

**DEVELOPMENT OF MODERN HIGH RESOLUTION MASS SPECTROMETRY
PLATFORM FOR GLYCOLIPID MAPPING IN DEFINED HUMAN BRAIN
REGIONS**

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Abstract

Gangliosides (GGs) are present and concentrated on cell surfaces, with the two lipid chains of the ceramide moiety embedded in the plasma membrane and the oligosaccharide chain located on the extracellular surface, where they constitute points of recognition for extracellular molecules or surfaces of neighbouring cells. Gangliosides are found predominantly in the nervous system, were involved in a series of biological and pathological processes.

The introduction of electrospray (ESI) ion sources into biological mass spectrometry (MS) addressed the fundamental issue of how to analyze minute amounts of complex biological samples. A strategy to characterize and monitor the changes with age of the GG profile in different developmental stages of human cerebellum, by ESI Orbitrap MS and tandem MS (MS²) is presented here. Two native ganglioside mixtures originating from normal human fetal cerebellum in the 15th (Cc15) and 40th (Cc40) gestational week were subjected to Orbitrap MS and multistage MS (MSⁿ) by collision induced dissociation (CID) analysis under thoroughly optimized experimental conditions. Both native GGs were dissolved in pure methanol up to final concentration of 10 pmol/μL. After only 2 min of signal acquisition in the negative ion mode, over 100 species have been detected and identified, among them several potential biomarkers. Although a similar number of species were identified in both mixtures, the GG profile was found to be essentially different. Obtained results also indicated differences in the expression of polysialylated species in the two ganglioside mixtures, which support an earlier hypothesis regarding the direct correlation between sialylation degree and brain developmental stage.

The method provided elevated ionization efficiency, high speed of analysis, almost 100% in-run and run-to-run reproducibility at a sample consumption per experiment situated in the femtomole range.

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