Received: 16 August 2023 | Revised: 17 March 2024 | Accepted: 10 April 2024

DOI: 10.1002/epi4.12951

Epilepsia Open® Open Access

NARRATIVE REVIEW

Epilepsy, EEG and chromosomal rearrangements

Justyna Paprocka[1] | **Antonietta Coppola**[2] | **Claudia Cuccurullo**[2] | **Elżbieta Stawicka**[3] | **Pasquale Striano**[4,5]

[1]Pediatric Neurology Department, Faculty of Medical Sciences, Medical University of Silesia, Katowice, Poland

[2]Epilepsy Centre, Neurology Department of Neurology, Reproductive and Odontostomatology, Federico II University, Naples, Italy

[3]Clinic of Paediatric Neurology, Institute of Mother and Child, Warsaw, Poland

[4]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, IRCCS Istituto Giannina Gaslini, Genoa, Italy

[5]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy

Correspondence
Justyna Paprocka, Pediatric Neurology Department, Faculty of Medical Sciences, Medical University of Silesia, Katowice, Poland.
Email: justyna.paprocka@interia.pl and jpaprocka@sum.edu.pl

Abstract

Chromosomal abnormalities are associated with a broad spectrum of clinical manifestations, one of the more commonly observed of which is epilepsy. The frequency, severity, and type of epileptic seizures vary according to the macro- and microrearrangements present. Even within a single chromosomal anomaly, we most often deal with a phenotypic spectrum. The aim of the study was to look for chromosomal rearrangements with a characteristic electroencephalographic pattern. Only a few disorders have peculiar electroclinical abnormalities: 1p36, 4p16, 6q terminal or trisomy 12p, Angelman syndrome, inv dup 15, 15q13.3 deletions, ring 20, Down syndrome, or Xp11.22–11.23 duplication. We also reviewed studies on epileptic seizures and typical electroencephalographic patterns described in certain chromosomal rearrangements, focusing on the quest for potential electroclinical biomarkers. The comprehensive review concludes with clinical presentations of the most common micro and macro chromosomal rearrangements, such as 17q21.31 microdeletion, 6q terminal deletion, 15q inv dup syndrome, 2q24.4 deletion, Xp11.22–11.23 duplication, 15q13.3 microdeletion, 1p36 terminal deletion, 5q14.3 microdeletion, and Xq28 duplication. The papers reviewed did not identify any specific interictal electroencephalographic patterns that were unique and significant biomarkers for a given chromosomal microrearrangement. The types of seizures described varied, with both generalized and focal seizures of various morphologies being reported. Patients with chromosomal anomalies may also meet the criteria for specific epileptic syndromes such as Infantile Epilepsy Spasms Syndrome (IESS, West syndrome): 16p13.11, 15q13.3 and 17q21.31 microdeletions, 5q inv dup. syndrome; Dravet syndrome (2q24.4 deletion), Lennox–Gastaut syndrome (15q11 duplication. 1q13.3, 5q inv dup.); or Self-Limited Epilepsy with Autonomic Features (SeLEAS, Panayiotopoulos syndrome: terminal deletion of 6q.n), Self-Limited Epilepsy with Centrotemporal Spikes (SeLECT): fragile X syndrome. It is essential to better characterize groups of patients to more accurately define patterns of epilepsy and EEG abnormalities. This could lead to new treatment strategies. Future research is required to better understand epileptic syndromes and chromosomal rearrangements.

Plain Language Summary: This paper presents EEG recording abnormalities in patients with various gene abnormalities that can cause epilepsy. The authors summarize these EEG variations based on a literature review to see if they occur frequently enough in other chromosomal abnormalities (in addition to those already known) to be a clue for further diagnosis.

KEYWORDS

children, chromosomal complex rearrangements, chromosomal microrearrangements, EEG, epilepsy

1 | INTRODUCTION

Chromosomal abnormalities are often associated with a broad spectrum of neurological symptoms, predominantly epilepsy. The frequency and severity of epileptic seizures observed in different macro- and microrearrangements may vary. Singh et al.[1] reported more than 400 different chromosome aberrations associated with epileptic seizures and/or EEG abnormalities. However, only a few chromosome anomalies have a characteristic electroclinical pattern, such as 1p36 deletion, 4p16 deletion, 6q terminal deletion, trisomy 12p, Angelman syndrome, inv dup 15, 15q13.3 deletions, ring 20, 21 trisomy, and Xp11.22–11.23 duplication.[2] This review provides an update on recent research on epileptic seizures and electroencephalographic patterns reported in selected chromosomal rearrangements, focusing on chromosomal microrearrangements.

Key points

- Only a few disorders feature a peculiar electroclinical pattern: 1p36, 4p16, 6q terminal or trisomy 12p, Angelman syndrome, inv dup 15, 15q13.3 deletions, ring 20, Down syndrome, or Xp11.22–11.23 duplication.
- The authors describe clinical presentations of the most common micro and macro chromosomal rearrangements, such as 17q21.31 microdeletion, 6q terminal deletion, 15q inv dup syndrome, 2q24.4 deletion, Xp11.22–11.23 duplication, 15q13.3 microdeletion, 1p36 terminal deletion, 5q14.3 microdeletion, and Xq28 duplication.
- The papers reviewed did not identify any specific interictal electroencephalographic patterns that were unique and significant biomarkers for a given chromosomal microrearr angement.

2 | MATERIALS AND METHODS

2.1 | Search strategy

A systematic search was conducted in the PubMed, Medline, and Google Scholar databases to identify the literature related to epilepsy, EEG, and chromosomal rearrangements. Two authors independently (J.P., E.S.) screened the above-mentioned databases. Each database was searched individually, and search terms were applied line by line and replicated in every source. The following terms were used for the search: "EEG," "electroencephalography," in combination with terms such as "epilepsy," "seizures," "chromosomal abnormalities," and "chromosomal rearrangements." The entire process of searching relevant papers by two reviewers (period for establishing a database of relevant articles) lasted from September 2023 to October 2023, with numerous subsequent updates based on the latest scientific reports.

2.2 | Study selection and appraisal

Manuscripts were reviewed for titles, abstracts, and entire texts based on the following criteria: The inclusion criteria were as follows: (1) original papers; (2) reviews. The exclusion criteria were as follows: (1) methodological studies, editorials, commentaries, letters, and hypotheses; (2) no available abstract; (3) manuscripts in a language other than English. Titles, abstracts, and full-text articles were screened regarding the inclusion criteria by two reviewers. Next, manual search, reference, and citation tracking were undertaken by two reviewers (J.P. and E.S.), who established the final selection of papers.

2.3 | Development of the review

The analysis was conducted in the following steps: The first step was related to the analysis of selected papers based on titles and abstracts, the second step was connected with the analysis of full-text papers and the last step included the analysis of the collected data.

3 | RESULTS

The preliminary search of the database showed 159 studies, of which 59 were verified based on the entire manuscript. A total of 43 studies were finally included in the analysis.

3.1 | Complex chromosomal rearrangements

Many seizures are connected with rearrangements on macro- and microchromosomal levels. Significant chromosomal abnormalities connected with the epilepsy phenotype are well recognized (Table 1), and the EEG pattern is precisely characterized.

Febrile seizures are more frequent in Angelman and Prader-Willi syndromes than in other chromosomal abnormalities and more frequent than the prevalence of 3%–4% in the general population.[3] Also, the prognosis of IESS with Down syndrome is better than symptomatic IESS in the general population.[12] The EEG findings in many chromosomal abnormalities, like in Prader-Willi syndrome, tend to improve over time, most except for subjects with refractory epilepsy.[1,2] The disappearance of epileptiform discharges seems to be an age-related phenomenon rather than a mutation-dependent fact, likewise other neurodevelopmental genetic syndromes.[2]

Although Rett syndrome (RTT) does not belong to complex chromosomal rearrangements, it should be considered during a differential diagnosis. More than 80 genes are related to the RTT-like phenotype, and some of them are identified as causative for the aRTT or RTT-like phenotype in these patients: *TCF4*, *CNTNAP2*, and *NRXN1* genes (Pitt-Hopkins syndrome), *SHANK3* gene (Phelan-McDermid syndrome), *UBE3A* gene (Angelman syndrome), *EHMT1 gene (*Kleefstra syndrome), *SMC1A* gene (Cornelia de Lange syndrome), and other genes, such as *STXBP1*, *SCN1A*, *SCN2A*, *SCN8A*, *GRIN2A*, *GRIN2B*, *HCN1*, *SLC6A1*, *KCNA2*, *EEF1A2*, *KCNB1*, and *SYNGAP1* (related to epileptic encephalopathies).[17,18] Since the number of genes responsible for the Rett-like syndrome phenotype is constantly increasing, it is crucial to consider the EEG abnormalities in this disease, focusing on different stages of abnormal EEG findings in Rett syndrome[17,18]:

1. Stage 1: normal.
2. Stage 2: focal spikes in the centrotemporal regions.
3. Stage 3: abnormal sleep patterns, bilaterally synchronous bursts of pseudoperiodic delta activity, and generalized rhythmic spike discharges.
4. Stage 4: slowing of background activity, theta activity in central and frontal regions, multifocal epileptiform activity in the awake state, and generalized slow spike–wave activity in sleep.

3.2 | Chromosomal microrearrangements

Paroxysmal abnormalities in chromosomal microrearrangements are mainly focal or multifocal (Tables 2 and 3). The question is about the localization and pattern of EEG changes and the possibility of considering them as a potential marker. Until now, no peculiar interictal electroencephalographic patterns have been identified. Antiseizure medications with mono- or polytherapy were adjusted to the semiology of seizures. For example, in 15q inv dup syndrome, based on published reports, valproate was the most effective against generalized seizures, with the decreased frequency used following CBZ, LTG, TPM, and LEV.

Among presented microrearrangements there are several with the epilepsy syndrome phenotype, for example:

1. IESS: 16p13.11, 15q13.3, and 17q21.31 microdeletions, 5q inv dup syndrome.
2. Lennox-Gastaut syndrome: 15q11.1q13.3 duplication, 5q inv dup syndrome.
3. Dravet syndrome (DS): 2q24.4 deletion.
4. SeLEAS (Panayiotopoulos syndrome): 6q terminal deletion.

The attempt to connect some chromosomal abnormalities to epilepsy syndrome is challenging.

In IESS, pathogenic mutations have been detected in over 30 genes, and cyclin-dependent kinase-like 5 (*CDKL5*) (~10%), *STXBP1* (~2%), and *ARX* are among the most frequent genes observed.[33]

Although DS is usually caused by loss-of-function variants in *SCN1A*, other genes have also been reported to produce the Dravet phenotype, including *SCN2A*, *SCN8A*, *SCN9A*, *SCN1B*, *PCDH19*, *GABRA1*, *GABRG2*, *STXBP1*, *HCN1*, *CHD2*, and KCNA.[34–36]

Refractory epilepsy is associated with sudden, unexpected death in epileptic patients (SUDEP). The reported

TABLE 1 Epilepsy and EEG pattern in complex chromosomal rearrangements.

Chromosomal aberrations	Epilepsy onset	Seizures rate	Semiology of seizures	EEG tracing	Brain MRI	Treatment efficacy
Wolf-Hirschhorn syndrome (4p-syndrome),[1,3,4] Figures 1 and 2	During the first 3 years of life, mainly 6–13 months (average 9 months)	90%–100% of patients	Alternate hemiconvulsions, febrile seizures, epileptic spasms, generalized tonic–clonic, and clonic seizures	70% of patients-distinctive EEG pattern: 1. Frequent, diffuse atypical spike and wave complexes occurring in long bursts 2. Frequent high amplitude, fast spikes-polyspikes, and wave complexes over the posterior areas triggered by eye closure	Corpus callosum hypoplasia, enlargements of the lateral ventricles, cortical/subcortical atrophy, delayed myelination, cerebellar anomalies, and schizencephaly	Well controlled by monotherapy
Angelman syndrome[1,3–5] Figures 3–11	1–3 years of age, 25% before 1 year of age	80%–90%, status epilepticus: 35%–85%	Deletion type- prevalence of tonic–clonic seizures, infantile spasms, myoclonic status epilepticus Non-deletion type- atypical absence, myoclonic seizures	1. Persistent rhythmic 4–6 Hz, 200 mV theta waves during wakefulness 2. Prolonged runs of anterior dominant, rhythmic 2–3 Hz (200–500 mV) with or without mixed spike-wave complexes 3. Posterior dominant 3–4 c/s, 200 mV notched delta, and theta waves (mixed with ill-defined spike-wave) facilitated with eye closure	Corpus callosum hypoplasia, lateral ventricle enlargement, cerebral atrophy diffuse white matter changes delayed myelination	Antiseizure medications (ASM) that target GABAergic signaling, such as VPA PB and CLZ as former first-line therapies and other effective: TPM, LTG, ESM, LEV, CLB; According to questionnaires: VPA, TPM, LTG are the most frequently used
Prader-Willi syndrome (PWS)[1,2,6]	Before 2 years	4%–26%	Mainly focal seizures, but tonic–clonic seizures may occur and, more rarely, atypical absences and atonic seizures, febrile seizures in 6.4%–39.2% of children with PWS	Focal or multifocal, localized mainly over the middle–posterior regions, generalized epileptiform discharges, rarely high-voltage theta activities at 4–6 Hz	Myelination anomalies, corpus callosum hypoplasia, pituitary hypoplasia, subarachnoid space enlargement, enlargement of the lateral ventricles, arachnoid cyst, cerebral atrophy, cerebellar hypoplasia, pituitary hypoplasia	Well controlled by monotherapy

TABLE 1 (Continued)

Chromosomal aberrations	Epilepsy onset	Seizures rate	Semiology of seizures	EEG tracing	Brain MRI	Treatment efficacy
Miller-Dieker syndrome[1,4]	First months of life		Epileptic spasms (50%) tonic, myoclonic, tonic–clonic, and focal seizures	High-amplitude alpha or beta activity altering with high amplitude slow rhythms and slow-wave complexes or hypsarrhythmia	Lissencephaly corpus callosum dysgenesis/agenesis, ventriculomegaly	Refractory epilepsy
Ring chromosome 20[1,3,4,7–9]	Infancy to 14 years	Almost all patients	Nonconvulsive status epilepticus, focal seizures associated with ictal terror and hallucinations with loss of consciousness, oro-alimentary automatisms and hypertonia	-Normal or nearly normal EEG pattern with runs of theta waves activity of 5 Hz in fronto-centro-temporal areas or background slowing (interictal) -Long-lasting bifrontal high voltage slow waves with occasional spikes, sometimes unilateral side (ictal)	Usually normal, potential functional dysfunction of the frontal lobe and basal ganglia network	Refractory epilepsy, VPA and LTG, often in combination, are generally the most effective ASMs Single papers about the beneficial effect of the KD, VNS, steroids
Ring chromosome 14[1,4,9,10]	Early onset	Not determined	Polymorphic seizures: generalized tonic–clonic, myoclonic, focal motor seizures; seizure cluster tendency, and frequent status epilepticus	Slow and poorly organized background activity during wakefulness and sleep, frequent bursts of asynchronous rhythmic high amplitude slow waves over the frontal and temporal-posterior regions, and multifocal spikes and spike-wave complexes over the posterior regions, sometimes diffuse and activated by eye closure, followed by secondary generalization	Cerebral atrophy, lateral ventricular dilatation	Refractory epilepsy

(Continues)

TABLE 1 (Continued)

Chromosomal aberrations	Epilepsy onset	Seizures rate	Semiology of seizures	EEG tracing	Brain MRI	Treatment efficacy
18 trisomy[11]	Infancy	25%–50%	Complex partial, tonic–clonic seizures; in some patients, generalized seizures preceded by spasms and asymmetric tonic seizures or by periodic reflex spasms triggered by eating, autonomic epileptic seizures with cardiac arrhythmia, and apnea stimulating non-epileptic syncope, focal and generalized seizures	Generalized and focal discharges mainly over the posterior region	Cerebellar hypoplasia, disturbed myelination pattern, hydrocephalus	
Down syndrome[3,4,12–15] Figures 12–14	40%-before 12 months, 40%-within the 3rd decade of life	8% (1–13%)	47%- focal seizures, 37%-epileptic spasms (94% of all seizures in children with Down syndrome younger than 1-year, male predominance), 21%- generalized tonic–clonic seizures, myoclonic seizures	The commonest EEG pattern: symmetrical hypsarrhythmia, Single rather than clustered spasms on ictal EEG No interictal paroxysmal activity between consecutive spasms, Electrographic seizure initiated by or combined with focal discharges	Decreased total brain volume, total gray matter and white matter, cortical lobar, hippocampal, and cerebellar volumes	The long-term epileptic spasms control rate reportedly as high as 90%, the most effective ASM- ACTH
Klinefelter syndrome[4]	The onset ranges between childhood and adulthood more frequent among males	5%–17%, 2%–10%	Febrile seizures, generalized tonic–clonic seizures, focal seizures, and absences	Without typical or more frequent abnormalities	Decreased total brain volume, total gray matter volume, and total white matter volume, significant volumetric differences in the ventral and central parts of the brain have been reported, including amygdala, hippocampus, insula, and striatum	Usually, based on a few reports, not problematic

TABLE 1 (Continued)

Chromosomal aberrations	Epilepsy onset	Seizures rate	Semiology of seizures	EEG tracing	Brain MRI	Treatment efficacy
Fragile X syndrome[1,3,4,16] Figure 15	>80% below 10 years (the mean age of seizure onset was 6 years)	13%–14%-41%–44%, on average 25%	Seizures semiology like in SeLEAS (Panayiotopoulos syndrome), the most common type- focal onset with/without impaired awareness, and generalized tonic–clonic seizures, and status epilepticus have also been observed	Many children have abnormal electroencephalograms without overt epileptic seizures, frequently with a pattern of centrotemporal spikes	Enlargement of the caudate nuclei and parietal lobes and of the right brainstem, and a significant decrease in volume of the left frontal lobe	Well-controlled epilepsy to seizures unresponsiveness to treatment, the most commonly used anticonvulsants: OXC, VPA, LTG, LEV

