Development of the standardised, multilingual Mini Linguistic State Examination (MLSE) to classify and monitor primary progressive aphasia

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Summary

- Language loss is common in dementia (including in primary progressive aphasia [PPA]), but language tests are time-consuming and not readily comparable across languages.
- Current criteria to identify three main variants of PPA based on lengthy clinical tests or imaging.1
- Improved tools to screen, diagnose, and monitor PPA are essential.
- In this study, we develop English and Italian versions of a brief (<20 minutes) language screening tool which includes the major domains affected in PPA symptoms.

Background: clinical features of the three main variants of PPA1

PPA has three main forms: (1) the nonfluent variant of PPA (nvPPA) (2) the semantic variant of PPA (svPPA), and (3) the logopenic variant of PPA (lvPPA). The three variants have differing linguistic profiles, as summarised below:

<table>
<thead>
<tr>
<th>nrPPA</th>
<th>svPPA</th>
<th>lvPPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor speech production</td>
<td>Preserved</td>
<td>Impaired</td>
</tr>
<tr>
<td>Single-word repetition</td>
<td>Not considered</td>
<td>Preserved</td>
</tr>
<tr>
<td>Sentence repetition</td>
<td>Not considered</td>
<td>Impaired</td>
</tr>
<tr>
<td>Word/ sentence comprehension</td>
<td>Not considered</td>
<td>Preserved</td>
</tr>
<tr>
<td>Naming</td>
<td>Preserved</td>
<td>Impaired</td>
</tr>
<tr>
<td>Semantic knowledge</td>
<td>Preserved</td>
<td>Impaired</td>
</tr>
<tr>
<td>Reading/ writing</td>
<td>Preserved</td>
<td>Impaired</td>
</tr>
</tbody>
</table>

The linguistic profiles of the three variants of PPA are associated with characteristic impairing features, and underlying pathologies:

<table>
<thead>
<tr>
<th>nrPPA</th>
<th>svPPA</th>
<th>lvPPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging features</td>
<td>Left inferior frontal atrophy</td>
<td>Bilateral anterior temporal atrophy</td>
</tr>
<tr>
<td>Associated pathology</td>
<td>FTD-Tau; Cortico-basal degeneration; FTD-TDP; Alzheimer’s disease</td>
<td>FTD-TDP</td>
</tr>
</tbody>
</table>

The Mini Linguistic State Examination (MLSE)

MLSE test items are selected by the relevant domains, and based on the recommendations of current diagnostic guidelines1:

Confrontation naming
- for assessing anomia, semantic/phonemic errors
- Featuring 9 items (non-living and living); all with low values of familiarity/spoken frequency to be sensitive to mild deficits

Single-word comprehension (repeat and point)
- for assessing semantic knowledge
- 1 target and 5 distractors from same semantic category

Repetition
- Includes single words of varying syllabic length, repeated production of a polysyllabic word, polysyllabic nonsense words, and sentences for assessing difficulties with phonology, articulation, and working memory

Semantic association
- for assessing semantic knowledge

Reading (words and non-words)
- Like repetition, reading aloud can indicate problems with phonology and articulation, but is also sensitive to impaired lexical-semantic word knowledge as indicated in English by regularisation errors such as SEW pronounced as “sue”. This task features regular and irregular words (and regular/irregular stress words for the Italian version)

Sentence comprehension
- for assessing the effects of sentence length and grammatical complexity
- Tasks include matching orally presented sentences to pictures, and answering questions about orally presented sentences. Sentences vary in grammatical complexity, length, and predictability

Writing
- for assessing modifications (e.g. allography, micrography) and errors (e.g. orthographic, semantic, grammatical/syntactic)
- Instructed writing task

Picture description
- for connected speech analysis, including assessment of narrative structure, vocabulary, grammar, phonology, and fluency

Study Outline

Phase 1: Pre-norming and pilot data
- 180 English- and Italian-speaking controls complete MLSE test items
- Results from Phase 1 were used to inform the design of the MLSE for use in Phase 2

Phase 2: Principal study
- 120 English- or Italian-speaking patients with:
  - one of the three main variants of PPA, or
  - other neurodegenerative syndromes affecting motor or cognitive function (e.g. PSP, CBS, AD, FTD)
- 70 English- or Italian-speaking controls (age 45-75)

Procedure
- Baseline: participants complete the MLSE, the Addenbrooke’s cognitive examination (ACE-III), and 3T MRI. The MLSE is validated against the Boston Diagnostic Aphasia Examination for English-speaking participants or the Screening for Aphasia in NeuroDegeneration battery2 for Italian-speaking participants
- Follow-up: repeat assessment at 1 year

Conclusions

- The MLSE will provide a much needed short screening tool to assess aphasia, especially in diagnosis and monitoring of progressive aphasia
- Translation of the MLSE into other languages will increase sample sizes; and aid cross-linguistic/cultural investigation of language impairment associated with dementia
- The English version of the MLSE will provide a template for the development of further language-specific versions

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References