

Supplementary Table 1. Demographic and clinical characteristics of FTLD patients grouped according to the global CDR plus NACC FTLD and mutational status.

| Variable | Global CDR plus NACC FTLD | | | |
|--------------------------|---------------------------|-------------------------------|---------------------|-------------------------------|
| | 0.5 sporadic | 0.5 genetic | 1 sporadic | 1 genetic |
| Number | 112 | 26 | 108 | 22 |
| Age, years | 66.8 (59.8-71.9) | 61.4 (55.9-66.7) [†] | 69.6 (63.6-74.8) | 62.8 (56.6-70.7) [†] |
| Sex male, n (%) | 66 (58.9) | 14 (53.8) | 56 (51.9) | 16 (72.7) |
| Education, years | 8.0 (5.0-13.0) | 9.0 (7.8-13.0) | 8.0 (5.0-13.0) | 8.0 (5.0-13.0) |
| Age at onset, years | 65.0 (57.3-69.0) | 57.5 (53.8-64.0) [†] | 66.5 (61.0-72.0) | 60.5 (54.0-68.3) [†] |
| Disease duration, years | 1.9 (1.3-3.1) | 1.7 (1.1-3.0) | 2.1 (1.3-3.3) | 2.0 (1.5-2.8) |
| Serum NfL (pg/mL)* | 27.2 (20.1-37.7) | 24.8 (19.1-46.5) | 39.0 (27.5-48.7) | 66.9 (52.4-78.0) [†] |
| bvFTD/avPPA/svPPA, n | 75/18/19 | 17/7/2 | 75/20/13 | 14/7/1 |
| MMSE | 25.9 (24.4-26.9) | 26.0 (24.0-27.9) | 23.2 (20.4-26.0) | 22.8 (20.2-25.5) |
| FBI | 7.0 (3.0-10.8) | 9.0 (4.0-12.5) | 11.5 (6.3-17.0) | 12.0 (7.8-21.3) |
| BADL lost | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) |
| IADL lost | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-1.0) | 0.0 (0.0-1.0) |
| Short story | 9.5 (8.0-13.0) | 9.0 (6.8-11.6) | 8.5 (5.8-10.9) | 8.1 (6.6-11.1) |
| Rey figure copy | 30.5 (26.4-32.8) | 29.7 (23.5-32.8) | 27.9 (22.4-32.7) | 26.4 (18.1-32.3) |
| Rey figure recall | 11.3 (8.5-16.5) | 13.8 (10.5-17.8) | 9.8 (6.5-13.3) | 9.6 (6.5-13.4) |
| Phonological fluency | 24.0 (19.0-29.8) | 22.6 (14.2-28.3) | 20.5 (15.0-29.0) | 16.0 (9.8-26.8) |
| Semantic fluency | 31.5 (24.3-36.8) | 31.0 (24.0-38.3) | 27.0 (20.0-33.0) | 26.6 (18.5-32.5) |
| Digit span | 5.0 (4.5-5.7) | 5.0 (4.6-5.8) | 4.9 (4.3-5.5) | 4.5 (3.5-5.9) |
| Token test | 30.1 (28.0-32.3) | 28.7 (27.4-31.3) | 28.3 (26.4-30.1) | 28.3 (22.8-30.5) |
| Trail making test part A | 51.0 (28.0-73.0) | 48.5 (27.0-72.5) | 64.0 (42.3-108.0) | 59.0 (39.0-115.8) |