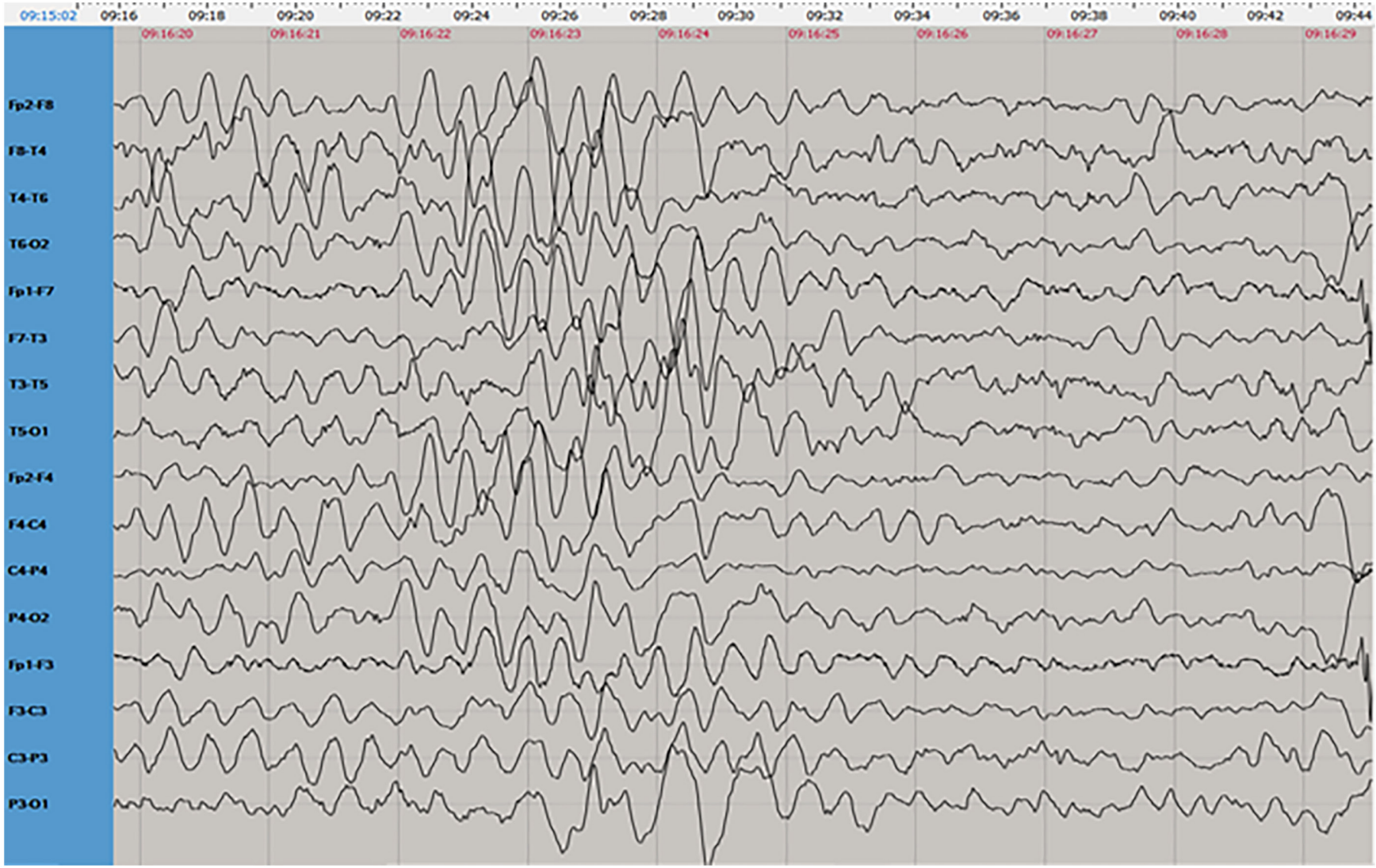
Abbreviations: ACTH, adrenocorticotropic hormone; CLB, clobazam; CLZ, clonazepam; ESM, ethosuximide; KD, ketogenic diet; LEV, levetiracetam; LTG-lamotrigine; OXC, oxcarbazepine; PB, phenobarbital; TPM, topiramate; VNS, vagal nerve stimulation; VPA, valproate.

incidence of SUDEP by the American Academy of Neurology (AAN) and American Epilepsy Society (AES) was 0.22 (95% CI 0.16–0.31) per 1000 patient-years in children aged 0–17 years.[35,37] Sveinsson et al. reported SUDEP incidence under the age of 16 years was 1.11 per 1000 person-years based on Annegers criteria. A Canadian cohort study based on Nashef criteria calculated an overall incidence of 1.17 (95% CI 0.68–1.88) per 1000 pediatric epilepsy-person-years.[35,37] SUDEP had been reported due to mutations of the following genes: *DEPDC5*, *TBC1D24*, *FHF1*, or 5q14.3 deletion. Although in some channelopathies like Dravet syndrome (SUDEP accounts for 49% of deaths in Dravet syndrome; 15.84 per 1000 patient-years), SCN8A-DEE (risk ranging from 1% to 10%), and duplication of chromosome 15q11.2q13 SUDEP is reported more frequently.[36] In the study of Conant et al. 8% of patients with 5q inv dup syndrome experienced SUDEP.[18] Chromosomal rearrangements involving the 1p36, 5p15, and 7q11 regions have also been reported in association with periventricular heterotopia, but the genes implicated remain unknown.[26]

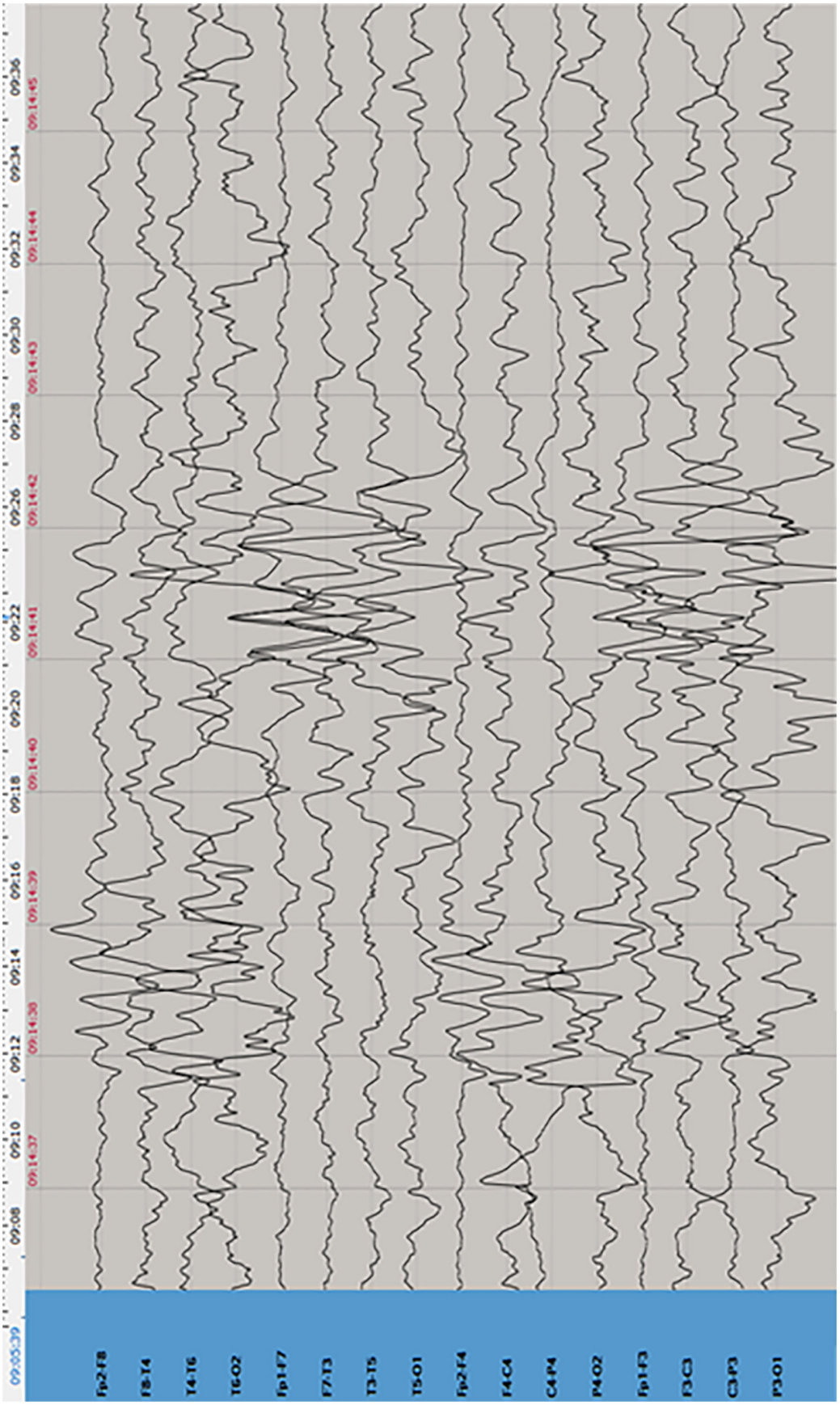
The micro-chromosomal rearrangements with clinical features resembling known epileptic syndrome phenotypes are discussed below.

3.3 | 17q21.31 microdeletion

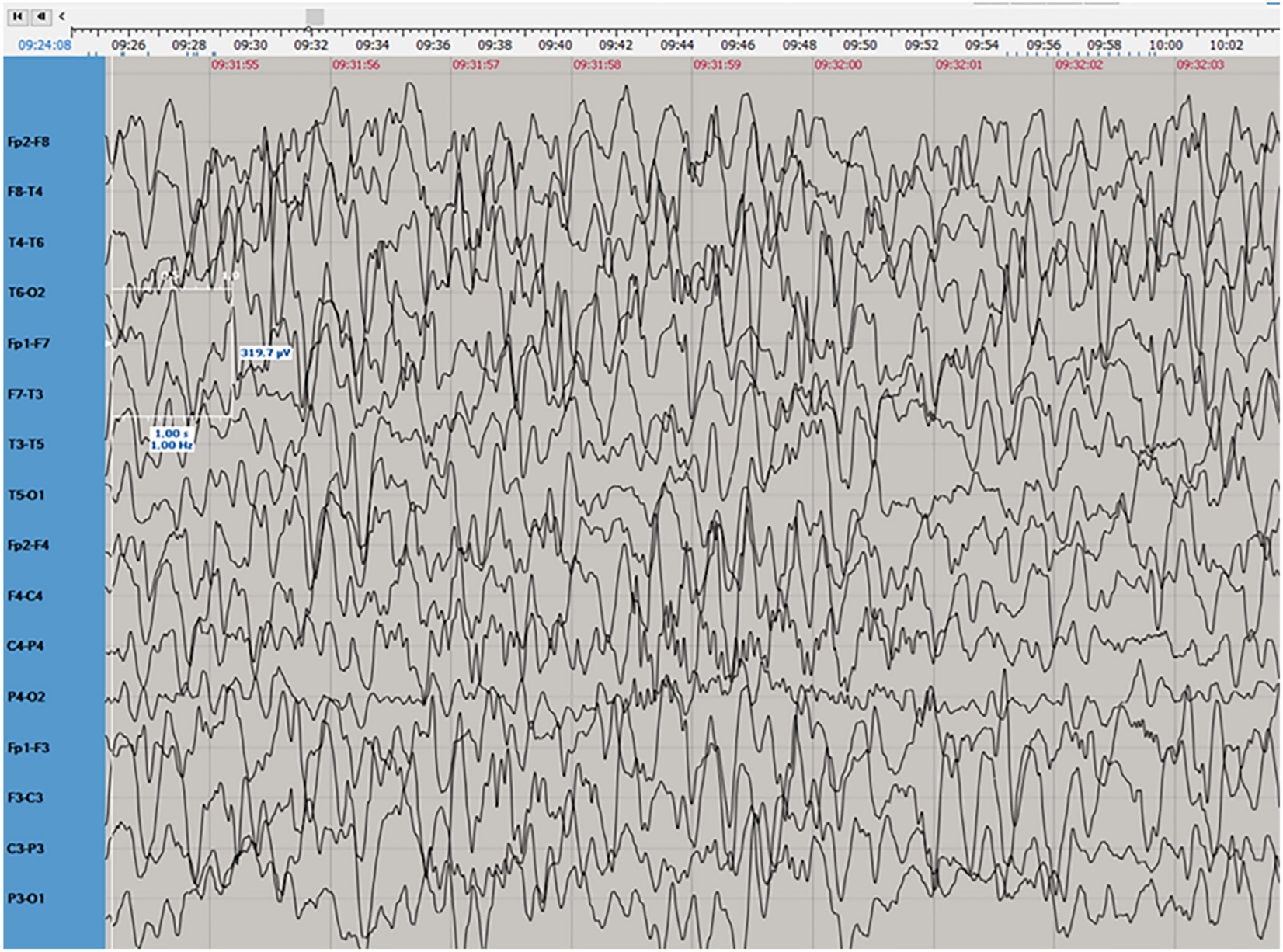
The literature indicates chromosome 17q21.31 microdeletion as one of the first genomic disorders identified by chromosome microarrays.[19] It is associated with epilepsy, although the specific seizure phenotype has not been well described. Koolen et al. reported 22 patients with 17q21.31 microdeletion,[2,38] all presented with global psychomotor developmental delay from an early age. Epilepsy had been diagnosed in 11 patients (50% of cases). Generalized seizures were observed in 8 patients (36% of cases). Only 1 patient presented with focal clonic seizures and hypotonia 48 h after birth. Wray described a child with 17q21.31 microdeletion and epileptic spasms not specifically described in this syndrome, with the onset at the age of 5 months[21] (Table 4). ACTH treatment allowed for the spasms' cessation. Tan et al.[20] presented another 11 patients with 17q21.31 microdeletion, and the significant EEG and CNS findings are shown in Table 5. Table 6 presents an evolution of EEG recordings as a function of age in a male patient with 17q21.31 microdeletion.[39] That patient experienced epilepsy onset at the age of 11 years with hemiclonic seizures preceded by the expression of fear. The treatment with valproic acid was partially effective, but since the introduction of oxcarbazepine, he has been seizure-free. A brain MRI performed at the age of 11 years showed partial corpus callosum agenesis.



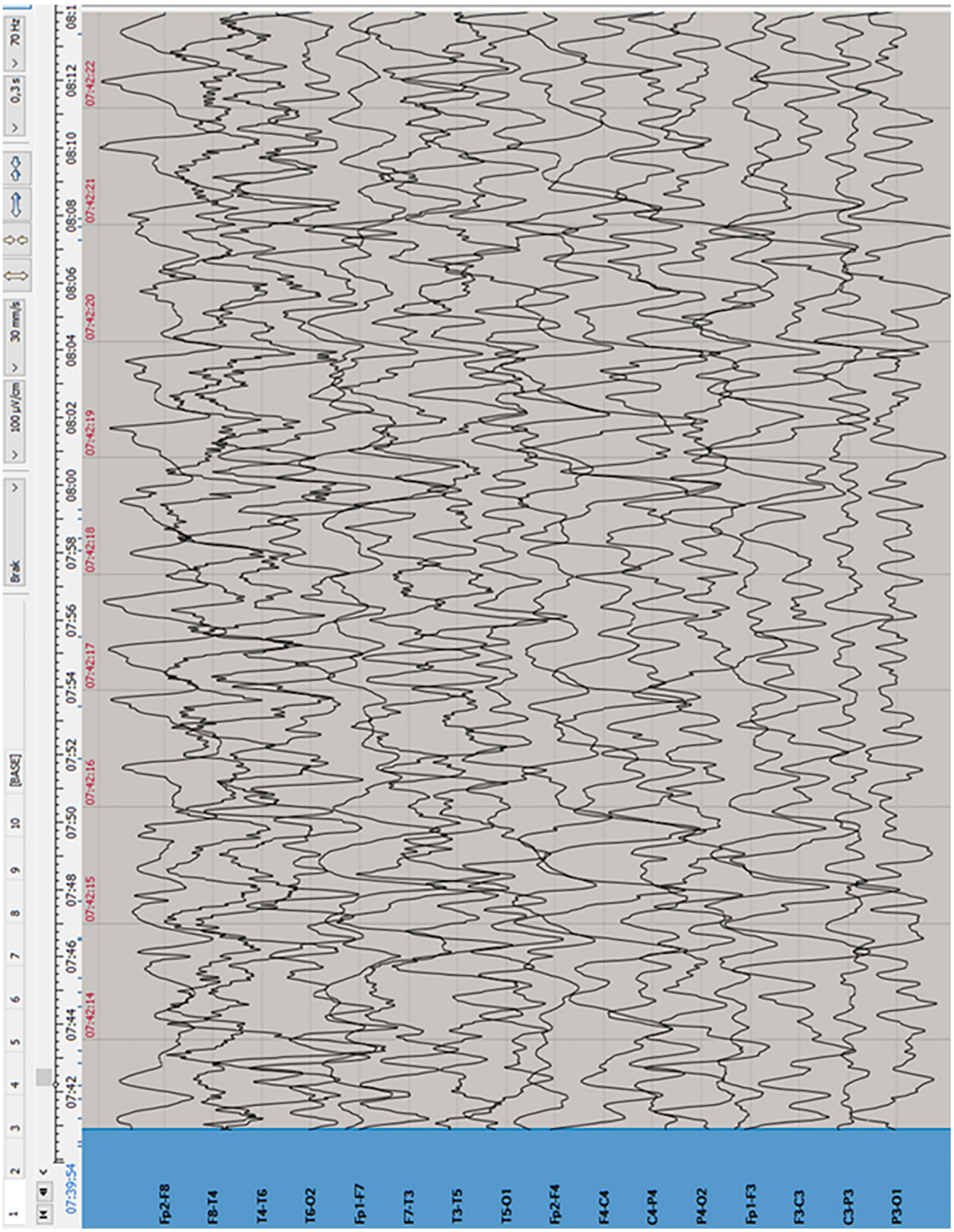
FIGURES 1 AND 2 Wolf-Hirschhorn syndrome (4p-syndrome). Poor basal activity and poorly expressed sleep features. Periodically 2–3 s generalized series consisting of slow waves 3–6 Hz (arrows) with amplitudes up to 400 μV with the presence of intruded sharp waves, spikes, and abortive spike-and-wave complexes.



FIGURES 1 AND 2 (Continued)



FIGURES 3 AND 4 Angelman Syndrome. Before treatment. Multiple generalized discharges (groups and series, sometimes fragmented, with a duration of up to 3 s) composed in various combinations of spikes/polyspikes/spike-and-wave complexes 2–5 Hz and slow waves of similar frequency and amplitudes up to 750 μV.



