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for rare or low prevalence complex diseases
⚙ Network
Neurological Diseases (ERN-RND)

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Neuromuscular Diseases (ERN EURO-NMD)

DG 'FTD'
8. eptember 2020

Joint webinar series

'Semantic variant of primary progressive aphasia'

Robert Rusina, Charles University, Thomayer Hospital Praha, Czech Republic &
Zsolt Cséfalvay, Comenius University, Bratislava, Slovakia

General information about the webinars

- RARE neurological, neuromuscular and movement disorders

- 30-35min presentation

- 15min Q&A session at the end (please write your questions in the Q&A)

- Target audience: neurologists, residents, paediatric neurologists, geneticists and other para-medical personnel involved in patient care

- Recorded Webinar and presentation to be found at the latest 2 weeks after on: http://www.ern-rnd.eu/education-training/past-webinars/

- For more information on this diseases group visit: http://www.ern-rnd.eu/disease-knowledge-hub/frontotemporal-dementia/

- Post-webinar survey (2-3min): satisfaction, topic/speaker ideas for next webinars
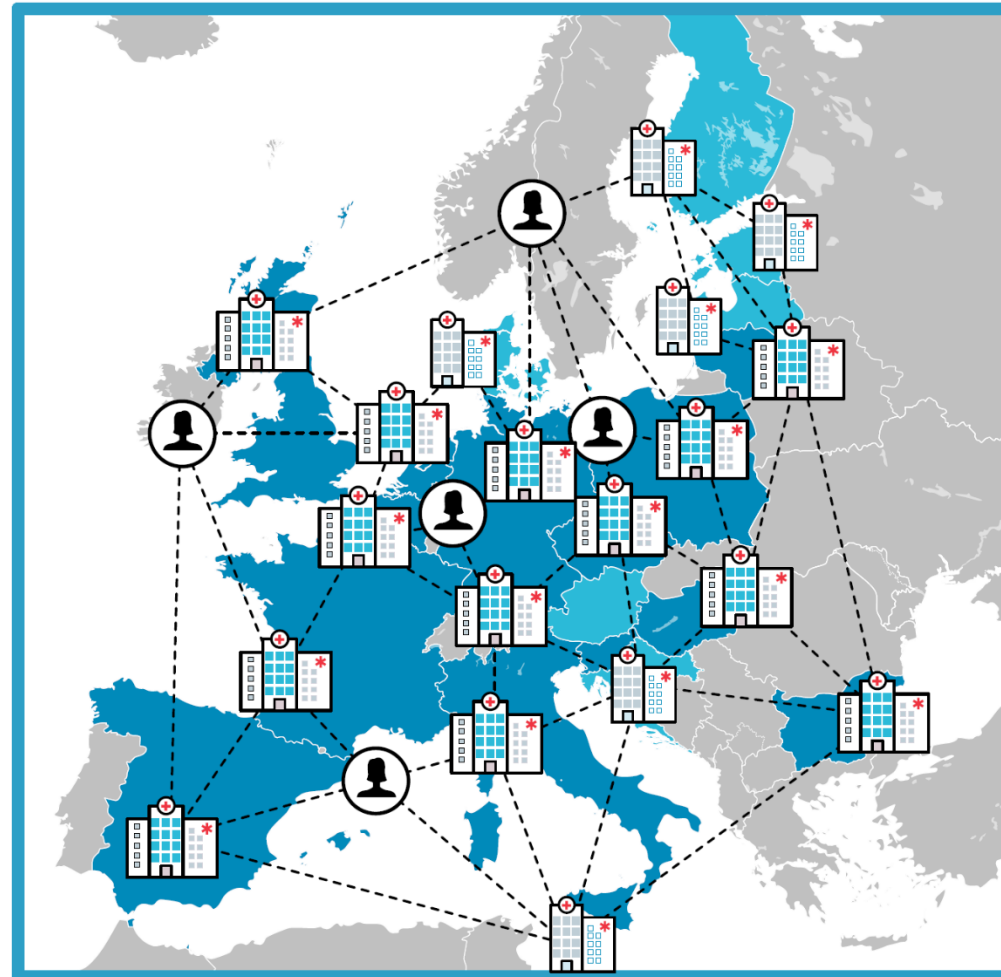
European Reference Network for RARE Neurological Diseases (ERN-RND)

- Countries with Full Members
- Countries with Affiliated Partners

ERN-RND covers 6 disease groups:
1. Ataxia and HSP
2. Leukodystrophies
3. Dystonias /NBIA/Paroxysmal disorders
4. Chorea and HD
5. FTD
6. Atypical Parkinsonism

Speaker: Robert Rusina & Zsolt Cséfalvay

Robert Rusina, MD.,Ph.D.

- graduated at Charles University in Prague and obtained the Interuniversity degree of specialization in Neurology in Paris, France

- head of the Department of Neurology in Thomayer Hospital, Prague

- chair of the Section of Cognitive Neurology, Czech Neurological Society.

His main research interests include cognitive neurology, progressive aphasia, frontotemporal dementia a human prion disorders

Speaker: Robert Rusina & Zsolt Cséfalvay

Zsolt Cséfalvay, Ph.D.

- graduated at Comenius University in Bratislava (Slovakia): speech and language pathology
- worked for 10 years as clincial speech and language pathologist at Department of Neurology at University Hospital in Bratislava
- professor and head of the Department of Communication Disorders at Comenius University in Bratislava

His main clinical and research topic is acquired neurogenic communication disorders: stroke induced aphasia, primary progressive aphasia, dysarthria and cognitive-communication disorders in neurodegenerativne disaeses such Alzheimer´s disease, Parkinson´s disease, etc.

Learning objectives

By the end of this webinar you will be able to:

- identify clinical hallmarks of svPPA
- assess focal atrophy on MR in svPPA
- discuss the neuropathological and genetic background of svPPA

- understand typical language profile of svPPA
- understand core aspects of assessment of language in svPPA
- outline possible intervention approaches in individuals with svPPA

Outline

Neurologist's perspective
- definition
- hallmarks
- neuroimaging
- neuropathology
- anatomy & behavior

Language aspects
- confrontation naming
- single word comprehension
- object knowledge
- surface alexia

Case 1 – early stage of svPPA
Case 2 – advanced stage of svPPA

svPPA:
clinical, MRI and neuropathological aspects

PPA – definition, short recap…

1990-2005

Isolated aphasia without structural correlates (tumor, ischemia…)

After 2 years progression into *frontal lobe dementia*
primary nonfluent aphasia(PNFA)
semantic dementia (SD)

Logopenic form after 2 years progression into *dementia*
logopenic progressivní aphasia (LPA)

Hodges 1996, Miller 2004

PPA – definition, short recap...

