Supplementary material

Addendum items of the ACE-III

The addendum items of the ACE-III include the following: i) in the Language domain, the three-step command is replaced by three single-step commands of increasing complexity, ii) comprehension of the written command (“close your eyes”) is removed, iii) the sentence writing task is modified so that participants are required to write two or more sentences with a maximum score of 2 points, iv) two common proverbs replace the phrase repetition items, and v) naming of the two easiest items (“pencil” and “watch”) are replaced by other highly familiar objects (“spoon” and “book”); vi) in the Visuospatial domain, the intersecting pentagons are replaced by overlapping infinity loops (see Hsieh et al., 2013). Of note, the ACE-III Attention and Orientation domain no longer includes the option to spell the word ‘WORLD’ backwards upon failure of the serial 7 subtraction task

Neuropsychological tests routinely administered to patients and controls at the Frontier research clinic

i) Digit Span Forward and Backward subtests of the Wechsler Memory Scale–Third edition ([WMS-III Wechsler, 1997](#_ENREF_12)), ii) the Rey Complex Figure Test Copy and Recall ([RCFT; Rey, 1941](#_ENREF_8)), iii) the Rey Auditory Verbal Learning Test ([RAVLT; Schmidt, 1996](#_ENREF_10)), iv) the Doors Test from the Doors and People memory battery ([Baddeley, Emslie, & Nimmo-Smith, 1994](#_ENREF_1)), v) the Sydney Language Battery (SydBat), which includes measures of confrontation naming, single-word repetition, word comprehension and semantic association ([Savage et al., 2013](#_ENREF_9)), vi) verbal letter fluency ([with letters F, A and S; Strauss, Sherman, & Spreen, 2006](#_ENREF_11)), vii) the Test for Reception of Grammar–Second edition ([TROG-2; Bishop, 2003](#_ENREF_3)), viii) the Sentence Repetition task from the Multilingual Aphasia Examination ([Benton, 1994](#_ENREF_2)), ix) Trail Making Test ([Reitan, 1955](#_ENREF_7)), x) the Hayling Sentence Completion Test ([Burgess & Shallice, 1997](#_ENREF_4)) and, xi) the Face and Emotion Processing Battery ([Kumfor et al., 2014](#_ENREF_5); [Miller et al., 2012](#_ENREF_6)).

*Supplementary Table 1*. Study 2 Demographic characteristics for the healthy controls and patient groups

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Controls**  **(n=87)** | **bvFTD (n=82)** | **AD (n=69)** | **NOS (n=38)** | **SD (n=34)** | **LPA (n=28)** | **PNFA (n=26)** | **CBS (n=21)** | **FTD-MND, MND or mixed FTD (n=18)** | **PSP (n=11)** | **PCA (n=4)** |
| **Age** | 67.3 (7.2) | 63.4 (9.0) | 66.0 (9.5) | 60.2 (11.0) | 64.1 (6.7) | 65.8 (6.9) | 65.7 (9.9) | 66.4 (5.8) | 63.1 (8.0) | 70.3 (5.9) | 62.5 (5.1) |
| **Education** | 13.9 (2.7) | 12.1 (2.8) | 11.9 (3.1) | 11.9 (2.7) | 12.9 (3.1) | 11.8 (3.2) | 12.8 (3.0) | 12.4 (4.0) | 12.8 (3.5) | 11.3 (3.5) | 12.0 (0.0) |
| **Disease Duration** | - | 5.4 (3.5) | 4.5 (3.0) | 4.7 (3.2) | 5.6 (2.3) | 3.9 (2.7) | 3.7 (2.1) | 3.7 (2.1) | 2.3 (1.1) | 5.4 (4.9) | 3.3 (2.7) |
| **ACE-III Total** | 95.3 (3.3) | 74.0 (18.6) | 62.8 (18.7) | 77.9 (21.2) | 55.2 (18.0) | 56.8 (21.3) | 73.2 (15.5) | 75.4 (11.5) | 71.4 (18.7) | 75.3 (7.1) | 40.8 (16.9) |
| **CDR SoB a** | 0.3 (0.6) | 5.2 (2.6) | 4.3 (2.3) | 4.1 (3.0) | 4.5 (3.7) | 3.9 (2.6) | 2.6 (3.1) | 3.2 (2.5) | 3.9 (2.7) | 5.0 (2.5) | 7.3 (3.2) |
| **CDR severity (0/0.5/1/2/3)** | 27/10/0/0/0 | 1/28/33/5/0 | 1/26/25/2/0 | 3/10/13/1/0 | 0/16/9/1/1 | 3/10/7/3/0 | 9/9/3/2/0 | 3/11/2/0/0 | 2/7/4/1/0 | 0/5/5/1/0 | 0/0/2/0/0 |

*Note,* Values are mean (standard deviation). bvFTD = behavioural-variant frontotemporal dementia, AD = Alzheimer’s disease, SD = semantic dementia, NOS = dementia not otherwise specified, PNFA = progressive nonfluent aphasia, LPA = logopenic progressive aphasia, CBS = corticobasal syndrome, mixed FTD = mixed frontotemporal dementia, MND = motor neurone disease, FTD-MND = frontotemporal dementia-motor neurone disease, PSP = progressive supranuclear palsy, PCA = posterior cortical atrophy. a Number of missing values: Controls = 50, bvFTD = 15, AD = 15, NOS = 11, SD = 7, LPA = 5, PNFA = 3, CBS = 5, FTD-MND, MND or mixed FTD = 4, PCA = 2

