

Original article:

Neurobehavioral disorders in childhood epilepsy : a prospective, cross-sectional survey

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Abstract:

Objective: Epilepsy is the commonest neurological disorder of childhood and 1 in 5 epileptic has a behavioural disorder

Participants: After IRB clearance, 100 consecutive, aged 4-12 years children with a history of epilepsy of at least one year duration were enrolled as cases and 100 controls. A baseline IQ test was performed .

Intervention: All the participants were administered an SDQ (Strength and Difficulty Questionnaire), available in Hindi, that records competencies of children in five domains such as emotional issues (fear, nervousness), behavioral issues (hyperactivity), prosocial tendencies, conduct problems (tantrums, lying, stealing) and problems in peer relationships. The data was analysed using the chi – square test also age, sex adjusted logistic regression multivariate analysis for outcome variables such as conduct disorders, hyperactivity and no specific complaints was done.

Results: The mean (SD) ages of the cases and controls were 9.05 (1.99) and 8.65 (2/05) years respectively (p=0.17). A higher proportion of cases had conduct disorders and hyperactivity compared with controls (conduct disorders: 16% vs 6%, p=0.02 and hyperactivity: 16% vs 6%, p=0.02). Four epileptic children were school dropouts. With logistic regression multivariate analysis cases were significantly more likely to have conduct disorders (OR: 3.11, 95% [CI]: 1.15-8.39) and hyperactivity (OR: 3.35, 95% CI: 1.22-9.19) compared with controls.

Discussion: Neurobehavioral comorbidity of epilepsy is now accepted as a major cause of potentially treated disability. In our study epileptic children had significantly higher externalizing behavior problems such as conduct disorders and hyperactivity compared with healthy siblings.

Conclusions: Neurobehavioral disorders are significant comorbid conditions seen in epileptics which cannot be ignored ; these require timely assessment and intervention for a holistic qualitative outcome.

Keywords: Neurobehavioral disorders, Epilepsy, SDQ

Introduction:

Childhood epilepsy is a common, chronic and challenging illness for children and their families (1). Epilepsy is a heterogeneous condition of recurrent seizures with varied etiologies and

consisting of different syndromes with different seizures types. The unpredictability and distressing nature of the seizures and social stigma associated with epilepsy are assumed to influence psychological development and often impact the

quality of life, causing neurobehavioral disorders. (2,3). A spectrum of neurodevelopmental disorders are found to occur at a higher rate in children and adolescents with epilepsy. These include intellectual disabilities, autism, attention problems and / or attention deficits / hyperactivity disorders (ADHD), depression, anxiety and psychotic disorders (4).

Methods:

A case control study was conducted at the paediatric epilepsy clinic in a tertiary care metropolitan hospital in Mumbai, India after institutional review board clearance. We included 100 consecutive children aged between four and 12 years with a history of epilepsy of at least one year duration as cases for the present study. We excluded children with neuro-developmental disorders (such as cerebral palsy, autism, genetic abnormalities, intellectual disabilities, febrile or metabolic seizures). We included children in the same group with no history of epilepsy, of similar age, gender and socio economic status as controls. All the cases and controls were evaluated by the Kamat Binet Test of Intelligence and had an IQ level above 80-85.

We administered the Strengths and Difficulties Questionnaire (SDQ)(5), a validated tool, includes 25 questions covering the following five domains: emotional (fear, nervousness); hyperactivity; prosocial behavior; conduct problems (lying, tantrums, stealing); and peer problems. We also collected information on the type of epilepsy, etiology, medications, outcome of treatment, any other medical diagnosis, demographic details in all the cases and controls.

Data were entered in Ms Excel (Microsoft, USA) and converted to Stata Version 13 (Stata Corp, College Station, Texas, USA) for analysis. Descriptive analysis included means and standard deviations (SD) for linear variables and proportions

for categorical variables. The means were compared using the t-test and the proportions were compared using the chi square test or Fisher's exact test for low expected cell counts. We also used the logistic regression for multivariate analysis, the outcome variables in the models were: conduct disorders, hyperactivity; and no specific complaints. We adjusted for age and sex in these logistic regression models.

Results

The mean (SD) ages of the cases and controls were 9.05 (1.99) and 8.65 (2/05) years respectively ($p=0.17$). About 51% of the cases and 49% of the controls were males; the difference in the proportions was not statistically significant ($p=0.77$). We found that 81% of the cases had generalised epilepsy and 92% were idiopathic in etiology. About 89% of the cases were on monotherapy and 11% were on polytherapy; a higher proportion of children on polytherapy had uncontrolled epilepsy compared with those on monotherapy even though the difference was not statistically significant (27% vs 12%, $p=0.18$). Most of the children were on sodium valproate (70%) or carbamazepine (38%) and a small proportion of them were on phenytoin (2%) or newer drugs (4%). About 8% of the cases were diagnosed with a neuropsychiatric problem and 4% were on medications.

We found that a significantly higher proportion of cases had conduct disorders and hyperactivity compared with controls (conduct disorders: 16% vs 6%, $p=0.02$ and hyperactivity: 16% vs 6%, $p=0.02$). Furthermore, we also found that only cases had emotional disorders (6% vs 0%, $p=0.03$) and other non specific complaints (6% vs 0%, $p=0.03$) and lack of prosocial skills (1% vs 0%, $p>0.99$). The non specific complaints were few overactivity, inattention traits, difficultness, resistance to control, unadaptability. Certain

demographic and clinical characteristics of cases and controls are presented in Table 1.

