White Paper

noselab
GATEWAY TO THE BRAIN

Nasal Fluid from the Brain-Nose Interface Captures Brain-Relevant Proteome

A minimally invasive, repeatable way to sample fluid biomarkers in brain disorders would be game-changing for treating and monitoring diseases of the central nervous system (CNS). Cerebrospinal fluid (CSF) sampling gives a direct reading of brain biology, but it is invasive enough that repeated collection is not practical. Blood samples are easy to draw, but they reflect biology from the whole body with very little brain-derived content. So far, no biofluid between invasive CSF sampling and easily accessible but non-specific blood testing has been available to aid clinical management of CNS disorders.

The brain-nose interface (BNI) is evolving as an alternative minimally invasive route to brain biology. At the BNI, olfactory nerve fibers run from the brain, through small perforations in a bone called the cribriform plate, directly into the upper nasal cavity, creating a unique and direct connection between the brain and the nose. This anatomy at the BNI provides a conduit through which brain fluids such as CSF and brain-derived molecules can drain into the nasal cavity, making them accessible through nasal sampling. Earlier studies using nasal samples either flushed saline through the whole nose to collect nasal fluid (lavage), diluting it in the process, or sampled lower regions of the nose, farther from the BNI. To facilitate nasal fluid collection precisely from the BNI region of the upper nasal cavity, we developed nosecollect®, a minimally invasive device for routine clinical sampling. Next, we asked whether fluid collected from the BNI carries a proteome profile that is relevant to brain disorders and of interest to neurologists.

To quantify the proteomic profile of nasal fluid from the BNI, we analyzed samples collected from cognitively impaired patients using three different technologies, including untargeted mass spectrometry, the Olink Target Neurology panel, and the NULISAseq CNS Disease 120 panel. Our results from targeted proteomics panels showed that nasal fluid captures broad proteomic coverage which overlaps substantially with matched CSF and plasma proteomes. On Olink's neurology panel, we reliably detected about 97% of targeted proteins in nasal fluid, closely matching plasma (98%) and outperforming CSF (90%) (Fig 1. A). NULISA also showed a similar pattern, with 92% of targeted proteins detected in nasal fluid, 93% in plasma, and 80% in CSF (Fig 1. B). Majority of the

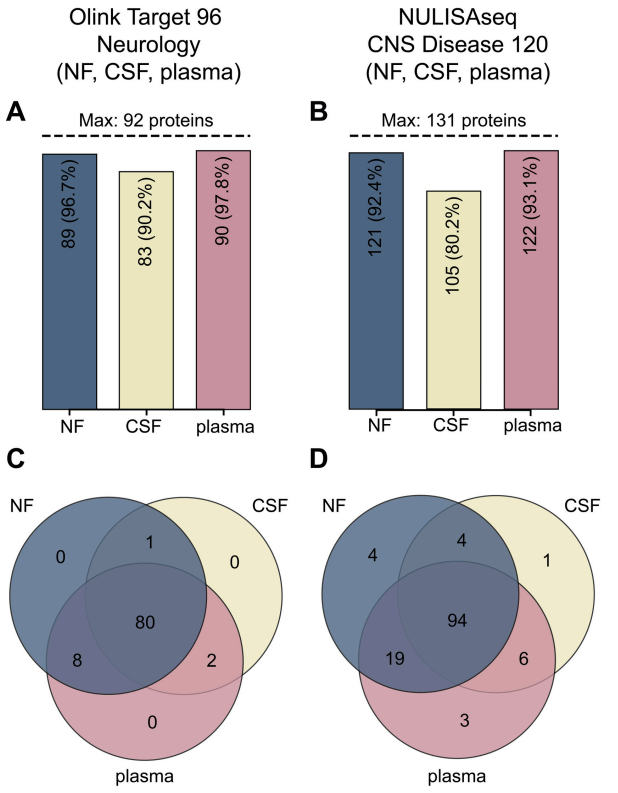

Figure 1. Detection of the Olink Target 96 Neurology and NULISAseq CNS Disease 120 panels in nasal fluid (NF), cerebrospinal fluid (CSF), and plasma. A, B) Bar plots showing the percentage of proteins detected by Olink neurology (A) and the NULISA CNS 120 (B) panels in NF (blue), CSF (yellow), and plasma (pink). **C, D)** Venn diagrams showing the overlap of proteins detected across the three matrices for the Olink Neurology (C) and the NULISA CNS 120 (D) panels. (Adapted with permission from Bashiri et al., medRxiv 2026: 2026-06)

