Review article
Korean J Pediatr 2016;59(4):155-164
http://dx.doi.org/10.3345/kjp.2016.59.4.155
pISSN 1738-1061•eISSN 2092-7258

Korean J Pediatr

Cognitive impairment in childhood onset epilepsy: up-to-date information about its causes

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Cognitive impairment associated with childhood-onset epilepsy is an important consequence in the developing brain owing to its negative effects on neurodevelopmental and social outcomes. While the cause of cognitive impairment in epilepsy appears to be multifactorial, epilepsy-related factors such as type of epilepsy and underlying etiology, age at onset, frequency of seizures, duration of epilepsy, and its treatment are considered important. In recent studies, antecedent cognitive impairment before the first recognized seizure and microstructural and functional alteration of the brain at onset of epilepsy suggest the presence of a common neurobiological mechanism between epilepsy and cognitive comorbidity. However, the overall impact of cognitive comorbidity in children with epilepsy and the independent contribution of each of these factors to cognitive impairment have not been clearly delineated. This review article focuses on the significant contributors to cognitive impairment in children with epilepsy.

Key words: Epilepsy, Child, Seizure, Cognition

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Received: 21 August, 2015
Revised: 2 November, 2015
Accepted: 16 November, 2015

Introduction

Many children with epilepsy are affected by various neuropsychiatric comorbidities, which significantly affect the quality of their lives. Above all, cognitive impairments, such as memory impairments, mental slowness, and attention deficits, are the most common comorbid disorders in epilepsy[1-3]. Such impairments affect children in developing stages as well as their family members, and may be more deleterious for a patient than the seizures. Therefore, it is crucial to explore the factors leading to cognitive impairment. Various factors can have a debilitating effect on cognitive function in epilepsy, including underlying structural lesions and disorders that cause epilepsy, severity of epileptic activity, psychosocial factors, and surgical or pharmacological treatment of seizures[1]. As all factors are strongly intercorrelated and their contribution to cognitive impairment is complex, the exact cause of cognitive impairment in epilepsy is not completely established. However, three factors are clearly confirmed: the underlying etiology of epilepsy, electroclinical seizures, and central nervous system side effects of antiepileptic drugs (AEDs). Depending on which factor has a larger effect on cognitive function, the timing, degree, and course of cognitive impairment can vary[1-3]. All these factors need to be considered in an individual patient evaluation and optimization of therapy.

The association of epilepsy related factors and AEDs with cognitive impairment in childhood epilepsy have been consistently investigated[3-7]. Aggregation of specific cognitive difficulties in the families of some children with epilepsy suggests potential genetic and environmental contributions to cognitive impairment in childhood epilepsy[8]. Recent

studies indicate that abnormalities in cognition, brain structure, and behavior can be apparent at or near the time of epilepsy diagnosis[2,9-11], suggesting the possibility of common neurobiological mechanisms. Apart from the structural alteration, pathological abnormalities including abnormal pattern of apoptosis, channelopathies, bad synapses, and improper dendrites are suggested as underlying disturbances responsible for the cognitive impairment in childhood epilepsy.

In this review, we present the degree of cognitive impairment according to the type of epilepsy or epileptic syndrome, and the impact of electroclinical seizures and antiepileptic medication on cognition function in childhood onset epilepsy.

Cognitive assessment of children with epilepsy

Cognitive assessment is an important component of diagnosing learning and behavior problems in children with epilepsy. A thorough assessment will depend on functional information gleaned from careful clinical interviewing, observations of how the child performs, and finally, the results of psychiatric tests. Clinical assessment of children with epilepsy need to take into account the child's age and developmental level, and factors related to epilepsy. The underlying neuropathology may lead to different problems at different ages. In addition, not only will appropriate tests differ radically depending on the age of the child, but the child's age at testing and age at onset of epilepsy will also affect their performance on assessment and outcomes. There are two main types of instruments used for assessing cognitive function in children with epilepsy. One group consists of tools aimed to give a global assessment of cognitive performance, whereas the other comprises tests that specifically assess certain cognitive functions, such as memory, attention, or executive function. A selection of generally used test is shown in Table 1.

