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Mental deterioration in childhood epilepsy

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Abstract

Mental retardation is detected in 20-30% of children with epilepsy at hospitals specializing in treatment of childhood epilepsy. However, the incidence of mental deterioration in childhood epilepsy is not high. In this study, mental deterioration was found in 52 (1.8%) of the 2,880 children with epilepsy at Okayama University Hospital. The patients showing mental deterioration mostly suffered from specific epileptic syndromes, such as West syndrome, Lennox-Gastaut syndrome, severe myoclonic epilepsy in infancy and epilepsy with continuous spike-waves during slow wave sleep. These types of epilepsy show generalized electroencephalographic (EEG) abnormalities. It is presumed that mental deterioration is caused by the total effects of prolonged diffuse EEG abnormalities and the age of the patients. Antiepileptic drugs exert a relatively minor effect on mental deterioration.

KEYWORDS: mental deterioration, mental retardation, epilepsy, EEG, children

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Review

Mental Deterioration in Childhood Epilepsy

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Mental retardation is detected in 20-30% of children with epilepsy at hospitals specializing in treatment of childhood epilepsy. However, the incidence of mental deterioration in childhood epilepsy is not high. In this study, mental deterioration was found in 52 (1.8%) of the 2,880 children with epilepsy at Okayama University Hospital. The patients showing mental deterioration mostly suffered from specific epileptic syndromes, such as West syndrome, Lennox-Gastaut syndrome, severe myoclonic epilepsy in infancy and epilepsy with continuous spike-waves during slow wave sleep. These types of epilepsy show generalized electroencephalographic (EEG) abnormalities. It is presumed that mental deterioration is caused by the total effects of prolonged diffuse EEG abnormalities and the age of the patients. Antiepileptic drugs exert a relative minor effect on mental deterioration.

Key words: mental deterioration, mental retardation, epilepsy, EEG, children

Mental handicap in childhood is divided into two subtypes: mental retardation and mental deterioration. Mental retardation is defined as a kind of developmental disorder seen in those whose peak IQ development is less than 75. In contrast, mental deterioration is a condition where mental ability that has developed normally, declines due to various etiologies other than acquired acute brain damage as shown in Fig. 1.

Possible mental impairment resulting from convulsions is a matter of the gravest concern to parents of children who suffer from convulsion. Whether their children's convulsion is a severe or mild febrile convulsion is a

question commonly raised by parents of epileptic children. However, in general, the incidence of mental deterioration in childhood epilepsy is by no means high.

In a comparative study of 98 children with afebrile convulsions and their siblings without convulsions, Ellenberg *et al.* (1) found that although mental retardation was frequent in the group with convulsions, IQ levels remained undeteriorated during the period of their follow-up until 4-7 years of age.

O'Donohoe (2) likewise found that mental deterioration occurred in only a very limited number of epileptic children, not in a large majority. He considered it important that parents of epileptic children be advised of this information to relieve their anxiety. However, it is a stern fact that mental deterioration occurs in some cases of childhood epilepsy. It is found especially in age dependent epileptic encephalopathies such as West syndrome.

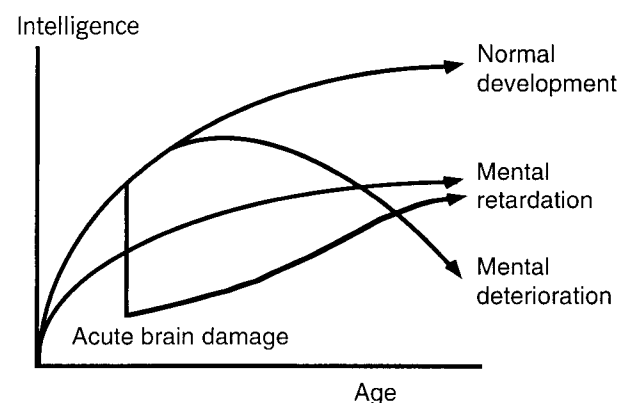


Fig. 1 Mental handicap in childhood.

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In a prospective study of 72 new, untreated epileptic children, Bourgeois *et al.* (3) found a decrease in IQ in more than 10 points in 8 (11.1%) cases. This is a relatively high rate of IQ deterioration but should be interpreted as the result of an investigation conducted at epilepsy-specialized institutions where large numbers of patients with severe epilepsy were enrolled.

