Spatial cognition is impaired in preterm relative to term born pigs

A.D. Andersen[1], K. Ryom[1], P.T. Sangild[1], T. Thymann[1]
[1]Comparative Pediatrics and Nutrition, University of Copenhagen, Denmark

Background & Aim: Impaired neurodevelopment is a concern following preterm birth. A preterm animal model to assess cognition within the first weeks after birth could help identify supportive interventions. The perinatal brain growth spurt in both man and pig suggests that the preterm pig may be a relevant model to investigate functional brain deficits. We hypothesized that preterm pigs could learn a spatial cognitive task but that learning would be impaired, relative to term pigs.
Methods: Caesarean-delivered, preterm pigs (n=17, 90% gestation) were compared with term born pigs (n=6). From day 15, pigs were tested in a spatial T-maze where they learned to navigate via extra maze cues to obtain a milk reward. Performance was assessed for six acquisition days (10 trials/day) until reaching the learning criterion (80% correct). Pig movements were tracked using EthoVision XT10.
Results: Performance was affected by gestational age ($P<0.01$), and generally increased over time ($P<0.001$). Initially, all pigs performed according to chance (~50% correct), and after transiently displaying a response strategy (e.g. always choosing left-turn), the preterm pigs also gradually learned to use the visual cues. Consequently, preterm pigs required three more days to reach the criterion with a correspondingly lower proportion of correct choices relative to term pigs (64.2 ± 1.9 vs. 80.2 ± 3.2 %, $P<0.01$).
Conclusion: Preterm pigs can learn this T-maze task, but learning is delayed relative to term born pigs. This test may be useful to investigate effects of dietary or pharmacological interventions on spatial cognition early after preterm birth.
Conflict of interest statement: Supported by NEOMUNE, Danish Research Councils

The preterm pig as a model of premature infant gait ataxia

Bergström A.[1], 1Ryom K., Vanden Hole C.[2], Andersen A.D[1]., Skovgaard K.[3], Van Ginneken C.[2], Thymann T[1]., Sangild P.T.[1,4]
[1]Comparative Pediatrics and Nutrition, Department of Clinical Veterinary and Animal Science, Faculty of Health and Medical Sciences, University of Copenhagen, Frederiksberg, Denmark; [2]Applied Veterinary Morphology, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp, Belgium; [3]Section for Immunology and Vaccinology, National Veterinary Institute, Technical University of Denmark, 1870 Frederiksberg C, Denmark; [4]Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark.

Aims/background: Compromised gait, balance and motor coordination (ataxia) as observed in cases of cerebral palsy is a serious complication to premature birth. The cerebellum is a central region with regards to these brain functions and its development shows high sensitivity to premature birth. Our group has over many years refined a pig model of premature birth focusing on gut and immune system development. Phenotypically, we have observed distinct motoric problems e.g. falls, tiptoe walking and swaying in preterm pigs relative to term born counterparts, indicating compromised brain function. The aim of this study was to compare gait patterns and cerebellar neurodevelopmental gene expression of preterm and term piglets.
Methods: We compared gait patterns and T-maze performance of caesarean born preterm (3 litters, 90% gestation) and term born pigs (1 litter, 100% gestation) recorded at five distinct postnatal days. MatLab was used to determine a list of spatiotemporal gait characteristics e.g. stride length/ frequency, ”duty factor” and asymmetry indices. These data were paralleled by qPCR of >60 selected neurodevelopmental genes of isolated cerebellar tissue.
ResultsWhile most genes did not differ significantly, we found higher (fold change [1,5-2]) mRNA levels of Midkine, Doublecortin, Neurotrophin3, p75 and Ephrin-B1 in preterms. Preliminary results from gait and T-maze showed significant functional differences between terms and preterms.
Conclusions: The preterm pig shows functional delays relative to terms, yet the limited cerebellar gene expression differences (mainly related to angiogenesis) suggest other brain regions e.g. motor cortex and basal ganglia to also be involved in compromised gait.