Monitoring Progress of Neurological and Functional Outcomes in the Paediatric HIV Cohort in the UK

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Summary

This document aims to summarise the current understanding of neurological and functional outcomes for children living with HIV and provide recommendations for screening and monitoring, as well as the process for deciding when to refer for or carry out additional assessments.

This guideline gives a summary of some of the literature relating to the neurological and functioning outcomes of children and young people living with HIV. It is aimed at multidisciplinary clinicians working in HIV services around screening for difficulties in these areas. It gives guidance on significant time points to assess, an example screening proforma, a list of potential assessments to undertake and the actions to take if needs are identified. It also gives two case examples. Assessing and reviewing neurological and functioning outcomes continues to be a priority.

Ethos of developmental care

Echoing the 'Every Child Matters' paper in 2004 the ethos of paediatric HIV care is to enhance wellbeing and quality of life outcomes as well as improve the management of the condition and treatment demands. To achieve these, careful attention needs to be given to monitoring all aspects of progress (physical, cognitive, behavioural, learning, social and emotional) and address the changing demands of daily life as a child moves through childhood and adolescence.

Background

The developing brain is known to be particularly vulnerable to the effects of early biological and / or psychosocial adversity. Long term developmental, cognitive and behavioural consequences, of varying severity, are noted in children with early exposure to perinatal risks such as prematurity, neonatal infection or traumas and chronic deprivation.

Biological Factors

The first cases of paediatric HIV encephalopathy were found in children with AIDS in 1985. Prior to the introduction of Highly Active Antiretroviral Treatment (HAART) treatment, HIV associated neurological disease was recorded in 76% of children with a diagnosis of acquired immune deficiency syndrome (AIDS) and 21 to 33% of all children infected with HIV (Cooper et al, 1998). This rate has subsequently fallen to 1.6 to 10% following the introduction of HAART in the mid-1990s (Chiriboga et al, 2005). Starting HAART at an early age has been shown to attenuate the neuropathic effects of HIV infection (Sánchez-Ramón et al. 2003; Laughton et al. 2012). Not all HAART drugs are equal in their ability to penetrate the blood-brain barrier. A recent South African study has also shown that even when HAART was started between 8 and 12 weeks of life, a large proportion of infants already presented with advanced HIV disease (Innes et al. 2014), which would predispose them to neurological involvement. Neuroscience and neuropsychology evidence suggests that HAART alone is not enough to correct or resolve the neurodevelopmental consequences of Paediatric HIV (PHIV) (Lyall et al, 2010). Some young people may also be at risk of Central Nervous System (CNS) side effects of HAART, which may impact on behaviour and cognitive processes (Brown et al, 2008). It is also possible that host genetics play a part in whether a young person living with HIV is susceptible to disease progression and neuropathology (Lorente et al 2006).

Environmental & Psychosocial Factors

As of the end of March 2018, a total of 801 young people were in active follow up at a Paediatric Clinic in the UK or Ireland. The vast majority of those (93%) were known to be infected through mother-to-child transmission (Collaborative HIV Paediatric Study – CHIPS, 2016). The fact that the

diagnosis is usually shared with the mother may also contribute to the child's neurodevelopmental outcome. For example, parents or carers may not highlight any concerns they may have about their child's development with school or other services due to fears about the child's or their own HIV status being shared. Parents or carers living with HIV may also have their own mental health, cognitive or functioning difficulties, which impacts on the recognition, reporting or support of impairments. This could lead to difficulties remaining unidentified and unsupported. In addition, children with HIV in the UK are overrepresented by minority ethnic populations (Collaborative HIV Paediatric Study, 2015). Many are bilingual and the majority are likely to have experienced stressful life events growing up, such as family bereavement, health diagnosis in the family, and migration to a different country (Elliott-DeSorbo et al, 2009, Melvin et al., 2014). These represent added potential risk factors and complexities when understanding neurodevelopment and are important additional considerations for clinical services. Many children with HIV may have additional neurodevelopmental risk factors, such as co-infections, premature birth, perinatal drug and alcohol exposure (Laughton et al, 2013), and environmental factors such as lower socioeconomic status (SES) and changes in primary caregiver add further to the risk of poorer cognitive and educational outcomes (Smith & Wilkins, 2015). Social stigma, including devaluing and stereotyping of individuals can be related to lower social support, increased risk of mental health symptoms and poor physical health (Logie & Gadalla, 2009).