Lennox (4) attributed mental impairment in epilepsy etiologically to (A) genetic predisposition, (B) organic brain lesions pre-existent to the onset of epilepsy, (C) epilepsy itself, (D) psychoenvironmental background and (E) excess dosages of antiepileptic drugs. (A) and (B) relate to mental retardation, and (C), (D) and (E) to mental deterioration. Epilepsy itself (C) refers to effects of epileptic seizures and epileptic EEG abnormality.

Chaudhry and Pond (5) proposed 'frequent seizures', 'intractableness' and 'coexistence of localized and diffuse EEG abnormalities' as factors associated with mental impairment due to epilepsy itself. Bourgeois *et al.* (3) suggested intractableness and onset at low ages.

Very few studies have been performed on the effect of epilepsy itself on the brain during development, namely, the actual state of mental deterioration due to epileptic seizures or epileptic EEG abnormalities in large populations of children with epilepsy. This paper gives an outline of studies conducted at the Department of Child Neurology, Okayama University Hospital.

Frequency of Mental Deterioration in Childhood Epilepsy

From 2,880 epileptic patients receiving medical treatment at the Department of Child Neurology, Okayama University Hospital, patients for this study were selected according to the following criteria:

- 1, Patients who grew normally until the onset of epilepsy and manifested mental impairment after the onset, with IQ reduced to less than 75 were included. Developmental quotient (DQ by the Enjoji Developmental Test) was substituted for IQ in some cases of early childhood.
- 2, Patients with underlying gross organic brain lesion were excluded (*e.g.*, tuberous sclerosis, hydrocephalus, sequellae of intracranial hemorrhage, cerebral palsy and progressive degenerative disease).
- 3, Patients with epilepsy associated with acute encephalopathy or hemiconvulsion, hemiplegia (H.H.) syndrome were excluded.
- 4, Patients with irreversible mental impairment induced

by antiepileptic drugs were excluded.

Of the 2,880 patients, 52 (1.8%) fitted these criteria. These 52 did not include patients who had already developmental retardation before the onset of epilepsy, with mental impairment progressing further during the clinical course. They consisted of 28 boys and 24 girls, and thus there was no significant sex difference in distribution. The 28 cases of mental deterioration reported by Chaudhry and Pond (5) consisted of 18 boys and 10 girls. The ratio of boys was higher, but the difference is not significant.

Types of Epilepsy Leading to Mental Deterioration

Table 1 shows the types of epilepsy leading to mental deterioration. Since the type of epilepsy may vary during childhood, this list shows the types of epilepsy believed to be the ones primarily responsible for mental deterioration.

Nine cases (17.3%) were categorized as symptomatic localization-related epilepsy. These consisted of 5 temporal lobe epilepsies, 3 frontal lobe epilepsies and 1 other. The 3 frontal lobe epilepsies included motor cortex seizure in 2 cases and Kojewnikow syndrome in 1.

Thirty-two cases (61.6%) were categorized as generalized epilepsy. These consisted of 6 West syndrome, 21 Lennox-Gastaut syndrome (LGS), 3 myoclonic variants of LGS (6) and 2 intermediate petit mal (6) cases.

Eleven cases (21.1%) were categorized as undetermined epilepsy. These consisted of 6 severe myoclonic epilepsy in infancy (SME) cases, 4 epilepsy with continuous spike-waves during slow wave sleep (ECSWS) cases and 1 minor epileptic status (7) case. Thus, specific syndromes constituted the majority, and the types of epilepsy which led to mental deterioration were relatively few.

In West syndrome cases, mental deterioration is inevitable if treatment is begun belatedly. In LGS cases, mental deterioration also often occurs in intractable cases. SME is extremely intractable, and mental deterioration inevitably appears after 1 year of age. Mental deterioration was recognized in all 20 cases reported by Dravet (8) and in all 14 cases reported by Ogino (9).

