PRIMARY PROGRESSIVE APHASIAS

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Disclosure

• None
Learning objectives

• The learner will be able to:
  • Diagnose primary progressive aphasia (PPA) on the basis of a clinical examination
  • Request the appropriate tests to support the diagnosis
  • Diagnose the subtype of PPA and the most likely pathological cause
  • Propose a management plan to patient and family
Key message

• PPAs are a group of phenotypic presentations of different neurodegenerative disorders

• PPA is not rare in cognitive/behavioural neurology practice

• A correct diagnosis has prognostic and management relevance
Classification of primary progressive aphasia and its variants

A progressive disorder of language associated with atrophy of the frontal and temporal regions, PPA was first described in the 1990s by Pick and Curschmann. In the modern literature, Mesulam’s classical series of cases with ‘primary progressive aphasia,’ subsequently renamed primary progressive aphasia (PPA), described a progressive disorder of fluent language, similar to the language impairment seen in semantic dementia, in the early 1990s. Variants described subsequently, including an additional clinical form—non-fluent progressive primary aphasia, a common clinical presentation in developing countries due to its condition in non-fluent aphasia—were initially described in 2001. Today, PPA is used primarily to describe clinical syndromes with dementia, and the term ‘primary progressive aphasia’ is now used as a synonym for PPA. PPA is a heterogeneous group of disorders with varying clinical presentations, and the diagnosis of PPA should be made with caution. The current classification of PPA includes three main subtypes: semantic dementia, non-fluent progressive aphasia, and logopenic progressive aphasia. This classification is based on the clinical features of language impairment, such as the pattern of comprehension, production, and repetition. The subtypes of PPA are characterized by different patterns of language impairment and progression, and the diagnosis of PPA is made by excluding other possible causes of cognitive decline and language impairment. The classification of PPA is important for improving the understanding of the underlying neuroanatomical and neurophysiological mechanisms, and for developing targeted treatments for these disorders. Future research will likely lead to a better understanding of the pathogenesis of PPA and the development of new therapeutic strategies.
When to suspect a PPA?
(Mesulam 2003 criteria, modified)

• Inclusion
  • Most prominent clinical feature is a language impairment (aphasia)
  • This impairment is the only determinant of difficulties in the activities of daily living
  • Aphasia is the most prominent disorder at onset and in the early phase of disease

• Exclusion
  • Aphasia can be due to non neurodegenerative or other medical causes
  • Aphasia can be attributed to a psychiatric disorder
  • Prominent early episodic memory or visuo-spatial disorders
  • Prominent early behavioural disturbances
How to diagnose a PPA?

• Quantitative/qualitative analysis of connected speech
• Naming and comprehension of single words
• Repetition
• Comprehension of grammatically complex sentences
The analysis of connected speech
What to look for?

• Motor speech production
• Other disorders of fluency (pauses and repetitions)
• Lexical/semantic errors
• Grammar (morphology, syntax)
How to diagnose a PPA?

- Quantitative/qualitative analysis of extended production
- Naming and comprehension of single words
- Repetition
- Comprehension of syntactically complex sentences
A comprehensive semantic memory test

• Picture naming
• Naming from verbal description
• Word-picture matching
• Picture sorting
• Feature generation and verification
Naming from verbal description

“It is a fruit, it is yellow, with the shape of a half-moon. Monkeys like them very much”

Picture naming

Word-picture matching

Sorting

Feature generation and verification

Distracters

Target
How to diagnose a PPA?

• Quantitative/qualitative analysis of extended production
• Naming and comprehension of single words
• Repetition
• Comprehension of syntactically complex sentences
A comprehensive assessment of repetition

- Vowels and syllables
- Digits
- Words
- Pseudowords
- Sentences of increasing length
A “core” assessment procedure

• Quantitative/qualitative analysis of extended production
• Naming and comprehension of single words
• Repetition

• Comprehension of syntactically complex sentences
The boy and the dog are being followed by the girl
The new screening battery for aphasia

Italian version

1. Picture naming (14)
2. Sentence comprehension (8)
3. Single word comprehension (12)
4. Repetition (6 words, 4 nwds)
5. Repetition of sentence (6)
6. Reading (16)
7. Written description (1)
8. Semantic knowledge (pictures) (4)
9. Connected speech (1)

Test Materials:

User’s Manual
Norms Guide
Scoring Template

10-15 min
Clinical variants

• Non fluent/agrammatic

• Semantic

• Logopenic/phonological

• Other variants
Semantic variant

- Fluent speech, with anomias and semantic paraphasias
- **Naming and single word comprehension impairment**
- Impaired nonverbal semantics
Case S.P. ♂ 63 years old, 13 years of education, svPPA (GRN +)
Non fluent/agrammatic variant

• Nonfluent production with articulation impairment and agrammatism

• Naming moderately impaired

• Preserved single word comprehension

• Defective comprehension of syntactically complex sentences
Case M.G. ♀ 62 years old, 17 years education

