IMPACT OF EPILEPSY SURGERY IN CHILDHOOD

motor function, health related quality of life
and self perceived competence

R. van Empelen

Impact of epilepsy surgery in childhood
Thesis, University of Utrecht, the Netherlands
ISBN 90-393-3971-6

Cover design and layout: Marco van Brussel and
Multimedia, UMC Utrecht

Scan, department of radiology UMC Utrecht
EEG, department of neurophysiology UMC Utrecht

Photography: Afra van Empelen-Stein
Printed by: Drukkerij Zuidam, Utrecht

IMPACT OF EPILEPSY SURGERY IN CHILDHOOD

motor function, health related quality of life
and self perceived competence

Effecten van epilepsiechirurgie op de kinderleeftijd

motorische functie, gezondheidsgerelateerde kwaliteit van leven
en competentie beleving

(met een samenvatting in het Nederlands)

Proefschrift

Ter verkrijging van de graad van doctor aan de Universiteit Utrecht,
op gezag van de Rector Magnificus, Prof. dr. W.H. Gispen
ingevolge het besluit van het College voor Promoties
in het openbaar te verdedigen
op dinsdag 1 november 2005 des middags te 2.30 uur

door

Ronald van Empelen

Geboren op 5 november 1950, te Amsterdam

Promotores:

Prof. dr. O. van Nieuwenhuizen, Universiteit Utrecht
Prof. dr. P.J.M. Helders, Universiteit Utrecht

Copromotor:

Dr. A. Jennekens-Schinkel, Universiteit Utrecht

Dit proefschrift werd mede mogelijk gemaakt met financiële steun voor het onderzoek van:
- Johanna Kinderfonds
- Phelps Stichting

De uitgave van dit proefschrift werd financieel ondersteund door:
- Divisie Kinderen, Universitair Medisch Centrum Utrecht
- Koninklijk Nederlands Genootschap voor Fysiotherapie
- Nederlandse Vereniging voor Fysiotherapie in de Kinder- en Jeugdgezondheidszorg
- Johanna Kinderfonds
- Nationaal Epilepsie Fonds
- Phelps Stichting

LOCKED-IN

Dat dit de hersenen zijn, dat dat de wereld is,
Dat heeft de taal mij aan het verstand gebracht.
Het alfabet komt langs, bij iedere oogopslag
Staat weer een letter vast. Betekenis.
[Wiel Kusters in: “Stof zijn wij” Brein en poëzie, 2002]

Voor de kinderen met epilepsie en hun ouders

A disabled child should enjoy a full and
decent life in conditions which ensure dignity,
promotes self reliance and facilitates the child’s
active participation in the community
(UN Convention on the Rights of the Child, 1989, Art 23.Sec 1)

CONTENTS

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
AED	Anti-Epileptic Drug
ANOVA	Analysis of variance
BSID II	Bayley Scales of Infant Development (2e Edition)
CP	Cerebral Palsy
CPG	Central Pattern Generator
DI	Developmental Index
DNET	Dysembryoplastic NeuroEpithelioma Tumor
DuCESP	Dutch Collaborative Epilepsy Surgery Program
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
HARCES	Hague Restrictions in Childhood Epilepsy Scale
HASS	Hague Seizure Severity Scale
HAY	How Are You (questionnaires for children and parents)
HHE	Hemiplegia, Hemiconvulsions, Epilepsy syndrome,
HrQoL	Health-related Quality of Life
ICF	International Classification of Functioning, Disability and Health
ILAE	International League Against Epilepsy
IQ	Intelligence Quotient
JAM	Joint Alignment and Motion scale
LSD	Least Significant Difference
M-ABC	Movement Assessment Battery for Children
MAS	Modified Ashworth Scale
MCA	congenital Middle Cerebral Artery infarction
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
MTS	Mesial Temporal Sclerosis
NetChild	Network for Childhood Disability Research in The Netherlands
PEDI	Pediatric Evaluation of Disability Inventory
PDI	Psychomotor Developmental Index
ROM	Range of Motion

SD	Standard Deviation
SPP (C) (A)	Self-Perception Profile Competence (Children) (Adolescents)
SPPS	Statistical Package of Social Sciences
SWS	Sturge-Weber Syndrome
TS	Tuberous Sclerosis
WHO	World Health Organization
WISC-R.	Wechsler Intelligence Scale for Children – Revised
WPPSI-R	Wechsler Preschool and Primary Scale of Intelligence – Revised

Chapter 1

Introduction

Ron van Empelen

Intractable epilepsy and epilepsy surgery

Although most children (0-16 years) with epilepsy do well on anti-epileptic drugs, some develop medically intractable epilepsy. The incidence rate of epilepsy per year in children is 73 to 86 per 100,000 children and prevelance is 4-6 per 1,000, 10% of these cases are intractable (Berg et al., 2004). Intractability is defined as failure of more than 2 first-line anti-epileptic drugs (AED) to control seizures in patients (Berg et al., 2004).
Epilepsy surgery has become a prominent intervention for these children and adolescents with pharmacologically untreatable epilepsy (Wyllie et al., 1998; Graveline et al., 2000; Devlin et al., 2003). Favourable effects on seizure outcome have been reported for different types of surgery, like hemispherectomy, temporal or extra-temporal resections, (Chen et al., 2002; Devlin et al., 2003) and the psychosocial benefits of surgery have been studied (Lendt et al., 2000; Birbeck et al., 2002; Ronen et al., 2003; Ronen et al., 2003; Smith et al., 2004). Knowledge of the impact of epilepsy surgery on motor development and activities of daily life of children is as yet in an exploratory phase.

