Alterations in lipid profile of a depression model detected by MALDI imaging mass spectrometry

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Overview

Long-term administration of tricyclic antidepressants to neonatal mice can lead to behavioral changes and disrupt the stress response system during adulthood. This treatment may therefore produce an animal model for depressive disorders. The clomipramine model (20 mg/kg dose) produces changes in the serotonin or norepinephrine systems through the continuous administration of antidepressants from days 6 to 22. Mouse brains were removed and immediately frozen at −80 °C. Brain slices of 12 μm thickness were produced using a cryostat, the 1,5-diaminonaphthalene (DAN) matrix using HTX-M5 was applied, and the distribution of lipids was compared at a spatial resolution of 50 μm per image pixel using 9.4T Fourier-transform ion cyclotron resonance mass spectrometry imaging(FT-ICR MSI). The ion peaks of lipids (*m/z* 200–2,000) were used to create mass ion visualization. Most of these peaks corresponded to corticosterone. These data show for the first time that MSI is suitable for the visualization of the spatial distribution of an animal depression model. The data may be valuable for research and clinical practice.

Key words: Antidepressants, MALDI-MSI, Clomipramine model

Conclusions

● Direct tissue analysis by MALDI-FT-ICRMS imaging is an important technology for assessing the localization of molecular species and for revealing the underlying molecular signatures indicative of disease in the etiology.

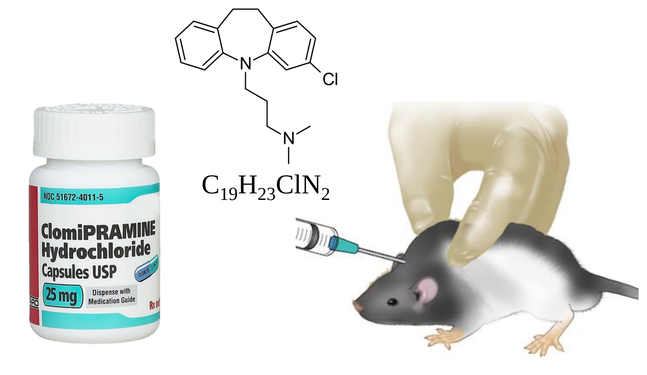
● In this study, we examined whether the neonatal administrations of CLI exert the similar effects to mice in order to establish a useful mouse model for studying major depression.

● The molecular species identified in these experiments can provide insight into mechanisms of major depression in the etiology.

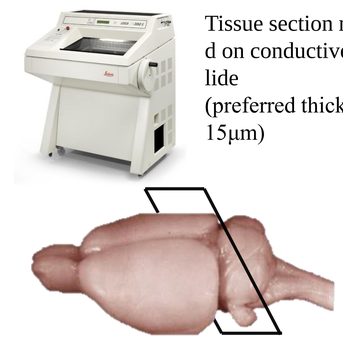
Introduction

Brain undergoes plastic changes that are essential for refining functional brain circuits in the early period of life. A number of studies, including human studies, have made links between early-life experiences and propensity for depressive episodes in later life. Neonatal administration of clomipramine(CLI), a drug that inhibits the reuptake of serotonin and norepinephrine, causes behavioral changes during adulthood that resemble the human depression. This animal model can be helpful to elucidate molecular changes incurred during early-life experiences that predispose to later depressive episodes. Stress is a prominent precipitating factor for depression and anxiety disorder. The social defeat stress paradigm, kind of chronic stress, appears useful for studying the interactions between genetic predispositions and environmental influences. In addition, it is reported that the genetic polymorphism of serotonin transporter (5-HTT) gene and the altered expression of 5-HT receptors play critical roles in major depression.

Materials and Methods

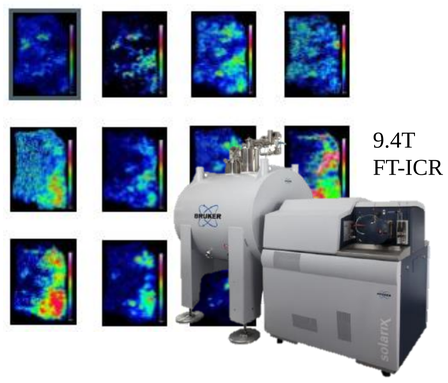


<Injection of clomipramine in the mouse>



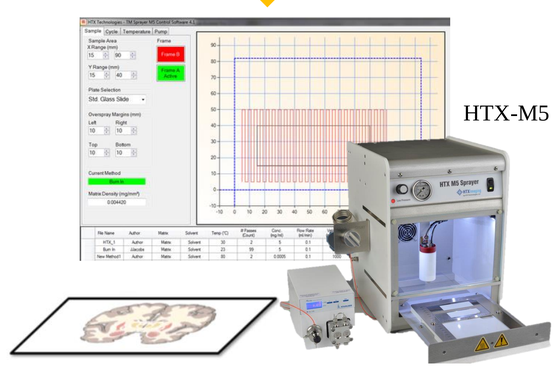
Tissue section mounted on conductive ITO slide (preferred thickness ≤ 15μm)

<Cryosection of brain tissue>



9.4T FT-ICR MS

<High resolution MALDI imaging>



HTX-M5

<Sprayer for tissue imaging>

Results

Saline(SAL) vs clomipramine(CLI)

