Language Dysfunction in Pediatric Epilepsy

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Epilepsy is one of the most common and severe neurologic diseases in children, affecting 0.9%-2% of the pediatric population.[1,2] Children and adolescents with epilepsy and their parents indicate that quality of life is driven as much or more by cognitive comorbidities as by seizure control.[3-5] Surveys of these families found that cognitive problems were second only to medication side effects in terms of decreasing quality of life.[6] The new International League Against Epilepsy classification considers the cognitive comorbidities seen in epilepsy to be part of the condition.[7] Of the cognitive problems seen in epilepsy, language disorders (**Table**) are particularly important to identify and address, as language dysfunction can contribute to academic underachievement and long-term social, professional, and psychological problems.[10]

The impact of epilepsy on language is relevant not only from a clinical perspective but also because it sheds light on the underlying neurobiology of both processes. Advances in imaging and neurophysiology techniques have demonstrated that normal language development is a complex process, subserved by bilateral but usually left-predominant networks (**Figure 1**).[13] We increasingly are understanding that epilepsy is a network disorder in which even focal seizures have widespread impact on many parts of the brain. Given this, childhood epilepsy likely affects the normal development of language on several levels. First, common underlying pathophysiology, such as a genetic mutations or a structural lesion, may lead to both language disorders and seizures. This is supported by the fact that language problems are noted in children with new-onset seizures and do not always resolve completely even with excellent seizure control.[14-16] Second, interictal epileptiform discharges (IEDs), spike waves that occur outside of seizures, are known to cause transient disruptions in local cortical function and likely also affect the function of more widespread networks. Finally, childhood is a critical window for the development of language pathways, and abnormal electrical activity during this time may interfere with typical development. Multiple neurocognitive and imaging studies have shown atypical language lateralization and network connectivity in pediatric subjects with epilepsy, which does not always resolve even after the seizures and IEDs have ceased.

Many children with epilepsy have underlying conditions that lead to significant intellectual disability (ID), making specific assessment of language extremely difficult; this review will therefore focus on studies of children with normal or near-normal intelligence. This paper will first review studies characterizing language deficits in pediatric epilepsy from the most severe forms with total loss of language to the more common forms of language impairment found in the inappropriately termed "benign" epilepsies of childhood. Next, we will describe what is known about the structural and electrophysiologic changes associated with language dysfunction, reviewing the neuroimaging, electroencephalogram (EEG), and genetic studies related to language dysfunction. Epilepsy surgery planning and resection of epileptic foci provide additional tools to understand the impact of focal epilepsy on language network development and interaction with overall cognition in children with epilepsy. We will review studies on language mapping in children highlighting the unique challenges and emerging promising techniques to ensure preservation of language.

BECTS	Benign epilepsy with centrotemporal spikes
CSWS	Continuous spike waves in slow-wave sleep
EEG	Electroencephalogram
ESES	Electrical status epilepticus of sleep
fMRI	Functional magnetic resonance imaging
ID	Intellectual disability
IED	Interictal epileptiform discharge
LKS	Landau-Kleffner syndrome

Clinical Overview

Epilepsy–Aphasia Spectrum

Much of what we know regarding language and epilepsy in children is derived from disorders on the epilepsy–aphasia spectrum. Landau and Kleffner in 1957 first described the relationship between epilepsy and language dysfunction in an article detailing 6 children with previously normal language development who became aphasic after the onset of focal seizures. These patients all had EEGs with a significant burden of spike waves, especially in sleep. In general, the severity of the patients' language disorder fluctuated with the degree of EEG epileptiform activity.[17] Since then, a spectrum of disorders, often referred to collectively as the epilepsy–aphasia spectrum, have been described that share features of sleep-potentiated EEG abnormalities, cognitive problems, and rare or even absent clinical seizures.[18] The 2 best-characterized disorders are Landau-Kleffner syndrome (LKS) and benign epilepsy with centrotemporal spikes (BECTS).

Landau-Kleffner Syndrome. LKS is the canonical example of the epilepsy–aphasia spectrum. Children with previously normal development undergo a progressive language regression over weeks to months in which they lose the ability to understand

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Table. Speech and language disorders[8]

