O-060 ASSESSING AUTISM IN TODDLERS BORN

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The Autism Diagnostic Observation Schedule (ADOS) is the only available semi-structured observational assessment of autism and has not been used extensively in preterm toddlers. We used a screening and diagnostic method to determine the diagnostic prevalence of autism and the characteristics of screen positive cases.

Methods A 12-month birth-cohort of toddlers (2-and-4-years-old) born with a gestational age <29-weeks were administered the Modified Checklist of Autism in Toddlers (M-CHAT)-and follow-up interview (FI™) screen, the ADOS and neurodevelopmental assessments (Bayley Scales of Infant and Toddler Development III-2-year-olds, Wechsler Preschool and Primary Scale of Intelligence-III and Adaptive Behaviour Assessment System-Second Edition-4-year-olds). The ADOS was conducted on toddlers with M-CHAT-FI™ positive screens.

Results Complete data were available on 88% (169/192) of children. Thirteen-percent screened M-CHAT-FI™ positive. ADOS (DSM-IV-criteria) classified 1.8% with autistic disorder and none with ASD. Multivariate analysis showed that social emotional delay (p = <0.001) was the only neurodevelopmental factor independently associated with M-CHAT-FI™ positive screens even after adjusting for psychosocial risk and child gender. All but one of the M-CHAT-FI™ positive screens scored some level of abnormality at the domain and item level on the ADOS testing, one third of these reached the Communication Total category cut off for ASD for the combined Communication and Social Interaction Total Score. Four children displayed comorbid atypical development (DQ/IQ <-2SD).

Conclusion The ADOS reports a lower incidence of autistic disorder in children born very preterm compared to studies using diagnostic interview based tools. The distinguishing features of the M-CHAT-FI™ positive cases suggest a sub-threshold communication dysfunction profile.

O-061 CELL-BASED THERAPY FOR HYPOXIC-ISCHAEMIC INJURY IN THE PRETERM BRAIN

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Background and aims Preterm infants are prone to hypoxic-ischaemic encephalopathy. No therapy exists to treat this brain injury. The objective of this study was to assess the neuroprotective effect of exogenous administration of stem cells and the mobilisation of endogenous stem cells in the ovine preterm brain after global hypoxia-ischemia.

Methods Instrumented preterm sheep were subjected to global hypoxia-ischemia by 25 min of umbilical cord occlusion at a gestational age of 104 (term is 150) days. During a 7 day reperfusion period all vital parameters, including (amplitude-integrated) electroencephalogram, were recorded. At the end of the experiment, the preterm brain was assessed by histology and diffusion tensor imaging (DTI).

Results Systemic administration of exogenous mesenchymal stem cells (MSCs) reduced cerebral inflammation (i.e. microglia proliferation) and white matter injury. MSCs induced T-cell tolerance, which was paralleled with diminished mobilisation and invasion of these cells in the preterm brain. In addition, MSCs decreased number of seizures after global hypoxia-ischemia, indicating functional improvement.

Similarly, mobilisation of endogenous stem cells using systemic granulocyte-colony stimulating factor (G-CSF) reduced cerebral inflammation and white matter injury. However, G-CSF did not reduce the number of seizures after global hypoxia-ischemia.

Conclusion We have shown for the first time in a translational animal model that cell-based therapy is effective in protecting the preterm brain against the cerebral and peripheral inflammatory responses which are involved in the aetiology of white matter injury in the preterm brain after global hypoxia-ischemia. Our studies form the basis for future clinical trials studying feasibility of cell-based therapy in preterm infants with hypoxic-ischaemic encephalopathy.

Neonatal Brain and Development – Evolving Techniques

O-062 EARLY BRAIN ACTIVITY AND CORTICAL DEVELOPMENT IN PRETERM INFANTS

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Background and aim Early brain activity is crucial for neuronal growth. It is well known that the cerebral cortex develops rapidly in the last trimester of pregnancy. We investigated whether early brain activity was related to the rate of cortical

development over the 10 wks before term equivalent age in preterm infants.