FIGURES 3 AND 4 (Continued)

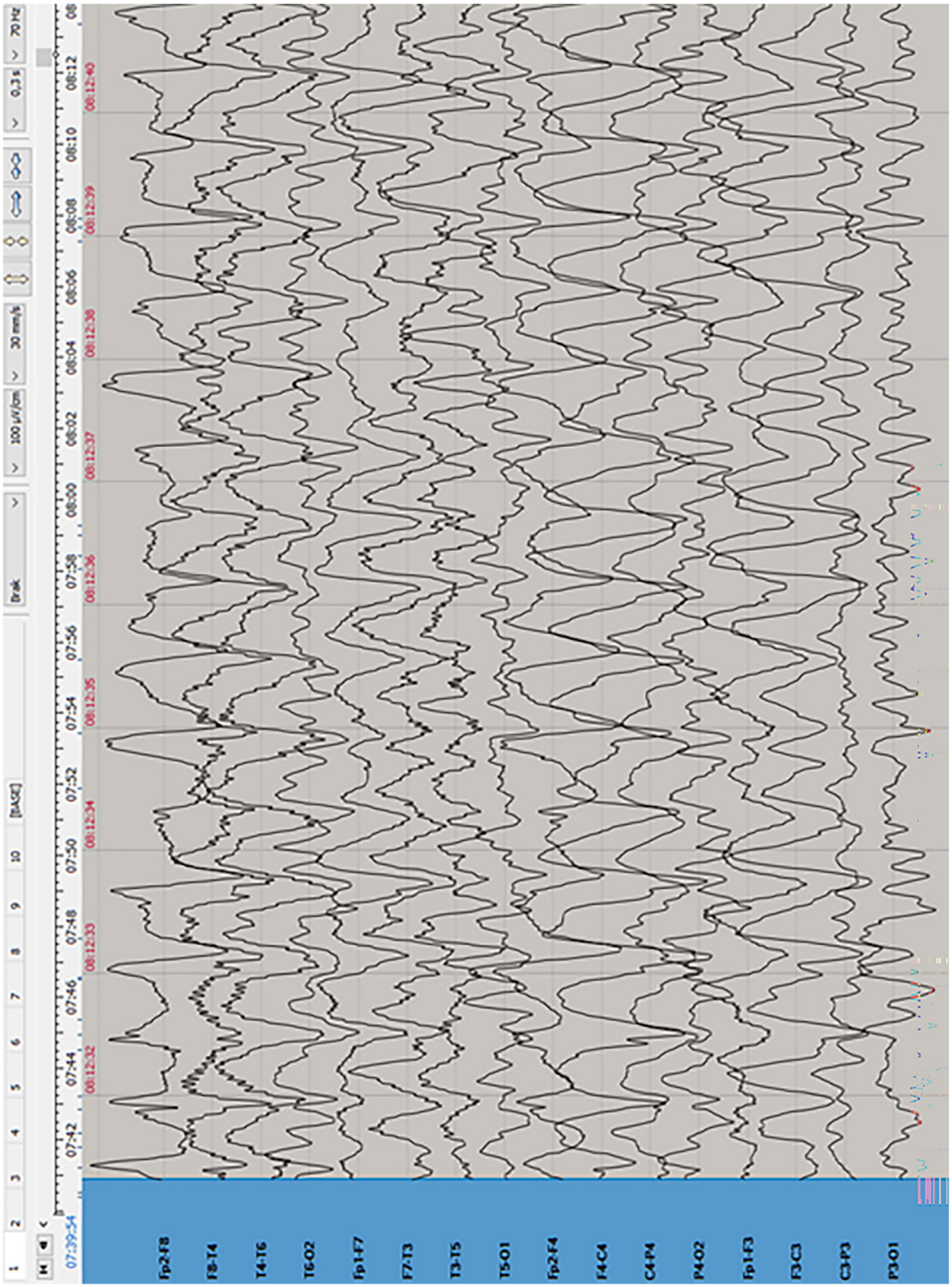


FIGURE 5 The same patient (Angelman Syndrome) after treatment (valproate and lamotrigine). Multiple generalized series consisting of polymorphic, asynchronous delta waves (arrows) with amplitudes up to 500 μV sometimes with the presence of singles and groups of low spike-and-wave complexes/sharp-slow waves.

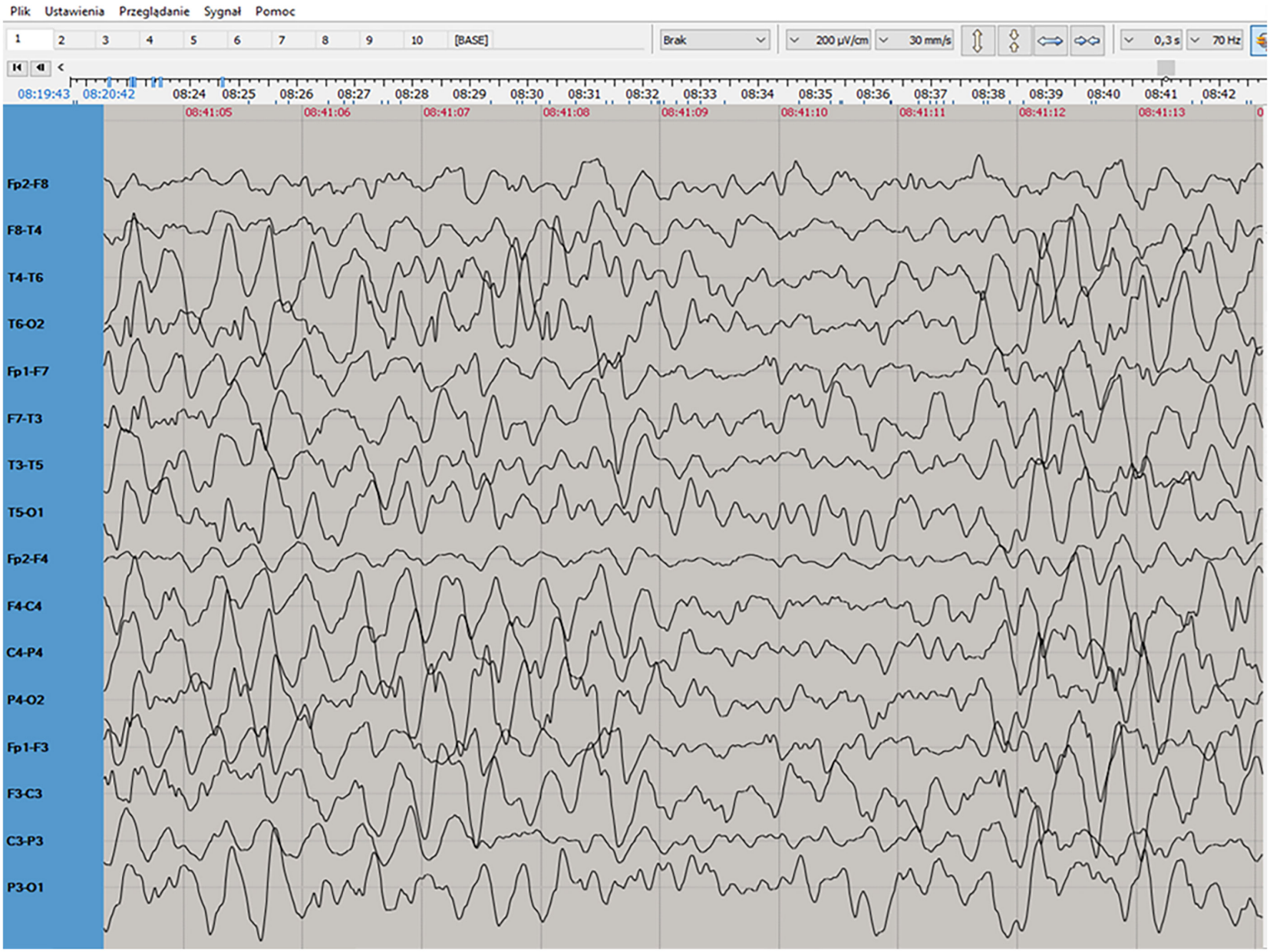


FIGURE 6 Angelman syndrome. Rhythmic and widespread monomorphic theta waves (arrows) are recorded during wakefulness.

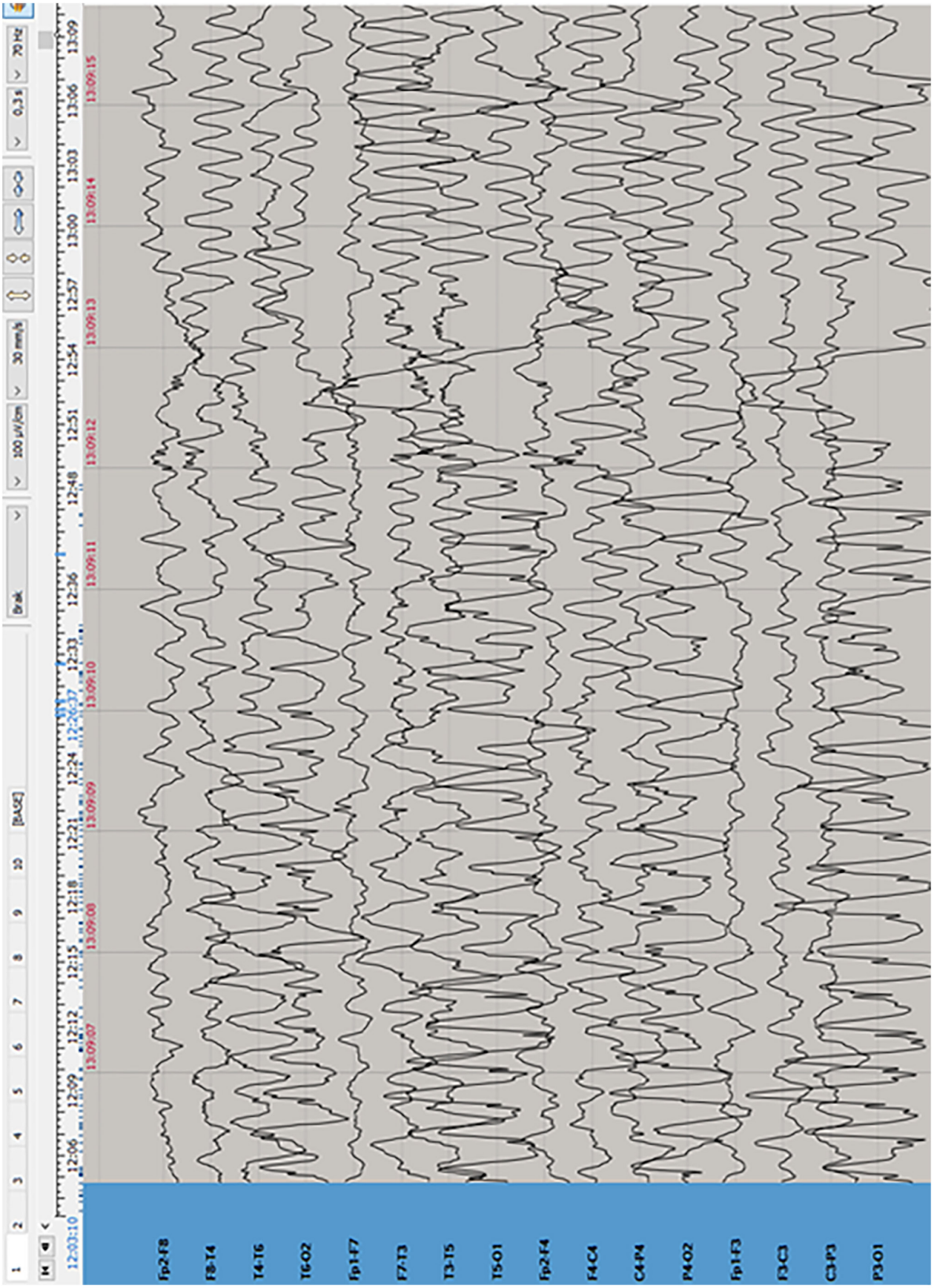


FIGURE 7 Angelman syndrome. Monomorphic theta wave activity, discharges of spike-and wave complexes (spikes of low amplitude, slow waves of high amplitude—arrows) over the occipital regions, and mainly on the left.

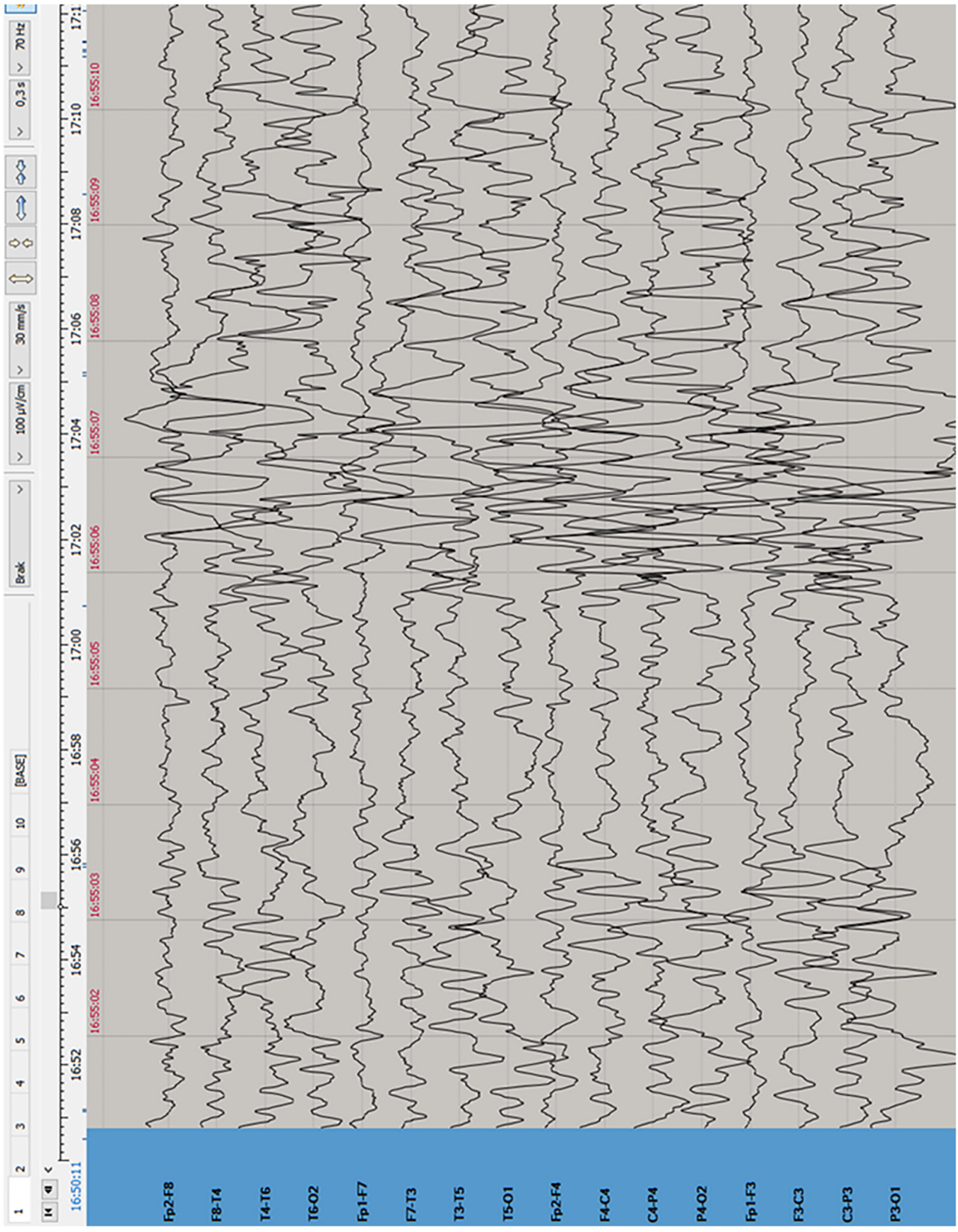


FIGURE 8 Angelman syndrome Triphasic sharp waves.

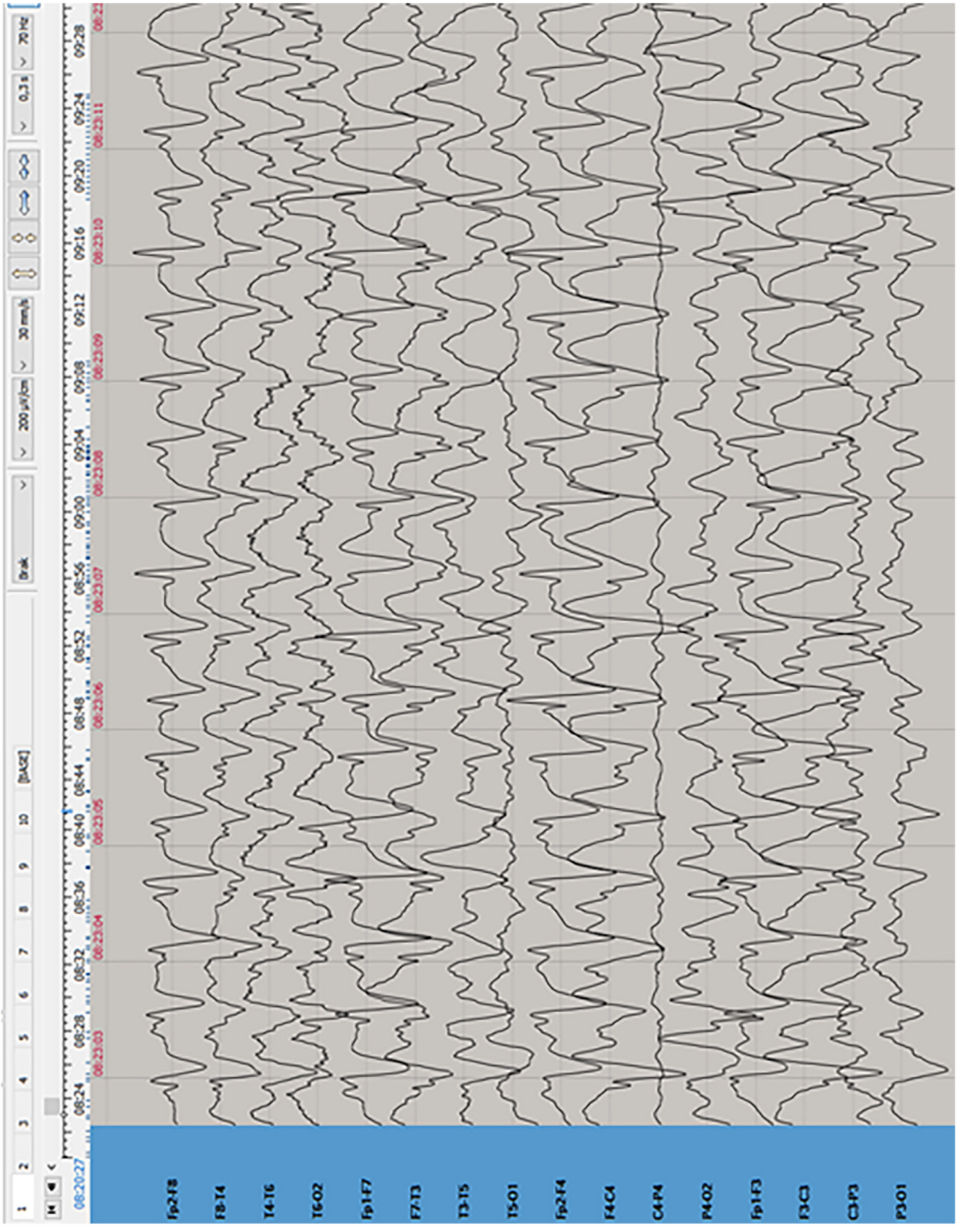


FIGURE 9 Angelman syndrome. Almost continuous generalized high voltage (up to 800 μV) slow spike-wave complexes at a frequency of 1.5 Hz.