It is becoming clearer that as children with perinatally acquired HIV are living longer and healthier lives, the impact of the subtle as well as more severe effects of HIV on cognitive and behavioural processes, becomes more significant. Some impairment may not be evident until later years and affect learning, independence and the ability to realise their full potential in education, social relationships or employment. Such weaknesses may also make coping with HIV, including adherence to treatments, more challenging.

UK Cohort

There is a paucity of available neurological and developmental data for children with HIV in the UK, particularly comparison data with uninfected children. The UK's largest neurocognitive research study, Adolescents & Adults Living with Perinatal HIV (AALPHI) addressed this gap. AALPHI used brief cognitive screening measures in a cohort of 270 PHIV+ aged 12-21. The study found significant differences only in those children who had clinical AIDS stage disease; overall (HIV negative and HIV positive) performance was substantially lower than in the general population (Judd et al., 2016). A greater understanding of the neurocognitive areas that underpin the observed difficulties in learning will help to inform clinic interventions for this population (Freeman, 2017).

At the St Mary's Family clinic 10 - 15 % of the paediatric population were identified as having abnormal neurological signs and a common profile of developmental weakness has been observed (Biggs & Melvin, 2007). A later review of over 70 children, aged 9-11 years, from this clinic cohort found 27% were receiving some kind of extra learning support in school and 11% were significantly behind in aspects of literacy than predicted by their general cognitive ability (Krechevsky & Melvin, 2010). A neurodevelopmental audit completed in 2011 on behalf of the North West Perinatal & Paediatric HIV Network across clinics in Manchester, Liverpool and Stoke found that 14% of young people had abnormal neurological signs, 22% were receiving extra help in school and 27% were known to child development services (O'Riordan A, 2012).

Patterns of Impairment

The most commonly used measure of neurodevelopment in older youth with PHIV in the HAART era is global intelligence, which is the name used for general verbal and non-verbal problem solving skills, typically assessed by the Wechsler scales. Studies have typically found small or no differences between global intelligence scores for young people with PHIV and those who have been perinatally exposed but uninfected (i.e. Smith et al, 2012). Measures of general intelligence may mask subtle impairments in functioning (Smith & Wilkins, 2015). Recent research has found specific impairments in domains such as executive functioning (Llorente et al, 2014), hearing and language (Torre et al, 2012) memory (Keller et al 2004), attention (Koekkoek et al, 2008), visual-spatial processing (Martin et al, 2006), achievement (Franklin et al, 2005) and adaptive functioning (Smith et al, 2012). Furthermore, Pearlstein et al (2014) found that older youth with PHIV had lower daily skill mastery, and this can be important when considering how much independence a young person would be expected to have in relation to accessing adult health care following transition, taking medication etc.

The children who have evidence of severe disease progression early in life have consistently been found to be more at risk of later difficulties (Laughton et al, 2003; Smith et al, 2006; Smith et al, 2012). However, psychosocial factors such as family income level, caregiver functioning (Smith et al, 2012), nutrition (Govender et al, 2011), education level and amount of stimulation in the home (Bangirana, 2009) have been shown to mediate the relationship between PHIV and these impairments. Therefore, the outcomes for young people are likely to be the result of complex relationships between a number of factors.

Aims of Developmental Monitoring

The primary aim is the early detection of potential developmental weaknesses in order to facilitate interventions which prevent and/or reduce the impact of problems on functions and the young person's quality of life.

Further aims:

- To provide ongoing data about specific population needs to allow for planning of service provision.
- To help understand the effects of treatments (ART exposure, length of treatments, timing of starting etc)
- To promote a greater understanding of the chronic influence of HIV infection on developmental processes and identify possible risk and resilience factors which may help identify new potential interventions

Core Outcome Measures

In order to identify levels of need in the HIV infected population and plan for service provision at both a specialist and local level, the collection of the following core outcome measures are recommended:

- Number of patients with neurological signs (and description)
- Number of patients with significant motor or speech delays in early years.
- Any sensory impairment (hearing & vision) requiring additional aids / equipment.
- Number of patients referred to local developmental services e.g. Physiotherapy, Speech and Language Therapy, (SALT) Child Development Centre (CDC) and for what reason.
- Number of patients attending special schools or units, and those that require an Education Health and Care Plan (EHCP) or additional educational support.
- Number of patients referred to Child and Adolescent Mental Health (CAMHS) services and the nature of the referral.