2006 –

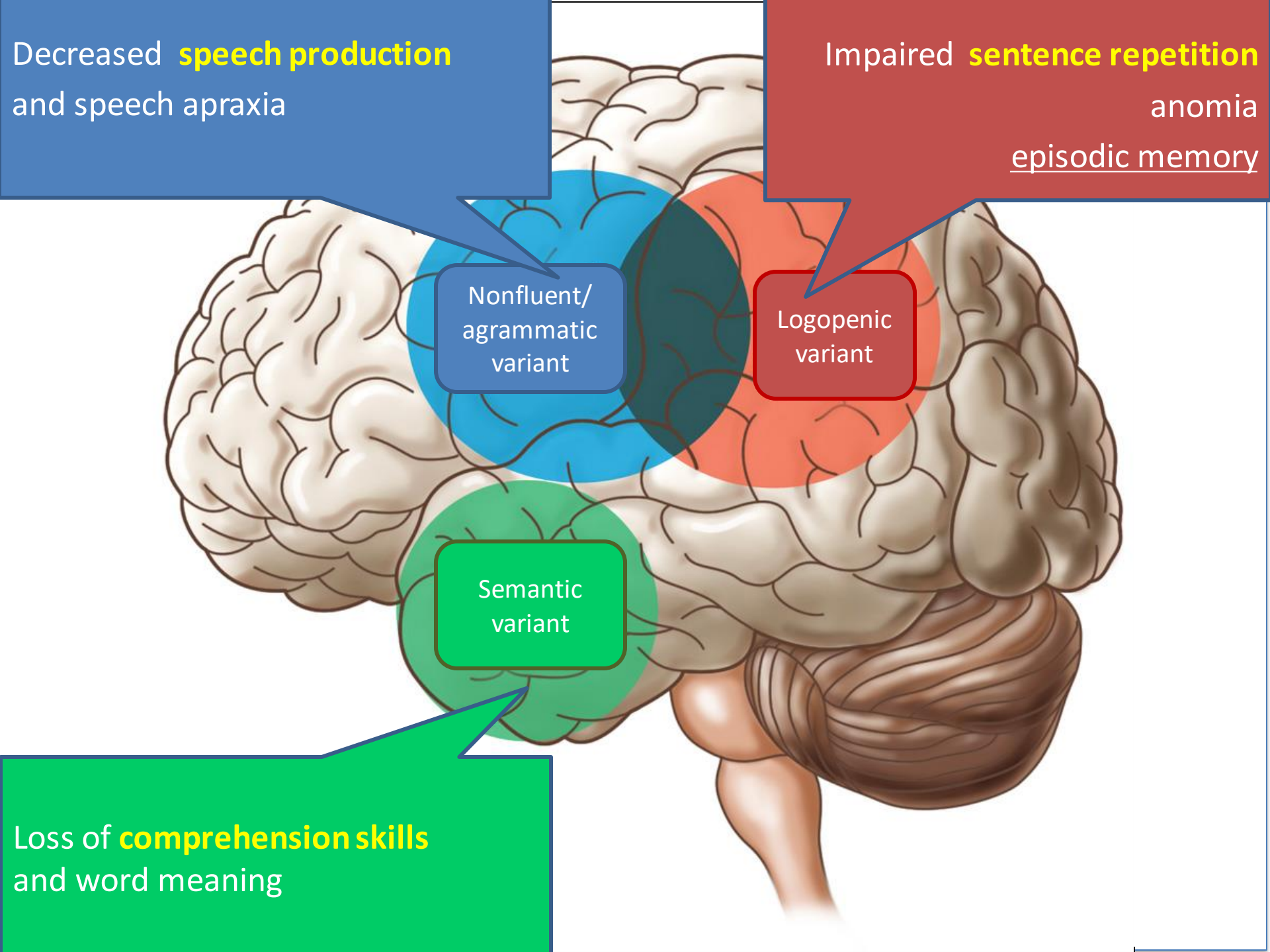Isolated aphasia without structural correlates (tumor, ischemia…)

After 2 years progression into *frontal lobe dementia*
> **nonfluent/agrammatical variant** (nvPPA)
> **semantic variant** (svPPA)

Logopenic form after 2 years progression into *dementia*
> **logopenic variant** (lvPPA)

Gorno-Tempini 2009

Nonfluent/ agrammatic variant

Logopenic variant

Semantic variant

Loss of **comprehension skills** and word meaning

Severely reduced speech comprehension

Anomia
Paraphasias
Fluent speech

Surface alexia (ability to read words, but not to understand)

Preserved autobiographic memory

Semantics:
Loss of understanding
single word meaning

Quizz ???

Typical MR findings in svPPA include:

(a) Posterior fronto-insular atrophy
(b) Symmetrical hippocampal atrophy
(c) <u>Atrophy of the left anterior temporal lobe</u>
(d) Atrophy of the inferior parietal lobe

svPPA – neuroimaging...

Atrophy predominates in the left temporal lobe

Anteroposterior gradient of atrophy (anterior hippocampal areas and amygdala are more atrophic then posterior areas)

Late right-sided temporal atrophy

svPPA – neuroimaging ...

Atrophy:
anterotemporal
asymmetric
dominant hemisphere
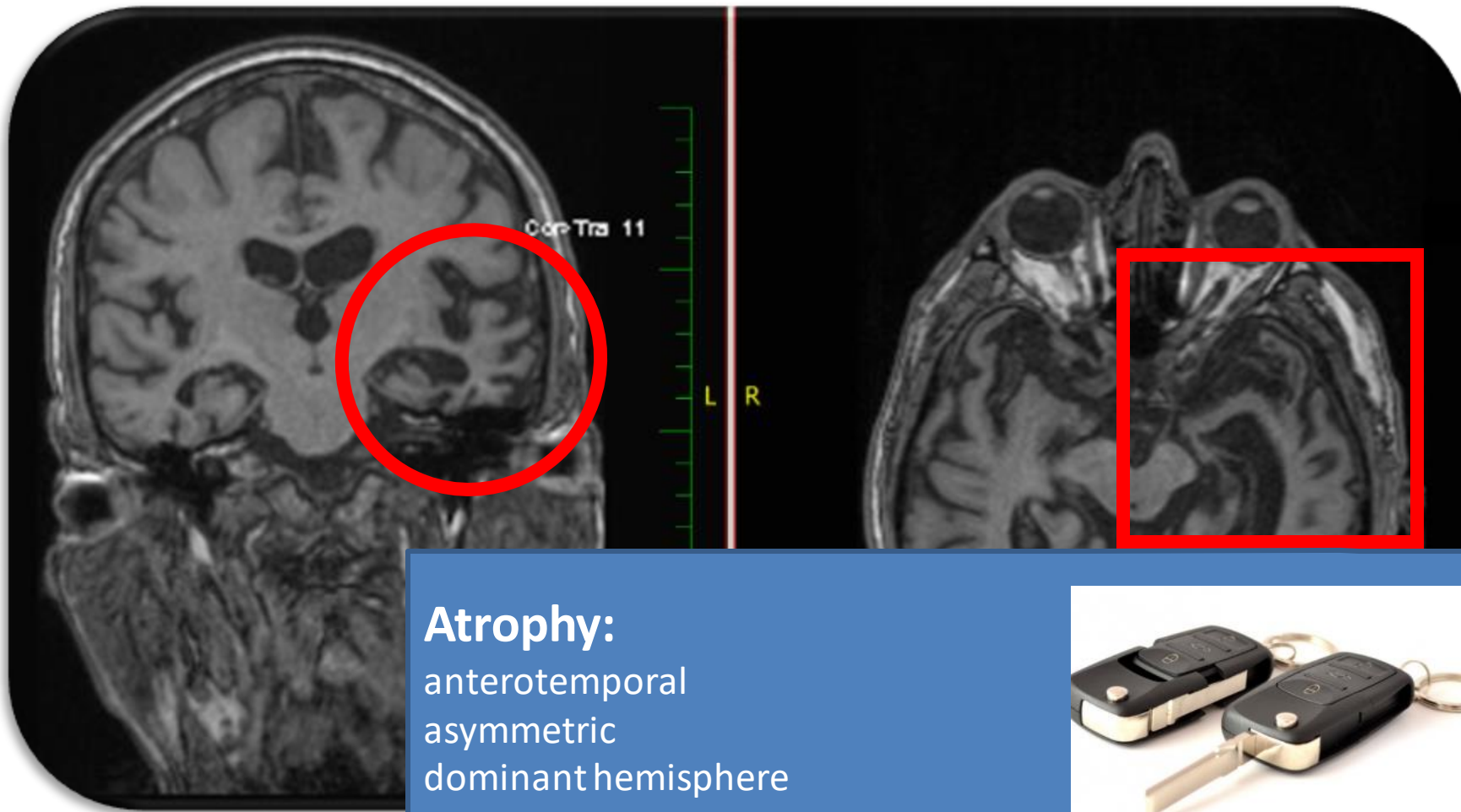
Quizz ???

The most common neuropathological background of svPPA is

(a) Alzheimer's disease
(b) Tauopathy
(c) TDP-43 proteinopathy
(d) Prion disorder

svPPA – neuropathology...

