

Supplementary Material

Time Trends of Cerebrospinal Fluid Biomarkers of Neurodegeneration in Idiopathic Normal Pressure Hydrocephalus

Supplementary Table 1. Demographic data

Group	n=201	n=41
Age; mean (SD)	74.9 (6.9)	74.7 (5.2)
Male; n (%)	99 (49)	25 (61)
Biopsy positive; n (%)		
A β	103 (51)	25 (61)
HP-Tau	33 (16)	6 (15)
Shunt response; n (%)	163 (81)	33 (80)
iNPHGS	97 (48)	25 (61)
Gait velocity	76 (38)	26 (63)
Other ¹	48 (24)	4 (10)
iNPHGS; mean (0-12, SD)		
Pre	5.9 (2.7)	5.9 (2.5)
Post	5.4 (2.9)*	4.4 (2.3)*
Gait velocity ² ; mean (SD)		
Pre	0.6 (0.3)	0.6 (0.3)
Post	0.7 (0.3)	0.7 (0.4)
MMSE; mean (SD)		
Pre	22.1 (4.8)*	23.9 (3.2)*
Post	22.5 (4.8)	23.3 (3.9)

Demographic data of the source cohort and study cohort. Values presented as mean and standard deviation (SD) or as number and percent. Significances are calculated between the source cohort and study cohort with students t-test, Mann-Whitney test or χ^2 -test (*p<0.05).

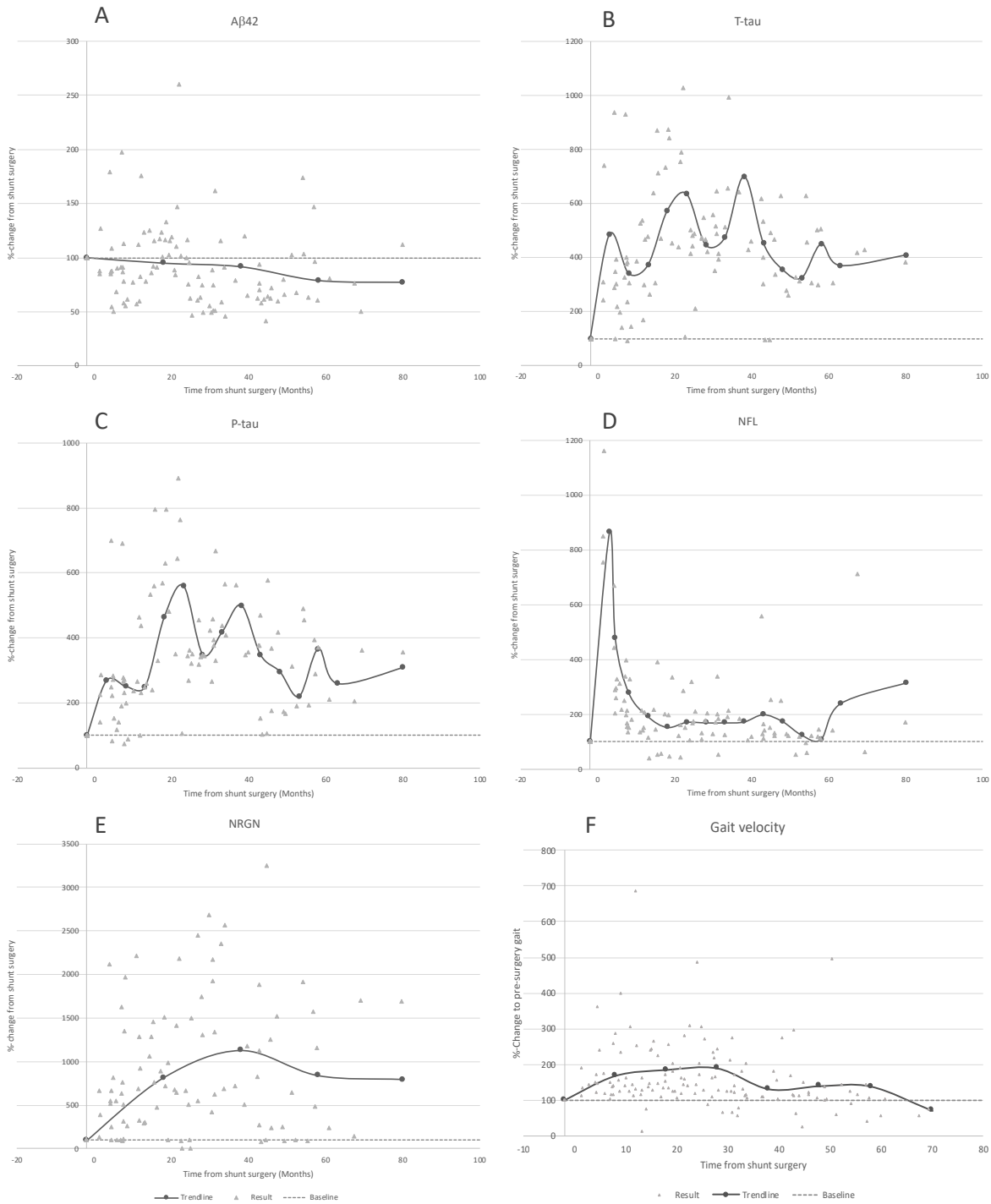
¹The “other” stands for the clinical evaluation of practitioner about the shunt response. The protocol used in diagnostic parameters is previously reported in Junkkari et al. [1]. The shunt response and iNPHGS are based on the study of Kubo et al. [2].

²Gait velocity measured in meters per second.

B0, baseline visit of the follow-up; MMSE, Mini-Mental State Examination; iNPHGS, idiopathic normal pressure hydrocephalus grading scale; A β , amyloid- β protein aggregates; HP-Tau, hyperphosphorylated Tau; Pre, Pre-shunt surgery; Post, Post-shunt surgery.

REFERENCES

- [1] Junkkari A, Luikku AJ, Danner N, Jyrkkänen HK, Rauramaa T, Korhonen VE, Koivisto AM, Nerg O, Kojoukhova M, Huttunen TJ, Jääskeläinen JE, Leinonen V (2019) The Kuopio idiopathic normal pressure hydrocephalus protocol: initial outcome of 175 patients. *Fluids Barriers CNS* **16**, 21.
- [2] Kubo Y, Kazui H, Yoshida T, Kito Y, Kimura N, Tokunaga H, Ogino A, Miyake H, Ishikawa M, Takeda M (2008) Validation of grading scale for evaluating symptoms of idiopathic normal-pressure hydrocephalus. *Dement Geriatr Cogn Disord* **25**, 37-45.



Supplementary Figure 1. Longitudinal change of the biomarkers of neurodegeneration from L-CSF plotted with the time from shunt surgery and percentual change from the pre-surgery value (A-E). Results are presented as individual datapoints (gray triangle) and as mean values and trendlines with either 5 (B-D)- or 20 (A, E)- month averaging. In addition, the longitudinal change of gait velocity (F) is presented with the 10-month trendline and individual datapoints (gray triangle). Gait velocity is calculated as percentual change from pre-surgery value and plotted with the time form shunt surgery. L-CSF, cerebrospinal fluid collected with lumbar puncture; Aβ₄₂, Amyloid-β 42; T-tau, total tau; P-tau, tau phosphorylated at threonine 181; NFL, neurofilament light; NRGN, neurogranin.