SUMMARY

Speech and language dysfunction are a common developmental problem observed in children with epilepsy. These patients need a complex assessment and chronic therapy, conducted by neurologists, psychologists and speech therapists, as well as other specialists. Abnormal cerebral activity in epilepsy, and its treatment results in disturbances in a variety of cognitive functions, and may also affect the development of a child. However, it is still not known how epileptiform discharges influence the speech and language skills. Published studies concentrate mainly on a characteristics of speech and language disorders, its potential underlying nature or additional disabilities. In recent studies, performed through the application of new techniques, researchers have attempted to find genetic and neuromolecular explanations for the origin of childhood speech and language disorders. Nevertheless, research, concerning the area of speech and language dysfunctions in children with epilepsy, is rare and still requires detailed attention. The aim of the present study is to review the available data in order to establish the factors affecting chiefly the language and speech in children with epilepsy.

Key words: centrotemporal-spikes, epilepsy, acquired epileptic aphasia
INTRODUCTION

There are a large number of children with epilepsy who are in need of special services relating to cognitive functions and school achievements. Problems with attention, memory and language have been reported in this group (Mefford 2014; Melbourne 2014; Shinnar 2010). The type and frequency of seizures, the age of onset, and the duration of epilepsy are reported to affect the severity of cognitive symptoms (Jones et al. 2010). There is also the impact of antiepileptic drugs used in therapy (their number and dose) on cognitive functions (Aldenkamp 2001; Mula 2012). There are not so many studies which deal with the prevalence of speech and language disorders in children with epilepsy. The aim of the present study is to review the available data in order to establish the factors affecting chiefly the language and speech in children with epilepsy.

ANTIEPILEPTIC DRUGS

Among children, with no concomitant diseases, with epilepsy only, there are some specific speech, language and neuropsychological difficulties, although verbal intelligence and comprehension are usually not particularly affected. Children with an early onset of epilepsy, and on more than one AED, appear to experience more difficulties (Helmstaedter and Witt 2008). There are some studies reporting that antiepileptic drugs can induce clinically meaningful adverse cognitive and behavioral side effects (Hirsch, Schmitz and Carreno 2003). In the studies evaluating the cognitive effects of antiepileptic drugs it has been shown that phenobarbital has a negative impact on short term memory (Calandre et al. 1990; MacLeod, Dekabian and Hunt 1978), but no special findings concerning language and speech delay were observed. For phenytoine there are studies available where cognitive impairment in the areas of attention, memory and mental speed was observed (Meador et al. 1991). The most important cognitive side effects with the biggest influence on speech and language contain topiramate (Koo et al. 2013; Ojemann et al. 2001). It has been reported that topiramate has a negative impact on verbal fluency, verbal memory span and verbal memory (delayed recall and recognition) (Kockelmann, Elger and Helmstaedter 2004). There is also some evidence which shows a similar cognitive “profile” for zonisamide when compared to topiramate. The use of most popular conventional antiepileptic drugs carbamazepine and valproate, is connected with no impairment for carbamazepine, and a mild to moderate impairment of psychomotor and mental speed for valproate (Aldenkamp et al. 1993; Prevey et al. 1996). Lamotrigine, levetiracetam and oxcarbazepine showed promising cognitive profiles with no particular effects on cognition (Aikia et al. 1992; Kim et al. 2014; Koo et al. 2013; Marciani et al. 1998; Mazurkiewicz-Beldzińska and Olszewska 2000; Wu et al. 2009). Based on the available data, clinicians should consider the cognitive side effect profiles of antiepileptic medications, particularly in extreme age groups, especially children. While no effective treatments are available for cognitive and behavioral impairments in epilepsy, comprehensive pretreat-
ment evaluation and the careful selection of antiepileptic drugs may minimize these unwanted effects.

What is even more important, there are equally studies which emphasize the language skills delay in children prenatally exposed to antiepileptic drugs (Nadebaum et al. 2011). It has been shown that children born of mothers who were taking valproic acid or taking polytherapy with valproic acid during pregnancy are at risk of language impairment. In the cohort studied by Nadebaum et al. (2011) 18.6% of studied children met the criteria for moderate or severe language delay. This was significantly higher than the expected population rate of 6%.

SPEECH AND LANGUAGE DISTURBANCES IN SPECIFIC EPILEPSY SYNDROMES.