Most frequent finding are **TDP-43 deposits**

(transactive response DNA-binding protein 43
encoded by the *TARDBP* gene on choromosome 1)

Recent findings: "new tauopathies"
ARTAG – aging-related tau astrogliopathy
PART – primary age related tauopathy).
GGT – globular glial tauopathy

svPPA – neuropathology...

svPPA is mostly a **FTLD-TDP proteinopathy**
(frontotemporal lobar degenerations associated with TDP-43)

"Harmonized FTLD-TDP classification" 2012: four subtypes (A,B,C,D)
      Type A: frontotemporal dementia, nvPPA
      Type C: svPPA

Genetic forms: mutations in *TARDBP* or *PGRN* (progranulin) genes

svPPA – neuropathology …
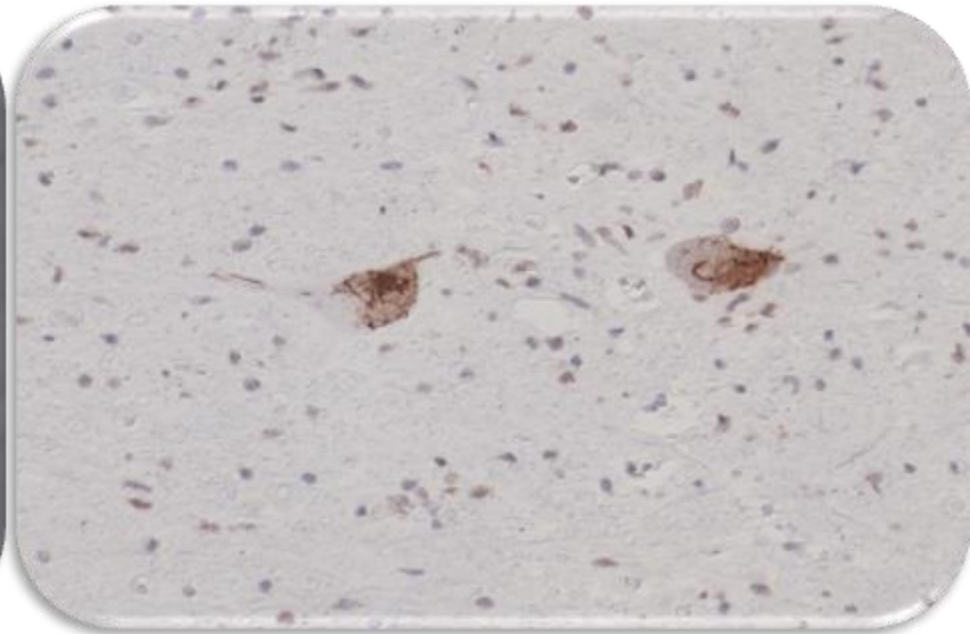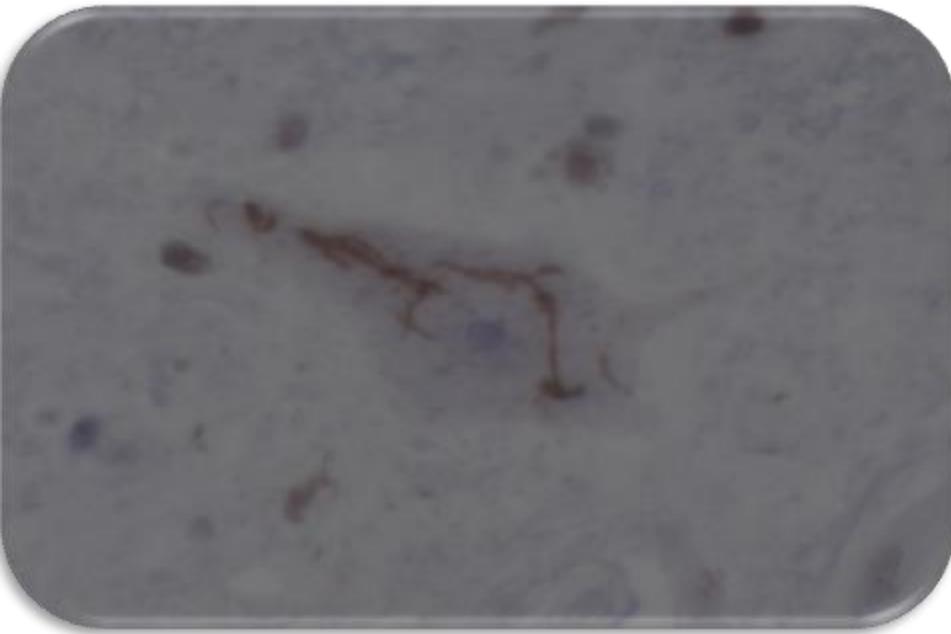
intracytoplasmatic **TDP-43** inclusions
(positive staining with monoclonal antibodies)

svPPA – anatomical framework…

Broca's area
      (inferior frontal cortex)

Wernicke's area
      (superior temporal cortex)

connected
via long fiber bundles
dorsally and ventrally
to the Sylvian fissure

Ventral stream = semantics

- dominant angular gyrus
- superior temporal gyrus
- temporal pole
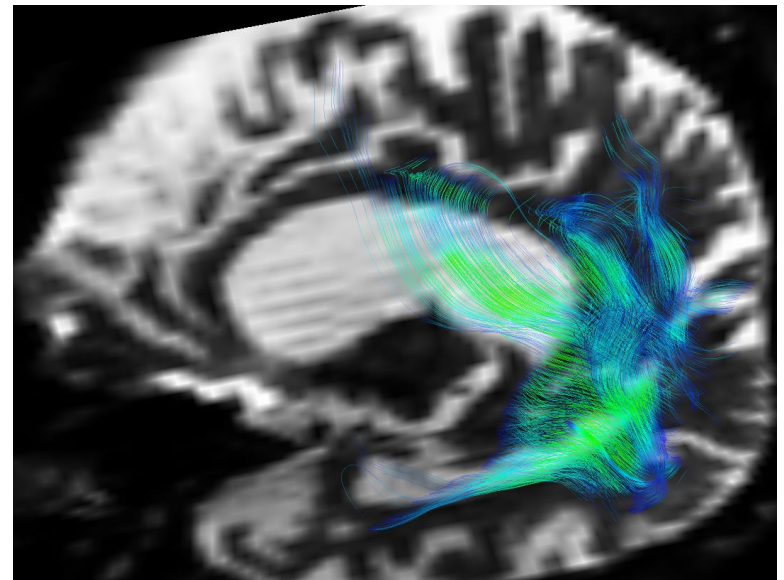
Anterotemporal cortex	Loss of empathy
Uncinate fascicle	Impulsivity, hyperorality
TDP-43 proteinopathy	Frontotemporal dementia

Clinical features and language assessment of svPPA
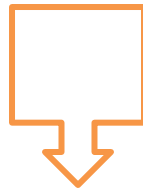
The core deficit in sv PPA is thought to involve semantic memory

component of long-term memory which contains the permanent representation of our knowledge about things in the world: facts, concepts and words, culturally shared, acquired early in life

Language pathways in the brain

The language-relevant brain regions are connected via long-range fiber bundles, which are located dorsally and ventrally to the sylvian fissure

Dorsal pathway (stream)

motor speech

Grammar (morphology, syntax)

Phonology (word sounds)

Ventral pathway (stream)

Hickok G, Poeppel D *(Cognition, 2004)*

Diagnostic criteria for svPPA
(Gorno-Tempini et al. 2011)

Both of the following core features must be present:

1) **Impaired confrontation naming**
2) **Impaired single word comprehension**

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

1) Impaired object knowledge, particularly for low-frequency items
2) Surface dyslexia or dysgraphia
3) Spared repetition
4) Spared speech production (grammar and motor speech)

Problem or inability to retrieve the word from mental lexicon

1. Impaired naming

- substitute the name of prototype (apple – orange)

- superordinate term

  (orange as fruit)

- „empty words" (that, thing)

Assessment of confrontation naming

Both of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

At least 3 of the following other features must be present:
Impaired object knowledge, particularly for low-frequency item
Surface dyslexia or dysgraphia
Spared repetition
Spared speech production (grammar and motor speech)

real objects

pictures, drawings of objects or actions

standardized test (norms: age, education)

