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Multimodal Imaging of Ischaemic Rat Brain, 1-3 months on: A MALDI MS insight into long term molecular expression

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Philippa Hart[1], Fiona Henderson[2], Omar Belgacem[1], Herve Boutin[2], Adam McMahon[2].
[1]Shimadzu, Manchester, UK;
[2]Wolfson Molecular Imaging Centre, Manchester University.

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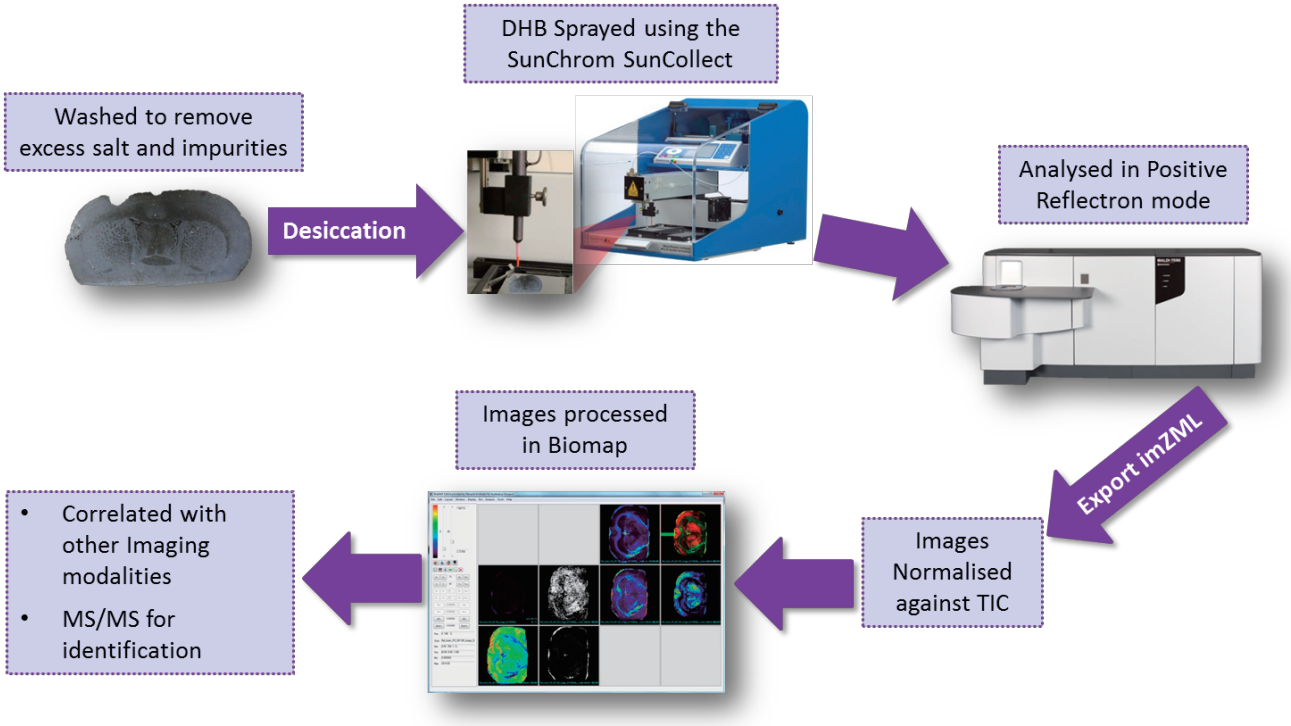
Overview

- Inflammatory responses are observed in the brain most acutely after stroke. This neuroinflammation can be seen with various imaging techniques: PET scans, Immunohistochemistry (IHC) and MALDI-MS imaging.
- Many studies have investigated the immediate molecular response (24 – 96 hours).
- In this study we are interested in long term observations running from 1-3 months subsequent to stroke.

Introduction

Inflammatory responses are observed in the brain mostly acutely after stroke. This neuroinflammation can be seen with various imaging techniques: PET scans, MR scans, Immunohistochemistry (IHC) and MALDI-MS imaging. In this study we have taken a further look at molecular expression/distribution between one and three months post-stroke. In this case the proteins targeted in PET and IHC did not highlight any significant differences between healthy brain tissue and regions of the brain damaged by stroke. As such, our aim in these analyses was to look at a broader range of molecules using a data mining approach to determine whether MALDI would elucidate any additional information.

