The spectrum of acquired cognitive disturbances in children with partial epilepsy and continuous spikewaves during sleep: A 1-year follow-up case study with prolonged reversible learning arrest and dysfluency

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Abstract
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The spectrum of acquired cognitive disturbances in children with partial epilepsy and continuous spike-waves during sleep
A 4-year follow-up case study with prolonged reversible learning arrest and dysfluency

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We report a longitudinal study (7–11 years) of a previously normal boy (MR) who presented from the age of 5 years with rare partial motor seizures and atypical ‘absences’. The history revealed a stagnation in development and speech difficulties a few months before onset of his epilepsy. The first waking electroencephalogram (EEG) showed rare generalized discharges during hyperventilation. Magnetic resonance imaging revealed an arachnoid cyst in the frontotemporal region. Although his epilepsy never became severe, he experienced important learning difficulties. Subsequent EEGs became increasingly active with left focal epileptic activity and continuous spike-waves during sleep (CSWS) present from the first sleep EEG. The first neuropsychological evaluation (7 years) showed a speech dysfluency, word finding and naming problems, inattention and low intelligence quotient. Carbamazepine was changed to clobazam and later ethosuximide was added with a rapid improvement (within 1 month) in linguistic and cognitive performances as well as in behaviour. Furthermore, the patient showed considerable progress in acquisition over the next months whereas learning to read had previously been very difficult. The epileptic activity gradually disappeared and he was able to follow regular school at an age-appropriate level. This case adds a new facet to the already recognized more obvious acquired neuropsychological disturbances known to occur in some partial childhood epilepsy syndromes with CSWS (aphasia, dementia). It manifested as prolonged insidious stagnation in learning and subtle language disability. This study documents rapid specific language improvement with change in anti-epileptic drugs and a restored immediate and long-term learning capacity, suggesting a direct but ‘hidden’ role of epilepsy.

Keywords: Cognitive disturbances in children. Partial epilepsy. CSWS. Prolonged reversible learning arrest.

Introduction

Some childhood partial epilepsy syndromes with persistent focal electroencephalographic discharges and continuous spike-waves during sleep (CSWS) can lead to acquired neuropsychological disturbances. The classical example is ‘acquired epileptic aphasia’ or Landau-Kleffner syndrome.1 An increasing amount of clinical and electrophysiological data indicate that the cognitive deficits are directly related to the disturbed focal electrical abnormality. The specific clinical symptoms depend mainly on the functional role of the
cortical areas or areas affected by the epileptic process, at the time it becomes active.2

When the cognitive deficit is severe and specific (i.e. language loss) with an acute onset and/or marked fluctuations, or if it improves rapidly with treatment, the epileptic nature of the problem is now generally accepted. When the onset of the deficit is more protracted and if the symptoms are non-specific such as attention problems, behavioural difficulties, slowness or non-fluent speech, the relationship to the epilepsy is more difficult to establish or can remain unsuspected. This is particularly so if there is no real loss of cognitive abilities but only an insidious stagnation in learning.

The proof that such situations are real can only be provided if it can be shown that a rapid improvement of cognitive abilities occurs with effective anti-epileptic treatment and if a 'catch-up' in the learning of a given skill which was previously impossible is observed.

We report a longitudinal observation of an 11-year-old boy whose epilepsy was first diagnosed at age 5 years, and who illustrates this situation. He was followed from ages 7 to 11 years. We want to show the place of his epilepsy among the already recognized disorders within the spectrum of the neuropsychological disturbances observed in children with partial idiopathic epilepsies and CSWS. We suspect that it is probably a frequent manifestation, but also the most difficult to recognize and document.

Our case also indicates that after a prolonged period of stagnation, a learning ability can develop in these situations.

Materials and methods

Summary of case report

The course of the disorder and the major clinical data are summarized in Fig. 1.

