News Release

Title

Intact metabolite profiling of mouse brain by probe electrospray ionization/triple quadrupole tandem mass spectrometry (PESI/MS/MS) and its potential use for local distribution analysis of the brain

Key Points

- PESI/MS/MS enabled us to analyze intact metabolites in mouse brain without sample preparation.
- PESI/MS/MS discriminated the metabolic profiles of energy metabolism disruption model mice from control mice.
- PESI/MS/MS allowed us to perform local distribution analysis of mouse brain.

Summary

The research group of Assoc. Prof. Kei Zaitsu (Legal medicine and Bioethics, Graduate School of Medicine and In Vivo Real-time Omics Unit, Nagoya University) and Assist. Prof. Yumi Hayashi (Pathophysiological Laboratory Sciences, Graduate School of Medicine and In Vivo Real-time Omics Unit, Nagoya University), and Shimadzu Corporation have succeeded in developing a novel analytical technique for intact metabolites in mouse brain using probe electrospray ionization/tandem mass spectrometry (PESI/MS/MS).

Metabolome analysis (metabolomics) has recently been applied to various fields including life sciences. In 2016, our group developed a new analytical method to detect intact metabolites in mouse liver by PESI/MS/MS without sample preparation.

In brain, the high abundance of lipids can easily interfere with ionization of target metabolites. Therefore, tedious sample preparation to separate those lipids from target metabolites is mandatory for metabolome analysis in the brain thus far. In the present study, we have applied this technique to mouse brain, resulting in the detection of intact metabolites without any sample preparation. Since PESI uses an extremely thin solid needle (tip diameter: 700 nm) for simultaneous sampling and ionization, we have also succeeded in profiling the local distribution of metabolites between the frontal cortex and hippocampus. Our established analytical method for the intact metabolites in brain will highly contribute not only to analytical improvement in metabolomics, but also to pathophysiological analysis for brain diseases such as dementia or cognitive impairment.

Our study has been published in Analytica Chimica Acta online on June 30, 2017.

Research Background

Expanding the capability of analytical methods, mass spectrometric applications combined with ambient ionization techniques have been developed over the last decade. Probe electrospray ionization (PESI) is one of the ambient ionization techniques, first invented by Hiraoka in 2007. Special uniqueness of this ionization technique lies in the use of a thin needle (700 nm tip diameter) as the probe to work for both sampling and ionization units. Our research group was the first to develop the combinational use of PESI and tandem mass spectrometry (MS/MS) and to report PESI/MS/MS in achieving higher specific identification of hepatic metabolites (K. Zaitsu, Y. Hayashi et al., Anal. Chem. 2016, 88(7), 3556-3561.).

Our previous results motivated us to apply PESI/MS/MS to other mouse tissues, especially the brain. A brain works with regional functions, and therefore its metabolites are distributed locally. In order to investigate the metabolic profiles of each area of the brain by MS-based metabolomics, however, tedious sample preparation including delipidation is mandatory because the brain contains high concentrations of lipids and fats, acting as interference in conventional metabolome analyses. In addition, bias caused from sample preparation can affect the results. Thus, analytical method for intact metabolites in brain is required for obtaining more reliable results.

Research Results

As shown in Fig. 1, we used PESI ionization source and mass spectrometer (Shimadzu, LCMS-8040). PESI/MS/MS directly detected 25 metabolites in mouse frontal cortex, and clearly discriminated the metabolic profiles of mice model with energy metabolism disruption from control mice (Fig. 2). Loading plots can easily extract the primarily important metabolites that contributed to group separation.

Also, there is high potential for applying this technique to the local distribution analysis owing to the use of such a thin probe needle (Fig. 1). As a result, PESI/MS/MS allowed us to perform local distribution analysis of the hippocampus as well as the frontal cortex in each mouse (n=5), discriminating their subtle metabolic differences (Fig. 3). In conclusion, high potential of PESI/MS/MS use not only for direct metabolome profiling of mouse brain, but also for local distribution analysis is demonstrated in this study.

Research Summary and Future Perspective

In the present study, we succeeded in the detection of intact metabolites without any sample preparation by PESI/MS/MS. We have also achieved local distribution profiling of metabolites of the frontal cortex and hippocampus. The present analytical technique for intact metabolites in brain will highly contribute not only to analytical improvement in metabolomics, but also to pathophysiological analysis for some brain disease such as dementia or cognitive impairment.

