

(0:10) *aktovka* - *af...af...av..aktov... ehm..
aktovka*

(0:21) *sloučenina* - *slou..ni...ni (laughter) ...
snou...ne...ne...nedeli...*

REPETITION



Sentence repetition

0:5

SLT: It's not raining outside today

P: but it's going to be bad here.

0:12

SLT: So try it, I'll say it again. It's not raining outside today

P: ne... it's long for me

0:24

SLT: Ok, I'll say it again. It's not raining outside today

P: no..no...not raining...

0:40

SLT: the water sailed away from me

P: aw... awa...away...drop...dropped

1:05

SLT: I forgot my keys at home

*P: for...for...forgot.. at
home...kh..key..khee..khethi...*

1:20

He apologised politely to me for this.

P:.....ap.....aph...poli...polit...polite...



Sentence repetition

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home...kh..key..khee..khethi...*

1:20

He apologised politely to me for this.

P:.....ap.....aph...poli...polit...polite...

Quizz ???...

Which symptom was not present in speech production and repetition in this patient?

- a. phonological errors
- b. motor speech impairment
- c. word finding problems
- d. a sentence repetition problem



Reminder: diagnostic criteria lvPPA...

Both of the following core features must be present:

- ☐ Impaired single-word retrieval in spontaneous speech and naming
- ☐ Impaired repetition of sentences and phrases

At least 3 of the following other features must be present:

- ☐ Speech (phonologic) errors in spontaneous speech and naming
- ☐ Spared single-word comprehension and object knowledge
- ☐ Spared motor speech
- ☐ Absence of frank agrammatism





Take-home message

1. Significant correlation: lvPPA symptoms – **MRI findings**
2. Early lvPPA: careful **evaluation of language** features
3. Enhance language analysis: **video/audio**
4. Key features: **anomia, impaired repetition and episodic memory**