LANDAU-KLEFFNER SYNDROME

Landau-Kleffner syndrome (LKS), also known as acquired epileptic aphasia, is a rare disorder appearing in children between 2 and 10 years of age (peak age 5 – 7 years), twice more frequently in boys than in girls. It is characterized by acquired aphasia and electroencephalographic (EEG) abnormalities in previously healthy and normal children. Focal epileptic seizures, generalised tonic-clonic, atonic seizures or atypical absences may also be present, however 20 to 30% of patients never experience them. If seizures occur, they are usually easy to treat, but the language and behavioral disturbances persist (Caraballo et al. 2014; Deonna and Roulet-Perez 2010; Duran et al. 2009; Smith and Spitz 2002). Epileptiform activity is responsible for the deterioration of auditory processing abilities. The loss of receptive language is followed by expressive aphasia, with a marked reduction in spontaneous speech. In almost 90% of children a receptive aphasia appears first, then subsequently a rapid and severe reduction in spontaneous speech occurs, leading even to mutism. The type of aphasia is usually a verbal auditory agnosia, which is the failure to give a semantic significance to the different sounds (Caraballo et al. 2014; Deonna and Roulet-Perez 2010; Duran et al. 2009). The aphasia has a subacute onset and a progressive course, with a fluctuating pattern of spontaneous improvements and exacerbations. When auditory agnosia occurs, autistic-like symptoms may be identified. Nevertheless, the child with LKS never loses the ability to relate socially to others or properly participate in social relations (Pačhalska et al 2012). Psychotic behavior has been reported in a small number of patients. On neuropsychological examination, children with LKS have normal or minimally impaired nonverbal cognitive functions. Starting from a few months to several years the aphasia stabilizes and usually improves before adulthood (Pačhalska et al 2012). Other clinical findings in children include cognitive impairment and global autistic behavioral regression (Caraballo et al. 2014; Deonna and Roulet-Perez 2010; Duran et al. 2009; Smith and Spitz 2002). The most frequently observed behavioral problems are attention deficits, impulsivity, distractibility, and hyperactivity (Duran et al. 2009).
An awake electroencephalogram (EEG) usually reveals normal background activity and focal epileptiform discharges, mostly on the temporal lobes: bilateral centrotemporal, posterior temporal, and parieto-occipital spikes and waves (Caraballo et al. 2014; Duran et al. 2009). During sleep there is an activation and diffusion of the epileptiform discharges, forming into the pattern of electrical status epilepticus during sleep (ESES) or continuous spikes and waves during slow sleep (CSWS) (Fig. 1) (Caraballo et al. 2014; Duran et al. 2009). EEG abnormalities in sleep correlate with the continuation of language impairment, and if evident for a few (more than 3) years may be associated with long-term language deficits (Caraballo et al. 2014).

A neuroimaging investigation in LKS is on the whole normal (Duran et al. 2009). However, there are also reports of LKS in patients with a congenital or acquired brain lesion (Caraballo et al. 2014; Duran et al. 2009).

The prognosis in LKS is variable: seizures and epileptiform discharges usually disappear with time, while language abnormalities tend to persist. Currently, LKS is considered as a clinical variant or subtype of encephalopathy related to ESES or CSWS, however, in the new diagnostic scheme of the ILAE (International League against Epilepsy) they are considered as separate clinical states (Pąchalska et al 2012).

Fig 1. EEG recording in patient with Landau-Kleffner syndrome – continuous generalized paroxysmal activity during sleep.
EPILEPSY WITH CENTROTEMPORAL-SPIKES