Scope of this study and International Classification of Functioning, Disability and Health

As one of the main questions in this study is "Do we harm children in their motor development and activities of daily life by performing epilepsy surgery?", our focus was on health-related consequences of epilepsy surgery. Historically, the medical definition of outcome has long been confined to impairments, and in this vein the effects of epilepsy surgery have been assessed in terms of seizure reduction (Carter Snead, 2001). But the disablement research of the last decade has strongly contributed to a change with perhaps the importance of a paradigm shift, in the sense that not only biological, organ-bound impairments, but also wider spheres of health-related human functioning have become a focus for clinicians and researchers.

To classify health-related consequences of diseases or disorders, the World Health Organization (WHO) has developed an internationally accepted framework, The International Classification of Functioning, Disability and Health (ICF) (WHO, 2002). The ICF is applicable across cultures, age groups and sexes, and allows the collection of reliable and comparable data on health outcomes (WHO, 2002). Using the ICF, one can classify functioning and disability, both of which can be considered at three main levels, i.e., body functions and structures or anatomical features, activity and participation (WHO 2002; Steiner et al., 2002; Stucki et al., 2003; Battaglai et al., 2004). In the ICF, the term functioning refers to all body functions, activities and participation, and disability is defined as impairments, limitations in activities and restrictions in participation, depending on the level under consideration:

1. Body functions are defined as physiological functions of body systems (including mental functions). Body structures are anatomical parts of the body such as organs, limbs and the nervous system. An example of body functions relevant to the present study is range of motion, which is an aspect of the function of movement. Deficits or abnormalities on this level are denoted as impairments, such as decreased or insufficient range of motion or loss of strength.
2. Activities are defined as components of a person's action. Mobility and self-care are examples with relevance for the present study. Deficits or any abnormalities in the level of activities are pooled under the concept of limitations. These are difficulties that a person has when taking an action: examples are difficulties grasping objects or climbing stairs.
3. Participation refers to involvement in social life. Restrictions of participation are problems that a person experiences when becoming involved in social or societal situations. An example is not being able or not being allowed to go independently to school or to a sports club.

The ICF classification (WHO, 2002) served as a framework for the present study. At the three levels of human functioning, we measured functioning: at the level of body, we scored the impairments;

at the level of the whole person, we scored motor development and activity limitations; and at the level of social participation, we scored the restrictions. Impairments were assessed a) in terms of seizure frequency and seizure severity, and b) with respect to muscle strength, range of motion and muscle tone. Limitations in activities were assessed in terms of motor functioning and self-care, mobility and social function. At the level of participation, epilepsy-related restrictions were assessed.
The ICF integrates the medical model and the social model and has been described as having a bio-psycho-social focus (WHO, 2002; Simeonsson et al., 2003; Battaglia et al., 2004). In terms of the ICF, the health condition may affect every level of functioning. For example: in many cases of intractable epilepsy the underlying lesion leads to impairments in cognitive and/or motor functioning, activities are limited because the risk of seizures necessitates chaperoning and the child is restricted in social participation because the danger of seizures prohibits practice of, e.g., sports. Environmental and personal factors are also elaborated in the ICF but remain beyond the scope of this thesis.

Epilepsy, health-related quality of life and self-perceived competence

In addition to impairments, limitations and restrictions, health-related quality of life (HrQoL) is an important outcome measure for epilepsy surgery, because the ultimate goal of surgery for epilepsy is to improve overall functioning and well-being. One, therefore, has to ask the question: might epilepsy surgery have an effect on HrQoL? To assess HrQoL, defined in terms of mental, physical and social functioning, we used a questionnaire that assesses generic as well as disease-specific areas related to the life of children with epilepsy. This questionnaire is called the How Are You (HAY) and has been developed by Bruil (1999). A strong point of this questionnaire is that it allows one to study the child's HrQoL as perceived by the parents but also as perceived by the child herself/himself.

When the goal is to improve autonomy of the patient, indices of outcome may also be found in the child's perceptions of the competence with which she/he adapts. Self-perceived competence denotes the evaluations of self-worth that are part of the self-concept. Because children with epilepsy perceive their competence as being poorer than healthy children do, one must study whether self-perceived competence might change after surgery.

