

# Supplementary Material

## Subtle Differences in Cognition in 70-Year-Olds with Elevated Cerebrospinal Fluid Neurofilament Light and Neurogranin: A H70 Cross-Sectional Study

**Supplementary Table 1.** Cognitive performance in 70-year-olds with Clinical Dementia Rating 0 - CSF neurofilament light (NfL) divided into tertials (n = 256)

|                                 | 1 <sup>st</sup> T<br>N=84 | 1 <sup>st</sup> T<br>Mean<br>(SD) | 2 <sup>nd</sup> T<br>N=85 | 2 <sup>nd</sup> T<br>Mean (SD) | p     | 3 <sup>rd</sup> T<br>N=87 | 3 <sup>rd</sup> T<br>Mean<br>(SD) | p            |
|---------------------------------|---------------------------|-----------------------------------|---------------------------|--------------------------------|-------|---------------------------|-----------------------------------|--------------|
| MMSE                            | 84                        | 29.3 (0.9)                        | 85                        | 29.2 (1.0)                     | 0.460 | 86                        | 29.2 (0.9)                        | 0.328        |
| <b>Memory</b>                   |                           |                                   |                           |                                |       |                           |                                   |              |
| Immediate recall                | 84                        | <b>8.5 (1.5)</b>                  | 84                        | 8.3 (1.6)                      | 0.627 | 87                        | <b>7.9 (1.7)</b>                  | <b>0.021</b> |
| Delayed recall                  | 84                        | <b>7.9 (1.6)</b>                  | 84                        | 7.8 (1.7)                      | 0.716 | 87                        | <b>7.4 (1.8)</b>                  | <b>0.041</b> |
| Word memory                     | 83                        | 5.8 (1.8)                         | 82                        | 5.5 (1.5)                      | 0.298 | 86                        | 5.6 (2.0)                         | 0.374        |
| Supra Span                      | 82                        | 7.7 (1.6)                         | 80                        | 7.8 (1.3)                      | 0.769 | 80                        | 7.6 (1.4)                         | 0.650        |
| Thurstone's picture memory test | 78                        | 22.9 (3.4)                        | 78                        | 22.4 (4.2)                     | 0.400 | 80                        | 23.1 (4.1)                        | 0.750        |
| <b>Language</b>                 |                           |                                   |                           |                                |       |                           |                                   |              |
| Word fluency                    | 84                        | 25.6 (7.3)                        | 84                        | 25.2 (5.7)                     | 0.682 | 87                        | 24.5 (6.3)                        | 0.321        |
| FAS                             | 82                        | 43.7 (14.1)                       | 79                        | 42.3 (13.3)                    | 0.525 | 82                        | 39.9 (13.9)                       | 0.083        |
| <b>Executive function</b>       |                           |                                   |                           |                                |       |                           |                                   |              |
| SRB2                            | 83                        | 20.2 (4.1)                        | 82                        | 20.8 (4.1)                     | 0.378 | 85                        | 20.5 (4.2)                        | 0.677        |
| Digit span backwards            | 84                        | 4.5 (1.2)                         | 82                        | 4.6 (1.2)                      | 0.589 | 84                        | 4.7 (1.0)                         | 0.261        |
| <b>Visuospatial</b>             |                           |                                   |                           |                                |       |                           |                                   |              |
| SRB3                            | 83                        | 22.3 (6.6)                        | 79                        | 21.5 (6.2)                     | 0.476 | 84                        | 21.9 (7.5)                        | 0.742        |
| <b>Mental speed</b>             |                           |                                   |                           |                                |       |                           |                                   |              |
| Psif                            | 84                        | 29.5 (7.8)                        | 82                        | 30.8 (7.4)                     | 0.277 | 85                        | 28.8 (7.7)                        | 0.565        |

T, tertile. The 1<sup>st</sup> tertile was the reference group.

NfL was log-transformed before divided into tertiles.