Experimental Methods



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Results and Discussion

The findings of the PET and IHC analyses, showed little significant change in expression across the ischaemic and healthy regions of the brain.
Many of the MALDI-MS images (MSI) generated in this study corroborate the findings of the IHC analyses (not displayed here), showing no significant change in expression across the ischaemic and healthy regions of the brain. However, a number of MSI generated show variation in expression and localisation that may be associated with the expected long term effects of stroke. Some phosphatidylcholine species were found to be almost entirely absent in scar tissue surrounding the area of the infarct (the region at which the stroke was initiated).

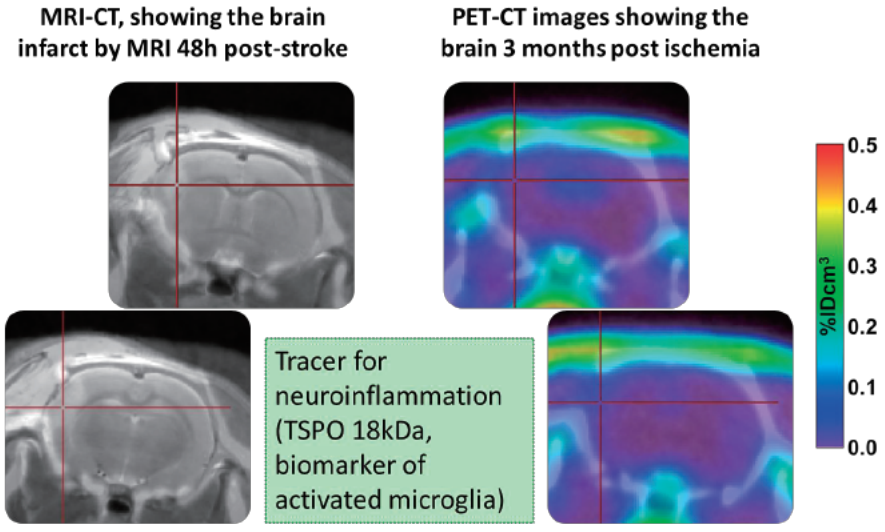

Figure 1: MRI CT images taken at 48 hours post stroke and PET-CT images taken at 3 months post ischaemia. No significant uptake of the tracer is seen.

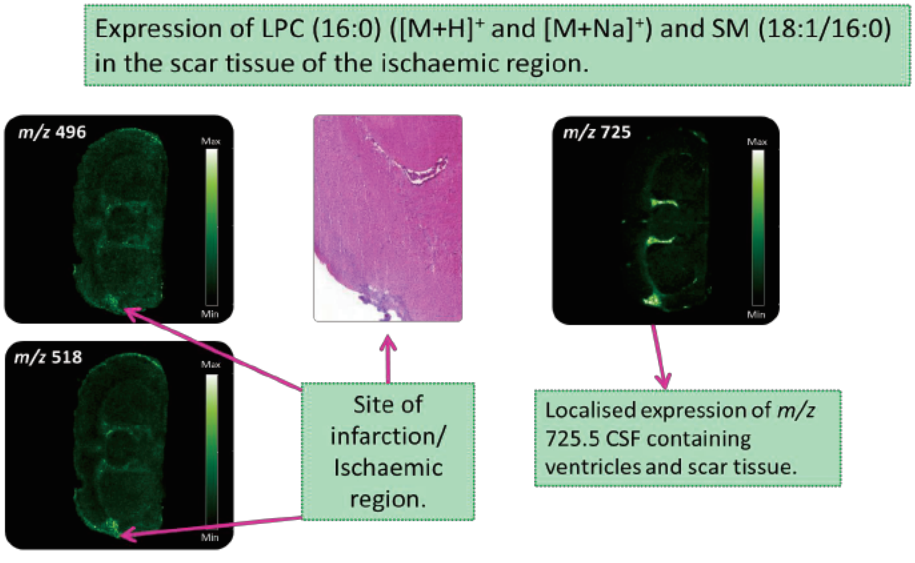

Figure 2: Ion images acquired with a spatial resolution of 80 µm on the MALDI 7090. Images show localisation specific to the cerebral spinal fluid (CSF) containing ventricles and scar tissue (see H&E stain for scar tissue).

