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BECTS evolving to Landau–Kleffner Syndrome and back by subsequent recovery: A longitudinal language reorganization case study using fMRI, source EEG, and neuropsychological testing

A.N. Datta [a,*], N. Oser [a,b], G.P. Ramelli [c], N. Zanda Gobbin [c], G. Lantz [d], I.K. Penner [a,b], P. Weber [a]

[a] Division of Pediatric Neurology and Developmental Medicine, University Children's Hospital Basel, Switzerland
[b] Department of Cognitive Psychology and Methodology, University of Basel, Switzerland
[c] Pediatric Neurology, Department of Pediatrics, Ospedale Regionale di Bellinzona e valli, Switzerland
[d] Functional Brain Mapping Laboratory, Department of Neurology, University Hospital, Geneva, Switzerland

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ABSTRACT

By means of a longitudinal case study, we demonstrated the course of cerebral reorganization of language representation due to epilepsy in a child with benign epilepsy with centro-temporal spikes (BECTS) evolving to Landau–Kleffner Syndrome (LKS) and returning to BECTS.
The child underwent the following procedures at the ages of 8.2, 8.6, and 9.3 years: 3D source EEG imaging, language fMRI (sentence generation and reading), and neuropsychological testing. He had a follow-up testing at the age of 10.8 years. Further, 24-h EEGs were regularly performed.
At the age of around 8 years, the child was diagnosed initially with left-hemispheric BECTS, which evolved to LKS with continuous bilateral discharges. In addition, 3D source imaging data revealed a left anterior temporal focus with a spreading to the right parietal and left centro-parietal areas. The patient had verbal agnosia with poor verbal yet good performance indices. Functional magnetic resonance imaging (fMRI) showed a left-hemispheric reading network but sentence generation was impossible to perform. After initiation of adequate treatment, continuous discharges disappeared, and only very rare left-hemispheric centro-temporal spikes remained. Verbal IQ and performance IQ increased at the age of 8.6 years. Functional magnetic resonance imaging showed, at this time, a right-hemispheric language activation pattern for sentence generation and reading. At the ages of 9.3 and 10.8 years, language tasks remained right-hemispheric and verbal IQ remained stable, but right-hemispheric non-verbal functions decreased due to possible crowding-out mechanisms.

1. Introduction

First described in 1957 [1], the Landau–Kleffner Syndrome (LKS) was defined as a convulsive disorder with abrupt acquired aphasia and verbal auditory agnosia, behavioral disturbances, and a bilateral activation of focal, predominantly temporal spikes, sharp waves, or spike-slow wave complexes in children with an onset at 3 to 10 years of age. These bilateral epileptic discharges are typically continuously present during NREM sleep and fulfill the criteria of (focal) continuous spike–waves during slow sleep (CSWS) [2–4]. Acquired aphasia in LKS is secondary to epileptic disturbances involving the cortical language network. By hampering functional reorganization, bilateral discharges are assumed as the basis of language decline. They not only have an immediate effect on the functional language network but also tend to induce permanent dysfunction, which may explain poor verbal outcome [5]. Landau–Kleffner Syndrome is nowadays seen as the severe end of the continuum of cognitive manifestations that can be observed in benign focal epilepsies [6].

We present a longitudinal language fMRI and a 64-channel EEG study of a patient with initially typical left-hemispheric benign epilepsy with centro-temporal spikes (BECTS) at the age of 7 years evolving to a LKS at the age of around 8 years. In addition, 24-h EEGs were performed 2 months before and 1, 2, 3, 4, and 13 months after the diagnosis of LKS. Under adequate antiepileptic treatment, he showed a near disappearance of epileptic activity during wake and sleep cycles.

The aim of this longitudinal case study was to show the relevance of continuous focal epileptic activity on language and visuo-constructive functions in a brain under development. Cerebral plasticity led to a reorganization of the language network and a return of verbal functions. However, verbal agnosia due to bilateral continuous discharges in the posterior language network demonstrated limitations of reorganization and was only overcome with antiepileptic treatment. In addition, mechanisms of crowding-out led to a secondary decrease of non-verbal functions.

* Corresponding author at: Division of Pediatric Neurology and Developmental Medicine, Basel, Switzerland. Fax: +41 61 704 12 13.
E-mail address: alexandre.datta@ukbb.ch (A.N. Datta).

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2. Case history

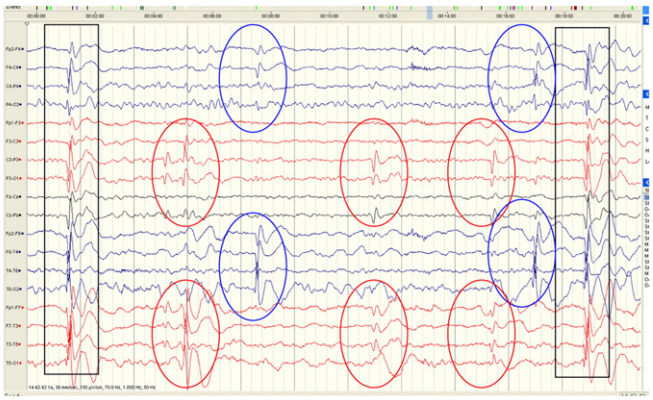
After having been normally delivered, this boy showed a strictly normal development, adequately achieving all the developmental milestones including expressive and receptive language; a very good vocabulary was already available at the age of 2 years when he generated sentences of 3 and 4 words with a good verbal comprehension. At the age of 7.4 years, he had his first focal seizure early in the morning with right hemifacial jerks, pharyngeal sound, and a short secondary generalization. Electroencephalogram (EEG) data showed a spike and sharp wave focus over the left centro-temporal area. The second seizure followed one month later, when the diagnosis of BECTS was made, and antiepileptic treatment with sultiam was initiated.