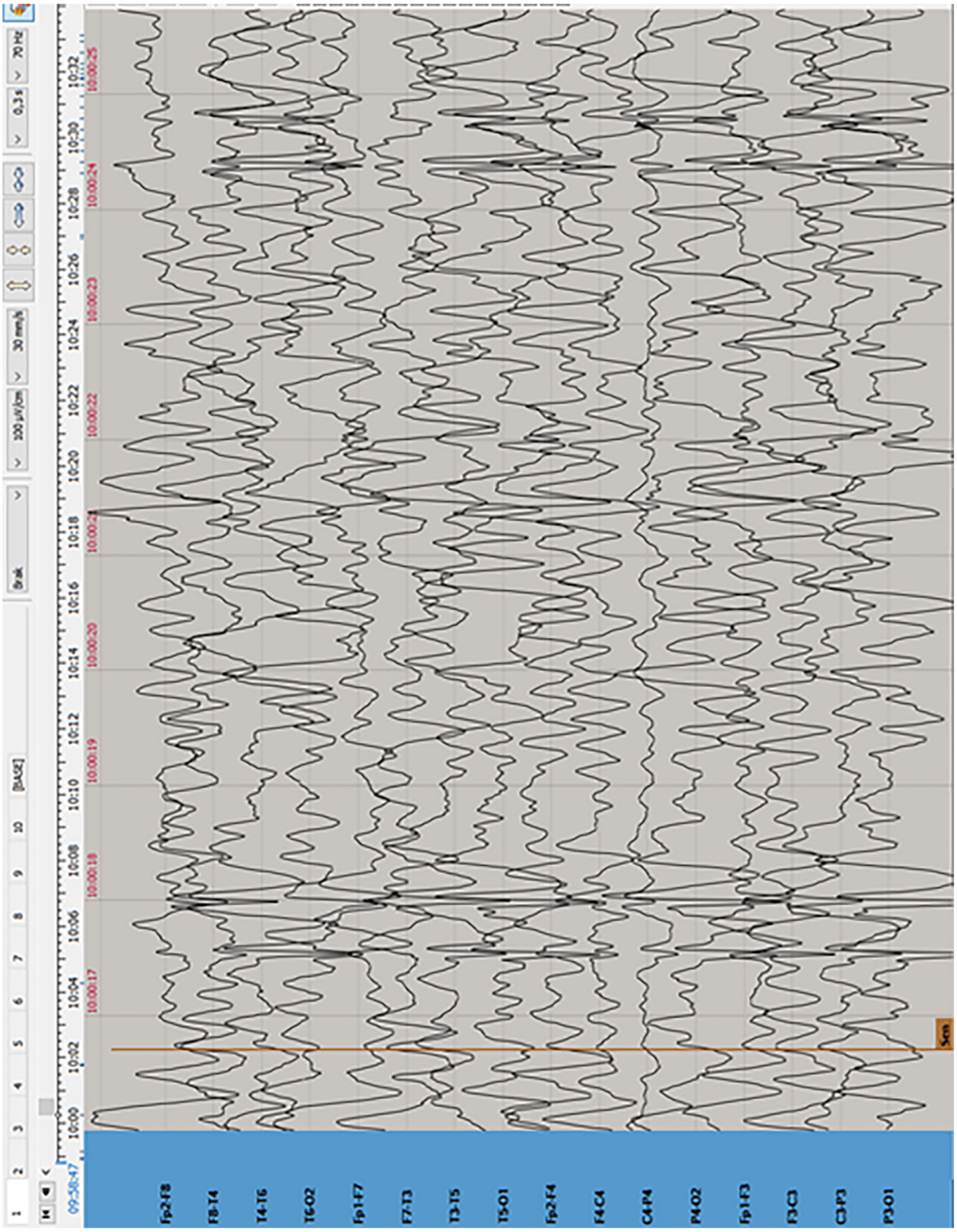


FIGURE 10 Angelman syndrome. Multiple pseudorhythmic discharges of triphasic sharp waves and sharp slow wave complexes with amplitudes up to 600 μV: generalized with max. in posterior regions and less frequently localized in temporal and central parietal-occipital regions, bilaterally.

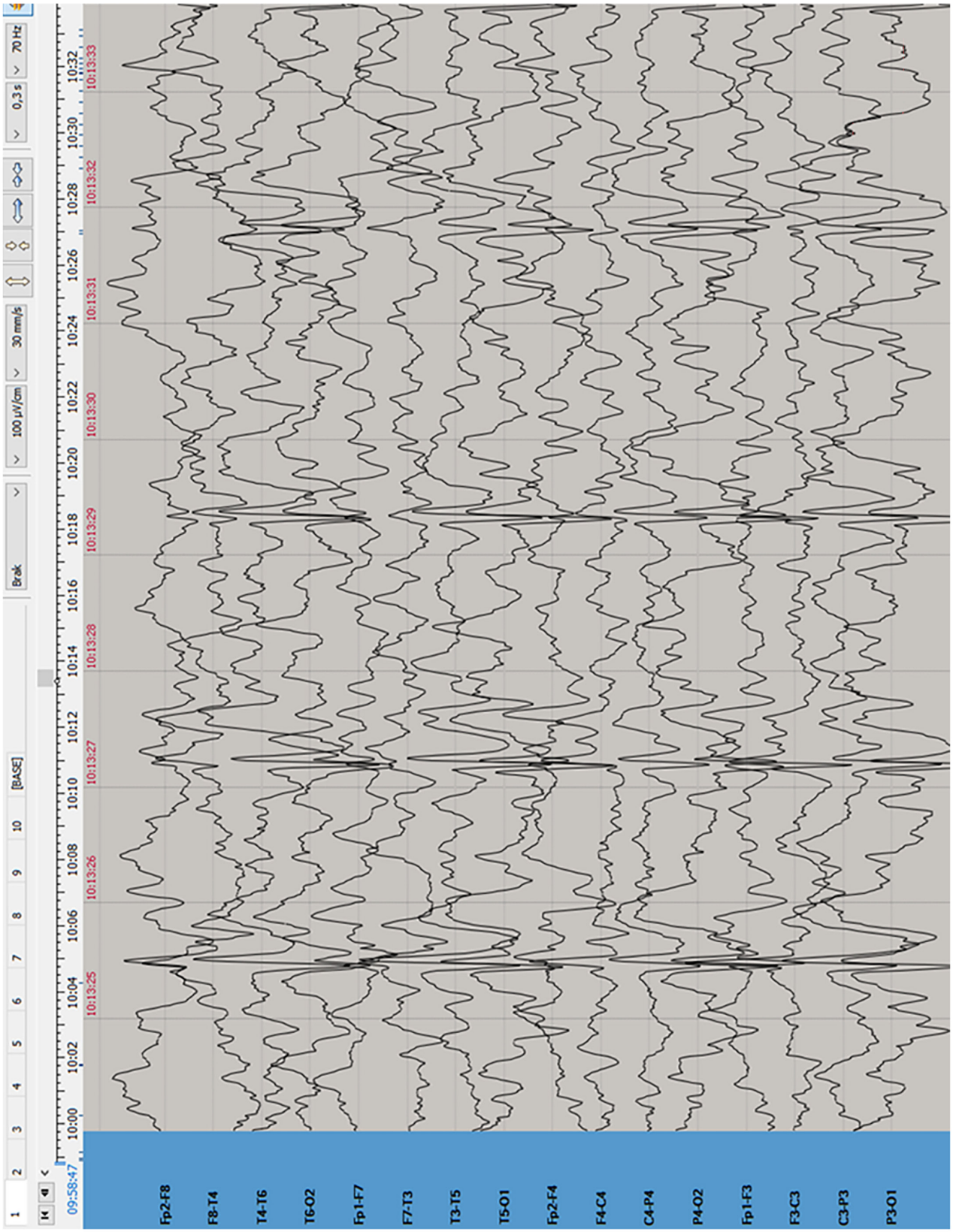


FIGURE 11 Angelman syndrome. Generalized spike-wave complex discharges.

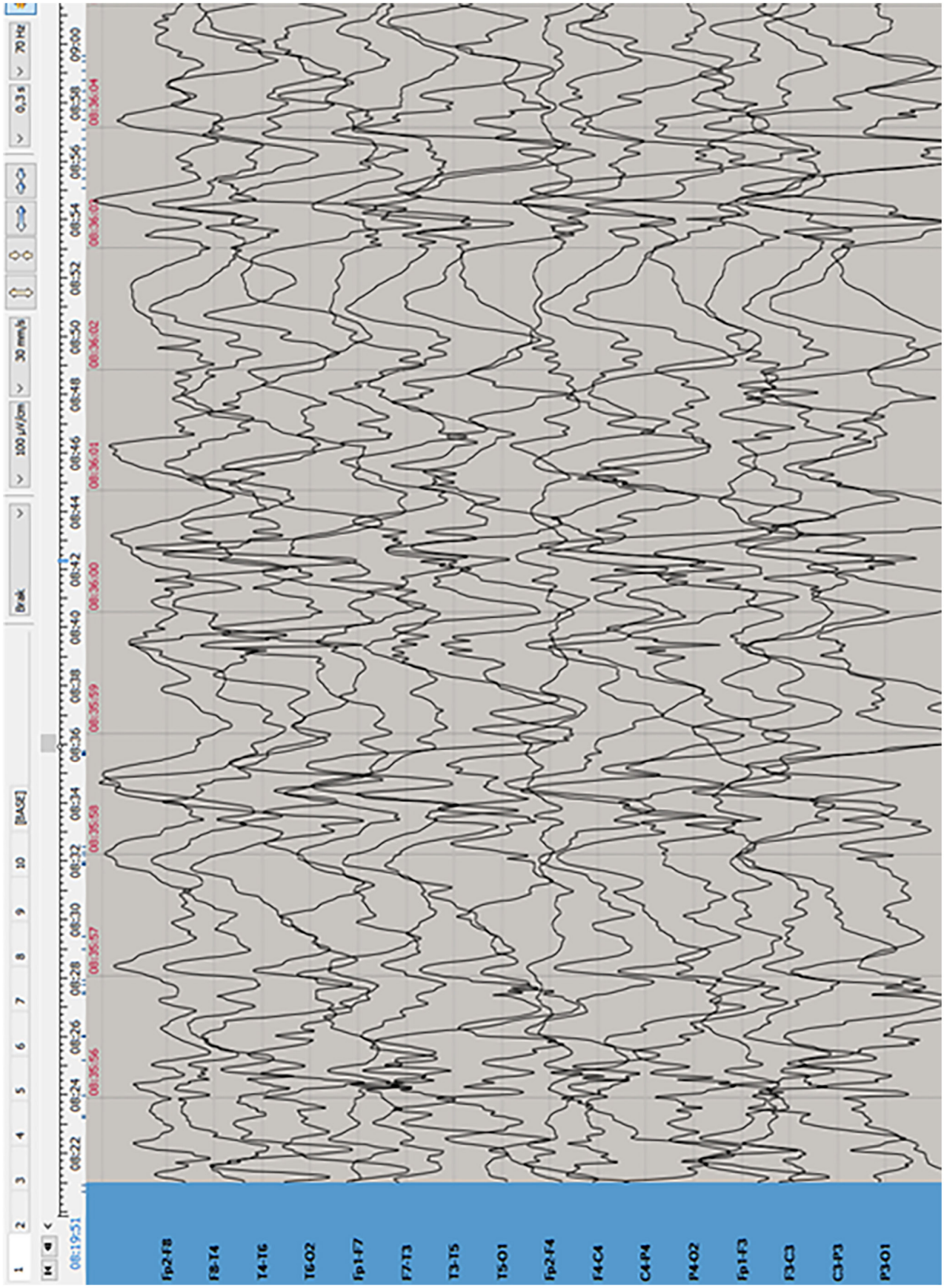


FIGURE 12 Down syndrome. Hypsarrhythmia.

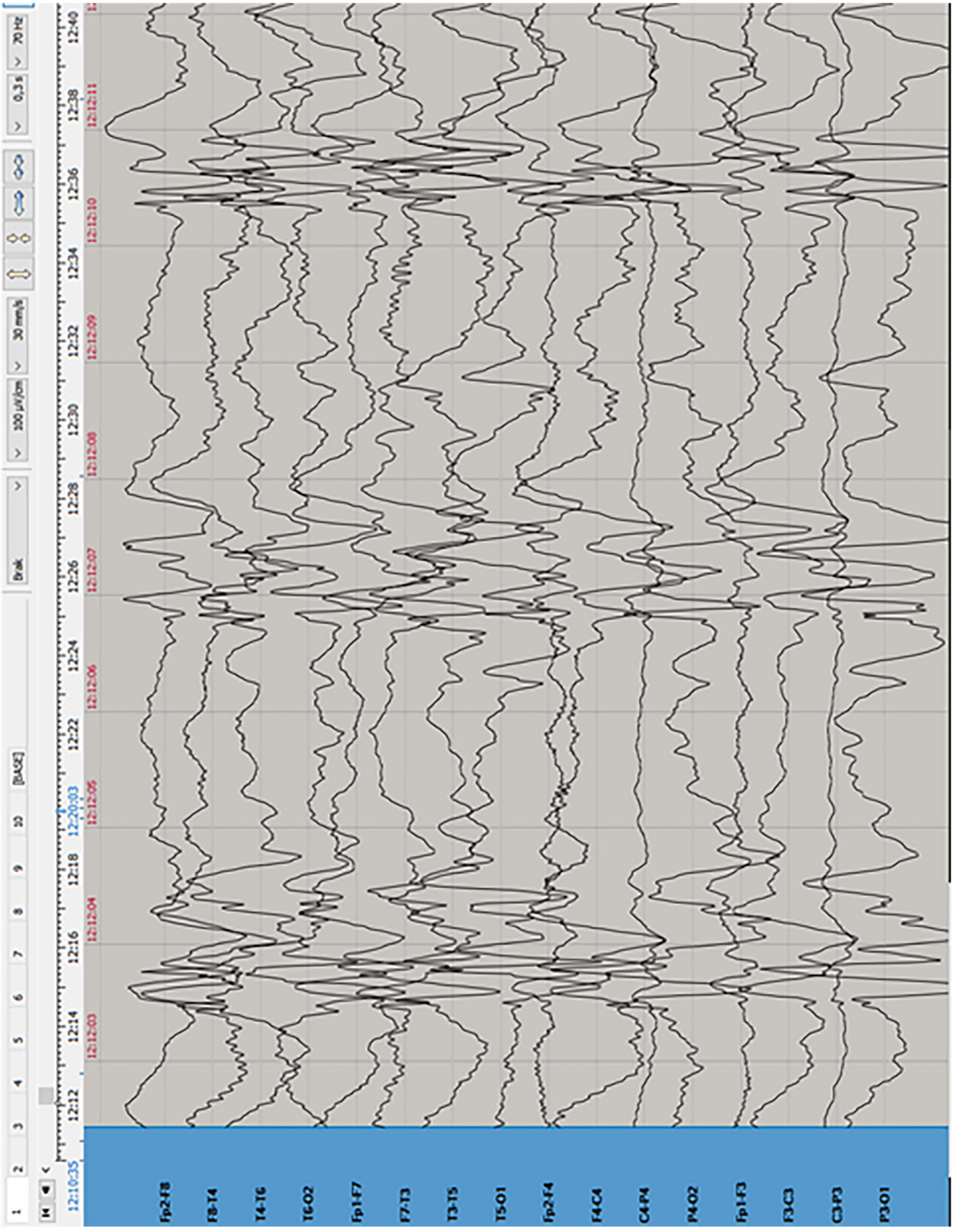


FIGURE 13 Down syndrome. Hypsarrhythmia (burst-suppression) variant.

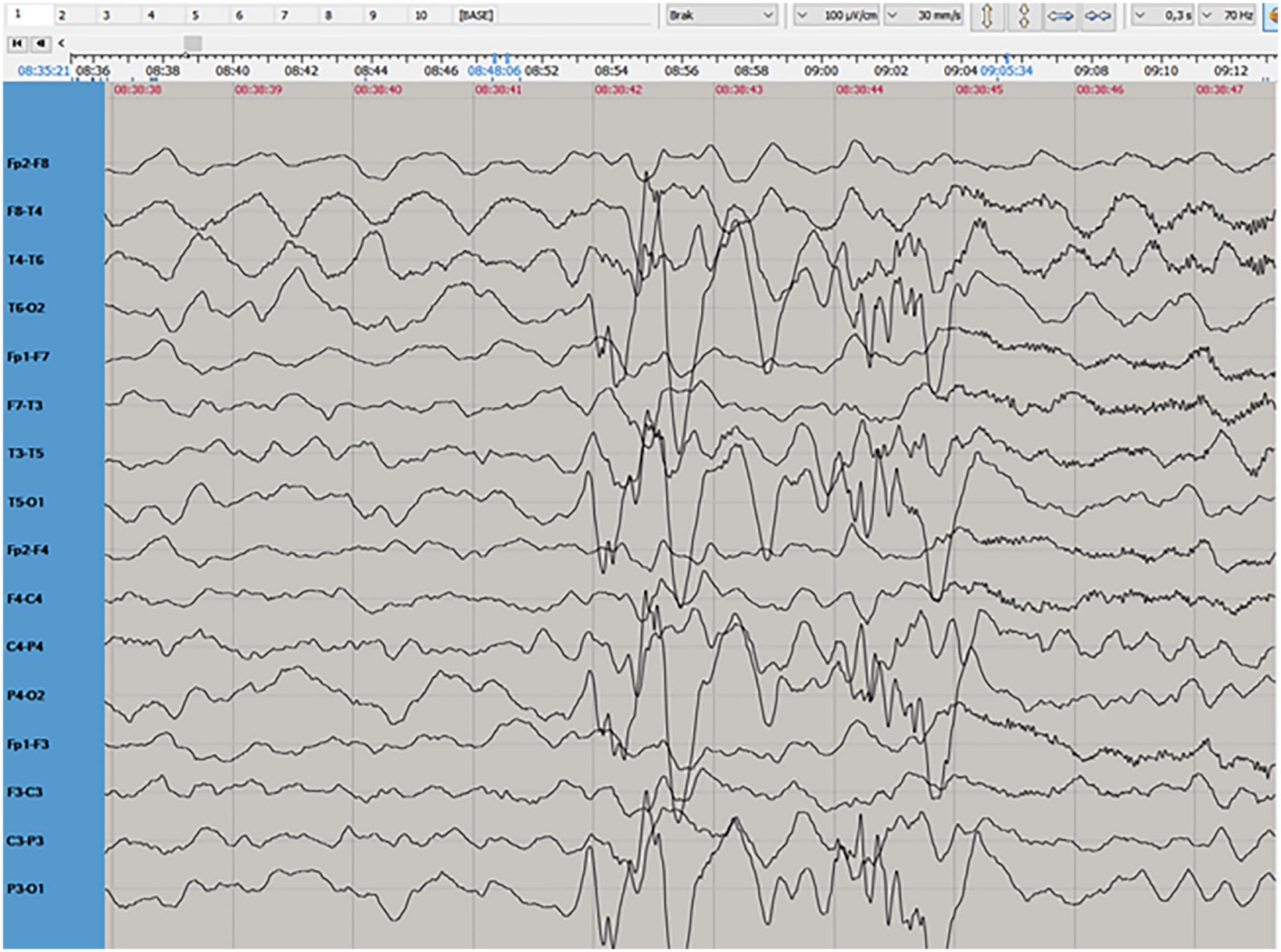


FIGURE 14 Down syndrome. After treatment (vigabatrin).Medium-volume groups and series composed in various combinations of sharp waves/spikes, slow spike-wave complexes, spike-wave complexes 100–600 μV: over the posterior temporal–parietal-occipital region bilaterally.