ECSWS and minor epileptic status represent non-convulsive status epilepticus. Diffuse EEG abnormalities are seen in non-convulsive status epilepticus. If not appropriately treated, status epilepticus can persist from several months to more than 1 year, and the rate of mental deterioration is high. The risk of brain damage

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Table 1 Types of epilepsy and epileptic syndromes leading to mental deterioration

Type and syndrome	Number of cases ^a	
Symptomatic localization-related epilepsies		9
1) Temporal lobe epilepsy	5	
2) Frontal lobe epilepsy	3	
Motor cortex seizure	2	
Kojewnikow syndrome	1	
3) Others	1	
Cryptogenic or symptomatic generalized epilepsies		32
4) West syndrome	6	
5) Lennox-Gastaut syndrome (LGS)	21	
6) Myoclonic variant of LGS	3	
7) Intermediate petit mal	2	
Undetermined Epilepsies		11
8) Severe myoclonic epilepsy in infancy	6	
9) Epilepsy with continuous spike-waves during slow wave sleep	4	
10) Minor epileptic status	1	
Total	52 ^a /2,880 ^b (1.8%)	

a: Number of mentally-deteriorated children with epilepsy.

b: Total number of children with epilepsy treated at Okayama University Hospital.

being caused by clinical convulsive seizure is very low in nonconvulsive status epilepticus. Irreversible mental dysfunction is, therefore, believed to result from diffuse EEG abnormality itself.

Temporal lobe epilepsy was most frequent in the localization-related epilepsies. Three of the five cases had both temporal focal discharge and diffuse discharge on EEGs. The clinical seizures consisted of complex partial and generalized tonic seizures. Among childhood epilepsies, temporal lobe epilepsy is relatively often intractable, and the prognosis is known to be poor in many cases, if diffuse EEG abnormality is concurrently present. However, mental deterioration does not appear in mesial temporal lobe epilepsy which is intractable in temporal lobe epilepsies (10). Secondarily generalized seizure is the most frequent type of seizure seen in childhood epilepsy. As shown in Table 1, mental deterioration occurred in only 1 case. In a follow-up of the 98 children with afebrile convulsion, Ellenberg *et al.* (1) found mental deterioration in none of them.

Ages at the Onset of Epileptic Seizures Leading to Mental Deterioration

Epileptic seizure initially broke out at ages 0–12

months in 14 children (26.9%), ages 1–3 years in 15 (28.8%), ages 3–6 years in 15 (28.8%), ages 6–10 years in 7 (13.6%) and at ages 10–12 years in 1 (1.9%). The last mentioned case (onset of initial seizure at an age above 10 years) was a child who developed Kojewnikow syndrome at 11 years of age. The number of children who developed epilepsy at ages less than 6 years amounted to 44 (84.6%). Compared to the especially high incidence of mental retardation-accompanied epilepsy in children who developed epilepsy in infancy and early childhood, the incidence of mental deterioration is not significantly high in early-onset childhood epilepsy. Of the children with mental deterioration reported by Chaudhry and Pond (5), five developed epilepsy within 6 months after birth and 11 at ages 6 months to 4 years, and 12 after 4 years.

Ages at the Onset of Mental Deterioration

Fig. 2 shows the ages when mental deterioration was detected. The ages were distributed over all ages from the latter half of infancy to 14 years, but mental deterioration was detected in many cases during early childhood and at school ages. The types of epilepsy in which mental deterioration was perceived at ages less than 4 years were West syndrome, LGS and variants of LGS and SME. In the localization-related epilepsies, mental deterioration was perceived after 4 years of age, mostly during school ages.

Duration from the Onset of Epilepsy to the

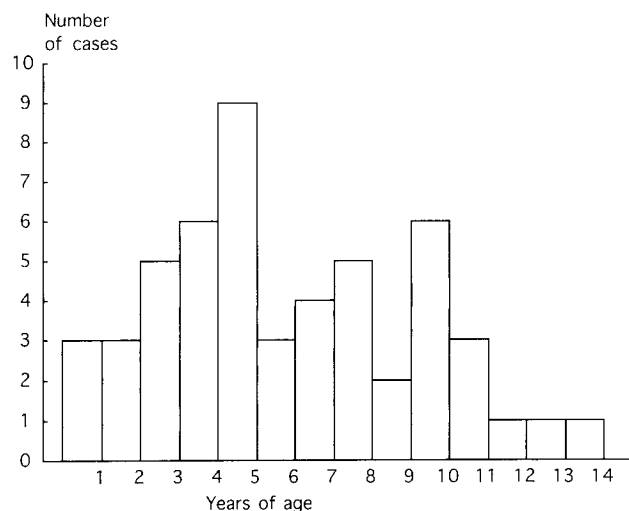


Fig. 2 Age at onset of mental deterioration.

