Prognostication and the unpredictable nature of HIV encephalopathy

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This commentary is on the original articles by Mann, Laughton et al. and Mann, Donald et al. on pages 407–411 and 412–419 of this issue.

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 varied outcomes. Defining the causes and courses of disease and determining treatment effects are essential for building a body of knowledge to inform 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 as well as confound. Recent papers exploring the outcomes of neonates with hypoxic-ischemic encephalopathy (HIE) indicate 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, and 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 percentage 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 thus help mitigate some activity limitations 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 timely and focussed intervention minimized the impact of disease (or who may have done well notwithstanding). There are others who defy expectation with or without intervention (no treatment with hypothermia or delayed ART) and achieve more positive outcomes. This is illustrated in the study by Mann et al.1 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 some 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)? What are the interactions between these that link children who exceed or confound our expectations? Addressing these questions 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.6

Understanding the dynamic and multidimensional nature of child development has a number of challenges. An ecological (and interdisciplinary) 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.
Sleep disorders in cerebral palsy

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The study by Jacquier and Newman1 is a valuable reminder of the challenges faced by carers managing the sleep of young people with cerebral palsy and other motor disabilities. Sleep problems in this population begin at a young age, tend to persist, and can be detrimental to the physical and mental health of young people and their caregivers. This particular study focuses on the prevalence and determinants of co-sleeping using questionnaires for cases and unmatched controls. Co-sleeping is a difficult outcome to define, and is not necessarily a ‘bad thing’, being the preferred sleeping arrangement for many cultures around the world. In this study, although no causality can be determined, co-sleeping was associated with improved sleep in the young people and worse sleep for their carers.

While the study goes on to explore medical factors that might explain increased rates of co-sleeping, it is also likely that in some cases sleep association difficulties have arisen and have never been adequately addressed. There is a tendency to overlook basic sleep association disorders when faced with a child requiring overnight postural changes and tube feeding, for example. However, it is nearly always possible to time such interventions to still allow the child to learn appropriate sleep associations and ‘self-soothe’. In this group of families, who are often exhausted and at their wits’ end, it is important to emphasize that such behavioural interventions are as powerful as any sleep medications, without the risk of adverse effects. Well-timed support either in the form of more frequent initial face-to-face or telephone follow-up can boost therapeutic success.

Sleep can be disrupted in almost every conceivable manner in this group of young people, for whom a combination of intrinsic and extrinsic factors often come together in a perfect storm to disturb sleep rhythms and fragment sleep throughout the night.2

Intrinsic factors include neurological factors, of which the presence of nocturnal seizures is the most important. The mechanisms are complex and probably include sleep fragmentation secondary to seizures, anticonvulsants compromising sleep and daytime alertness, and alteration in caregivers’ approach to sleep associations. The degree of intellectual disability, and frequent presence of comorbid autism or attention-deficit-hyperactivity disorder, predict poor sleep in this group of young children, just as in those with no motor impairment. Brainstem dysfunction and intrinsic sleep rhythm disorders are often seen, with visual impairments affecting circadian rhythms and worsening sleep.

Sleep-related breathing problems are common and underestimated; they include obstructive events secondary to abnormal upper airway tone and central events secondary to poor brainstem control, aspiration, and gastro-oesophageal reflux. Sleep-related breathing disorder questionnaires have particularly poor sensitivity and are no substitute for standardized objective overnight sleep studies.

Unsurprisingly, studies indicate that sleep disorders are positively associated with level of motor functioning using Gross Motor Function Classification System. The more severe grades are likely to experience pain from muscle spasms, hip dislocations, and inability to alter sleeping positions. This is a particularly vicious circle whereby poor sleep also affects pain perception thresholds.

Extrinsic factors include caregiver variables around employment, single parents, and co-sleeping. This group of young children are frequently prescribed many medications, including anticonvulsants and medications to reduce muscle tone. These can all, singly or in combination, alter sleep maintenance, increase risk of sleep-related breathing difficulties and reduce levels of daytime alertness.

With this background knowledge it is now time to conduct well-designed randomized controlled studies that will