

Autism: Electroencephalogram Abnormalities and Clinical Improvement With Valproic Acid

Autism is a severe disorder of social and communicative development. Although there are a number of biomedical causes of autistic symptoms,¹ a cause has not been identified for the majority of children with this condition. There is a much higher prevalence of epilepsy and electroencephalographic (EEG) abnormalities in autistic children as compared with controls.^{2,3} However, it is not clear whether autistic children with epileptiform abnormalities on EEGs (spikes and/or sharp waves) who have never had seizures would benefit from anticonvulsants. In a comprehensive review of autism, Minshew et al⁴ mentioned nonconvulsive seizures as a possible association with autism but recommended further testing and anticonvulsants only in those children with clinical indications of possible epileptic phenomena. More significantly, in a recent review of autism, Rapin⁵ wrote: "There is little evidence to suggest that seizure-free children with rare spikes or other paroxysmal EEG discharges will benefit from anticonvulsants."

In my report, I describe three children with autism who had no clinical suggestion of seizures. Each child had epileptiform findings on EEGs. Each significantly improved with the use of valproic acid.

Report of Patients. *Patient 1.* A boy, aged 5 years 2 months, was seen for assessment of speech delay and autistic symptoms. The pregnancy was without complications. Labor was full term and started spontaneously. Because the labor failed to progress, he was delivered by cesarean section at a birth weight of 3.9 kg. There were no complications at the time of birth and his postnatal course was unremarkable. His only past medical problem was recurrent otitis media. His gross motor developmental milestones were normal. He started saying his first words at 4 years of age. Owing to delayed development of language, he underwent a speech therapy assessment at 4 years of age. His receptive language skills were from 14 to 16 months of developmental age and expressive language skills, 13 to 15 months. Results of formal hearing and ophthalmologic assessments were normal. There was no relevant family history, and he was taking no medications. There was no history of seizures

or of any events that could have been interpreted as being potentially ictal or episodic in nature.

At the time when he was first seen, his only spoken words were yes and no, besides fairly continuous babbling sounds with no communicative intent. He would not engage with peers in any activities and displayed no imaginative use of toys. He would place toys in lines and would not use them appropriately. His head circumference was 52.0 cm (50th percentile). His general physical

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examination only revealed one café au lait spot on the dorsum of his left wrist. His neurologic examination did not reveal any abnormalities. He qualified for the diagnosis of autism by satisfying the following *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R)*⁶ criteria for autism: A1, A4, A5, B1, B3, B4, B5, and C5.

Results of additional laboratory testing that included screening for thyroid functioning, levels of serum amino acid, lactate, and pyruvate, complete blood cell count, blood chemistry studies, and chromosome analysis, including cultures for fragile X, were normal. During sleep, the EEG revealed single and short runs of spike discharges from the right frontal-temporal area, with phase reversals at T₄. A computed tomographic scan of the head was normal.

At the age of 5 years 3 months, he started valproic acid therapy, 125 mg three times a day. Within a month his language and social skills started to improve significantly. When he was seen for a reevaluation at the age of 5 years 8 months, he was freely speaking in four- to five-word sentences, he knew his telephone number and address, he made inquiries about friends and relatives, and he had made strides in socially interacting with peers and adults. He technically no longer qualified for the diagnosis of autism since the following *DSM-III-R*⁶ criteria for autism no longer applied to him: A1, A4, A5, B1, B3, B4, and B5. He has maintained his clinical improvement and has remained clinically stable for 11 months.

Patient 2. A 3-year-old girl was seen for assessment of speech delay. The pregnancy was without complications. Labor was full term and started spontaneously. She was born of a vaginal, vertex presentation at a birth weight of 3.4 kg. There were no difficulties at the time of birth or subsequently. Her only medical history was an episode of mild croup at 1 year of age, one bout of bronchi-