Supplementary Material

Utility of the Addenbrooke’s Cognitive Examination-III online calculator to differentiate the primary progressive aphasia variants

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METHODS

Participants

The current consensus criteria states that ‘a clear parkinsonian syndrome (rigidity, tremor) ’should not be present at the time of diagnosis, although mild limb apraxia and difficulty with fine finger movements can be noted.’\(^1\) The consensus criteria, however, do not elaborate on the definition of ‘clear’. Accordingly, in the current study, we took a precautionary approach and excluded patients with frank parkinsonism and/or patients with suspected parkinsonian or motor neuron features. Supplementary Figure 1 provides a comprehensive illustration of the parkinsonian and motor neuron profiles of nfv-PPA patients i) included and ii) excluded in Phase 1 of this study.

Neuropsychological tests routinely administered to PPA patients and controls at the FRONTIER Research Group clinic

i) Digit Span Forward and Backward subtests of the Wechsler Memory Scale–Third edition WMS-III,\(^2\) ii) Rey Complex Figure Test Copy and Recall (RCFT),\(^3\) iii) Sydney Language Battery (SYDBAT), which includes measures of confrontation naming, single-word repetition, word comprehension and semantic association,\(^4\) iv) verbal letter fluency (with letters F, A and S),\(^5\) v) the Sentence Repetition
task from the Multilingual Aphasia Examination,\textsuperscript{6} vi) Trail Making Test, \textsuperscript{7} and, vii) the Face and Emotion Processing Battery.\textsuperscript{8,9}

Results

Demographics

Overall group differences were present for all baseline ACE-III subdomain raw scores (all \( p \) values < .001): Attention \( F(3, 190) = 45.049; \) Memory \( F(3, 190) = 88.127; \) Verbal Fluency \( F(3, 190) = 169.899; \) Language \( F(3, 190) = 136.932; \) Visuospatial \( F(3, 190) = 31.452 \) (Table 1). Compared to Controls, patient groups were impaired on all ACE-III subdomains (all \( p \) values < .001), with the exception of the sv-PPA group which showed relatively intact performance on the Visuospatial subdomain (\( p = .162 \)).

Direct comparisons of the patient groups on the baseline ACE-III subdomain raw scores are presented in Table 1. On the Attention subdomain, the lv-PPA group were more impaired than the nfv-PPA groups (\( p \) values < .003), whereas no differences were observed between the nfv-PPA and sv-PPA groups on this measure (\( p = .418 \)). On the Memory subdomain, the lv-PPA and sv-PPA groups performed worse than the nfv-PPA group (\( p \) values < .001). Performances among the lv-PPA and sv-PPA on this measure did not differ significantly (\( p = .212 \)). On the Fluency subdomain, the nfv-PPA were more impaired than the sv-PPA group (\( p < .001 \)). Performances did not differ on this measure among the lv-PPA and nfv-PPA group (\( p = .593 \)) or among the lv-PPA and sv-PPA groups (\( p = .065 \)). The lv-PPA and nfv-PPA groups were similarly impaired on the Language (\( p = 1.000 \)) but less impaired than the sv-PPA group (\( p \) values < .001). Lastly, on the Visuospatial subdomain, the lv-PPA and nfv-PPA groups were more impaired than the sv-PPA group (\( p \) values < .002). Performances on this measure did not differ significantly between the lv-PPA and nfv-PPA groups (\( p = .461 \)).

ACE-III items
The PPA groups showed distinct ACE-III profiles at the item-by-item level. Relative to controls, the PPA groups were impaired on most ACE-III items. Notable exceptions across PPA groups were, however, present. The sv-PPA group did not differ significantly from controls on all visuospatial items (i.e., loops, cube, clock, dot counting, fragmented letters), most repetition items (i.e., single words, ‘glitters’ sentence), three step commands, and on several attention items (orientation to time, three-word registration/learning, serial 7s). Relative to controls, the nfv-PPA group’s performance was spared on aspects of visuospatial ability (i.e., clock drawing, fragmented letters), semantic association, and on free recall of a name and address. The lv-PPA group did not differ significantly from controls on basic visuoperceptual skills (i.e., dot counting, fragmented letters) and the semantic association item.

Direct comparisons of the PPA groups revealed cognitive profiles characteristic of each variant. Comparison of the two non-fluent variants (i.e., lv-PPA, nfv-PPA) revealed the lv-PPA group were disproportionately impaired on the name and address learning item and clock drawing, whereas the nfv-PPA group were disproportionately impaired on single word repetition and dot counting. Relative to the non-fluent groups, the sv-PPA were more impaired on retrograde memory, confrontation naming, semantic knowledge (i.e., word-picture matching) and reading, and were additionally more impaired than the nfv-PPA group on orientation to location (i.e., geography), and aspects of memory (i.e., three-word recall, free memory recall of name and address). By contrast, the sv-PPA group performed better than the non-fluent groups on aspects of attention (i.e., orientation to time, serial 7s), repetition (i.e., single word, sentences) and visuospatial abilities (i.e., loops, cube); the sv-PPA group were also superior to the nfv-PPA group on letter fluency, writing and dot counting, and superior to lv-PPA on clock drawing.
Supplementary Table 1. Progressive aphasia language scale (PALS) scoring criteria