A tiered approach to developmental monitoring within clinics

Detailed developmental and cognitive assessments are time consuming and require access to specific tests and staff trained in their administration and interpretation. Furthermore, this is a culturally diverse population and some available tests may have norms which give an unreliable reflection of these children's abilities and needs. With the high percentage of those with HIV being

from ethnic minorities, this monitoring should be mindful of the young person's language and cultural influences, especially if they have recently moved to the UK and the use of some of the tests should be considered carefully, particularly if they have been standardised in the UK or US. Access to psychology, physiotherapy or other child development professionals may be possible in some centres but generally only for those individuals with significant concerns about their development progress.

The following may be most effective in collecting outcomes about general neurodevelopmental and psychological progress of all children attending HIV services.

On-going screening of all children at clinic

AIM: to collect reported levels of 'concern' from carers, child and staff and as a first step to help identify who requires further referral or assessment

Completing a developmental checklist or screening tool with the parent/carer and child in clinic (an example is included as Appendix 1), which could be administered with all young people on an annual basis by a range of clinic staff would be a good first step. Feedback from this will indicate whether further follow up, referral or more detailed assessment is required. Screening in clinic should also assess for subtle or specific impairments (i.e. processing speed or attentional deficits), as well as global issues, as suggested by Smith & Wilkins (2015) and Freeman (2017). Clinic screening should also include any psychosocial factors, which may be having an impact on functioning. It is acknowledged that for some clinics, there may be a need to refer outside of the clinic for more specialist screening or review. There will be some young people who are at increased risk of neurodevelopmental vulnerability, i.e. children who experienced severe disease progression early in life. It will be of increased importance that children at increased vulnerability have access to on-going screening in clinic. In addition, routine screening at clinics also allow for discussion and review of potential side effects of HAART, ways HAART could be optimised or whether there are any issues with adherence of treatment.

Assessment at key times

AIM: For those clinics that have access to a psychology service to consider developmental screening at key times:

- Newly referred children and young people
- A young person who has arrived in the country in the past 6-12 months

- Where concerns are raised at routine clinic visits or annual screening (Appendix 1), including issues around adherence , naming safeguarding, change in home circumstances, transition within education (e.g. primary and secondary school entry) or issues in school
- As part of the transition process to adult care (1 year prior); particularly with young people where learning needs have been identified, to inform transition planning and service provision around vulnerability, engagement with care and mental capacity decisions.

CASE Example 1:

A 10-year old boy who is currently in Year 6 of mainstream education reports finding school difficult and needs some support keeping up in lessons. He is nervous about going to secondary school. No formal educational health and care plan or educational support is in place. Parent unconcerned about academic ability but is expressing concern regarding his motivation and ability to organise himself at home, suggesting he is lazy.

Assessment could include:

- Educational and clinical review - Review of last school report and clinical interview including: early developmental milestones, history of identified difficulties, objective examples, any exception to examples, and medical history/treatment.
- Cognitive screening - Broad cognitive assessment to establish overall cognitive ability level including a measure of processing speed
- Psychology screen – include screening measure of mood and quality or life/strengths and difficulties.
- Hypothesis testing - Based on school report, parental and self-report and cognitive assessment include cognitive assessment of relevant attainments assessment, and/or measures of cognitive flexibility planning organising and self-regulation.
- Reporting – prove accessible summary of cognitive assessment results and behavioural observations for parent and young person, including recommendation to support and identified weaknesses.
- Dissemination – If relevant, a family agree share report with education and health team, and any appropriate service.

