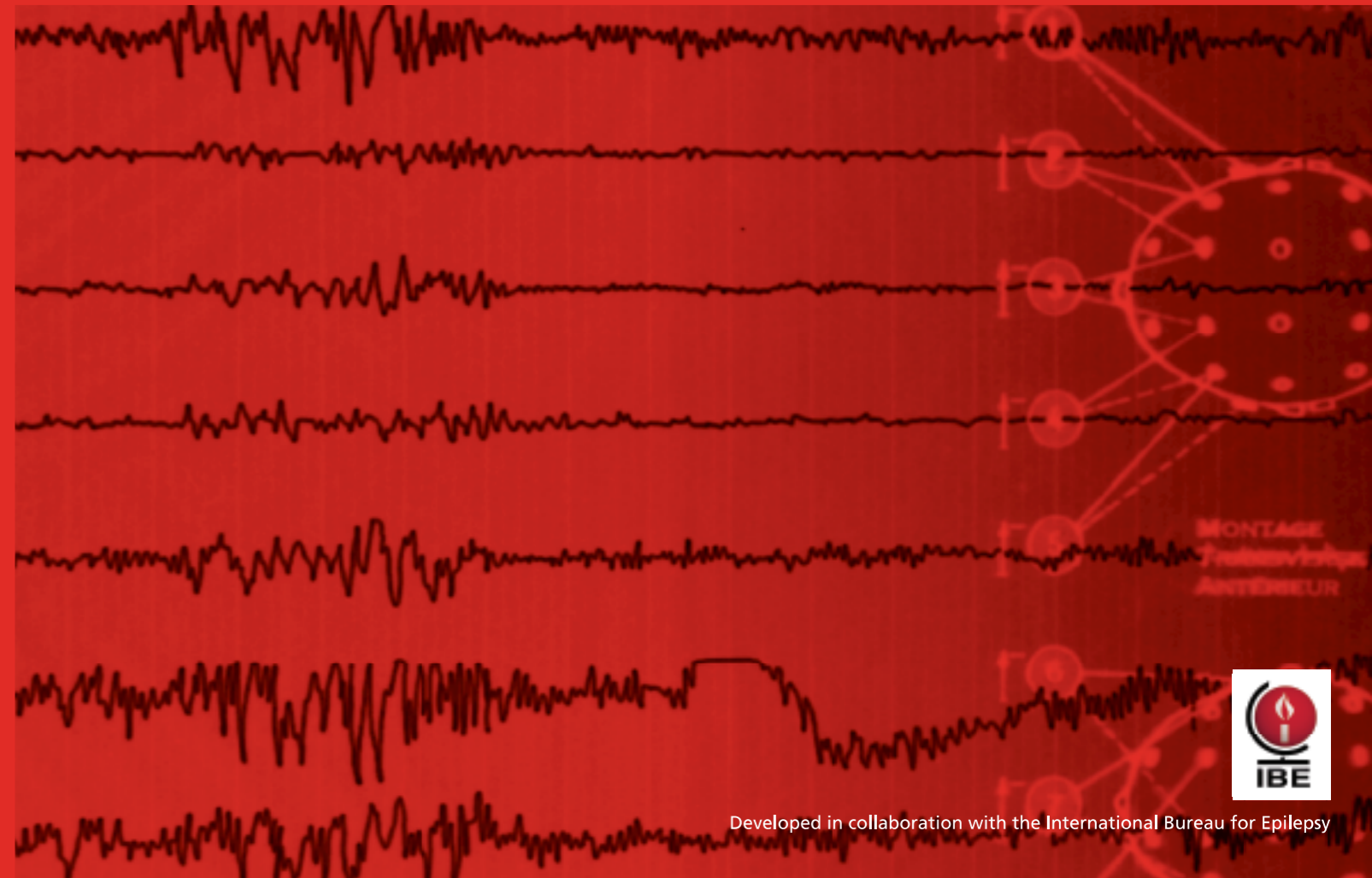


Future in Mind Report

Critical Years Review

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About 'Future in Mind'

'Future in Mind' is an educational initiative by the International Bureau for Epilepsy (IBE) to raise awareness of the considerations and consequences of childhood epilepsy. The 'Future in Mind' initiative should be of interest to healthcare professionals, parents and families, teachers and caregivers.



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Introduction

'Critical Years' is a review of published evidence on childhood epilepsy, which explores factors influencing development and outcomes. This report has been developed by authors as part of the 'Future in Mind' initiative and is in collaboration with the IBE.

