Two Platforms, One Biomarker: Concordance of Simoa and Lumipulse NfL Assays in Alzheimer's Cerebrospinal Fluid

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Background

Alzheimer's disease (AD) is the most common neurodegenerative disorder and the leading cause of dementia in older adults [1]. Cerebrospinal fluid (CSF) biomarkers, decreased Aβ42 and increased total tau and phosphorylated tau, do not fully capture the extent of axonal damage. Elevated CSF neurofilament light chain (NfL) levels, has emerged as a sensitive marker of neurodegeneration [2] and in AD correlate with brain atrophy, cognitive decline, and disease progression, even at preclinical stages. Reliable quantification requires ultrasensitive immunoassays, with Simoa providing very high analytical sensitivity and Lumipulse offering automated, clinically scalable testing [3]. Establishing concordance between these two platforms is essential for standardization and broader clinical implementation of NfL in AD diagnostics and monitoring.

Methods

We included 28 patients with cognitive impairment referred to the Aging Brain and Memory Clinic at the University Hospital "Città della Salute e della Scienza" of Torino, Italy. Only cases fulfilling ATN-based biological criteria for AD according to the 2018 NIA-AA framework were selected. Patients underwent neurological examination, neuropsychological testing, and neuroimaging, and were classified as MCI due to AD (CDR = 0.5) or AD dementia (CDR ≥ 1). CSF samples were collected under standardized conditions; APOE genotyping was also performed. Core AD CSF biomarkers (Aβ42, Aβ40, t-tau, p-tau181) were measured using Lumipulse G1200II (Fujirebio). CSF NfL was quantified with two immunoassays: Simoa™ Neurology 2-Plex B kit on the SR-X platform (Quanterix) and Lumipulse G NfL CLEIA assay (Fujirebio). All analyses were run in duplicate with CV <10%. Statistical analyses were performed in Jamovi and R. Significance was set at $p < 0.05$.

Results

We included 28 patients, of whom 18 were classified as MCI due to AD and 10 as AD dementia. Mean age was comparable between groups (~71 years), with females representing 58% of the overall cohort. In sex and APOE stratified analyses, correlations between platforms remained consistently high.

CSF NfL concentrations were highly comparable across methods. In MCI patients, mean NfL values were 1044 ± 602 pg/mL with Lumipulse and 1034 ± 598 pg/mL with Simoa; in dementia patients, they were 1156 ± 500 pg/mL and 1208 ± 513 pg/mL, respectively (Table 1). The Wilcoxon signed-rank test showed no significant difference between platforms ($p = 0.316$).

Correlations between Lumipulse and Simoa were very strong (Spearman's $\rho = 0.965$, $p < 0.001$), with excellent agreement (CCC = 0.981, 95% CI 0.960–0.991) (Figure 1). Bland–Altman analyses revealed minimal mean bias (−11.8 pg/mL) but wide limits of agreement, consistent with expected inter-assay variability. Overall, the two assays demonstrated near-equivalent performance in quantifying CSF NfL in AD patients.

	MCI	Dementia	MCI	Dementia	*p*-Value
Age at sampling	N = 18	N = 10	70.7 ± 5.5	70.7 ± 10.7	0.993
Gender	N = 18	N = 10	7 (38.9%)	9 (90%)	0.007
APOE	N = 16	N = 8	9 (56.25%)	5 (62.5%)	0.781
CSF Aβ42 (pg/mL)	N = 18	N = 10	371 ± 131	362 ± 95	0.846
CSF ratio Aβ42/40	N = 17	N = 10	0.038 ± 0.008	0.042 ± 0.011	0.287
CSF t-tau (pg/mL)	N = 18	N = 10	676 ± 317	845 ± 377	0.252
CSF p-tau 181 (pg/mL)	N = 18	N = 10	103 ± 54	134 ± 69	0.289
CSF NfL Lumipulse (pg/mL)	N = 18	N = 10	1044 ± 602	1156 ± 500	0.606
CSF NfL Simoa (pg/mL)	N = 18	N = 10	1034 ± 598	1208 ± 513	0.426
Education	N = 18	N = 10	12.1 ± 3.8	11.4 ± 3.8	0.643
Mini-Mental State Examination	N = 18	N = 10	26.9 ± 1.8	15.1 ± 7.2	<0.001
Montreal Cognitive Assessment	N = 18	N = 5	20.7 ± 3.0	13.0 ± 4.9	0.020
Frontal Assessment Battery	N = 17	N = 8	13.5 ± 2.6	8.4 ± 3.0	0.001
Clock Drawing Test	N = 18	N = 8	11.5 ± 3.3	4.6 ± 3.7	<0.001

Table 1. Clinical and biomarker characteristics of subjects with Mild Cognitive Impairment (MCI) and dementia.

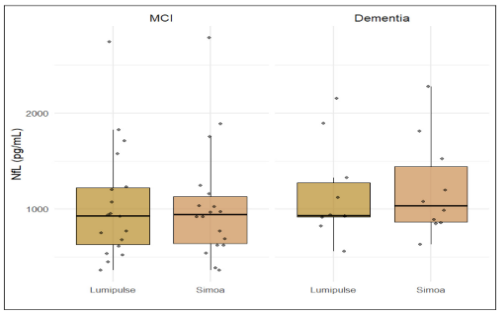

Figure 1. Boxplot showing CSF NfL concentrations measured with the Simoa and Lumipulse platforms across all participants (n = 28).

Conclusion and discussion

In this study, we compared CSF NfL concentrations measured with two analytical platforms, Simoa and Lumipulse, in patients fulfilling ATN criteria for Alzheimer's disease. We observed excellent agreement between assays, with no significant differences in absolute concentrations and a near-perfect correlation ($\rho = 0.965$). These findings provide preliminary evidence that both platforms can generate consistent results, supporting the role of NfL as a reliable biomarker of neurodegeneration.

Although mean NfL levels were higher in dementia than in MCI, the difference did not reach significance, likely due to the modest sample size. Still, the observed trend aligns with prior evidence linking NfL to disease severity and progression. Limitations include the small cohort, gender imbalance, and absence of healthy controls, which restrict generalizability.

References

1. Alzheimer's disease facts and figures. Alzheimers Dement. Apr;19(4):1598–695.
2. Vecchio D, Puricelli C, Malucchi S, Virgilio E, Martire S, Perga S, et al. Serum and cerebrospinal fluid neurofilament light chains measured by SIMOA™, Ella™, and Lumipulse™ in multiple sclerosis naïve patients. Multiple Sclerosis and Related Disorders. 2024 Feb 1;82:105412.
3. Preische O, Schultz SA, Apel A, Kuhle J, Kaeser SA, Barro C, et al. Serum neurofilament dynamics predicts neurodegeneration and clinical progression in presymptomatic Alzheimer's disease. Nat Med. 2019 Feb;25(2):277–83.