Those clinics that offer routine cognitive screenings at key educational transitional stages have identified a proportion of children and young people that have undiagnosed specific learning needs (e.g. slowed processing speed, weaknesses in executive functioning abilities). An assessment and recommendations support the educational processes required to access additional resources and more specialist interventions. Gaining explicit consent from families prior to liaison with school is essential. In some circumstances where families have not shared the child's HIV status with school or other services and do not wish to, it may be necessary to omit the HIV status of the child in feedback. Similarly, schools carry out assessments and gather important information about a child's progress, which would inform screening. Where possible when concerns are identified, liaison with school can be a helpful first step to inform decisions about whether a child's developmental needs are being met and if further assessment is appropriate.It is also recognised that a neurodevelopmental review is a helpful part of discharge planning during the transitional process prior to transfer to adolescent/adult services (e.g. Cervia, 2013, Nichols, 2013). This review can be informative to adult services, highlighting a potential need for additional support or mental capacity considerations. A pre-transition neurodevelopmental review can also provide a baseline of general cognitive ability by which any future assessments can be based. A review of adaptive functioning in particular can be important around the time of transition to adult services (see Appendix 2 for suggested measures).

CASE Example 2:

A 17-year old girl that is currently in full time education in local college and reporting that she did not do as well as she hoped in GCSE exams. She has an early history of developmental delay and category C diagnosis in infancy, but otherwise well managed HIV and no neurological follow up. Her clinic are preparing for transition to adult services. She reports that her mum still reminds her to take her medication. She is not sexually active.

Assessment could include:

- Clinical review - Review of educational attainments and clinical interview including: early developmental milestones, histology of identified difficulties, objective examples, any exception to examples, and medical history/treatment including neurology assessments.
- Cognitive screening - Broad cognitive assessment to establish overall cognitive ability level including a measures of processing speed and executive functioning.
- Psychology screen – include screening measure of mood and quality or life/strengths and difficulties.
- Health understanding: review knowledge and understanding of diagnosis and treatment to identify any areas she will need support with. Include support needed to achieve greater independence in own health management.
- Hypothesis testing - Based on self-report, clinical review and cognitive assessment.
- Reporting – prove accessible summary of cognitive assessment results and behavioural observations for young person and her clinicians, including recommendation to support and identified strengths and weaknesses.
- Dissemination – If relevant, a family agree share report with education and health team, and any appropriate service.

Further in-depth assessment or onward referral

AIM: To assess detailed developmental, learning and cognitive profiles in order to identify those in need of interventions and/or to look for changes associated with condition and treatment effects. It is important that children get referred early for more in-depth assessments and interventions when their difficulties are interfering with the ability to manage age appropriate functioning and activities.

Families may be anxious about a referral to a developmental or educational service through fear of a confidentiality breach as HIV remains a stigmatising condition. Unfortunately there is often a lack of up to date information within general paediatric, educational and community services about the treatment and prognosis of living with HIV. This means discussions about confidentiality are paramount and before sharing a person's HIV status this needs to be discussed with parents/carers and children. It is useful to discuss with families if and why services may 'need to know' about the

diagnosis and if there are any benefits for the child's care. It may not always be appropriate or necessary to share the HIV diagnosis at the beginning of finding out what services are available. Instead it may be preferable in a referral to describe the child's needs and difficulties (i.e. that they have mobility problems, speech and language delay, are struggling with work at school etc.) to assess if the service is appropriate for the young person.

Any child that is identified as having significant learning difficulties or in need of additional educational or social care support, should be referred to a local Learning Disability (LD) and/or child development services at the earliest opportunity. On-going liaison with LD health and social care organisations is crucial to support the young person's health, education and transition through education and to adult health services in the future. The health team should support young people to gain age appropriate levels of understanding and independence in their health care, through joint working with carers and other support organisations.

CONCLUSIONS

To ensure the best functional outcomes and wellbeing of the child, culturally sensitive developmental monitoring and school progress should be a core part of the management of Paediatric HIV at all centres. This monitoring helps inform health care management, as well as identify appropriate educational and psychological interventions. Psychosocial and biological factors should be considered in these assessments, as well as resilience factors that can be used for intervention planning.

Regular screening for cognitive strengths and difficulties should be part of clinical practice. When more potential difficulties are identified, the young person should be referred for more in-depth cognitive and developmental assessments and/or to specialist services. While this monitoring should be continual, the suggested key times for more in-depth assessments are at the time of new referral, transition to secondary school and adult HIV servicesWhen a child or young person has complex needs there will be a need for the health teams to jointly work with the child/young person and their professional and carer network.

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