**Supplementary material**

### Comparison between PA-MND and PPA:

### Comparison of neuropsychological profile for nfvPA-MND vs nfvPPA-TDP and for svPA-MND vs svPPA:

The direct comparison of neuropsychologic scores between the nfvPA-MND cases (n=3) vs the nfvPPA-TDP cases of the UCSF cohort (n=2) and between the svPA-MND cases (=7) vs a group of svPPA-TDP-C cases of the UCSF cohort (n=5) is shown in Supplementary table 1. Even if no statistically significant differences emerged in this analysis, likely due to the limited sample size, a globally similar cognitive profile between nfvPA-MND and nfvPPA, and between svPA-MND and svPPA, respectively, was observed. In particular, AOS and dysarthria are unique to the non-fluent variant groups while, conversely, naming test (BNT) and semantic fluency are mostly compromised in the semantic groups.

### Comparison of imaging profile for nfvPA-MND vs nfvPPA and for svPA-MND vs svPPA:

A comparison between non fluent PA cases with and without MND was conducted by matching two of the three nfvPA-MND cases with two nfvPPA cases with TDP pathology (type A) present in the UCSF NDBB. nfvPA-MND showed GM atrophy in the left temporal pole, the right cerebellum, the left thalamus and BA 44; nfvPPA (n=2) were mainly atrophic in the left BA 44 and the left rolandic operculum, while no atrophy was found in the cerebellar hemispheres. Bilateral hippocampal atrophy was present due to hippocampal sclerosis in one nfvPPA-TDP case (Supplementary figure 1A).The same comparison was taken between semantic PA cases with and without MND, by matching five svPA-MND cases (four TDP-B and one TDP-A cases) with five svPPA-TDP (type C) cases. The svPA-MND (n=5) (TDP-A/B) showed atrophy in the left temporal pole, hippocampus, fusiform gyrus, medial temporal pole and inferior temporal gyrus, with the second most eminent cluster in the right parahippocampal, hippocampal and fusiform gyrus. A smaller cluster was detected in the left inferior frontal gyrus, pars orbitalis, and in the left insula. Conversely, svPPA (TDP type C) showed the peak of GM atrophy in the left temporal pole, inferior temporal gyrus, fusiform gyrus, amygdala, with the second cluster was in the right fusiform gyrus, medial temporal pole, and inferior temporal gyrus (Supplementary figure 1B).

