Supplementary Table 1: Cognitive performance in patients with and without prior overt HE

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Combined | | | VA | | | OH | | | AR | | |
|  | OHE-  (n = 277) | OHE+  (n= 155) | p-value | OHE-  (n =132) | OHE+  (n = 93) | p-value | OHE-  (n = 75) | OHE+  (n = 32) | p-value | OHE-  (n = 70) | OHE+  (n = 30) | p-value |
| PHES components | | | | | | | | | | | | |
| NCT-A | 31.00  (26.00, 42.00) | 38.00  (28.00, 50.00) | 0.0009 | 31.00  (26.00, 44.00) | 40.00  (31.00, 58.00) | 0.001 | 31.00  (25.00, 37.00) | 28.50  (24.00, 36.50) | 0.15 | 31.43  (24.76, 39.91) | 41.23  (29.96 47.62) | 0.01 |
| NCT-B | 75.68  (59.00, 109.00) | 94.00  (69.90, 125.00) | <0.0001 | 78.50  (59.00, 114.50) | 104.00  (76.00, 144.00) | 0.0002 | 89.00  (72.00, 115.00) | 97.00  (80.50, 122.50) | 0.35 | 63.62  (53.62, 78.29) | 68.99  (64.84, 92.18) | 0.05 |
| DST | 50.00  (43.00, 62.00) | 46.00  (39.00, 54.00) | <0.0001 | 56.50  (43.00, 69.00) | 46.00  (34.00, 54.00) | <0.0001 | 51.00  (42.00, 63.00) | 49.50  (40.50, 60.50) | 0.46 | 45.00  (43.00, 49.00) | 44.00  (41.00, 46.00) | 0.04 |
| LTT | 119.62  (99.00, 143.00) | 136.00  (111.66, 172.00) | <0.0001 | 123.00  (106.00, 150.00) | 147.00  (125.00, 187.00) | 0.0001 | 110.00  (95.00, 134.00) | 114.00  (91.00, 138.50) | 0.90 | 113.61  (94.31, 139.20) | 133.27  (116.97, 160.92) | 0.003 |
| SDT | 66.00  (55.00, 81.14) | 76.15  (59.00, 96.00) | <0.0001 | 58.50  (50.00, 75.00) | 76.00  (58.00, 96.00) | <0.0001 | 67.00  (57.00, 82.00) | 67.00  (58.50, 86.00) | 0.62 | 75.95  (65.11, 85.41) | 82.60  (74.48, 97.55) | 0.01 |
| ICT components | | | | | | | | | | | | |
| ICT Lures | 11.50  (5.00, 19.00) | 13.00  (7.00, 21.00) | 0.05 | 7.00  (3.00, 14.00) | 10.00  (6.00, 18.00) | 0.006 | 15.00  (8.00, 22.00) | 14.00  (9.50, 22.00) | 0.83 | 14.00  (10.00, 22.00) | 19.00  (11.00, 23.00) | 0.33 |
| ICT % Targets | 96.85  (91.00, 99.00) | 94.81  (88.00, 98.00) | 0.004 | 98.58  (96.70, 99.53) | 96.70  (92.45, 98.58) | 0.0001 | 95.00  (90.00, 98.00) | 94.00  (86.50, 96.00) | 0.14 | 91.51  (87.50, 95.99) | 91.741  (79.71, 94.81) | 0.41 |
| EncephalApp | | | | | | | | | | | | |
| OffTime | 82.71  (70.47, 92.97) | 90.71  (78.94, 101.65) | <0.0001 | 79.40  (66.57, 90.69) | 92.22  (77.80, 109.06) | <0.0001 | 83.93  (70.47, 97.49) | 85.62  (74.72, 100.33) | 0.45 | 86.92  (80.50, 95.18) | 89.42  (81.56, 99.59) | 0.28 |
| OnTime | 96.84  (82.68, 109.57) | 104.78  (90.19, 123.94) | <0.0001 | 96.87  (79.63, 109.57) | 108.66  (92.16, 130.00) | <0.0001 | 97.26  (84.81, 117.89) | 106.32  (85.03, 129.57) | 0.49 | 96.21  (88.03, 101.74) | 97.19  (90.30, 103.04) | 0.65 |
| OffTime+  OnTime | 180.63  (153.51, 200.43) | 195.88  (168.10, 221.39) | <0.0001 | 178.63  (145.17, 196.97) | 200.50  (173.27, 237.57) | <0.0001 | 183.94  (155.69, 210.36) | 192.55  (162.58, 229.00) | 0.43 | 183.12  (169.90, 195.29) | 182.84  (175.42, 198.54) | 0.40 |
| OnTime – OffTime | 14.44  (5.87, 21.14) | 12.95  (7.27, 25.58) | 0.27 | 15.56  (8.64, 21.90) | 16.53  (9.19, 29.05) | 0.13 | 15.15  (8.61, 23.15) | 14.43  (7.20, 31.08) | 0.98 | 7.88  (-0.04, 16.31) | 6.75  (2.79, 10.21) | 0.57 |
| No. of Off runs | 6.00  (5.00, 6.00) | 6.00  (5.00, 7.00) | 0.62 | 5.00  (5.00, 6.00) | 5.00  (5.00, 6.00) | 0.70 | 5.00  (5.00, 7.00) | 6.00  (5.00, 7.00) | 0.29 | 6.00  (5.00, 7.00) | 6.50  (6.00, 7.00) | 0.11 |
| No. of On runs | 6.00  (5.00, 7.00) | 6.00  (5.00, 7.00) | 0.19 | 5.00  (5.00, 7.00) | 6.00  (5.00, 7.00) | 0.23 | 6.00  (5.00, 8.00) | 6.00  (5.00, 7.00) | 0.92 | 7.00  (6.00, 7.00) | 7.00  (6.00, 8.00) | 0.03 |