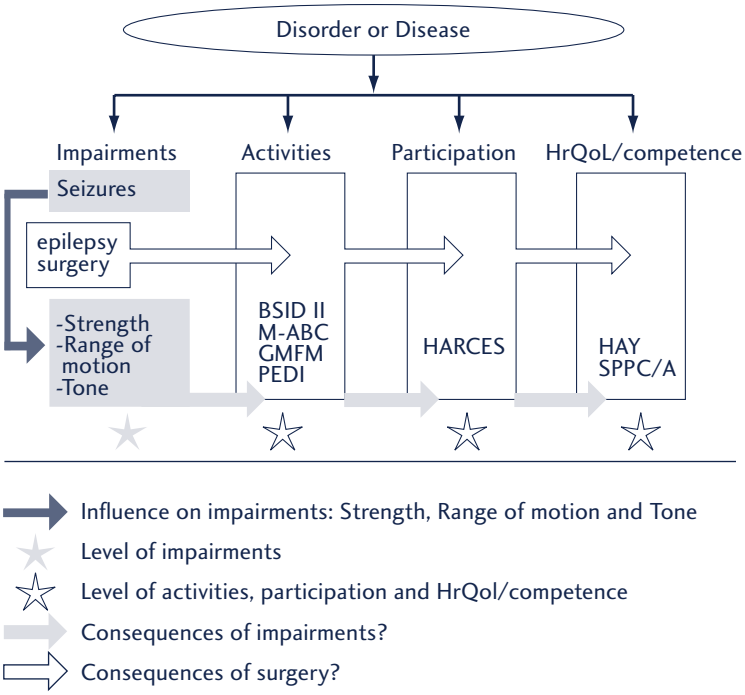
Outline of the study

Children with pharmacologically intractable epilepsies are referred to the Dutch Collaborative Epilepsy Surgery Programme (DuCESP). The referrals are from neurologists, paediatric neurologists and epileptologists working at epilepsy centres, secondary and tertiary institutions of health care all over the country. After careful screening, about 10-15 children can be operated per year. But not all intractable seizures in childhood offer the prospect of successful surgical treatment. In The Netherlands, almost 75% of the children who are presented to DuCESP do not fulfil the criteria for surgery and, hence, are not offered this treatment. Reasons for not being eligible for surgery include multifocal localisation or localisation of the epileptogenic zone in an eloquent cerebral area. All the children referred to DuCESP between 1996 and 2001 were enrolled into the study, as we were interested in the impact of epilepsy surgery, but also in the course of development in children who were not eligible for epilepsy surgery.
In fact, we followed two groups. One comprised 52 children who underwent epilepsy surgery between 1996 and 2001 at the Wilhelmina University Children's Hospital. The other group consisted of 45 children who were not eligible for epilepsy surgery between 1996 and 2001.
In both groups, patients were assessed using a standard protocol with fixed intervals: baseline assessment, 6 months, 1 year and 2 years after surgery or after baseline, at the outpatient clinic of the Wilhelmina Children's Hospital.

Instruments

At the level of impairments, surgical outcome in terms of seizure frequency was assessed by the child neurologist using Engel et al.'s (1993) modified classification. Seizure severity as perceived by the parent or caregiver was quantified using the Hague Seizure Severity Scale (HASS), and muscle strength (MRC), range of motion (JAM score) and muscle tone (modified Ashworth scale) (MAS) were assessed by the physical therapist. IQ's were determined by the neuropsychologist using instruments validated for Dutch children (WISC-R and WPPSI-R) or equivalent instruments.
At the level of activities, motor performance and motor development were assessed with the following instruments: Bayley Motor Scales of Infant Development 2nd edition (BSID-II) and Movement Assessment Battery for Children (M-ABC). For children with spasticity we used the Gross Motor Function Measure (GMFM-88), together with the Gross Motor Function Classification System (GMFCS). The Pediatric Evaluation of Disability Inventory (PEDI) was used as a functional assessment of activities of daily life.
Participation was assessed in terms of epilepsy-related restrictions and quantified by means of the Hague Restrictions in Childhood Epilepsy Scale (HARCES).
For health-related quality of life we used the How Are You (HAY) questionnaire. The HAY is a questionnaire adapted to life in The Netherlands, designed for children with epilepsy.
Perceived competence was measured using the Dutch adaptation of the Harter Self Perception Profile for Children (SPP-C) or the Self Perception Profile for Adolescents (SPP-A).

The impact of epilepsy surgery and the different assessments used in this study can be represented in the following scheme.



Questions addressed by the study

Our intention was to improve knowledge about the impact of epilepsy surgery on motor impairments, activities, participation, HrQoL and competence, by evaluating change over a period of two years in:

- Motor impairments, motor development, daily functional activities (ADL), caregiver assistance and social participation before and after epilepsy surgery,
- HrQoL and perceived competence.

Because of the scarcity of knowledge regarding the impact of not being eligible for epilepsy surgery, other issues addressed by this thesis are:

- Whether motor impairments, severity of epilepsy, motor functioning and epilepsy-related restrictions worsen in children with intractable epilepsy,
- Whether children with intractable epilepsy have poorer health-related quality of life (HrQoL) and self-perceived competence compared to a healthy reference group and how this changes over time.

References

Battaglia M, Russo E, Bolla A, Chiusso A, Bertelli S, Pellegri A, Borri G, Martinuzzi A. International Classification of Functioning, Disability and Health in a cohort of children with cognitive, motor, and complex disabilities. Dev Med Child Neurol 2004;46:98-106.

Berg AT, Smith SN, Frobish D, Beckerman B, Levy SR, Testa FM, Shinnar S. Longitudinal assessment of adaptive behavior in infants and young children with newly diagnosed epilepsy: influences of etiology, syndrome, and seizure control. Pediatrics 2004;114:645-50.

Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. Epilepsia 2002;43:535-538.

Bruil J. Development of quality of life questionnaire for children with a chronic illness. (Thesis) Universiteit Leiden. (FSW) 1999.

Carter Snead O 3rd. Surgical treatment of medically refractory epilepsy in childhood. Brain Dev 2001;23(4):199-207. [Review].

Chen LS, Wang N, Lin M. Seizure outcome of intractable partial epilepsy in children. Pediatric Neurology 2002;26:282-7.

Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003;126:556-66.

Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel JJ (ed.) Surgical treatment of the epilepsies. 2nd ed. New York: Raven Press, 1993:609–21.