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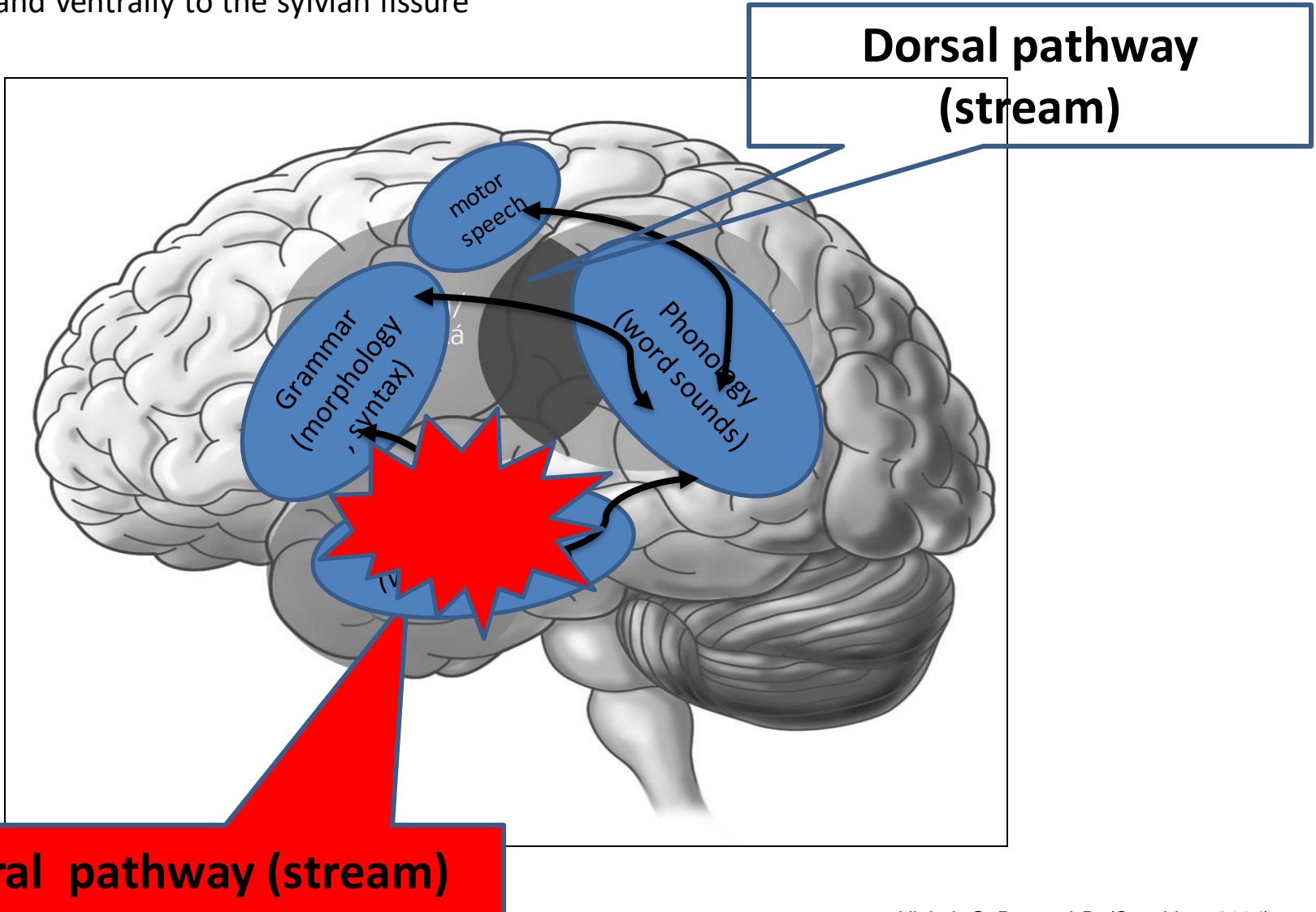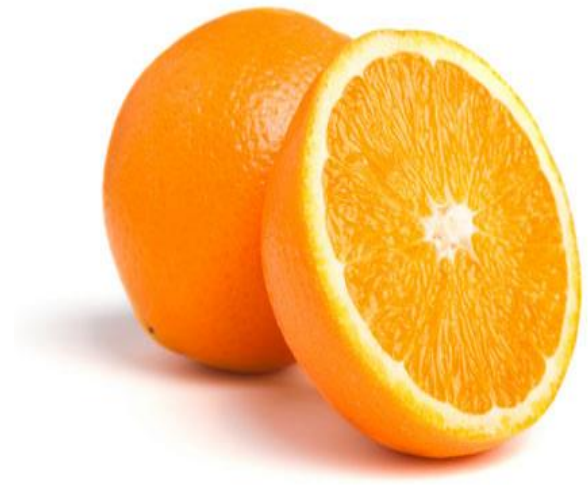Neuromuscular
Diseases (ERN EURO-NMD)

Assessment of confrontation naming

Both of the following core features must be present:

Impaired confrontation naming

Boston
Naming Test

SECOND EDITION

Edith Kaplan
Harold Goodglass
Sandra Weintraub
drawings by Osa Segal

Assessment of confrontation naming

Diagnostic criteria for svPPA

(Gorno-Tempini et al. 2011)

Both of the following core features must be present:

Impaired confrontation naming
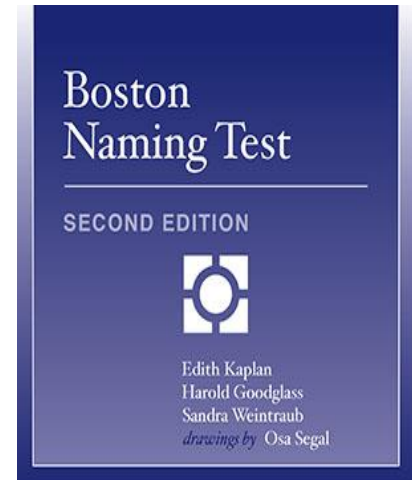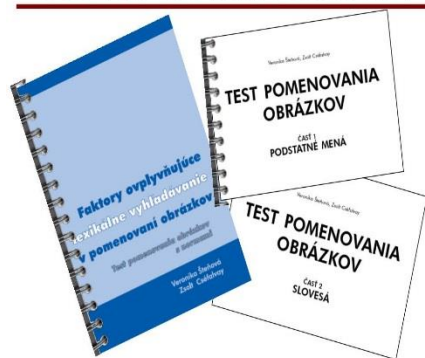
SYDBAT

Savage et al. 2013, Distinguishing Subtypes in Primary Progressive Aphasia: Application of the Sydney Language Battery, 2013, Dementia and Geriatric Cognitive Disorders 35(3-4)

Savage et al. 2013, Distinguishing Subtypes in Primary Progressive Aphasia:
Application of the **Sydney Language Battery,** 2013, Dementia and Geriatric Cognitive Disorders 35(3-4)

"I'm going to show you some pictures, and I'd like you to tell me what each one is called. Please give me the *full name* for each item (that is, without using abbreviations). For each one, you should be able to tell me the name of each picture by using a single word only. [Show Picture] What is this called?" *Discontinue test if patient has failed more than 6 consecutive items and appears distressed.*

Item	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
11. caterpillar		
12. cauliflower		
13. screwdriver		
14. dinosaur		
15. thermometer		
16. escalator		
17. shuttlecock		
18. asparagus		
19. leotard		
20. dandelion		Subtotal = _____ / 10
21. rhinoceros		
22. stethoscope		
23. hippopotamus		
24. chandelier		
25. tiara		
26. secateurs		
27. hieroglyphics		
28. balaclava		
29. orangutan		
30. pagoda		Subtotal = _____ / 10
		GRAND TOTAL = _____ / 30

Clinical features of semantic variant PPA

At least one of the following core features must be present:

1) Impaired confrontation naming

2) Impaired single word comprehension

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

Impaired object knowledge, particularly for low-frequency items

Surface dyslexia or dysgraphia

Spared repetition
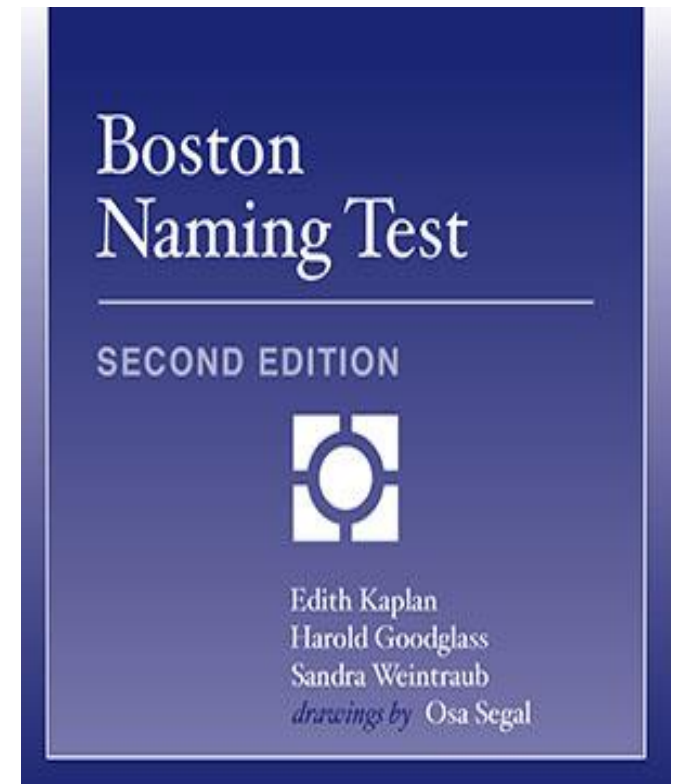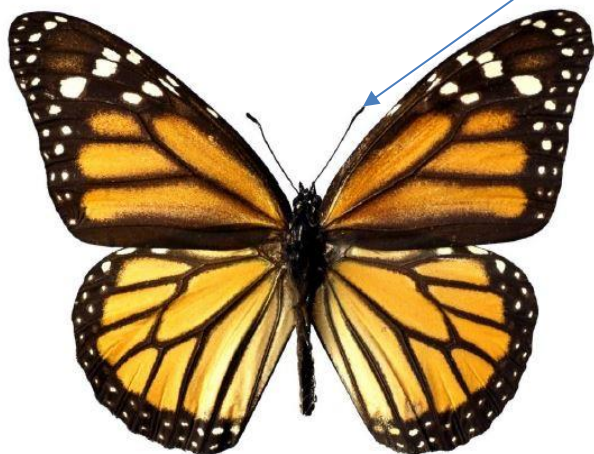
Spared speech production (grammar and motor speech)