Appearance of Mental Deterioration

Fig. 3 shows the number of years from the onset of epilepsy to the appearance of mental deterioration. Mental deterioration occurred within 4 years in 45 cases (86.5%). Five of the children who developed mental deterioration 4 to 8 years after the onset of epilepsy suffered from frequent episodes of grand mal during infancy and early childhood

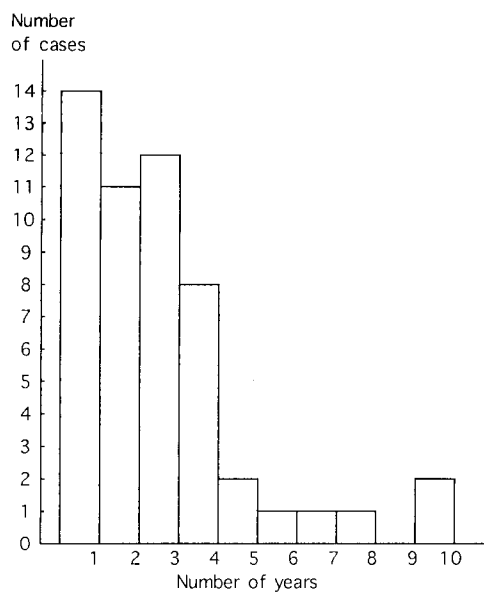


Fig. 3 Number of years from the onset of epilepsy to the appearance of mental deterioration.

and developed LGS at school ages. Two children in whom mental deterioration manifested itself more than 9 years after the onset of epilepsy consisted of 1 with LGS and 1 with Jacksonian seizure.

Severity of Mental Impairment

On assessing the severity of mental impairment after more than 3 years of follow-up, IQ was below 24 in 4 cases (7.7%), 25-49 in 12 (23.1%), 50-69 in 30 (57.7%), and 70-74 in 6 (11.5%). Mental impairment was generally mild. Chaudhry and Pond (5) also obtained similar results. Of their 16 patients whose IQ could be determined during the follow-up, 67.5% had an IQ above 50.

Past History of Status Epilepticus

Status epilepticus (SE) seen during the clinical course is shown in Table 2. SE was seen in a total of 22 cases (42.4%); convulsive SE in 11 (21.2%) and nonconvulsive SE in 11 (21.2%). All of the remaining 30 patients experienced periods of frequent seizures; either those occurring more than 10 times a day or those occurring more than once a day but persisting for more than 10 days.

Chaudhry and Pond (5) also pointed out that frequently occurring SE, grand mal or minor seizures is a significant cause of mental deterioration.

Convulsive SE is not rare during childhood. It appears frequently in LGS and various other types of

Table 2 Past history of status epilepticus

Type of epilepsy	Number of patients with			Total
	Convulsive status epilepticus	Nonconvulsive status epilepticus	Periods of frequent seizures ^a	
West syndrome			6	6
Lennox-Gastaut syndrome (LGS)	4	4	13	21
Myoclonic variant of LGS		1	2	3
Intermediate petit mal	1	1		2
Severe myoclonic epilepsy in infancy	2		4	6
ECSWS ^b		4		4
Minor epileptic status		1		1
Temporal lobe epilepsy	1		4	5
Frontal lobe epilepsy	2		1	3
Others	1			1
Total	11 (21.2%)	11 (21.2%)	30 (57.6%)	52

^a: Either occurring more than 10 times a day or occurring more than once a day but persisting for more than 10 days.

^b: Epilepsy with continuous spike-waves during slow wave sleep.

