

P013 Role of MyD88 in LPS induced hypoxic-ischemic brain injury in neonatal mice

Xiaoyang Wang¹, Chunxia Nie¹, Kristina Eriksson³, Henrik Hagberg² and Carina Mallard¹

Perinatal Center, Institute of Neuroscience and Physiology¹, Dept of Obstetrics and Gynecology² and Dept of Rheumatology³, Sahlgrenska Academy, Göteborg, Sweden

Neurological deficits in children, including cerebral palsy, are associated with infection before or after birth. We have shown that LPS exposure potentiates hypoxic-ischemic (HI) brain injury in newborn animals and this effect is dependent on TLR-4. However, the role of MyD88 in neonatal brain injury is not known. Littermates of mixed genotype (MyD88 KO, heterozygotes and wild type (WT)) were subjected to left carotid artery ligation and 10% O₂ for 45min (HI) on PND9. In a second set of experiments pups were exposed to LPS (0.3mg/kg, i.p.) or saline, 14h before HI. Brain injury was evaluated 5d after HI. MyD88 deficiency did not reduce overall brain injury after HI (MyD88 KO 15.14±1.03mm³, n=19 vs WT 17.64±1.14mm³, n=25, p=0.14). However, further analysis revealed less brain injury in female MyD88 KO mice (15.28±0.92mm³, n=6) compared with female WT mice (20.07±1.32mm³, n=14, p<0.05). Furthermore, in WT mice brain injury score was increased after the combination of LPS/HI (3.2, n=10) compared HI alone (1.3, n=12, p<0.05). In contrast, the sensitizing effect of LPS did not occur in MyD88 KO mice (Saline: 0.7, n=11 vs LPS: 1.0, n=5). In conclusion, the MyD88 dependent pathway plays a critical role in LPS induced HI brain injury in neonatal mice. This effect appears to be mainly LPS related as MyD88 deficiency only had a minor effect in females on brain injury induced by hypoxia-ischemia alone.