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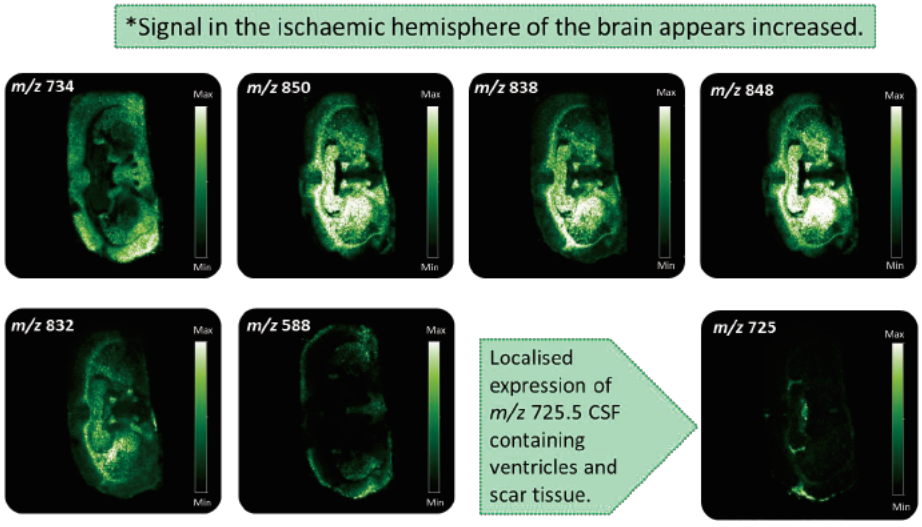

Figure 3: Ion images acquired at a spatial resolution of 80 µm on the MALDI 7090. Images show multiple lipids conveying varied localisation, some with increased expression in the ischaemic region and others less so.

Further to MS imaging experiments lipid identifications were obtained through direct on-tissue analysis from highly resolved spectra produced using high energy CID and Axial spatial distribution focusing (ASDF) technology, coupled to a curved field reflectron. Monoisotopic resolution of lipid fragment ions was possible. Overall, the lipid species detected included sphingomyelin, lysophosphatidylcholine, other phosphatidylcholines and glycerolipids.

