

BRAIN MS IMAGING AFTER ISCHEMIC STROKE IN MICE – INSIGHT FOR BRAIN INJURY BY ABNORMAL PROTEOLYSIS

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Stroke, the 3rd leading cause of death in the US, is caused by blood clotting in the cerebral arteries leading to brain oxygen deprivation and cerebral infarction. To represent the stroke condition, we produced a mouse model of focal cerebral ischemia followed by reperfusion. We then employed matrix-based mass spectrometry imaging to compare the molecular differences between the ischemic versus non-ischemic regions and attempted to identify mass signatures that correlate with abnormal brain proteolytic activity and disease. In response to ischemia, the brain showed swelling due to traumatic injury to the brain. The optical image indicates the ischemic area (A, dotted red line). The total averaged spectra shows ion rich features throughout the measured mass range (B). The overall anatomical brain structure was intact evidenced by selective localization of a number of molecular ions (C, color-coded) while other distinct ions are shown to co-localize well to the area of injury (D). The ions which localized to the area of injury were found in between 5 to 20 kilodaltons (kD) in size. Based on such information, tissues in the ischemic regions were homogenized and molecules were selectively separated by gel electrophoresis and subsequently extracted from the gel. Attempts to adequately enrich these molecules for identification by mass spectrometry are still in process. Identification of these molecules, which are specifically present in the ischemic regions of the brain, may have profound application in the development of novel biomarkers for diagnosis and/or therapies of stroke.

