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Determinants of intelligence in childhood-onset epilepsy: A single-center study

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ABSTRACT

The purpose of this study was to quantify the intelligence of children with epilepsy and to determine the clinical factors associated with intellectual impairment.

The medical records of patients diagnosed with childhood-onset epilepsy at a single tertiary medical center in Korea between 2006 and 2011 were retrospectively reviewed. The Korean Education Development Institute—Wechsler Intelligence Scale for Children or Korean Wechsler Intelligence Scale for adults was used to quantify the level of intelligence. Age at seizure onset, etiology, epilepsy duration, number of seizures in the last year, use of antiepileptic drugs, EEG/MRI findings, and epilepsy classification were recorded. The association between clinical factors and the intelligence was determined using logistic regression.

Three hundred and twenty-two patients were included in the analysis. One hundred and seventy-six (54.7%) patients had low intelligence (intelligence quotient [IQ] < 80) with 18 (5.6%) defined as borderline mental retardation (IQ 70–79), 47 (14.6%) as mild mental retardation (IQ 60–69), and 111 (34.5%) as moderate-to-severe mental retardation (IQ < 60). Epilepsy duration, number of seizures in the last year, and epilepsy classification were significantly associated with low intelligence in multivariate logistic regression ($p < 0.05$). However, when analyzed according to etiology, these factors were not associated with low intelligence in children with idiopathic epilepsy.

The most important factors associated with low intelligence in childhood-onset epilepsy are the underlying etiology and, in cryptogenic and symptomatic epilepsy, seizure burden. The results of this study underscore the importance of seizure control to alleviate the harmful impact of epilepsy on cognition.

1. Introduction

Cognition is the mental process of knowing from the environment and includes aspects of awareness, perception, memory, reasoning, and judgment. Cognition and intelligence are often considered synonymous. However, intelligence is only one aspect of cognition and is evaluated by a standardized intelligence test [1]. Epilepsy is a disorder of the brain that is caused by abnormal electrical activity in neurons and is closely associated with cognitive comorbidities, which are major concerns in children with epilepsy [2,3].

The prevalence of mental retardation is more frequent in children with epilepsy than in the general population [4,5], and a large number of studies have shown that poor achievement and learning disability are associated with childhood epilepsy [6–10]. Childhood-onset epilepsy is associated with greater risk of cognitive impairment compared with adult-onset epilepsy [11]. Even in patients with benign childhood epilepsy with centrotemporal spikes (BCECTS), which has been associated with normal cognitive function and benign progression, many studies have found a negative impact of epilepsy on cognition including intelligence and school difficulties [12–14].

Epilepsy is not a single disease entity but a complex group of disorders embracing a large number of diseases that cause neuronal excitability. Multiple interrelated factors influence cognitive function in childhood epilepsy. Brain pathology or etiological factors have a critical impact on cognition. Patients with symptomatic epilepsy are more likely to have cognitive impairment than patients without detectable brain lesions [15], and patients with temporal lobe epilepsy often suffer memory deficits [16]. The frequency, duration, and severity of seizures can also impact cognitive function, and a younger age at onset of seizures is a risk factor for intellectual impairment [17,18]. There are also treatment-related factors that can impact cognitive function, including the use of antiepileptic drugs (AEDs) and sequelae of epilepsy surgery [19].

Abbreviations: AED, Antiepileptic drug; IGE, Idiopathic generalized epilepsy; ILRE, Idiopathic localization-related epilepsy; LGS, Lennox–Gastaut syndrome; EE, Epileptic encephalopathy.

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Children undergo a process of brain maturation and intellectual growth, and, as such, the intellectual impact of epilepsy is one of the most critical aspects of treatment. The aim of this study was to evaluate intelligence in patients with childhood-onset epilepsy, to determine the prevalence of low intelligence in patients with childhood-onset epilepsy, and to determine the factors that are associated with intellectual impairment.

2. Methods

2.1. Subjects

Between January 2006 and March 2011, a total of 1834 patients with childhood-onset epilepsy over 5 years old have been actively managed in the pediatric neurology clinic at Asan Medical Center in Seoul, Korea. Among them, the medical records of 322 patients with childhood-onset epilepsy who were evaluated by an intelligence test were retrospectively reviewed. Demographic data and clinical history were obtained from the medical records.

2.2. Cognitive assessment

The Korean Education Development Institute—Wechsler Intelligence Scale for Children was used to evaluate intelligence in patients younger than 18 years of age, and the Korean Wechsler Intelligence Scale for adults was used to evaluate intelligence in patients aged 18 years or above. A licensed psychologist or psychometrician administered all evaluations. The level of intelligence was categorized as normal (intelligence quotient [IQ] ≥ 80), borderline mental retardation (IQ 70–79), mild mental retardation (IQ 60–69), moderate-to-severe mental retardation (IQ < 60), or neurologically devastated (not testable). When repeated tests were undertaken, data from the first evaluation were used.