Cognitive impairment in childhood onset epilepsy or epileptic syndrome

Cognitive impairment occurs more frequently in children with epilepsy than in children without epilepsy, irrespective of other chronic illnesses[12]. Although the underlying causes of cognitive impairment are generally complex and multifactorial, epilepsy or seizures themselves is one of the important causes of cognitive disability. Besides the underlying etiology of epilepsy, seizure type and frequency, age at onset of epilepsy, ongoing subclinical epileptiform discharges, and duration of epilepsy could affect the cognitive function in children with epilepsy. One of the strongest factors influencing cognitive function is the etiology of epilepsy, especially in children with new onset epilepsy. The high prevalence of cognitive impairments at epilepsy onset suggests the intrinsic abnormalities attributable to genetics and the underlying abnormality of the brain in children with new onset epilepsy at baseline[13]. The developing brain may be affected by some epileptic syndromes, and certain cognitive dysfunction may ensue. Certain pediatric epilepsy syndromes are associated with significant cognitive or behavioral declines with a devastating impact. The cognitive function in specific epilepsy and epileptic syndrome in childhood are summarized in Table 2.

1. Benign focal epilepsies in childhood

Although benign focal epilepsies in childhood are known to have no structural brain lesion, easily controlled seizure, and good prognosis, recent evidence suggests that children with benign focal epilepsy may present with impairment of overall cognitive function, or difficulties with visual perception, attention, and memory[14]. Children with benign childhood epilepsy with centrotemporal spikes (BCECTS) demonstrate attention impairment, learning difficulties, and memory impairment in the presence of overall normal intelligence[10,15]. Reading disability and phonological processing difficulties are reportedly strongly comorbid in children with BCECTS[16]. In addition to the consequence of epilepsy itself, these deficits are considered as independently inherited traits with increased odds among relatives

Table 1. Cognitive assessment tools in children with epilepsy

Test name	Age range	Functions assessed/subscales
Bayley Scales of Infant Development III	1–42 mo	Motor scale, mental scale, behavioral rating scale
Wechsler Preschool and Primary Scale of Intelligence III	3–7 yr	Verbal scale, performance scale
Stanford-Binet Intelligence Scale (5th ed)	2–19 yr	Composite IQ score
Kaufman Assessment Battery for Children II	3–13 yr	Sequential processing scale, simultaneous processing scale, achievement scale
Wechsler Intelligence Scale for Children (WISC-IV)	6–17 yr	Verbal scale, performance scale, full scale, verbal comprehension index, Perceptual organization index, freedom of distractibility index
Basic test of memory and learning	6–12 yr	Memory, learning
ADHD Diagnostic System	5–19 yr	Attention

IQ, intelligence quotient; ADHD, attention deficit/hyperactivity disorder.

 http://dx.doi.org/10.3345/kjp.2016.59.4.155

Table 2. Childhood epilepsy syndromes with an indication of age of onset, duration of epilepsy, prognosis of epilepsy, and cognitive function