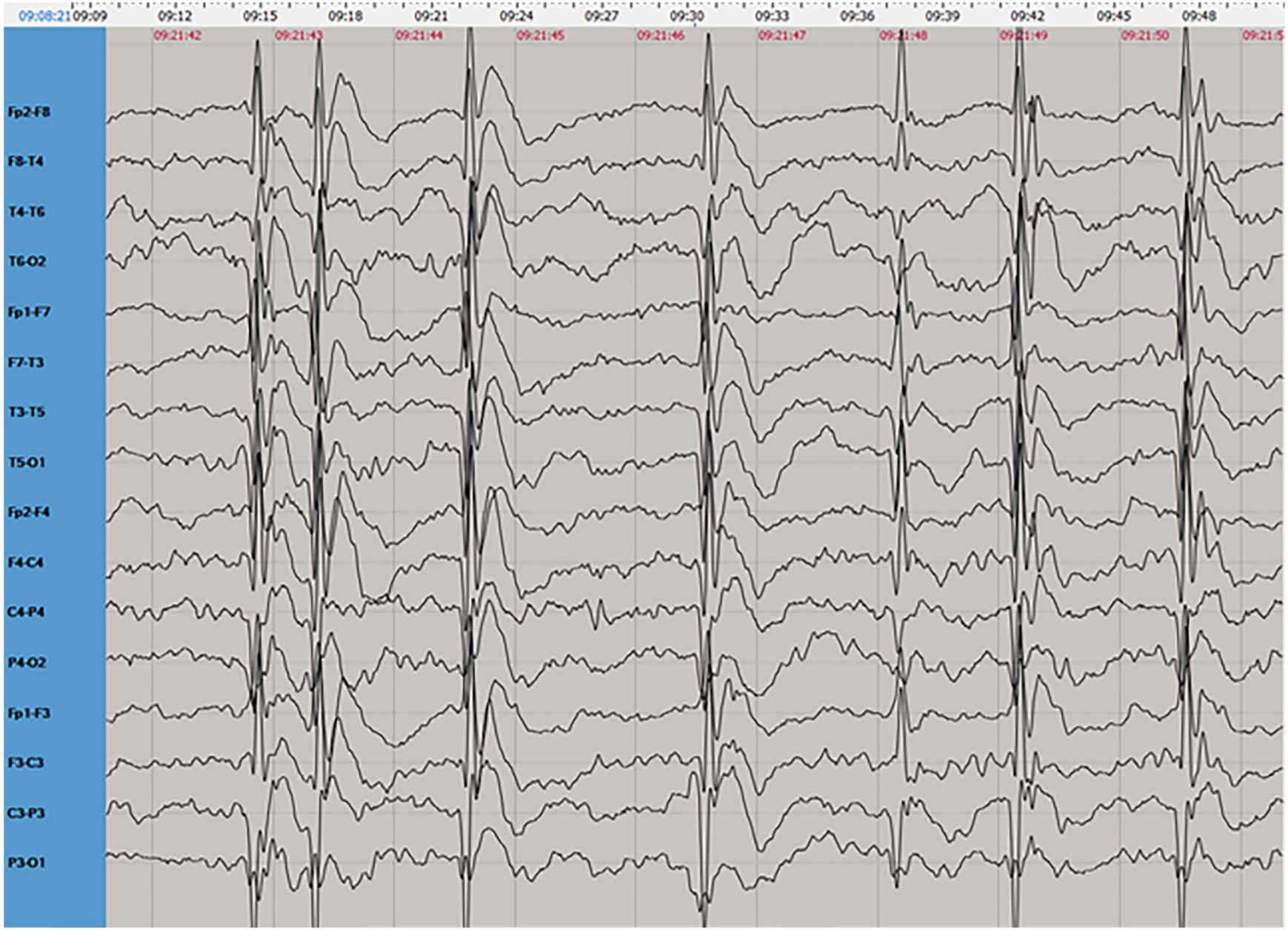


FIGURE 15 Fra-X syndrome. Generalized sharp waves and sharp-slow wave complexes with amplitudes up to 600 μV: In drowsiness and sleep almost continuous pseudo rhythmic (every about 1–2 s).

TABLE 2 Epilepsy and EEG pattern in chromosomal microrearrangements.

Chromosomal aberrations	Epilepsy onset	Seizures prevalence	Semiology of seizures	EEG tracing	Brain MRI
17q21.31 microdeletion[19–21]	Childhood onset focal seizures	Not determined	Focal impaired awareness seizures, usually with prominent autonomic features	Focal/multifocal epileptiform discharges	Corpus callosum dysgenesis, abnormal hippocampi, dilated ventricles, periventricular nodular heterotopia, focal cortical dysplasia, abnormal sulcation
15q13.3 microdeletion[4,22,23] Figures 16–19	Childhood, the median age of onset around 5 years	Breakpoints 4 and 5 (BP4 and BP5) have been associated with the epilepsy phenotype	Absence seizures, generalized seizures (tonic–clonic, myoclonic), overlapping with impaired awareness, non-motor onset seizures	Ictal EEG showed generalized polyspike and wave or spike and waves discharges Interictal EEG: generalized and focal epileptiform discharges with posterior dominant rhythm slowing	Usually normal, rare reports on ventricular dilatation, arachnoid cysts, cerebellar vermis hypoplasia, corpus callosum agenesis, focal cortical dysplasia, heterotopias
14q microdeletion[24] 14q duplication Figures 20–25	Infancy period 3–8 months	Not determined Not determined	Generalized tonic–clonic Epileptic spasms	Multifocal pattern with spikes and sharp waves Hypsarrhythmic pattern	Thinning of corpus callosum
6q terminal deletion[25,26]	First or second decade of life, frequently between ages 4 months and 4 years	Not determined	Focal onset, characterized by the ictal signs of vomiting, cyanosis, and head and eye version with or without loss of consciousness, similar to SeLEAS	Multifocal epileptiform discharges	Colpocephaly, dysgenesis of the corpus callosum and brainstem, hypertrophic massa intermedia, dilatation of ventricles, massive hydrocephalus, cerebral aqueductal stenosis, cortical atrophy, rarely periventricular nodular heterotopias or neuronal migration defects
1p36 terminal deletion[3,4,27,28]	Infancy period, from 6th month of life, rarely neonatal seizures	Present in around 60% of patients with female predominance	First seizures are usually generalized tonic, tonic–clonic, or clonic epileptic spasms in 31%	Focal and multifocal spikes, generalized spike/wave complexes and fast recruiting rhythms and hypsarrhythmia	Enlargement of the lateral ventricles sometimes associated with cortical atrophy, cerebral atrophy, white matter abnormalities, polymicrogyria, thin corpus callosum, cortical hypoplasia, Chiari malformation, and subependymal heterotopias

(Continues)

TABLE 2 (Continued)

Chromosomal aberrations	Epilepsy onset	Seizures prevalence	Semiology of seizures	EEG tracing	Brain MRI
2q24.4 deletion[29]	Within the first year of life	2%–3% of all Dravet syndrome (DS) and 12.5% of patients with DS negative for mutations on sequencing	The clinical picture of Dravet syndrome	Electroclinical picture of Dravet syndrome	Usually normal, rare report of diffuse lesions in the periventricular white matter and basal ganglia
5q14.3 deletion[30]	Infancy period	A Rett-like phenotype	Beginning with infantile spasms, febrile seizures, myoclonic and complex partial seizures	Variety of EEG abnormalities	Sometimes periventricular heterotopia, polymicrogyria
Xp11.22–11.23 duplication[31]	From 5 to 13 years	Not determined	Clonic jerks of the limbs and stare, generalized tonic–clonic seizures during sleep, and absences	Continuous Spike-Waves during Sleep (CSWS)	No abnormalities
15q inv dup syndrome[2,32]	62.3%, age of onset below 10 years	1% of idiopathic generalized epilepsy	Multiple seizure types (tonic–clonic, tonic, atonic, atypical absence, myoclonic, focal motor seizures) with a predominance (40.4%) of tonic–clonic seizures and epileptic spasms (30%); IESS and/or Lennox–Gastaut phenotype	Variety of EEG abnormalities, generalized spike activity being the most frequent	Thinning of corpus callosum, enlargement of ventricles

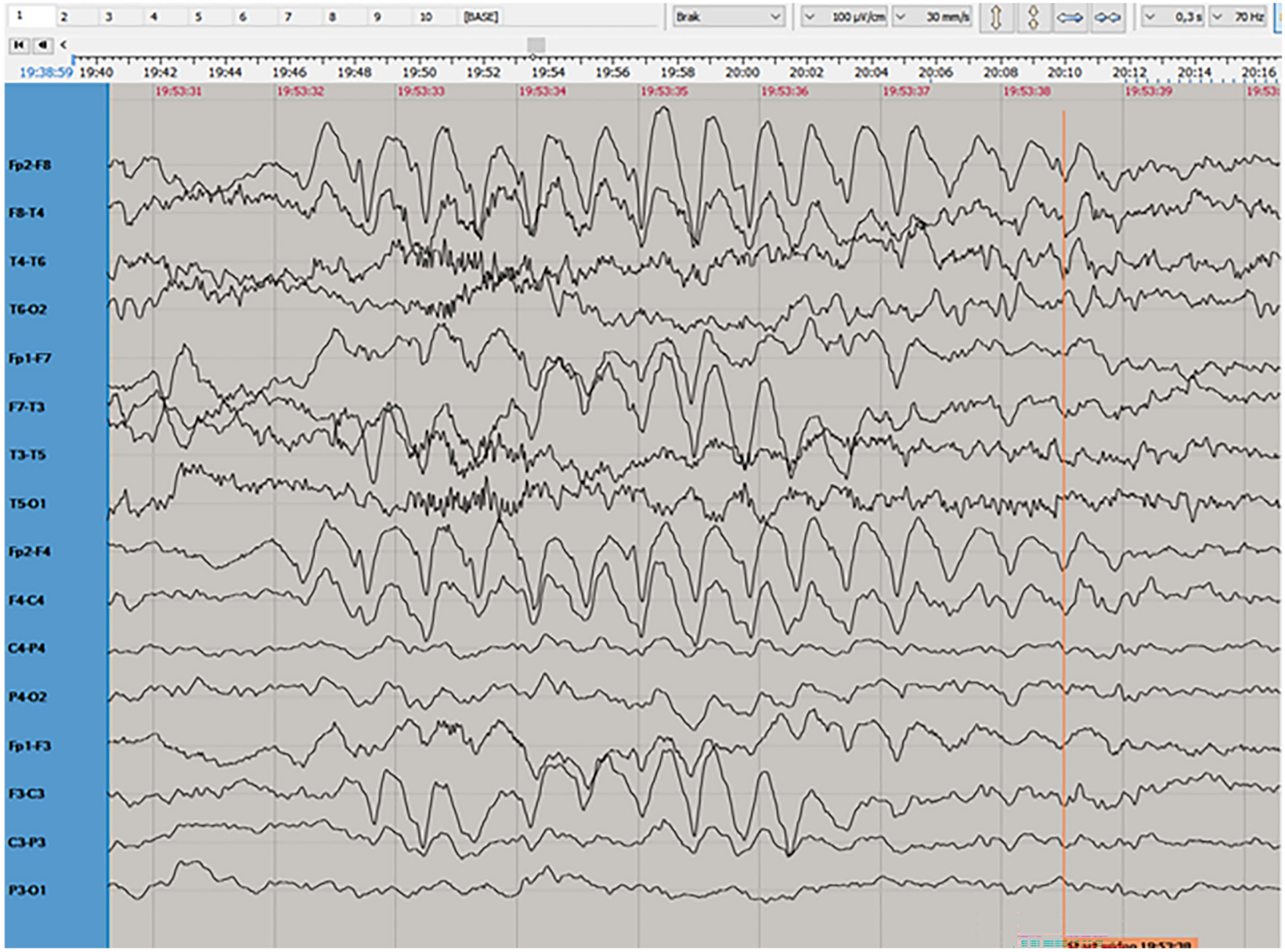


FIGURE 16 Del 15q13.3. Frontal and central regions bilateral discharges (groups and series of up to 40 s duration) with sharp wave- slow wave/spike wave complexes 2–2.5 Hz or 3–3.5 Hz and slow waves 2–4 Hz with amplitudes 200–700 μV with a tendency to become continuous in sleep.

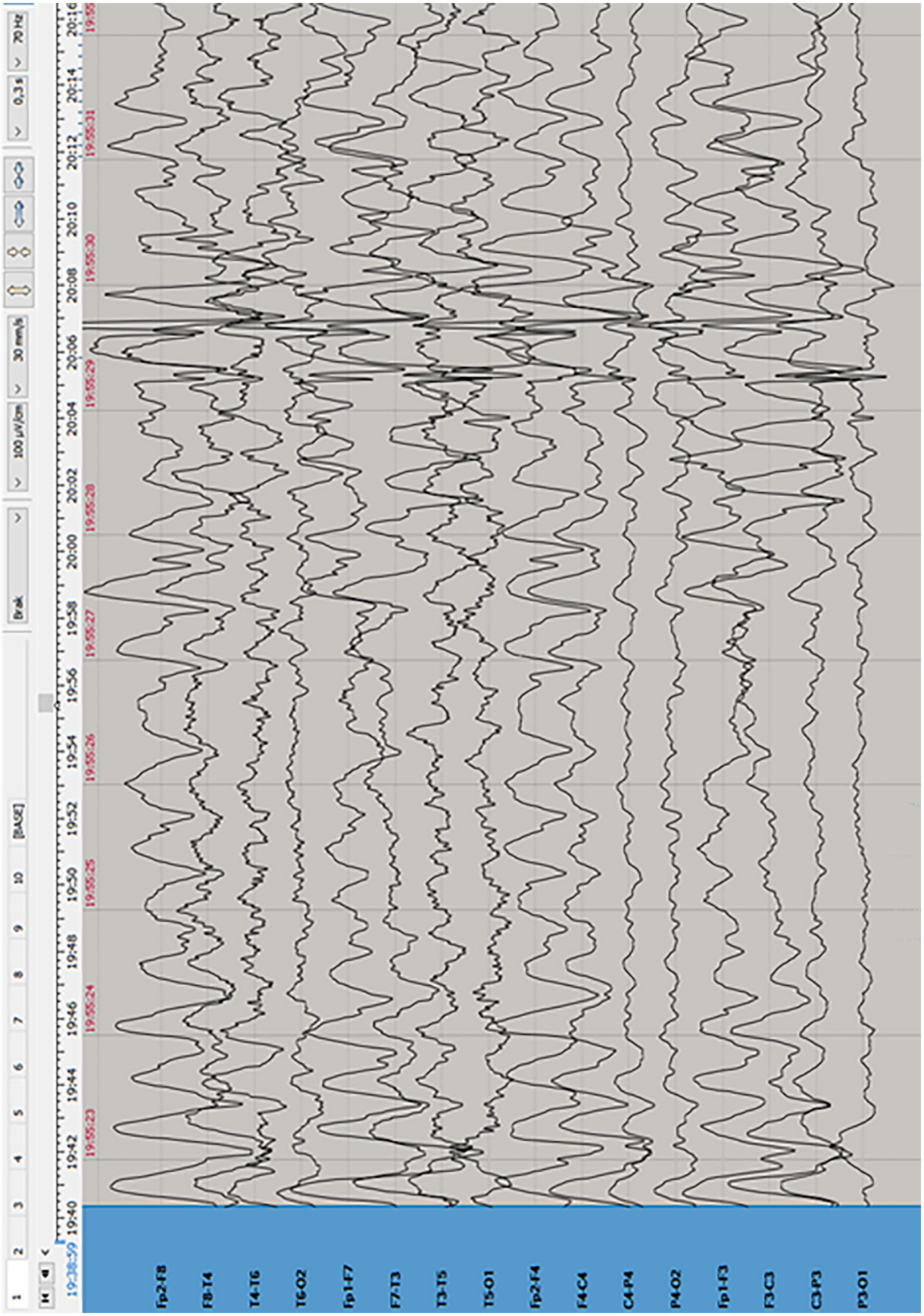


FIGURE 17 Del 15q13.3 Multiple 2–25 s series composed of sharp slow wave complexes 1.5–2.5 Hz and slow waves of similar frequency with amplitudes 100–650 μV, generalized with max. in frontal and central areas or only in these areas bilaterally or with predominance once on the right and once on the left side.