MR the eldest of three brothers born 28.11.1984, after a full-term pregnancy and normal delivery, developed without problems. Onset of speech was
‘slightly late’ but he spoke fluently in sentences at 3 years. His first seizure occurred in June 1990 at the age of 5 years 6 months. It was generalized and motor and occurred during sleep with a right-sided predominance. However, from May 1990, coincidental with the period of his grandfather’s death, he had frequent mood changes, was often sad and became sometimes aggressive. He was never inadequate or impulsive nor did he have a thought disorder. He expressed himself with more difficulties, but never stopped speaking, nor did he have difficulties in understanding. His speech problems were considered as being psychogenic. He had individual psychotherapy from May 1990. A specific speech or language problem was not suspected at this time. He was prescribed carbamazepine 400 then 600 mg/day from August 1990 and valproate was added in December 1990. Clinically atypical absences and focal motor seizures were neither frequent nor severe. His electroencephalograms (EEGs) became increasingly abnormal, with left focal and generalized discharges. A marked increase of the discharges during sleep was noted from the first sleep EEG obtained 6 months after onset of epilepsy. A computed tomography scan after the first seizure showed a focal hypodensity in the left frontal region initially interpreted as an atrophic lesion. Magnetic resonance imaging (MRI) 18 months later showed a probable arachnoid cyst in the frontal region extending into the left sylvian fissure, without signs of focal cortical destruction, mass effect or cortical dysplasia (Fig. 2).

A spectacular improvement was seen by the family within days of the introduction of clobazam 15 mg/day in February 1992 preceded by withdrawal of carbamazepine (Table 1). In September 1992, ethosuximide 500 mg/day was added to clobazam because of recurrence of suspected ‘absences’ and because of persistent, although decreased EEG discharges. The boy is currently 11 years old and following regular school at the age-appropriate level and continuing to receive ethosuximide and clobazam.

Objectives of the study and methods

MR was first referred to us in December 1991 at the age of 7 years for detailed evaluation of his cognitive difficulties, associated with worsening of his paroxysmal EEG activity. He has been followed from that period until the age of 11 years 6 months. Further inquiry from his parents and school teachers revealed that he had suffered an insidious stagnation after normal development and had a dysfluent speech, possibly linked to a subtle-acquired dysphasia. We hypothesized that this could be a direct consequence of his epileptic syndrome and that we could be in a position to confirm this if his epilepsy (or EEG discharges) was responsive to a change in therapy. Thus, we needed to answer the three following questions:

1) What has been his developmental course and what is the nature of his present neuropsychological problem. Can a specific cognitive dysfunction be demonstrated?

The developmental history was extensively reviewed with the parents, the paediatrician, the child psychiatrist, the kindergarten and elementary school teachers.

Cognitive and language evaluations were videotaped and standardized tests were used (Weschler Intelligence Scale for Children, form R &is&e (WISC-R), McCarthy, language tests from Chevre-Muller, Raven Progressive matrices, Rey complex figure, Piaget’s number concepts, etc). We also focused on the fluency of speech which appeared particularly affected, whereas no obvious aphasic problems were noticed. Fluency of speech was judged from videorecorded sessions which included comparative samples during free conversation, description of images and retelling of a read story.

The child’s parents also completed an extensive behavioural questionnaire (257 questions) that we
Table 1  Short-term cognitive improvement: results of the neuropsychological tests performed before and after the therapy change (interruption of carbamazepine and introduction of clobazam)