Accounting for 24% of all children with epilepsy between the age 5 and 14, childhood Rolandic epilepsy (benign partial epilepsy with centrotemporal spikes BCECTS) is the most common idiopathic partial epilepsy. Rolandic epilepsy is regarded as the classic example of benign focal epilepsy. However, neuropsychological deficits have been noted in affected children. As Rolandic discharges are mainly distributed over the centrotemporal region, specific interference with language function might be suspected. Studies which specifically investigated language/speech performance in children with Rolandic epilepsy found atypical hemispheric specialization, impairments in phonological production and verbal fluency (Northcott et al. 2005; Northcott et al. 2006; Northcott et al. 2007; Riva et al. 2007). In one study patients with Rolandic epilepsy failed five of the twelve standardized language tests significantly more often than the normative population and consequently showed impairment of the following functions: reading, spelling, auditory verbal learning, auditory discrimination with background noise and expressive grammar (Volkl-Kernstock et al. 2009). Language dysfunction was closely associated with learning difficulties at school (Northcott et al. 2007; Volkl-Kernstock et al. 2009).
Although the prognosis of seizure outcome is excellent, evidence indicates that BCECTS is not always a benign condition (de Saint-Martin et al. 2000). Studies over the last few years period have reported a large range of often conflicting findings of specific cognitive deficits. Most of the studies found language delay connected with the presence of interictal epileptic discharges (Baglietto et al. 2001; Fonseca, Tedrus, and Pacheco 2007) (Fig. 2), whereas other studies did not find such a correlation (Monjauze et al. 2005). In some studies there was a remarkable improvement in the language skills after remission (Berroya et al. 2004; Lindgren et al. 2004) others reported the persistence of significant impairment (Northcott et al. 2005). The nature of the deficits reported in patients with BCECTS has been inconsistent. Verbal (Baglietto et al. 2001; Massa et al. 2001), visuomotor (D’Alessandro et al. 1990), nonverbal (Baglietto et al. 2001; Massa et al. 2001) language (Staden et al. 1998), executive functioning (D’Alessandro et al. 1990) and memory deficits (Massa et al. 2001) have been described. The varied nature of these results is likely an artefact of the heterogeneity of the populations studied and the methods used. Recent studies with appropriate design, direct comparison to healthy controls and careful EEG analysis, show that children with BCECTS have a normal level of intelligence, but there is a specific pattern of difficulties in memory and phonologic awareness despite having an IQ within the normal range (Lopes et al. 2014; Metz-Lutz et al. 1999; Volkl-Kernstock et al. 2009).

In the literature the beneficial effect of behavioral methods to improve cognitive deficits and changes in the EEG have been reported (Mirski et al. 2014). In another study the authors draw attention to the usefulness of neurofeedback training (RBNT) in patients with Rolandic epilepsy. The rolandic spikes decreased after the sessions of RBNT and cognitive function improved (Pąchalska et al. 2012). There is an agreement that patients with Rolandic epilepsy should be investigated in the areas of pre-reading, reading, spelling, mathematics, and memory, and receive input from the teacher (Mefford 2014; Northcott et al. 2007; Volkl-Kernstock et al. 2009; Pąchalska et al. 2012). Children with Rolandic epilepsy should be followed up, as the impact of any difficulties may not be apparent early in the child’s education (Pąchalska et al. 2012).

**GENETIC FACTORS**

It has been recently shown that about 20% of cases of Landau-Kleffner syndrome, CSWS and atypical Rolandic epilepsy, often associated with speech impairment, can have a genetic origin sustained by de novo or inherited mutations in the GRIN2A gene (encoding the N-methyl-D-separate) (NMDA) glutamate receptor α2 subunit, GluN2A) (Dimassi et al. 2014; Lesca et al. 2013). GRIN2A is now considered a crucial genetic link between different epileptic and speech disorders of the same continuum (Lesca et al. 2013) from atypical Rolandic epilepsy to CSWS and Landau-Kleffner Syndrome. This is of prime importance because of the possible treatment options involving the NMDA-receptors mediated mechanisms in order to prevent seizures, and what is equally important - the language
and other neuropsychological deficits (Pachalska et al. 2012). It has been stated by Lesca et al, 2013 (Lesca et al. 2013) that the identification of GRIN2A as a major gene for particular epileptic encephalopathies connected with speech disorders provides the crucial insights into the mechanisms underlying these syndromes and their relationship.

**SYMPTOMATIC TEMPORAL LOBE EPILEPSY**

It has been found that in patients with symptomatic temporal lobe epilepsy, not only do the factors which were mentioned at the beginning of this review – the age of onset, localization of brain injury, but also the epileptic activity (ictal and interictal) by itself has a great impact on speech and language reorganization. It has been proved that not only structural elements, but also functional factors may have an effect on the language organization of the brain.

There are a lot of challenges with speech and language delay in children with epilepsy, awareness of them can lead to a better outcome through the implementation of therapeutic methods. Therefore the role of speech and language therapists is very important (Pachalska 2011; Pachalska et al. 2012).

**REFERENCES**


Aldenkamp, A.P., Effects of antiepileptic drugs on cognition. Epilepsia, 2001; Suppl. 46-51.


epilepsies contains candidate or known epilepsy genes including GRIN2A and PRRT2. Epilepsia 2014; 55: 370-378.


Mefford, H.C., Thinking about cognition and epilepsy. Epilepsy Behav 2014; 41:276.


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