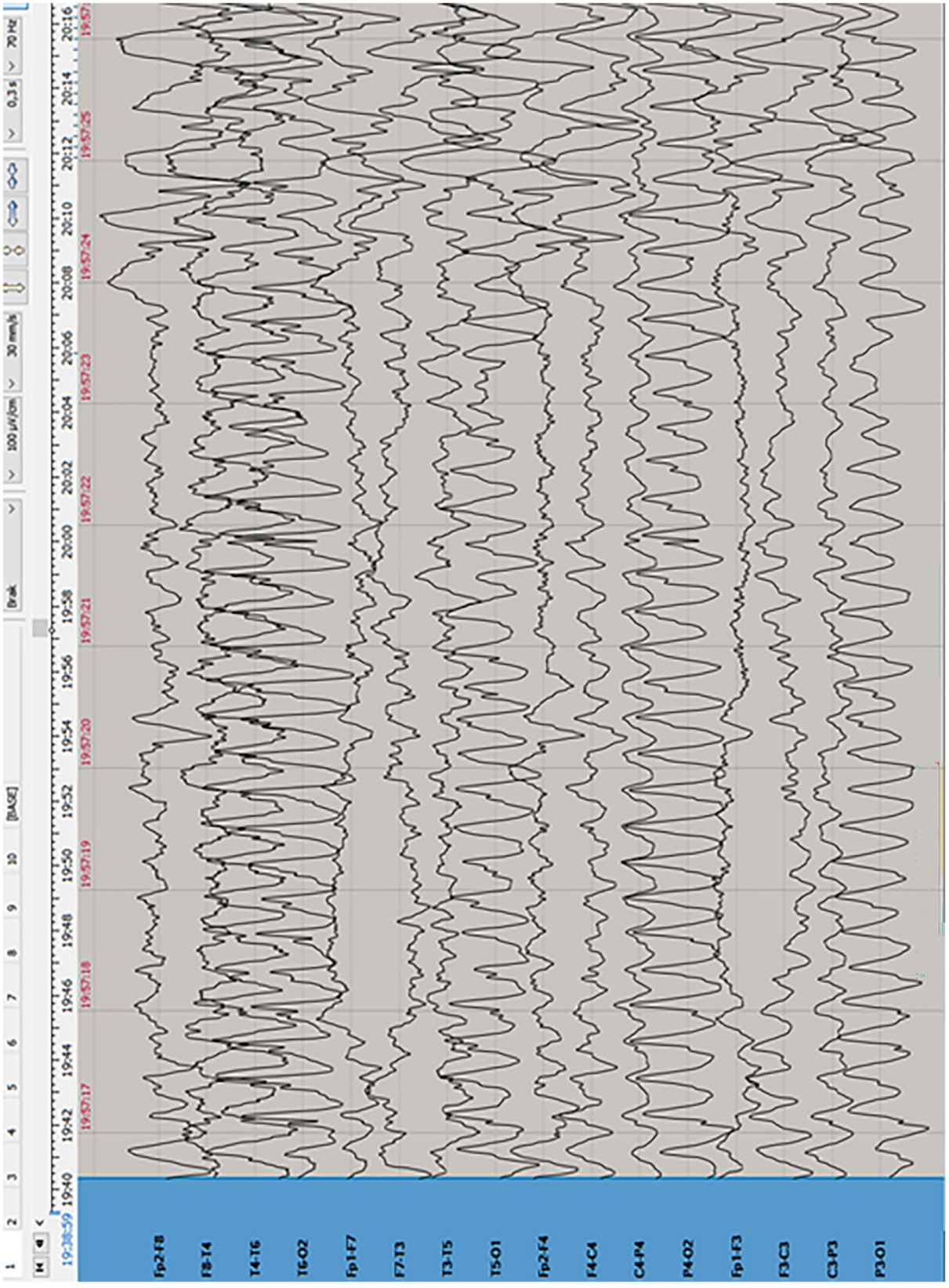


FIGURE 18 Del 15q13.3. Continuous discharges of slow waves 4–5 Hz and abortive spike-wave complexes 4–5 Hz in occipital regions with predominance on the right side with secondary generalization.

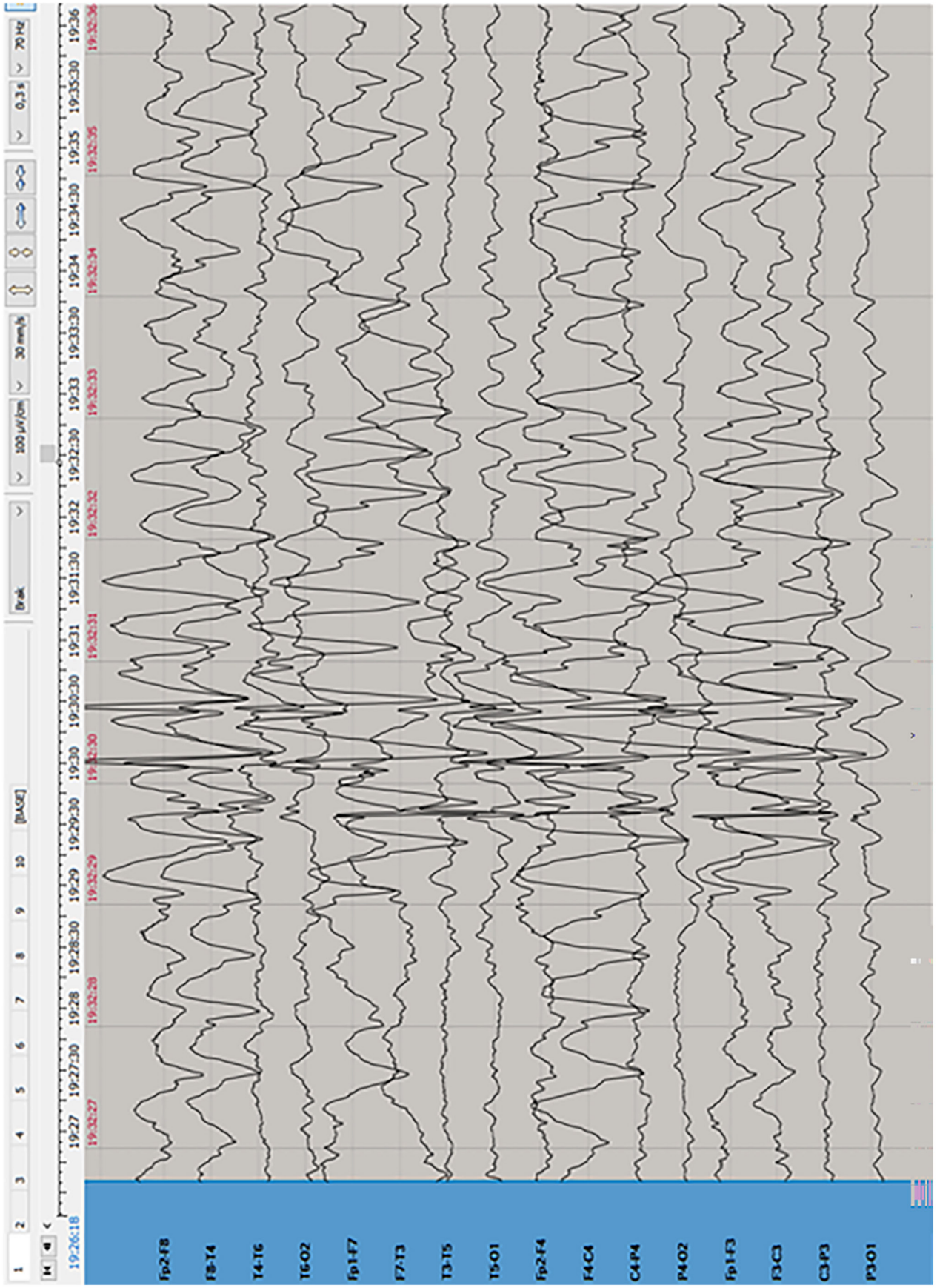
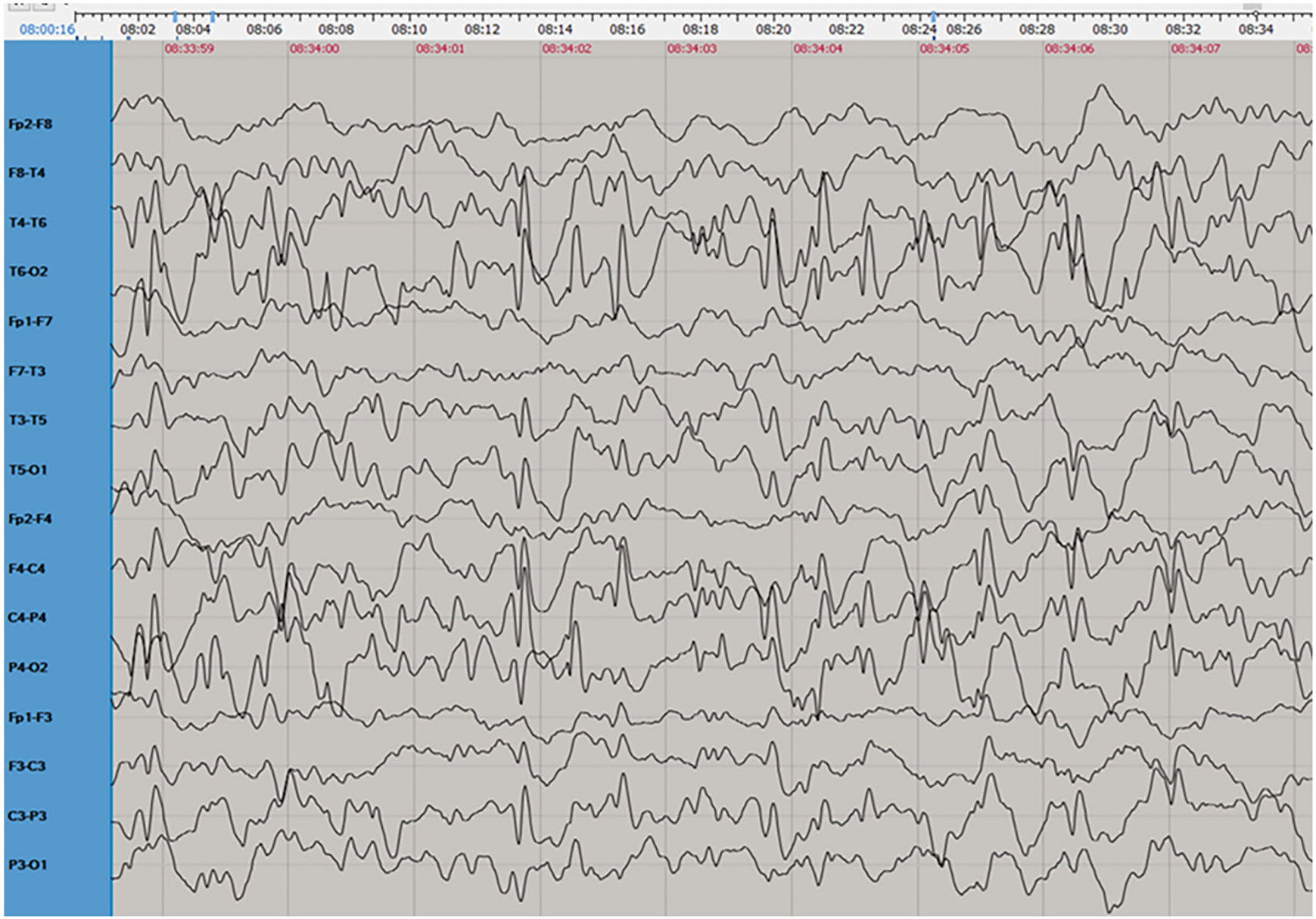
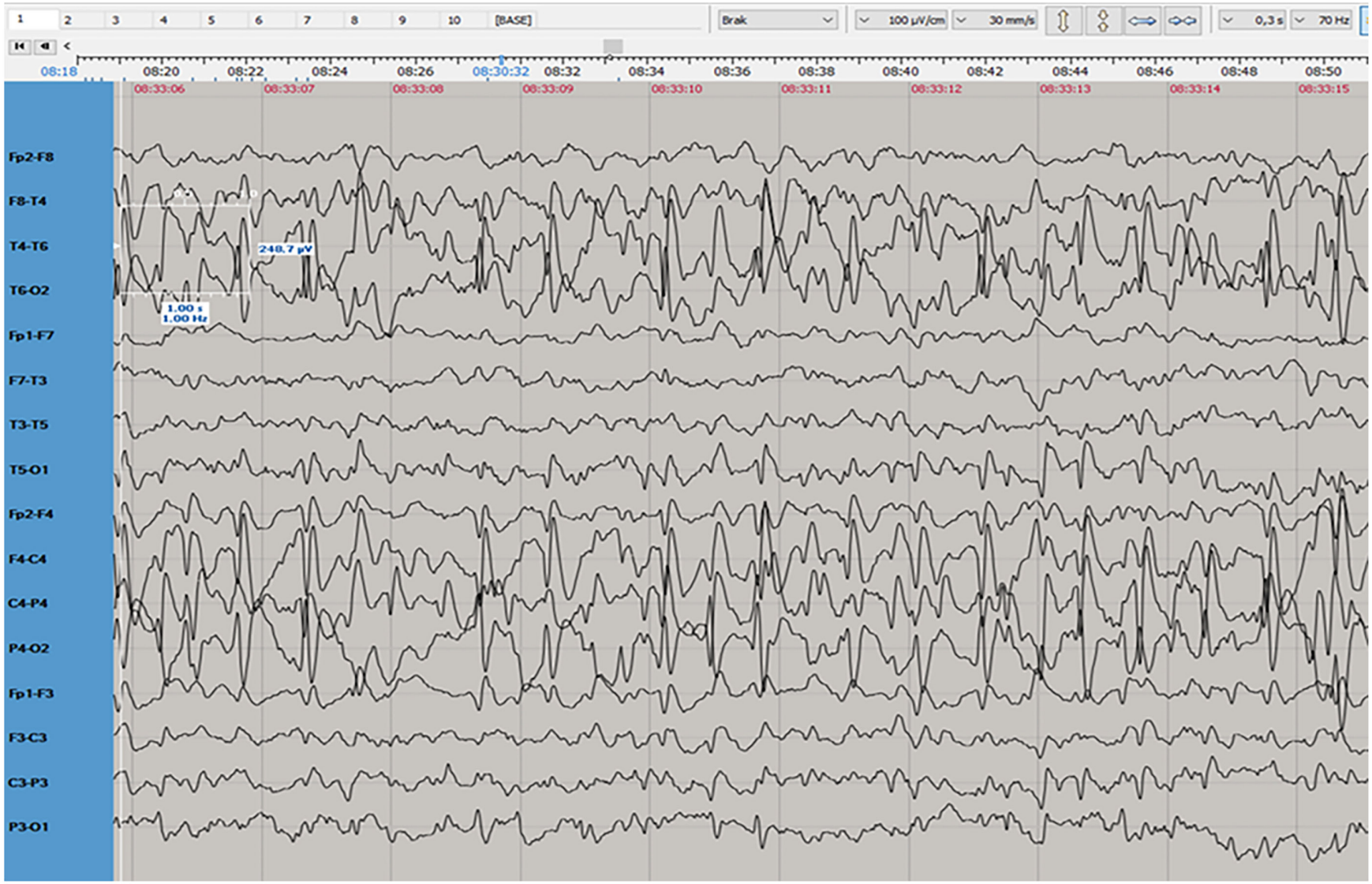


FIGURE 19 Del 15q13.3. Multiple 2–25 s series composed of sharp slow wave complexes 1.5–2.5 Hz and slow waves of similar frequency with amplitudes 100–650 μV, generalized with max. in frontal and central areas or only in these areas bilaterally or with predominance once on the right and once on the left side.



FIGURES 20 AND 21 14q duplication (14q11.2). A patient with a CNS defect (cortical dysplasia within the cingulate gyrus major on the right side). In the temporal and central-parietal-occipital regions of the right hemisphere, sharp wave discharges and combinations of sharp-slow waves, spikes with amplitudes up to 380–400 μV were registered in drowsiness multiple (groups and series) (Figure 21), and in sleep continuous (Figure 22).



FIGURES 20 AND 21 (Continued)

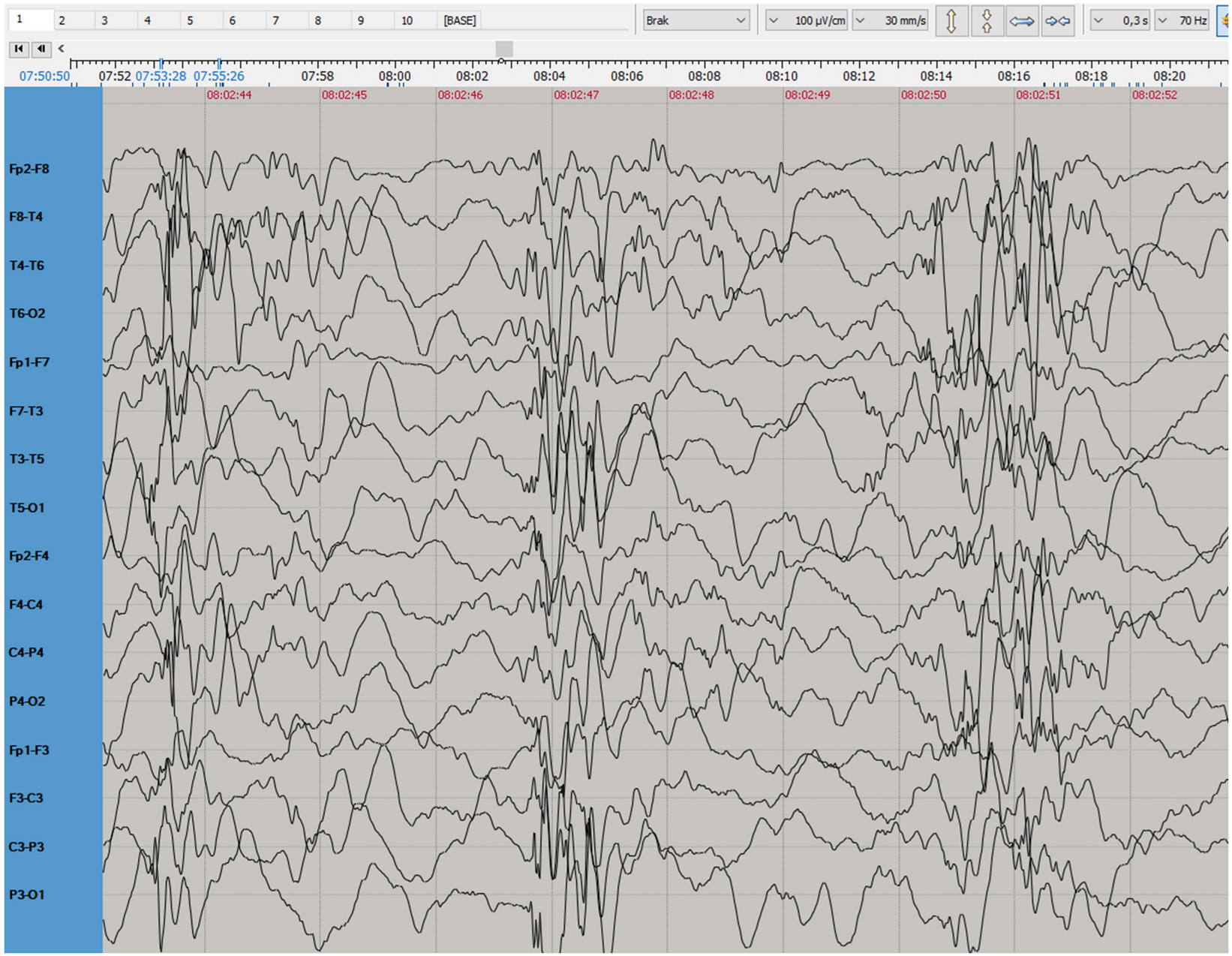


FIGURE 22 14q duplication (14q11.2q21.3). Hypsarrhythmia (burst-suppression) variant.