(Gorno-Tempini et al., 2011)

inability to identify
the meaning of stimuly
(object, picture..)
despite preserved perception

Assessment of word comprehension

- picture naming

- word-picture matching

- semantic association

- repetition

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. caterpillar		

Assessment of word comprehension

At least one of the following core features must be present:

Impaired confrontation naming

2) Impaired single word comprehension ➡️

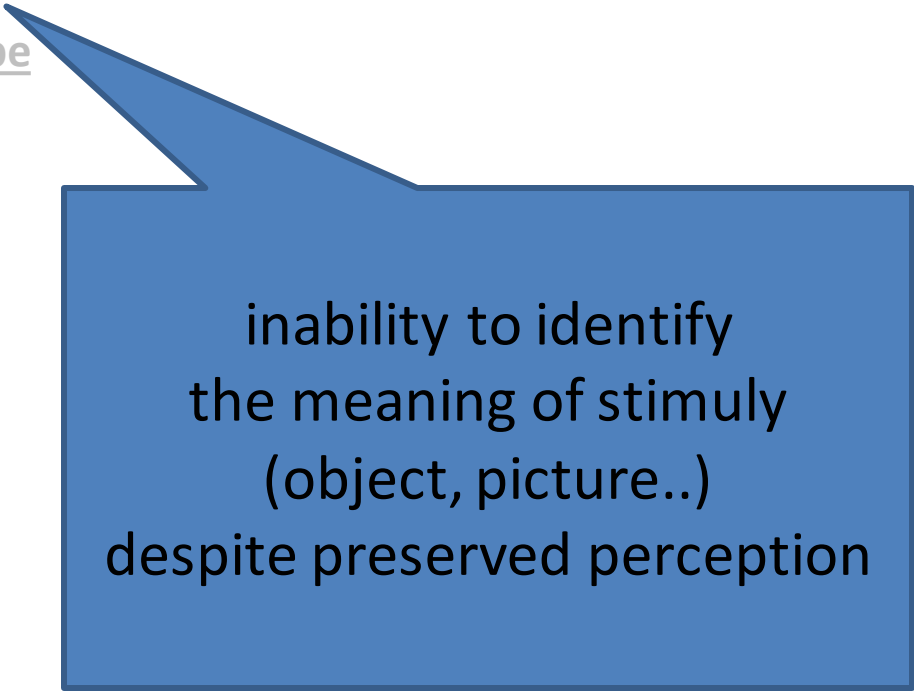**At least 3 of the following other features must be present:**

Impaired object knowledge, particularly for low-frequency items

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

Clinical features of semantic variant PPA

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

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

- Impaired object knowledge (particularly for low-frequency items)

- Surface dyslexia or dysgraphia

- Spared repetition

- Spared speech production (grammar and motor speech)

Assessment of object knowledge

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

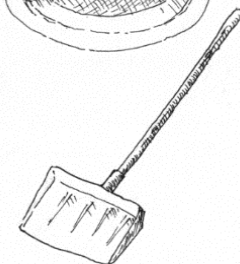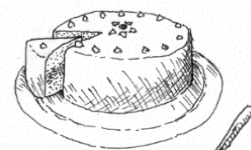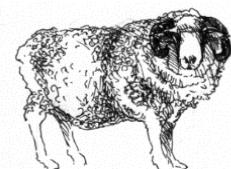**At least 3 of the following other features must be present:**

Impaired object knowledge ➡️

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

12

Howard, Patterson (1992):
The Pyramids and Palm Trees Test
(accessing meaning from pictures, words)

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Assessment of object knowledge

At least one of the following core features must be present:

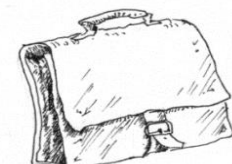Impaired confrontation naming

Impaired single word comprehension

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

Impaired object knowledge

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

Beeson, P.M. (unpublished).
The Arizona Semantic Test
https://aphasia.sites.arizona.edu

Assessment of object knowledge

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

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

Impaired object knowledge

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

Original Research Article

Distinguishing Subtypes in Primary Progressive Aphasia: Application of the Sydney Language Battery

Sharon Savage[a–c]   Sharpley Hsieh[a, c]   Felicity Leslie[a, c]   David Foxe[a, c]
Olivier Piguet[a–c]   John R. Hodges[a–c]

Assessment of object knowledge

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

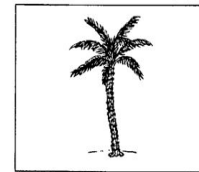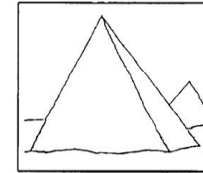**At least 3 of the following other features must be present:**

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Clinical features of semantic variant PPA

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Impaired single word comprehension

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

Impaired object knowledge
(particularly for low-frequency items)

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

PRINT

Letter Identification

Lexical Route — Orthographic Lexical — Non-lexical Route

Semantic System

Grapheme–Phoneme Correspondence

Phonological

READ ALOUD

M. Coltheart, 2006

Clinical features of semantic variant PPA

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

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

Impaired object knowledge

(particularly for low-frequency items)

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

M. Coltheart, 2006

Clinical features of semantic variant PPA

At least one of the following core features must be present:

Impaired confrontation naming

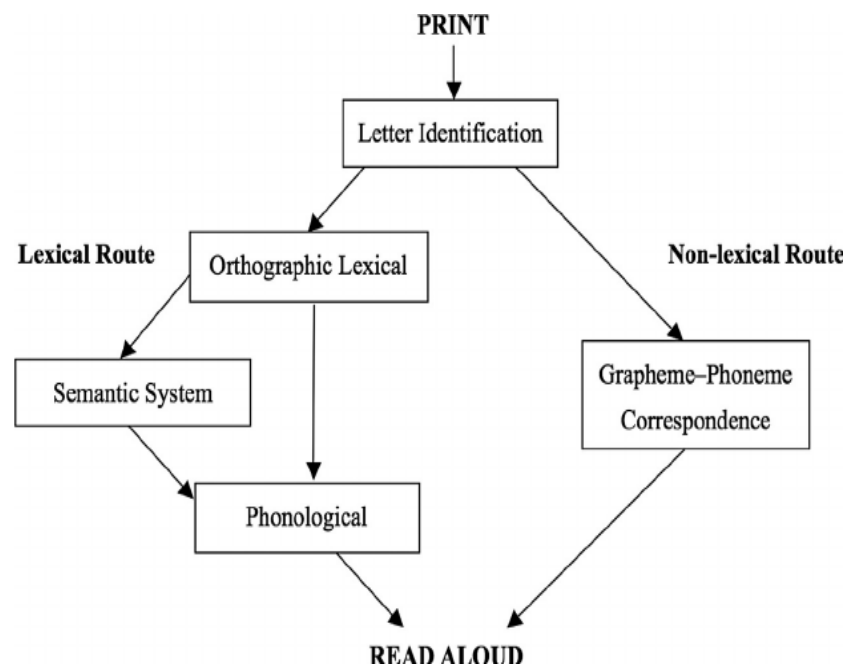Impaired single word comprehension

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

Impaired object knowledge

(particularly for low-frequency items)

