

Principles and practices of behavior management in epilepsy

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Abstract

People with epilepsy (PWE) can have cognitive and behavioral disturbances caused by many factors, including epileptic seizures, interictal electroencephalographic discharges, brain pathology, psychological factors, and side effects of antiepileptic drugs (AEDs). Recent studies suggest that factors other than seizures themselves play a crucial role in the cognitive dysfunction in PWE. Neuropsychologic deficits due to cognitive effects of interictal epileptic activity have been demonstrated (transitory cognitive impairment). With regard to the cognitive side effects of AEDs, new generation drugs have a less significant negative impact compared to older AEDs. PWE are more likely to have neuropsychiatric co-morbidities (depression, anxiety, and aggression), which should be attended to. Increasing evidence suggests that subtle cognitive and behavioral disorders can be seen in association with benign epilepsy of childhood with centrotemporal spikes.

INTRODUCTION

It has been acknowledged that the majority of people with epilepsy (PWE) have cognitive and behavioral disturbances.¹ Many factors can coexist and contribute to the cognitive and behavioral dysfunction in epilepsy, including epileptic seizures, interictal electroencephalographic (EEG) discharges, brain pathology, psychological factors, and side effects of antiepileptic drugs (AEDs).¹ In addition, epilepsy-related sleep disruption has recently been reported to have a negative impact on cognition.² As a consequence of these factors, affected children can have developmental problems such as learning difficulties in school; and some psychiatric disorders may occur in adults.

EFFECTS OF EPILEPSY-RELATED FACTORS ON COGNITION

1. Seizures

It is well known that risk factors of global intellectual impairment in epilepsy include symptomatic causes or epileptic encephalopathy. Generalized tonic-clonic seizures are thought to have a greater negative impact on intelligence than partial seizures. In addition, an early onset of epilepsy before 5 years of age, a high seizure frequency, and a history of status epilepticus

are risk factors. However, it is challenging to elucidate the neuropsychologic impact of seizures themselves because of methodological difficulties, such as the many interrelated factors mentioned earlier. In a recent prospective study, Taylor *et al.* examined the cognitive status of 155 untreated PWE and 87 healthy controls, and found that memory and psychomotor speed were impaired in PWE without structural brain abnormalities, following a few seizures and before AED treatment.³ Although the mechanisms underlying the cognitive deficits were unknown, the study indicated that factors other than seizures play a crucial role in the cognitive dysfunction in PWE.

2. Interictal EEG discharges

In 1984, Aarts *et al.* demonstrated transitory cognitive impairment (TCI), which comprises neuropsychologic deficits due to cognitive effects of interictal epileptic activity.⁴ TCI is more prominent during generalized spike-wave activities, but is also seen in focal discharges. TCI is not necessarily a consequence of general impairment of attention, but comprises a specific disruption of a certain cerebral process. However, there is no evidence for use of AEDs for cognitive problems in individuals with subclinical EEG discharges.

3. Antiepileptic drugs

According to the psychotropic properties, there are two main categories of AEDs, i.e., GABAergic drugs and anti-glutamatergic drugs. The former AEDs have sedating, axiolytic and antimanic properties, and include barbiturates, benzodiazepine, valproate, vigabatrin, tiagabine, and gabapentine. The latter drugs have activating, axiogenic, and antidepressant properties, and include felbamate and lamotrigine. Topiramate has both properties. From a psychiatric point of view, there are negative and positive effects of older generation AEDs. Among them, barbiturates and benzodiazepines should be carefully used because they tend to cause more serious depressive or hyperactive side effects, especially in children. On the other hand, new generation AEDs show less significant negative side effects compared to the older generation AEDs.⁵ Topiramate is an exception that frequently causes serious cognitive side effects, such as depression, psychomotor slowing, and psychosis. However, double-blind controlled studies with behavioral measures are still needed, especially for newer generation AEDs.

NEUROPSYCHIATRIC IMPAIRMENT IN EPILEPSY

1. Depression

Depression is common in PWE, occurring three times more than in normal controls. Risk factors for depression are temporal or frontal epilepsy and the presence of hippocampal atrophy. Depressive patients frequently exhibit neuroanatomical structural changes in the limbic-cortical-striatal-pallidal-thalamic-circuit.⁶ The severity of hippocampal atrophy correlates with the duration of untreated depression. Conversely, treatment with antidepressant drugs can prevent hippocampal atrophy in depressive patients.⁷ Management of depression associated with epilepsy includes (1) re-evaluation to assess whether AEDs may be contributing to the depression, (2) attempts to reduce AEDs to those with the least adverse psychotropic effects, (3) observation for several weeks to evaluate the need for antidepressant drugs, and (4) if necessary, selective serotonin reuptake inhibitors as the first choice drugs for treating the depression, which may also improve the seizure frequency.

