HYPEROXIA-INDUCED INJURY IN OLIGODENDROGLIAL PRECURSOR CELLS (OPC) IS ATTENUATED BY MINOCYCLINE

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Background: In very preterm infants, exposure to hyperoxia has been associated with worse neurological outcome. In the immature rodent brain, white matter damage (WMD) and perturbed myelination can be caused by hyperoxia via oxidative stress, inflammation, and apoptotic cell death. Decreased proliferation and delayed maturation of oligodendroglial precursor cells (OPC) have been found to contribute to WMD. The antibiotic minocycline exerts pleiotropic neuroprotective effects in various models of hypoxia/ischemia or inflammatory neurodegenerative diseases and is therefore a promising candidate for protection against hyperoxia-mediated brain injury.

Methods: Rat pups and their mothers were kept at 80% oxygen for 24 hours from P6 to P7. Treatment with minocycline was performed i.p. 12 hours before, at the beginning and at 12 hours of hyperoxia exposure. Control animals were kept at room air. P7 rat brains (n=4) were then perfused for cryosections. Immunohistochemistry was performed for Ki67 (proliferation), NG2 (OPC), TUNEL (apoptosis) with a DAPI (DNA) mounting medium followed by analysis using confocal microscopy.

Results: Hyperoxia induced a marked reduction of OPC numbers in the white matter both through reduction of proliferation (NG2/Ki67 co-staining) and increased rates of apoptosis. In hyperoxia-exposed animals, treatment with minocycline led to significantly higher OPC numbers and proliferation and to decreased apoptosis as compared to pups not receiving minocycline.

Summary: In immature rat brains, minocycline reduces the toxic effects of hyperoxia on white matter OPCs.