<table>
<thead>
<tr>
<th>Domain test</th>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18.2.92</td>
</tr>
<tr>
<td>Language production</td>
<td></td>
</tr>
<tr>
<td>Speech</td>
<td></td>
</tr>
<tr>
<td>Number of words per minute</td>
<td>45.79</td>
</tr>
<tr>
<td>Mean length of utterances</td>
<td>5.28</td>
</tr>
<tr>
<td>Per cent of complete utterances</td>
<td>40.63</td>
</tr>
<tr>
<td>Verbal fluency (McCarthy)</td>
<td>—</td>
</tr>
<tr>
<td>Picture naming (Chevrie-Muller)</td>
<td>50/100</td>
</tr>
<tr>
<td>Verbal memory (McCarthy)</td>
<td>18 (normal)</td>
</tr>
<tr>
<td>Language comprehension</td>
<td></td>
</tr>
<tr>
<td>Verbal comprehension (Chevrie-Muller)</td>
<td>70/100</td>
</tr>
<tr>
<td>Syntactic comprehension (Chevrie-Muller)</td>
<td>27/40</td>
</tr>
<tr>
<td>Non-verbal tests</td>
<td></td>
</tr>
<tr>
<td>Code (standard score) (WISC-R)</td>
<td>3 (normal)</td>
</tr>
<tr>
<td>Tapping (McCarthy)</td>
<td>3 (&lt;normal)</td>
</tr>
<tr>
<td>Rey’s figure</td>
<td>—</td>
</tr>
<tr>
<td>Raven’s matrices</td>
<td>—</td>
</tr>
</tbody>
</table>

have developed to evaluate and follow similar situations.8

2) Should there be positive response with a change in anti-epileptic therapy, is it possible to demonstrate a rapid cognitive improvement by comparative psychometric tests with parallel EEG improvement?

As soon as we saw the parental impression of rapid improvement with change in anti-epileptic drug therapy, the initial tests were repeated and the results were compared (Table 1).

3) If a rapid positive response occurs with anti-epileptic drugs, it is possible to demonstrate a ‘catch-up’ in a specific learning achievement which he should have made at his age and which was previously impossible?

We chose to study his ability and speed of learning to read as a possible index of cognitive ‘catch-up’ as soon as the rapid movement of general cognitive ability and behaviour was noted clinically. This choice was made because he had learned to recognize letters early and easily by 3 years of age, but had not progressed much beyond this stage from the onset or even before diagnosis of his epilepsy, despite regular exposure to written language in the first 2 years of elementary school and systematic teaching in the first grade. It was hypothesized that this could be related directly to his epilepsy and that rapid progresses could be anticipated with an effective anti-epileptic drug therapy.

His learning to read was evaluated with regular sessions over an 11-month period from the age of 7.4 to 8.1 years during which he moved to the reading of simple regular words to reading and understanding of complex sentences.9 A detailed examination of written language (Batterie d’Évaluation du Langage Écrit) (BELEC) was performed at age 11.5.10

Progress was also monitored by regular telephone calls with his teacher.
EEG evaluation

All standard records but one were registered with 21 electrodes using the 10 to 20 international system. Repeated records were obtained as close as possible to the time of the neuropsychological tests. The first four sleep EEGs were only brief sleep records, but the following six whole-night EEGs were monitored during the course of the next 4 years by ambulatory eight-channel EEG, Medilog Oxford 9200. When spike-wave activity was very active, almost continuous, it was quantified during 10s intervals, for example spike-wave activity during 8s out of 10s gave a density of 80%. This was repeated frequently through the whole night recording, especially if important fluctuations in the epileptic activity was observed. In this way the density of the epileptic activity could be plotted against time and the fluctuations of the density of the epileptic activity could be determined in a semi-quantitative way. This allowed us to study the fluctuations of the epileptic activity during the whole night and also compare one recording with another.

Results

Psychological development and initial cognitive evaluation (Fig. 1, Table 1)

The child’s early development had caused no concern. At 3 years, he had an excellent vocabulary, he knew the alphabet, several colours, finger names and right and left. His behaviour caused no problems and he learned eagerly. During the first 2 years of elementary school (from 5 to 7 years), he was passive and did not make any significant progress. Later on, MR was described by his parents and child psychiatrist as anxious and immature and he was very much helped by regular professional support. He was easily upset, had mood changes and was sometimes aggressive. The main problems were his passivity, poor attention, fatiguability and infantile behaviour. Results of the behavioural questionnaire did not show hyperactivity, autistic symptoms or specific abnormal behaviours in the multiple areas evaluated. He did not have phobias, hallucinations, or a thought disorder. His speech had also changed from the time of his first seizure. He was slow to initiate sentences, made pauses, searched for current words, sometimes said a word for another, made circumlocutions. He did not stutter and his speech comprehensions did not seem affected. The difficulties were quite variable.

