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BRAIN IMAGING AND OUTCOME IN EXTREMELY PRETERM INFANTS

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ABSTRACT

In parallel to the dawn of modern neonatal intensive care, the survival after extremely preterm birth has greatly improved. These very immature children are born during a vulnerable phase of brain maturation, and are at high risk of brain injury and subsequent neurodevelopmental impairments. The overall aim of the works compiled in this thesis is to study brain development and damage of extremely preterm (EPT) infants using different neuroimaging techniques, and to investigate the relations to toddler age outcomes.

All infants born before gestational week 27 + 0 days in Stockholm during a 3-year period were invited to participate. Infants underwent Magnetic Resonance Imaging (MRI, n=109) including Diffusion Tensor Imaging (DTI, n=54) at term equivalent age. Paper I describes the brain damage panorama in the cohort, and the rates of major injuries were low; only 14% had moderate or severe white matter (WM) abnormalities. Subtle WM changes, so called DEHSI (diffuse excessive high signal intensities), were found in 56% of infants and were verified as changes on DTI, indicating possible alterations in WM microstructure.

To study functional connectivity in the WM we used non-stimulated functional MRI in EPT infants at rest. In Paper II, we present evidence of five unique resting state networks at term age in healthy preterm infants.

In Paper III we demonstrate that, provided that imaging was performed on the same day, cranial ultrasound (cUS) detected all infants with moderate or severe WM abnormalities on MRI. However, one third of infants with mild WM abnormalities and four infants with small cerebellar haemorrhages on MRI were overlooked with cUS.

Follow-up was conducted at age 30 months corrected to study the consequences of extreme prematurity. In Paper IV, infants underwent a neurological examination and were evaluated using the Bayley Scales of Infant and Toddler Development (BSID-III) to assess cognitive, language and motor function. Overall, the preterm group performed within the normal range for test standards, but significantly lower than a full term control group. The rates of severe impairments were low: 2% had a severe cognitive delay, 5% had a severe language delay and 7% had cerebral palsy.

Moreover in Paper IV, we demonstrate a high negative predictive value of a normal MRI at term age. Cystic changes, delayed myelination and severe WM reduction were factors most strongly related to adverse outcomes. DEHSI showed no relation to later cognitive, language and motor performances.

Finally, in Paper V, we found poorer cognitive and language function in EPT boys than girls at age 30 months. These differences could neither be explained by an altered WM microstructure assessed with MR-DTI and Tract-Based Spatial Statistics, nor by any individual perinatal factor.

In summary, the rates of brain injuries and later impairments were low in this very high-risk population. The present results suggest that survival without major disability is likely even at extremely low gestational ages. Long-term follow-up after extremely preterm birth is essential.

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