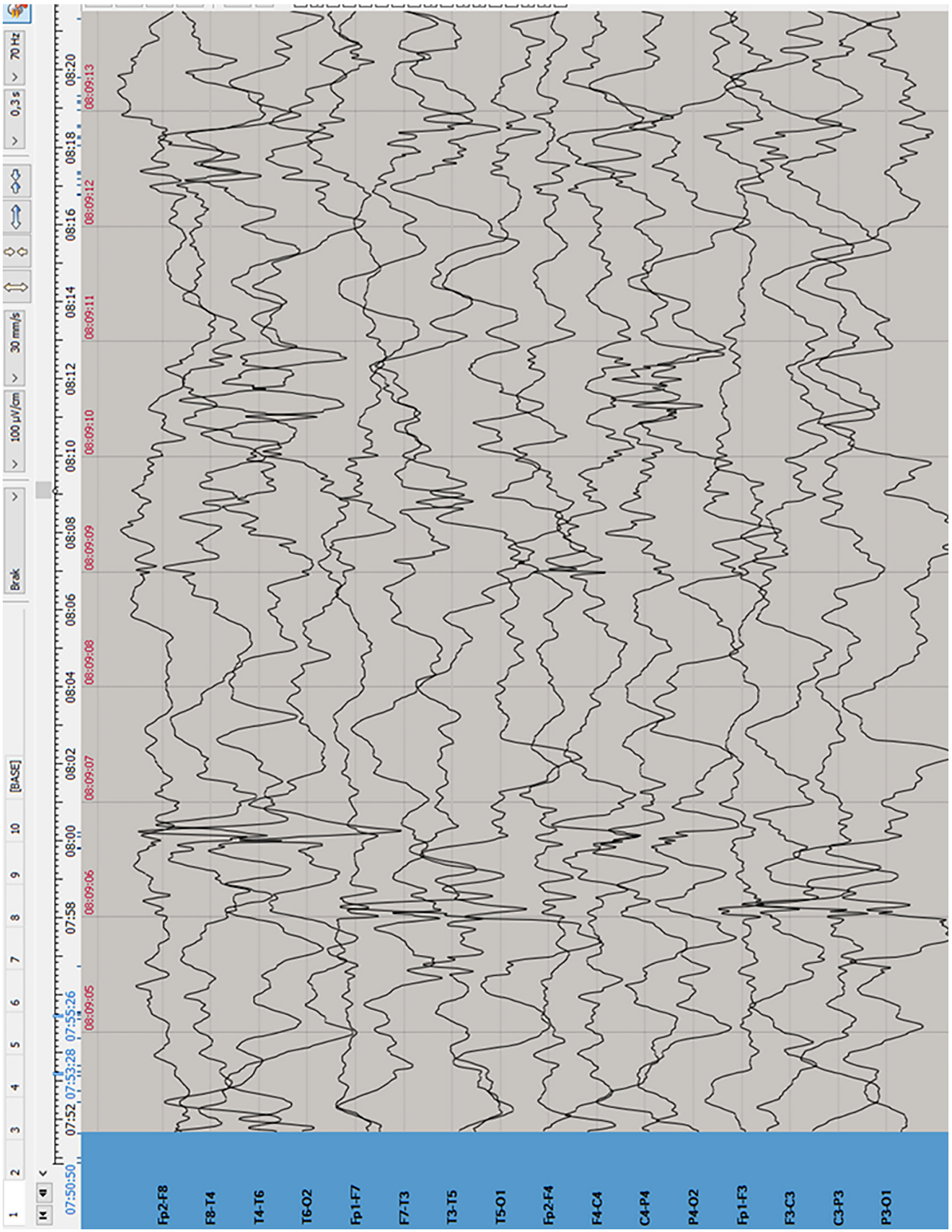


FIGURE 23 14q duplication (14q11.2q21.3). Multifocal asynchronous discharge of polyspikes and spike-wave complexes.

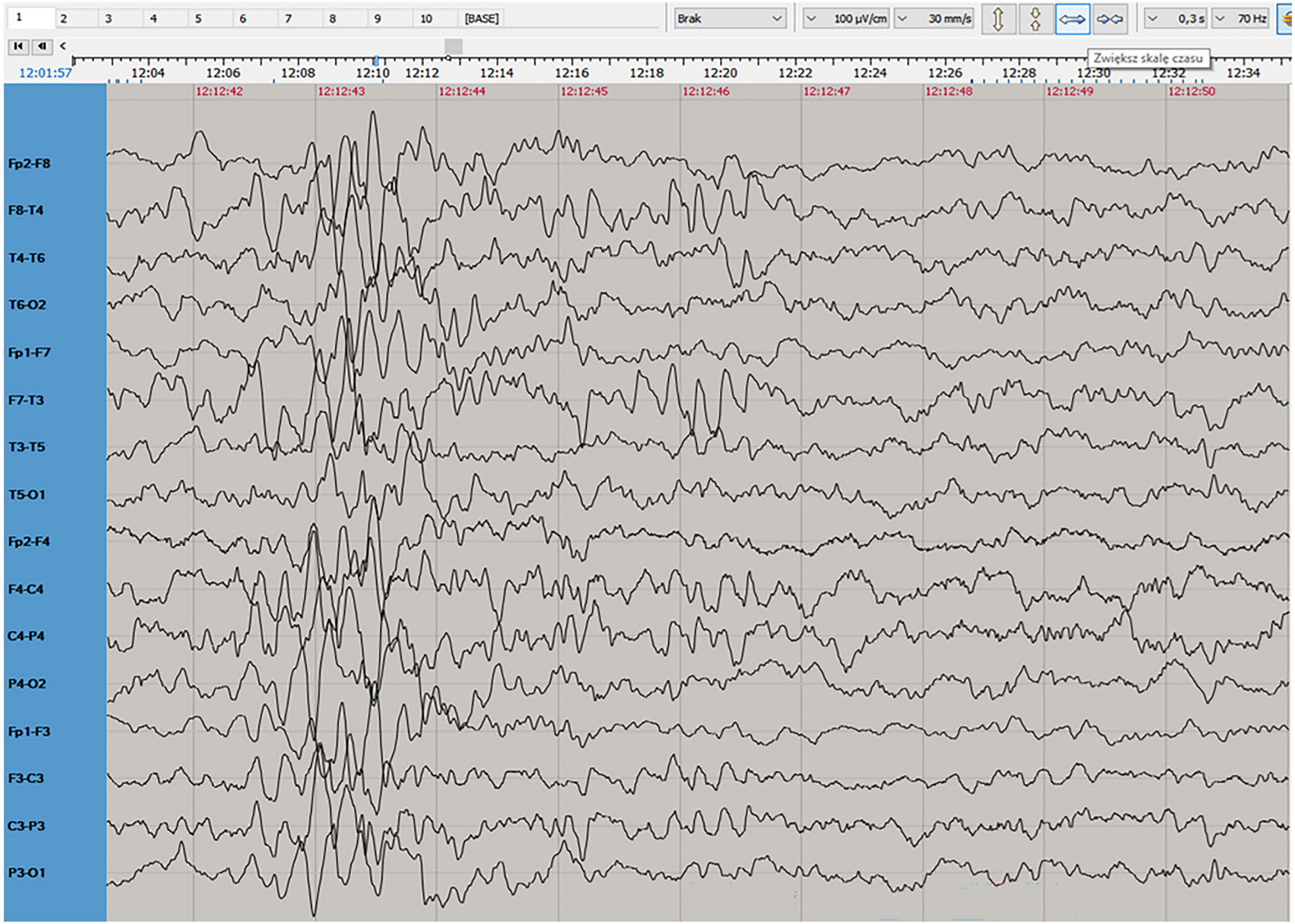


FIGURE 24 14q duplication (14q11.2). In drowsiness and sleep, multiple generalized 3–5-s series consisting of 3–4 Hz slow waves interspersed with sharp waves, spikes, and spike-wave complexes with amplitudes up to 600 μV.

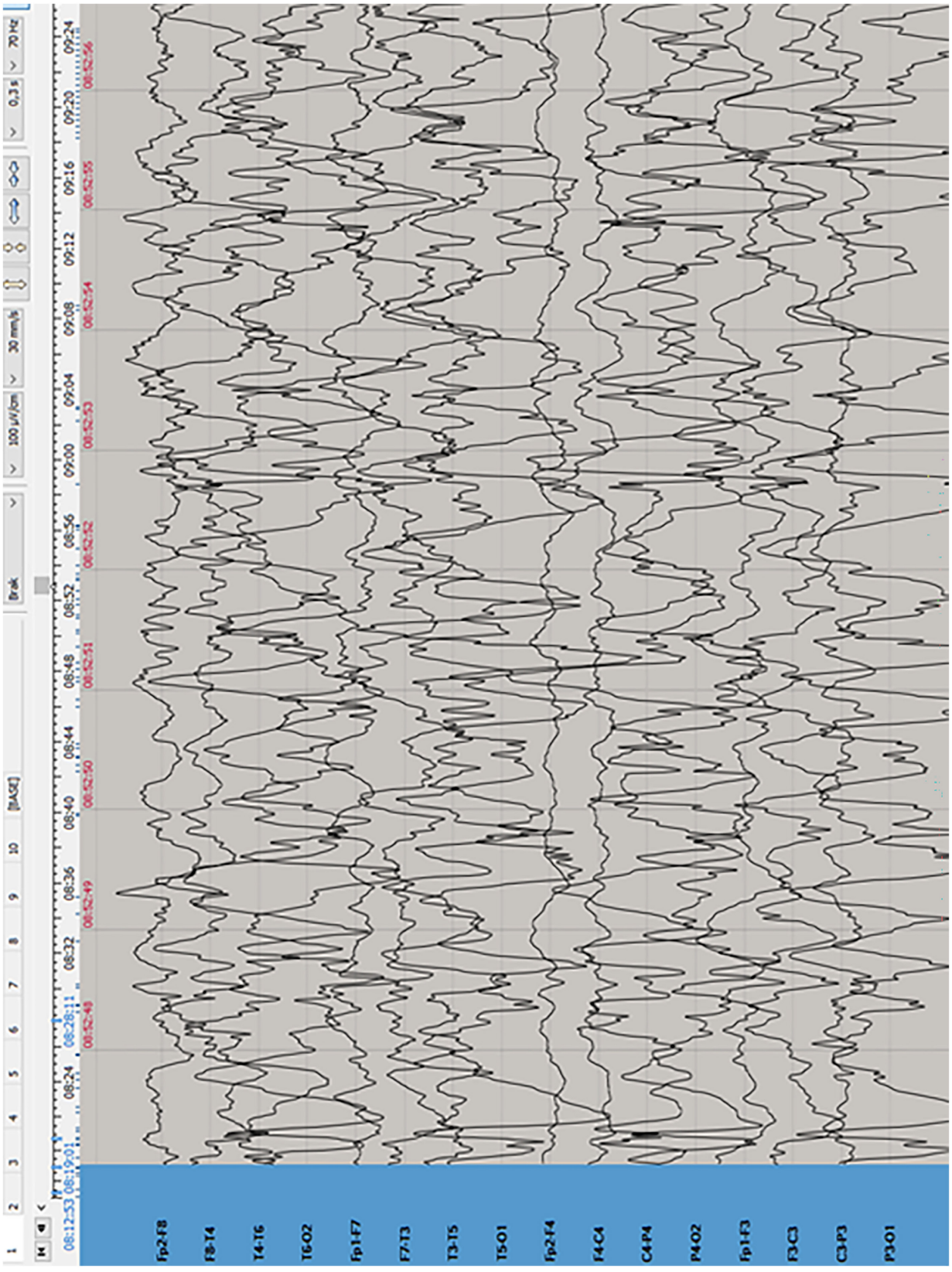


FIGURE 25 14q duplication (14q11.2). Hypsarrhythmia.

TABLE 3 Chromosomal microrearrangements.

Chromosomal micro	Face dysmorphism	Other dysmorphic features	Congenital abnormalities	Developmental delay	Important comorbidities
17q21.31 microdeletion[19–21]	High/broad forehead, long face, upward slanting palpebral fissures, epicanthic folds, and an abnormally formed nose (either "tubular" or "pear" shaped, high nasal bridge, a broad nasal root, long columella, and hypoplastic and/or thick alae nasi), bulbous nasal tip, large prominent ears, and everted lower lip, with time elongation of the face and broadening of the chin	No	Congenital heart defects, urogenital malformations, and ectodermal anomalies	Moderate psychomotor delay	No
15q13.3 microdeletion[4,20,21]	Subtle dysmorphic features	No	Cardiac malformations	Mild intellectual disability	Autism, psychiatric disorders: schizophrenia, language disorders
14q microdeletion[24] 14q duplication	Down slanting palpebral fissures, bilateral epicanthic folds, depressed nasal bridge, bulbous nasal tip, tented upper lip, everted lower lip, and large ears High frontal hairline, deep-set eyes, and hypotelorism	No No	No No	Normal development in infancy Various degrees of developmental delay	Without autonomic symptoms typical for Rett syndrome Delayed or absent speech
6q terminal deletion[25,26]	Microcephaly, low frontal hairline, abnormal hair pattern, asymmetric face, bilateral epicanthus, horizontal or upslanting or short palpebral fissures, broad nasal bridge, micrognathia, high palate, long philtrum, and characteristic mouth shape (described as "fish-like"), with downturned corners, a large gap between upper central incisors, posteriorly rotated or low-set ears	Short neck, skeletal malformations (camptodactyly, flat feet with valgus position of the calcaneus), genital (phimosis, hypospadias), and renal abnormalities	Nuchal cyst, diaphragmatic hernia, multicystic kidney, and cardiac septal defects	Mild–moderate intellectual disability	Retinal abnormalities, strabismus, growth failure, and diffuse joint laxity
1p36 terminal deletion[3,4,27,28]	Straight eyebrows, deep-set eyes, flat nasal bridge, midface hypoplasia, and pointed chin	No	Congenital heart defects, cardiomyopathy, and renal abnormalities	Developmental delay or intellectual disability ranging from profound or severe (the majority of the cases, about 90%) to moderate (about 10%)	Vision problems, hearing loss, behavioral disorders (temper tantrums, self-biting), manual apraxia, feeding difficulties, poor social interactions, and short stature

(Continues)

TABLE 3 (Continued)

Chromosomal micro	Face dysmorphism	Other dysmorphic features	Congenital abnormalities	Developmental delay	Important comorbidities
2q24.4microdeletion[29]	Microcephaly, craniosynostosis, micrognathia, bitemporal narrowing, or frontal bossing, down-slanting or short palpebral fissures, bulbous nose or broad nasal bridge, low-implanted ears, thick helix, bow-shaped mouth, and anterior open bite	Hands and feet dysmorphia (single palmar creases bilaterally, and partial syndactyly between the second and third toes)	Cardiac abnormalities (hypoplastic left heart, atrial septic defects, and arrhythmia), scoliosis	Mild to severe intellectual disability	Autistic behavior, ataxia, muscle hypotonia, and growth retardation
5q14.3 microdeletion[30]	Microcephaly, broad, high forehead, relatively large, backward rotated ear lobes, mildly upward-slanting palpebral fissures, and cupid bowed or tented upper lip	No	Ophthalmologic abnormalities, rarely dental anomaly	From normal intelligence to severe motor and intellectual disability	Occasionally autistic behavior, stereotypic hand movements, and episodic hyperventilation, no speech acquisition
Xp11.22–11.23 duplication[31]	No specific facial dysmorphism	Dysmorphic features of the feet (flat or arched feet, fifth-toe hypoplasia, and syndactyly)	No	Cognitive disturbance (from borderline functioning to severe intellectual disability)	Speech delay, hoarse or nasal voice, early puberty, and overweight
15q inv dup syndrome[2,32]	Down-slanting palpebral fissures, epicanthic folds, low-set eyes, and/or posteriorly rotated ears, highly arched palate, broad nose, anteverted nostrils; fifth finger clinodactyly and abnormal dermatoglyphics; partial 2nd and 3rd toe syndactyly, brachycephaly, frontal bossing, synophrys, short philtrum, cleft palate, a prominent mandible in adults, and brachydactyly	No	No	Moderate to profound developmental delay	Speech delay, autistic features, hypotonia, and joint hypermobility

TABLE 4 EEG and epilepsy findings in patients (described as 1, 2, 3, 4, 6, 8, 9, 10, and 11) with 17q21.31 microdeletion (according to Tan et al. 20).

Patient	1	2	3	4	6	8	9	10	11
Age at the time of report	4 years	5 years	21 months	10 years	24 months	11 years	25 months	7 years 8 months	18 months
Gender	F	F	F	F	M	F	M	M	M
Brain abnormalities	Partial corpus callosum agenesis		Mild ventricular enlargement, abnormal periventricular white matter		Partial corpus callosum agenesis, increased T2 signal central tegmental tract, high T2 signal periventricular white matter parieto-occipital regions	Prominent ventricles	Thinning of rostral portion of corpus callosum, and abnormally shaped hippocampus	Short corpus callosum and abnormal positioning of occipital lobes and cerebellum with the normal myelinisation	
EEG findings		Normal EEG		Widespread epileptogenic activity, mainly in centro-temporal regions.		Independent right central and left parietal spike discharges		Frequent sharp waves and spikes from occipital lead 1 and occasional sharp waves from Cz, T3, T5, C4, P4 during sleep	Normal EEG
Seizures		Transient epileptic seizures		Afebrile focal seizures	Generalized seizure at 26 months	Focal seizures	Generalized tonic–clonic seizures	Staring spells	Neonatal seizures

Abbreviation: SW, spike-and-wave.

