ASTROGLIAL RESPONSE AFTER NEONATAL HYPEROXIA IS ASSOCIATED WITH LONG-TERM CHANGES OF WHITE MATTER INTEGRITY

T. Schmitz¹, J. Ritter², S. Mueller³, L.-J. Chew², V. Gallo², C. Bührer¹

¹Neonatology, Charité Universitätsmedizin Berlin, Berlin, Germany, ²Center for Neuroscience Research, Children's National Medical Center, Washington, DC, USA, ³Center for Stroke Research Berlin, Charité Universitätsmedizin Berlin, Berlin, Germany

Impaired neurological development in premature infants is often caused by periventricular white matter injury (PVM) in association with myelin damage. Exposure to hyperoxia (80% O₂) was reported to perturb myelination process during development in neonatal rodents. We analyzed cellular changes in neonatal mice that were exposed to 48 hours of 80% oxygen from postnatal day 6 (P6) to postnatal day 8 (P8). We found that MBP expression was reduced and apoptosis in NG2+ oligodendroglial progenitor cells (OPC) was induced by hyperoxia at P8 and after four days recovery in room air at P12, whereas MBP returned to control levels at P15 and P30. In order to identify hyperoxia-induced changes in astrocytes that might contribute to oligodendroglial cell damage, we characterized expression of GFAP and GLAST in the WM. Hyperoxia did not affect survival or proliferation of astrocytes in the WM, but protein levels of GFAP and GLAST were decreased at P8. These returned to control levels after four days of recovery in room air (P12). Cultured astrocytes exposed to 24h hyperoxia displayed a decreased maximal uptake velocity (V_{max}) of 3H-D-aspartate and a decrease in GLAST expression. MRI measurement using diffusion tensor imaging in animals at P30 and P60 revealed a long term impact of oxygen toxicity on the WM as indicated by decreased fractional anisotropy in adult animals after prior exposure to hyperoxia. Our data suggest that hyperoxia causes a long-term disturbance of WM integrity under involvement of altered astroglial glutamate homeostasis. (T. Schmitz and J. Ritter: equal contributions to this work).