| Item                          | Score                        |
|-------------------------------|------------------------------|
|                               | 0 (None)                     | 1 (Questionable)              | 2 (Definite)               | 3 (Severe)               |
| Spontaneous Speech            |                              |                              |                            |                            |
| Motor speech disorders        | No evidence                  | Isolated and inconsistent articulatory errors. Groping speech is occasionally present. | Consistent or evident distortions, especially for less common polysyllabic words, leading to evident slurred speech. Loss of prosody is often present. | Speech is continuously distorted or slurred, often causing unintelligible pronunciation or slow output. Consistently abnormal prosody, rate of speech, and resolution of utterances |
| Agrammatism                   | No evidence                  | Avoidance of complex grammatical structures. Syntax and word inflection are largely preserved. There are only isolated and questionable errors. | Consistent oversimplification of sentence structures, with evidence of grammatical errors, especially for syntax and verb conjugation (i.e., inflection). Closed-type words (e.g., prepositions, auxiliary verbs, or articles) are omitted or incorrectly used. | Frequent omission of closed-type words while open-type words are often incorrectly inflected. Language production is telegraphic, with evident oversimplification of sentence structure. |
|                               |                              |                              |                            |                            |
| Tasks                         |                              |                              |                            |                            |
| Naming                        | No anomia                    | Nearly normal with just one or two naming errors or omissions, usually for uncommon items (e.g., tongs, rhinoceros, etc.). Frequent and marked self-corrections, subtle delays in retrieving names, or naming doubtfully should be included in this level. | Although may correctly name some well-known items, there is consistent and unmistakable naming errors. | Just able to correctly name a few well-known items (less than a third of items), with marked delays in retrieving names. |
| Single word repetition        | Flawless repetition          | Occasional (1-2) and subtle errors mainly due to mispronunciation or word fragmentation, involving only longer, or more complex words. | Evident and consistent mistakes due to mispronunciation, omissions, substitutions, phoneme reversal or word fragmentation. | Frequent and evident errors. Only able to repeat the simpler-more-common words (e.g., banana, potato) or one to two syllables of the longer-more-complex words. |
| Single word comprehension     | Normal comprehension         | Low frequency words (e.g., ferocious, indigenous) are occasionally unknown. In general, most words are somehow correctly defined, pointed to, or related to their concept. | Marked impairment in defining or object-word matching, able to provide broad superordinate category (e.g., an animal), but not able to elaborate on details. Preservation of more familiar items. | Only a few highly familiar words might be correctly recognised, with consistent failures in pointing to, or matching well-known items, such as tiger or crocodile. |
| Sentence repetition           | Flawless repetition          | Subtle mistakes due to word errors, self-corrections, or long latency. Although minimal omissions may be present, there is frequent repetition of the main sentence’s components. | Consistent errors (namely disorganisation, omissions, or mispronunciation) when the patient tries to repeat longer sequences (e.g., The Chinese fan...). | Unable to correctly repeat phrases with more than two short words. |
| Sentence comprehension        | Normal comprehension         | Occasional or minimal mistakes. Longer latency in replying, asking for instructions to be repeated, and self-corrections should be considered. | Consistent mistakes involving complex instructions. | Marked and consistent mistakes in direct instructions (e.g., touch the pen then the toothbrush). |
## Supplementary Table 2. Terms used in this study and in the online PPA ACE-III diagnostic calculator

| Terms used in Figures and Tables                                                                 | Terms used in the PPA ACE-III calculator                                      |
|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Attention_Time                                                                                   | Attention: Orientation to Time (0-5)                                         |
| Attention_Geography                                                                             | Attention: Orientation to Location (0-5)                                     |
| Attention_3_Word_Registration                                                                   | Attention: Registration of Three Words (0-3)                                 |
| Attention_Serial_7s                                                                             | Attention: Serial 7 Subtraction (0-5)                                        |
| Memory_3_Word_Recall                                                                            | Memory: Recall of Three Words (0-3)                                          |
| Fluency_Letter_Score                                                                            | Verbal Fluency: Letter Score (0-7)                                           |
| Fluency_Animal_Score                                                                            | Verbal Fluency: Animal Score (0-7)                                           |
| Memory_Learning_Address                                                                         | Memory: Learning of Name and Address (0-7)                                   |
| Memory_Retrograde                                                                              | Memory: Retrograde (i.e., Prime Minister etc.) (0-4)                         |
| Language_3_Commands                                                                            | Language: Comprehension (pencil and paper) (0-3)                             |
| Language_Writing                                                                               | Language: Sentence Writing (0-2)                                             |
| Language_Repetition_Single_Words                                                                | Language: Word Repetition ('caterpillar' etc.) (0-2)                         |
| Language_Repetition_Glitters                                                                    | Language: Sentence Repetition 1 ('All that glitters...') (0-1)               |
| Language_Repetition_A_Stitch                                                                   | Language: Sentence Repetition 2 ('A stitch in time...') (0-1)                |
| Language_Confrontation_Naming                                                                  | Language: Object Naming (0-12)                                                |
| Language_Semantics                                                                             | Language: Object Comprehension (0-4)                                         |
| Language_Reading                                                                               | Language: Reading (0-1)                                                      |
| Visuospatial_Loops                                                                             | Visuospatial: Intersecting Infinity Loops (0-1)                              |
| Visuospatial_Cube                                                                              | Visuospatial: 3D Wire Cube                                                   |
| Visuospatial_Clock                                                                              | Visuospatial: Clock Drawing (0-5)                                            |
| Visuospatial_Dots                                                                              | Visuospatial: Dot Counting (0-4)                                             |
| Visuospatial_Letters                                                                            | Visuospatial: Fragmented Letters (0-4)                                       |
| Memory_Recall_Address                                                                           | Memory: Recall of Name and Address (0-7)                                     |
| Memory_Recognition_Address                                                                      | Memory: Recognition of Name and Address (0-5)                                |
Supplementary Table 3. Performances on the ACE-III items in a sample of 30 healthy controls and 104 controls