Graveline C, Young N, Hwang P. Disability evaluation in children with hemidecorticectomy: use of the activity scales for kids and the pediatric evaluation disability inventory. J Child Neurol 2000;15:7-14.

Lendt M, Helmstaedter C, Kuczaty S, Schramm J, Elger CE. Behavioural disorders in children with epilepsy: Early improvement after surgery. J Neurol Neurosurg and Psychiatry 2000;69:739-44.

Ronen GM, Streiner DL, Rosenbaum P; Canadian Pediatric Epilepsy Network. Health-related quality of life in children with epilepsy: development and validation of self-report and parent proxy measures. Epilepsia 2003;44:598-612.

Ronen GM, Streiner DL, Rosenbaum P. Health-related quality of life in childhood epilepsy: Moving beyond 'seizure control with minimal adverse effects'. Health Qual Life Outcomes 2003;1:36.

Simeonsson RJ, Leonardi M, Lollar D, Bjorck-Akesson E, Hollenweger J, Martinuzzi A. Applying the International Classification of Functioning, Disability and Health (ICF) to measure childhood disability. Disabil Rehabil 2003;25:602-10. [Review].

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Steiner WA, Ryser L, Huber E. Use of the ICF model as a clinical problem-solving tool in physical therapy and rehabilitation medicine. Phys Ther 2002;82:1098-1107.

Stucki G, Ewert T, Cieza A. Value and application of the ICF in rehabilitation medicine. Disabil Rehabil 2003;25:628-34.

W.H.O. The International Classification of Functioning, Disability and Health (2002). ICF: introduction. Geneva: World Health Organization. Available on the WHO Internet site, 2002. http://www.who.int/classification/icf.

Wyllie E, Comair YG, Kotagal P, Bulacio J, Bingaman W, Ruggieri P. Seizure outcome after epilepsy surgery in children and adolescents. Annals of Neurology 1998;44:740-8.

Chapter 2

Functional consequences of hemispherectomy

R. van Empelen[1*]
A. Jennekens-Schinkel[2*]
E. Buskens[3]
P.J.M. Helders[1]
O. van Nieuwenhuizen[4*]

On behalf of the Dutch Collaborative Epilepsy Surgery Programme.

1 Department of Paediatric Physical Therapy and Exercise Physiology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands. NetChild, Network for Childhood Disability Research in The Netherlands
2 Department of Neuropsychology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
3 Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, The Netherlands.
4 Department of Child Neurology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.

* Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands.

Brain 2004; 127: 2071-2079.

Summary

Purpose: Using the International Classification of Functioning (WHO, 2002), impairments, activities and social participation are reported in twelve children (mean age at surgery 5.9 years) investigated prior to and 6 months, one and two years after hemispherectomy.
Methods: Impairments were assessed a) in terms of seizure frequency (Engel classification) and seizure severity (HASS), and b) with respect to muscle strength (MRC), range of motion (JAM score) and muscle tone (modified Ashworth scale). Activities were assessed in terms of gross motor functioning (GMFM) and self-care, mobility and social function (PEDI). Participation was assessed in terms of epilepsy-related restrictions and quantified by means of the Hague Restrictions in Childhood Epilepsy Scale (HARCES).
Results: Nine out of 12 children could be classified as free of seizures (Engel Class I) and in the remaining three, seizure frequency belonged to Engel Class III. HASS scores improved maximally in 10 out of 12 children, and almost maximally in the two remaining children. Muscle strength and muscle tone in the side of the body contralateral to the hemispherectomy, which were already decreased preoperatively, decreased even further in the first six months after surgery, but returned to pre-surgical baseline thereafter, except for the distal part of the arm. Range of motion was abnormal prior to operation and remained so post-surgically. Mean GMFM increase was 20% after two years (95% confidence interval 10-33), while mean PEDI-increase was even more than 20 scale-points (95% confidence interval 10-35). In nearly all children HARCES scores had normalized two years after surgery.
Conclusion: decrease of seizure frequency and severity widens the scope of motor and social functioning, which overrides the effects of remaining motor impairments.

Introduction

In children with pharmaco-resistant seizure disorders, epilepsy surgery reduces and even eliminates seizure activity. Until recently, effectiveness of epilepsy surgery was measured predominantly in terms of seizure reduction. Alongside the intended seizure reduction, motor function – a valid marker of development (Beissner et al., 2000) – is an important pre-surgical consideration, as it strongly influences social participation in infancy and later childhood (Wyllie et al., 1998; Graveline et al., 2000). Change in motor functioning, if addressed as a consequence of hemispherectomy, has been estimated in terms of clinical impression (Carson et al., 1996) or determined by the level of impairment (Beckung and Uvebrant, 1993; Beckung et al., 1994; Graveline et al., 1999). In a series of 33 hemispherectomised children, Devlin et al. (2003) reported that hemiplegia had not changed in the majority (22 children), had improved in five and worsened in six. To date there has been no assessment of the course of motor impairments, limitations in activities and restrictions when participating in social life following hemispherectomy in childhood.

