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Citation of this paper:
Prasad, Asuri N.; Burneo, Jorge G.; and Corbett, Bradley, "Epilepsy, comorbid conditions in Canadian children: Analysis of cross-sectional data from cycle 3 of the national longitudinal study of children and youth" (2014). *Paediatrics Publications*. 1874.
https://ir.lib.uwo.ca/paedpub/1874

Seizure 23 (2014) 869–873

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Epilepsy, comorbid conditions in Canadian children: Analysis of cross-sectional data from Cycle 3 of the National Longitudinal Study of Children and Youth

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ARTICLE INFO

Article history:
Received 21 December 2013
Received in revised form 18 July 2014
Accepted 20 July 2014

Keywords:
Epilepsy
Comorbid
Children
Population studies
Cerebral palsy
Learning disability

ABSTRACT

Purpose: The purpose of this study was to analyze national survey data to provide estimates of prevalence of epilepsy and associated developmental disabilities and comorbid conditions.
Methods: We analyzed data from Cycle 3 of Canada's National Longitudinal Survey of Children and Youth. The NLSCY captured, socio-demographic information, as well as age, sex, education, ethnicity, household income, chronic health related conditions from birth to 15 years old. The main survey question intended to identify "epilepsy", "cerebral palsy", "intellectual disability", "learning disability", and "emotional and nervous difficulties" in the population of children surveyed. Prevalence was based on the national cross-sectional sample and used 1000 bootstrap weights to account for survey design factors.
Results: Cycle 3 of the NLSCY had the largest number of patients with diagnosed epilepsy. Prevalence figures (n/1000) for epilepsy and cerebral palsy (EPI_CP), epilepsy and intellectual disability (EPI_ID), epilepsy and learning disability (EPI_LD), and epilepsy and emotional nervous difficulties (EPI_EMO_NERV) were 1.1, 1.17, 2.58 and 1.34 respectively. Amongst children with epilepsy, 43.17% reported the presence of one or more of the above comorbid conditions.
Conclusion: These results provide an initial prevalence estimate of comorbid conditions with epilepsy in Canadian children. In a high proportion of children with epilepsy, the PMK had reported at least one comorbid disorder. These findings carry implications for health care utilization and long-term outcomes. We discuss methodological aspects related to the ascertainment of epilepsy in both surveys, and to the validity and implications of our findings.
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1. Introduction

Epidemiological studies of chronic conditions are useful in determining the distribution and impact of such diseases on child health. Childhood epilepsy is a heterogeneous collection of neurological conditions where epileptic seizures are recurrent, unprovoked and paroxysmal in occurrence. Epilepsy can be the consequence of heritable conditions (genetic) and secondary to a coexistent neurological insult to the brain that is acute or remote in origin. Incidence and prevalence are the most frequently used measures of disease frequency.

Prevalence rates measure the existing number of cases in the population (old and new cases) at a particular point in time (Point prevalence) or over a defined time period (Period prevalence). Prevalence rates estimated through different studies vary depending on how cases are included ("active cases" only vs "active and inactive" and whether cases included single seizures, febrile seizures, and acute symptomatic seizures). Children with epilepsy frequently carry comorbid conditions like cerebral palsy, mental retardation and learning disabilities.[1] Prevalence data on epilepsy vary by geographic region and ethnic group, as well as differ in terms of methods of case ascertainment as well as time trends that reflect changes with age.[2] Population-based studies on prevalence of epilepsy and comorbid conditions are listed among the priorities for the public health dimension of epilepsy in the recent report issued by the Institute of Medicine (IOM).[3]

We previously determined prevalence of epilepsy in Canadian children using Cycles 2 and 3 of National Longitudinal Survey of

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http://dx.doi.org/10.1016/j.seizure.2014.07.012
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Children and Youth (NLSCY) data and found our estimates to be comparable to other published studies.[4] In the present study, we extend the analysis to focus on the comorbid conditions associated with epilepsy in children; namely cerebral palsy, mental handicap (intellectual disability), learning disability, emotional and nervous difficulties using data from Cycle 3 which had the largest number of children diagnosed with epilepsy. The results will allow a comparison with population-based studies of prevalence of epilepsy and comorbidities in other countries.

2. Methods

2.1. About the NLSCY survey

The National Longitudinal Survey of Children and Youth (NLSCY) was designed to study long-term trends in the physical well being and social development of Canadian children from birth to adulthood under the auspices of Social Program Information and Analysis Directorate, Strategic Policy, Human Resources Development Canada and the Special Surveys Division, Statistics Canada.[5]

The study started in 1994 with an initial cohort of children aged 0–11 years, and repeated every 2 years (1994/95, 1996/97, 1998/99, and 2000/2001).