|                           | 30 Controls | 104 Controls |
|---------------------------|-------------|--------------|
| Sex (m : f)               | 12:18       | 49:55        |
| Age (y)                   | 66.8 (8.3)  | 67 (7.8)     |
| Education (y)             | 13.7 (2.5)  | 14.1 (2.9)   |
| ACE-III Total (100)       | 96.3 (2.6)  | 95.2 (2.9)   |
| ACE-III Attention (18)    | 17.5 (0.8)  | 17.3 (1)     |
| ACE-III Memory (26)       | 24.7 (1.5)  | 24.7 (1.4)   |
| ACE-III Fluency (14)      | 12.8 (1)    | 12.2 (1.5)   |
| ACE-III Language (26)     | 25.7 (0.6)  | 25.5 (0.8)   |
| ACE-III Visuospatial (16) | 15.6 (0.6)  | 15.6 (0.7)   |
| Attention_Time            | 4.9 (0.3)   | 4.9 (0.3)    |
| Attention_Geography       | 4.9 (0.4)   | 4.9 (0.4)    |
| Attention_3_Word_Registration | 2.9 (0.4)  | 3 (0.2)      |
| Attention_Serial_7s       | 4.8 (0.4)   | 4.7 (0.8)    |
| Memory_3_Word_Recall      | 2.8 (0.4)   | 2.9 (0.4)    |
| Fluency_Letter_Score      | 6.5 (0.6)   | 6.1 (1)      |
| Fluency_Animal_Score      | 6.3 (0.6)   | 6.1 (0.9)    |
| Memory_Learning_Address   | 7 (0)       | 7 (0.1)      |
| Memory_Retrograde         | 3.8 (0.4)   | 3.8 (0.4)    |
| Language_3_Commands       | 3 (0)       | 3 (0.3)      |
| Language_Writing          | 2 (0.2)     | 1.9 (0.3)    |
| Language_Repetition_Single_Words | 2 (0) | 1.9 (0.3) |
| Language_Repetition_Glitters | 1 (0)       | 1 (0)        |
| Language_Repetition_A_Stitch | 1 (0)       | 1 (0.1)     |
| Language_Confrontation_Naming | 11.9 (0.3) | 11.9 (0.4)  |
| Language_Semantics        | 3.9 (0.3)   | 3.9 (0.3)    |
| Language_Reading          | 0.9 (0.3)   | 0.9 (0.3)    |
| Visuospatial_Loops        | 0.9 (0.3)   | 1 (0.2)      |
| Visuospatial_Cube         | 1.9 (0.3)   | 1.9 (0.3)    |
| Visuospatial_Clock        | 4.8 (0.4)   | 4.8 (0.5)    |
| Visuospatial_Dots         | 3.9 (0.3)   | 3.9 (0.3)    |
| Visuospatial_Letters      | 4 (0)       | 4 (0)        |
| Memory_Recall_Address     | 6.2 (1.1)   | 6.1 (1)      |
| Memory_Recognition_Address| 4.9 (0.3)   | 4.9 (0.3)    |

Notes: Values are mean ± standard deviation. The 104 controls were included in the characterisation of PPA performance profiles on the ACE-III (Phase 1 Step 1). The sample of 30 controls were included in the PPA ACE-III diagnostic calculator (Phase 1 Step 2 and 3).
| Term                  | Definition and Examples                                                                 |
|----------------------|-----------------------------------------------------------------------------------------|
| Visuospatial         | Broad term relating to visual and spatial abilities. The visuospatial ACE-III subdomain incorporates measures of visuoconstruction and visuoperception. |
| Visuoconstruction    | Involves the ability to organise and manually manipulate visual and/or spatial information to make a design (i.e., drawing). Visuoconstruction items on the ACE-III includes drawing the infinity loops, 3-dimensional cube, and clock. |
| Visuoperceptual      | Involves recognising objects based on their form, pattern, and colour. Visuoperceptual items on the ACE-III includes counting dots and identifying fragmented letters. |
### Supplementary Table 5. Performances on the ACE-III items in primary progressive aphasia patients (n = 90) and healthy controls (n = 104)

| Item                                | lv-PPA Mean (SD) | nfv-PPA Mean (SD) | sv-PPA Mean (SD) | Controls Mean (SD) | H or χ² Value | p     | Post hoc test                                      |
|-------------------------------------|------------------|-------------------|------------------|--------------------|---------------|-------|---------------------------------------------------|
| Attention_Time                      | 4.1 (1.3)        | 4.4 (0.8)         | 4.9 (0.3)        | 4.9 (0.3)          | 34.988        | <.001 | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Attention_Geography                | 3.8 (1)          | 4.4 (0.7)         | 3.7 (0.9)        | 4.9 (0.4)          | 73.169        | <.001 | sv-PPA < nfv-PPA; PPA < Controls                 |
| Attention_3_Word_Registration      | 2.7 (0.7)        | 2.8 (0.4)         | 3 (0.2)          | 3 (0.2)            | 12.884        | .005  | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Attention_Serial_7s                | 2.5 (2)          | 3.4 (1.8)         | 4.4 (1.2)        | 4.7 (0.8)          | 46.296        | <.001 | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Memory_3_Word_Recall               | 1.8 (1)          | 2.4 (0.7)         | 1.3 (1.2)        | 2.9 (0.4)          | 75.458        | <.001 | sv-PPA < nfv-PPA; PPA < Controls                 |
| Fluency_Letter_Score               | 2.8 (1.9)        | 1.7 (1.3)         | 3.9 (1.5)        | 6.1 (1)            | 116.636       | <.001 | nfv-PPA < sv-PPA; PPA < Controls                 |
| Fluency_Animal_Score               | 2.1 (1.6)        | 2.3 (1.4)         | 2.4 (2)          | 6.1 (0.9)          | 131.046       | <.001 | PPA < Controls                                   |
| Memory_Learning_Address            | 4.8 (2.1)        | 6.1 (1.7)         | 6.2 (1.3)        | 7 (0.1)            | 74.627        | <.001 | lv-PPA < nfv-PPA; Controls                       |
| Memory_Retrograde                 | 2.3 (1.4)        | 2.5 (1.3)         | 1.2 (1.2)        | 3.8 (0.4)          | 104.629       | <.001 | sv-PPA < lv-PPA, nfv-PPA < Controls             |
| Language_3_Commands               | 2.3 (1.1)        | 2.3 (0.9)         | 2.9 (0.3)        | 3 (0.3)            | 49.562        | <.001 | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Language_Writing                  | 1.3 (0.8)        | 0.8 (0.7)         | 1.5 (0.7)        | 1.9 (0.3)          | 66.989        | <.001 | nfv-PPA < sv-PPA; PPA < Controls                 |
| Language_Repetition_Single_Words  | 1.1 (1)          | 0.4 (0.8)         | 1.8 (0.4)        | 1.9 (0.3)          | 85.147        | <.001 | nfv-PPA < lv-PPA, sv-PPA, Controls               |
| Language_Repetition_Glitters      | 0.8 (0.4)        | 0.5 (0.5)         | 1 (0.2)          | 1 (0)              | 65.007^       | <.001 | nfv-PPA < sv-PPA; lv-PPA, nfv-PPA < Controls    |
| Language_Repetition_A_Stitch      | 0.5 (0.5)        | 0.5 (0.5)         | 0.9 (0.3)        | 1 (0.1)            | 61.702^       | <.001 | lv-PPA, nfv-PPA < sv-PPA < Controls             |
| Language_Confrontation_Naming     | 9.6 (3.1)        | 11 (1.3)          | 4.4 (2.9)        | 11.9 (0.4)         | 121.413       | <.001 | sv-PPA < lv-PPA, nfv-PPA < Controls             |
| Language_Semantics               | 3.5 (0.9)        | 3.6 (0.7)         | 1.6 (1.4)        | 3.9 (0.3)          | 93.11         | <.001 | sv-PPA < lv-PPA, nfv-PPA, Controls               |
| Language_Reading                  | 0.6 (0.5)        | 0.4 (0.5)         | 0.1 (0.3)        | 0.9 (0.3)          | 84.599^       | <.001 | sv-PPA < lv-PPA; PPA < Controls                 |
| Visuospatial_Loops                | 0.6 (0.5)        | 0.6 (0.5)         | 0.9 (0.3)        | 1 (0.2)            | 38.151^       | <.001 | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Visuospatial_Cube                 | 1.4 (0.8)        | 1.4 (0.7)         | 1.9 (0.4)        | 1.9 (0.3)          | 35.615        | <.001 | lv-PPA, nfv-PPA < sv-PPA, Controls               |
| Visuospatial_Clock                | 3.2 (1.3)        | 4.2 (1.1)         | 4.2 (1.2)        | 4.8 (0.5)          | 54.085        | <.001 | lv-PPA < sv-PPA, sv-PPA, Controls                |
| Visuospatial_Dots                 | 3.7 (0.7)        | 3.3 (1)           | 3.9 (0.3)        | 3.9 (0.3)          | 22.958        | <.001 | nfv-PPA < sv-PPA; lv-PPA, sv-PPA, Controls       |
| Visuospatial_Letters              | 4 (0.2)          | 4 (0.2)           | 4 (0)            | 4 (0)              | 5.372         | .146  | Nil                                              |
| Memory_Recall_Address             | 3.1 (2.4)        | 4.8 (2.4)         | 1.7 (1.9)        | 6.1 (1)            | 91.474        | <.001 | sv-PPA < nfv-PPA; sv-PPA, lv-PPA < Controls     |
| Memory_Recognition_Address        | 4.2 (1)          | 4.3 (1.1)         | 3.8 (1.2)        | 4.9 (0.3)          | 47.646        | <.001 | PPA < Controls                                   |