Table 3 Findings of the electroencephalograms in mentally-deteriorated children

Diffuse discharge	33 (63.5%)
Hypsarhythmia	6
Diffuse slow spike-waves	16
Diffuse multiple spike-waves	9
Diffuse irregular spike-waves	2
Both diffuse and focal discharge	14 (26.9%)
Focal discharge	5 (9.6%)
Total	52 cases

epilepsy. On the other hand, nonconvulsive SE is generally a rare phenomenon. In epilepsy with mental deterioration, therefore, the incidence of nonconvulsive SE gives an impression of being considerably prominent. Nonconvulsive SE is also likely to appear in LGS and its variant types.

Electroencephalographic Characteristics

Table 3 shows seizure discharges. Diffuse discharge was most frequent (33 cases; 63.5%). Of these 33 cases, 6 had hypsarhythmia, 16 diffuse slow spike-waves, 9 diffuse multiple spike-waves and 2 diffuse irregular spike-waves. Diffuse discharge was mixed with focal discharge in 14 (26.9%) cases. Including these 14 cases, diffuse discharge was recorded in a total of 47 (90.4%) cases. Focal discharge was recorded in 5 (9.6%) cases, which were all multifocal. The EEG findings in Chaudhry and Pond's (5) study were similar to ours. They found that of the 28 epileptic children with mental deterioration, 8 had diffuse discharge, 16 both diffuse and focal discharges and 4 only focal discharge.

The seizure type most closely related to mental deterioration in epilepsy is hypsarhythmia. If left untreated, mental deterioration may be unavoidable. Diffuse slow spike-waves, an EEG pattern frequently associated with mental deterioration, is not necessarily a cause of mental deterioration. An EEG pattern with a surge of focal discharge in diffuse discharge is present in the Landau-Kleffner syndrome. In this case, IQ is maintained, although speech is disturbed (11).

Nishibayashi (12) carried out a study on diffuse EEG abnormalities in ECSWS, and stressed that mental deterioration was observed in patients whose spike-wave index during slow wave sleep exceeded 50%, or whose continuous spike-waves during slow wave sleep continued for

more than two years. As described, the active appearance of diffuse EEG abnormality does not necessarily lead to mental deterioration. It is presumed that mental deterioration is caused by the total effect of two combined factors: the duration of diffuse EEG abnormality and the age of the patients. It may be said that mental deterioration in epilepsy can be prevented to some extent by early diagnosis and appropriate treatment.

Antiepileptic Drugs and Mental Deterioration

Since medication for epilepsy extends over a long period of time, the influence of antiepileptic drugs (AED) on mental function needs to be taken into consideration. Generally speaking, even long-term medication does not result in chronic brain dysfunction, if blood concentrations of AED are maintained within therapeutic levels. Many numbers of our patient population of 2,880 received long-term medication, but the 52 who developed mental deterioration displayed specific types of epilepsy. The incidence of mental deterioration in the whole epileptic population was very low. This suggests that drugs exert a relatively small deleterious impact on the brain.

The possible risk of not only acute toxic symptoms but also irreversible brain damage being induced by a high, albeit temporary, blood concentration of AED has been shown for Phenytoin.

Bourgeois *et al.* (3) emphasized that in the treatment of epilepsy in infancy and early childhood, complete control of seizures should not be attempted if it involves a risk of raising blood concentrations of AEDs to toxic levels. This is because toxic levels of AEDs in the blood were often observed in children suffering from 10 point IQ reductions. In such cases, the duration of seizures and the development of mental deterioration were not necessarily in direct proportion. This is an admonition to those who have recently started using high-dose monotherapy with AEDs. However, high-dose monotherapy is prescribed strictly for specific patients, and should be regarded as a special treatment for intractable patients with imminent dangers (such as mental deterioration) due to intense epileptic activity. Evaluation of drug-related toxicity should not wait until the manifestation of clinical symptoms. Detection of a pretoxic condition, by neurophysiological examination such as auditory brainstem response (13) and event-related potential checks (14), is important to prevent toxic-levels of AEDs and resultant mental deterioration.

Conclusion

We herein described the actual conditions of mental deterioration in childhood epilepsy. The occurrence of mental deterioration is, on the whole, rather rare in childhood epilepsy. It is seen mostly in specific epileptic syndromes. Complete prevention of mental deterioration in childhood epilepsy, even by early diagnosis and early treatment, is difficult. However, prevention or relief of mental impairment may be possible to some degree.

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