Specific syndrome	Age at onset	Age at remission/prognosis	Cognitive function
Benign focal epilepsies in childhood			
Benign childhood epilepsy with centrotemporal spikes	3–13 yr	16 yr/good	Normal or mildly subnormal IQ
Idiopathic occipital epilepsy	2–8 yr; 6–17 yr	12 yr or earlier/good	Learning difficulties
			Inattention, hyperactivity, language disability
Cryptogenic or symptomatic focal epilepsies			
Frontal lobe epilepsy	Childhood	Unclear/variable	Normal or mildly subnormal IQ
			Impairment of executive function
			Inattention, hyperactivity
Temporal lobe epilepsy	School age or earlier	Long-standing/variable	Memory impairment
			Impairment of executive function
Rasmussen syndrome	6–12 yr	Progressive/ominous	Progressive cognitive decline
Hemiconvulsion-hemiplegia syndrome	1–5y r	Chronic/severe	Progressive cognitive decline
Idiopathic generalized epilepsies			
Benign myoclonic epilepsy in infancy	3 mo–3 yr	3–5 yr/variable	Normal or mildly subnormal IQ
			Learning difficulties
Epilepsy with myoclonic astatic seizures	3–5 yr	Variable/variable	Normal or cognitive impairment
Childhood absence epilepsy	5–6 yr	10–12 yr/good	Normal or mildly subnormal IQ
			Inattention, memory impairment
			Deficit of visuospatial skill
			Language disability
Juvenile myoclonic epilepsy	12–18 yr	Usually lifelong/good	Normal or mildly subnormal IQ
			Inattention, hyperactivity
Epileptic encephalopathies			Memory impairment, language disability
Early infantile epileptic encephalopathy (Ohtahara syndrome)	Newborn–infant	No remission/ominous	Severe psychomotor retardation
Infantile spasms (West syndrome)	Infant	Variable/variable	Severe intellectual disability
Severe myoclonic epilepsy in infancy (Dravet syndrome)	Infant	No remission/severe	Progressive cognitive decline
Lennox-Gastaut syndrome	3–10 yr	No remission/severe	Severe intellectual disability
Landau-Kleffner syndrome	3–6 yr	8–12 yr/guarded	Regression of language
Epilepsy with continuous spike waves during slow-wave sleep	4–7 yr	8–12 yr/guarded	Expressive aphasia, regression of global skills

IQ, intelligence quotient.
Adapted from Guerrini R. Lancet 2006;367:499-524[100].

of the proband[17]. Benign childhood epilepsy with occipital paroxysms is reportedly associated with impairment in attention and memory ability, visual perception, reading and writing abilities, and arithmetic abilities[18].

Recent reports on quantitative and functional brain imaging analyses demonstrate multifocal abnormalities in white matter integrity by cortical and subcortical morphometry in children with new onset idiopathic focal epilepsies, particularly with BCECTS[9,19-22]. Multiple structural abnormalities outside the seizure onset zone include the frontal and temporal lobes, putamen, and amygdala. Theses abnormalities are regarded as disruption of neurodevelopmental processes or secondary pathology of distal regions by the propagation of epileptiform discharges[9,19-22]. Although the reported abnormalities across studies are inconsistent and the cross-sectional findings cannot demonstrate causality, these findings suggest that microstructural alterations of the brain may underlie and contribute to early cognitive disruption in childhood epilepsy[9,23,24].

2. Symptomatic focal epilepsies

Specific cognitive impairments could originate in focal epilepsies in correlation with seizure focus. In frontal lobe epilepsy, attention deficits and impairment of executive function are frequently described[25]. Both, a structural lesion and an epileptogenic zone, in the frontal lobe can interfere with a variety of frontal lobe functions such as planning, organizing, paying attention, and problem solving, leading to cognitive impairment and executive dysfunction. The most prominent cognitive impairment in temporal lobe epilepsy (TLE), particularly if caused by mesial temporal sclerosis, involves episodic memory deficits due to

the involvement of the limbic structures for memory consolidation[26,27]. In addition, as both mesial and lateral temporal lesions can implicate wide spread neural network disturbance, children with TLE can have executive dysfunction and inattention[28].

Rasmussen syndrome and hemiconvulsion-hemiplegia syndrome are rare disorders, but their chronic and progressive courses usually affect unilateral hemispheric function. These conditions cause intractable focal seizures, epilepsia partialis continua, contralateral hemiplegia, and variable degree of progressive intellectual deterioration[29,30]. If the dominant hemisphere is affected, patients frequently have complications of language disabilities[29].