The International Classification of Functioning, Disability and Health (ICF) provided a useful guide for the present prospective, longitudinal study (WHO, 2002). The ICF is the generally accepted framework for classification of functional consequences of diseases or disorders (Steiner et al., 2002; Stucki et al., 2003; von Wild, 2003). Whereas impairments reflect consequences of a disease at the organ level (Bilbao et al., 2003), limitations in activities reflect changes in performance and motor activity, while restrictions refer to difficulties encountered in social participation. Assessment of daily activities and participation in social life is more comprehensive and closer to the patient's needs than assessment of impairment. Environmental and personal factors are also elaborated in the ICF but remain beyond the scope of this paper. The ICF is applicable across cultures, age groups and sexes, and allows the collection of reliable and comparable data on health outcomes (WHO, 2002).

The study addresses the questions to what degree motor impairments, motor activities and aspects of social participation exist before hemispherectomy and change thereafter.

Patients

Between 1996 and 2000, 12 children (9 girls, 3 boys), all of whom had been referred to the Dutch Collaborative Epilepsy Surgery Programme (DuCESP) underwent functional hemispherectomy. Exclusion criteria were: age older than 16 years at the time of surgery and tumours and metabolic disease. Pre- and post-surgery patient characteristics including pathology, age at surgery, seizure outcome (frequency), gross motor function (classification score) (Palisano et al., 2000) and cognitive/developmental level (Intelligence quotient/ developmental index [IQ/DI]) are given in Table 1. The pathology had been ascertained both by imaging and pathological examination of the surgical specimen. In four children there was evidence of vascular pathology (3 cases with congenital middle cerebral artery (MCA) infarction and 1 child with Sturge-Weber syndrome), in five acquired pathology (4 cases with Rasmussen encephalitis and 1 child with Hemiplegia, hemiconvulsions, epilepsy syndrome (HHE), three children exhibited developmental pathology (Hemimegalencephaly). Six children underwent a right-sided and 6 children a left-sided hemispherectomy. Mean age at time of surgery was 5.9 years (range: 0.3 – 12.1 years). All patients attended a rehabilitation programme at a regional rehabilitation centre after hemispherectomy. Three of them have used a splint for hand-positioning. All parents gave informed written consent and all children were followed for two years.

Table 1

Characteristics of patients: demographic (sex, ages at onset and at surgery), illness (resected hemisphere, pathology/aetiology, Engel classification), cognitive (IQ/DI) and gross motor function (classification system)

Nr.	Sex	Age (yrs;mo) at onset of epilepsy	Age (yrs;mo) at surgery	Hemisphere resection	Pathology/ aetiology	Engel Classification	IQ/DI Pre-surgery	2 yrs post-surgery	GMFCS Pre-surgery	2 yr post-surgery
1	F	1.2	4.4	Right	Vas (MCA)	I	79	87	3	2
2	F	0.1	6.4	Right	Vas (MCA)	I	60	68	2	2
3	F	0.9	11.10	Left	Vas (MCA)	I	52	54	1	1
4	F	0.5	7.6	Left	Vas (SWS)	I	54	53	2	2
5	F	5.1	8.5	Right	Acq (Ras)	III	67	56	5	3
6	F	2.6	3.0	Left	Acq (Ras)	I	<50	55	2	2
7	F	7.11	11.5	Left	Acq (Ras)	III	67	64	2	2
8	M	10.3	12.1	Left	Acq (Ras)	I	69	77	3	2
9	M	0.2	3.9	Left	Acq (HHE)	III	<50	<50	4	4
10	F	0.0	0.6	Right	Devel (Hem)	I	54	53	3	3
11	F	0.0	0.3	Right	Devel (Hem)	I	54	55	4	3
12	M	0.4	1.6	Right	Devel (Hem)	I	<50	<50	4	4

Abbreviations: Acq = Acquired pathology, Age (yrs;mo) at surgery = age in years and months at the time of surgery, Devel = Developmental pathology, DI= Developmental Index, GMFCS = Gross Motor Function Classification System, Hem = Hemimegalencephaly, HHE = Hemiplegia, hemiconvulsions, epilepsy syndrome, IQ = full scale Intelligence Quotient, MCA = congenital middle cerebral artery infarction, Ras = Rasmussen encephalitis, Sex: F = Female, M = Male, SWS = Sturge-Weber syndrome, Vas = vascular pathology.

Methods

Patients were assessed using a standard protocol with fixed intervals: 1- 3 months before surgery, and 6 months, 1 year and 2 years after surgery, at the outpatient clinic of the Wilhelmina Children's Hospital.

Epilepsy-related impairments were assessed by means of two measures. Surgical outcomes in terms of seizure frequency were assessed using Engel et al.'s (1993) modified classification.

Class I = free of seizures or residual auras, Class II = intermittent, infrequent seizures or relapse after a significant seizure-free period and Class III = worthwhile improvement, i.e., more than 75% reduction in seizure frequency. The outcome of children who experience less than 75% reduction in seizure frequency is classified as Engel Class IV.

Seizure severity as perceived by the parent or caregiver was quantified using the Hague Seizure Severity Scale (HASS), an inventory of 13 ictal and postictal problems that may have been encountered in the previous three months (Carpay et al., 1997). This scale is reliable in terms of test-retest stability and internal consistency (Carpay et al., 1997) and produces ranging from 13 (no seizures) to 52 (maximal seizure severity).

To assess motor impairments, we selected muscle strength as an expression of the degree of paresis, and furthermore range of motion and muscle tone.

