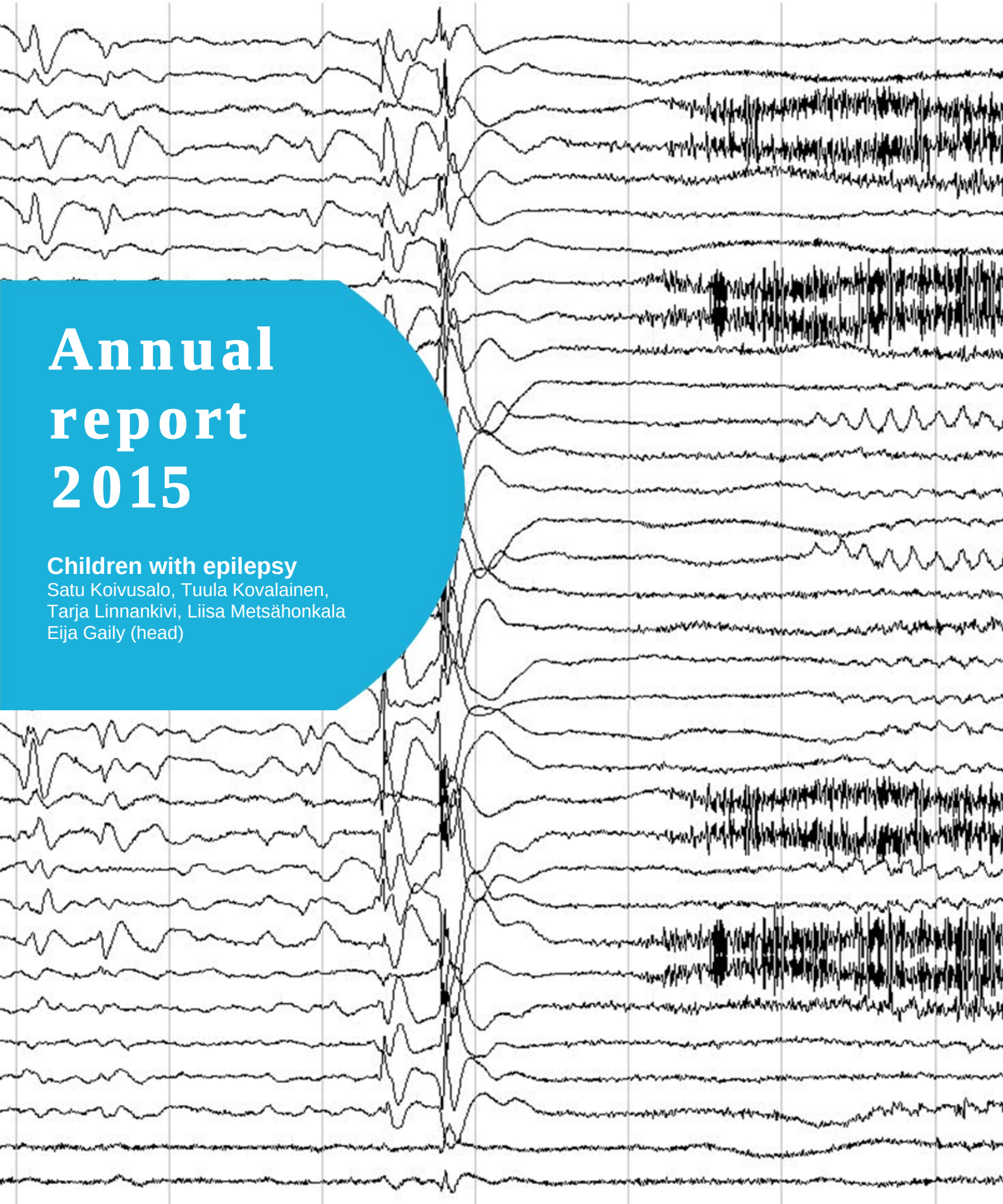
HUS



Annual report 2015

Children with epilepsy

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Eija Gaily (head)

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Abbreviations used
Children's epilepsy unit = Children's Epilepsy Ward L11 and video EEG and outpatient clinic
EEG = Electroencephalography
MEG = magnetoencephalography, a technique for mapping brain activity by recording magnetic fields produced by the brain
PET = positron emission tomography, a technique measuring glucose metabolism in the brain
SPECT = single-photon emission computed tomography, a technique measuring blood flow in the brain tissue
Stereo-EEG = video EEG performed with stereotactically placed depth electrodes, used in planning epilepsy surgery
Video-EEG = an examination lasting several hours or days, in which an EEG and video of the patient's symptoms are simultaneously recorded
VNS = vagus nerve stimulator, a treatment method based on the stimulation of the vagus nerve
HUS = Helsinki and Uusimaa Hospital District

Background information on epilepsy

Epilepsy is a tendency toward recurrent, unprovoked seizures. The illness may be associated with other brain disorders, including learning disorders. Approximately 30,000 people in Finland have epilepsy. The prevalence under the age of 15 years is approximately 0.7/1000. The causes and manifestations of epilepsy are highly varied. Some children and adolescents have benign forms of epilepsy, which are either self-limiting or respond well to medication. One fourth have drug-resistant forms of epilepsy. The majority of difficult-to-treat epilepsies are characterized by onset in childhood or adolescence.

Therapy is based on accurate epilepsy syndrome diagnosis and the determination of the underlying causes. These include many rare diseases. Inappropriate or excessive medication is not effective against seizures and may further impair functionality. Drug-resistant epilepsy is associated with increased risk of cognitive disorders, psychiatric comorbidity, accidents and death.

