

TREATING NEONATAL SEIZURES: IS GABA STILL EXCITING AFTER BIRTH?S.M. Miller, V.P. Kalanjati, Z. Ireland, P.B. Colditz, **S.T. Bjorkman***Perinatal Research Centre, UQ Centre for Clinical Research, The University of Queensland, Brisbane, QLD, Australia*

Background and aims: Antiepileptic drugs (AEDs) do not effectively control seizures in newborn brain and there is growing concern that use of standard AEDs such as phenobarbital may exacerbate seizures and brain injury. Recent data suggests this may be due to the changing role of the GABA_A receptor (an AED target) during normal neurodevelopment, a process tightly coupled to developmental expression of the chloride co-transporter proteins NKCC1 and KCC2. The timing of the 'switch' in GABA_A receptor function from excitation to inhibition is unclear and in human may not be completed until 3-4 months of age. The aim of this project was to establish the developmental profile of NKCC1, KCC2 and the GABA_A receptor α_1 and α_3 subunits in piglet brain.

Methods: Preterm and term piglets of several different gestational ages around birth were obtained by caesarean section or spontaneous delivery. Brain tissue was collected from several brain regions and expression analysed by western blot.

Results: In parietal cortex the switch between NKCC1 and KCC2 and, GABA_A receptor α_1 and α_3 expression was evident by P3. The switch in GABA_A receptor α_1 and α_3 expression had not yet occurred in the frontal, temporal or occipital cortex. NKCC1, KCC2 analysis is ongoing.

Conclusions: Efficacy of AEDs in neonatal brain may depend on regional and temporal maturation of inhibition. Furthermore changes in GABA_A receptor expression as we have demonstrated following HI and seizures will influence receptor pharmacology. There is a critical need to develop effective treatment strategies specific to the neonatal brain.