The first formal evaluation was made at the age of 7 years 3 months (Table 1). In spontaneous oral production, MR showed no significant phonological or syntactic errors. Language comprehension (Chevrie-Muller’s test) was at the lower range of normal performance. He had some difficulties in naming current objects and made occasional paraphrases. He had marked difficulties in generating words of a given category. His speech was mainly characterized by a dysfluency with unnatural pauses between words or phrases, especially when he had to tell a story or answer open questions. Discourse was slow and he resented conversations or other imposed speech productions. His full scale intelligence quotient (IQ) on the WISC-R was 86 (verbal IQ:85, performance IQ:96). He was slow in timed items requiring speed and sustained attention (e.g. WISC-R code and McCarthy’s tapping test). Basic reasoning, visuospatial skills (Raven’s matrices, Rey’s complex figure, WISC-R puzzles) were within or above the normal range.

The overall impression was that he did have a specific language disorder with dysfluent speech, and that this was not only the result of his general slowness, immaturity and poor attention.

Evolution with change in anti-epileptic therapy (Table 1)

First phase (rapid change)

Comparative evaluations were performed within 1 month of the therapy change (three sessions) because the parents reported a spectacular improvement with the introduction of clonazepam (see Table 1). Notable improvements were observed in all tasks, in particular in the verbal domain. Speech fluency seemed better and confirmed the parent’s impression that his spontaneous speech production was more abundant, faster and contained fewer hesitations. This could also be documented with quantitative measures (dysfluency measures).

Word generation, picture naming, verbal memory were clearly better.

Written language acquisition (Table 2)

When first tested at age 7 years 2 months and 7 years 3 months, he could only read respectively 2/13 and 3/11 simple words and sometimes he misidentified letters. He was then seen repeatedly
during that year from the age of 7 years 6 months (Table 2) and asked each time to read a list of selected words (regular, irregular and nonsense words). He was not given the correct answer nor did he rehearse in between sessions. During that year, he was in a private school where he received the same teaching as the other children without special tutoring. Reading efficiency (Claire and Bruno) and comprehension of written sentences (Khomsi) were measured at the end of the year and showed surprisingly good results (normal high scores, respectively 15/15 and 17/20). These data show that within 9 months, he moved from hardly decoding a few simple words to understanding complex written sentences. He continued to progress normally in the following years in reading and spelling. A detailed examination of written language (BELEC) performed in April 1996 (at age 11 years 5 months) revealed normal to superior performances in reading isolated words, in written comprehension and spelling.

**Long-term follow-up (Table 3)**

MR was examined at ages 8 years 2 months, 9 years 3 months and 11 years 4 months. His results on the WISC-R showed significant improvement the first year after change of treatment, then stable scores indicating that he continued to develop normally. There was no more discrepancy between the verbal and the non-verbal scores. He could follow the regular school programme although he was a little slower than his classmates and is still immature in his behaviour.

**Electroencephalographic data** (Table 4 and Fig. 3)

During the study from 5 years 6 months to 11 years, 15 recordings were obtained, five awake EEGs, three nap EEGs and six whole night recordings (Table 4).

**Discussion**

This child's problems when we first met him were not spectacular and he could have been described
Table 4  Summary of EEG findings from 5 years to 11 years