*Supplementary Table 2.* Effects of age and education on ACE-III performance in healthy controls

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ACE-III total** | | **Attention** | | **Memory** | | **Fluency** | | **Language** | | **Visuospatial** | |
|  | F value | *p* | F value | *p* | F value | *p* | F value | *p* | F value | *p* | F value | *p* |
| **Age** | 1.483 | 0.234 | 0.477 | 0.623 | 0.901 | 0.411 | 1.328 | 0.271 | 2.047 | 0.136 | 0.297 | 0.744 |
| **Education** | 11.626 | 0.001\*\* | 0.983 | 0.325 | 11.203 | 0.001\*\* | 1.202 | 0.277 | 5.820 | 0.018\* | 2.434 | 0.123 |
| **Age\*Education** | 1.986 | 0.145 | 0.314 | 0.731 | 1.374 | 0.259 | 0.402 | 0.671 | 0.641 | 0.530 | 1.281 | 0.284 |

*Note,* results of the two-way ANOVAs investigating the effects of age and education (independent variables) on ACE-III total and domain scores (dependent variables).*\** =significant at the p < 0.05 level*, \*\** = significant at the p < 0.01 level*.* ACE-III = Addenbrooke’s Cognitive Examination – Third edition.

*Supplementary Table 3*. ACE-III performance scores of the control group, stratified by age and education

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age** | **Education** | **n** | **ACE-III total** | **Attention** | **Memory** | **Fluency** | **Language** | **Visuospatial** |
| 50-65 | ≥14 | 18 | 96.9 (2.6) | 17.5 (0.6) | 25.1 (1.1) | 12.9 (1.2) | 25.8 (0.5) | 15.7 (0.5) |
|  | <14 | 9 | 94.1 (4.8) | 17.4 (1.0) | 23.4 (2.4) | 12.3 (1.8) | 25.3 (1.3) | 15.6 (0.7) |
| 66-71 | ≥14 | 9 | 95.8 (2.7) | 17.3 (1.3) | 24.9 (1.1) | 12.3 (1.1) | 25.7 (0.7) | 15.6 (0.5) |
|  | <14 | 16 | 94.8 (3.4) | 17.1 (1.7) | 24.4 (1.7) | 12.3 (1.2) | 25.5 (0.7) | 15.5 (0.7) |
| 72+ | ≥14 | 14 | 96.2 (2.2) | 17.6 (0.6) | 24.9 (1.2) | 12.2 (1.2) | 25.6 (0.6) | 15.9 (0.5) |
|  | <14 | 13 | 92.9 (3.8) | 17.2 (1.2) | 23.8 (1.8) | 11.8 (1.2) | 24.9 (1.0) | 15.2 (1.4) |

*Note*, values are mean (standard deviation). ACE-III = Addenbrooke’s Cognitive Examination – Third edition.

*Supplementary Online Conversion Calculator.* Addenbrooke’s Cognitive Examination–Revised to Addenbrooke’s Cognitive Examination–Third edition conversion calculator

**References**

Baddeley, A., Emslie, H., & Nimmo-Smith, I. (1994). *Doors and People*. Bury St Edmunds: Thames Valley Test Company.

Benton, A. L., Hamsher, K. deS., & Sivian, A.B. (1994). *Multilingual Aphasia Examination (3rd ed.)*. Iowa City: AJA Associates, Inc.

Bishop, D. V. M. (2003). *The Test for Reception of Grammar, version 2 (TROG-2)*. London: Pearson Assessment.

Burgess, P., & Shallice, T. (1997). The Hayling and Brixton Tests: Thames Valley Test Company Bury St. *Edmonds, England*.

Kumfor, F., Sapey-Triomphe, L.-A., Leyton, C. E., Burrell, J. R., Hodges, J. R., & Piguet, O. (2014). Degradation of emotion processing ability in corticobasal syndrome and Alzheimer’s disease. *Brain, 137*(11), 3061-3072.

Miller, L. A., Hsieh, S., Lah, S., Savage, S., Hodges, J. R., & Piguet, O. (2012). One size does not fit all: face emotion processing impairments in semantic dementia, behavioural-variant frontotemporal dementia and Alzheimer’s disease are mediated by distinct cognitive deficits. *Behavioural neurology, 25*(1), 53-60.

Reitan, R. M. (1955). The relation of the trail making test to organic brain damage. *Journal of Consulting Psychology, 19*(5), 393-394.

Rey, A. (1941). L'examen psychologique dans les cas d'encéphalopathie traumatique. *Archives de psychologie, 28*, 286-340.

Savage, S., Hsieh, S., Leslie, F., Foxe, D., Piguet, O., & Hodges, J. R. (2013). Distinguishing subtypes in primary progressive aphasia: application of the Sydney language battery. *Dementia and Geriatric Cognitive Disorders, 35*(3-4), 208-218. doi: 10.1159/000346389

Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook*: Western Psychological Services Los Angeles, CA.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary, 3rd ed*. New York, NY, US: Oxford University Press.

Wechsler, D. (1997). *Wechsler Memory Scale: Administration and Scoring Manual* (3rd ed.). San Antonio, TX: The Psychological Corporation.