**Supplementary table 1. Demographic and cognitive findings of nfvPA-MND and svPA-MND compared to nfvPPA and svPPA.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Group** | **nfvPA- MND** | **nfvPPA-TDP-A** | **svPA-MND** | **svPPA-TDP-C** | **Controls** |
|  | **1** | **2** | **3** | **4** |  |
| **Demographic data** |  |  |  |  |  |
| Gender (M/F) | 2/1 | 0/2 | 5/2 | 3/2 | 7/14 |
| Handedness (R/L) | 3/0 | 2/0 | 7/0 | 5/0 | 19/2 |
| Education, y | 16 ± 2 | 19, 12 | 16.7 ± 2.9 | 16.4 ± 2.3 | 17.5 ± 2.2 |
| Age at onset (general), y | 55 ± 6.2 | 68, 63 | 57.3 ± 6.8 | 60.2 ± 6.3 | n/a |
| Age at onset (motor), y | 56 ± 6.2 | n/a | 65.7 ± 6.8 | n/a | n/a |
| Age at initial evaluation, y | 56.7 ± 6.4 | 70, 66 | 63.9 ± 9.5 | 63.8 ± 6.2 | 67 ± 8.0 |
| Illness duration at initial evaluation, y | 1.4 ± 0.2 | 1.17, 3 | 6.6 ± 4.7 | 3.6 ± 1.3 | n/a |
| Presence of motor symptoms at initial evaluation | 3/3 | n/a | 4/7 | n/a | n/a |
| Presence of motor symptoms at any point | 3/3 | n/a | 6/7 | n/a | n/a |
| Survival, y | 3.2 ± 0.6 | 9.33, 9.75 | 11.6 ± 6.0 | 10.2 ± 3.5 | n/a |
| **General function and cognition** |  |  |  |  |  |
| MMSE | 25.3 ± 3.1 | 28, 30 | 26.7 ± 1.2 | 27 ± 2.0 | 29.7 ± 0.5 |
| CDR Total | 0.5 ± 0.0 | 0, 0.5 | 0.8 ± 0.6 | 0.5 ± 0.3 | 0.0 ± 0.0 |
| CDR Sum of boxes | 2.5 ± 1.3 | 0, 0.5 | 4.7 ± 3.2 | 1.7 ± 2.4 | 0.0 ± 0.0 |
| NPI Total | 22.0 ± 3.6 | 0, 0 | 41.0 ± 20.8 | 10.7 ± 9.3 | 0.5 ± 0.7 |
| GDS Total | 10.0 ± 7.2 | 6, 12 | 8.9 ± 5.2 | 6.4 ± 2.2 | 3.9 ± 3.4 |
| Total behavior ratings | 1, 3 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| **Cognition** |  |  |  |  |  |
| CVLT-MS Total free recall | 23.3 ± 6.7 | 29, 32 | 15.9 ± 3.3 | 16.0 ± 3.9 | 29.9 ± 3.3 |
| CVLT-MS free recall at 10 minutes | 6.3 ± 2.5 | 7, 9 | 2.1 ± 1.3 | 2.6 ± 2.8 | 7.9 ± 1.0 |
| Benson figure recall | 11.7 ± 1.5 | 8, 10 | 8.9 ± 3.0 | 7.2 ± 5.3 | 12.8 ± 3.2 |
| Benson figure copy | 15.3 ± 0.6 | 14, 16 | 15.6 ± 1.1 | 14.6 ± 1.9 | 16.3 ± 1.0 |
| Modified Trails | 0.02, 0.02 | 0.02, 0.03 | 0.02 ± 0.02 | 0.03 ± 0.02 | 0.04 ± 0.02 |
| Calculation | 3.7 ± 1.5 | 5, 5 | 4.7 ± 0.5 | 4.2 ± 1.1 | 4.9 ± 0.3 |
| Digits Backward | 3.3 ± 0.6 | 4, 4 | 4.4 ± 1.3 | 5.2 ± 0.8 | 5.3 ± 1.3 |
| **Speech and Language** |  |  |  |  |  |
| AOS Severity (MSE, 7) | 2 | 4, 7 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Dysarthria Serverity (MSE, 7) | 5 | 0, 4 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Verbal agility | 0, 4 | n/a | 5.7 ± 0.6 | 3, 6 | 5.7 ± 0.5 |
| Speech fluency (WAB, 10) | 6 | 0, 0 | 9.7 ± 0.6 | 9.4 ± 0.5 | 10.0 ± 0.0 |
| Information Content (WAB, 10) | 10 | 0, 0 | 9.0 ± 1.0 | 9.2 ± 0.8 | 4.3 ± 5.1 |
| Sentence repetition (3) | 2.3 ± 0.6 | 0, 2 | 3.0 ± 0.0 | 2.8 ± 0.4 | 3.0 ± 0.0 |
| Sentence repetition (5) | 2, 5 | n/a | 4.0 ± 1.0 | 5, 5 | 5.0 ± 0.0 |
| Syntax comprehesion (Short CYCLE, 55) | 39 | 53, 53 | 50.5 ± 5.1 | 50.0 ± 6.0 | 54.3 ± 1.1 |
| Sentence comprehension (5) | 3, 4 | n/a | 5.0 ± 0.0 | 4, 5 | 5.0 ± 0.0 |
| Single-word comprehension (16) | 14.3 ± 1.5 | n/a | 10.2 ± 0.5 | 10, 10 | 15.7 ± 0.6 |
| Boston Naming Test (15) | 11.7 ± 2.1 | 13, 15 | 6.3 ± 4.0 | 5.0 ± 1.6 | 14.8 ± 0.7 |
| Phonemic fluency (D-words/minute) | 3.0 ± 1.7 | 6, 7 | 8.4 ± 3.5 | 8.0 ± 2.7 | 15.2 ± 4.7 |
| Semantic fluency (animals/minute) | 9.0 ± 3.6 | 12, 18 | 6.9 ± 1.9 | 7.2 ± 2.9 | 23.9 ± 5.4 |
| PPTP Total (52) | 50.0 ± 1.0 | n/a | 36.7 ± 10.7 | 15.8 ± 21.9 | 51.7 ± 0.6 |
| Irregular word reading (6) | 4, 5 | n/a | 5.7 ± 0.6 | 5, 5 | 6.0 ± 0.0 |
| Reading, regular words (PALPA, 30) | n/a | 30 | 29.7 ± 0.6 | 28.4 ± 1.8 | 30.0 ± 0.0 |
| Reading, irregular words (PALPA, 30) | n/a | 30 | 25.0 ± 6.2 | 23.4 ± 5.1 | 29.8 ± 0.4 |

Abbreviations: MMSE: Mini-Mental State Examination; CDR: Clinical Dementia Rating; NPI: Neuropsychiatric Inventory; GDS: Geriatric Dementia Scale; CVLT-MS: California Verbal Learning Test-Mental Status; AOS: apraxia of speech; MSE: motor speech evaluation; WAB: Western Aphasia Battery; CYCLE: Curtiss-Yamada Comprehensive Language Evaluation; PPTP: Pyramids and Palm Trees-Pictures; PALPA: Psycholinguistic Assessments of Language Processing in Aphasia; n/a= not applicable; nfvPA-MND: non fluent variant of progressive aphasia with motor neuron disease; nfvPPA: non fluent variant of primary progressive aphasia; TDP-A: transactive response DNA binding protein of 43 kD type A; svPA-MND: semantic variant of progressive aphasia with motor neuron disease; svPPA: semantic variant of primary progressive aphasia; TDP-C: transactive response DNA binding protein of 43 kD type C. Reported values are mean ± SD, except when data were available for two cases only, in which case single values are shown.