| Trail making test part B | 187.5 (105.3-345.5) | 238.0 (92.0-401.3) | 324.0 (121.3-408.8) | 394.0 (176.5-442.5) |
| Clock drawing | 8.0 (6.0-9.0) | 8.0 (6.0-9.0) | 7.0 (5.0-8.8) | 8.0 (5.0-10.0) |
| Variable | 2 sporadic | 2 genetic | 3 sporadic | 3 genetic |
| Number | 141 | 34 | 94 | 26 |
| Age, years | 66.7 (61.0-71.9) | 61.0 (54.7-66.5) [†] | 67.7 (61.1-74.6) | 65.5 (61.5-69.9) |
| Sex male, n (%) | 76 (53.9) | 15 (44.1) | 43 (45.7) | 10 (38.5) |
| Education, years | 8.0 (5.0-8.0) | 10.0 (7.3-13.0) | 8.0 (5.0-11.3) | 8.0 (5.0-13.0) |
| Age at onset, years | 63.0 (58.0-69.0) | 58.0 (51.8-64.0) [†] | 64.0 (56.8-71.0) | 61.5 (59.5-67.0) |
| Disease duration, years | 2.6 (1.7-4.2) | 2.4 (1.6-3.2) | 3.2 (2.0-5.2) | 2.6 (1.8-4.2) |
| Serum NfL (pg/mL)* | 43.4 (36.1-59.8) | 55.3 (37.8-108.8) | 47.7 (39.9-55.4) | 74.1 (60.1-88.8) [†] |
| bvFTD/avPPA/svPPA, n | 99/25/17 | 22/10/2 | 73/13/8 | 17/8/1 |
| MMSE | 20.0 (15.0-23.0) | 20.6 (16.7-24.0) | 11.6 (4.0-19.1) | 7.5 (0.0-14.5) |
| FBI | 19.0 (11.5-27.0) | 22.5 (14.8-25.3) | 30.5 (24.0-37.0) | 32.5 (25.3-36.3) |
| BADL lost | 0.0 (0.0-1.0) | 0.0 (0.0-1.0) | 3.0 (1.0-4.0) | 3.0 (2.0-5.0) |
| IADL lost | 2.0 (1.0-3.0) | 2.0 (0.0-4.0) | 5.0 (3.8-7.0) | 6.0 (5.0-7.3) |
| Short story | 6.0 (3.5-8.0) | 6.2 (3.5-8.4) | 5.2 (3.8-7.5) | 5.7 (4.4-8.1) |
| Rey figure copy | 20.8 (13.6-29.0) | 22.0 (17.6-28.3) | 13.6 (6.9-20.1) | 10.0 (6.8-13.6) |
| Rey figure recall | 6.1 (3.2-9.7) | 7.1 (4.4-9.6) | 5.2 (3.1-7.3) | 5.8 (4.0-7.5) |
| Phonological fluency | 15.0 (9.6-21.5) | 12.0 (7.0-20.5) | 10.1 (5.0-15.6) | 7.4 (2.3-11.5) |
| Semantic fluency | 18.0 (13.0-25.0) | 22.3 (14.5-26.8) | 10.9 (5.3-18.1) | 7.4 (3.1-17.0) |
| Digit span | 4.5 (3.8-5.5) | 4.5 (4.0-5.0) | 3.8 (2.8-4.5) | 3.4 (2.8-4.0) |
| Token test | 24.1 (19.3-28.0) | 23.7 (21.3-27.5) | 18.8 (14.7-24.6) | 17.0 (11.0-21.6) |
| Trail making test part A | 115.0 (68.0-297.0) | 86.5 (48.5-173.3) | 212.5 (131.0-394.5) | 321.5 (184.5-387.0) |
| Trail making test part B | 403.0 (345.0-426.5) | 407.5 (299.0-447.8) | 398.5 (364.8-422.3) | 421.5 (395.5-463.3) |
| Clock drawing | 5.0 (3.0-6.0) | 5.0 (3.0-7.0) | 3.0 (1.0-4.3) | 2.0 (0.0-3.3) |