Notes: Values are mean ± standard deviation. ^ + χ² test.
| Patient (Dx according to neurologist) | Dx certainty | Differential Dx | Sex | Education (y) | Age at PALS and/or ACE-R | PALS diagnosis | ACE-R Total score | PIB-PET result | Brain pathology | ACE-III PPA diagnostic calculator |
|-------------------------------------|-------------|-----------------|-----|---------------|------------------------|----------------|------------------|---------------|----------------|-----------------------------------|
| lv-PPA case 1                       | Certain     |                 | Male | 19            | 68                     | lv-PPA         | 72               | Positive       | AD*            | Uncertain lv-PPA vs. nfv-PPA calculator probability 0.46 0.22 0.24 |
| lv-PPA case 2                       | Certain     |                 | Female | 16           | 73                     | Unclassifiable | 69               | Positive       |                | lv-PPA Not sv-PPA 0.73 0.12 0.10 |
| lv-PPA case 3                       | Certain     |                 | Female | 18           | 56                     | lv-PPA         | 58               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.70 0.08 0.21 |
| lv-PPA case 4                       | Certain     |                 | Male | 11.5          | 72                     | lv-PPA         | 74               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.36 0.13 0.45 |
| lv-PPA case 5                       | Certain     |                 | Male | 13.5          | 59                     | lv-PPA         | 63               | Positive       | AD            | Uncertain lv-PPA Not sv-PPA 0.39 0.11 0.48 |
| lv-PPA case 6                       | Certain     |                 | Male | 12            | 61                     | nfv-PPA        | 58               | Positive       | AD            | Uncertain lv-PPA Not sv-PPA 0.52 0.41 0.05 |
| lv-PPA case 7                       | Certain     |                 | Female | 15           | 69                     | lv-PPA         | 55               | Positive       |                | lv-PPA Not sv-PPA 0.87 0.07 0.05 |
| lv-PPA case 8                       | Certain     |                 | Female | 9            | 77                     | Unclassifiable | 90               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.23 0.40 0.04 |
| lv-PPA case 9                       | Certain     |                 | Female | 11           | 63                     | Unclassifiable | 56               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.32 0.30 0.36 |
| lv-PPA case 10                      | Certain     |                 | Female | 12           | 75                     | Not available  | 44               | N/A            | AD*            | Uncertain lv-PPA Not sv-PPA 0.63 0.23 0.15 |
| lv-PPA case 11                      | Certain     |                 | Female | 18           | 53                     | lv-PPA         | 68               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.36 0.25 0.38 |
| lv-PPA case 12                      | Certain     |                 | Male | 12            | 59                     | lv-PPA         | 63               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.36 0.22 0.39 |
| lv-PPA case 13                      | Certain     | Atypical AD-Aphasic | Male | 11           | 70                     | nfv-PPA        | 74               | Positive       | FTLD-Tau¹  | lv-PPA Not sv-PPA 0.73 0.04 0.13 |
| lv-PPA case 14                      | Uncertain   | Atypical AD-Aphasic | Male | 12           | 65                     | lv-PPA         | 44               | Positive       |                | lv-PPA Not sv-PPA 0.94 0.04 0.03 |
| lv-PPA case 15                      | Uncertain   | Atypical AD-Aphasic | Female | 11          | 71                     | Unclassifiable | 64               | Positive       |                | Uncertain lv-PPA Not sv-PPA 0.40 0.19 0.39 |
| lv-PPA case 16                      | Uncertain   | sv-PPA           | Female | 16           | 65                     | lv-PPA         | 60               | Equivocal      | AD            | Not lv-PPA; Not nfv-PPA sv-PPA 0.11 0.02 0.86 |
| lv-PPA case 17                      | Uncertain   | nfv-PPA          | Female | 14           | 65                     | Unclassifiable | 75               | Negative       |                | Uncertain lv-PPA Not sv-PPA 0.60 0.14 0.17 |
| nfv-PPA case 1                      | Certain     |                 | Male | 17.5          | 55                     | nfv-PPA        | 62               | Negative       |                | Uncertain lv-PPA Not sv-PPA 0.31 0.48 0.19 |
| nfv-PPA case 2                      | Certain     |                 | Female | 8            | 80                     | Not available  | 41               | N/A            | FTLD-Tau²  | Uncertain lv-PPA Not sv-PPA 0.54 0.43 0.00 |
| nfv-PPA case 3                      | Certain     |                 | Male | 9            | 78                     | nfv-PPA        | 56               | Equivocal      | FTLD-Tau³  | Uncertain lv-PPA Not sv-PPA 0.35 0.63 0.01 |
| nfv-PPA case 4                      | Certain     |                 | Female | 9            | 71                     | Unclassifiable | 83               | Negative       | FTLD-Tau³  | Uncertain lv-PPA Not sv-PPA 0.20 0.39 0.20 |
| nfv-PPA case 5                      | Certain     |                 | Male | 15            | 47                     | nfv-PPA        | 87               | Negative       | FTLD-Tau³  | Uncertain lv-PPA Not sv-PPA 0.24 0.53 0.05 |