2. Anxiety

Anxiety disorders are twice as common in PWE as in the general population. Risk factors are frequent seizures, polytherapy, and drug withdrawal. If anxiety is an ictal symptom, it most likely indicates that the epileptic focus typically lies in the amygdale, and also may be located in the anterior cingulate, orbitofrontal cortex, and other limbic structures. In addition, ictal anxiety should be differentiated from panic attacks.⁸ The main deferential point is that PWE hesitate to disclose affective ictal symptoms, while patients readily report panic attacks. Treatment of anxiety in association with epilepsy includes (1) administration of GABAergic AEDs with axiolytic potential if the drugs are suitable for the seizure type, (2) psychologic intervention with the collaboration of a psychotherapist, and (3) if necessary, antidepressants, including selective serotonin reuptake inhibitors, tricyclic antidepressants, benzodiazepine, and buspiron.

3. Aggression

Aggression can be seen during interictal, ictal, or postictal periods. However, most of it is considered to be defensive or reactive aggression.⁹ "Aggressivity" is not synonymous with "violence". Aggressive behavior resulting in physical violence is exceptionally rare. Risk factor is complex partial seizures involving the mesial temporal and prefrontal cortex. Aggressive behavior often occurs in response to unpleasant stimulation to PWE with transiently disrupted frontotemporal limbic networks. Management of aggression includes (1) isolation of the patient until control of the seizures has been established, (2) special supervised nursing care to prevent patients from hurting themselves and/or other patients, and (3) in severe cases, antipsychotic medication, for example, haloperidol.

NEUROPSYCHOLOGIC DEFICITS IN BENIGN EPILEPSY OF CHILDHOOD WITH CENTROTEMPORAL SPIKES

Benign epilepsy of childhood with centrotemporal spikes (BECTS) is one of the most common epilepsy syndromes occurring in 15-25% of pediatric epilepsy patients. In BECTS, seizures begin in middle childhood and resolve by puberty. Over the last 10 years, a number of studies have indicated that patients with BECTS have a variety of subtle cognitive and behavioral disorders.¹⁰ Therefore, there should be adequate intervention

in patients with such previously considered benign epilepsy. For this purpose, neuropsychologic tests are suggested and beneficial, especially in children with the first recognized seizures. Unnecessary cognitive side effects of AEDs should be avoided, because the administration of AEDs to achieve a relative reduction in seizure frequency may adversely impact the patient's quality of life.

REFERENCES

1. Motamedi GK, Meador KJ. Epilepsy and cognition. *Epilepsy Behav* 2003; 4:S25-S38.
2. Parisi P, Bruni O, Pia Villa M, *et al.* The relationship between sleep and epilepsy: the effect on cognitive functioning in children. *Dev Med Child Neurol* 2010; 52:805-13.
3. Taylor J, Kolamunnage-Dona R, Marson AG, Smith PE, Aldenkamp AP, Baker GA. Patients with epilepsy: cognitively compromised before the start of antiepileptic drug treatment? *Epilepsia* 2010; 51:48-56.
4. Aarts JH, Binnie CD, Smit AM, Wilkins AJ. Selective cognitive impairment during focal and generalized epileptiform EEG activity. *Brain* 1984; 107:293-308.
5. Meador KJ. Cognitive side effects of epilepsy and of antiepileptic medications. In: Wyllie E, ed: *The treatment of epilepsy. Principles and practice*. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005:1215-26.
6. Sheline YI. Neuroimaging studies of mood disorder effects on the brain. *Biol Psychiatry* 2003; 54:338-52.
7. Sheline YI, Gado MH, Kraemer HC. Untreated depression and hippocampal volume loss. *Am J Psychiatry* 2003; 160:1516-8.
8. Beyenburg S, Mitchell AJ, Schmidt D, Elger CE, Reuber M. Anxiety in patients with epilepsy: systematic review and suggestions for clinical management. *Epilepsy Behav* 2005; 7:161-71.
9. Gerard ME, Spitz MC, Towbin JA, Shantz D. Subacute postictal aggression. *Neurology* 1998; 50:384-8.
10. Metz MN, Filippini M. Neuropsychological findings in Rolandic epilepsy and Landau-Kleffner syndrome. *Epilepsia* 2006; 47 (Suppl 2):71-5.