<table>
<thead>
<tr>
<th>Year (no)</th>
<th>EEG Age (years:months)</th>
<th>Awake (SW), maximum focal activity</th>
<th>Sleep (SW)</th>
<th>Comment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990 1</td>
<td>5:6</td>
<td>PL (+)</td>
<td>ND</td>
<td>only during HV</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>5:7</td>
<td>gen (+)</td>
<td>ND</td>
<td></td>
<td>CBZ</td>
</tr>
<tr>
<td>3</td>
<td>5:9</td>
<td>T-FL+PL+</td>
<td>ND</td>
<td></td>
<td>CBZ</td>
</tr>
<tr>
<td>4</td>
<td>6 years</td>
<td>TPL +</td>
<td>Nap (9 min)</td>
<td></td>
<td>VPA+CBZ</td>
</tr>
<tr>
<td>1991 5</td>
<td>6:7</td>
<td>gen (+)</td>
<td>ND</td>
<td></td>
<td>VPA+CBZ</td>
</tr>
<tr>
<td>1992 6</td>
<td>7:2</td>
<td>PL ++</td>
<td>Nap (35 min)</td>
<td></td>
<td>VPA+CRZ</td>
</tr>
<tr>
<td>7</td>
<td>7:3</td>
<td>PL ++</td>
<td>Nap (45 min)</td>
<td></td>
<td>CLB+VPA</td>
</tr>
<tr>
<td>8</td>
<td>7:6</td>
<td>FL ++</td>
<td>Nap (16 min)</td>
<td></td>
<td>CLB+VPA</td>
</tr>
<tr>
<td>9</td>
<td>7:9</td>
<td>gen ++</td>
<td>whole night (WN)</td>
<td></td>
<td>CLB+VPA</td>
</tr>
<tr>
<td>1993 10</td>
<td>8:1</td>
<td>gen ++</td>
<td>WN, CSWS</td>
<td></td>
<td>CLB+ESM</td>
</tr>
<tr>
<td>11</td>
<td>8:6</td>
<td>TFL (+)</td>
<td>ND</td>
<td></td>
<td>CLB+ESM</td>
</tr>
<tr>
<td>12</td>
<td>8:10</td>
<td>L (+)</td>
<td>WN, CSWS lat. L</td>
<td></td>
<td>CLB+ESM</td>
</tr>
<tr>
<td>1994 13</td>
<td>9:3</td>
<td>L (+)</td>
<td>WN, CSWS lat. L</td>
<td>see Fig. 5</td>
<td>CLB+ESM</td>
</tr>
<tr>
<td>14</td>
<td>9:11</td>
<td>—</td>
<td>WN (+)</td>
<td></td>
<td>CLB+ESM</td>
</tr>
<tr>
<td>1996 15</td>
<td>11:4</td>
<td>—</td>
<td>WN (+)</td>
<td></td>
<td>CLB+ESM</td>
</tr>
</tbody>
</table>

SW: spike-wave activity; P: parietal; T: temporal; F: frontal; L: left; gen: generalized epileptic activity and no clear focalization; CSWS: continuous spike-waves during slow wave sleep; DZP: diazepam; CBZ: carbamazepine; VPA: valproate; CLB: clobazam; ESM: ethosuximide; — absent; (+) rare; + present; ++ frequent; ND: not done.

as an immature, anxious, slow, inattentive epileptic child with poor speech and well controlled seizures. The questions we asked at onset and the data we gathered to answer them gave, however, a different picture.

First, the detailed development history and the results of the neuropsychological evaluation showed that he had been initially a bright and rapidly learning child who underwent subtle behavioural changes and an insidious stagnation in cognitive development with learning problems starting a few months prior to the recognized epilepsy. These difficulties were clearly fluctuating. His neuropsychological profile showed both non-specific problems (slowness, inattention) but also an unusual language difficulty (dysfluency) associated with subtle dysphasic symptoms. By analogy with the more typical partial epilepsy syndromes with CSWS, these results made us postulate a potentially direct but relatively hidden effect of his epilepsy.

Second, a rapid improvement with change of anti-epileptic medication could be measured by comparative cognitive tasks (word generation, naming, subtests of the WISC-R). It coincided with the introduction of clobazam which had a sustained effect (without the often observed escape phenomenon). An aggravating effect of carbamazepine, which had been gradually withdrawn prior to its introduction can not be ruled out.

It is very unlikely that such significant, specific and rapid changes were due to maturational changes or to a psychotropic drug effect (anxiolytic role of diazepines), independent from the antiepileptic effect of the drug.