| NFV-PPA Case | Diagnosis | Sex | Age | Language | MMSE | FTLD-Tau | FTLD-TDP | Uncertainty | sv-PPA | 0.06 | 0.04 | 0.80 |
|--------------|-----------|-----|-----|----------|------|----------|----------|-------------|--------|-------|-------|------|
| 6            | Certain Pseudobulbar Palsy | Female | 11 | 70 | NFV-PPA | 89 | Negative | Uncertain | Not sv-PPA | 0.21 | 0.52 | 0.03 |
| 7            | Certain | Female | 12.5 | 72 | Not available | 75 | Negative | FTLD-Tau | NFV-PPA | Not sv-PPA | 0.08 | 0.86 | 0.03 |
| 8            | Certain | Male | 14 | 77 | Not available | 74 | Negative | NFV-PPA | Not sv-PPA | 0.13 | 0.74 | 0.11 |
| 9            | Certain | Male | 15 | 73 | Not available | 87 | Negative | Uncertain | Not sv-PPA | 0.36 | 0.26 | 0.19 |
| 10           | Certain Pure Apraxia of Speech | Female | 14 | 60 | Not available | 85 | Negative | FTLD-Tau | Uncertain | Not sv-PPA | 0.14 | 0.63 | 0.11 |
| 11           | Certain | Female | 15 | 70 | NFV-PPA | 85 | Negative | FTLD-Tau | Uncertain | Not sv-PPA | 0.34 | 0.40 | 0.04 |
| 12           | Certain | Female | 15 | 63 | Not available | 74 | Negative | FTLD-Tau | Uncertain | Not sv-PPA | 0.39 | 0.52 | 0.05 |
| 13           | Uncertain CBS | Male | 8 | 71 | Not available | 45 | Equivocal | Uncertain | Not sv-PPA | 0.68 | 0.30 | 0.02 |
| 14           | Uncertain lv-PPA | Male | 12 | 70 | Not available | 71 | Negative | Uncertain | Not sv-PPA | 0.30 | 0.57 | 0.11 |
| 15           | Certain | Male | 15.5 | 59 | Unclassifiable | 70 | Positive | Uncertain | Not sv-PPA | 0.53 | 0.37 | 0.08 |
| 16           | Certain | Male | 9 | 71 | NFV-PPA | 83 | Positive | Uncertain | Not sv-PPA | 0.45 | 0.31 | 0.06 |
| 17           | Uncertain PSP | Male | 18 | 76 | NFV-PPA | 95 | Negative | NFV-PPA | Not sv-PPA | 0.26 | 0.05 | 0.07 |
| 18           | Uncertain lv-PPA | Female | 9 | 72 | Unclassifiable | 68 | Negative | NFV-PPA | Not sv-PPA | 0.17 | 0.74 | 0.07 |
| 19           | Uncertain PSP | Female | 11 | 69 | NFV-PPA | 86 | Negative | Uncertain | Not sv-PPA | 0.44 | 0.21 | 0.09 |
| 1            | Certain | Female | 9 | 68 | SV-PPA | 52 | Negative | FTLD-Tau | Not lv-PPA; Not nfV-PPA | 0.15 | 0.04 | 0.80 |
| 2            | Certain | Male | 19 | 53 | SV-PPA | 66 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.03 | 0.02 | 0.94 |
| 3            | Certain | Male | 11.5 | 60 | SV-PPA | 65 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.08 | 0.03 | 0.87 |
| 4            | Certain | Male | 11 | 53 | SV-PPA | 61 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.04 | 0.02 | 0.94 |
| 5            | Certain | Male | 11.5 | 69 | SV-PPA | 46 | Negative | Uncertain | Not sv-PPA | 0.25 | 0.06 | 0.69 |
| 6            | Certain | Female | 9.5 | 63 | SV-PPA | 64 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.10 | 0.07 | 0.83 |
| 7            | Certain | Female | 12.5 | 65 | Not available | 60 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.04 | 0.03 | 0.93 |
| 8            | Certain | Female | 9 | 58 | Not available | 44 | Negative | Uncertain | Not sv-PPA | 0.19 | 0.01 | 0.79 |
| 9            | Certain | Female | 6 | 73 | SV-PPA | 74 | Negative | Uncertain | Not sv-PPA | 0.09 | 0.12 | 0.71 |
| 10           | Uncertain | Female | 12 | 81 | Not available | 58 | N/A | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.06 | 0.04 | 0.89 |
| 11           | Uncertain AD | Male | 9 | 71 | SV-PPA | 48 | Negative | FTLD-TDP Type C | Not lv-PPA; Not nfV-PPA | 0.11 | 0.06 | 0.83 |
Note, all PPA patients completed the Addenbrooke’s Cognitive Examination-Revised (ACE-R). Details on how ACE-R performance scores were converted to equivalent ACE-III scores are reported in Supplementary Table 7. Patients shaded in grey were deemed atypical due to either the neurologist’s clinical opinion or atypical findings on PiB-PET or brain autopsy. ^ Patient 12 was included in the initial ACE-III evaluation and modelled data (i.e., Phase 1) but was also included in Phase 2 based on the recent availability of autopsy findings. Abbreviations: * = co-occurring Lewy body pathology; ACE-III = Addenbrooke’s Cognitive Examination-Third edition; ACE-R = Addenbrooke’s Cognitive Examination-Revised; AD = Alzheimer’s disease; CBS = corticobasal syndrome; Dx according to the neurologist = the most up-to-date clinical diagnosis according to the neurologist based on the patients’ clinical history, brain imaging, and most recent clinical and neuropsychological assessment; Education = total years (y) of formal education; FTLD = frontotemporal lobar degeneration; lv-PPA = logopenic variant of primary progressive aphasia; nfv-PPA = non-fluent variant of primary progressive aphasia; PALS = progressive aphasia language scale; PiB-PET = [11C] Pittsburgh compound B positron emission tomography; PSP = progressive supranuclear palsy; sv-PPA = semantic variant of primary progressive aphasia; tau\textsuperscript{1} = corticobasal degeneration type of tau pathology; tau\textsuperscript{2} = globular glial tauopathy ; tau\textsuperscript{3} = progressive supranuclear palsy type of tau pathology; tau\textsuperscript{4} = Pick’s type of tau pathology; TDP-43 = Transactive response DNA binding protein-43.
Supplementary Table 7. How ACE-R performance scores in the PiB-PET or pathology confirmed PPA patients were converted to equivalent ACE-III performance scores (Phase 2)

