The role of autophagy in oligodendrocyte differentiation in an ex vivo model of neonatal hypoxia-ischemia

Zofia Klich

Hypoxic-Ischemic Encephalopathy (HIE) can lead to abnormal development of the white matter and disturbances in the myelination process, which is carried out by oligodendrocytes in the CNS. These cells are particularly susceptible to the effects of asphyxia, which can impair their proliferation, maturation, and differentiation, potentially leading to the development of various neurological and neurodevelopmental complications. Autophagy is a molecular process essential for maintaining cellular homeostasis regulating key functions including cell viability. The role of this process in the response of oligodendrocytes to hypoxic-ischemic injury has not yet been sufficiently elucidated and may present a potential therapeutic target for reducing the consequences of cerebral asphyxia. The aim of this study was to evaluate the role of autophagy in the differentiation of oligodendrocytes in a neonatal hypoxia-ischemia model using ex vivo rat hippocampal slice cultures. Hypoxic-ischemic conditions were modeled using oxygen-glucose deprivation (OGD), a well-established method for reproducing ischemic injury ex vivo. OGD-induced changes in oligodendrocyte viability, development, and autophagic activity were assessed. These parameters were evaluated using microscopy, Western blot, propidium iodide staining, and immunofluorescence staining. This study demonstrates the first novel application of the Premo Autophagy Tandem Sensor (RFP-GFP-LC3B) to monitor autophagic flux in organotypic tissue slice cultures. The hippocampal slices were successfully transduced, proving that this assay works well in a tissue model. The experiments demonstrated that OGD induces cell death in hippocampal slices and may contribute to increased proliferation of oligodendrocyte progenitors and inhibition of their differentiation. The studies indicated that enhanced autophagy may play a key role in these cellular processes. A low concentration of the autophagy inhibitor tended to increase myelin protein expression.