Notes: 1) Median (IQR)

2) Tests done using Mann-Whitney U test (Wilcoxon Rank-Sum test)

Supplementary Table 2: Individual test results in the validation cohort; data is presented as median (IQR)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Combined  (n = 121) | No prior overt HE  (n = 76) | Prior overt HE  (n = 45) | p-value |
| NCT-A (seconds) | 40.00  (30.00, 54.00) | 35.00  (26.00, 46.00) | 51.00  (38.00, 65.00) | <0.0001 |
| NCT-B (seconds) | 104.00  (73.00, 140.00) | 86.00  (65.00, 115.00) | 128.00  (100.00, 176.00) | <0.0001 |
| DST (raw score) | 48.00  (39.00, 58.00) | 54.00  (44.00, 66.50) | 42.00  (34.00, 49.00) | <0.0001 |
| SDT (seconds) | 68.00  (54.00, 91.00) | 64.50  (52.00, 77.00) | 87.00  (67.00, 121.00) | <0.0001 |
| LTTe+Time (number+seconds) | 137.00  (111.00, 163.00) | 126.00  (107.00, 156.00) | 155.00  (129.00, 190.00) | 0.0005 |
| ICT Lures (number) | 7.00  (6.00, 9.00) | 7.00  (6.00, 9.00) | 8.00  (6.00, 12.00) | 0.12 |
| ICT % Targets | 96.70  (92.92, 99.06) | 97.17  (93.87, 99.06) | 95.28  (90.57, 98.58) | 0.10 |
| OffTime (seconds) | 85.35  (73.23, 98.30) | 80.31  (70.92, 91.08) | 95.47  (80.71, 114.73) | <0.0001 |
| OnTime (seconds) | 100.62  (87.77, 121.54) | 96.00  (83.16, 109.44) | 110.57  (100.39, 135.05) | <0.0001 |
| OffTime+OnTime (seconds) | 185.94  (162.57, (222.94) | 175.31  (154.90, 200.89) | 207.58  (182.58, 243.72) | <0.0001 |
| OnTime – OffTime (seconds) | 15.54  (10.60, 23.59) | 14.65  (9.60, 20.68) | 18.12  (11.58, 27.08) | 0.02 |
| No. of Off runs | 5.00  (5.00, 6.00) | 5.00  (5.00, 6.00) | 5.00  (5.00, 6.00) | 0.64 |
| No. of On runs | 6.00  (5.00, 7.00) | 6.00  (5.00, 6.00) | 6.00  (5.00, 7.00) | 0.17 |

HE: hepatic encephalopathy, ICT: inhibitory control test, NCT-A: number connection test-A, NCT-B: number connection test-B, DST: digit symbol test, LTT: line tracing test (errors+time)