| ACE-III Item                  | How ACE-R performance scores were converted to ACE-III scores |
|-------------------------------|---------------------------------------------------------------|
| Attention_Time                | Same as ACE-III (no conversion)                              |
| Attention_Geography           | Same as ACE-III (no conversion)                              |
| Attention_3_Word_Registration | Same as ACE-III (no conversion)                              |
| Attention_Serial_7s           | Same as ACE-III (no conversion)                              |
| Memory_3_Word_Recall          | Same as ACE-III (no conversion)                              |
| Fluency_Letter_Score          | Same as ACE-III (no conversion)                              |
| Fluency_Animal_Score          | Same as ACE-III (no conversion)                              |
| Memory_Learning_Address       | Same as ACE-III (no conversion)                              |
| Memory_Retrograde             | Same as ACE-III (no conversion)                              |

Language_3_Commands

Performance scores on the ACE-R three-stage command were used for the ACE-III three single-step item.

Language_Writing

The ACE-R writing item is out of /1 but the ACE-III writing item is out of /2. ACE-R performance scores were converted to equivalent ACE-III scores: If the patient scored 1/1 on the ACE-R, then their performance was converted to 2/2. If the patient scored 0/1 on the ACE-R, then their score on the ACE-III writing item remained as 0/2.

Language_Repetition_Single_Words

Same as ACE-III (no conversion)

Language_Repetition_Glitters

Performance scores on the ACE-R sentence item 'Above beyond and below' were used for the ACE-III sentence item 'All that glitters is not gold'

Language_Repetition_A_Stitch

Performance scores on the ACE-R sentence item 'No ifs and or buts' were used for the ACE-III sentence item 'A stitch in time saves nine'

Language_Confrontation_Naming

Similar to ACE-III* (no conversion)

Language_Semantics

Same as ACE-III (no conversion)

Language_Reading

Same as ACE-III (no conversion)
| Task                        | Description                                                                 |
|-----------------------------|----------------------------------------------------------------------------|
| Visuospatial Loops          | Performance scores on the ACE-R intersecting pentagons item were used for the ACE-III intersecting infinity loops item |
| Visuospatial Cube           | Same as ACE-III (no conversion)                                            |
| Visuospatial Clock          | Same as ACE-III (no conversion)                                            |
| Visuospatial Dots           | Same as ACE-III (no conversion)                                            |
| Visuospatial Letters        | Same as ACE-III (no conversion)                                            |
| Memory Recall Address       | Same as ACE-III (no conversion)                                            |
| Memory Recognition Address  | Same as ACE-III (no conversion)                                            |