A common neuropathology of medically intractable focal epilepsy is focal cortical dysplasia (FCD), which has accounted for >50% of intractable epilepsy in children[31]. There is a high rate of cognitive impairment in children with FCD, particularly with FCD type I, ranging from 50% to 80%[32,33]. The major contributor to cognitive impairment in FCD is considered the underlying brain substrates. The widespread alterations with impaired cortical inhibition and the subsequent increased excitation, and disrupted cognitive networks in dysplastic lesions are known to have profound effect on cognitive function in children with FCD. In addition, the age of epilepsy onset, duration and severity of epilepsy, FCD lesion location, lesion extent, and specific histopathological features can be related to the variation in neuropsychological profiles[32]. Children with tuberous sclerosis complex (TSC) are also at increased risk for cognitive impairment as well as refractory focal epilepsy. Fifty to sixty-five percent of children with TSC have various degree of cognitive impairment including mental retardation, autism, and learning disabilities[34]. The number of tubers and their location seem to play an important role in the cognitive outcome. Early onset of epilepsy, genetics, and timing and type of AEDs have been proposed as risk factors for cognitive impairment[35,36].

3. Idiopathic generalized epilepsies

Risk of pervasive or specific cognitive impairment and learning disability despite normal intelligence and well-controlled seizures exists in children with idiopathic generalized epilepsy (IGE)[37,38]. In benign myoclonic epilepsy in infancy, the long-term prognosis of epilepsy and neuropsychological outcome are good[39]. However, cognitive impairment or learning difficulties are reported in some cases with a long delay between seizure onset and diagnosis or high seizure frequency[39]. Neurocognitive outcome of myoclonic-astatic epilepsy is documented as highly variable, ranging from normal cognitive development to cognitive delay[40]. The cognitive impairment detected in children with childhood absence epilepsies involves deficits in visual sustained attention, verbal and nonverbal attention and memory, execution of visual-motor tasks, and language disabilities[37,41,42]. Patients with juvenile myoclonic epilepsy also often have impairment of attention, control of inhibition, verbal or working memory, mental processing and flexibility, or verbal fluency[43,44].

Similar to idiopathic focal epilepsy, quantitative and functional brain imaging analysis in IGE demonstrates multifocal abnormalities in white matter integrity by cortical and subcortical morphometry[21,22,45]. As in the syndrome-specific anatomic abnormalities, abnormal neurodevelopmental changes in brain structure and connectivity attributable to active epilepsy and medical treatment result in structural alterations in mainly the subcortical structures or the frontal and temporal lobes[21-23,46]. The reported abnormalities in IGE are inconsistent across studies, but these findings also support that cognitive impairment in IGE is associated with structural disruption of the brain network[21-23,46].

4. Epileptic encephalopathies

Many epileptic encephalopathies with neonatal to childhood onset are frequently associated with drug-resistant epilepsy and significant cognitive impairment. Apart from the frequent and paroxysmal electroclinical seizures, metabolic or genetic causes may be important contributors. In early myoclonic encephalopathy and early infantile epileptic encephalopathy (or Ohtahara syndrome), defined as epileptic encephalopathies with neonatal onset, a typical suppression-burst electroencephalography (EEG) pattern and severe intractable seizures are highly associated with poor prognosis and severe psychomotor retardation[47]. West syndrome, an epileptic syndrome characterized by clinical spasms with hypsarrhythmia on interictal EEG, leads to intellectual disability and specific cognitive and behavioral deficits such as speech difficulties and visuospatial disabilities in majority of patients[48]. On the other hand, prognostic factors for a better cognitive outcome in West syndrome include effective early treatment of spasms, absence of atypical spasms and partial seizures, and age at onset older than 4 months[49,50]. In severe myoclonic epilepsy of infancy (or Dravet syndrome), early development is normal but progressive cognitive decline occurs by 1–4 years of age, with intellectual disability and an autism phenotype[51]. Lennox-Gastaut syndrome (LGS) consisting of multiple seizure types and characteristic EEG pattern of slow spike-and-wave complexes also frequently accompanies or induces severe intellectual disability in most cases[52]. It is suggested that the epileptic processes associated with infantile spasms and LGS lead to abnormal patterns of neuronal connectivity during brain development, thus resulting in subsequent impairment or regression of cognition[48,53].