Third, he became able to learn complex reading skills in less than 1 year. Considering the marked difficulties he had shown in this domain before, we think that this is related to the better control of his epilepsy and not simply an unusually rapid ‘normal’ acquisition.

We could not demonstrate a close clinical-EEG correlation as there was no significant decrease of EEG discharges at the time of rapid clinical improvement. Parallel clinical-EFG improvement can sometimes be seen in these syndromes with anti-epileptic drugs or steroids, but this is not a regular feature and dissociations can be observed. This indicates that anti-epileptic drug therapy should be guided by the clinical situation, as much as by the presence of EEG discharges, whose intensity can be quite variable, as in this case (see Table 4). It must also be noted that at this period, only short comparative sleep tracings had been obtained. Whole night EEG recordings obtained later showed almost continuous CSWS in the early part of the night with a progressive decrease of the density of the discharges (‘fragmentation’) later in the night. As expected in the course of such an epileptic syndrome, a gradual
Fig. 3. EEG showing diffuse spike-waves (A) with appearance of left-sided focus (B) when diazepam was given during the same tracing.
Fig. 4. Evolution of whole-night sleep EEG recordings from 7 years 9 months to 11 years 4 months showing the 'density' (percentage) of diffuse spike-waves throughout the night which decreases markedly ('fragmentation') from 8 years 2 months and disappears completely from the age of 9 years 11 months (see also Methods and Results).

reduction of epileptic activity was seen progressively over time with no CSWS in the last 2 whole night recordings at 10 and 11 years.

From the nosological point of view, our case belongs to the syndrome of idiopathic partial epilepsies and CSWS whose physiopathology is ill-understood and possibly different from the classical lesional epilepsies. The possible role of a cyst in the region of the EEG focus must, however, be discussed. It is known that such cysts can be found incidentally and their epileptic potential has not been demonstrated. The improvement in symptoms with anti-epileptic drugs only, also argues against a local pressure effect of the cyst as postulated in one publication. At the present time, it appears reasonable to envisage a continuum of syndromes from the genetically determined functional partial epilepsies with no or minimal neuropsychological consequences to the severe cases in which sometimes a focal lesion
will be an additional or main factor in the deterioration of the patient.\textsuperscript{2,14}

Our observation must be added to the more spectacular cognitive and behavioural syndromes already described in childhood partial epilepsy syndromes with CSWS (Table 5)\textsuperscript{16-20} and which can be related to the function of the cortical area or areas primarily involved in the epileptic process.

When the deficit is slowly progressive, not severe, or if the involved cortical zone does not have a critical role at the time, the disorder can remain inapparent or unrecognized because the symptoms can be non-specific or subtle, as was the language disorder of our child. This may also explain why some children with CSWS and no apparent problems have been described.

One must consider the influence on outcome, of age at onset, intensity of the epileptic process during the period it is active, as well as total duration during development (months, years). These factors will also determine the neuropsychological and behavioural consequences of these special partial epilepsy syndromes. They can be conceptualized in the way shown in Table 6. Children may have fluctuations in performances and still score within average ranges on IQ tests, without loss of a specific ability (such as aphasia or apraxia). At the other extreme are those children whose epilepsy starts so early that it is impossible to distinguish between a developmental and acquired disorder and because so many more psychological and educational confounding factors exist.

Cases such as the one described in this paper are rarely reported because of the difficulty of suspecting symptoms and study them at the appropriate time and also because currently available anti-epileptic drugs are often ineffective or can even worsen the symptoms. Thus, it is often impossible to bring a definite proof of the role of epilepsy in these special epileptic syndromes.\textsuperscript{15} Hopefully, awareness of their existence and new effective drugs will change this situation.

### Acknowledgements

The study was supported by Swiss National Research Fund No. 32-032. The authors gratefully acknowledge the help of the Fondation pour la recherche en faveur des handicaps! and also of the Fondation Charles Leopold pour le progrès de l'homme for their financial support.

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