**Supplementary Table 2.** Cognitive performance in 70-year-olds with Clinical Dementia Rating 0 - CSF-Neurogranin (Ng) divided into tertiles (n = 258)

|                                 | 1 <sup>st</sup> T<br>N=91 | 1 <sup>st</sup> T<br>Mean<br>(SD) | 2 <sup>nd</sup> T<br>N=76 | 2 <sup>nd</sup> T<br>Mean<br>(SD) | p     | 3 <sup>rd</sup> T<br>N=91 | 3 <sup>rd</sup> T<br>Mean<br>(SD) | p     |
|---------------------------------|---------------------------|-----------------------------------|---------------------------|-----------------------------------|-------|---------------------------|-----------------------------------|-------|
| MMSE                            | 91                        | 29.2 (1.0)                        | 76                        | 29.3 (0.8)                        | 0.471 | 90                        | 29.2 (1.0)                        | 0.673 |
| <b>Memory</b>                   |                           |                                   |                           |                                   |       |                           |                                   |       |
| Immediate recall                | 91                        | 8.2 (1.6)                         | 76                        | 8.0 (1.8)                         | 0.475 | 90                        | 8.3 (1.5)                         | 0.623 |
| Delayed recall                  | 91                        | 7.8 (1.7)                         | 76                        | 7.5 (1.9)                         | 0.244 | 90                        | 7.8 (1.6)                         | 0.780 |
| Word memory                     | 90                        | 5.6 (1.8)                         | 75                        | 5.5 (1.8)                         | 0.843 | 88                        | 5.7 (1.8)                         | 0.701 |
| Supra Span                      | 86                        | 7.8 (1.4)                         | 72                        | 7.7 (1.5)                         | 0.644 | 86                        | 7.6 (1.5)                         | 0.245 |
| Thurstone's picture memory test | 84                        | 22.6 (4.0)                        | 68                        | 22.9 (4.3)                        | 0.662 | 85                        | 22.8 (3.4)                        | 0.751 |
| <b>Language</b>                 |                           |                                   |                           |                                   |       |                           |                                   |       |
| Word fluency                    | 91                        | 25.2 (6.6)                        | 76                        | 25.3 (7.1)                        | 0.904 | 90                        | 24.8 (5.9)                        | 0.660 |
| FAS                             | 87                        | 41.8 (13.2)                       | 73                        | 41.8 (13.2)                       | 0.990 | 85                        | 42.3 (14.9)                       | 0.824 |
| <b>Executive function</b>       |                           |                                   |                           |                                   |       |                           |                                   |       |
| SRB2                            | 89                        | 20.6 (4.1)                        | 75                        | 20.9 (4.2)                        | 0.657 | 88                        | 20.2 (4.0)                        | 0.557 |
| Digit span backwards            | 90                        | 4.7 (1.2)                         | 76                        | 4.5 (1.1)                         | 0.224 | 86                        | 4.6 (1.1)                         | 0.574 |
| <b>Visuospatial</b>             |                           |                                   |                           |                                   |       |                           |                                   |       |
| SRB3                            | 88                        | 22.2 (5.7)                        | 75                        | 22.0 (7.7)                        | 0.843 | 85                        | 21.4 (7.0)                        | 0.402 |
| <b>Mental speed</b>             |                           |                                   |                           |                                   |       |                           |                                   |       |
| Psif                            | 89                        | 29.4 (7.6)                        | 76                        | 30.0 (8.0)                        | 0.605 | 88                        | 29.8 (7.5)                        | 0.694 |

T, tertile. The 1<sup>st</sup> tertile was the reference group

Ng was log-transformed before divided into tertiles.