Methods 35 infants (GA: 27.1 ± 0.7; BW: 937 ± 172) without morphine, were monitored with EEG/aEEG. Three periods were selected at 20–24 h, 32–36 h, 44–48 h. Minimum amplitude,% of time

Results Increased SATrate was positively associated with deltaGMv, inner and outer surface (resp β:7.4, p:0.001; β:46.6, p:0.002; β:57.5, p:0.001). Consistent with these findings, ISI was negatively associated with changes in GMv, inner and outer surface (β:-3.4, p: 0.007; β:-17.8, p: 0.034; β:-27.7, p: 0.006). Min aEEG and% of time <5 μV were associated with inner and outer surface at 40 wks (respectively: β:46.2, p:0.043; β:53.0, p:0.041; and β:-2.9, p:0.025; β:-3.5, p:0.019). No effect on thickness and gyrification was found.

Conclusions Early brain activity seems to be associated with cortical development suggesting that adequate brain activity in the early neuronal networks is necessary to lead to growth and development of neonatal cerebral cortical brain, measured by structural MRI.

O-063 DATA QUALITY IN DIFFUSION TENSOR IMAGING STUDIES OF THE PRETERM BRAIN

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Background and aims Quantitative measurement of brain maturation is increasingly performed in preterm infants using diffusion tensor imaging (DTI). To study white matter properly, reliability of underlying DTI data is of paramount importance, as acquisition and processing steps can substantially affect DTI analyses. We systematically reviewed literature to raise awareness regarding these matters.

Methods We systematically reviewed studies published between 1991 and September 2013, in which DTI scanning of preterm infants was performed within 28 days after term-equivalent age. Based on our inclusion criteria, 75 preterm DTI studies were considered relevant and further analysed. We primarily focused on use of dedicated neonatal equipment, DTI acquisition parameters and processing methodology.

Results There was wide variation among different studies in acquisition and processing methodology, and frequently incomplete reporting of these settings. 25.3% reported the use of dedicated neonatal equipment. Data quality assessment was not reported in 34.7%. Correction for artefacts and exclusion of datasets was not reported in 45.3% respectively 30.7%. Only 54.7% of the studies reported specific correction methods. Tensor estimation methodology was reported in 82.7%. Fast but less accurate tensor calculation algorithms were applied more frequently than advanced algorithms.

Conclusion

DTI acquisition and processing settings are described incompletely in current literature, and vary considerably among different neonatal DTI research groups. In addition, described settings do frequently not meet the highest standards possible. Hence the premature population should be regarded as one of the most challenging groups to image using DTI, maximal awareness regarding these matters is a prerequisite.

Neonatal Immunity

O-064 DEVELOPMENT AND MATURATION OF MAIT CELLS IN HUMAN NEONATES: RELATIONS WITH GESTATIONAL AGE AND MICROBIAL INFECTION

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Newborns, in particular preterm neonates, suffer a high frequency of microbial infections. MAIT cells are innate-like T cells expressing a semi-invariant Vα7.2-Jα33 TCR which recognises MR1-restricted, microbial-derived riboflavin (vitamin B2) metabolites unique to bacteria and yeast.

We studied 151 newborns admitted in the Neonatology Department at Robert Debré Hospital divided into four groups according to gestational age (group 1: 24–27 wks; group 2: 28–31 wks; group 3: 32–36 wks; group 4: >37 wks). The rate and kinetics of MAIT cell expansion and maturation were determined longitudinally at birth (day 0), day 3, day 30 and day 60. We performed multiparametric 10-colour flow cytometry analyses using combinations of antibodies to CD45, CD3, CD4, CD8, TCR Vα7.2, CD161, CD45RA, TCR Vα24 and TCRγδ on 100 ml residual whole blood (left over of blood count), allowing characterisation of MAIT cells in parallel with other non-conventional and conventional T cells.

Our results show that the frequency of MAIT at birth is low and significantly differs according to gestational age (median at D0 group 1: 0.21%; group 2: 0.14%; group 3: 0.12%; group 4: 0.06%).

Of note, this frequency remains relatively stable over the first 2 months of life. However, the phenotype of MAIT cell changes after birth with rapid maturation and increased proportion of CD8aa cells. Significant difference was observed between high preterm neonates with and without maternofetal infection. Analysis of MAIT cell frequency in 20 twin pairs showed it was very similar, suggesting that it might be controlled by a genetic and/or early environmental factor.

In conclusion, the frequency of MAIT cells at birth is inversely correlated with gestational age, and is correlated with the presence of maternofetal microbial infection in preterm neonates. Whether it may reflect the presence of microbial products in amniotic liquid, and/or differences in the gut microbiota immediately after birth is under investigation.

O-065 MACROPHAGE MIGRATION INHIBITORY FACTOR BALANCES NEONATAL INNATE IMMUNE RESPONSES

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