In the logistic models, we found that after adjusting for age and sex cases were significantly more likely to have conduct disorders compared with controls (Odds ratio [OR]: 3.11, 95% confidence intervals [CI]: 1.15 to 8.39). Similarly, cases were significantly more likely to report hyperactivity compared with controls (OR: 3.35, 95% CI: 1.22 to 9.19). However, cases were significantly less likely to report non specific complaints compared with controls (OR: 0.28, 95% CI: 0.13 to 0.59). Overall, we found that children in the age group of 10 to 12 years were less likely to report hyperactivity compared with children aged 4 to 7 years (OR: 0.25, 95% CI: 0.06 to 1.02). In addition, girls were less likely to report hyperactivity compared with boys (OR: 0.36, 95% CI: 0.12 to 1.04). We have presented the unadjusted and adjusted estimates for three outcomes (conduct disorders, hyperactivity, and non-specific complaints) in Table 2.

Discussion

Neurobehavioral comorbidity of epilepsy is now accepted as a major cause of potentially treated disability and is also an important area of epilepsy research (6). Psychiatric comorbidity can precede or follow the development of epilepsy and there is increasing evidence that this bidirectionality reflects the existence of common mechanisms underlying both epilepsy and psychopathology involving frontotemporal limbic structures and an increased cortisol production due to a hyperactive hypothalamic – pituitary – adrenal axis(7).

Epileptic children are up to 4.7 times more likely to have behavior problems than controls (8) similar to our study. Children with epilepsy also have more behavior problems than children with other chronic non neurological conditions(9).In comparison to generalised seizures, focal type especially temporal lobe epilepsy is associated with a higher risk of

psychopathology in children, which is consistent with the majority of adult studies(10).

The potential risk of emotional side effects in polytherapy regiments has been widely studied. Although certain studies (11) found a significant relationship between polytherapy and behavior problems, in contrast, other studies have offered more equivocal results(12).

In our study epileptic children had significantly higher externalizing behavior problems such as conduct disorders and hyperactivity compared with healthy siblings. Other factors significantly associated with hyperactivity were male gender, younger children. These observations are similar to findings of Austin et al(13). Certain studies have identified more boys with behavior problems (14) , particularly disruptive disorders (15) . Other studies reports no gender differences (16) or greater risk in girls . Similar conflicting findings have been demonstrated for chronological age (17).

The prevalence of ADHD in epileptics is much higher than the general population, ranging widely between 8% and 77% (18) .Our results showed that 16% of epileptic children had ADHD when they had normal intelligence and their seizures were well-controlled. In addition , there was no difference in ADHD accompaniment in comparison with healthy siblings controls. Disorders of attention may be the most frequent behavioral problems in children with epilepsy (19). Mc Dermott et al. reported hyperactivity in 28% of children with epilepsy as compared to 13% of those with heart disease and 5% of controls (20).

Conclusion

The study indicates that a clear association of neurobehavioral disorders in epileptic children exists. Often in clinical practise, neuropsychiatric co morbidities is either missed or if identified is considered an integral part of epilepsy. Therefore routine monitoring through a multidisciplinary

approach with an early intervention is necessary to provide a holistic quality of care for children with epilepsy.

What this paper adds :

1. The prevalence of behavior problems in children with epilepsy in India is high .
2. These children with epilepsy have particular problem with hyperactivity and conduct.
3. In epileptic children with hyperactivity a clear predeliction for male gender and younger ages was seen.

Table 1: Demographic data and SDQ domain characteristics of 100 epileptic cases and controls

	Cases n (%)	Controls n (%)	p value
All	100 (100)	100 (100)	
<i>Demographic characteristics</i>			
<i>Age (years)</i>			
4-7	32 (32)	25 (25)	0.45
7.1 – 10	39 (39)	39(39)	
10.1 - 12	29 (29)	36 (36)	
<i>Sex</i>			
Male	58 (58)	60 (60)	0.77
Female	42 (42)	40 (40)	
<i>Clinical Domains on SDQ</i>			
<i>Conducttraits</i>			
Present	16 (16)	6 (6)	0.02
Absent	84 (84)	94 (94)	
<i>Hyperactivity traits</i>			
Present	16(16)	6(6)	0.02
Absent	84(84)	94(94)	
<i>Emotional Problems</i>			
Present	6(6)	0 (0)	0.03
Absent	94(94)	100(100)	
<i>Peer relationships affected</i>			
Present	6(6)	0 (0)	0.03
Absent	94(94)	100(100)	
<i>Prosocial skills</i>			
Present	1 (1)	0 (0)	>0.99
Absent	99(99)	100(100)	
<i>Nothing significant</i>			
Present	68(68)	88(88)	0.001
Absent	32(32)	12(12)	

Table 2: Table showing the unadjusted and adjusted(for age and gender) estimates for three outcomes of conduct disorders, hyperactivity and non-specific complaints

	Unadjusted Models	Adjusted Models		
		Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Clinical features				
Conduct				
Cases	2.98 (1.12 to 7.98)	3.11 (1.15 to 8.39)	--	--
Controls	Reference	Reference		
Hyperactivity				
Cases	2.98 (1.12 to 7.98)	--	3.35 (1.22 to 9.19)	--
Controls	Reference		Reference	
No specific complaints				
Cases	0.28 (0.13 to 0.60)	--	--	0.28 (0.13 to 0.59)
Controls	Reference			Reference
Age (years)				
10.1 – 12		0.75 (0.24 to 2.35)	0.25 (0.06 to 1.02)	1.24 (0.50 to 3.07)
7.1 – 10		0.72 (0.24 to 2.17)	1.03 (0.37 to 2.87)	0.87 (0.37 to 2.05)
4 – 7		Reference	Reference	Reference
Sex				
Female		1.59 (0.64 to 3.94)	0.36 (0.12 to 1.04)	1.14 (0.56 to 2.32)
Male		Reference	Reference	Reference

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