

O-014 PRETERM PIGLETS DISPLAY IMPAIRED PHYSICAL ACTIVITY AND ALTERED BEHAVIOUR DURING THE FIRST WEEKS OF LIFE

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Background and aims Premature birth interrupts normal growth and may affect postnatal brain development. We hypothesised that prematurity in pigs would affect neuromuscular control and behaviour also beyond the neonatal period.

Methods Caesarean-delivered preterm (n = 44, 90% gestation) and term (n = 33, 100% gestation) piglets were fed parenterally for five days and then enterally with milk-replacer until d26. Time until basic motor skill (BMS) acquisition (eye lid opening, first walk and stand) were recorded, coordination assessed, and locomotion and general exploration were tracked from open field video recordings on d4, d9, d16 and d23. A novel-object recognition test was performed on d24 (assessing both specific exploration and short-term memory), and learning ability was assessed with a clicker-based poke-reward test from d18-d25 in a subset of piglets.

Results BMS acquisition was delayed in preterm piglets (all p < 0.001). Coordination scores were lower in preterm piglets at all ages whereas locomotion and exploration were reduced only on d4 (all p < 0.05). Preterm piglets explored novel objects less (p < 0.001) but short-term memory assessments were not different. Poke-reward performance improved over time in both preterm and term pigs but did not differ significantly between groups, which partly reflects that only clinically healthy preterm piglets could be tested. In preterm piglets, locomotion on d23 was increased (p < 0.01) when parenteral nutrition had been supplemented with enteral nutrition the first five days after birth.

Conclusion Acquisition of neuromuscular control, locomotion and exploration are quantifiable functional neurological endpoints in preterm piglets that may be used to characterise developmental disturbances and nutritional interventions.

O-015 TEMPORARY THERAPEUTIC WINDOW OF CANNABIDIOL EXTENDS BEYOND 12 HOURS IN HYPOXIC-ISCHAEMIC NEWBORN MICE

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Background and aim cannabidiol (CBD) leads to significant and long-term sustained neuroprotection in hypoxic-ischaemic (HI) newborn rodents. We aim to determine the temporary therapeutic window (TTW) of CBD. Such TTW is established in 6 h for the standard therapy, hypothermia.

Methods 9-day old C57BL6 mice underwent a HI insult (10% oxygen for 90 min after left carotid artery electrocoagulation). Then, 0.1 mL of vehicle (ethanol:solutol:saline 2:1:17) (HV,

n = 25) or CBD (1 mg/kg) was administered s.c. 15 min, or 1, 3, 6, 12 or 24 h after the end of the HI insult (HC0.15 n = 10; HC1, n = 10; HC3, n = 10; HC6, n = 10; HC12, n = 10; HC24, n = 9, respectively). Seven days later MRI scan (T2W) were carried out in formaline-included pup brains (ipsilateral hemisphere volume loss, IVHL), whereas the penumbral perilesional area (parieto-occipital cortex) was studied using Nissl staining (necrotic damage, by a neuropathological score, NPS), TUNEL staining (apoptotic damage) and GFAP immunohistochemistry (astrocyte viability). Non-HI mice served as controls (SHM, n = 15).

Results CBD, administered up to 12 h after HI, showed a significant neuroprotective effect, reducing HI-induced IHVL and NPS by 60%, TUNEL+ count by 90% and astrocyte damage by 50%. When CBD administration was delayed 24 h, however, mild neuroprotective effect was still observable regarding NPS or TUNEL, but not IVH loss or astrocyte viability

Conclusions TTW for CBD seems to be between 12 and 24 h after the end of the HI insult.

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O-015a IMPROVED DEVELOPMENT OF CULTURED OLIGODENDROGLIA AT 5% IN COMPARISON TO 21% OXYGEN

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Immature oligodendroglia of the developing brain are highly susceptible to hyperoxia. As the *in-vivo* O₂ saturation of the brain parenchyma is about 3–7%, we hypothesised that the 21% O₂ commonly sustained in cell culture poses a hyperoxic challenge to immature oligodendroglia affecting their development.

We cultured primary rat oligodendroglial precursor cells (OPC) for 24 h, 48 h and 96 h at 5% and 21% and assessed their developmental progress through analysis of cell numbers of different oligodendroglial stages. For immunocytochemistry, A2B5+, O4+, and O1+ markers were used to label precursor, immature and mature stages respectively, combined with Ki67 for proliferation or TUNEL for apoptosis. qPCR was used to determine gene expression of factors important for development (Olig1, Olig2, Sox9, Sox10) and maturation (MBP, CNP). NRF2 and SOD2 expression was measured to quantify responses to oxidative stress.

Morphology of OLC varied greatly between 21% and 5% at all time points. At 48 h, O4 positive immature oligodendroglia frequently had multiple processes with typical shape at 5% but rarely at 21% oxygen. Gene expression of MBP, CNP, Olig1, and Olig2 was significantly reduced and antioxidant genes NRF2 and SOD2 were significantly up-regulated after 48 h at 21% immunohistochemistry (each p < 0.05). However, there was no difference in cell death as analysed by NG2+TUNEL+ OPCs.

Altogether, these findings indicate that 21% O₂ *in vitro* has negative effects on oligodendroglial development. It has to be debated whether 5% O₂ resemble physiological oxygen conditions more appropriately than current standard protocols with 21% for oligodendroglial cultures.