Autism And Epilepsy: The Complex Relationship Between Cognition, Behavior And Seizure

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Citation

R Anand. *Autism And Epilepsy: The Complex Relationship Between Cognition, Behavior And Seizure*. The Internet Journal of Neurology. 2004 Volume 4 Number 1.

Abstract

There is an increased and variable association between autism and epilepsy. Autism is a complex neurodevelopmental disorder. When associated with epilepsy, it places the child and the family in a very demanding and stressful situation to cope with. In order to help these children and their families, it is important to understand the relationship between behavior patterns, cognitive processes, language development and occurrence of seizures. So far we are yet to fully understand this relationship. I have tried to present here a brief review of what we know so far, using a case example emphasizing the fact that behind the diseases there are the people.

"It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has." – William Osler

THE STORY OF LITTLE C

I met little C for the first time in the follow-up clinic with his mother. He was seven years old but looked much younger. He was well dressed and groomed with bright eyes, short fair hair and was shorter than the average child of that age. He walked into the room, making no eye contact. He took a blank sheet of paper that lay on the desk to a smaller table that stood in one corner of the room and started drawing. He had a sad and blank expression on his face with no reciprocal interaction and never spoke a word all through the session which lasted nearly two hours. He seemed to be in his own world engrossed in his drawing, oblivious to the happenings in the room. By the end of the session he had filled the page with figures of little trees in neat rows and columns that looked uncannily identical. His mother pointed out that this was pretty much the routine in every follow-up clinic for the last two years.

C was born full term after a normal pregnancy and was delivered normally. As far as the mother could remember, his early motor developmental milestones were normally achieved but he was late to develop speech. He would have some restless nights when he tossed and turned in bed. He was a very easy child to look after as he was not at all demanding. He had no problems feeding and was adequately toilet trained. He was fully immunized. One day, when he was around two years of age while his mother was feeding him, C suddenly 'went blank' with a vacant stare and started making clicking noises with his tongue, which lasted for less than a minute. This did not recur and so the mother never consulted a doctor. As he grew older, there appeared clear changes in his behavior. He very much liked routines. The least change would bring on a tantrum, when he would become quite aggressive. These were frequent with violence mostly directed towards objects and sometimes towards mother and siblings. By contrast, he was unusually caring towards the pet cat and they seemed to like each others company. He could indicate his needs but was less verbal and was very literal in the use of language. He preferred playing alone for long hours and never mixed with his siblings, a brother 3 years older to him and a sister who was a year younger. His play was unimaginative and was repetitive. He had a fascination for trees. He liked to look at pictures of trees in books again and again. He liked drawing only pictures of trees. From the age of five years, very often and very suddenly, he would demonstrate behavior out of character. His eyes would suddenly appear glazed and his face would become pale. He would then make strange clicking noises with his tongue and repeated movements in the air as if trying to climb. This would last for a few seconds to several minutes. He would then sleep for several hours.

A maternal uncle had learning disability. Mother had separated from his father when C was about one and a half

years old and there was no contact with him. Father had a history of violent behavior and was seeing a psychiatrist, but more details were not available. There were no problems reported with the siblings. Mother, who had received high school education, was unemployed. The family received emotional support from mother's mother and sister.

C had been fully assessed by a child psychiatrist, a pediatrician, a child neurologist, speech and language therapist and a clinical psychologist. He had undergone general-physical and neurological examinations. His laboratory investigations included routine blood and urine analysis and genetic testing which did not reveal any abnormalities. Psychometric tests reported a below average intelligence in the borderline range. Routine and sleep EEGs showed paroxysmal abnormalities over the left temporal lobe. An MRI scan of the head was normal.

From the history, C demonstrates a qualitative impairment in the development of reciprocal social interaction and communication. It appears that this was evident from infancy though in a subtle form. At two years of age he appears to have had an absence seizure. Whether this contributed to cause further impairments or, the progress was natural is hard to tell. He shows some restriction and repetition in his interests and activities. Speech was late to develop but he was able to use it though in a concrete way. Psychological testing revealed only borderline impairments in intelligence. These features are consistent with a diagnosis of autism. At the age of five he started having clear cut seizures. Whether the behavioral difficulties were subtle forms of seizures is hard to tell. EEG revealed abnormalities with a left temporal lobe focus. These are consistent with a diagnosis of complex partial seizures.

C was receiving the antiepileptic medication valproic acid. He was identified as having special educational needs and was receiving specialized help in school. His mother was a very patient person. She showed a lot of interest in the problem. She never blamed C or anyone else for the situation. She was willing to learn and understand. She understood that C was suffering and made it her goal to make things better for him. The seizures were under control. He was showing very small and slow improvements in his communication. His behavior was much improved. His school work was showing a gradual progress.

