

Blood-based biomarkers in epilepsy

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Sahlgrenska akademien, den 12 juni 2025, klockan 13.00

av Sarah Akel

Fakultetsopponent:

Professor Aristeia Galanopoulou

Albert Einstein College of Medicine, Bronx NY, USA

Avhandlingen baseras på följande delarbeten

- I. **Akel, S**, Asztely, F, Banote, RK, Axelsson, M, Zetterberg, H, Zelano J. Neurofilament light, glial fibrillary acidic protein, and tau in a regional epilepsy cohort: High plasma levels are rare but related to seizures. *Epilepsia*. 2023; 64(10):2690-2700.
- II. **Akel, S**, Banote, RK, Asztely, F, Zelano J. Protein profiling in plasma for biomarkers of seizure. *Epilepsy Res*. 2023; 197:107241.
- III. **Akel, S**, Axelsson, M, Asztely, F, Zetterberg, H, Zelano J. Higher plasma neurofilament-light chain concentration in drug-resistant epilepsy. *Brain Commun*. 2025;7(2):fcf108.
- IV. **Akel, S**, Ashtiani, SH, Sarangdhar, MA, Axelsson, M, Zelano J. Blood biomarkers of seizures in epilepsy: machine learning reveals altered plasma proteome. Manuscript. Preprint on medRxiv: (<https://doi.org/10.1101/2025.02.04.25321586>).

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Abstract

Blood-based biomarkers hold promise as minimally invasive and scalable tools to complement current diagnostic methods and potentially support clinical decision-making in epilepsy. This thesis explores blood biomarkers in four original research papers to identify candidate markers through proteomics and to further characterize existing markers of brain injury and neurodegeneration in epilepsy.

In Paper I, levels of neurofilament-light (NfL), glial fibrillary acidic protein (GFAP), and total-tau were analyzed in plasma. The findings revealed elevated NfL and GFAP in individuals with recent seizures compared to those with seizure freedom. Paper III expands on this by comparing the same markers, along with serum S100 calcium-binding protein B and neuron-specific enolase, between drug-resistant epilepsy (DRE) and monotherapy-controlled epilepsy. As in the previous study, higher levels of NfL and GFAP were observed in the DRE group. NfL levels remained elevated even after excluding participants with prior strokes or brain lesions.

Papers II and IV investigated seizure-related changes of proteins using plasma proteomics. Paper II identified four differentially expressed proteins (CDH15, PHOSPHO1, LTBP3, and PAEP) in individuals with recent seizures. Paper IV applied a machine-learning (ML) approach to analyze four larger protein panels, revealing 51 consensus proteins between the two ML models, of which 23 were considered top differentially expressed. Enrichment analysis highlighted several inflammatory and immune processes and pathways.

This research further emphasizes the potential of integrating blood biomarkers into epilepsy care and research. Longitudinal studies are necessary to track biomarker fluctuations over time in relation to seizures and treatment responses. Such studies will also help to identify optimal time frames for sampling.

Keywords: epilepsy, seizures, biomarkers, blood-biomarkers, proteomics.

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