Children's epilepsy unit

The children's epilepsy unit includes the epilepsy ward L11, video-EEG and outpatient clinic. It is Finland's largest unit specializing in the diagnostics, treatment and differential diagnostics of pediatric and adolescent epilepsy. Epilepsy surgery in Finland is centralized in two hospitals, Helsinki University Hospital (HUH) and Kuopio University Hospital, by virtue of Government Degree 336/2011 Section 5 (6 April 2011). HUH has the most extensive experience of epilepsy surgery in children and adolescents, particularly of extratemporal operations and examinations carried out with intracranial

depth electrodes. In 2015, 20% of our patients came from outside the HUS catchment area and 14% from outside HUS area of special responsibility (Figure 1).

The task of the children's epilepsy unit is to perform diagnostics and treatment for children and adolescents with epilepsy within the HUS catchment area, in collaboration with the general pediatric neurology outpatient clinics (the Children's Castle Hospital, Jorvi Hospital, Peijas Hospital, Hyvinkää Hospital). In addition, it provides nation-wide consultations on severe epilepsies in children and adolescents, pre-operative assessments and epilepsy surgery. The unit engages in international clinical and research cooperation regarding surgical and non-surgical treatments of severe and rare epileptic syndromes.

The epilepsy ward L11 and the video EEG unit manage the care of all children and adolescents from all over the country who are undergoing a pre-operative assessment due to severe epilepsy (Figure 1). Post-operative care takes place at L11 from the first post-operative day. In addition, ward L11 manages patients with epilepsy who require inpatient care for a severe seizures or demanding examinations and treatments (onset of diets, immunological treatments). All children and adolescents with drug-resistant epilepsies within the HUS's specialized area of responsibility, and their treatment consultations, have been centralized in the children's epilepsy unit. The video-EEG unit carries out all video-EEG examinations required for children and adults under HUH care; at least one third of these examinations are pre-operative assessments of severe epilepsy.

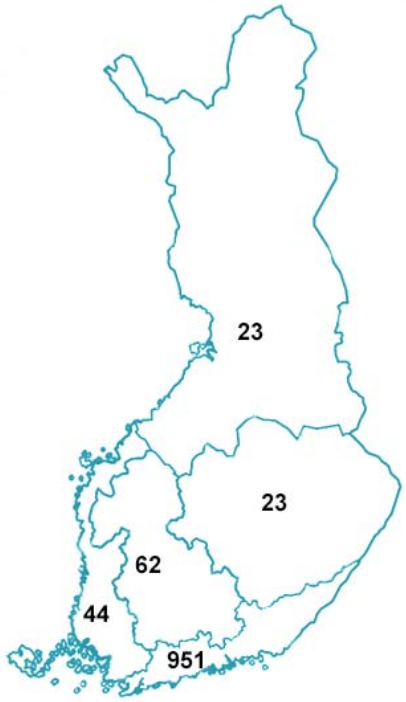
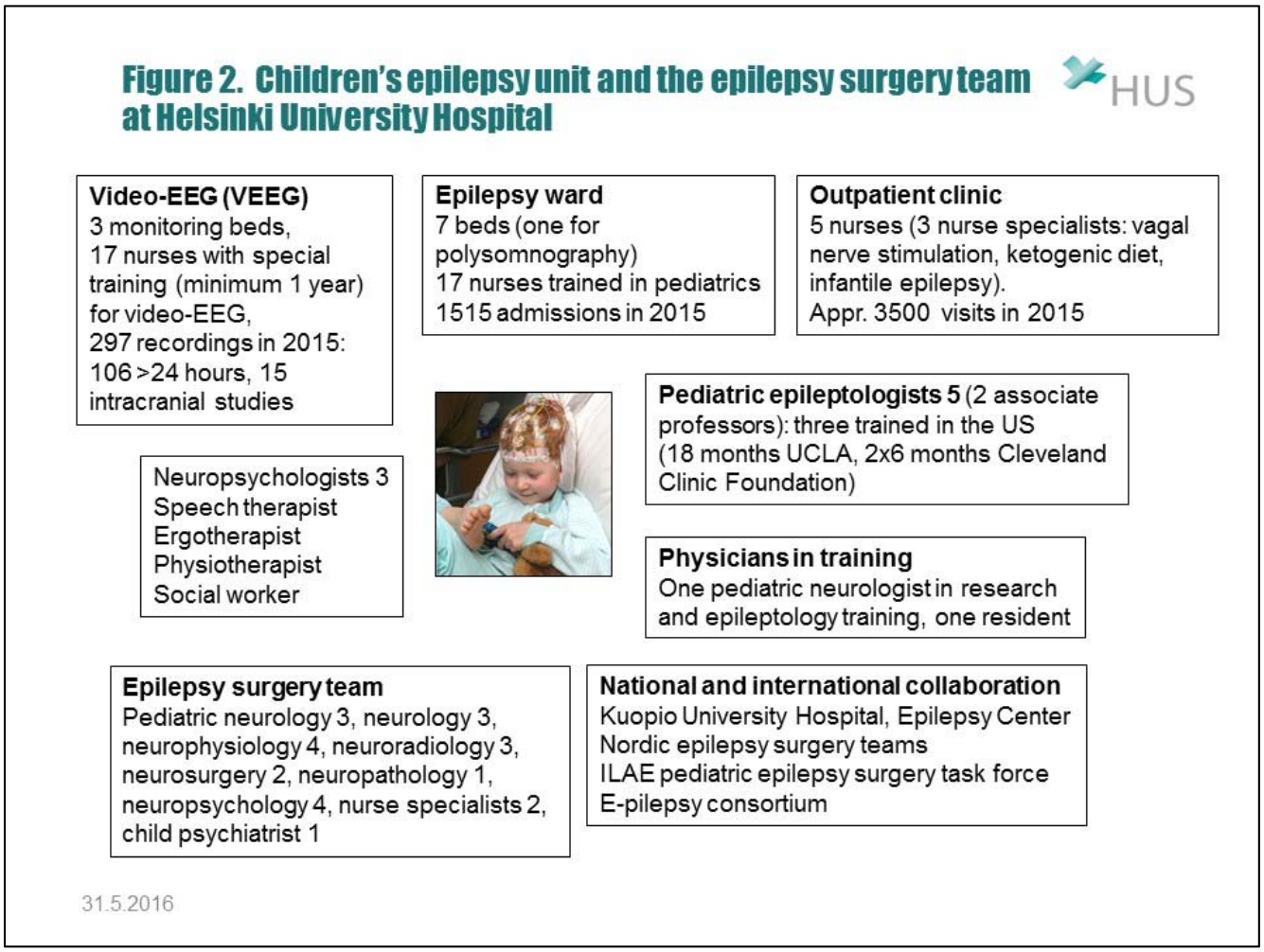