The questions that arose in my mind in this case were, were seizures a cause of autism in this child, or an association? Could there be other causes? Were the improvements shown, due to the treatment of epilepsy or due to other factors? What is the relationship between cognition, behavior and seizures? I decided to 'dig' into the literature and find out.

AUTISM AND EPILEPSY

Autism was first described by Leo Kanner in 1943. In his 11 cases of children with "autistic disturbances of affective contact", Kanner noted an "inability to relate" in usual ways to people, from the beginning of life, unusual responses to the environment, which could include stereotyped motor mannerisms and resistance to change (or insistence on sameness) as well as communication idiosyncrasies such as pronoun reversal and tendency to echo language (echolalia). The current criteria for diagnosis of autistic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-VI) requires at least six criteria, one from each of the areas of disturbance in social interaction, communication and restricted, repetitive, stereotyped patterns of behavior, interests and activities. The onset is before three years of age.

Autism can present in two ways. In most autistic children, the difference can be recognized from an early age. They move and cry less, they do not like to be held and they are quite happy to be left alone. In approximately one-third of children the development proceeds normally until the second year of life. Then they gradually regress into autism usually in association with emotional or physical trauma and with seizures. Kanner reported one case of epilepsy among his 11 children. The prevalence of epilepsy among autistics is much higher than the normal population. There is also an increased prevalence of abnormal potentially epileptogenic activity in children with autistic spectrum disorder. About one in four autistic children develop seizures at puberty.

EPILEPSY AND AUTISM

Hughlings Jackson in 1870 postulated about epilepsy as an intermittent derangement of the nervous system due to "an excessive and disorderly discharge of cerebral nervous tissue on muscles." This has been supported by modern electrophysiology. As a result of the discharge, there may be an instantaneous loss of consciousness, altered perception or impaired psychic function, convulsive movements, disturbance of sensation, or some combination thereof. Seizure always indicates that the cerebral cortex has been affected by disease, either primary or secondary. Epilepsy is often associated with global central nervous system disorders like cerebral palsy, mental retardation and autism. In autistic children, the risk of seizures increases if they have

certain specific neurological disorders like neurofibromatosis, tuberous sclerosis, phenylketonuria (untreated). Children with symptomatic infantile spasms (sudden generalized muscle contractions usually beginning between the ages of three and eight months) tend to develop both epilepsy and autism. Complex partial seizures or temporal lobe epilepsies show different clinical features in children of different ages. The general course tends to be favorable. Adverse course may be seen in children with perinatal complications, spike-wave complexes in the EEG and those with psychomotor and psychosensory seizures. Hashimoto et al reported a tendency for epileptic foci to occur in the frontal region in autistic children and they suggest that frontal dysfunctions may be important in the mechanism of symptoms of autism.

AUTISM, EPILEPSY AND LANDAU-KLEFFNER SYNDROME

Landau-Kleffner syndrome (LKS), also known as acquired epileptic aphasia usually affects children between the ages of three and seven years. These children previously have no developmental, language or interactional difficulties. They have an abrupt onset of loss of language comprehension and a decrease in their ability to express themselves. Seizures are usually present. Their EEGs, especially sleep EEGs are abnormal. There may be some cause for confusion with autism. But it would be rare for an autistic child to have LKS. The syndrome denotes aphasia acquired after two to three years of age in a normally developing child and coinciding with onset of seizures. If doubt exists, a sleep EEG should be obtained. If it is normal, LKS is unlikely. Anticonvulsants improve the condition along with speech and language therapy. Corticosteroids and neurosurgery have yielded positive results in certain cases.

GENES

Duplications of chromosome 15 have been reported in individuals with atypical autism, varying degrees of mental retardation and epilepsy. Mutations in the Aristaless related homeobox gene (ARX) cause a diverse spectrum of diseases including cognitive impairment, epilepsy and in another group, severe cortical malformations. The precise prevalence of ARX mutation is not known, but may be an important cause of developmental disorders and epilepsy in males which in the future may provide important treatment options.

INFECTION

A possible association with viral CNS infection with autism and epilepsy has been reported.

NUTRITION

There is also an interesting study which hypothesizes that developing fetuses of pregnant women with deficiency of zinc and excess of copper experience major difficulties in early brain development which may later manifest as schizophrenia, autism or epilepsy.