**Supplementary Table 3.** Linear regression with cognitive tests as dependent variables and Neurofilament light or Neurogranin as independent variables in a population-based sample of 70-year-olds with Clinical Dementia Rating 0

| <b>Model 1:</b> No covariates   |  |          |  |          |
|---------------------------------|--|----------|--|----------|
| <b>Cognitive tests</b>          | <b>Neurofilament light</b>             |          | <b>Neurogranin</b>                     |          |
|                                 | <b>Standardized <math>\beta</math></b> | <b>p</b> | <b>Standardized <math>\beta</math></b> | <b>p</b> |
| MMSE                            | 0.065                                  | 0.298    | -0.049                                 | 0.432    |
| Immediate recall                | 0.010                                  | 0.874    | -0.015                                 | 0.808    |
| Delayed recall                  | <0.001                                 | 0.994    | -0.027                                 | 0.664    |
| Word memory                     | 0.030                                  | 0.633    | 0.026                                  | 0.686    |
| Supra Span                      | -0.010                                 | 0.883    | -0.021                                 | 0.748    |
| Thurstone's picture memory test | 0.123                                  | 0.059    | 0.023                                  | 0.724    |
| Word fluency                    | 0.043                                  | 0.491    | -0.016                                 | 0.796    |
| FAS                             | 0.001                                  | 0.986    | -0.012                                 | 0.852    |
| SRB2                            | -0.002                                 | 0.976    | -0.054                                 | 0.396    |
| Digit span backwards            | 0.038                                  | 0.551    | -0.035                                 | 0.582    |
| SRB3                            | 0.031                                  | 0.625    | -0.087                                 | 0.173    |
| Psif                            | -0.023                                 | 0.713    | 0.021                                  | 0.734    |

  

| <b>Model 2:</b> Age, education, sex, and <i>APOE ε4</i> as covariates |  |          |  |          |
|---|--|----------|--|----------|
| <b>Cognitive tests</b>  | <b>Standardized <math>\beta</math></b> | <b>p</b> | <b>Standardized <math>\beta</math></b> | <b>p</b> |
| MMSE  | 0.066                                  | 0.295    | -0.026                                 | 0.683    |
| Immediate recall  | 0.009                                  | 0.884    | -0.024                                 | 0.703    |
| Delayed recall  | -0.005                                 | 0.934    | -0.037                                 | 0.558    |
| Word memory   | 0.031                                  | 0.631    | 0.028                                  | 0.660    |
| Supra Span  | -0.018                                 | 0.782    | -0.035                                 | 0.586    |
| Thurstone's picture memory test                                       | 0.123                                  | 0.056    | 0.037                                  | 0.571    |
| Word fluency  | 0.046                                  | 0.463    | 0.012                                  | 0.850    |
| FAS   | 0.001                                  | 0.992    | 0.005                                  | 0.940    |
| SRB2  | -0.001                                 | 0.993    | -0.026                                 | 0.671    |
| Digit span backwards  | 0.037                                  | 0.564    | -0.018                                 | 0.774    |
| SRB3  | 0.037                                  | 0.546    | -0.062                                 | 0.318    |
| Psif  | -0.024                                 | 0.706    | 0.054                                  | 0.393    |

**Supplementary Table 4.** Mann-Whitney U-test with neurofilament light and neurogranin divided by the median in cognitive performance in 70-year-olds with Clinical Dementia Rating 0

|                                 | NfL          | Ng           |
|---------------------------------|--------------|--------------|
| Cognitive tests                 | Significance | Significance |
| MMSE                            | 0.574        | 0.557        |
| Immediate recall                | <b>0.025</b> | 0.392        |
| Delayed recall                  | 0.164        | 0.055        |
| Word memory                     | 0.154        | 0.969        |
| Supra Span                      | 0.151        | 0.110        |
| Thurstone's picture memory test | 0.709        | 0.728        |
| Word fluency                    | 0.767        | 0.407        |
| FAS                             | <b>0.021</b> | 0.847        |
| SRB2                            | 0.592        | 0.275        |
| Digit span backwards            | 0.165        | 0.653        |
| SRB3                            | 0.632        | 0.380        |
| Psif                            | 0.135        | 0.874        |