Appendix – Supplementary material

Supplementary Table 1. Descriptive statistics for the BrANCH cohort from which the Myelin and Aging cohort and the subcohort with visual evoked potential measurements were extracted.

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| Characteristics\* | BrANCH cohort (N = 861) | Myelin and Aging cohort (N = 231) |
| Females at birth, N (%) | 517 (60.0%) | 121 (52.4%) |
| Age (years) | 70.0 [64.0 – 75.0] | 71.2 [67.3 – 76.4] |
| Education (years) | 18.0 [16.0 – 19.0] (N = 812) | 18 [16 – 20] |
| BMI (kg/m2) | 25.2 [22.7 – 28.1] (N = 664) | 25.2 [22.9 – 27.4] |
| Hemoglobin A1C (%) | 5.5 [5.3 – 5.7] (N = 387) | 5.5 [5.3 – 5.8] (N = 229) |
| APOEε4 allele, N (%) | 174 (25.1%) (N = 694) | 58 (25.2%) (N = 230) |

\*Values are reported as median [25th percentile – 75th percentile] unless specified otherwise.



Supplementary figure 1. Quadratic relationship of mfVEP latency and total measured B12 values. Both the linear and the polynomial regression were compared. The quadratic model was a better fit (R2 = 0.023) than the linear relationship (R2 = 0.007), suggesting a nonlinear correlation between B12 and VEP. The quadratic association has a point of inflexion around the geometric mean of B12 levels.

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Supplementary figure 2. Non-significant association between mfVEP and biologically unavailable B12 fraction holo-haptocorrin (Holo-HC). Mixed linear model of mfVEP latency with Holo-HC as the independent variable, correcting for age (years), sex at birth, education (years), BMI, CVRF, HbA1C and APOEε4, as well as accounting for the eye as a random factor.



Supplementary Figure 3. Analysis of the association between processing speed and B12, Holo-TC and Holo-HC. A. Linear regression for processing speed and log transformed values of total B12 as the independent variable showed a weak association approaching significance. B. Similarly, the same model as in A with Holo-TC as the independent variable associated weakly but again without reaching significance. C. No association between the processing speed and the log Holo-HC. Linear regression of processing speed with log Holo-HC as the independent variable, correcting for sex, age, education, HbA1C and APOEε4.

Supplementary Table 3. Number of samples included for analysis after excluding those with high variability (CV: coefficient of variability).

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| Biomarker | Available samples/n with CV<20% |
| NfL (pg/ml), % CV | 153/153 |
| Tau (pg/ml), %CV | 153/142 |
| UCH-L1 (pg/ml), %CV | 153/96 |
| GFAP (pg/ml), %CV | 153/153 |
| Aß42 (pg/ml), %CV | 118/112 |
| Aß40 (pg/ml), %CV | 108/107 |
| NfL: neurofilament light chain, UCH-L1: Ubiquitin C-terminal hydrolase L1, GFAP: glial fibrillary acidic protein, Aß: amyloid-beta. | |



Supplementary Figure 4. No significant association between white (A, C, E) and grey (B, D, F) matter volumes with log B12 (A, B), Holo-TC (C, D) and Holo-HC (E, F) after correcting for age, sex, BMI, education, HbA1C, APOEε4, total intracranial volume and cardiovascular risk factors. WMV = white matter volume; GMV = grey matter volume.