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Prognostication and the unpredictable nature of HIV encephalopathy,

Diseases affecting the structure or function of the brain in infancy and early childhood can have devastating and long term effects on function and quality of life for children and families. There are as many causes of encephalopathies as there are multiple and varied outcomes. Defining the causes and courses of disease and impact of interventions are essential for helping to build a body of knowledge to inform on the type and timing of interventions that may have a more positive impact on outcomes.

The complexity of the brain and its capacity for adaptation never cease to amaze if not also to confound. Recent papers exploring the outcomes of neonates with hypoxic-ischemic encephalopathy (HIE) indicated that the presence of moderate to severe HIE when accompanied by prolonged/severe seizures may contribute to an abnormal outcome irrespective of treatment with hypothermia, albeit at somewhat reduced odds.^{1,2} Two recent papers have taken a different approach to focus on encephalopathies associated with human immune deficiency virus (HIVE).^{3,4} These are interesting and important studies highlighting the broader impact of HIVE but which also reflect some unexpected outcomes with implications for medical and therapeutic management. A number of factors related to the extent of viral infection (CD4%- and viral load) and the timing of initiation of antiretroviral therapy (ART) were explored with respect to motor outcomes of children with HIVE presenting with bilateral lower limb spasticity. As with neonatal treatment of HIE with hypothermia, neither severity of viral infection nor timing of ART initiation reliably predicted functional (motor) status in later childhood. Notable though were significant associations between severity of gross motor impairment and upper limb capacity and subsequent impact on participation. Early recognition and intervention for fine motor difficulties may help mitigate some disabling aspects associated with HIVE.

When looking more closely at the data, extensive individual differences linked to outcomes are evident across all of these studies. There may be some children for whom specific early timely and focussed intervention minimised the impact of disease (or who may have done well notwithstanding) and others who have defied expectation with or without intervention (no treatment with hypothermia or delayed ART) and achieved more positive outcomes. This is illustrated in the study by Mann et al (2016a), in which 50% (4/8) of children with severe motor impairment (Gross Motor Classification Scale (GMFCS) Level III) had early initiation of ART while one child in GMFCS Level I had a relatively delayed ART initiation.

Separating infants and children into groups according to the severity of disease at onset, or impairment at outcome, has limitations. Information is required about the infants and children who lie outside of our expectations; outliers potentially forming distinct subgroups.⁵ What might be the common factors? Are these clinical (e.g. severity of disease), personal and familial (e.g. resilience, education) or environmental (e.g. access to and receipt of medical, physical, social and educational

interventions), and what are the interactions between these that link children who exceed or confound our expectations? This will require a unified and comprehensive approach to define a common minimum data set that transcends disciplines, allows for merging of information across motor, cognitive, social and behavioural domains and helps transcend limitations of these small sample sizes (e.g. utilise the Disabilities Complexity Scale for routine data collection).⁶

Understanding the dynamic and multi-dimensional nature of child development has a number of challenges. An ecological (and inter-disciplinary) perspective will enable consideration of the transactional elements within and between individuals and the many contexts for behaviour and the environments in which they occur. An integrated approach can help us untangle some of the mysteries surrounding the similarities and singularities of differing infant brain diseases, neural and behavioural adaptations, and influence of structured and naturally occurring interventions.

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