2.3. Epilepsy variables

The following information was obtained from the medical records: 1) age at first unprovoked seizure (<5 years, 5–9 years, ≥10 years), 2) epilepsy duration (<1 year, 1–5 years, 6–9 years, ≥10 years), 3) number of AEDs (0, 1, 2, ≥3), 4) number of seizures in the year preceding the cognitive evaluation (0–1, 2–9, ≥10), 5) EEG findings (focal, generalized, focal and generalized, normal), 6) MRI findings (abnormal, normal), 7) epilepsy classification (idiopathic localization-related epilepsy [ILRE], symptomatic focal epilepsy, cryptogenic focal epilepsy, idiopathic generalized epilepsy [IGE], Lennox–Gastaut syndrome/epileptic encephalopathy [LGS/EE]), and 8) etiology of epilepsy (idiopathic, cryptogenic, symptomatic). Epilepsy duration was defined as time between seizure onset and the day of cognitive evaluation. Antiepileptic drug status, EEG findings, and MRI findings were determined at the time of cognitive evaluation.

2.4. Statistics

Kruskal–Wallis or Mann–Whitney tests were used to determine if the IQ differed across the different categories of clinical characteristics. Low intelligence was defined as an IQ score <80, and logistic regression analysis was used to identify the risk factors for low intelligence. Univariate logistic regression analysis was used to identify the variables that were significantly associated with low intelligence, and these were entered into a multiple logistic regression. Backward elimination was used to identify significant risk factors for low intelligence. Statistical significance was set as $p < 0.05$.

3. Results

3.1. Baseline characteristics

Clinical characteristics are summarized in Table 1. Age at the time of cognitive evaluation ranged from 4 to 29 years (mean ± SD, 12.4 ± 4.8 years), and age at onset of seizures ranged from 0 to 16 years (mean ± SD, 5.8 ± 4.2 years). Epilepsy duration at the time of cognitive evaluation ranged from 0 to 29 years (mean ± SD, 6.5 ± 5.1 years). Intelligence was normal in 146 (45.3%) patients and low in 176 (54.7%) patients. Three neurologically devastated patients could not perform the Wechsler Intelligence Scale and were excluded for the risk factor analysis.

3.2. Risk factors for low intelligence

Mean IQ (Table 2) and low intelligence (IQ < 80; Table 3) were strongly associated with multiple risk factors including age at onset of seizures, epilepsy duration, AED number, number of seizures in the preceding year, MRI abnormalities, epilepsy classification, and etiology. In multivariate logistic regression model with backward elimination, epilepsy duration, number of seizures in the preceding year, and epilepsy classification were significant risk variables for low intelligence. Longer epilepsy duration was associated with higher risk of low intelligence compared with epilepsy duration of <1 year, and ten or more seizures in the preceding year were associated with higher risk of low intelligence than zero or one seizure in the preceding year. Epilepsy classification was also a strong risk variable (Table 3). The etiology of epilepsy

Table 1
Patient characteristics.

Age at onset of seizures[a]	
<5 years	147 (47.7%)
5–9 years	103 (33.4%)
≥10 years	58 (18.8%)
Epilepsy duration[a]	
<1 year	37 (12.0%)
1–5 years	101 (32.8%)
6–9 years	100 (32.5%)
≥10 years	70 (22.7%)
Number of seizures in preceding year	
0–1	196 (60.9%)
2–9	66 (20.5%)
≥10	60 (18.6%)
Number of antiepileptic drugs	
0	52 (16.1%)
1	151 (46.9%)
2	48 (14.9%)
≥3	71 (22.0%)
Epilepsy classification	
ILRE	25 (7.8%)
CFE	119 (37.0%)
SFE	96 (29.8%)
IGE	55 (17.1%)
LGS/EE	27 (8.4%)
MRI findings[b]	
Normal	172 (56.2%)
Abnormal	134 (43.8%)
Etiology of epilepsy	
Idiopathic	80 (24.8%)
Cryptogenic	135 (41.9%)
Symptomatic	107 (33.2%)
Overall global cognitive function	
Normal (IQ ≥ 80)	146 (45.3%)
Borderline mental retardation (IQ 70–79)	18 (5.6%)
Mild mental retardation (IQ 60–69)	47 (14.6%)
Moderate-to-severe mental retardation (IQ < 60)	111 (34.5%)

ILRE, idiopathic localization-related epilepsy; CFE, cryptogenic focal epilepsy; SFE, symptomatic focal epilepsy; IGE, idiopathic generalized epilepsy; LGS/EE, Lennox–Gastaut syndrome/epileptic encephalopathy.
[a] 14 patients who did not know the age at seizure onset were excluded.
[b] 13 patients who did not have brain magnetic resonance images were excluded.