VACCINE

An important study was conducted by Steffenburg, Steffenburg and Gillberg. They found that partial seizures were more common and generalized seizures less common in autistic spectrum disorder (ASD) group compared with non-ASD group. Seizure onset was later in the ASD group. Established etiology was more often present in the prenatal period than in the peri- or post-natal periods in the ASD group. There was no increase neither in the prevalence of active epilepsy and learning disability nor in the rate of autism with active epilepsy and learning disability in children born between 1981 and 1986 compared with those born between 1976 and 1980, indicating no statistical association with the general measles-mumps-rubella (MMR) vaccination introduced in the early 1980s.

VAGUS NERVE STIMULATION

Preliminary studies have indicated that vagal nerve stimulation (VNS) therapy which can reduce pharmacoresistant seizures in epilepsy, may improve neurocognitive performance. Park reported a study with 59 autistic patients and 6 with LKS, with epilepsy. Improvements were reported in all areas of quality of life monitored particularly for alertness (76% at 12 months). But better standardized and long term studies are required to assess the results better.

MAGNETOENCEPHALOGRAM

Lewine et al used magnetoencephalogram (MEG) to evaluate patterns of epileptiform activity during stage III sleep in six children with LKS and 50 children with regressive autistic spectrum disorder (ASD). MEG of all children with LKS showed epileptiform involvement of the left intra/perisylvian region with one child showing additional involvement of right sylvian region. Epileptiform activity was identified in 82% of children with ASD. The same intra/perisylvian regions involved in LKS were found in 85% with ASD. They also found that when epileptiform activity was present in ASD, therapeutic strategies (antiepileptic drugs, steroids and even neurosurgery) aimed at its control can lead to a significant reduction in autistic symptoms and improvement in language skills.

TREATMENT

The most important aspect of treatment of epilepsy is the use of antiepileptic drugs. Epilepsies which have not responded to prolonged and intensive therapy have benefited from surgical excision of the epileptic foci. Other treatments that have shown some positive results in intractable epilepsy are vagal nerve stimulation and ketogenic diet. The aims of treatment in autism are promoting learning, especially developing language and communication and self help skills and reducing disruptive behavior. The children require intensive, highly structured special educational support, speech and language therapy, behavior therapy and psychotherapy for older children focusing on problem solving skills. The family needs education and support. Tuchman and Rapin reported an important study looking at the relationship between epilepsy, epleptiform EEGs and autistic regression. Epilepsy and epileptiform EEGs occur in a significant minority of autistic children with a history of regression and in a small minority without regression. They conclude that prompt recognition of regression and recording of prolonged sleep EEGs is recommended, even though information on the potential efficacy of antiepileptic treatment to improve language and behavior in autistic children with epilepsy or epileptiform EEG is still lacking.

WHAT'S THE LAST WORD?

The relationship between epilepsy, language, behavior and cognition is not well understood. Tuchman and Rapin, in their review in the Lancet concluded that there is an increased but variable risk of epilepsy in autism. Age, cognitive level and type of language disorder account for the variability in the reported prevalence of epilepsy. In some cases the association between the two conditions may denote common genetic factors. The effect of subclinical epilepsy on language, cognition and behavior is debated as is the relation of autistic regression with an epileptiform EEG to LKS. They conclude that there is no evidence-based treatment recommendation for individuals with autism, regression and subclinical epilepsy, and double-blind studies with sufficient power are urgently required to resolve the issue.

LITTLE C SPEAKS

As far as little C is concerned, seizures were clearly present and responded to treatment well. Weather the treatment helped improve the autistic symptoms is difficult to say. I can say with some certainty that treatment of epilepsy did have a positive physical and emotional impact on C and the family. The most important factor to my mind is the mother's attitude. Treatment of epilepsy and control of seizures I feel played an important role in reducing the burden of care. At the end of the session I asked C what he would like to be when he grew up. Without looking up he said, "archeologist" I asked him why? He said, "I don't know... that's why." I rest my case.

"Care more for the individual patient than for the special features of the disease. Put yourself in his place... The kindly word, the cheerful greeting, the sympathetic look... these the patient understands." – William Osler

DECLARATION

The case of little C is a typical case and not a case report and as such used here to demonstrate the complexity of the issues discussed and to draw attention to the fact that at first we are treating patients and not diseases. There is no conflict of interest and no financial support was received from any source.

ACKNOWLEDGEMENT

I am grateful to Professor A.S.Starikov MD, DSc and Dr V.A.Zhadnov MD, DSc, Department of Neurology and Neurosurgery, Ryazan Regional Clinical Hospital, I.P.Pavlov Medical University, Ryazan, Russia, for their kind support.

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