Landau-Kleffner syndrome (LKS, acquired epileptic aphasia) and continuous spike-and-wave activity in sleep (CSWS) are epileptic encephalopathies with common clinical features, including seizures, neurodevelopmental regression, and EEG pattern of electrical status epilepticus during slow-wave sleep. In LKS, the primary clinical manifestation is an acquired regression of language, while in CSWS, there is a regression in global skills.

Impact of clinical or electrical seizures on cognitive function

Neurologic disturbances such as electroclinical seizures can have an impact on brain maturation and cognitive function in childhood, the most vulnerable period of brain development. The seizure itself may directly disrupt the daily activities, and transient cognitive impairment can occur during interictal or postictal period, depending on seizure severity[54,55]. In addition, anoxia, lactic acidosis, or excessive excitatory neurotransmitters by repetitive or prolonged seizures may permanently damage the cerebral substrate resulting in cognitive impairment.

Age at onset of epilepsy, seizure type and frequency, ongoing subclinical epileptiform discharges, and duration of epilepsy are known to impact on the cognitive impairment in children with epilepsy. These findings indicate that electroclinical seizures have an effect on brain maturation and cognitive functioning[25,56]. The degree and course of cognitive impairment can vary depending on the developmental stage of the brain affected by electroclinical seizures[1-3]. In general, young age at seizure onset is strongly associated with cognitive impairment in most childhood epilepsies[57]. Widespread propagation of epileptiform discharges at young age could have a negative impact on neurodevelopmental processes including synaptogenesis and apoptosis[58]. In addition, prolonged and frequently repeated seizures are typically associated with more severe adverse effects on cognition, particularly if epilepsy is symptomatic[3,59]. Some studies report that children with generalized seizures or nonconvulsive seizures have lower cognitive scores than children with focal seizures or convulsive seizures[13,60]. However, findings across studies inconsistently implicate these epilepsy related factors[57]. Chronic progressive effects of epilepsy on brain structure may also be associated with cognitive impairment[59]. However, some evidence indicates that the cognitive impairments at epilepsy onset do not seem to worsen over time but remain on a trajectory[4,61], suggesting the importance of intrinsic abnormalities at epilepsy onset and early detection and intervention rather than the effect of chronic epilepsy[62,63].

Distinct from ictal effects and long-term stable interictal effects caused by the underlying etiology or clinical syndrome, evidence for the impact of interictal epileptiform discharges on cognitive function are conflicting[64]. Some studies demonstrate transient cognitive impairment with slowness of reaction times and inaccurate perception during interictal epileptiform discharges[65], but some indicate low incidence of such impairments and failure to attain statistical significance[66]. It is suggested that subtle seizures can lead to presumed transient cognitive impairment, while interictal epileptic activity has less effect on cognitive functioning[64]. However, in epileptic encephalopathies such as West syndrome, Dravet syndrome, and LGS, the epileptic activity itself may contribute to severe cognitive and behavioral impairments, interfering with the development of brain functions during critical periods[1,48,53].

Cognitive side effects of AEDs

AEDs reduce neuronal irritability, and thus, may reduce neuronal excitability and impair cognition[5,67], although the magnitude of AED effect on cognition is commonly smaller than other epilepsy-related factors. Because AEDs are the major therapeutic intervention in epilepsy, neurologists have to consider the risk-to-benefit ratio of any treatment and assess the patient's cognitive condition before starting treatment with an AED. Particularly, as the modest effects of AEDs on attention and memory might be additive over long-term during neurodevelopment, children may be at a higher risk for developing cognitive side effects from AEDs[67,68]. Further, the detrimental effects of AEDs might interact with seizures and underlying cerebral abnormalities to produce even greater impairments in neurodevelopment[69]. Currently, investigations in children are insufficient to fully explain the effects of each AED[68].