In the first 24-h standard EEG, at the age of 8 years, the boy's EEG showed a predominantly left-hemispheric sharp-wave and spike activity over the fronto-centro-temporal area (Fig. 1a). Additionally, a right-hemispheric sharp-wave focus appeared and an intermittent bilateral centro-temporo-parietal sharp-and-slow-wave activity (Fig. 1a) with intermittent continuous discharges during 10–20 s and short breaks during NREM sleep stages N1, N2, and N3 (Fig. 1b) was diagnosed. At this point, no continuous epileptic activity during the whole night NREM sleep was detectable.

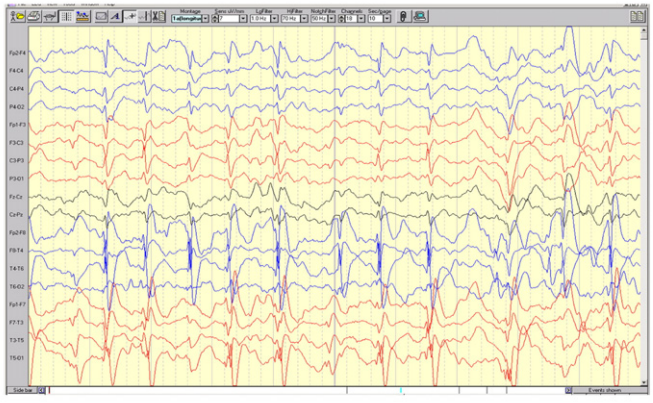
Over a short period of weeks, the school situation worsened. Teachers were wondering why the boy, all of a sudden, was having more and more difficulties at school; instructions had to be repeated several times and were nevertheless not entirely completed. In sum, he was unable to understand the meaning of oral and written sentences. While reading a text, he was only able to read letter by letter, without understanding the meaning of the words or sentences. Two months later, a 64-channel EEG examination (Electrical Geodesic Inc., Eugene, Oregon, USA) revealed that a continuous bilateral spike and sharp wave activity was present during drowsiness as well as during NREM sleep stage N1. A first neuropsychological testing (WISC-III), at the same time, showed a very poor word understanding, inability to recognize well-known words (verbal agnosia), and deficient expressive speech (verbal IQ 71). Non-verbal tasks were in the superior limits of the normal range (non-verbal IQ 113) (Table 1), whereas elaboration speed was slow. As a result, LKS was diagnosed, sultiam treatment was increased from 5 mg/kg/day to 10 mg/kg/day and an evening dosage of 12.5 mg (0.4 mg/kg) of clobazam was added. Further, speech therapy was initiated and his school situation adapted to his needs to allow for maximal stimulation.

A 12-hour long-term night EEG, 1.5 months later, showed a clear reduction of the epileptic activity. Bilateral discharges especially decreased considerably in frequency. At the age of 8.5 years, only some sharp wave activities on the left and some on the right hemisphere were detectable with the 24-h EEG, and continuous epileptic discharges completely disappeared. Over the following months, he improved gradually in his speech fluency, vocabulary, and understanding, although major deficits remained. His verbal IQ increased 10 points and remained stable at the age of 8.6 years. An increase in non-verbal IQ was revealed in the first follow-up, while a decrease was found in the second and third neuropsychological follow-up testing at the ages of 9.3 and 10.8 years (for details see the Results section).

The following 24-h EEGs confirmed the absence of CSWS. Only isolated sharp waves on the left and some on the right centro-temporal areas were detectable during NREM sleep, whereas bilateral discharges and sharp-and-slow-wave complexes were completely absent.



a)



b)

Fig. 1. EEG at transition from BECTS to LKS. a: Bilateral centro-temporo-parietal spike–slow wave complexes [ ], visible over the whole hemisphere. Left centro-temporal spike and sharp wave focus, corresponding to the initial focus ( ), independent right centro-parietal spike and sharp wave focus ( ). b: Continuous focal sharp–slow wave activity phases during NREM sleep.

3. Methods

A neuropsychological examination was performed with the Wechsler Intelligence Scale for Children-III (WISC-III) [7], including an age-adequate verbal and non-verbal intelligence scale. This test battery assesses various aspects of oral language including denomination, comprehension, verbal fluency, logical reasoning, processing speed, and verbal memory. The WISC-III was done at the ages of 8.2, 8.6, 9.3, and 10.8 years.

Twenty-four-hour long-term EEG recordings were performed in clinical settings on a Nicolet EEG system (10/20 electrode configuration) at the ages of 8.0, 8.3, 8.4, 8.5, 8.6, and 9.3 years.

For 3D-EEG source imaging, our patient underwent, at three different time points (at the ages of 8.2, 8.6, and 9.3 years), a 64-channel scalp surface recording on an EGI-EEG system (Electrical Geodesic Inc., Eugene, Oregon, USA). For source imaging, 50 artifact-free interictal spikes or sharp waves with similar surface voltage distribution were selected from the recordings with 64 electrodes.

The marking and averaging of spikes were performed using the NetStation software, and the source reconstructions were performed with the GeoSource software (both from EGI, Electrical Geodesic, Inc., 2008; www.egi.com). Localization of intracerebral generators from the scalp EEG, developed during the last few years, has been effectively applied to epileptic data [8–11].

During functional MRI, two language tasks were applied. Acquisitions in blocks were made on a 3 T MR scanner (Siemens VERIO), as described in previous studies [12–15]. Functional magnetic resonance imaging investigations were performed at the ages of 8.3, 8.6, 9.3, and 10.8 years.