NfL = neurofilament light chain; CDR plus NACC FTLD SB = clinical dementia rating plus National Alzheimer's Coordinating Center behaviour and language domains FTLD sum-of-boxes; MMSE = mini mental state examination; FBI = frontal behavioural inventory; BADL = basic activities of daily living; IADL = instrumental activities of daily living. Results are expressed as median (interquartile range), unless otherwise specified.

*results for serum NfL are reported for a subgroup of patients; [†]significant difference vs sporadic cases at Mann-Whitney U test or Fisher's test, as appropriate, FDR-corrected for multiple comparisons.

Supplementary Table 2. Demographic and clinical characteristics of FTLD patients grouped according to the global CDR plus NACC FTLD and conversion at 12-months follow-up.

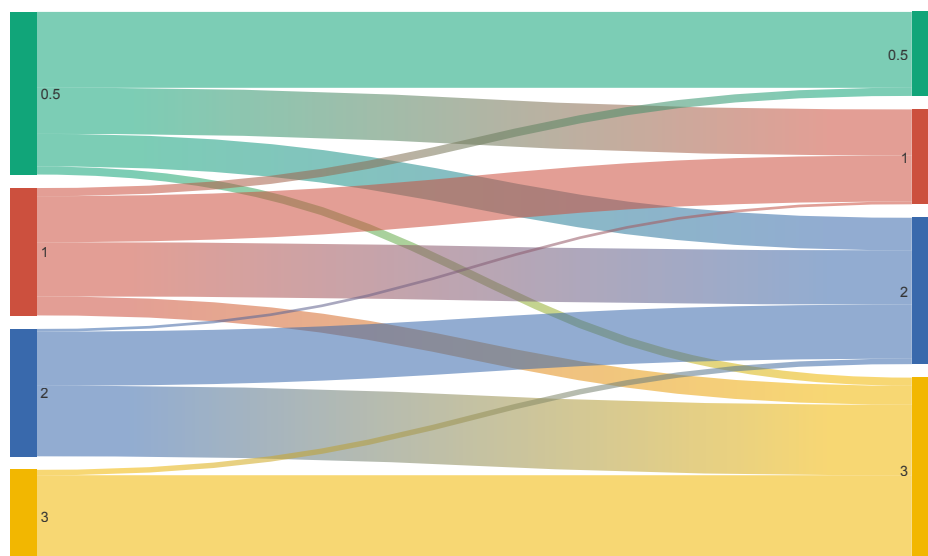
| Variable | Global CDR plus NACC FTLD | | | | | | |
|--------------------------|---------------------------|----------------------------------|--------------------|-------------------------------|---------------------|---------------------|---------------------|
| | 0.5 non-converters | 0.5 converters | 1 non-converters | 1 converters | 2 non-converters | 2 converters | 3 |
| Number | 41 | 43 | 26 | 42 | 28 | 40 | 38 |
| Age, years | 66.7 (60.4-72.1) | 65.1 (56.9-70.7) | 68.7 (63.9-75.4) | 64.9 (57.5-74.1) | 62.6 (57.7-68.8) | 66.6 (61.0-71.9) | 65.8 (62.0-73.4) |
| Sex male, n (%) | 22 (53.7) | 27 (62.8) | 17 (65.4) | 19 (45.2) | 16 (57.1) | 16 (40.0) | 18 (47.4) |
| Education, years | 8.0 (5.0-13.0) | 8.0 (5.0-13.0) | 8.0 (5.0-8.3) | 8.0 (5.0-13.0) | 7.0 (5.0-8.0) | 8.0 (5.0-8.0) | 5.0 (5.0-11.0) |
| Age at onset, years | 64.0 (57.5-69.5) | 64.0 (56.0-69.0) | 65.0 (61.8-69.8) | 63.0 (55.8-71.3) | 60.0 (55.3-65.8) | 62.5 (58.0-68.0) | 63.5 (56.0-68.8) |
| Disease duration, years | 2.2 (1.3-3.5) | 1.9 (1.2-2.8) | 2.1 (1.2-3.5) | 2.2 (1.4-3.2) | 1.8 (1.4-2.6) | 2.8 (1.9-4.4) | 2.4 (1.6-4.4) |
| Monogenic disease, n (%) | 6 (14.6) | 11 (25.6) | 4 (15.4) | 7 (16.7) | 2 (7.1) | 8 (20.0) | 9 (23.7) |
| Serum NfL (pg/mL)* | 20.4 (18.1-28.9) | 36.0 (24.0-47.0) [†] | 29.5 (18.2-37.3) | 47.2 (37.0-66.9) [†] | 41.1 (28.9-49.8) | 46.0 (38.1-62.8) | 51.9 (44.1-76.9) |