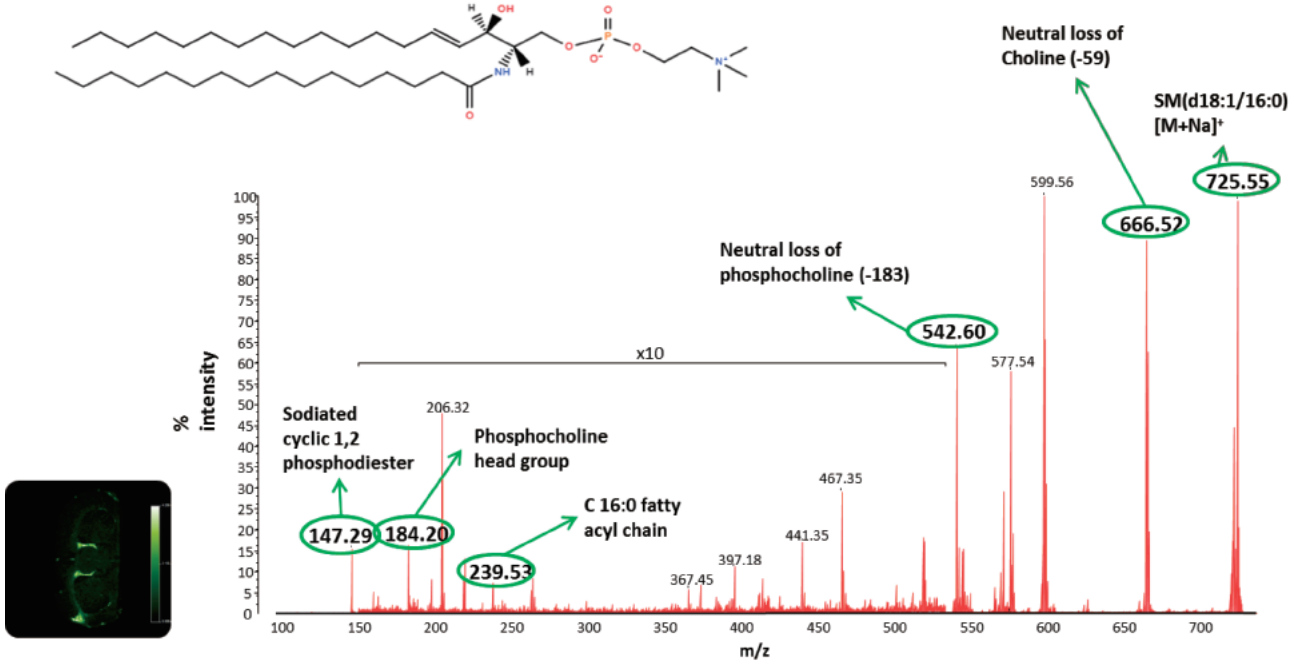

Figure 4: An example of an MS/MS spectrum generated in experiments, showing peaks characteristic of sodiated sphingomyelin (d18:1/16:0). The structure and the corresponding ion image (at 80 µm) are also pictured.

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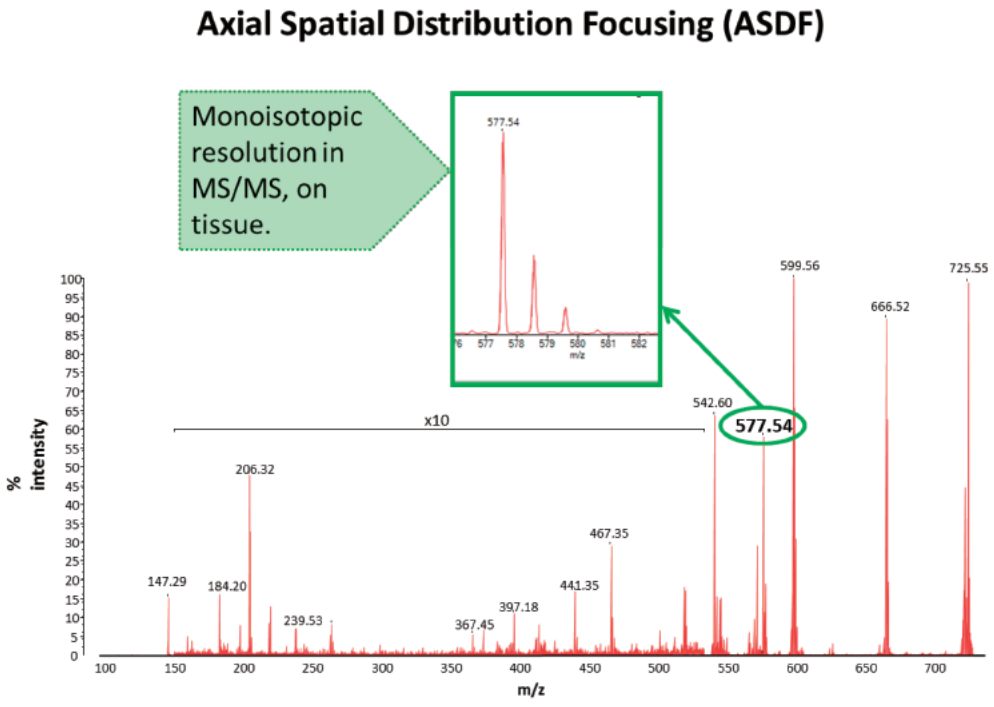

Figure 5: Magnification of the MS/MS spectrum seen in figure 4, showing the high resolution provided via the use of ASDF technology. Monoisotopic resolution was observed.

Conclusion

In this case MALDI-MSI served as a valuable complementary tool for the investigation of molecular changes in long term rat stroke models, going further to exploit a less targeted approach that is not possible with the other imaging modalities employed in the study.

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