Auditory agnosia	Inability to recognize the symbolic meaning behind a sound, including an inability to understand speech or meaningful noises (such as a telephone ring)
Aphasia	Disorders affecting the production or comprehension of spoken and written language due to acquired damage to the language regions of the dominant (typically left) hemisphere. Different components of language are affected depending on the area of brain damage. Although the disorders described herein are the canonical aphasias, patients typically have mixed symptoms. Receptive/fluent/Wernicke aphasia: Inability to understand spoken or written language, classically attributed to damage of the superior temporal gyrus of the dominant temporal lobe. Speech is fluent but nonsensical. Expressive/nonfluent/Broca aphasia: Inability to produce speech or writing, classically attributed to damage of the inferior frontal gyrus of the dominant frontal lobe. Speech is halting and grammar is significantly affected, but comprehension is typically spared. Conduction aphasia: Inability to repeat secondary to damage to the arcuate fasciculus, which connects Wernicke and Broca areas.
Dysarthria	Impairment of speech due to difficulty with strength or coordination of the muscles of speech. This can be a primary muscle problem or secondary to damage to the nerves or brain structures that control the muscles. Mistakes in speech are usually consistent, and there can be difficulty in other functions like chewing or swallowing. Dysarthria can be a congenital or acquired condition.
Prosody	The varying rhythm, intensity, or frequency of speech that, when interpreted as stress or intonation, aid in transmission of meaning. Aprosody: Absence of rhythm or normal pitch variations; "robotic" voicing. Dysprosody: Impairment in normal speech intonation patterns.
Speech dyspraxia/apraxia	Difficulty in articulation of syllables or words due to impaired motor planning; mistakes are inconsistent, with intermixed fragments of intact speech. There is often impaired pitch and prosody.[9] Unlike in dysarthria, muscle strength and coordination are otherwise intact. Dyspraxia can be a congenital or acquired condition.

speech and sometimes other meaningful sounds, such as a telephone ring. Eventually, speech production diminishes. Neuropsychological testing in LKS suggests that impaired phonologic decoding is the primary deficit that leads to the language regression.[19] Children with LKS may simultaneously develop psychiatric symptoms, including irritability, inattention, and autistic traits. Rare and easily controlled seizures, including generalized tonic clonic, focal motor, and atypical absence seizures, emerge. Age of onset is typically between 3 and 8 years.[20] Corresponding with the acquired auditory agnosia, an EEG pattern of electrical status epilepticus of sleep (ESES) appears in which extremely frequent spike and slow waves

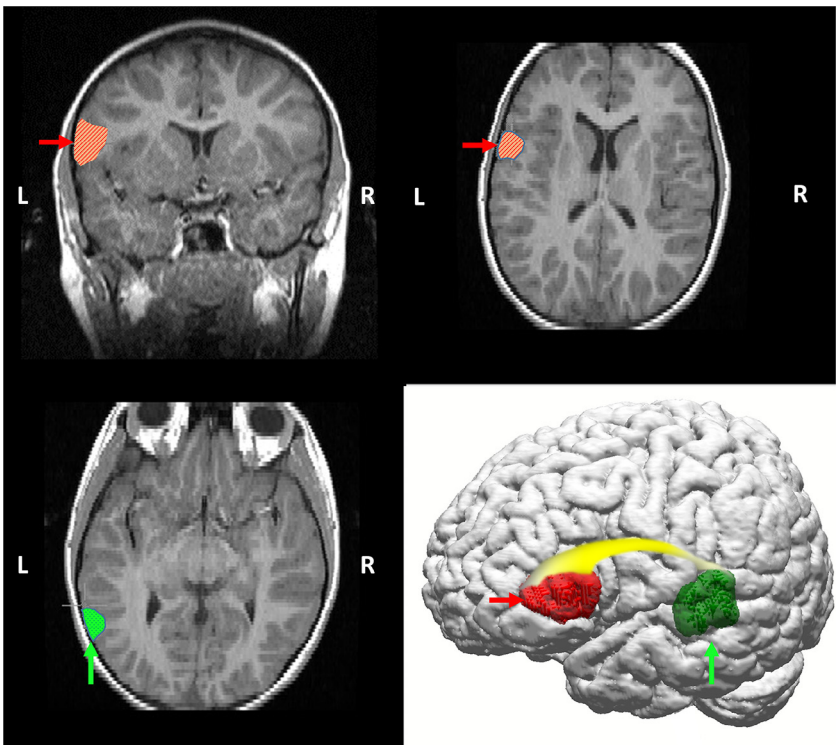

Figure 1. Diagrammatic representation of primary language areas on anatomical T2-weighted fluid-attenuation inversion recovery MRI and 3D reconstruction images,[11] highlighting left temporal lobe (Wernicke area in posterior temporal region, *vertical arrows/dotted hatching*), frontal lobe (Broca area in middle frontal region, *horizontal arrows/diagonal hatching*), and the white matter (arcuate fasciculus, *gradient shading*) that connects these regions. Historically, language has been conceptualized as a lateralized function, with dominance typically in the left hemisphere. fMRI studies confirm that language is a left-hemispheric dominant process in the vast majority of healthy adults[12] but also that language requires input from distributed networks, including homologous right hemispheric regions.

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