| bvFTD/avPPA/svPPA, n | 28/7/6 | 31/5/7 | 20/4/2 | 27/8/7 | 21/5/2 | 26/8/6 | 34/3/1 |
| MMSE | 26.2 (25.3-27.5) | 25.9 (23.9-26.9) | 25.0 (23.2-26.1) | 22.5 (19.8-25.5) | 20.0 (16.9-22.7) | 20.0 (14.8-22.3) | 12.9 (2.7-16.0) |
| FBI | 5.0 (2.0-9.0) | 10.0 (7.0-13.0) [†] | 11.5 (5.0-19.0) | 13.0 (8.0-17.5) | 16.0 (12.0-22.8) | 19.5 (10.0-26.8) | 30.5 (23.8-36.0) |
| BADL lost | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.8) | 0.0 (0.0-0.0) | 3.0 (1.0-5.0) |
| IADL lost | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-0.0) | 0.0 (0.0-1.0) | 2.0 (1.3-3.8) | 2.0 (1.0-4.0) | 5.0 (4.0-7.0) |
| Short story | 12.5 (8.5-15.0) | 9.1 (6.5-11.5) [†] | 9.8 (6.3-14.6) | 7.0 (4.0-10.5) | 5.6 (4.1-8.0) | 5.2 (0.6-7.5) | 5.7 (2.8-8.1) |
| Rey figure copy | 30.5 (27.7-32.7) | 27.5 (23.3-31.8) | 29.0 (24.7-32.4) | 27.7 (21.2-33.6) | 20.9 (17.4-29.4) | 19.2 (12.9-26.7) | 10.7 (6.2-19.2) |
| Rey figure recall | 16.3 (10.7-19.5) | 10.5 (7.3-15.0) [†] | 9.8 (7.1-14.8) | 9.2 (3.7-13.6) | 6.7 (1.3-10.0) | 5.4 (0.4-8.5) | 4.5 (2.7-7.4) |
| Phonological fluency | 28.0 (22.0-36.5) | 23.0 (15.0-28.0) [†] | 25.5 (16.8-31.5) | 17.0 (11.0-28.1) | 17.5 (9.9-23.0) | 11.0 (8.3-20.5) | 11.5 (4.1-19.2) |
| Semantic fluency | 35.0 (27.5-42.0) | 29.0 (26.0-36.0) [†] | 31.0 (20.8-38.3) | 26.0 (18.5-32.0) | 22.5 (15.3-28.5) | 15.0 (11.4-22.8) | 11.3 (3.1-19.8) |
| Digit span | 5.0 (4.4-6.0) | 5.2 (4.5-5.8) | 5.3 (4.5-5.6) | 4.5 (3.8-5.8) | 5.0 (4.0-5.5) | 4.3 (3.4-5.5) | 3.5 (2.4-4.5) |
| Token test | 31.0 (29.4-33.0) | 29.4 (27.8-32.5) | 29.3 (27.5-31.6) | 27.0 (23.1-29.6) [†] | 24.4 (22.4-28.9) | 23.8 (19.4-27.0) | 18.1 (12.0-22.9) |
| Trail making test part A | 49.0 (24.5-73.5) | 51.0 (28.0-80.0) | 53.0 (26.5-73.5) | 68.5 (41.8-111.0) | 101.0 (50.5-212.0) | 141.5 (70.0-472.0) | 353.5 (168.0-476.0) |
| Trail making test part B | 144.0 (73.5-253.0) | 223.0 (140.0-396.0) [†] | 306.5 (94.8-409.0) | 349.5 (157.0-432.3) | 408.0 (315.3-430.5) | 411.0 (393.8-431.5) | 405.0 (370.0-424.0) |
| Clock drawing | 9.0 (7.0-10.0) | 7.0 (5.0-9.0) [†] | 7.0 (5.0-9.0) | 7.0 (4.0-8.0) | 5.0 (4.0-6.0) | 4.5 (2.0-6.0) | 3.0 (1.0-5.0) |