Muscle strength of the extremities was assessed proximally and distally and scored according to the criteria for manual muscle testing, using the 6-point scale (MRC range 5-0) of the Medical Research Council (Medical Research Council, 1943). In children under the age of 5 years, functional muscle strength was tested as described by Hislop (Hislop and Montgomery, 2002). Because of the age of the children and the presence of muscle strength lower than grade 4, manual muscle testing and functional testing were indicated. Despite the subjectivity of manual muscle testing, its reliability and validity are both adequate for use in clinical assessments (Hislop and Montgomery, 2002).

Strength was assessed in the following muscles: flexors and abductors of the shoulder and hip (proximal), dorsal and palmar flexors in the wrist and plantar and dorsal flexors in the ankle (distal). We measured the strength of flexors and extensors in the neck and trunk. Scores: 6 strength scores were calculated by averaging the scale values per muscle group across directions of movement.
Range of motion (ROM) was measured using the Joint Alignment and Motion (JAM) scale, Which consists of a five-point scale of motion decrease (0 = no decrease, 1 = 1-5%, 2 = 6-25%, 3 = 26-75% and 4 = 76-100%). Each individual joint is scored according to an estimate of the percentage of normal motion, based on the knowledge of a joint's normal ROM (Bernbeck, 1983). The examiner visually estimates whether a joint's ROM is normal or limited (Spiegel et al., 1987). Inter- and intra-reliability are high (r = 0.91 and r = 0.85). In the upper extremities, range of flexion and abduction of the shoulder and of dorsal and palmar flexion of the wrist were determined. In the lower extremities, flexion, extension, abduction and adduction of the hip and plantar and dorsal flexion of the ankle were measured. Scores: 4 mean JAM scores were calculated by averaging the scale values of motion decrease per joint across directions of movement.
Muscle Tone was assessed using the Modified Ashworth Scale (MAS) (Bohannon and Smit, 1987), a very well known and reliable method consisting of a 5-point scale of tone increase (0 = no resistance, 1 = slight 'catch' when limb is moved, 2 = resistance in whole range of movement, 3 = strong increase with decreased range of movement, 4 = limb rigidly in flexion or extension). Kendall's tau correlation for inter-tester reliability was 0.85 (Bohannon and Smit, 1987). Scores: six mean scores were calculated by averaging the scale values of tone increase over movement directions (0 = normal; 1 and 2 = mild, 3 = moderate and 4 = severe impairment).

Within the activity domain (WHO, 2002) we administered three measures. Gross Motor Function Classification Scale (GMFCS) (Palisano et al. 2000). The GMFCS for children with cerebral palsy

is based on self-initiated movement with particular emphasis on sitting (truncal control) and walking. The manual provides separate descriptions for children in the age bands of 0-2 years, 2nd to 4th birthday, 4th to 6th birthday, 6 to 12 years and older children. Mobility is classified into 5 levels, taking age band into account (for children above the age of two years, level I = walks without restrictions, limitations in more advanced gross motor skills; level V = self-mobility is severely limited even with the use of assistive technology) (Table 1).

The Gross Motor Function Measure (GMFM-88) is a standardized clinical observational instrument designed to evaluate change in gross motor activities in children with cerebral palsy. It assesses how much of an activity a child can accomplish, rather than how well the activity is performed (Russell et al., 1989; Russell et al., 2002). The GMFM-88 (Russell et al., 2002) consists of 88 items grouped into five dimensions: lying and rolling (17 items), sitting (20 items), crawling and kneeling (14 items), standing (13 items), and walking, running and jumping (24 items). The items are scored on 4-point ordinal scales (0 = cannot initiate, 1 = initiates, but completes less than 10%, 2 = partially completes item (11-99%), 3 = completes item independently). Good reliability using intra-class correlation coefficient has been reported, the values varied from 0.87 to 0.99 (Russell et al., 1989; Russell et al., 2002). Score: percent scores for each of the five GMFM dimensions and a total GMFM percentage score are calculated. Higher scores mean better performance.

The Pediatric Evaluation of Disability Inventory (PEDI) (Haley et al., 1992; Custers et al., 2002) is a structured parent′s interview that assesses functional skills (capability) and caregiver assistance. It covers the domains of self-care (73 items), mobility (59 items) and social functioning (65 items). Functional skill is measured by counting the items in which the child is perceived as having mastery and competence. Caregiver assistance is measured by counting the daily functional activities in which the caregiver provides factual assistance. Although the instrument has been designed for children aged from 6 months to 7.5 years, the scaled scores offer

the opportunity to estimate skills in older children whose functional abilities lag behind those expected of 7.5 year-old healthy children (Feldman et al., 1990; Haley et al., 1992; Nichols and Case-Smith, 1996; Custers et al., 2002). As the aim of the present study was to map individual change rather than to compare with healthy peers, we used the scaled scores rather than the age-norms. The PEDI is sensitive to changes over time.
The Internal Consistency for PEDI scales has alpha scores ranging from 0.95 to 0.99 and a mean standard error of measurement of 0.09 (Haley et al., 1992; Custers et al., 2002).
The scaled scores provide estimates of the level of skill in each domain (0 = no measurable functional skill, 100 = intact functional skill; 0 = complete caregiver assistance, 100 = no caregiver assistance).

Independence refers to the ICF's participation domain. Restrictions, or difficulties when participating in social life (WHO, 2002) due to the effects of seizures, were assessed using the Hague Restrictions in Childhood Epilepsy Scale (HARCES) (Carpay et al., 1997), a 10-item scale that quantifies the parent's/caregiver's perception of epilepsy-related restrictions imposed on the child to avoid seizure-related injuries. The scale is based on the Liverpool Seizure Severity Scale (Scott et al., 2001) and is reliable in terms of test-retest validity and internal consistency (Carpay et al., 1997). Score: 10 (no restrictions) to 40 (maximal restrictions).