2.2. Sample size

Statistics Canada's Labor Force Survey sample frame was used to select a reliable random sample of the Canadian population in Cycle 1 and a new cohort of 0–2 year olds was added in each new cycle. The sample was intended to be longitudinal and cross-sectional for Cycles 1–4 but this study only used the cross-sectional design. The population sampling frame includes children and youth in Canada's 10 provinces but excludes respondents from the north, persons residing in institutions or children with parents serving in the military.

The population sample sizes were sufficiently large enough to produce reliable estimates of these neurological conditions in the Canadian population; however, the sample estimates may vary somewhat from cycle to cycle. Some variation in the sample estimates are expected and can be due to factors such as natural variations in cycle composition, attrition, changes in the age of individuals in the sample, missing data, some questions such as the presence of a learning disability, intellectual disability restricted to children older than 6 years, changes due to the inclusion of a new cohort of 0–2 year olds in subsequent cycles, and changes in the diagnosis of epilepsy as children age from cycle to cycle. For the purpose of this study, we analyzed data from Cycle 3 that had the largest number of respondents with a total of 31,963 children.

2.3. Measures

In keeping with the NLSCY's survey format the person in the household who was most knowledgeable (PMK) about the child (in most cases the mother) responded to the following questions (HLTQ45A and HLTQ51C in the survey)[5]:

"Does the child have any of the following long-term conditions that have been diagnosed by a health professional? ... Epilepsy?, Cerebral Palsy, Mental Handicap, Learning disability, Emotional, Psychological or nervous difficulties ...." Long-term conditions refer to conditions lasting 6 months or longer.

"Does the child take any of the following prescribed medication on a regular basis: Anti-convulsants or anti-epileptic pills?" (AED).

For comorbid estimates, respondents who reported both epilepsy and the comorbid conditions were assigned a value of 1 and those who did not indicate both conditions were assigned a value of 0.

3. Analysis

Descriptive statistics were generated for Cycle 3 respondents including the number reporting the comorbid condition, the prevalence per 1000 in the population and the estimated number of children and youth affected in Canada. The final estimate was conducted by applying cross-sectional weights, calculated for each cycle by Statistics Canada. Statistical analysis of the dataset was done using IBM®SPSS® v22 for Windows®.

Relative risk ratios indicate increased or decreased risk of having the condition for males compared to females. In addition, relative risk estimates for each of the comorbidities of epilepsy (CP, MR, LD, EMONERV) were obtained for the epilepsy group in comparison to the group of children without reported epilepsy. In a cross-sectional analysis of this nature both odds ratios and relative risks can be used. Relative risk calculations are considered to be more accurate, while odds ratios tend to overinflate the risk estimates. In this context relative risk calculations are considered to be more appropriate. For a discussion on the differences between odds ratios and relative risk the reader may consult the provided reference.[6,7] Relative risk calculations were done by creating a two by two table using an online calculator MEDCALC (URL: http://www.medcalc.org/calc/relative_risk.php).

3.1. Weights

Cross-sectional weights representing the cross-sectional sample were calculated by Statistics Canada, for each cycle. Statistics Canada also provides 1000 bootstrap sample weights for simulating the bootstrap method.[8] Both methods were used for producing point estimates with no observed differences in the estimates.

Cross-sectional weights were used to produce population estimates that were used to estimate the number of children and youth in the population with epilepsy alone and epilepsy and one of the four comorbidities.

3.2. Missing data

The overall response rate to questions in the survey pertinent to demographics and gender was 100%. The response rate however varied with different questions in the survey, as a result of which response rates were not uniform for all the questions posed in the survey. There were a total of 30,592 valid responses (95.7%) and 1371 missing responses (4.3%) in the dataset for the primary question on epilepsy (HLTQ45A). There were no missing responses to the question components addressing comorbid conditions surveyed. In an effort to understand missing data patterns in the Epilepsy variable we conducted a logistic regression where the dependent variable was coded as missing (coded as 1) or not missing (coded 0). This missing indicator variable was analyzed to determine if there was systematic "missingness" in the epilepsy variable.