NfL = neurofilament light chain; CDR plus NACC FTLD SB = clinical dementia rating plus National Alzheimer's Coordinating Center behaviour and language domains FTLD sum-of-boxes; MMSE = mini mental state examination; FBI = frontal behavioural inventory; BADL = basic activities of daily living; IADL = instrumental activities of daily living. Results are expressed as median (interquartile range), unless otherwise specified.

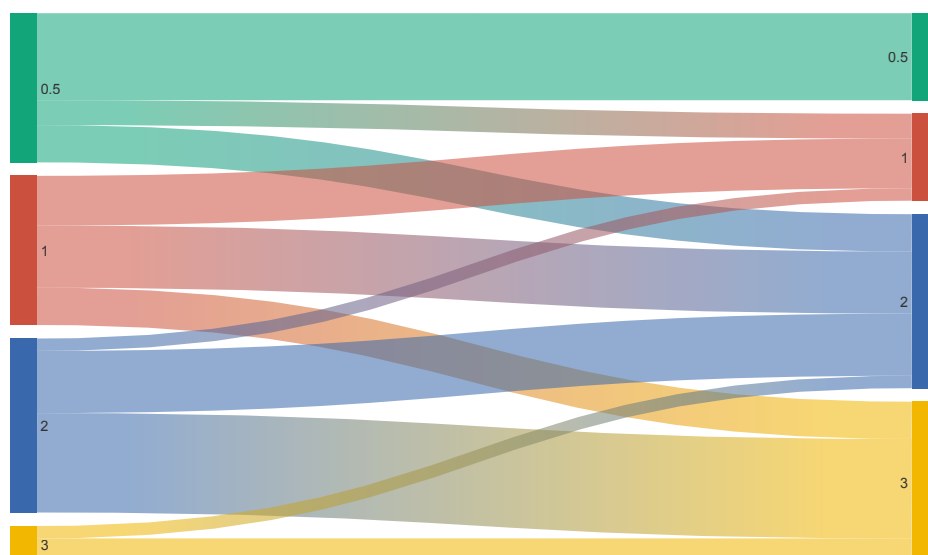
*results for serum NfL are reported for a subgroup of patients; [†]significant difference vs non-converters at Mann-Whitney U test or Fisher's test, as appropriate, FDR-corrected for multiple comparisons.

Supplementary Figure 1. Sankey diagram showing the evolution of patients according to the global CDR plus NACC FTLD and phenotype.

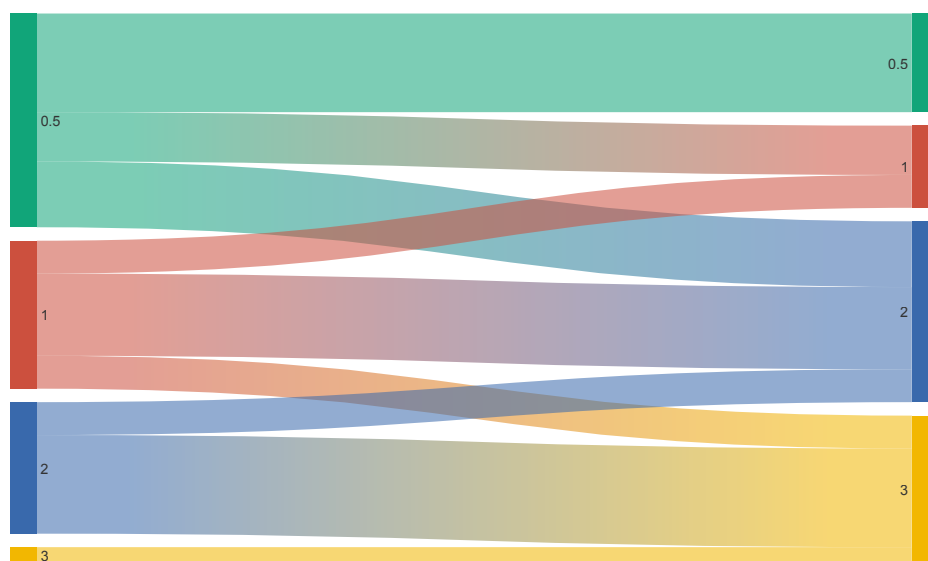
A. bvFTD



B. avPPA



C. svPPA



The changes of patients over time at different time points is represented in different global CDR plus NACC FTLD groups. The height of the boxes and the thickness of the stripes are proportional to the number of patients belonging to each group and moving from each group, respectively. bvFTD = behavioural variant frontotemporal dementia; avPPA = agrammatic variant primary progressive aphasia; svPPA = semantic variant primary progressive aphasia.