Data analysis

Descriptive statistics were calculated using SPSS software (version 11.01). Changes in seizure severity (HASS), IQ/DI values, muscle strength, muscle tone, range of motion, and restrictions (HARCES) were analyzed using non-parametric statistics (Wilcoxon signed ranks test). Data obtained before and after surgery were compared. Scores on the PEDI, GMFCS and GMFM were analysed using the Wilcoxon signed-ranks test and mean difference scores with 95% Confidence Interval (CI) were calculated. Analysis of vari-

ance (ANOVA) for repeated measures was also applied to analyse the scores on the GMFM and PEDI with Time (pre-, 6, 12 and 24 months post-surgery) as within-subject factor. A p-value of less than 0.05 was considered statistically significant.
Non-parametric Spearman's rho correlation was used to see whether differences in impairments between pre- and 2 years after surgery were related to differences in activities and social participation (restriction level) assessed over the same period, and to see whether decrease in caregiver assistance and increase in functional skills were correlated (PEDI).

Results

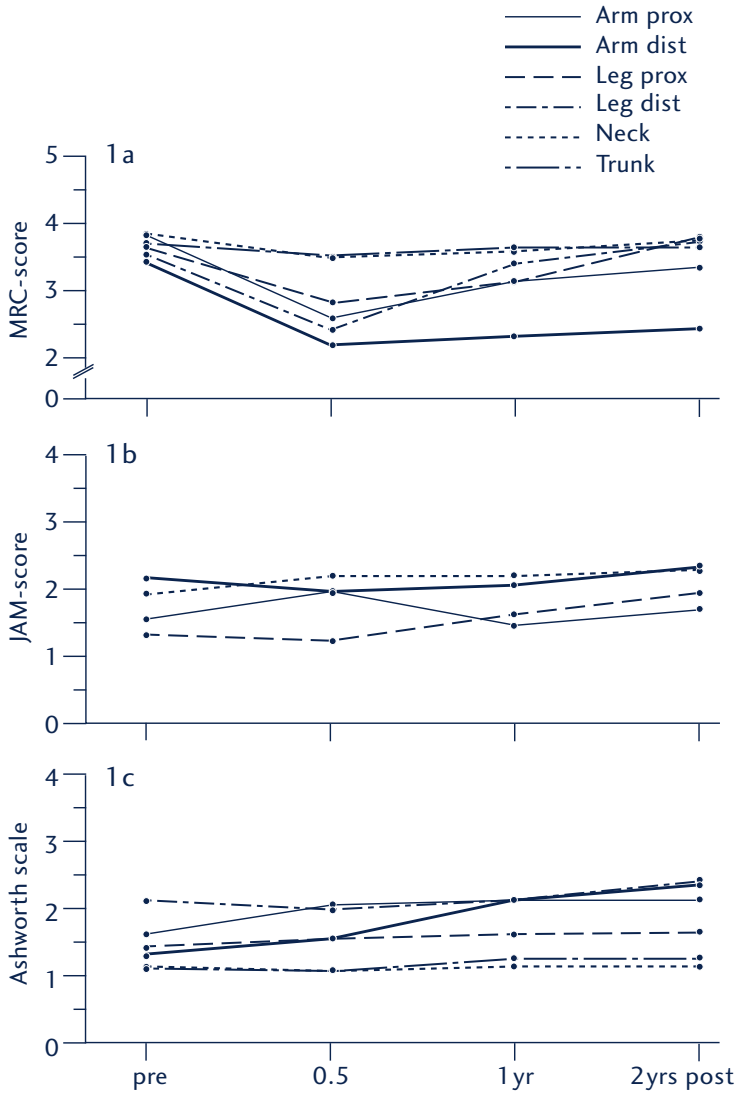
Impairments

Seizure frequency: In all children hemispherectomy had considerable effect in terms of seizure reduction: outcome classes I and III: 9 and 3 children (Engel et al., 1993) (Table 1).
Seizure severity: The group mean score on the HASS improved from 30.52 (SD 2.9, range 27-39) before surgery to 14.8 (SD 0.8, range 13-15) at six months post surgery ($p < 0.01$) and to 13.25 (SD 0.7, range 13-15 two years after surgery ($p < 0.01$). Two of the children with Engel III classification improved on the HASS to a score of 15 (almost maximally), the third one to a score of 13.
Cognition: Group-wise, mean IQ/DI changed statistically non-significantly from 58.7 (SD 9.8) before surgery to 60.3 (SD 9.7) two years thereafter.
Muscle strength (Fig.1a): At pre-surgical baseline, the muscle strength of the extremities on the affected side was mildly to moderately impaired. Six months after hemispherectomy, scores reflected post-surgical further significant decrease ($p < 0.05$) in the arm and, however statistically not significant, in the leg.
Two years after surgery, the affected leg had recovered to pre-surgery strength. In the arm however, strength remained very poor distally (MRC 2.4), whereas proximal strength recovered although

statistically not significantly. The pre-surgical mild impairment of strength in neck and trunk muscles did not change statistically significantly over time.
Range of motion (Fig.1b): Prior to surgery, all JAM scores were subnormal (range: 1.4-2.2), indicating a mild (5-25%) decrease of range of motion. JAM did not significantly change over the 2 years after surgery (range: 1.7-2.3).
Muscle Tone (Fig.1c): Prior to surgery, tone was mildly increased in the proximal and distal arm and in the proximal and distal leg. Six months after surgery, tone had increased, although statistically non-significantly, both proximally and distally in the paretic arm and remained so until 1 year after surgery.
At 24 months post-surgery muscle tone increased in the distal part of the arm ($p < 0.05$). In the hemiparetic leg and in neck and trunk no significant changes could be detected.

