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Multi-platform characterization of the human cerebrospinal fluid metabolome: a comprehensive and quantitative update

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Abstract

Background: Human cerebral spinal fluid (CSF) is known to be a rich source of small molecule biomarkers for neurological and neurodegenerative diseases. In 2007, we conducted a comprehensive metabolomic study and performed a detailed literature review on metabolites that could be detected (via metabolomics or other techniques) in CSF. A total of 308 detectable metabolites were identified, of which only 23% were shown to be routinely identifiable or quantifiable with the metabolomics technologies available at that time. The continuing advancement in analytical technologies along with the growing interest in CSF metabolomics has led us to re-visit the human CSF metabolome and to re-assess both its size and the level of coverage than can be achieved with today's technologies.

Methods: We used five analytical platforms, including nuclear magnetic resonance (NMR), gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS), direct flow injection-mass spectrometry (DFI-MS/MS) and inductively coupled plasmas-mass spectrometry (ICP-MS) to perform quantitative metabolomics on multiple human CSF samples. This experimental work was complemented with an extensive literature review to acquire additional information on reported CSF compounds, their concentrations and their disease associations.

Results: NMR, GC-MS and LC-MS methods allowed the identification and quantification of 70 CSF metabolites (as previously reported). DFI-MS/MS allowed the quantification of 78 metabolites (6 acylcarnitines, 13 amino acids, hexose, 42 phosphatidylcholines, 2 lyso-phosphatidylcholines and 14 sphingolipids), while ICP-MS provided quantitative results for 33 metal ions in CSF. Literature analysis led to the identification of 57 more metabolites. In total, 476 compounds have now been confirmed to exist in human CSF.

Conclusions: The use of improved metabolomic and other analytical techniques has led to a 54% increase in the known size of the human CSF metabolome over the past 5 years. Commonly available metabolomic methods, when combined, can now routinely identify and quantify 36% of the 'detectable' human CSF metabolome. Our experimental works measured 78 new metabolites that, as per our knowledge, have not been reported to be present in human CSF. An updated CSF metabolome database containing the complete set of 476 human CSF compounds, their concentrations, related literature references and links to their known disease associations is freely available at the CSF metabolome database.

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