

## **Abstract**

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease that damages white matter of the central nervous system (CNS). The exact cause of MS is still unknown, but various environmental and genetic factors are believed to be involved in its development. The pathophysiology of MS is a very complex. MS is currently an incurable disease, but specific therapy can be used to influence its course. Metabolomics is a systematic study that uses an analytical chemistry approach to profile endogenously small molecule metabolites present in the examined preparation. The main goal of this dissertation was to determine significant differences in the metabolome of the cerebrospinal fluid of patients in the initial stage of MS compared to controls. Furthermore, we performed a correlation analysis of these results over time with the clinical condition of the patients in the form of EDSS values. Subsequently, as part of further analyses, we also evaluated other potential biomarkers of MS, more precisely evoked potentials (EP), neurofilament light chains (NfL) and glial fibrillary acidic protein (GFAP). In total, we collected CSF samples from 40 patients in the early stages of MS, and CSF samples from 33 healthy controls. Subsequent analysis of these samples was performed using high-performance liquid chromatography with tandem mass spectrophotometry, with a high-resolution detector. Furthermore, some samples were analyzed with the help of Single Molecule Array (SIMOA) and in some patients, EP was performed and subsequently correlated with EDSS values. Statistically significant changes ( $p$ -value  $<0.05$ ) were observed in CSF for arginine, histidine, spermidine, glutamate, choline, tyrosine, serine, oleic, stearic and linoleic acids. Furthermore, we observed a significant correlation in the examination of EP and histidine metabolite with the EDSS values, thus pointing out their possible prognostic potential. In the case of NfL and GFAP, we did not observe a significant correlation with EDSS values for the other metabolites. In conclusion, we demonstrated statistically significant differences in the concentrations of some metabolites in the cerebrospinal fluid of patients in the initial stages of MS, which could be used as new biomarkers of MS. We further demonstrated that EPs correlate with current EDSS values. In patients in the early stages of MS evoked potentials seem to have the ability to predict, based on EDSS values, the development of the clinical condition in the following years of the disease.