Notes: * The first two naming items on the ACE-R (“pencil” and “watch”) were replaced/superseded in the ACE-III with other highly familiar objects (“spoon” and “book”). All other naming items in the ACE-R and ACE-III are the same.
| Patient   | Sex | Disease duration (years) | ACE-III Total | PIB-PET result | ACE-III PPA diagnostic calculator | lv-PPA probability | nfv-PPA probability | sv-PPA probability |
|-----------|-----|--------------------------|---------------|----------------|----------------------------------|---------------------|---------------------|---------------------|
| AD case 1 | Male | 7.82                     | 74            | Positive       | Uncertain                        | Not sv-PPA          | 0.6                 | 0.21                | 0.07                |
| AD case 2 | Male | 7.03                     | 45            | Positive       | lv-PPA                           | Not sv-PPA          | 0.75                | 0.14                | 0.11                |
| AD case 3 | Male | 5.57                     | 67            | N/A            | Not lv-PPA; Not nfv-PPA          | sv-PPA              | 0.18                | 0.03                | 0.75                |
| AD case 4 | Male | 4.30                     | 51            | N/A            | lv-PPA                           | Not sv-PPA          | 0.92                | 0.03                | 0.04                |
| AD case 5 | Male | 10.17                    | 73            | N/A            | lv-PPA                           | Not sv-PPA          | 0.42                | 0.08                | 0.36                |
| AD case 6 | Male | 13.17                    | 65            | N/A            | Uncertain                        | Not sv-PPA          | 0.4                 | 0.06                | 0.48                |
| AD case 7 | Male | 6.23                     | 62            | Positive       | lv-PPA                           | Not sv-PPA          | 0.8                 | 0.11                | 0.07                |
| AD case 8 | Female | 4.97                     | 51            | N/A            | lv-PPA                           | Not sv-PPA          | 0.97                | 0.01                | 0.01                |
| AD case 9 | Male | 6.96                     | 74            | N/A            | Uncertain                        | Not sv-PPA          | 0.36                | 0.12                | 0.36                |
| AD case 10| Male | 3.94                     | 72            | N/A            | Uncertain                        | Not sv-PPA          | 0.48                | 0.05                | 0.36                |
| AD case 11| Male | 4.06                     | 71            | N/A            | Uncertain                        | Not sv-PPA          | 0.2                 | 0.66                | 0.11                |
| AD case 12| Female | 2.06                     | 58            | Positive       | lv-PPA                           | Not sv-PPA          | 0.73                | 0.16                | 0.09                |
| AD case 13| Female | 3.05                     | 85            | N/A            | Uncertain                        | Not sv-PPA          | 0.38                | 0.15                | 0.11                |
| AD case 14| Male | 3.23                     | 56            | N/A            | lv-PPA                           | Not sv-PPA          | 0.94                | 0.03                | 0.03                |
| AD case 15| Female | 2.25                     | 70            | N/A            | Uncertain                        | Not sv-PPA          | 0.56                | 0.1                 | 0.27                |
| AD case 16| Female | 2.61                     | 78            | N/A            | Uncertain                        | Not sv-PPA          | 0.29                | 0.05                | 0.42                |
| AD case 17| Male | 2.79                     | 59            | N/A            | Uncertain                        | Not sv-PPA          | 0.41                | 0.16                | 0.42                |
| AD case 18| Male | 1.79                     | 57            | N/A            | Uncertain                        | Not sv-PPA          | 0.67                | 0.24                | 0.09                |
| AD case 19| Male | 2.72                     | 40            | N/A            | lv-PPA                           | Not sv-PPA          | 0.76                | 0.17                | 0.06                |
| AD case 20| Male | 4.19                     | 82            | Positive       | Uncertain                        | Not sv-PPA          | 0.27                | 0.16                | 0.29                |
| AD case 21| Female | 1.08                     | 62            | N/A            | Uncertain                        | Not sv-PPA          | 0.23                | 0.1                 | 0.64                |
| AD case 22| Male | 2.17                     | 49            | N/A            | Uncertain                        | Not sv-PPA          | 0.61                | 0.07                | 0.31                |
| AD case 23| Female | 1.26                     | 65            | N/A            | Uncertain                        | Not sv-PPA          | 0.56                | 0.08                | 0.33                |
| AD case 24| Female | 2.52                     | 73            | N/A            | Uncertain                        | Not sv-PPA          | 0.45                | 0.04                | 0.38                |
| AD case 25| Female | 1.19                     | 71            | N/A            | lv-PPA                           | Not sv-PPA          | 0.83                | 0.06                | 0.05                |
| AD case 26| Female | 2.87                     | 62            | N/A            | Uncertain                        | Not sv-PPA          | 0.44                | 0.26                | 0.29                |
| AD case | Gender | Age | Diagnosis | Uncertainty | Treatment | Duration |
|---------|--------|-----|-----------|-------------|-----------|----------|
| 27      | Female | 2.52| N/A       | Uncertain   | Not sv-PPA| 0.54     |
| 28      | Female | 6.40| N/A       |            | Not sv-PPA| 0.78     |
| 29      | Male   | 6.05| N/A       | Uncertain   | Not sv-PPA| 0.2      |
| 30      | Female | 4.47| N/A       | Uncertain   | Not sv-PPA| 0.58     |
| 31      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.78     |
| 32      | Male   | 1.93| N/A       | Uncertain   | Not sv-PPA| 0.65     |
| 33      | Male   | 6.40| N/A       | Uncertain   | Not sv-PPA| 0.48     |
| 34      | Male   | 6.05| N/A       | Uncertain   | Not sv-PPA| 0.78     |
| 35      | Male   | 4.47| N/A       | Uncertain   | Not sv-PPA| 0.63     |
| 36      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.96     |
| 37      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.48     |
| 38      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.21     |
| 39      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.09     |
| 40      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.57     |
| 41      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.68     |
| 42      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.5      |
| 43      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.68     |
| 44      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.34     |
| 45      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.4      |
| 46      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.88     |
| 47      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.82     |
| 48      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.35     |
| 49      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.74     |
| 50      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.31     |
| 51      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.34     |
| 52      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.83     |
| 53      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.86     |
| 54      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.6      |
| 55      | Female | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.27     |
| 56      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.56     |
| 57      | Male   | 4.55| N/A       | Uncertain   | Not sv-PPA| 0.38     |
| AD case | Gender | Age | Disease Duration | Diagnosis | PiB | ACE-III Score (AD) | ACE-III Score (Non AD) | ACE-III Score (Control) |
|---------|--------|-----|-----------------|-----------|-----|-------------------|------------------------|------------------------|
| 58      | Female | 1.67| 59              | Uncertain | Not sv-PPA | 0.62              | 0.08                   | 0.29                   |
| 59      | Male   | 1.20| 90              | Uncertain | Not sv-PPA | 0.18              | 0.06                   | 0.1                    |
| 60      | Male   | 3.35| 82              | Uncertain | Not sv-PPA | 0.32              | 0.09                   | 0.19                   |
| 61      | Female | 5.42| 71              | Uncertain | Not sv-PPA | 0.36              | 0.15                   | 0.36                   |
| 62      | Female | 3.54| 83              | Uncertain | Not sv-PPA | 0.31              | 0.07                   | 0.12                   |
| 63      | Female | 2.55| 54              | nfv-PPA   | Not sv-PPA | 0.17              | 0.72                   | 0.1                    |
| 64      | Female | 2.87| 43              | lv-PPA    | Not sv-PPA | 0.91              | 0.04                   | 0.05                   |
| 65      | Male   | 4.88| 74              | Uncertain | Not sv-PPA | 0.44              | 0.39                   | 0.08                   |
| 66      | Male   | 2.96| 71              | Uncertain | Not sv-PPA | 0.33              | 0.03                   | 0.57                   |
| 67      | Male   | 1.54| 54              | Uncertain | Not sv-PPA | 0.52              | 0.41                   | 0.05                   |
| 68      | Male   | 4.13| 52              | lv-PPA    | Not sv-PPA | 0.91              | 0.03                   | 0.06                   |

Notes: All Alzheimer’s disease patients completed the Addenbrooke’s Cognitive Examination-Third edition. Abbreviations: ACE-III = Addenbrooke’s Cognitive Examination-Third edition; AD = Alzheimer’s disease; Disease duration = time (years) since the onset of symptoms as described by the caregiver; lv-PPA = logopenic variant of primary progressive aphasia; nfv-PPA = non-fluent variant of primary progressive aphasia; PiB = [11C] Pittsburgh Compound B; sv-PPA = semantic variant of primary progressive aphasia.
Supplementary Figure 1. Phase 1 nfv-PPA patients a) included or b) excluded based on the presence or absence of parkinsonian and/or motor neuron features at baseline assessment (i.e., at the time of the first ACE-III assessment).