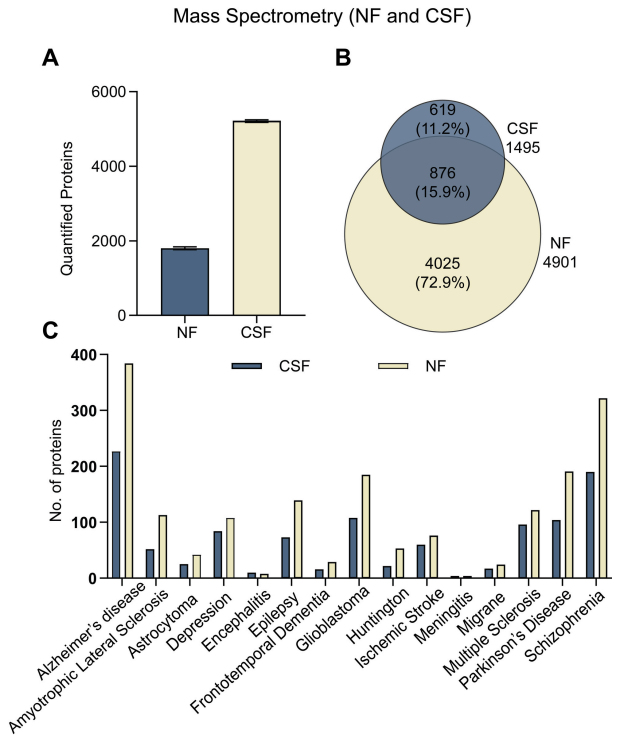

Figure 2. Untargeted mass spectrometry analysis of nasal fluid (NF) and cerebrospinal fluid (CSF). A) Bar plot showing the number of proteins detected by untargeted mass spectrometry in NF (blue) and CSF (yellow). **B)** Venn diagram showing the overlap of proteins consistently detected across NF and CSF. **C)** Bar plot showing the number of proteins detected in NF and CSF with gene-disease associations identified using DisGeNET (doi:10.64898/2026.01.05.697749), with an association score threshold of 0.3. (Adapted with permission from Mueller et al., medRxiv (2026): 2026-07)

proteins detected in CSF and plasma were also present in nasal fluid (Fig 1. C,D). Broader, untargeted mass spectrometry found the same pattern at a larger scale, identifying over 5,200 proteins in nasal fluid on average, which was nearly three times as many as in matched CSF (Fig 2. A). Among the proteome consistently detected across nasal fluid and CSF samples, about half of the CSF proteome were found to be present in nasal fluid (Fig 2. B).

Our proteomic studies using the above-mentioned methods revealed that nasal fluid contains a wide range of proteins relevant to brain diseases. We identified established biomarkers such as tau proteins (linked to Alzheimer's disease), alpha-synuclein (linked to Parkinson's disease), and TDP-43 (linked to amyotrophic lateral sclerosis/frontotemporal dementia), along with markers related to pathological changes in the brain such as axonal damage (e.g., NEFL, NEFH), synaptic loss (e.g., SNAP25, pretaxins), and glial activation (e.g., CHI3L1, S100B, TREM2). Of particular interest to us was the presence of brain-derived tau in nasal fluid, including their phosphorylated forms, at levels matching CSF and exceeding that in plasma, suggesting a direct connection between brain and nose. Among the proteins detected by mass spectrometry, we identified proteins associated with several brain disorders, including Alzheimer's disease, Parkinson's disease, multiple sclerosis, and brain cancer (Fig 2. C). Together, these findings suggest that nasal fluid may capture signals relevant to multiple brain diseases.

Put together, these findings point to something neurology has lacked: a sample that contains brain-related proteome content and can be easily and repeatedly collected. The proteomic signatures we have identified in nasal fluid provides a foundation for future biomarker discovery and clinical validation in brain disease groups. Ultimately, this approach could enable longitudinal monitoring of disease progression, tracking of therapeutic response, and earlier detection of neurodegeneration before it becomes irreversible.

References

Bashiri, Mohammad, et al. "Targeted Proteomic Profiling of Nasal Fluid from the Brain-Nose Interface." medRxiv (2026): 2026-06.

Mueller, Stephan A., et al. "Proteomic Profiling of Nasal Fluid from the Brain-Nose Interface using Mass Spectrometry." medRxiv (2026): 2026-07.