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Childhood epilepsy is among the most prevalent neurological conditions in the developing years

Fifty million people in the world have epilepsy, of whom, 33 million are children.¹ The risk of presenting with epilepsy peaks during the first 10 years of life,^{2,3} with prevalence rates of 3.6 to 4.2 per 1,000 children (0-16 years).^{4,5}

Epilepsy is a medical diagnosis and a social label with potential implications across all aspects of a child's development and family life

Epilepsy is characterised by its episodic and chronic nature. Seizures are commonly associated with periods of disruption including loss of, or changes in consciousness, physical distortion, risk of physical injury, incontinence and sometimes psychological problems including loss of self esteem, learning and behavioural difficulties and emotional problems. The unpredictable nature of seizures has a compounding effect, in terms of anxiety and fear of recurrence, consequences on independence, emotional and psychological well-being and overall quality of life.⁶

70% of people with epilepsy can be seizure-free with appropriate medication, however only about one third of children currently achieve this goal^{10,11}

Clinicians and scientists have long been aware that seizure activity in a child's brain differs from that in a mature, adult brain. These differences are seen across electroencephalogram (EEG) activity and manifestations of seizures.⁷ Differences are also seen in the consequences of seizure activity, including neuropsychological and behavioural outcomes.⁷

It is well established that children with epilepsy have more academic and behavioural problems than the general

population and are at a high risk of impaired social and emotional functioning.⁶ Risk factors are multiple and probably involve a combination of neurological, seizure, treatment, family and child factors (eg, family support, environment and co-morbidities).⁶

A diagnosis of epilepsy has been shown to have complex and far-reaching social consequences – for both the child and their family. Feelings of shame and apprehension, in addition to parental overprotection, and the risk of stigmatisation are among the factors that may contribute to challenges in social development and integration.^{8,9}

This review aims to enhance understanding of the complexities associated with epilepsies in children – from infancy, through puberty and into early adulthood. Insights into factors that have an influence on outcomes are gathered from an evaluation of scientific and clinical evidence across the following areas:

- Neurobiology and brain development
- Cognitive development and neuropsychological outcomes
- Educational and academic performance
- Psychosocial development and behavioural outcomes



Neurobiology and brain development

Seizures throughout childhood and puberty can have a damaging effect on crucial periods of brain development. Consequences include irreversible alterations in the 'hard wiring' of the brain eg, the connections between different parts of the brain and nervous system³

Recurrent seizures in an immature brain result in a reduction in nerve connections, which is more pronounced than the effects of seizures in an adult brain¹³

The nervous system develops over a long period of time, extending from the embryonic period, through puberty and into early adulthood.¹² As a result, the developing brain may be vulnerable to the potentially damaging effects of seizure activity during this extended period. Young people appear to be unusually susceptible to seizures, therefore, exacerbating this risk.³

A seizure is caused by excessive or uncoordinated neuronal activity that may spread across the brain. A risk of brain damage or impaired development due to uncontrolled seizures has long been suspected. Evidence has shown in animals that uncontrolled seizures may cause significant and irreversible effects on the connections between different groups of neurons and affect brain development.^{3,7}

Seizure freedom in children with epilepsy from the earliest opportunity is likely to have a beneficial effect in terms of brain development and long-term consequences

Pre-existing brain damage has been shown to predict difficulty in controlling seizures.¹⁴ This relationship may be additive to the individual effects of seizure activity and

brain pathology on neurodevelopment and, ultimately, outcomes in certain epilepsy syndromes.

Seizures have been shown to modify, either by slowing down or accelerating, a wide range of unique processes that take place during development.³ This has long-term consequences on the 'hard wiring' of the brain and hence causes disruption to common brain functions. This may lead to clinically significant impairment in function and development, for example, problems in thinking, learning, reasoning and behaviour in children with epilepsy.^{3,15}

The frequency of seizure activity in children has been shown to have a direct influence on changes in the developing brain.^{7,16} Clinically, this is supported by cognitive decline following the onset of seizures in some children who have no history of cognitive impairment and no underlying brain damage prior to seizure onset.¹³

Children with epilepsy show greater instability of cognitive functions compared with classmates without epilepsy – in particular measures of learning, memory span for words and attention are impaired¹⁷

Cognitive function includes the ability to plan, learn and remember new information, pay attention, solve problems, make mental decisions and understand and construct visual and verbal information. In general, individuals with epilepsy, across all age groups, have impaired cognitive performance compared with people without epilepsy of the same age and educational level.¹⁷ Impairment to cognitive performance however, is dependent on the epilepsy syndrome and individual characteristics of the child.

Multiple factors contribute to cognitive impairment associated with epilepsy, including:

- Underlying brain lesions and damage caused directly by seizure activity
- Etiology of seizures and epilepsy syndrome
- Seizure type
- Age of onset
- Seizure activity (frequency, duration and severity)
- Genetic factors
- Individual family and child variables, including co-morbidities eg, depression
- Side effects of anti-epileptic drug (AED) therapy

Disruption to brain development from seizure activity and potential side effects of some epilepsy medication, may have a detrimental effect on cognitive ability¹⁶ – the cornerstone of neuropsychological and social development and academic achievement

Cognitive abilities also vary according to age of seizure onset, with significant impairment most commonly seen when epilepsy occurs during childhood.¹⁸

Side effects of AED therapy

Some AEDs are known to be associated with cognitive side effects.^{7,19} Children are among the patients at highest risk for cognitive side effects from AEDs and impairment is most pronounced in those with lower than average IQs.^{7,18,19} Even modest cognitive side effects of epilepsy medications in children will have significant and cumulative consequences if they restrict the rate at which academic skills are initially learned and subsequently mastered.¹⁹

Animal studies suggest that there might be an interaction between AED treatment and early brain development.²⁰ Any associated clinical relevance in humans is not yet evaluated, but the results highlight the need for more information on specific relationships between epilepsy, brain development and treatment.