Notes: White spaces indicate unavailable data. ‘Suspected Parkinson’s + or MND’ = suspected Parkinson’s plus or motor neuron disease according to the neurologist’s (R.M.A., N.J.C, E.D., Y.T.H., J.R.H., J.R.B.) clinical notes. The parkinsonism, parkinsonism asymmetrical and postural instability
items were recorded as a ‘yes’ or ‘no’ by the neurologist. ‘Yes’ responses for these items were maroon colour coded (i.e., ‘potential exclusion criteria). All other items were rated as absent (0), mild (1), moderate (2), or severe (3).

In Figure 1a), patients 12, 18 and 24 had mild parkinsonism. In all cases, these features were asymmetrical (e.g., left side < right side). Further, patients 10 and 18 had postural instability. It was decided, however, that these features were not in keeping with a clear parkinsonian syndrome. Patient 25 did not undergo formal assessment for parkinsonism at our research clinic but was informally assessed by an experienced neurologist (R.M.A) at another clinic. In Figure 1b), 11/16 patients (i.e., patients 1-5, 7-8, 10, 12, 14-15) had features in keeping with a concomitant parkinsonian or motor neuron syndrome, and a further 5 patients (patients 6, 9, 11, 13, 16) had suspected (but unclear) parkinsonian or motor neuron features. Admittedly, while patient 11 went on to develop corticobasal syndrome at a follow up assessment, their parkinsonian features were very mild at baseline assessment and so should have been included in the Phase 1 data analysis. Fifteen out of the 16 patients in Figure 1b) went on to develop clear Parkinson’s plus (corticobasal syndrome: patients 1-8, 12, 14 and 15; progressive supranuclear palsy: patient 16) or motor neuron disease syndromes (patients 9, 10, 11) within 1-2 years post baseline assessment.
Supplementary Material Appendix 1

Instructions of the Progressive Aphasia Language Scale (PALS)

I. Spontaneous speech

Based upon 10 minutes of informal conversation on topics, such as previous occupation, hobbies, travel, and family, during which the examiner encourages free utterances and interrupts as little as possible.

1. Motor speech disorders. Features to observe:
   
   A. Distortions, articulatory groping and laboured speech.
   B. Changes in prosody, rhythm, intonation, and stress.
   C. Intelligibility of words.

2. Agrammatism. Features to observe:
   
   A. Omission of grammar structures, such as prepositions, articles, pronouns, and auxiliary verbs. Simplification and telegraphic speech.
   B. Incorrect inflection of verbs and other grammatical structures. Wrong usage of pronouns and arrangement of words.

II. Tasks

3. Naming: The subject is asked to name 10 animals (and then 10 tools).
   
   A. Animal models: Tiger, elephant, crocodile, kangaroo, giraffe, zebra, goat, sheep, horse, and donkey.
   B. Household objects: scissors, tongs, spoon, whisk, toothbrush, nutcracker, spanner, potato masher, grater, and can-opener.

   The examiner notes the types of errors – omission, semantic associative, or phonological. If errors are made in the naming, comprehension is tested by asking the subject to point to the ‘crocodile’, ‘giraffe’, and so forth. Then, knowledge is tested in all subjects by asking them to repeat the word (e.g., ‘domesticated’) and to point to the relevant animals, etc. (see 5A)

4. Single-word repetition (and definitions, see task 5B). The subject is asked to repeat (and then to define) words of increasing length and phonological complexity:
   
   - ‘Banana’
   - ‘Potato’
   - ‘Methodist’
   - ‘Artillery’
   - ‘Perimeter’
   - ‘Caterpillar’
   - ‘Catastrophe’
   - ‘Chrysanthemum’

   As with naming, the type of errors should be noted.
5. Single-word comprehension. This component is assessed simultaneously with the previous tasks:
   A. Selection of objects shown in the task 3: The subject is asked to select the animals according to the specified category; e.g., which one of these animals are ‘edible’, ‘ferocious’, ‘domesticated’, ‘indigenous’, ‘herbivorous’.
   B. Definition of words given in the task 4: After repeating the word ‘catastrophe’, the subject is asked to define it: What sort of thing is ‘catastrophe’? The examiner can classify the subject’s knowledge by probing or asking yes/no questions.

Word comprehension is judged, therefore, on three factors: pointing to the correct items if they make naming errors (e.g., point to the ‘crocodile’); comprehension of words like ‘domesticated’, ‘edible’; and definition of the words in the repeat and define task.

6. Sentence repetition. Subjects are asked to simply repeat a series of phrases or sentence:
   - ‘Not ifs ands or buts’
   - ‘The Chinese fan contained a rare emerald’
   - ‘Six small boys built a sizeable snowman’
   - ‘The lady delivered some delicious gingerbread’

Patients may omit words or produce errors as in naming and word repetition.

7. Sentence comprehension. The examiner places three common objects (e.g., pen, toothbrush, and spoon).
   A. Simple instructions: Direct two-step commands, such as ‘touch the pen then the toothbrush’; ‘pick up the pen and then the spoon’; etc. Typically, three such commands are given. If correct pass part B.
   B. Complex instructions: These include indirect instructions (e.g., ‘pass me the pen after touching the toothbrush’; ‘pick up the spoon after touching the pen’) and instructions with embedded clauses (e.g., ‘give me all the items that you find in the kitchen’).
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