Figure 1. Breakdown of patients at the epilepsy ward L11 by university hospital district in 2015. In addition, four patients were referred from Estonia.

The treatment of severe epilepsy is multi-professional teamwork. The treatment of children and adolescents with epilepsy involves pediatric neurologists, neuropsychologists, neuroradiologists, neurosurgeons and nurses specialized in epilepsy (Figure 2). It also requires close collaboration with child psychiatrists, pediatricians and nutritionists. Adult patients are managed through video-EEG monitoring in collaboration with HUH neurologists. All pre-operative assessments and recommendations are made by our common epilepsy team. A psychiatrist is consulted when necessary.



Antiepileptic medication

The clinical guidelines for children and adolescents with epilepsy were defined in the 2013 Current Care Guidelines (http://www.kaypahoito.fi/web/kh/suositukset/suositus?id=hoi50059), which were co-authored by two physicians from our unit. In addition, one of our physicians is currently co-authoring the update on Current Care Guidelines for prolonged epileptic seizure (http://www.kaypahoito.fi/web/kh/suositukset/suositus?id). The epilepsy unit has extensive expertise on orphan drugs, special permit drugs and immunological treatments used in severe epilepsies. Our unit has produced a care program for most rare forms of epilepsy.

Ketogenic diet

The efficacy of the ketogenic diet in the treatment of epilepsy was discovered as early as the 1920s, although it has been taken into moreextensive use some 20 years ago. The ketogenic diet is based on obtaining energy mainly from fat, and strict restriction of carbohydrates. According to the scientific literature, 40–50% of children benefit from the diet; a benefit is considered significant if the number of seizures is reduced by 50%. Serious complications are rare.

The use of ketogenic diets in the epilepsy unit increased in 2008, when physicians, nurses and nutritionists were provided with training in the dietary treatment of epilepsy and attended Nordic meetings focusing on the diet. Our own dietary guidelines were produced in 2010 and are currently being updated.

In 2014, 9 patients were on the ketogenic diet, which had been started between 2008–2013; one patient discontinued the diet during 2014 owing to lack of significant benefits. The other 8 patients were continuing with the diet on 31 December 2015. Table 1 presents dietary treatments started in 2014–2015.

Year	Started (median starting age; range of variation	Over 50% reduction in seizures	Diet discontinued before 31 Dec 2015 (duration)	Reason for discontinuation
2014	8 (4.5 yrs; 1–17 yrs)	4 (50%)	4 (3-9 months)	poor efficacy
2015	12 (6.2 yrs; 6 months–14 yrs)	Data available in 2016	5 (0-4 months)	poor efficacy

Table 1 Patients on ketogenic diet

Epilepsy surgery

Approximately one fifth of patients with epilepsy are diagnosed with severe epilepsy, defined by drug resistant seizures significantly interrupting daily life. According to conservative estimates, approximately 3% of new epilepsy cases would be optimally eligible for surgical treatment; for children, the percentage is probably slightly higher. This means that at least 90 new patients would be eligible for epilepsy surgery each year in Finland; of them, around one half undergo surgery at the present time. Recent research suggests that early surgical treatment improves the patient's long-term prognosis for seizures. In the future, we are likely to see an increase in the number of operations among patients under the age of 16, although most patients will continue to undergo surgery in adulthood. The success of epilepsy surgery largely depends on the region of the brain causing the seizures. The best outcomes in terms of a seizure-freedom are achieved in temporal lobe epilepsy; however, extratemporal epilepsy is a more common form of severe epilepsy.

The HUH epilepsy surgery team was launched in 1991 in collaboration between pediatric neurologists, neurosurgeons and neuroradiologists. The first specialists in the team were trained to conduct children's pre-operative assessments and epilepsy surgery in the United States (UCLA, Cleveland Clinic) and in Sweden (Umeå) between 1990 and 1993. From 2000 onwards, the team expanded the scope of its work, based on closer collaboration with neurologists and clinical neurophysiologists. Training at medical centers abroad is ongoing both for pediatric neurologists (Figure 2) and other professional groups. One neurophysiologist received further training in Marseille (Hôpital de la Timone) in 2013 and one neuropsychologist in Canada (Montreal Neurological Institute, Université de Montreal) in 2014.

The basic pre-operative assessment includes the review of earlier examination results and the monitoring of seizures during video-EEG, as well as high-quality MRI. In some cases, a video EEG and MRI performed in the referring hospital suffice for pre-operative assessment. In most cases, such examinations are also helpful in cases where the patient is deemed ineligible for surgery, as they may lead to a more accurate diagnosis of the epilepsy syndrome and the underlying cause of the epilepsy, which in turn may allow more specific treatment. Many patients with potential eligibility for surgery undergo additional examinations such as functional imaging (PET, SPECT during seizure) and MEG.