We recoded the age categories into indicator variables where children who were, for example, 5 years old would be coded as 1 in the variable age-five and children of any other age would be coded as 0. The age groups 0–2 were combined due to a low sample sizes in some age groups. Similarly, children who were 16 years old at the time of the survey were included in the 15 year old category for the same reason.

The findings indicated a much lower number of missing responses among the cohort of 6 years and younger in comparison with the group that was 7 years and older. The findings also indicate females are much approximately 25% more likely to have missing data on the epilepsy variable when compared to males. We believe that the missing data do not carry a major impact on the results and conclusions drawn in this study. Our suspicion is that

many of the missing values in the older children may relate to the self-reporting mechanism of the survey. The expected dissipation of symptoms in older children could lead to some confusion when parents tried to answer the question 'Does your child have epilepsy?'

4. Results

There were a total of 31,963 children in the survey (Males 51.3%, Females 48.7%). In Cycle 3, 161 children were identified as having epilepsy diagnosed by a health professional. In terms of age distribution, there were 11,190 children (birth to 5 years), 11,348 children (6–10 years) and 8054 children (10–15 years).

The prevalence of epilepsy in Cycle 3 (5.3/1000) children has already been published in a prior study while the prevalence of treated epilepsy was lower (3.82/1000) children. Not all children reported diagnosed with epilepsy were being actively treated with anticonvulsant/antiepileptic drugs. One can speculate as to whether the higher prevalence rates in response to the question HLTQ45A included those responses where the epilepsy was either untreated, as well those whose epilepsy was in remission. The survey data do not allow for the analysis of sub-groups and do not permit us to answer the question on the use of AED's for indications other than epilepsy in the survey population.

The comorbid disorders associated with epilepsy in the cross-sectional analysis were surveyed on the basis that the PMK had answered in the affirmative to both sections of the HLTQ45A that referred to the particular chronic conditions in the answers. In Cycle 3 the prevalence figures (n/1000) epilepsy and cerebral palsy (EPI_CP), epilepsy and intellectual disability (EPI_ID), epilepsy and learning disability (EPI_LD), and epilepsy and emotional nervous difficulties (EPI_EMO_NERV) were 1.1, 1.12, 2.58 and 1.34 respectively (Table 1). In the same cycle we surveyed, the relative proportion of children with epilepsy alone accounted for 56.87%, while 10.03% reported at least one comorbid condition, 23.57% had at least two comorbid conditions while 9.53% had three or more conditions.

In a further analysis of the Cycle 3 data the role of gender differences in the likelihood of having epilepsy and associated conditions was examined by calculating the relative risk (Table 2). Statistically significant relative risks ($p < 0.05$) indicate that male children in the survey were more likely to have epilepsy without any associated comorbidity (1.63, 95% CI 1.18–2.24, $p = 0.003$). Further, male children with epilepsy were less likely to carry an associated learning disability (0.502, 95% CI 0.28–0.902, $p = 0.025$) in comparison to females with epilepsy in the survey population. There were no statistically significant differences between male and female children with respect to epilepsy associated with cerebral palsy and intellectual disability (Table 2).

Finally, relative risk and confidence intervals for comorbidities in children with epilepsy and without epilepsy was significant ($p < 0.001$) revealing a greater risk for the epilepsy group. When the comorbid condition is itself treated as an independent variable the risk of epilepsy remains high (Table 3). The relative risk of cerebral palsy was (RR 136.08, 95% CI 91.27–202.90) and for intellectual disability/mental handicap was (RR 65.08, 95% CI 46.53–91.04) in children with epilepsy based on survey data.

5. Discussion

The NLSCY survey provides useful and valid estimates of the prevalence of epilepsy and use of AEDs in Canadian children birth to 15 years. In a previous study using the NLSCY data, robust estimates of prevalence figures were obtained in Cycles 2 and 3 (2: 1996–1997, 3: 1998–1999).[4] The prevalence rates estimated by the present survey in Canadian children from birth to 15 years is 5.3/1000, corresponding to a population-based estimate of 32,045 affected children in the Canadian population. These results are

Table 1
Prevalence of epilepsy and comorbid disorders in Canadian children – cross-sectional analysis (NLSCY data) from Cycle 3.