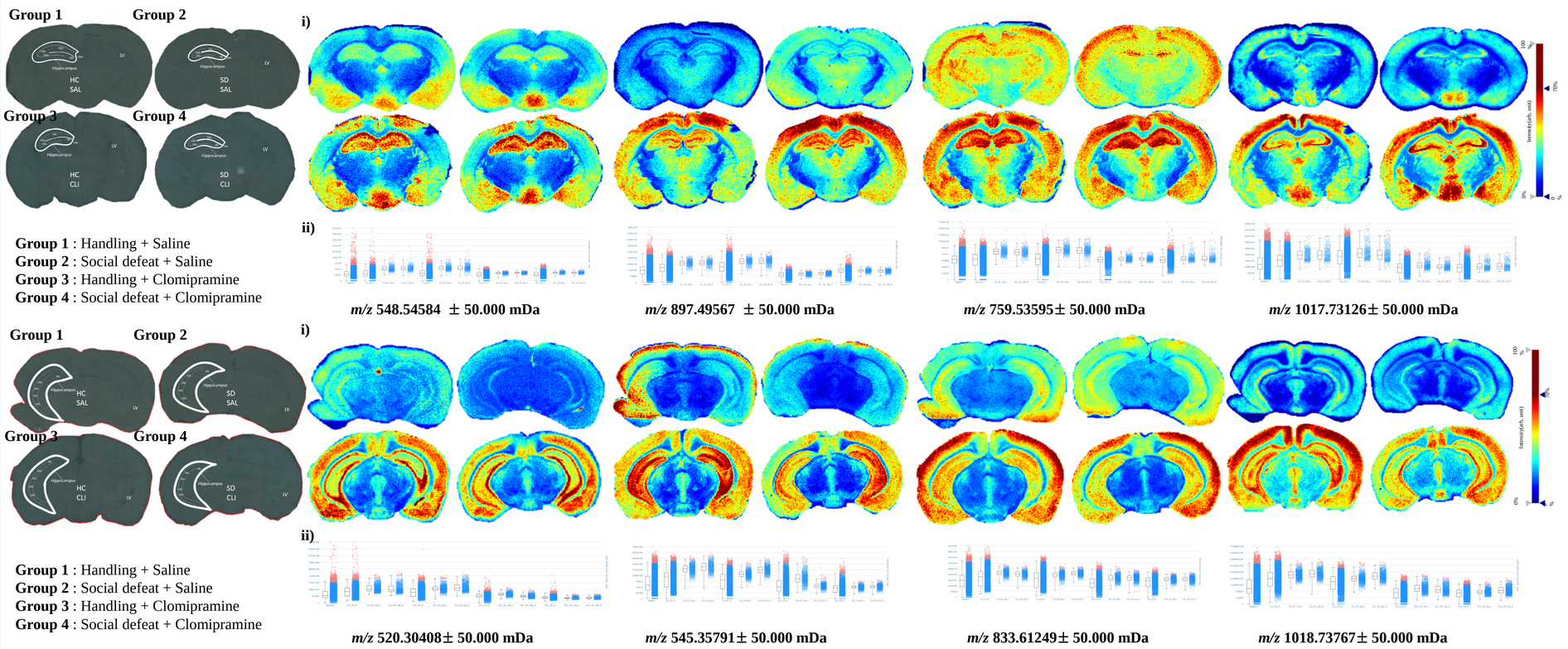


Figure 1. MALDI-FTICR MS imaging of a tissue section(i) and the intensity box plot(ii) shows the distribution of intensities in different regions of mouse brain.

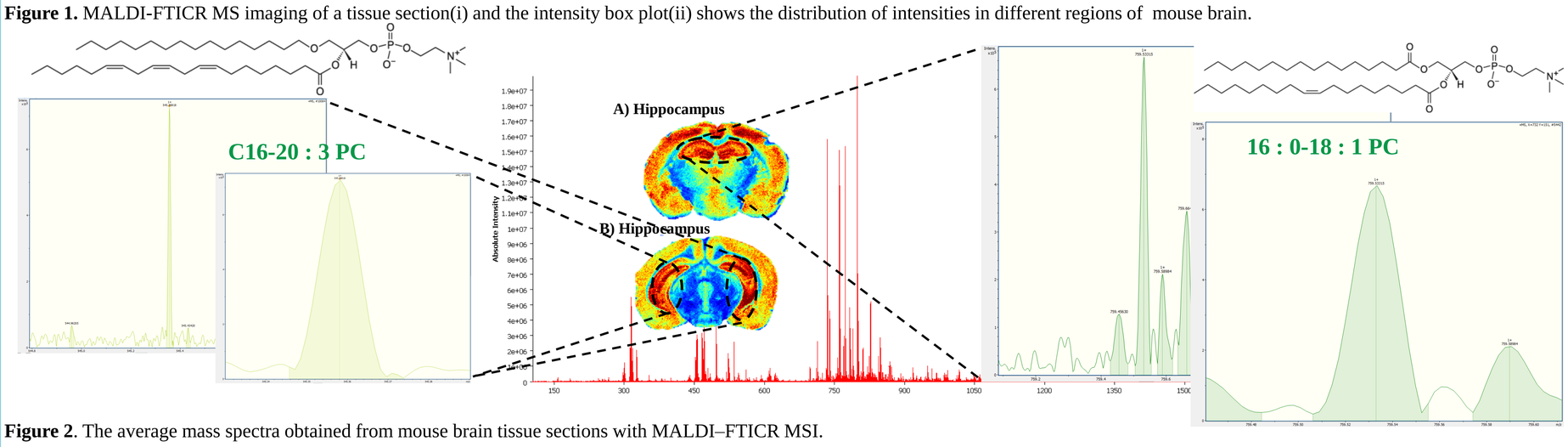


Figure 2. The average mass spectra obtained from mouse brain tissue sections with MALDI–FTICR MSI.

References

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