Approximately one quarter of patients referred to the unit for a video EEG with the purpose of pre-operative assessment end up having surgery. Intracranial examinations are carried out in 20–30% of patients who are operated. A neuropsychological examination is performed prior to surgery. There are usually three post-operative follow-up appointments, 2, 6 and 24 months after surgery. In addition to a physician's consultation, follow-up visits include a neuropsychological examination and, if necessary, other functionality assessments.

Intracranial examinations using grid and strip electrodes have been performed at HUH since 1992 (Figure 3). The Nordic countries' first ever stereo-EEG was performed at HUH in January 2011. This method significantly improves the potential for localizing epileptic foci in patients suffering from severe epilepsy for surgical treatment purposes. During stereo-EEG, depth electrodes with a diameter of less than 1 mm are implanted stereotactically into the brain, enabling the recording of events in deep cortical areas. By the end of 2015, we had conducted 55 stereo-EEG recordings in collaboration with the Neurosurgery Department.

France and Italy currently have the leading expertise in stereo-EEG; in those countries, the method has been in use for decades. The neurophysiologists of our epilepsy surgery team participate annually in stereo-EEG training courses organized by three French epilepsy surgery centers (Marseille, Lyon and Grenoble) covering different brain areas. The training includes theory and practical training in the planning, execution and interpretation of stereo-EEG examinations. When treating patients, we have been able to consult with two French epilepsy surgery and stereo-EEG specialists (in 2013 with Professor Philippe Kahane, Grenoble, and in 2015 with Professor Patrick Chauvel, Marseille/Cleveland Clinic Foundation).

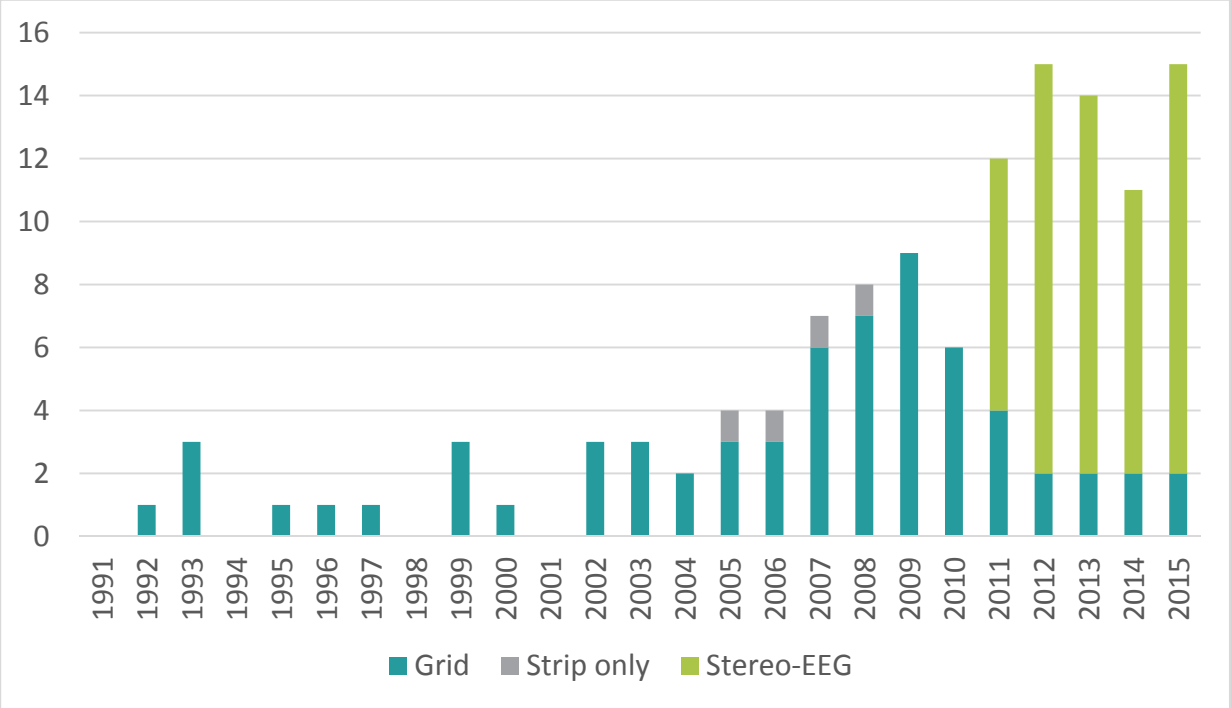


Figure 3. Intracranial examinations at HUH in 1991–2015.

HUH has the most extensive experience in Finland of the surgical treatment of drug-resistant epilepsy in children and adolescents. By the end of 2015, 453 epilepsy operations had been carried out, 13% of which were second operations. Of these, 271 (64%) were performed on patients under the age of 16 and 115 (27%) on patients under the age of 7 (Figure 4).