	Total valid responses	Yes	No	Prevalence/ 1000	Estimated number of affected children in Canada (Census data)
Epilepsy prevalence self reported	30,592[a]	161	30,431	5.3	32,045
Epilepsy prevalence (treated epilepsy)	31,963	122	31,841	3.82	18,952
Epilepsy and cerebral palsy	31,963	36	31,927	1.1	6949
Epilepsy and intellectual disability	31,963	38	30,925	1.17	7581
Epilepsy and learning disability	19,402[b]	50	19,352	2.58	10,107
Epilepsy and emotional and nervous symptoms	19,402[b]	26	19,376	1.34	5243

[a] There were 1371 missing responses for HLTQ45 from a total number of children 31,963 in Cycle 3 of the NLSCY.
[b] The denominator is smaller as these two questions were deemed to be not applicable to the children in the survey under the age of 6 years (12,564).

Table 2
Gender differences in children with epilepsy and comorbid conditions in Cycle 3 of NLSCY.

Condition	Total	Male	Female	Relative risk (male)	95% Confidence intervals	p value (significant ≤ 0.05)
Epilepsy +	161	102	59	1.63	1.18–2.24	0.003
Epilepsy –	30,431	15,656	14,775			
Epilepsy + and CP +	36	20	16	1.19	0.62–2.29	0.61
Epilepsy – and CP –	31,927	16,370	15,557			
Epilepsy + and intellectual disability +	37	18	19	0.90	0.47–1.71	0.75
Epilepsy – and intellectual disability –	31,925	16,371	15,554			
Epilepsy + and learning disability +	49[a]	17	32	0.502	0.28–0.902	0.025
Epilepsy – and learning disability –	31,914	16,373	15,541			
Epilepsy and emotional/nervous symptoms				Suppressed due to low n values[b]		

+ sign indicates that there was a "yes" response to the relevant survey question on the epilepsy and/or comorbid condition, while the "–" sign indicates a "no" response.
[a] In one case the value of the weight variable was zero, negative, or missing. Such cases are invisible to statistical procedures and graphs which need positively weighted cases, and hence a discrepancy of n of 1 in the total number of males and females in each category in comparison to Table 1 which gave total n values for each category in the survey.
[b] Low cell counts in this category; Statistics Canada confidentiality rules do not permit release of this data.

Table 3
Relative risk analysis of epilepsy and comorbid conditions.

	Variable +	Variable −	Relative risk (RR)	96% CI limits	Z statistic	*p* values
	Epilepsy+	Epilepsy−				
CP+	36	50	136.08	91.271–202.90	24.109	<0.0001
CP−	125	30,380				
	CP+	CP−				
Epilepsy+	36	125	102.1563	75.35–138.50	29.791	<0.0001
Epilepsy−	50	30,380				
	Epilepsy+	Epilepsy−				
ID+	38	109	65.08	46.53–91.04	24.38	<0.0001
ID−	123	30,322				
	ID+	ID−				
Epilepsy+	38	123	63.98	46.199–88.61	25.02	<0.0001
Epilepsy−	109	30,322				
	Epilepsy+	Epilepsy−				
LD+	50	1057	6.2823	4.98–7.92	15.533	<0.0001
LD−	95	18,200				
	LD+	LD−				
Epilepsy+	50	95	8.7	6.21–12.18	12.58	<0.0001
Epilepsy−	1057	18,200				
	Epilepsy+	Epilepsy−				
Emonerv+	26	394	8.76	6.10–12.60	11.8	<0.0001
Emonerv−	119	18,863				
	Emonerv+	Emonerv−				
Epilepsy+	26	119	9.87	6.53–14.92	10.86	<0.0001
Epilepsy−	394	18,863				

CP = cerebral palsy, ID = intellectual disability, LD = learning disability, Emonerv = emotional nervous symptoms, + sign indicates a Yes response in the survey, − sign indicates a No response in the survey.

similar to estimates obtained through other national and provincial surveys.[9]

Cycle 3 of the NLSCY had the largest number of respondent cases of epilepsy. For this reason, we have limited our discussion of prevalence of comorbid disorders to the respondents in this cycle. Based on the answers to the question HLQT45A in the survey, we were able to estimate the prevalence of four comorbid conditions i.e. cerebral palsy, intellectual disability, learning disability, and presence of emotional and nervous symptoms.