In general, polypharmacy, increasing AED dosage, and anticonvulsant blood levels increase the risk of cognitive side effects. However, cognitive effects differ across AEDs. Table 3 summarizes the cognitive impact of AEDs in children. The most consistent and marked adverse effects that affect attention and memory are observed with barbiturates and benzodiazepines, while the cognitive side effects of phenytoin, valproate, and carbamazepine do not differ significantly[5,68]. A double blind randomized crossover monotherapy study conducted in children with epilepsy[70] showed that the psychological and behavioral performance in children treated with phenobarbital was worse than in those treated with valproate. Adverse cognitive effects of phenobarbital were found in placebo-controlled, parallel-group studies on children with febrile convulsions[71]. Phenytoin and carbamazepine may affect mental speed, mainly in higher dosing and polytherapy. Valproate does not seem to impair cognition if the dosage is within the therapeutic range and without hyperammonemia. According to an earlier study, ethosuximide caused mild and temporary attention problems in children with idiopathic epilepsy (mostly absence seizures), as compared to a no treatment baseline[72]. However, more recently, a double-blind, randomized, controlled clinical trial in children with newly diagnosed childhood absence epilepsy showed that ethosuximide is associated with fewer adverse attention effects than valproic acid or lamotrigine[73].

Some new AEDs appear to have fewer cognitive side effects than old AEDs, but the comparative effects of the newer and older AEDs are not yet fully determined[5,74]. Properly designed monotherapy studies, either in comparison with placebo or in

Table 3. Summary of cognitive impact of antiepileptic drugs in children

Antiepileptic drug	Impairment or improvement	Area of cognitive impairment or improvement
Phenobarbital	↓↓↓	Memory and attention
Phenytoin	↓	Slowing of mental speed at high dosing
Ethosuximide	↔	
Carbamazepine	↔/↓	Probably only an effect with high dosing
Valproic acid	↔	Impaired cognition in hyperammonemia
Topiramate	↓↓↓	Attention, memory, and language function
Lamotrigine	↑	Cognitive enhancing effect on attention
Clobazam	↔	
Levetiracetam	↔	
Oxcarbazepine	↔/↑	Improvement of attention
Zonisamide	↓	Memory and language function
Gabapentin	No information in children	(No serious cognitive effect in adult)
Vigabatrin	↔	
Rufinamide	No information in children	(No serious cognitive effect in adult)
Lacosamide	No information in children	(No serious cognitive effect in adult)

↓, mild impairment; ↓↓, moderate impairment; ↓↓↓, severe impairment; ↑, mild improvement; ↑↑, moderate improvement; ↑↑↑, profound improvement; ↔, no impairment or improvement.

comparison with another antiepileptic demonstrate behavioral or cognitive measures. There is compelling clinical proof of topiramate-induced cognitive impairment (attention, memory, and language) in patients with childhood epilepsy[75,76]. Factors affecting these adverse effects include drug dosage, rate of dose titration, maintenance time, polytherapy, and individual susceptibility. On the contrary, lamotrigine has less harmful cognitive side effects in comparison with topiramate and old AEDs[77]. There were no significant differences between clobazam and standard monotherapy on the cognitive and behavioral effects in a randomized, double-blind, prospective study[78]. Levetiracetam also does not seem to have a negative impact on cognition. Three studies for levetiracetam indicate that it has significantly less neuropsychological effects, as compared with carbamazepine in adults[79,80] or almost no neuropsychological effects in children[81]. However, some aspects of behavioral and emotional aggravation, specifically aggressive behavior, seem to be affected by adjunctive treatment with levetiracetam[82]. No statistically significant differences in cognition were observed between oxcarbazepine, carbamazepine, and valproate in an open-label, randomized, parallel-group study in children and adolescents with newly diagnosed partial seizures[83]. Furthermore, a randomized, monotherapy, multidose, open-label study with zonisamide reported cognitive deficits and dose-related negative effects on delayed word recall, trail making test, and verbal fluency[84]. There is no evidence of cognitive side effects with vigabatrin. A small, open-label, randomized, parallel-group study of patients with epilepsy showed that vigabatrin produced fewer adverse effects on cognitive function than carbamazepine[85]. Studies on gabapentin, rufinamide, and lacosamide have not been conducted in children. However, studies in adults show no serious cognitive deficits[86-88].

