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The incidence of unprovoked seizures and occurrence of neurodevelopmental comorbidities in children at the time of their first epileptic seizure and during the subsequent six months

Eva Åndell[a,b,*], Torbjörn Tomson[c], Sofia Carlsson[d], Eva Hellebro[c], Tomas Andersson[d], Cecilia Adelöw[c], Per Åmark[a]

[a] Department of Women's and Children's Health, Karolinska Institutet, 171 77 Stockholm, Sweden
[b] Centre for Clinical Research Sörmland, Uppsala University, 611 85 Nykoping, Sweden
[c] Department of Clinical Neuroscience, Karolinska Institutet, 171 77 Stockholm, Sweden
[d] Institute of Environmental Medicine, Karolinska Institutet, 171 77 Stockholm, Sweden

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Summary
Purpose: To evaluate the incidence of unprovoked seizures in children and the prevalence of related neurodevelopmental comorbidities at the time of the presumed first seizure and six months thereafter.
Methods: The medical records of all children (0—18 years of age) seeking medical attention as the result of a first unprovoked seizure between September 1, 2001 and December 31, 2006, and registered in the population-based Stockholm Incidence Registry of Epilepsy (SIRE) were reviewed. Neurodevelopmental comorbidities were evaluated on the basis of the medical records from this first visit and from other healthcare during the following six months.
Results: The incidence of unprovoked seizures was between 30 and 204/100,000 person years ($n = 766$) in the different age groups. It was highest among the youngest children and lowest among the 18-year-olds with small gender differences. The most common neurodevelopment comorbidities were developmental delay (22%, CI: 19—25%), speech/language and learning

Abbreviations: CP, cerebral palsy; ID, intellectual disability; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorders; SIRE, Stockholm Incidence Registry of Epilepsy; ESSENCE, Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations; BECT, benign childhood epilepsy with centrotemporal spikes.

* Corresponding author at: Hållstavägen 14, 611 39 Nyköping, Sweden. Tel.: +46 0733 204048.
E-mail address: evaandell@gmail.com (E. Åndell).

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difficulties (23%, CI: 20—26%) and intellectual disability (16%, CI: 13—18%). The types of neurodevelopmental comorbidity varied by age at the time of seizure onset, with cerebral palsy being more common among the 0—5-year-olds, attention deficits among the 6—16-year-olds, and autism and psychiatric diagnosis among the older children. An associated neurodevelopmental comorbidity was more common among those experiencing recurrent than single seizures during follow-up six months from the index seizure (42% versus 66%). In 68% (CI: 64—71%) of the children there was no known or suspected neurodevelopmental comorbidity.

Conclusion: The incidence of unprovoked, non-febrile seizures among 0—18-year-olds included in the SIRE was 67/100,000 person-years. Neurodevelopmental comorbidities were common already at the time of onset of the seizure disorder, indicating that neither seizure treatment nor seizures were the underlying cause of other neurodevelopmental symptoms in these patients during the period studied.

Introduction

Among the 0.5—1.0% of children younger than 16 suffering from epilepsy, the most prevalent serious neurological condition in this age group (Kasteleijn-Nolst, 1996; Pellock, 2004), a number have additional neurological and cognitive problems (Pellock, 2004). Such neurodevelopmental comorbidities, including cerebral palsy (CP), intellectual disability (ID), attention deficit hyperactivity disorder (ADHD), autism spectrum disorders (ASD) (Pellock, 2004) and learning problems (Lhatoo and Sander, 2001), aggravate the epilepsy disease burden and must be taken into consideration in connection with treatment strategy and drug selection, as well as when looking for clues to underlying pathophysiological mechanisms. Analogously it has also been shown that that the presence of seizures is a negative prognostic factor for rehabilitation of neurodevelopmental disorders (Chiappedi et al., 2011). Most recent investigations have considered seizures as a comorbidity in neurodevelopmental conditions, rather than neurodevelopmental comorbidities in people with seizures or epilepsy. Neurodevelopmental comorbidities have mostly been assessed in studies involving smaller and sometimes not necessarily representative cohorts of patients (Besag, 2002).

Comparisons of neuropsychological functioning and behavioural and academic performance at the time of seizure onset to healthy siblings (Austin et al., 2011; Baum et al., 2010; Dunn et al., 2010; Fastenau et al., 2009) and to individuals with chronic epilepsy (Guilfoyle et al., 2012) have revealed an elevated risk for neurodevelopmental dysfunction already at the time of onset. Clinicians often disagree about whether the epileptic syndrome and/or the seizures per se, the medication, or other factors give rise to the neurodevelopmental comorbidities (Brown, 2006; Holmes, 2001). Accumulating evidence indicates that certain comorbid disorders, including ADHD (Hesdorffer et al., 2004; Jones et al., 2007), academic problems (Berg et al., 2005; Hermann et al., 2006; Oostrom et al., 2003), depression and suicidal ideation (Hesdorffer et al., 2006), may be present prior to the initial seizure. Our study includes these and additional neurodevelopmental comorbidities in a large, incident, population-based material.

A study design based on analysis of neurodevelopmental comorbidities in patients who have already developed epilepsy does not provide insight into the temporal or potential causal relationship between the onset of seizure and these comorbidities. Moreover, in light of the heterogeneity of seizures, and the possibility that neurodevelopmental comorbidities vary with, e.g., age and seizure type, larger study populations are needed. Accordingly, utilizing the population-based Stockholm Incidence Registry of Epilepsy (SIRE) (Adelow et al., 2009), we have examined here the incidences of first unprovoked epileptic seizures and the prevalence of neurodevelopmental comorbidities (developmental delay, speech/language and learning difficulties, intellectual disability, cerebral palsy, ADHD, autism spectrum disorders and other psychiatric diagnoses) in children (28 days—18 years old) at the time of this presumed first seizure and during the following six months.

Methods

Study population and data collection

From the children in northern Stockholm (an urban area with approximately 1 million inhabitants, of which about 230,000 were younger than 19) 766 cases with newly diagnosed unprovoked seizures were identified and documented in the SIRE from September 1, 2001 to December 31, 2006 as described previously in detail (Adelow et al., 2009). In brief, networks of medical professionals and the EEG laboratories in this area were requested repeatedly to report the unique individual identification numbers for everyone who sought medical advice for anything that could be suspected to be an epileptic seizure. Additional methods to identify cases included review of medical records of all patients discharged from department of paediatrics at the Karolinska University Hospital for the first time with an ICD code of G 40, G 41, or R 56.8, and review of paediatric emergency room records to evaluate possible cases not reported otherwise. Only a few new potential cases were found with the additional methods which showed that the reporting from the paediatric network worked well. Since medical care is free of charge in Sweden children with a noted suspected seizure normally would come to medical attention. If the patient for some reason would attend a medical institute away from home, copies of medical records are usually sent to the ''home-hospital'' and would this way have been identified by us. Looking at the complete register of SIRE