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SEIZURE DISORDERS

AUTISM AND EPILEPSY

The prevalence of autistic spectrum disorder (ASD) in children (2-18 years of age) with epilepsy was evaluated at a Tertiary Care Epilepsy Clinic at the Hospital for Sick Children, Toronto, Canada. ASD was assessed using parent questionnaires (ASQ), based on the DSM-IV diagnostic criteria, and age and language development of the child (Berument, Rutter, Lord, 1999). The questionnaire also related to sleep disorders, behavior, types of seizures, and antiepileptic medication (AED). Of 290 questionnaires distributed, 107 were returned, and 97 (32%) subjects were considered at risk of having ASD. The mean age was 12.7 years. A diagnosis of ASD had not previously been suspected in the majority. Patients with scores above the ASQ diagnostic cutoff of 15 (31 [32%]) were assigned to the ASD group, and those with scores below the ASQ cutoff (66 [68%]) were included in the non-ASD group. A comparison of ASD and non-ASD groups showed a similar mean age (10.53 and 11.07 years, respectively); similar body mass indices; male sex in 61% and 49% (difference NS); younger mean age at first seizure in ASD group (21 months vs 55 months; p=0.0001); greater mean number of AEDs (SD) used in ASD group (1.77+/-0.80 vs 1.45+/-0.91; p=0.04); average seizure frequency 10.5 and 5.38 per month (difference NS); number with generalized seizures 12/29 (41%) vs 29/61 (47%). Sleep-related problems in the ASD group included an increased frequency of nocturnal arousals, 38% vs 17% (p=0.06); difficulty in falling back to sleep after arousal (42% vs 18% [p=0.02]); early morning awakening in 55% vs 26% (p=0.01); and more daytime sleepiness reported by teachers, 73% vs 45% (p=0.01). Behavioral scores pertaining to attention, hyperactivity, and impulsiveness were worse in the ASD vs non-ASD groups, 3,7 vs 2.2 (p=0.001). Sleep-disordered breathing was strongly associated with a worse mean behavioral score of 3.45 in the ASD group vs 2.17 for non-ASD subjects. (Clarke DF, Roberts W, Daraksan M et al.

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The prevalence of autistic spectrum disorder in children surveyed in a tertiary care epilepsy clinic. **Epilepsia** December 2005;46:1970-1977). (Reprints: Dr Dave F Clarke, University of Tennessee Health Science Center, 777 Washington Ave, Suite 250, Memphis, TN 38105).

COMMENT. The Committee on Children with Disabilities of the American Academy of Pediatrics (AAP) recommends a prolonged sleep-deprived EEG in autistic children with regression.[1] Sleep disorders are reported in children with epilepsy,[2,3] and in those with autism.[4] Sleep EEGs are abnormal in children with autism and subclinical seizures, and treatment with the anticonvulsant, valproate results in improvement in language and social skills,[5] an observation confirmed in children with autism and epilepsy.[6]

The present report emphasizes the importance of clinical vigilance for symptoms of regression and autism in children with an onset of epilepsy. The authors also demonstrate the frequency of sleep and behavioral disorders in children with co-morbid symptoms of epilepsy and autistic spectrum disorder. Other co-morbidities frequently associated with epilepsy include ADHD, developmental disabilities, migraine, depression/anxiety, and accidental injury.[7] Children with autism and co-morbid cognitive impairment are at higher risk for epilepsy and abnormal EEGs ($p<0.05$), according to a recent retrospective study of 56 patients with autism referred for routine EEG.[8] The findings corroborate the recommendation of the AAP committee concerning EEG in children with autism and regression of language and communication, but do not support routine EEG in higher-functioning autistic children, unless they have episodic symptoms suggestive of epilepsy. 1) CCD AAP. **Pediatrics** 2001;107:1221-1226; 2) Cortesi F et al. **Epilepsia** 1999;40:1557-1565; 3) Becker DA et al. **Epilepsy & Behav** 2004;5:708-715; 4) Patzold LM et al. **J Paediatr Child Health** 1998;34:528-533; 5) Plioplys AV. **Arch Pediatr Adolesc Med** 1994;148:220-222; 6) Hollander E et al. **J Clin Psychiatry** 2001;62:530-534; 7) Pellock JM. **Neurology** 2004;62(Suppl 2):S17-S23; 8) Gabis L et al. **Epilepsy & Behav** 2005;7:652-656.

Genetics of autism and epilepsy. The inheritance patterns of both autism and epilepsy are heterogeneous and complex. In a search for autism loci by combined analysis of the Autism Genetic Resource Exchange (288 families) and 26 Finnish families, the most promising shared locus was on 3p24-26. Earlier identified loci on 3q25-27 or 17p12-q21 did not show increased linkage evidence by the combined data analysis. The oxytocin receptor gene (*OXTR)* was highlighted for further analysis as a gene for autism. (Ylisaukko-oja T et al. **Ann Neurol** Jan 2006;59:145-155). In contrast to autism, the genetics of epilepsy is better understood, particularly with regard to the idiopathic generalized epilepsies, and especially the syndromes of generalized epilepsy with febrile seizures plus (GEFS+). GEFS+ comprises a variety of phenotypes in a single family, ranging from typical febrile seizures to severe myoclonic epilepsy of infancy (Scheffer IE. **Acta Neurol Scand** Dec 2005;112(Suppl 181):47-51; Ottman R. **Epilepsia** 2005;46(Suppl 10):7-14). A family with both GEFS+ and autism in several members is described, showing a genetic relationship between epilepsy and autism. (Dixon-Salazar TJ. **J Child Neurol** Aug 2004;19:597-603).

New theories of autism: hyper-systemising and assortative mating. Autism spectrum disorder is the result of a systemizing mechanism (SM) being set too high, resisting change and preferring predictability and repetition (eg. mathematics, engineering). Autism in a child is the result of having 2 systemisers for parents (assortative mating). (Baron-Cohen S. **Arch Dis Child** Jan 2006;91:2-5).