Proposed possible mechanisms underlying the adverse effects of AEDs on cognitive function include actions of reactive intermediates, ischemia, apoptosis-related mechanisms, folate, and neuronal suppression. AEDs may be bioactivated to free-radical reactive intermediates, which may bind to DNA, protein, or lipids, resulting in teratogenesis[89]. Ischemia-induced embryopathy in animals resembles phenytoin-induced defects, and hyperoxic chamber treatment reduces malformations caused by phenytoin[90]. Phenobarbital, phenytoin, and primidone, but not carbamazepine, deplete folate[91,92], and valproate affects folate-dependent one-carbon metabolism[93]. Studies in neonatal rats reveal widespread apoptosis in the developing brain, as a result of exposure to clonazepam, diazepam, phenobarbital, phenytoin, vigabatrin, or valproate[94]. However, in this animal model, similar apoptotic effects were not seen at therapeutic dosages for carbamazepine, lamotrigine, levetiracetam, or topiramate monotherapy[95,96]. Reduction of neuronal excitation by AEDs in utero or in the neonatal period might also alter the synaptic growth and connectivity during these early stages, resulting in long-term deficits in cognition and behavior.

Recognition and treatment of cognitive impairment in epilepsy

Proper and early identification of cognitive impairment is necessary to provide early developmental interventions, ap-

propriate school programming, vocational counseling, supportive work settings, and a safe environment for promotion of independence across the life span in children with epilepsy. Early and complete seizure control and EEG normalization is mandatory for the prevention of developmental disablement in younger patients or of accelerated cognitive decline. Choosing AEDs that best control seizures with minimal cognitive side effects, slow titration and using the lowest effective dose of AEDs, avoiding polypharmacy, and treating comorbid neuropsychiatric disorders are also important to ameliorate the cognitive side effects of epilepsy. Despite the potential adverse effects of pharmacotherapy, achieving complete or acceptable seizure control using AEDs should be the initial approach to improve the cognitive impairment in epilepsy. The beneficial effect of reducing seizures may offset the adverse cognitive effects[68,97]. However, even if seizures are controlled, an ongoing epileptogenic process can irreversibly damage the brain, causing persistent cognitive changes, and finally global intellectual deficits. In patients with resectable cerebral lesions, particularly in TLE or FCD-related epilepsy, early surgical intervention may improve the cognitive impairment as well as seizures[98,99]. Recently, pharmacologic interventions for memory or attention deficit have gained some attention. Psychopharmacology may be another option to treat behavioral problems in patients with seizures, but this should not substitute the attempts to control the seizures or to treat any underlying conditions.

Conclusions

Children with epilepsy are at an increased risk for a broad range of cognitive disturbances and have substantial intellectual disability hindering their academic achievements. A variety of epilepsy-related factors including etiology of epilepsy, underlying pathology, severity of electroclinical seizures, and AED treatment are associated with cognitive impairment at or after diagnosis of epilepsy. Early identification, neuropsychological monitoring, and appropriate intervention for cognitive impairment are required to improve individual medical care, and prevent learning disabilities and social problems, particularly in children with earlier onset of seizure, symptomatic epilepsy, longer duration of illness, ongoing seizures, and polypharmacy.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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 http://dx.doi.org/10.3345/kjp.2016.59.4.155