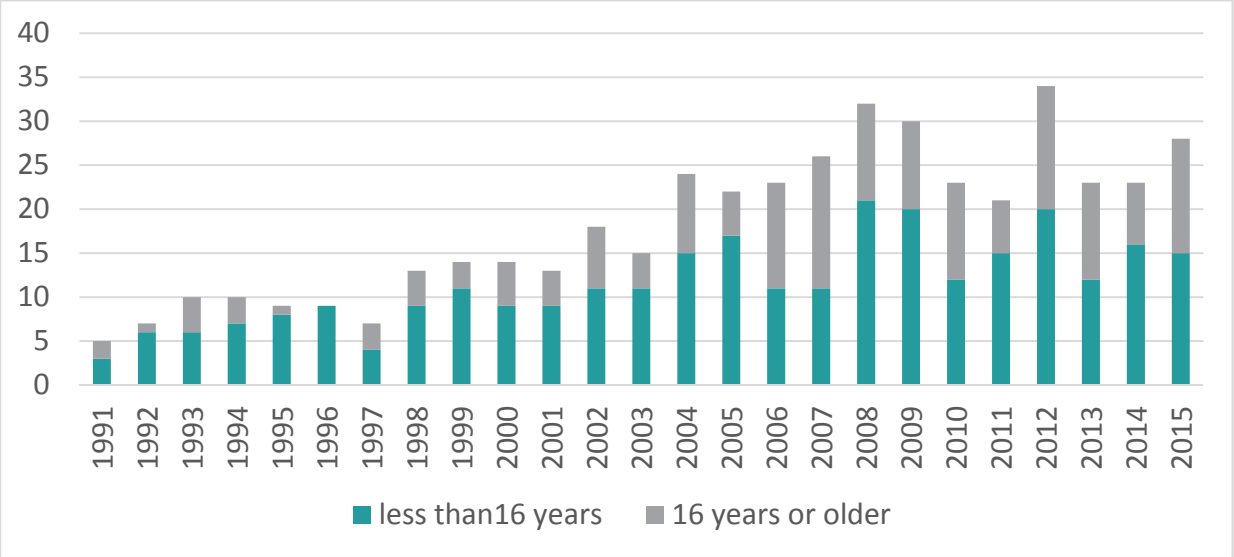


Figure 4. Epilepsy operations at HUH in 1991–2015 by age group, 453 operations in total. These figures do not include intracranial examinations or stimulator implantations..

By the end of 2015, 12 child patients from Estonia had been referred to us for pre-operative assessments. Six of them have now been operated on, two were diagnosed with a rare disease making them ineligible for surgery, a VNS was recommended for one patient, and for three the assessment process was still underway by the end of 2015.

Most of the studies reporting on the outcomes of operations on children and adolescents are based on the cohorts of single hospitals, probably with poor representation of the general population. Our results can best be compared with a national prospective and longitudinal study carried out in Sweden (Edelvik et al, Neurology 2013; 81:1244–1251), which reported that 53% of the 88 children and adolescents operated on were seizure-free during the two year follow-up period. Similarly, 51% of the patients operated on in HUH were seizure-free for at least two years following the surgery (Figure 5, Table 2). When making comparisons, it should be noted that, at HUH, the patients underwent fewer temporal procedures (24%) than in Sweden (43%), which by default decreases the likelihood of seizure-free outcomes.

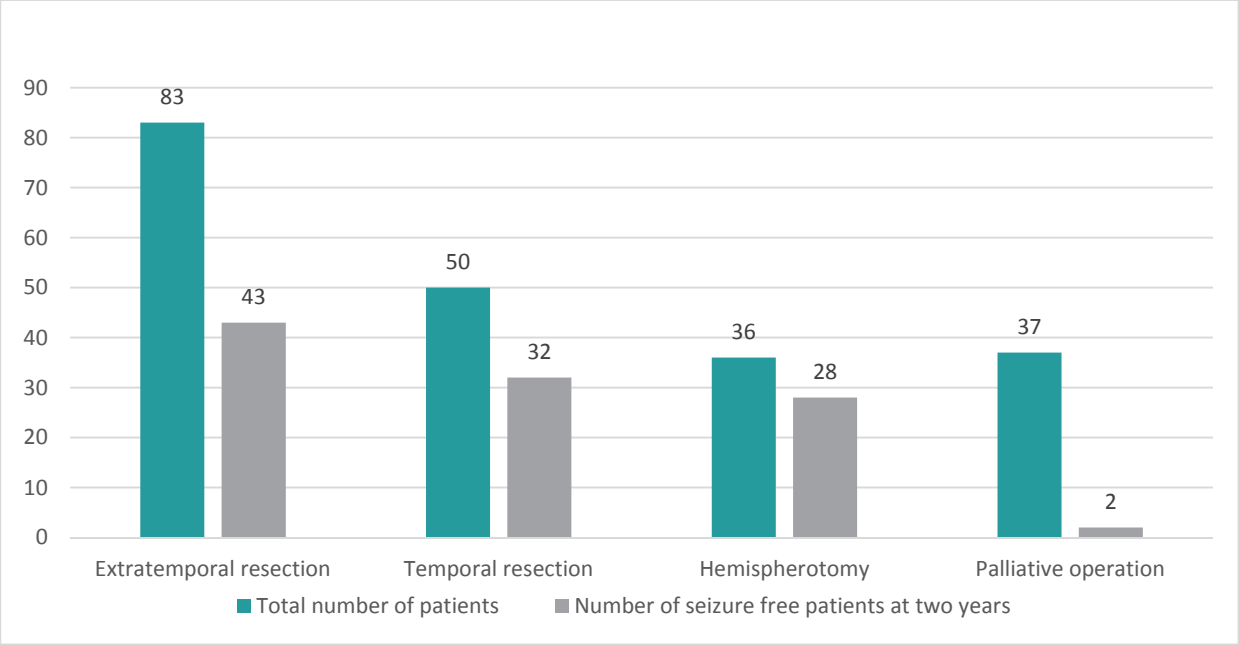


Figure 5. Outcomes of epilepsy surgery procedures performed at HUH in 1992–2012 on patients under the age of 16

Year	Seizure-free	Fewer than 3 seizures per year	Other significant reduction in seizures	No significant change	Data not available (monitoring under the age of 2)	Total
2013	8 (53%)	1	1	4 (27%)	1	15 (100%)

Table 2 Seizure outcomes at two-year post-operative follow-up of children and adolescents operated on in 2013 (12 extratemporal resections, 3 temporal resections)

Surgical complications at HUH (Table 3) can also best be compared with studies conducted in Sweden: in the 865 operations performed in 1996–2010, complications occurred in 10.5% of patients (Bjellvi et al. J Neurosurg 122:519–525, 2015).