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

Problems in reading exceptional. irregular words (in languages with deep orthography – English, French)

no 1:1 letter-sound correspondence

(less frequent in languages with shallow orthography, Czech or Slovak)

M. Coltheart, 2006

Clinical features of semantic variant PPA

At least one of the following core features must be present:

Impaired confrontation naming
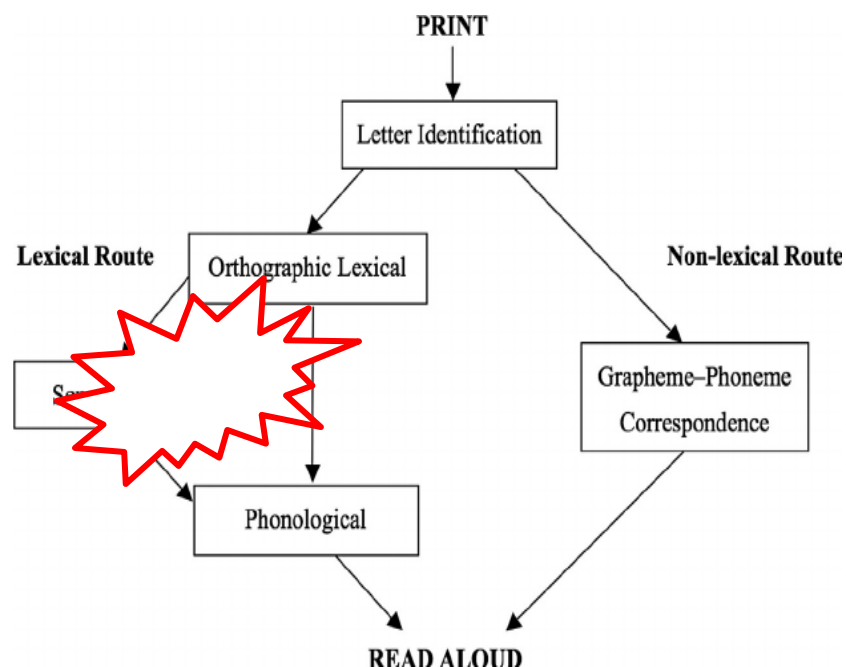
Impaired single word comprehension

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

Impaired object knowledge

(particularly for low-frequency items)

Surface dyslexia or dysgraphia

Spared repetition

Spared speech production (grammar and motor speech)

- mildly impaired of repetititon
- no arcuate fasciculus involvement (Grossman, Irwin, 2018)

regio Broca   regio Wernicke   fasciculus arcuatus

Assessment of connected speech

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

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

Impaired object knowledge

(particularly for low-frequency items)

Surface dyslexia or dysgraphia

Spared repetition

**Spared speech production
(grammar and motor speech)**

Western Aphasia Battery (WAB)

Boston Diagnostic Aphasia Examination (BDAE)

Clinical features of semantic variant PPA

At least one of the following core features must be present:

Impaired confrontation naming

Impaired single word comprehension

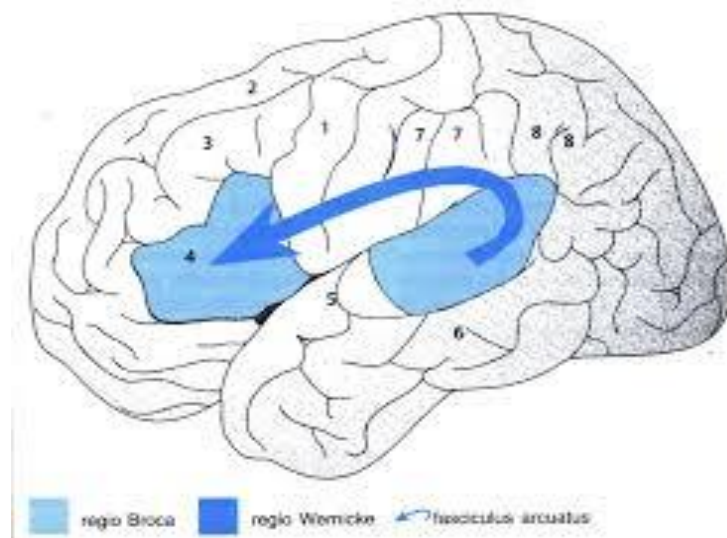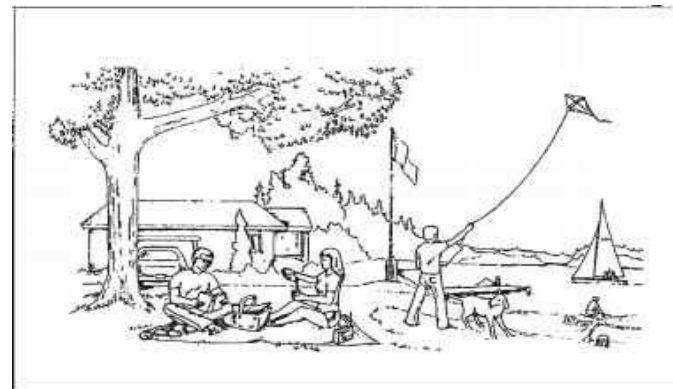**At least 3 of the following other features must be present:**

Impaired object knowledge
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Surface dyslexia or dysgraphia

Spared repetition

**Spared speech production
(grammar and motor speech)**

The picture description item from the VFF-R
(Cséfalvay, Košťálová, Klimešová, 2018)

Video

Clinical features of semantic variant PPA

The picture description item from the VFF-R
(Cséfalvay, Košťálová, Klimešová, 2018)

- fluent speech
- no sign of apraxia of speech
- no (frank) agrammatism
- empty, „non-sense" words
- word repetitions
- „singing like" intonation

Quizz ???

In a patient who has difficulties in single word comprehension, but can repeat them:

a.   svPPA can be excluded
b.   lvPPA can be excluded
c.   <u>svPPA is probable</u>
d.   lvPPA is probable

CASE 1: patient with mild svPPA

CASE 1: patient with mild svPPA

Language features

- 72 years old former high school teacher
- fluent speech, no grammatical erros
- word finding difficulties (low frequency words)
- speech comprehension problems in everyday conversations
  BUT...

CASE 1: conversation („My holiday")

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CASE 1:object naming

1: I'll put it aside like this.

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In formal tests – very mild impairments!!!

Object knowledge (AST) - mild impairment

Picture naming test - very mild impairment, delayed naming

Single word-comprehension

  a. word-picture matching task – not impaired

  b. lexical decision task „word/non-word" - mild impairment
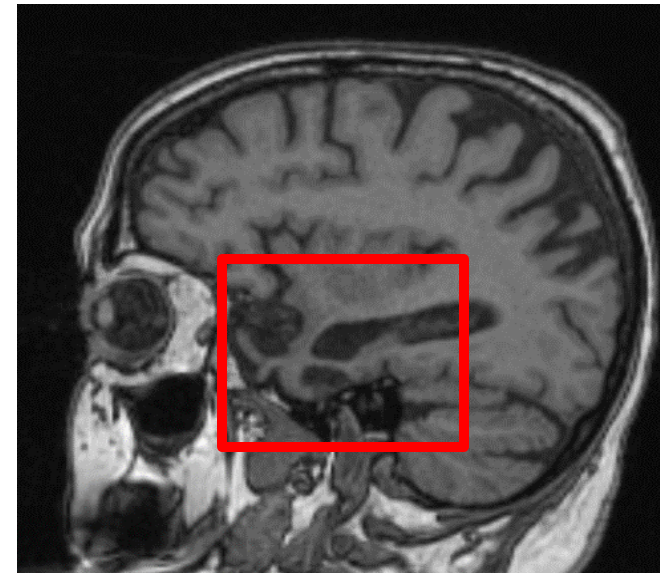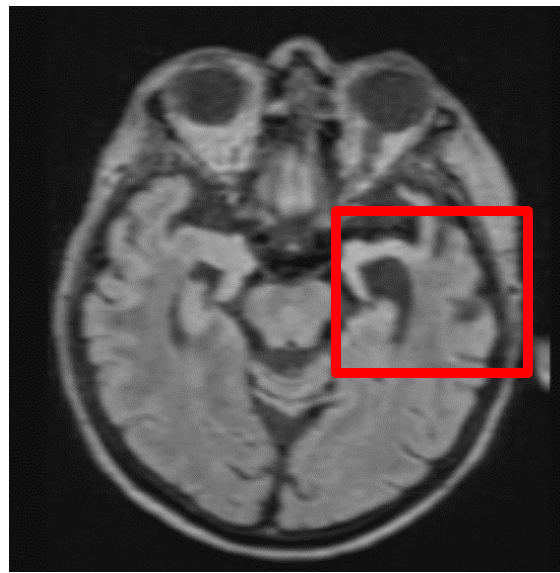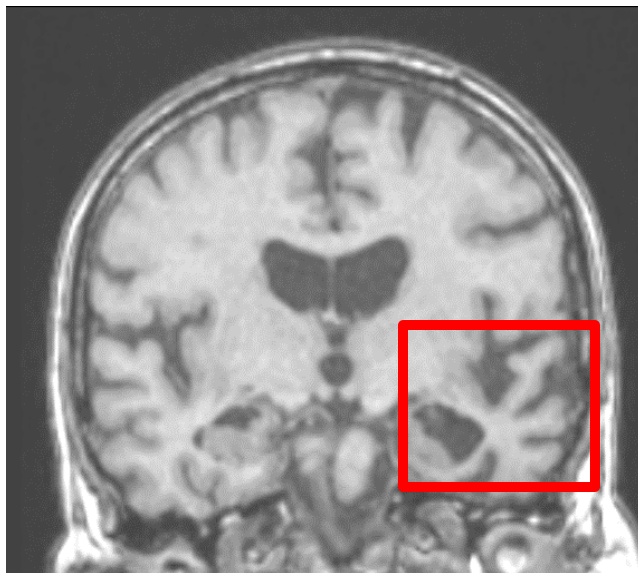
  c. word meaning comparison – mild impairment