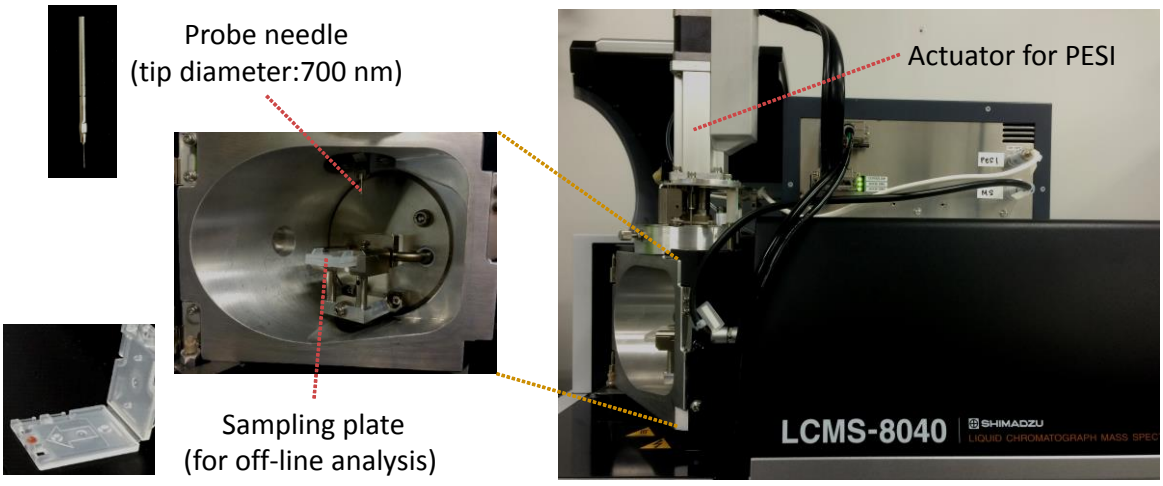

Fig. 1 Photograph of the probe electrospray ionization source combined with a triple quadrupole tandem mass spectrometer.

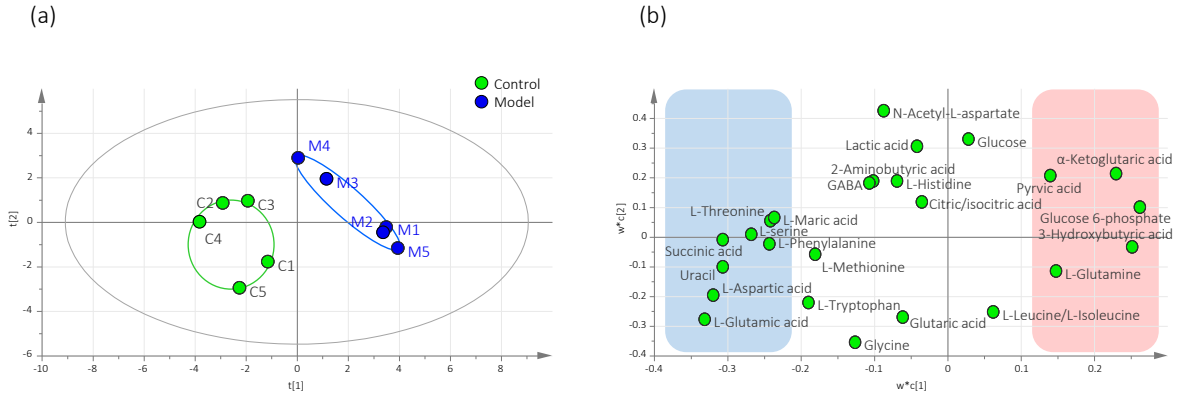

Fig. 2 Results of projection to latent structure-discriminant analysis (PLS-DA) for control and model groups: (a) score plot and (b) loading plot. Blue or red zones shown in the loading plot correspond to decreased or increased metabolite levels for the model group in comparison with those for the control group.

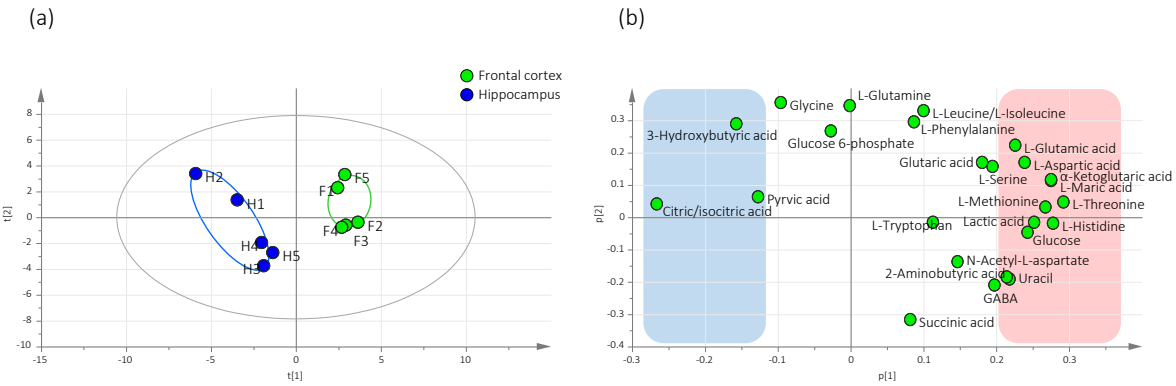

Fig. 3 Results of principal component analysis (PCA) for frontal cortex and hippocampus samples of the control group. Blue or red zones shown in the loading plot correspond to decreased or increased metabolite levels in the frontal cortex in comparison with those in the hippocampus.

Publication

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Analytica Chimica Acta
DOI：https://doi.org/10. j.aca.201016/ 17.06.047

Japanese ver.
https://www.med.nagoya-u.ac.jp/medical_J/research/pdf/Analytica_C_20170822.pdf