Adverse effect	1991-2013	2014	Comment
Visual field defect (hemianopia or inferior quandrantanopia)	10 (2.5%)	0	In one case probably present began prior to surgery, not examined
Shunt	8 (2.0%)	0	All hemispherotomies
Hemiparesis	8 (2.0%)	1 (4%)	Two very mild cases
Verbal dysfunction	6 (1.5%)	1 (4%)	
Psychiatric symptoms	4 (1.0%)	0	All adults
Visual dysfunction	1 (0.2%)	0	
Impairment of memory	1 (0.2%)	0	Prediction
Hypothalamic dysfunction	1 (0.2%)	0	
Bone infection	1 (0.2%)	0	
Cyst formation	1 (0.2%)	0	Required revision operation
Total	41 (10.2%)	2 (9%)	

Table 3 The adverse effects of surgical treatment still present at 6 months after surgery in all patients operated on at HUH (including adults)

Vagus nerve stimulation

A vagus nerve stimulator (VNS) can be used in the treatment of severe epilepsy together with drug therapies, in order to alleviate symptoms in patients who are ineligible for resective surgery. A neurosurgeon implants the VNS under the pectoral muscle, and the wires are coiled around the vagus nerve in the neck. The device sends electrical stimuli through the nerve, and can be adjusted using a sensor and small handheld computer through the skin. Based on controlled studies, VNS reduces the number of seizures in approximately half of all patients by at least 50% which is considered a significant benefit. The treatment response is difficult to predict at individual level. Adverse effects are usually rare and manageable by adjusting the electric current.

VNS therapies were begun with epilepsy patients at HUH in 1998. By the end of 2015, a VNS had been implanted in 58 children or adolescents. In 2014, eight patients under the age of 18 received a VNS. Four (50%) of them have reported a significant benefit, while in three cases the benefit has been less than 50% and, for one patient, sufficient follow-up data is yet to be gathered.

Rare epilepsies and epileptic syndromes

Many severe forms of epilepsy belong to the group of rare diseases and to conditions known as epileptic encephalopathies, defined as epileptic activity causing or exacerbating cognitive dysfunction, sometimes leading to intellectual disability. In addition to prompt diagnostics and correctly targeted treatment, these patients also require monitoring and care by a multi-professional team and experts in a number of specialties. Some examples are presented below.

*Infantile spasm*s is a severe form of epilepsy with onset in early infancy; when untreated, this condition may lead to a permanent arrest of the child's development and learning. Approximately 25 patients present annually with this syndrome in Finland. The underlying cause is the key determinant for prognosis, but delayed diagnosis and treatment also lead to learning disability even in those infants whose prognosis would be excellent with appropriate treatment. The first-line drugs are vigabatrin and ACTH, both of which are used almost exclusively for this specific syndrome. Our recently updated treatment program is based on both our own and international research as well as international treatment guidelines. Tables 4 and 5 present treatment outcomes at two years of age over a ten-year period in 1997–2006 and over a shorter period in 2014–2015 for children treated at the epilepsy unit.

Underlying cause	Seizure-free at the age of 2 years	Normal development at the age of 2 years	Mortality under the age of 2 years	Data not available	Patients total
Identified #	14 (41%)	6 (15%)	5 (15%)	2 (6%)	34 (100%)
Unknown	19 (100%)	17 (89%)	0	0	19 (100%)
Total	33 (62%)	23 (43%)	5 (9%)	2 (4%)	53 (100%)

Table 4 Treatment outcomes in patients with infantile spasms by the age of two years (HUH catchment area population-based 1997–2006, all infants treated at the epilepsy unit)
28 had structural, three genetic and three metabolic underlying causes

Year Underlying cause	New patients	Seizure-free latest by 3 months after treatment onset
2014 Identified Unknown	 8 2	 5 (63%) 2 (100%)
2015 Identified Unknown	 7 2	 4 (57%) 2 (100%)
Total	19	13 (68%)

Table 5 Short-term treatment outcomes in cases of infantile spasms in 2014-2015

Epileptic encephalopathy with electric status epilepticus during sleep (CSWS syndrome) is a form of epilepsy which is extremely difficult to treat and causes learning difficulties in children of pre-school and primary school age. EEG monitoring typically reveals continuous spikes and waves during sleep. The syndrome is difficult to diagnose and no accurate data are available on its prevalence. The children's epilepsy unit has conducted the largest clinical follow-up study to date on patients with this syndrome (Liukkonen et al. Epilepsia 2010: 51: 2023–2032). The study included 32 patients treated at

the epilepsy unit. The electric status during sleep was stopped by drug therapy in half of the patients. One third of them regained their previous intellectual capacity. The children's epilepsy unit has also published the first experience of surgical treatment of the syndrome (Peltola et al. Epilepsia 2011; 52:602–609). Based on our results and later research carried out elsewhere, surgery may significantly benefit some drug resistant patients with a structural abnormality as the underlying cause..

The children's epilepsy unit is currently developing better EEG methods for diagnosing CSWS syndrome, in collaboration with the pediatric clinical neurophysiology unit (Peltola et al. Clinical Neurophysiology 2012; 123:1284–12 and 2014; 125:1639–1646). The epilepsy unit is also participating in Rescue ESES, a randomized controlled multicenter European study comparing different treatments (http://www.isrctn.com/ISRCTN42686094). Our treatment program for CSWS is based on both our own previous experience and other available scientific evidence. Around 50 patients with CSWS syndrome are currently being treated at the unit.

Dravet syndrome is the most commonly known form of genetic epilepsy. Prevalence estimates indicate that 3–4 patients develop the condition each year in Finland. Typical symptoms include prolonged epileptic seizures (status epilepticus) provoked by fever and infection with onset in the first year of life, followed by polymorphic seizures and some level of cognitive dysfunction in the following years.An early diagnosis is important for starting appropriate drug treatment. The best response is usually achieved with the orphan medicine stiripentol combined with other suitable drugs; this combination stops episodes of epileptic status in nearly all patients. Some commonly used antiepileptic drugs may exacerbate the symptoms.