Repetition (words, non-words) – no impairment

Grammar – no impairmant,

Motor speech – no impairment

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CASE 2: patient with severe svPPA

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Diseases (ERN EURO-NMD)

CASE 2: patient with severe svPPA

Language features

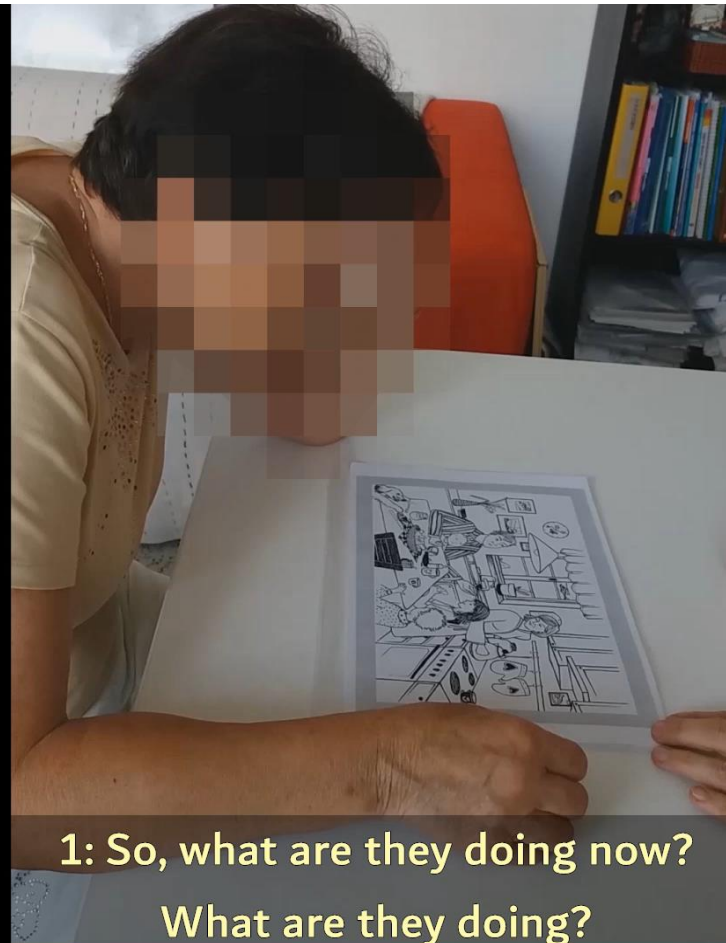first problems with language 7 years ago (now 65 years old woman)

- fluent speech production („empty speech")

- no motor speech problems

- no grammatical errors

- severe comprehension problems
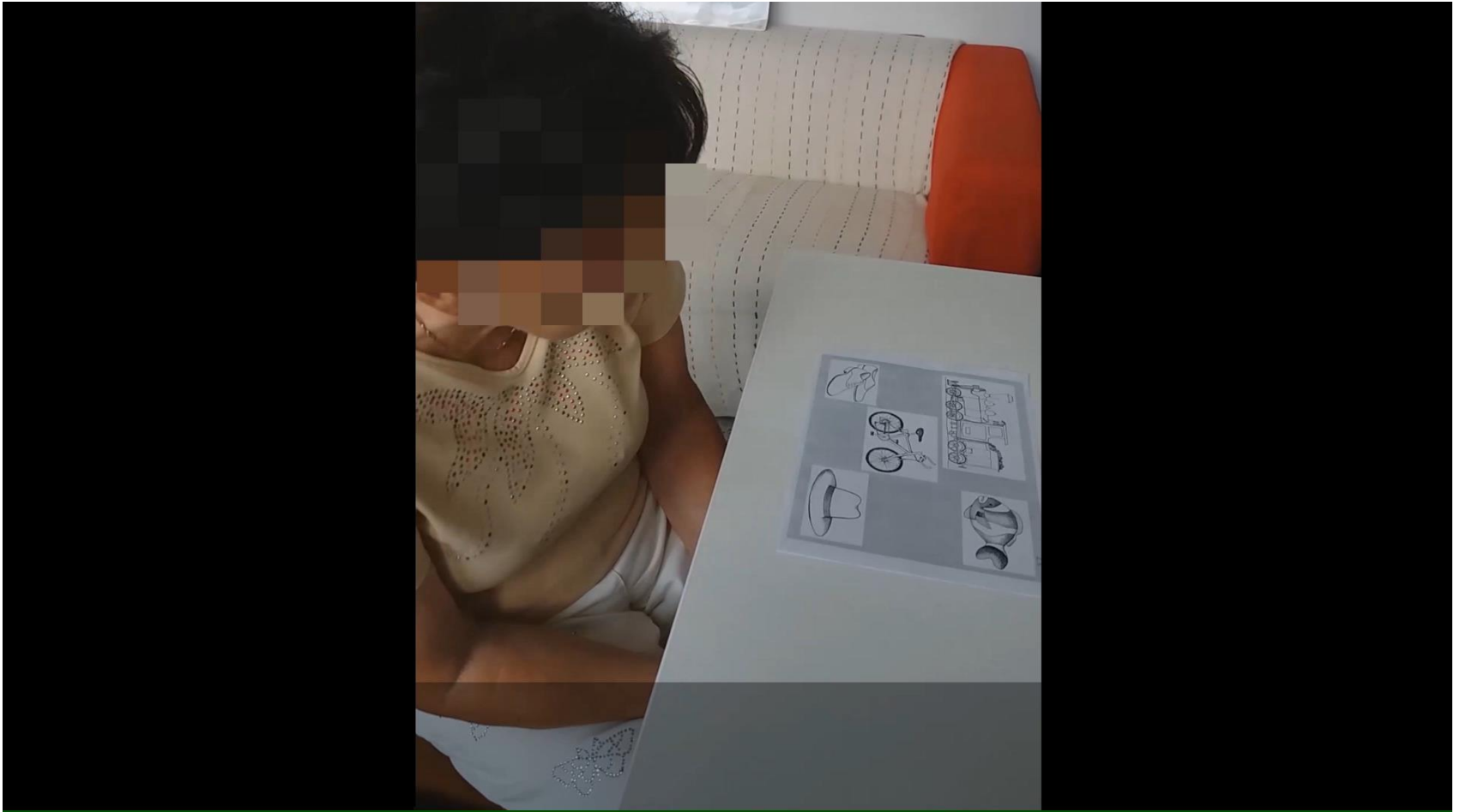
CASE 2:

Assessment

- AST (object semantics): 0
- Naming test : object naming 0, action naming: 0
- Single word comprehension 5/25
- Repetition (words) 9/10, pseudowords 8/10
- Oral reading words 17/20, pseudowords 11/15
- Reading comprehension (words) 6/15