Educational and academic performance

Children with epilepsy are at risk of academic difficulties and for underemployment as adults. Minimising cognitive impairment through achieving seizure freedom without cognitive side effects of AED therapy is critical to addressing academic underachievement in children with epilepsy¹⁴

Minimising cognitive side effects of epilepsy medication is important in achieving best possible educational outcomes in children with epilepsy

School and academic performance of children with epilepsy is often impaired and epilepsy is more common in children with learning disabilities:¹⁴

- Up to 30% of children with learning disabilities have epilepsy
- 30% of children with epilepsy attend special schools

This pattern of academic achievement for children with epilepsy has not changed for the last 35 years.¹⁴

Low stimulation and support in the family environment are related to poor academic achievement in children with epilepsy²²

Factors contributing to poor academic performance in children with epilepsy include:^{6,18,19,21,22}

- Underlying brain lesions
- Seizures and seizure activity
- Early age at onset
- Cognitive impairment
- Social demographics and family environment
- Choice of medication

Cognitive ability is a major predictor of academic performance.²² Furthermore, problems with the ability to pay attention have been shown to account for the majority of differences in academic achievement for children with well-controlled seizures compared with classmates without epilepsy.²³

For example, evidence suggests that phenobarbital may lower IQ. This IQ effect has been shown to decrease over time if the drug is stopped, however, there appears to be a longer-term negative effect on academic achievement where it is unclear whether the children ever 'catch up' in terms of performance.^{19,24}

In addition to seizure activity and cognitive ability, variables such as family environment and perceptions of the child and the people with whom they interact (eg, family members, teachers, peer group) have been shown to influence academic achievement in children with epilepsy.²²

Psychosocial development and behavioural outcomes

The effects of epilepsy on a child's psychological and social development are complex and cover all dimensions of a child's life and future. Enabling the child and family to lead a life as free as possible from the medical and psychosocial complications of epilepsy is the ultimate goal of management⁶

Children with epilepsy appear to have both the risk to behavioural and social development associated with chronic illness and the risk imposed by a central nervous system disorder

Children with epilepsy have been found to have relatively worse health-related quality of life in the psychological, social and school domains compared with children with other chronic conditions eg, asthma.²⁶ Because development of self-identity and peer relationships is of critical importance throughout late childhood and puberty, any stigma related to epilepsy encountered at this particular life stage may have a strong influence on future psychosocial health and self esteem.²⁶

Uncontrolled seizures contribute to poorer quality of life and psychosocial outcomes. Because of the detrimental effects of uncontrolled seizures on family dynamics and environment, uncontrolled seizures lead to a 'vicious circle' of events and poor outcomes

The presence of recurrent seizures in children seems to predict behavioural problems from very early in the course of epilepsy.²⁷ Children with frequent seizures tend to have poorer psychosocial outcomes than those with no or infrequent seizures.²⁷

Furthermore, families of children with uncontrolled seizures experience significantly more stress than those whose children have well-controlled seizures.²⁸ Maternal anxiety is higher in children with poorly controlled seizures and siblings have a higher rate of behavioural problems compared with siblings of children who have less frequent or completely controlled seizures.^{28,29}

Children with epilepsy may also find themselves excluded from group activity due to physical or psychological restrictions eg, sports and games because of the risk of physical injury. Parental overprotection may also restrict children, for instance, in making and maintaining friendships. Social exclusion and restrictions of this kind have been found to contribute to a lower quality of life in children with epilepsy.³⁰

Social exclusion and restrictions are further compounded by the risk of injury or mortality related to epilepsy. Long-term studies have shown that people with epilepsy, including children, have an increased mortality rate compared with the general population.³¹⁻³³ Sudden unexpected death in epilepsy (SUDEP) accounts for 3-31% of all deaths in people with epilepsy – almost one death per year in every 260 people with epilepsy.³⁴ Factors contributing to SUDEP are thought to include uncontrolled seizures or seizures that are refractory to treatment and underlying brain damage.³⁴

Conclusion

Achieving seizure freedom with minimum medication side effects must be the primary goal for the management of epilepsy in children and adolescents to provide the best possible potential for neurological, cognitive and psychosocial development and educational outcomes

Outcomes and quality of life in children and adolescents with epilepsy are influenced by, and related to a complex combination of different internal and external factors. It is therefore important to consider all aspects of a child's development and the long-term impact of different factors when managing childhood epilepsy.

Seizures are a key factor and predictor for the future development of a child who has epilepsy. Seizure activity has both a direct effect on development and outcomes (eg, disruption of normal brain development and related cognitive impairment) and indirect effects (eg, on family members and time missed from school). These effects are over and above the risks of increased mortality and disability or injury associated with epilepsy compared with the general population.

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