By the end of 2015 the children's epilepsy unit has been involved in the care of a total of 41 patients, of whom 34 (83%) were found to have the most common genetic abnormality associated with the syndrome, an *SCN1A* mutation. The *SCN1A* gene regulates the sodium channels within the neuronal membranes. Some other type of genetic etiology was identified in three patients and in four patients, the gene etiology remains unidentified. We have published research on on Dravet syndrome (Gaily ym. Epilepsia 2013; 54:1577-85) and have been involved in the multicenter study commissioned by the European Medicines Agency (EMEA) on the adverse effects of stiripentol. The epilepsy unit also participates in the Nordic working group which is developing treatment guidelines for Dravet syndrome. During 2015, we had a total of 21 patients in our care. Dravet syndrome was newly diagnosed in six patients in 2014–2015 (Table 6).

Key indicators/year	2014	2015
Number of new Dravet syndrome diagnoses	3	3
Genetic etiology*(SCN1A)*	3 (3)	2 (2)
Patiens' ages at the time of diagnosis	9, 14, 28 months	12, 14, 47 months
Stiripentol therapy in use	2	2
Patients with epileptic status after diagnosis	1	1

Table 6 New Dravet syndrome patients in 2014-2015

Others genetic epilepsies. During 2014–2015, the children's epilepsy unit identified an etiological diagnosis by gene panels for nine patients with severe forms of epilepsy (40% of those examined) and by conventional sequencing methods for two patients (Dravet patients not included). In addition, as part of our research project, a genetic diagnosis was determined for 20 children or families. The children's epilepsy unit participates in collaboration within EuroEpinomics, a research consortium which seeks to discover new genetic causes of epilepsy. New epilepsy genes have also been found in Finnish patients.

Tuberous sclerosis is a typical rare disease (incidence rate 17:100 000) caused by a gene defect. The symptoms include severe epilepsy (commonly infantile spasms), learning disabilities of varying degrees, and abnormalities in many other organs, such as renal angiomyolipomas, rabdomyomas,

skin abnormalities and ocular disorders. Patients need the expertise of a multi-professional team. International guidelines are available for follow-up, with the purpose of promoting early diagnosis of dangerous manifestations (e.g. infantile spasms, growing giant cell astrocytomas and kidney tumors) before they lead to complications. During 2015, 19 patients with tuberous sclerosis were treated. In 2016, the follow-up of patients will be improved to systematically to meet international recommendations. A joint multi-specialist outpatient clinic will be set up to arrange all necessary follow-up examinations at a single visit.

Rasmussen encephalitis is an autoimmune brain disease with typical onset at pre-school or primary school age. The symptoms include extremely drug-resistant epilepsy and gradually developing neurological deficiencies, most typically hemiparesis. The progression of neurological deficits can be delayed by immunological treatments, which do not, however, alleviate the seizures in most cases. Seizure freedom can only be achieved by hemispherotomy, i.e. disconnecting all neural connections of one hemisphere. The incidence rate of Rasmussen encephalitis is estimated at 0.017: 100,000, which in Finland means a maximum of one patient per year.

By the end of 2015, the children's epilepsy unit had treated 11 patients with Rasmussen encephalitis. Nine of our patients (82%) have received or are receiving immunological treatment (with the exception of one patient diagnosed in 1991 and another patient who arrived for examination only at the age of 20). Nine patients were treated surgically (82%). Hemispherotomies were performed for seven patients (64%) all of them are seizure-free and have retained ambulation. Resective surgery was performed on two patients resulting in alleviation of the seizures.

Limbic encephalitis, characterized by a clearly elevated level of GAD antibodies, responds poorly to immunological therapies and causes severe epilepsy. We have treated three patients, all of whom have undergone a temporal lobectomy during adolescence. Surgical treatment significantly alleviated the epileptic seizures.

Ongoing research projects (contact persons)

Outcome of pediatric epilepsy surgery and factors predicting outcome (Eija Gaily, Aki Laakso, Heta Leinonen)
Localization of epileptic foci using mathematical signal processing methods (Leena Lauronen, Maria Peltola)
Noninvasive localization of linguistic functions in children (Henri Lehtinen)
Localization of epileptic foci by MEG (Ritva Paetau, Juha Wilenius)
Developmental effects of prenatal antiepileptic drug exposure (Mari Videman, Sampsa Vanhatalo, Eija Gaily)
Cognitive development of children exposed to antiepileptic drugs at age 6; European multicenter study (coordinator Eija Gaily)
Genetic epilepsies, EuroEpinomics collaboration (Tarja Linnankivi, Anna-Elina Lehesjoki)
Early infantile epilepsies (Henna Jonsson, Tarja Linnankivi, Eija Gaily)
Development of EEG diagnostics for CSWS epilepsy (Maria Peltola)
A European multicenter study on the treatment of CSWS, coordinated by UMC Utrecht (Rescue ESES) (Liisa Metsähonkala)
NOPRES: Nordic Prospective study of outcome of Rare patient groups after Epilepsy Surgery (Liisa Metsähonkala, Eija Gaily) Physicians from the unit produced a total of 17 publications in 2014–2015.