The most salient finding in this study was the high association with comorbid developmental disabilities in children with epilepsy. Forty three percent of the children had comorbid conditions, as many as 33% had two or more conditions. Compared to children not reported to have epilepsy, the relative risk of a comorbid condition (CP, ID, LD, EMONERV) in the population of children with epilepsy is statistically significant. The risk is particularly high for cerebral palsy dependent on epilepsy, as well as for epilepsy dependent on cerebral palsy. This finding is biologically plausible as a significant proportion of childhood epilepsy is either cryptogenic or symptomatic in etiology, suggesting that epilepsy in these children is attributable to abnormalities in the developing nervous system, a feature common to cerebral palsy as well.[10]

In general, epilepsy prevalence estimates generated through this analysis are similar to other population-based studies in the developed world.[11,12] However, these estimates are lower in comparison to prevalence rates reported from Latin America, South Asia and other developing nations.[1,9,10] The higher prevalence of head injury, acute infections (meningitis and encephalitis), poor prenatal and intrapartum care, chronic CNS infections like neurocysticercosis and tuberculosis likely contribute to observed differences.[13]

In the Metropolitan Atlanta Developmental Disabilities study multiple source case ascertainment was used to confirm a diagnosis of epilepsy, the lifetime prevalence of epilepsy was 6/1000 (95% CI 5.5–6.5), and 35% reported an additional disability (MR, CP, LD, Visual or hearing impairment).[14] Similarly in the study reported from Turku, Finland an associated neurological deficit was reported in 39.9%, learning disabilities in 23.1%, mental retardation in 31.4%.[12] In a Swedish study a prevalence rate of 4.2/1000 was reported, the associated comorbidity of mental retardation was estimated to be 1.7/1000.[11] In a recent study on the profile of epilepsy in children 0–17 years of age in the US, a current prevalence rate was 6.3/1000 (95% CI 4.9–7.8) and a lifetime prevalence of epilepsy/seizure disorder was 10.2/1000 (95% CI 8.7–11.8). The study reported an increasing prevalence of epilepsy with age, a male preponderance as well as a larger number of mental health and developmental comorbidities.[10] Of particular significance is the occurrence of developmental delay (50%) and learning disabilities (56%) in this survey population.

The association between learning disability, mental retardation, and epilepsy has been documented in population-based studies. It is estimated that 20–25% of people with moderate to severe learning disabilities have epilepsy as a comorbid condition.[12,15]

A highly significant association of epilepsy with cerebral palsy has been noted in clinical studies. In one study, nearly half (47%) of the patients diagnosed with spastic quadriplegic cerebral palsy, also had epilepsy.[16] Similarly in a 10 year follow up of epilepsy the Dutch population-based study on cerebral palsy, epilepsy was a comorbid condition in 21.3%, and active epilepsy in 18.9%.[17]

The finding of a statistically significant male preponderance of epilepsy in Canadian children has not been previously reported. Similarly, the preponderance of learning disabilities in female children with epilepsy, observed in this survey, is surprising since a slight male preponderance has been suggested in other population studies. Furthermore, in healthy children, reading disabilities are reportedly more frequent in males. The issue of gender differences in the prevalence rates for epilepsy has been considered in other population studies and a slight male preponderance is generally accepted.[10,14] Gender differences in children with learning disability without epilepsy are considered to be controversial, a

male vulnerability has been suggested in some studies with regard to reading disability.[18] Whether there are biological or multifactorial causes underlying gender differences and learning disabilities still needs to explored.[19]

In conclusion, the findings of this national study provide valid and reliable estimates of prevalence rates for epilepsy in Canadian children, as well as for each of the four comorbid conditions selected. In addition, the findings suggest that a significant proportion of children with epilepsy have associated comorbid neurological impairment (cerebral palsy) and other developmental disabilities. The associated comorbid condition may be under diagnosed leaving these children at risk of academic under achievement, and any remedial interventions that could be of value may be delayed.

There are several limitations to this study as it utilizes survey data to understand the epidemiology of epilepsy. However, the estimates of epilepsy obtained in this analysis are remarkably close to the Canadian data from previous Canadian surveys as well as from those from other countries.[9,12]

Epilepsy is a dynamic condition; as children grow older new cases can be diagnosed in some, while others may go into remission. It is therefore difficult to precisely capture the total number of children who are impacted by epilepsy during childhood in cross-sectional surveys of this nature. A longitudinal study of the eight cycles of the NLSCY is planned, the results of which may shed further light on the direction and trajectories of epilepsy and comorbidities.

Another limitation that has to be considered is that the' report of epilepsy may be less reliable than measures diagnosed by a physician. To avoid this problem the survey question specifically asked if the condition had been chronic (lasting longer than 6 months) and had been diagnosed by a physician. Underreporting could still occur as families may not have accepted the diagnosis of epilepsy, or may have been given an alternate diagnosis such as seizure disorder, or may have been prescribed AEDs for conditions other than seizures (e.g. psychiatric diagnoses).

