MNN Seminar Feb 12th 2020 @ 12:15

Media & Knowledge Sciences (MAKS) Room 414

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Characterisation of hypoglycaemic white matter injury in the rodent brain.

Failure of white matter energy metabolism plays a major role in several neurological disorders. Over the years, several studies have focused on mechanisms of neuronal injury and death in the absence of sufficient substrate for oxidative metabolism. In so doing, a gap in the knowledge to central mechanisms of damage that are specific to white matter has been overlooked. In this study we explore how glucose deprivation (GD) cause delayed structural disruption to YFP-expressing axons, and functional loss in electrical activity. This was delayed by stimulation of the glycogenolytic pathway through β-adrenergic afferents using clenbuterol. Excitotoxicity has been shown to play a central role in hypoglycaemic white matter injury. Blocking AMPA/Kainate receptors with NBQX protects both axons and oligodendrocytes after GD. Combined therapy involving the specific GluN2C/D-containing NMDA receptor antagonist (QNZ-46) and the non-competitive AMPA-specific receptor antagonist (CP-465,022) show excellent preservation of axon integrity and function following GD. Sequential live imaging of Nitric Oxide (NO) during the course of GD shows that its increase preceded the loss of axonal electrical activity. At the same time, blocking NO release during GD with L-NAME partially protects axons. The findings from this study suggest a multimodal prophylactic therapy to protect patients that frequently suffer from hypoglycaemia and other forms of excitotoxic insults.