TABLE 5 EEG tracings in a male patient with 17q21.31 microdeletion as a function of age.[39]

Age	11 years- epilepsy onset	14 years	15 years	16 years	18 years	19 years
EEG findings	Low voltage background activity in the alpha range, occasional isolated SW complexes over the left posterior temporal and occipital regions with bilateral diffusion to the posterior areas, exacerbated by sleep	Low voltage inconstant background activity in the alpha range, frequent isolated sharp wave-slow wave, or SW complexes over the left posterior temporal and occipital regions, with bilateral diffusion to the contiguous areas, exacerbated by drowsiness	No significant change in background activity, absent epileptiform abnormalities	No significant change in background activity, isolated sharp wave-slow wave or SW complexes over the left posterior temporal and occipital regions, with bilateral diffusion to the contiguous areas, exacerbated by drowsiness	No significant change in background activity, isolated sharp wave-slow wave or SW complexes over the left posterior temporal and occipital regions, with bilateral diffusion to the contiguous areas, exacerbated by drowsiness	No significant change in background activity. Absent epileptiform abnormalities

Abbreviation: SW: Spike-Wave.

3.4 | 6q terminal deletion

The first clinical description of patients with 6q terminal deletion was reported in 1975. Lesieur-Sebellin et al. presented 22 case series of fetuses diagnosed with a pure 6q deletion.[40] The ultrasound findings showed cerebellar hypoplasia, ventriculomegaly, and corpus callosum abnormalities as the most common (70%), while gyration abnormalities occurred in 46% of patients. Cerebral heterotopia, aqueductal stenosis, vertebral malformations, dysmorphic features, or kidney abnormalities were described as rare. The distinctive EEG patterns are presented below. Elia et al.[25] reported 5 patients with 6q terminal deletion (Table 6).

3.5 | 15q inv dup syndrome

The authors indicate that most children with small inv dup(15)s characterize with a normal phenotype, while large inv dup(15)s are usually associated with multiple abnormalities. Still, little is known about EEG patterns and brain MRI findings in *15*q inv dup syndrome. Verrotti et al. summarized the seizures' semiology in 144 patients with *15*q inv dup syndrome,[6] shown in Table 7.

3.6 | 2q24.4 deletion

The EEG picture is typical of the classical DS with severe drug resistance, mild to severe mental retardation (MR), autistic behavior, ataxia, and muscle hypotonia.[29]

3.7 | Xp11.22–11.23 duplication

Broli et al. summarized the clinical features of Xp11.22–11.23 duplication patients[31] (Table 8).

3.8 | 15q13.3 microdeletion

15q13.3 microdeletions have been associated with various neurodevelopmental disorders, such as autism, intellectual disability, language disorders, psychiatric disorders, or schizophrenia.[3,20] The prevalence of this mutation in the general population is estimated at 1 in 40 000, and in samples submitted for array comparative genomic hybridization (aCGH), it is as high as 1 in 450–600. Whitney et al. reported 13 patients with the following microdeletion.[20] Thirteen children (9 females) were included in the study. The median age was 12 years, and the ages of children ranged from 3 to 15 years. Absence

TABLE 6 Epilepsy in 6q terminal deletion (according to Elia et al. 25).

Patient	Epilepsy- age at onset	Seizure type	Seizure frequency at the onset	EEG findings
Male 19	11 months	Cyanosis, vomiting, and loss of consciousness	>1/month	SW complexes over the right parietotemporooccipital regions
Male 4	4 months	Vomiting, head and eye deviation, hypertonia, and loss of contact	>1/month	High-voltage theta and delta waves over the posterior regions
Male 12	18 months	Cyanosis, vomiting	Daily	SW complexes over the posterior regions
Female 9	4 years	Cyanosis, clonic jerks, vomiting, and loss of contact	Daily	SW complexes over the posterior regions
Female 26	3 years	Cyanosis, vomiting, and loss of contact	Monthly	SW complexes over the parietotemporooccipital regions

Abbreviation: SW, spike-and-wave.

TABLE 7 Epilepsy in 15q inv dup syndrome (according to Verrotti et al. 6).

Seizures type	Number of patients (out of 144)	%
Generalized tonic–clonic	38	40.43
Epileptic spasms	30	31.91
Atypical absences	23	24.47
Status epilepticus	18	19.15
Generalized tonic	4	4.26
Complex partial	2	2.13
Generalized clonic	2	2.13
Axial tonic	1	1.06
Partial with secondary generalization	1	1.06
Focal	28	29.79
Tonic	27	28.72
Atonic	26	27.66
Myoclonic	25	26.60
Unconfirmed	4	4.08
Drop attack	2	2.13

TABLE 8 The clinical features of Xp11.22–11.23 duplication (Broli et al. 31).

Seizures type	Number of patients (out of 144)	%
Generalized tonic–clonic	38	40.43
Epileptic spasms	30	31.91
Atypical absences	23	24.47
Status epilepticus	18	19.15
Generalized tonic	4	4.26
Complex partial	2	2.13
Generalized clonic	2	2.13
Axial tonic	1	1.06
Partial with secondary generalization	1	1.06
Focal	28	29.79
Tonic	27	28.72
Atonic	26	27.66
Myoclonic	25	26.60
Unconfirmed	4	4.08
Drop attack	2	2.13

seizures dominated, and 5 children presented with spike and slow wave, and 11 with generalized spike–wave on the EEG.

3.9 | 1p36 terminal deletion

1p36 terminal deletion occurs approximately in 1 out of 5000 to 10000 live births and is the most common subtelomeric microdeletion observed in human.[27] Epilepsy is an important feature in patients with the following deletion syndrome. Greco et al. presented a great review of seizure occurrence and EEG findings in patients with 1p36 terminal deletion.[27] Thirty-one cases of focal spikes in interictal EEG at the onset, particularly 7 rolandic, 18 temporal-posterior or temporooccipital, 1 right centrotemporal, 1 bilateral frontal, and 4 no specific focal spikes. On the other hand, there were 20 cases of multifocal or generalized spikes or polyspikes, spike, and wave discharges in 10 cases: sharp waves in 4, slow waves in 5, and theta waves in 1. Abnormal delta-theta wave activity mainly on the posterior temporal–parietal-occipital areas and asymmetry of slow activities were observed in most patients. In 31 epilepsy patients, the EEG was normal, whereas 29 showed a hypsarrhythmic EEG pattern. The most common neuroimaging findings were enlargement of the lateral ventricles in 76 (40.6%) patients (in 41 patients associated with cortical atrophy) and global cerebral

atrophy in 62 patients (33%). White matter abnormalities were observed in 21 patients (11%), and polymicrogyria in 4 patients (2%). Other abnormalities, such as thin corpus callosum, cortical hypoplasia, Chiari malformation, or subependymal were also observed.

3.10 | 5q14.3 microdeletion

Brain malformations, intellectual disability, and epilepsy are associated with 5q14.3 microdeletion syndrome. Cardoso et al. reported 3 patients with 5q14.3.[41] In patient 1 (7-year-old boy), the seizures occurred at the age of 1 year and were described as febrile seizures. At 6 years, generalized tonic–clonic seizures appeared. The EEG showed normal background activity with no epileptiform discharges. Patient 2 (a 5-year-old girl) presented with refractory epileptic spasms at 9 months. The EEG revealed poorly organized background activity and multifocal epileptiform discharges. Patient 3 (a 5-year-old boy) presented with episodes of unresponsiveness lasting 10–20 s, occurring many times a day. Later, at the age of 18 months, the mentioned episodes ceased, but isolated myoclonic jerks appeared. EEG recordings showed bursts of multifocal and bilaterally synchronous epileptiform activity.

3.11 | Xq28 duplication

Duplication of the Xq28 region, involving *MECP2* (dupMECP2), has been primarily described in males with severe developmental delay, spasticity, epilepsy, stereotyped movements, and recurrent infections. Loss-of-function mutations of the *MECP2* gene lead to Rett syndrome (RTT).

The limitation of the study is the narrative form of a review.

4 | CONCLUSIONS

A unique interictal EEG pattern does not exist in many micro chromosomal abnormalities. The authors would like to stress the importance of describing novel patients to better characterize epilepsy patterns and EEG abnormalities. The treatment strategy may be based on clinical findings. Too few patients and an incomplete description of the seizure semiology in many reports make it often difficult to identify precise genotype–phenotype correlations. Further research must be conducted to better understand epileptic syndromes and chromosomal rearrangements.

AUTHOR CONTRIBUTIONS

J.P. and P.S.: study concept and design; J.P. and E.S.:drafting of the manuscript, literature search, and administrative and technical support; J.P., A.C., and P.S.: critical revision of the manuscript; J.P., A.C., C.C., E.S., and P.S.: editing, visualization. All authors have read and agreed to the published version of the manuscript.

CONFLICT OF INTEREST STATEMENT

Neither of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Justyna Paprocka https://orcid.org/0000-0003-1794-8546
Claudia Cuccurullo https://orcid.org/0000-0002-4845-4293
Elżbieta Stawicka https://orcid.org/0000-0003-1329-846X
Pasquale Striano https://orcid.org/0000-0002-6065-1476

REFERENCES

1. Singh R, McKinlay Gardner RJ, Crossland KM, Scheffer IE, Berkovic SF. Chromosomal abnormalities and epilepsy: a review for clinicians and gene hunters. Epilepsia. 2002;43(2):127–40.
2. Elia M, Rutigliano I, Sacco M, Madeo SF, Wasniewska M, Li Pomi A, et al. EEG patterns in patients with Prader–Willi syndrome. Brain Sci. 2021;11(8):1045.
3. Budisteanu M, Jurca C, Papuc SM, Focsa I, Riga D, Riga S, et al. Treatment of epilepsy associated with common chromosomal developmental diseases. Open Life Sci. 2020;15(1):21–9.
4. Sorge G, Sorge A. Epilepsy and chromosomal abnormalities. Ital J Pediatr. 2010;3(36):36.
5. Samanta D. Epilepsy in Angelman syndrome: a scoping review. Brain Dev. 2021;43(1):32–44.
6. Verrotti A, Sertorio F, Matricardi S, Ferrara P, Striano P. Electroclinical features of epilepsy in patients with InvDup(15). Seizure. 2017;47:87–91.
7. Vignoli A, Bisulli F, Darra F, Mastrangelo M, Barba C, Giordano L, et al. Epilepsy in ring chromosome 20 syndrome. Epilepsy Res. 2016;128:83–93.
8. Kishore VK, Viswanathan LG, Asranna A, Kenchiah R, Chowdary MR, Sinha S. Intravenous methylprednisolone is a potential add on therapy for ring chromosome 20 syndrome. Seizure. 2022;96:118–20.
9. Peron A, Catusi I, Recalcati MP, Calzari L, Larizza L, Vignoli A, et al. Ring chromosome 20 syndrome: genetics, clinical characteristics, and overlapping phenotypes. Front Neurol. 2020;11:613035.
10. Specchio N, Trivisano M, Serino D, Cappelletti S, Carotenuto A, Claps D, et al. Epilepsy in ring 14 chromosome syndrome. Epilepsy Behav. 2012;25(4):585–92.

11. Verrotti A, Carelli A, di Genova L, Striano P. Epilepsy and chromosome 18 abnormalities: a review. Seizure. 2015;32:78–83.
12. Arya R, Kabra M, Gulati S. Epilepsy in children with down syndrome. Epileptic Disord. 2011;13(1):1–7.
13. Kats DJ, Roche KJ, Skotko BG. Epileptic spasms in individuals with down syndrome: a review of the current literature. Epilepsia Open. 2020;5(3):344–53.
14. Sanmaneechai O, Sogawa Y, Silver W, Ballaban-Gil K, Moshé SL, Shinnar S. Treatment outcomes of west syndrome in infants with down syndrome. Pediatr Neurol. 2013;48(1):42–7.
15. Nishimoto S, Shimakawa S, Fukui M, Ogino M, Tsuda-Kitahara H, Toshikawa H, et al. Treatment outcomes for infantile spasms in Japanese children with down syndrome. Pediatr Int. 2021;63(12):1495–503.
16. Berry-Kravis E, Filipink RA, Frye RE, Golla S, Morris SM, Andrews H, et al. Seizures in fragile X syndrome: associations and longitudinal analysis of a large clinic-based cohort. Front Pediatr. 2021;9:736255.
17. Goodspeed K, Armstrong D, Dolce A, Evans P, Said R, Tsai P, et al. Electroencephalographic (EEG) biomarkers in genetic neurodevelopmental disorders. J Child Neurol. 2023;38(6–7):466–77. https://doi.org/10.1177/08830738231177386
18. Conant KD, Finucane B, Cleary N, Martin A, Muss C, Delany M, et al. A survey of seizuresand current treatments in 15q duplication syndrome. Epilepsia. 2014;55(3):396–402.
19. Koolen DA, Sharp AJ, Hurst JA, Firth HV, Knight SJL, Goldenberg A, et al. Clinical and molecular delineation of the 17q21.31 microdeletion syndrome. J Med Genet. 2008;45(11):710–20.
20. Tan TY, Aftimos S, Worgan L, Susman R, Wilson M, Ghedia S, et al. Phenotypic expansion and further characterisation of the 17q21.31 microdeletion syndrome. J Med Genet. 2009;46(7):480–9.
21. Wray CD. 17q21.31 microdeletion associated with infantile spasms. Eur J Med Genet. 2013;56(1):59–61.
22. Whitney R, Nair A, McCready E, Keller AE, Adil IS, Aziz AS, et al. The spectrum of epilepsy in children with 15q13.3 microdeletion syndrome. Seizure. 2021;92:221–9.
23. Budisteanu M, Papuc SM, Streata I, Cucu M, Pirvu A, Serban-Sosoi S, et al. The phenotypic Spectrum of 15q13.3 region duplications: report of 5 patients. Genes. 2021;12:1025.
24. Vaisfeld A, Spartano S, Gobbi G, Vezzani A, Neri G. Chromosome 14 deletions, rings, and epilepsy genes: a riddle wrapped in a mystery inside an enigma. Epilepsia. 2021;62(1):25–40.
25. Elia M, Striano P, Fichera M, Gaggero R, Castiglia L, Galesi O, et al. 6q terminal deletion syndrome associated with a distinctive EEG and clinical pattern: a report of five cases. Epilepsia. 2006;47(5):830–8.
26. Striano P, Malacarne M, Cavani S, Pierluigi M, Rinaldi R, Cavaliere ML, et al. Clinical phenotype and molecular characterisation of 6q terminal deletion syndrome: five new cases. Am J Med Genet. 2006;140A(18):1944–9.
27. Greco M, Ferrara P, Farello G, Striano P, Verrotti A. Electroclinical features of epilepsy associated with 1p36 deletion syndrome: a review. Epilepsy Res. 2018;139:92–101.
28. Verrotti A, Greco M, Varriale G, Tamborino A, Savasta S, Carotenuto M, et al. Electroclinical features of epilepsy monosomy 1p36 syndrome and their implications. Acta Neurol Scand. 2018;138(6):523–30.
29. Davidsson J, Collin A, Olsson ME, Lundgren J, Soller M. Deletion of the SCN gene cluster on 2q24.4 is associated with severe epilepsy: an array-based genotype–phenotype correlation and a comprehensive review of previously published cases. Epilepsy Res. 2008;81(1):69–79.
30. Sobreira N, Walsh MF, Batista D, Wang T. Interstitial deletion 5q14.3-q21 associated with iris coloboma, hearing loss, dental anomaly, moderate intellectual disability, and attention deficit and hyperactivity disorder. Am J Med Genet. 2009;149A(11):2581–3.
31. Broli M, Bisulli F, Mastrangelo M, Fontana E, Fiocchi I, Zucca C, et al. Definition of the neurological phenotype associated with dup (X) (p11.22-p11.23). Epileptic Disord. 2011;13(3):240–51.
32. Dangles MT, Malan V, Dumas G, Romana S, Raoul O, Coste-Zeitoun D. Electro-clinical features in epileptic children with chromosome 15q duplication syndrome. Clin Neurophysiol. 2021;132(5):1126–37.
33. Muir AM, Myers CT, Nguyen NT, Saykally J, Craiu D, De Jonghe P, et al. Genetic heterogeneity in infantile spasms. Epilepsy Res. 2019;156:106181.
34. Steel D, Symonds JD, Zuberi SM, Brunklaus A. Dravet syndrome and its mimics: beyond *SCN1A*. Epilepsia. 2017;58(11):1807–16.
35. Harden C, Tomson T, Gloss D, Buchhalter J, Cross JH, Donner E, et al. Practice guideline summary: sudden unexpected death in epilepsy incidence rates and risk factors: report of the guideline development, dissemination, and implementation Subcommittee of the American Academy of neurology and the American Epilepsy Society. Epilepsy Curr. 2017;17(3):180–7.
36. Cooper MS, Mcintosh A, Crompton DE, McMahon JM, Schneider A, Farrell K, et al. Mortality in Dravet syndrome. Epilepsy Res. 2016;128:43–7.
37. Sperling MR. Sudden unexplained death in epilepsy. Epilepsy Curr. 2001;1(1):21–3.
38. Saby JN, Peters SU, Roberts TPL, Nelson CA, Marsh ED. Evoked potentials and EEG analysis in Rett syndrome and related developmental encephalopathies: towards a biomarker for translational research. Front Integr Neurosci. 2020;28(14):30. https://doi.org/10.3389/fnint.2020.00030
39. Bernardo P, Madia F, Santulli L, Del Gaudio L, Caccavale C, Zara F, et al. 17q21.31 microdeletion syndrome: description of a case further contributing to the delineation of Koolen-de Vries syndrome. Brain and Development. 2016;38(7):663–8. https://doi.org/10.1016/j.braindev.2016.02.002
40. Lesieur-Sebellin M, Till M, Khau Van Kien P, Herve B, Bourgon N, Dupont C, et al. Terminal 6q deletions cause brain malformations, a phenotype mimicking heterozygous DLL1 pathogenic variants: a multicenter retrospective case series. Prenat Diagn. 2022;42(1):118–35.
41. Cardoso C, Boys A, Parrini E, Mignon-Ravix C, McMahon JM, Khantane S, et al. Periventricular heterotopia, mental retardation, and epilepsy associated with 5q14.3-q15 deletion. Neurology. 2009;72(9):784–92.

How to cite this article: Paprocka J, Coppola A, Cuccurullo C, Stawicka E, Striano P. Epilepsy, EEG and chromosomal rearrangements. Epilepsia Open. 2024;00:1–41. https://doi.org/10.1002/epi4.12951