

Supplementary Material

**A novel cognitive-neurophysiological state biomarker in  
premanifest Huntington's disease validated on longitudinal data**

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**Table 1:**

Means and standard deviations (SD) for pre-HD subjects in the different experimental conditions at all time points (longitudinal, 15-month, 21-month).

Parameter	Baseline (n = 27)	Follow-up 15-month	Follow-up 21-month
compatible switch	654 (50)	660 (53)	646 (55)
Incompatible switch	834 (49)	976 (65)	1023 (65)
compatible non-switch	601 (38)	611 (38)	598 (37)
Incompatible non-switch	666 (37)	672 (35)	658 (38)

**Table 2:**

Baseline group statistics of premanifest HD mutation carriers at baseline, 15 and 21 month follow up and controls. Data of matched controls are only shown at baseline. Of the 30 participants enrolled at baseline, 27 (90%) completed the 15 month and 27 (90%) completed the 21 month follow-up assessment. We included 27 participants who contributed to all three datasets in the statistical analysis. Values are given as mean  $\pm$  SD; range (min-max) in brackets; <sup>s</sup> = including two mutation carriers with a pheno-conversion to manifest HD, <sup>#</sup> = two manifest HD patients excluded, <sup>%</sup> = complete datasets for 26 participants; <sup>+</sup> = complete datasets for 25 participants (Cohen's d effect size for absolute MRI measures in ml: 15 month interval 0.14, for 6 month interval 0.11). Abbreviations: yr – years, OP – onset probability, YTO – years to onset, UHDRS – unified Huntington's disease rating scale, MS – motor score TFC – total functional capacity, IS – independence scale, CS – cognitive sum score; SDMT – symbol digit modality test.

Parameter	preHD Baseline (n = 27)	preHD (n = 27) <sup>s</sup> Follow-up 15 Month	preHD (n = 27) <sup>s</sup> Follow-up 21 Month
Age [yr]	39.3 $\pm$ 10.6 (23-63)	40.6 $\pm$ 10.7 (24-64)	41.1 $\pm$ 10.5 (25-64)
Gender (male/female)	12/15	12/15	12/15
CAG expanded	42.1 $\pm$ 2.2 (38-48)	42.1 $\pm$ 2.2 (38-48)	42.1 $\pm$ 2.2 (38-48)
Disease burden score	250.1 $\pm$ 79.3 (108.5-412.5)	258.3 $\pm$ 81.9 (115.5-427.5)	262.1 $\pm$ 82.4 (115.5-427.5)
5 year OP [%]	17.2 $\pm$ 17.4 (0.6-60.1)	16.9 $\pm$ 16.7 (0.7-52.9) <sup>#</sup>	18 $\pm$ 17.3 (0.7-52.9) <sup>#</sup>
YTO Langbehn [yr]	16.1 $\pm$ 8.7 (5.3-38.4)	16.4 $\pm$ 8.9 (5.9-36.4) <sup>#</sup>	16 $\pm$ 8.8 (5.9-36.4) <sup>#</sup>
YTO Ranen [yr]	6.6 $\pm$ 8 (-12.5-19.8)	6.8 $\pm$ 6.6 (-7.7-17.8) <sup>#</sup>	6.2 $\pm$ 6.5 (-7.7-17.8) <sup>#</sup>
UHDRS MS	2.9 $\pm$ 2.6 (0-8)	4.4 $\pm$ 4.8 (0-15)	4.4 $\pm$ 4.7 (0-17)
UHDRS TFC	12.9 $\pm$ 0.2 (12-13)	12.8 $\pm$ 0.3 (12-13)	12.8 $\pm$ 0.4 (12-13)
UHDRS IS	99.4 $\pm$ 1.6 (95-100)	98.7 $\pm$ 3.6 (85-100)	98.7 $\pm$ 3.3 (90-100)
UHDRS CS	332.4 $\pm$ 41.4 (238-423)	329.7 $\pm$ 44 (234-425)	342 $\pm$ 41.7 (242-433)
Verbal fluency	42.4 $\pm$ 10.9 (17-64)	41 $\pm$ 10.4 (21-64)	43.9 $\pm$ 14.8 (15-83)
SDMT	54.3 $\pm$ 9.9 (36-78)	53.4 $\pm$ 10.6 (36-76)	56.1 $\pm$ 10.5 (37-74)
Stroop interference	51.4 $\pm$ 8.9 (31-66)	50.4 $\pm$ 9.1 (31-78)	51 $\pm$ 9.2 (33-77)
Stroop color	77.5 $\pm$ 10.5 (59-101)	79.9 $\pm$ 11.8 (61-107)	81.7 $\pm$ 10.3 (58-104)
Stroop word	106.8 $\pm$ 14.2 (81-136)	105.1 $\pm$ 15.6 (76-137)	109.1 $\pm$ 13 (81-138)
Pegboard dominant <sup>36</sup>	42.8 $\pm$ 9.7 (32-56) <sup>%</sup>	43.7 $\pm$ 4.7 (33.7-52.6) <sup>%</sup>	42.4 $\pm$ 4.7 (33.8-52.8) <sup>%</sup>
Pegboard non dominant <sup>36</sup>	45.8 $\pm$ 11.3 (33.4-63.5) <sup>%</sup>	46.8 $\pm$ 6.2 (32.7-56.3) <sup>%</sup>	45.2 $\pm$ 6.4 (35.9-59.1) <sup>%</sup>

Tapping dominant <sup>37</sup>	195.2 ± 21.6 (143-226)	188.9 ± 24.2 (140-230)	192.1 ± 22.8 (147-238)
Tapping non dominant <sup>37</sup>	176.4 ± 24.1 (127-239)	170.6 ± 23.7 (128-221)	175 ± 23.2 (122-224)
Hamilton Depression Inventory	6.6 ± 6.2 (0-22)	6.4 ± 8.1 (0-28)	6.2 ± 5.5 (0-22)
Caudatum volume [ml] <sup>35</sup>	3.02 ± 0.76 (1.3-4.15) <sup>4</sup>	2.92 ± 0.75 (1.31 – 4.04) <sup>+</sup>	2.84 ± 0.75 (1.16-4.14) <sup>+</sup>