The NLSCY survey did not include questions about comorbidities associated with epilepsy syndromes, seizure type and severity of epilepsy. Therefore, we were unable to sub-classify epilepsy diagnoses providing added clinical data relevant to this discussion. Finally, there is lack of information about etiology as well as the temporal contiguity of the onset of the comorbid condition (before or after onset of epilepsy).

Notwithstanding these limitations, the NLSCY data proves to be a useful resource in understanding the epidemiology and the social determinants of epilepsy. Information in such studies should always be considered in concert with each other rather than on their own merit. The combined knowledge from both clinical and population studies find their strength when they find agreement on the issue and present opportunities for inquiry when they disagree.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Acknowledgements

This study was supported by a "Eplink" team grant funded by the Ontario Brain Institute (OBI) (Eplink-The Epilepsy Discovery Program Project #9). ANP and JB are Eplink investigators. Access to the NLSCY microdata files was granted through an application to the CISS-Access to the RDC's Program. While the research and analysis are based on data from Statistics Canada, the opinions expressed do not necessarily represent the views of Statistics Canada.

References

1. Cowan LD. The epidemiology of the epilepsies in children. *Ment Retard Dev Dis* 2002;**8**:171–81.
2. Leviton A, Cowan LD. Methodological issues in the epidemiology of seizure disorders in children. *Epidemiol Rev* 1981;**3**:67–89.
3. Berg AT, Baca CB, Loddenkemper T, Vickrey BG, Dlugos D. Priorities in pediatric epilepsy research: improving children's futures today. *Neurology* 2013;**81**:1166–75.
4. Prasad AN, Sang X, Corbett BA, Burneo JG. Prevalence of childhood epilepsy in Canada. *Can J Neurol Sci* 2011;**38**:719–22.
5. Statistics Canada Special Surveys Division, Human Resources Division Canada. *National Longitudinal Survey of Children and Youth (NLSCY): Cycles 1-8 [Canada] [longitudinal survey data]. Ottawa, Ontario*. 2010.
6. Davies HT, Crombie IK, Tavakoli M. When can odds ratios mislead? *BMJ* 1998;**316**:989–91.
7. Schmidt CO, Kohlmann T. When to use the odds ratio or the relative risk? *Int J Pub Health* 2008;**53**:165–7.
8. Mooney CZ, Duval RD. *Bootstrapping: a nonparametric approach to statistical inference*. Newbury Park, CA: Sage Publications; 1993.
9. Wiebe S, Camfield P, Jette N, Burneo JG. Epidemiology of epilepsy: prevalence, impact, comorbidity and disparities. *Can J Neurol Sci* 2009;**36**(Suppl. 2):S7–16.
10. Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. *Pediatrics* 2012;**129**:256–64.
11. Sidenvall R, Forsgren L, Heijbel J. Prevalence and characteristics of epilepsy in children in northern Sweden. *Seizure* 1996;**5**:139–46.
12. Sillanpaa M. Epilepsy in children: prevalence, disability, and handicap. *Epilepsia* 1992;**33**:444–9.
13. Newton CR, Garcia HH. Epilepsy in poor regions of the world. *Lancet* 2012;**380**:1193–201.
14. Murphy CC, Trevathan E, Yeargin-Allsopp M. Prevalence of epilepsy and epileptic seizures in 10-year-old children: results from the Metropolitan Atlanta Developmental Disabilities Study. *Epilepsia* 1995;**36**:866–72.
15. Lhatoo SD, Sander JW. The epidemiology of epilepsy and learning disability. *Epilepsia* 2001;**42**(Suppl. 1):6–9. discussion 19–20.
16. Venkateswaran S, Shevell MI. Comorbidities and clinical determinants of outcome in children with spastic quadriplegic cerebral palsy. *Dev Med Child Neurol* 2008;**50**:216–22.
17. Wichers MJ, Odding E, Stam HJ, van Nieuwenhuizen O. Clinical presentation, associated disorders and aetiological moments in cerebral palsy: a Dutch population-based study. *Disabil Rehabil* 2005;**27**:583–9.
18. Rutter M, Caspi A, Fergusson D, et al. Sex differences in developmental reading disability: new findings from 4 epidemiological studies. *JAMA* 2004;**291**:2007–12.
19. Liederman J, Kantrowitz L, Flannery K. Male vulnerability to reading disability is not likely to be a myth: a call for new data. *J Learn Disabil* 2005;**38**:109–29.