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**SPM-T map of hypometabolism of the single patient**

[^F]FDG-PET scan compared to 112 HC (FWE)

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**Neuropsychological Evaluation** Language assessment

<table>
<thead>
<tr>
<th>AREA INDAGATA</th>
<th>TEST</th>
<th>P. GREZZO</th>
<th>P. CORRETTO</th>
<th>P. EQUIVALENTE</th>
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<tbody>
<tr>
<td>LINGUAGGIO:</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>denominazione osca nono</td>
<td>CAS-7</td>
<td>40/40</td>
<td>40</td>
<td>4</td>
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<tr>
<td>comprensione word picture</td>
<td></td>
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<td></td>
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<tr>
<td>matching test</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>comprensione di ordini</td>
<td>Token Test</td>
<td>33/36</td>
<td>30/50</td>
<td>2</td>
</tr>
<tr>
<td>complessi:</td>
<td></td>
<td></td>
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<tr>
<td>Comprensione grammaticale utilitativa</td>
<td>BADA:</td>
<td>52/60</td>
<td>Cut off 50; Al limite</td>
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<tr>
<td>Comprensione grammaticale visiva.</td>
<td></td>
<td>42/45</td>
<td>Cut off 43; Deficitare</td>
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<tr>
<td>Accesso al lessico.............</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elencazione semantica.........</td>
<td>24</td>
<td>22</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Elencazione nominale.........</td>
<td>10</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Memoria semantica............</td>
<td>Test Palma Prisma</td>
<td>48/52</td>
<td>45,77</td>
<td>Nella norma</td>
</tr>
<tr>
<td>Ripetizione ..…………………</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Svuota</td>
<td>28/30</td>
<td></td>
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<tr>
<td>Parole</td>
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<tr>
<td>Parole stamane</td>
<td>30/30</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Parole e composti e sintagi</td>
<td>29/30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frasi</td>
<td>30/30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTALE</td>
<td>147/150</td>
<td>-</td>
<td>Nessun deficit</td>
<td></td>
</tr>
<tr>
<td>Lettura...........……………</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>AAT</td>
<td>30/30</td>
<td>-</td>
<td>Nessun deficit</td>
<td></td>
</tr>
<tr>
<td>Scrivere sotto detto..………</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAT</td>
<td>30/30</td>
<td>-</td>
<td>Nessun deficit</td>
<td></td>
</tr>
</tbody>
</table>
Logopenic/phonological variant (original definition)

• Dysfluent speech, with anomic pauses, hesitations and phonological errors, but normal articulation and grammar
• Preserved single word comprehension
• Defective repetition and auditory verbal short-term memory
• Defective sentence comprehension
Case E.M. ♀ 77 years old, 10 years schooling, suspected PPA

- **Instrumental Evaluations**

CSF Aβ42 and Tau measures

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
<th>Range</th>
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<tbody>
<tr>
<td>LCR-BETA AMILIOIDE (L-42)</td>
<td>269 ng/L</td>
<td>&gt; 500</td>
</tr>
<tr>
<td>LCR-PROTEINA TAU</td>
<td>322 ng/L</td>
<td>0.0 - 500.0</td>
</tr>
<tr>
<td>LCR-PROTEINA TAU FOSFORILATA</td>
<td>74 ng/L</td>
<td>0.00 - 81.00</td>
</tr>
</tbody>
</table>

SPM-T map of hypometabolism of the single patient

[18F]FDG-PET scan compared to 112 HC (FWE)
<table>
<thead>
<tr>
<th></th>
<th>NF/Av</th>
<th>Sv</th>
<th>L/Phv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor speech</td>
<td>Impaired (apraxia of speech)</td>
<td>normal</td>
<td>pauses, hesitations, phonological errors</td>
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<tr>
<td>Grammar</td>
<td>impaired</td>
<td>normal</td>
<td>preserved</td>
</tr>
<tr>
<td>Word-finding</td>
<td>mildly impaired</td>
<td>impaired, semantic errors</td>
<td>Impaired, anomias, phonemic paraphasias</td>
</tr>
<tr>
<td>Word comprehension</td>
<td>preserved</td>
<td>impaired early</td>
<td>preserved</td>
</tr>
<tr>
<td>Sentence repetition</td>
<td>motor impairment</td>
<td>preserved</td>
<td>impaired</td>
</tr>
<tr>
<td>Sentence comprehension</td>
<td>Impaired (grammatically complex sentences)</td>
<td>preserved</td>
<td>Impaired (long sentences)</td>
</tr>
</tbody>
</table>
Pathology
(Spinelli et al., 2017)

• Nf/Av
  • FTLD Tau 88%

• Sv
  • TDP-C 83%

• L/Phv
  • AD 100%
Management

• Advice and support
• Symptomatic treatment: depression, behavioural disorders
• Speech and language therapy
• Neuromodulation
References