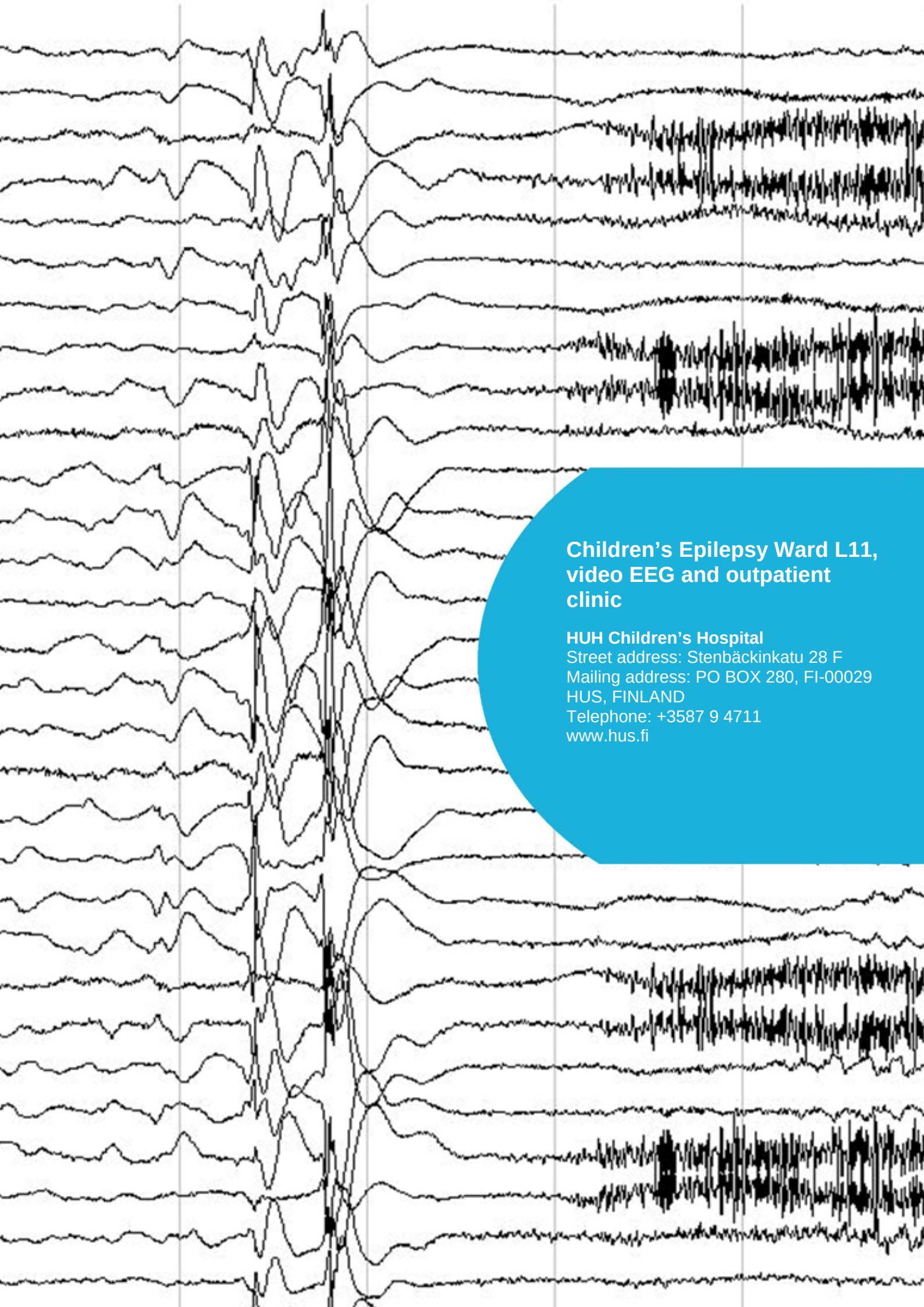
Summary and future plans

The children's epilepsy unit at HUH is Finland's largest unit specializing in the diagnostics, treatment and demanding differential diagnostics of epilepsy in children and adolescents. The unit has the most extensive experience of epilepsy surgery in children and adolescents in Finland, particularly in extratemporal operations, examinations carried out with intracranial depth electrodes and rare forms of epilepsy with onset in early childhood. Approximately one fifth of the patients come from outside the HUS catchment area. Our investigation methods and treatment outcomes correspond to high international standards.

The Epilepsy Unit is situated at the Children's Castle Hospital, separately from other acute pediatric care. This creates a challenge, particularly during out-of-hours service. With the completion of the new children's hospital in 2017, a new acute pediatric neurology ward will be established. The current three video-EEG recording rooms will be replaced by 4–5 rooms where recordings can also be carried out during the weekends. Increased capacity will further improve diagnostics and treatment. We will also have better resources for responding to the still existing treatment gap for patients with surgically remediable severe epilepsies. Patient safety will be improved by the proximity with the neurosurgical department, pediatric ICU and pediatric wards. The video-EEG unit will also continue to serve neurological patients at HUH, and collaboration with neurologists treating epilepsy patients will be further increased.

Maintaining a high standard in epilepsy surgery and the treatment and documentation of rare diseases will require substantial further efforts from our unit. We aim to establish an epilepsy center serving both pediatric and adult patients under the auspices of the Rare Diseases Unit, in order to develop and coordinate the treatment of severe and rare epilepsies in Finland in cooperation with the Kuopio University Hospital epilepsy team, other Finnish interest groups, European networks and other international partners. The reorganization of our processes will allow the provision of more consultations, investigations and special treatments including surgery in Finland and the neighboring countries, especially Estonia. We have launched the creation of a quality control epilepsy register which will improve measurement of the efficacy of epilepsy treatments and accumulate data for the development of treatments and scientific research.

In a country like Finland, with its small population, the number of patients with rare diseases or those needing epilepsy surgery are relatively low compared to epilepsy centers in many other European countries and the United States. The continuing education of specialists in international centers is crucial to maintaining high-standard practices within the unit, as well as regular attendance at the most important international congresses and the production of educational materials in the field of epilepsy.



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