European Reference Network
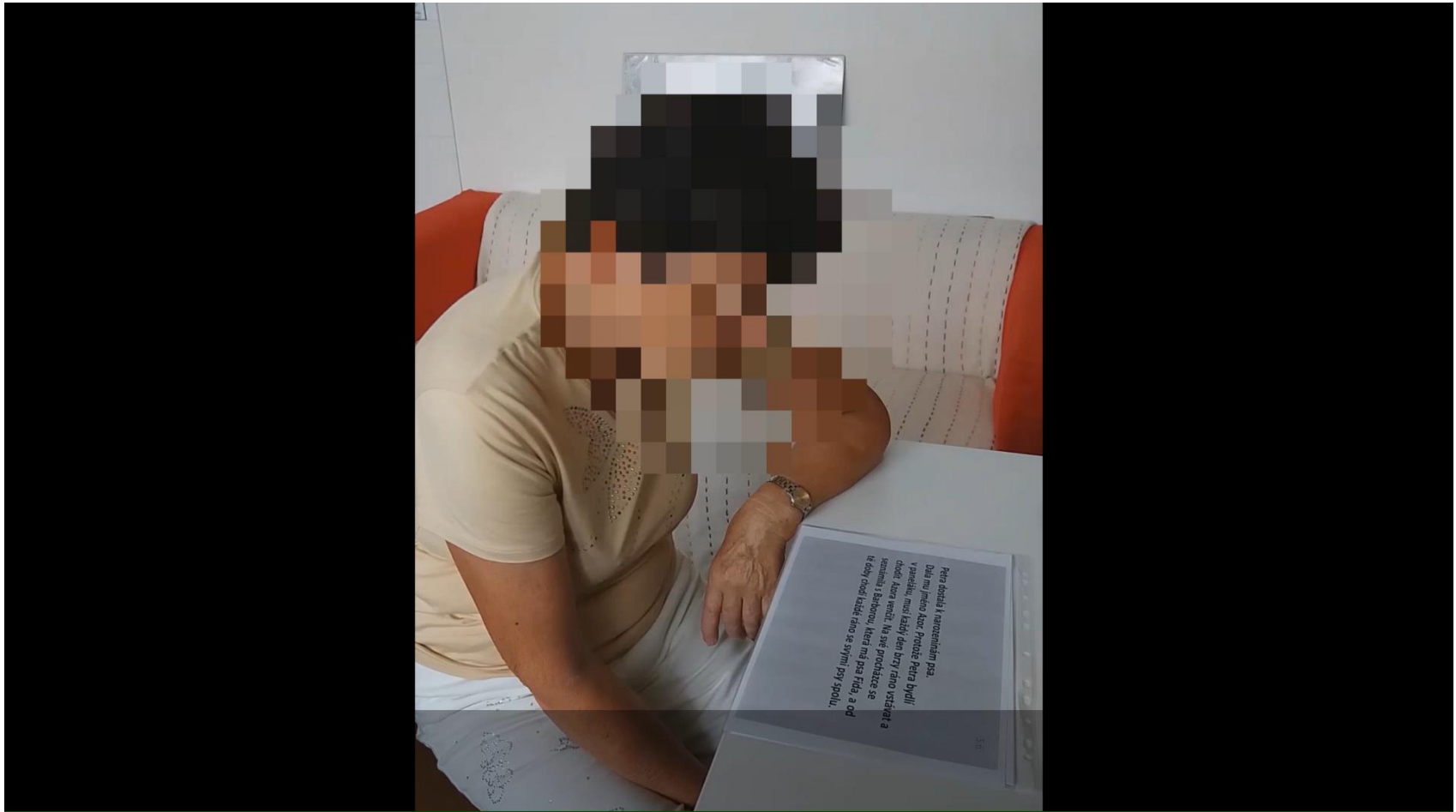for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

ean
european academy of neurology

European Reference Network
for rare or low prevalence complex diseases
Network Neuromuscular Diseases (ERN EURO-NMD)

CASE 2: picture description

CASE 2:
word comprehension (word-picture matching)

European Reference Network
for rare or low prevalence complex diseases
⚙ Network Neurological Diseases (ERN-RND)

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for rare or low prevalence complex diseases
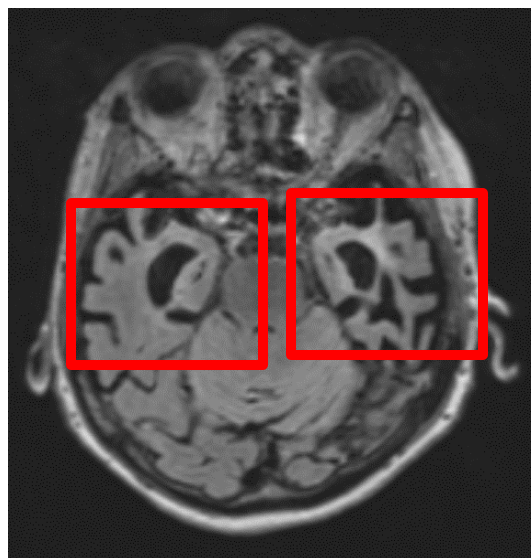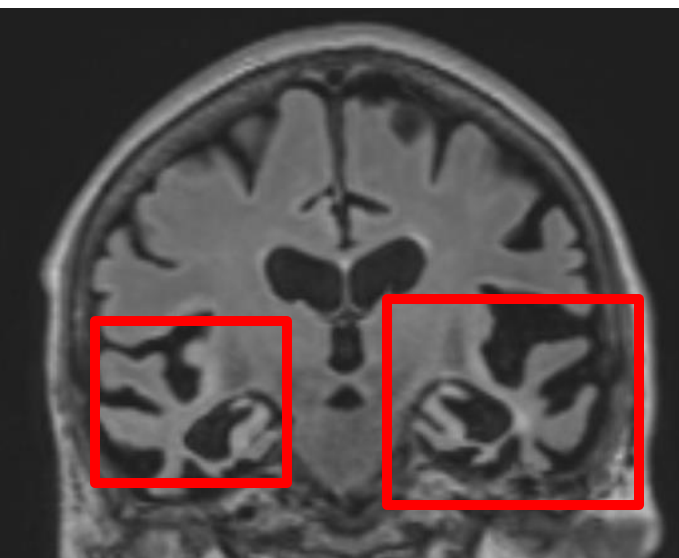⚙ Network Neuromuscular Diseases (ERN EURO-NMD)

CASE 2: oral reading

Intervention strategies

reviews on PPA treatment:

Croot et al., 2009

Rising et al., 2014

Tippett et al., 2015

SLT therapy **can** work
some promising results

Intervention strategies

Staged treatment approach (M. Fried-Oken, Henry, 2013)

1) Restorative approaches(lexical retrieval, writing...)

2) Shift toward aided approaches

3) Environmental support and partner training

Treatment strategies

Staged treatment approach (M. Fried-Oken, Henry, 2013)

1) Restorative

2) Shift toward

3) Environmen

lexical retrieval
- item specific improvement
- generalization …?
- maintenance …?

Treatment strategies

Staged treatment approach (M. Fried-Ok

1) Restorative

2) Shift

3) Envi

Self-cuing strategies   (Weintraub, Khayum):
- semantic circumlocution
- phonemic cueing
- writing the word
- visualizing the word
- using gestures

Treatment strategies

Staged treatment approach

1) Restorative

2) Shift toward aided approaches

3) Environmental support and partner training

low-tech
(i.e. communication books)

Treatment strategies

Staged treatment

High-tech (speech generating devices)

1) Restorative

   lexical retrieval, writing, sentence pr

1) **Shift toward aided approaches**

2) Environmental support and partner training

Treatment strategies

Staged treatment approach (M. Fried-Oken, Henry, 2013)

1) Restorative:

   lexical retrieval, writing, sentence pro...

1) Shift toward aided approaches

2) Environmental support and partner training

„sensitive, effective conversational partner"

Take-home message

1) Significant correlation: svPPA symptoms – **MRI findings**

2) Early svPPA: careful **evaluation of language** features

3) **Clinical impression prevails** over testing results
   („false negativity")

4) **Caregiver support** and training

Joint webinar series

THANK YOU

Next Webinar: '**How to assess and manage spastic gait in rare diseases?'**

10. September 2020, 15-16h CET