Multi-Modal Synchrotron Imaging Techniques Quantify Elemental and Molecular Changes After Acute Ischemic Stroke

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Introduction

Although the biochemical mechanisms that occur following a stroke have been extensively studied with conventional techniques, the spatial and temporal correlations between biochemical pathways at the cellular and sub-cellular level remain poorly understood. We have developed a novel multi-modal imaging approach, which incorporates synchrotron-based imaging techniques to reveal the spatial correlations between a wide range of elemental and biochemical markers of important physiological processes that can occur after an ischemic insult. In this study we have specifically focused on the application of our method to study the infarct and penumbra in a mouse photothrombotic stroke model.

Methods

Ischemic stroke is induced in mice using the previously validated photothrombotic model. Animals are sacrificed at various time-points after stroke. Fourier transform infrared spectroscopic imaging (FTIRI) is used to gather sub-cellular (< 1 µm spatial resolution) imaging data of lipid oxidation and protein aggregation in the areas of interest. X-ray fluorescence (XRF) imaging is used to image the distribution of bio-important elements at the cellular and sub-cellular spatial resolutions. Routine histology and immunohistochemistry are used to co-localize cell-types to areas of interest.

Results

Preliminary XRF results indicate significant reduction in the levels of multiple elements in the infarct, particularly diffusible ions (Cl-, K+, Ca++), compared to the penumbra, at day 1 post-stroke. Interestingly, elemental concentrations, particularly for the above mentioned ions, begin to return to normal levels in the penumbra at day 3, suggesting maximum disturbance to ion homeostasis occurs within a 3 day time frame post-stroke . FTIRI data shows that lipid and total protein levels decrease, correlating with the alterations observed for diffusible ions, however, aggregate protein levels increase in the penumbra.

Conclusions

Multi-modality synchrotron imaging can be used to map and correlate elements as well as bio-molecules in a stroke model. A better understanding of these changes can guide therapeutic interventions after stroke.

Learning Objectives

By the conclusion of this session, participants should be able to:

1) Discuss the theoretical underpinnings of multiple synchrotron-based imaging modalities for nervous tissue

2) Describe the changes that occur in the damaged brain after ischemic insult, in the acute and sub-acute setting.

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