Figure 1

Muscle strength (a), range of motion (b) and tone (c) of the paretic side and in the neck and trunk at pre-surgical baseline and 0.5, 1 and 2 years post-surgery, averaged over 12 children. Muscle strength as MRC-score: 0-5, higher score indicates greater muscle strength (5 = normal). ROM as expressed in Joint Alignment and motion (JAM) score (0 = normal). Tone increase as Modified Ashworth Scale Score: 0-4, higher score means more spasticity (0=normal)



Activities

The GMFCS, turned out to have improved statically significantly at 2 years post-surgery in comparison to pre-surgery ($p < 0.05$) (Table 2). GMFM-88 (Figure 2A).
Gross motor function was already limited before surgery, especially in the children with developmental pathology (hemimegalencephaly). In children 6, 7 and 10 (two children with Rasmussen encephalitis and one with hemimegalencephaly), motor function deteriorated in the first 6 months after surgery, but 12 and 24 months after surgery the percentage of completed items on the GMFM had increased, as in all other children. Overall, group mean increase after two years was 20% in each of the five dimensions and in the total score of the GMFM. The change between pre-surgical and 2-years post-surgical data was statistically significant ($p < 0.05$) in all domains of activities (Table 2).

Table 2

Recovery in Gross Motor Function Classification Scale (GMFCS) and Gross Motor Function Measure (GMFM) of 12 children. Median ratings on GMFCS and mean ratings on GMFM before and 6, 12 and 24 months after surgery, averaged per subscale and compared with pre-surgical score

	Before surgery	After surgery [1, 2]		
		6 months	12 months	24 months
GMFCS	Median (SD)	Median (SD)	Median (SD)	Median (SD)
	3.0 (1.3)	3.0 (1.1)	3.0 (1.0)	2.0 (1.1)*
GMFM	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Lying, rolling	58.27 (33.5)	72.01 (27.6)**	76.27 (22.1)**	82.73 (18.6)**
Sitting	49.82 (38.9)	59.73 (36.8)*	73.18 (25.2)**	80.45 (18.4)**
Crawling, kneeling	40.01 (33.3)	36.09 (32.1)	48.36 (40.3)	59.00 (41.3)*
Standing	38.71 (37.0)	38.82 (37.4)	51.91 (38.9)*	55.91 (40.6)*
Walking, running, jumping	37.90 (33.0)	35.11 (33.0)	44.36 (38.6)	51.91 (42.8)*
Total score	43.55 (37.2)	49.80 (31.6)	58.80 (31.9)*	65.38 (31.9)*

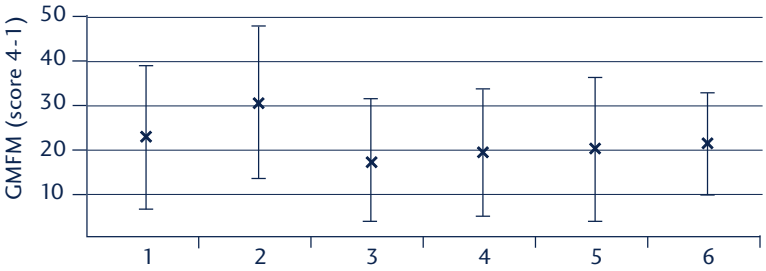
[1]Wilcoxon signed-ranks test for GMFCS

[2]Anova for Repeated Measures for GMFM

Statistically significant difference (* $p < 0.05$, ** $p < 0.01$) relative to presurgical scores

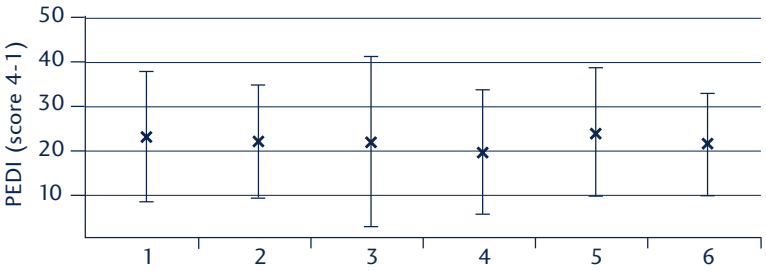
Figure 2

Improvement, averaged over 12 children in GMFM (A) and PEDI (B) over time (2 years post-surgery) (mean [x] and 95% CI)



2A

1 = lying and rolling
2 = sitting
3 = crawling and kneeling
4 = standing
5 = walking,running and jumping
6 = total score



2B

Functional Skills
1 = selfcare
2 = mobility
3 = soc.function

Caregiver Assistance
4 = selfcare
5 = mobility
6 = soc.function

PEDI

With respect to functional skills, a child with Rasmussen encephalitis (case 7) was the only one who, prior to surgery, scored maximally in all subscales and whose self-care worsened after surgery. All other children scored below 100 for self-care prior to the operation and increased their scores in the majority of skills after surgery (Appendix 1). When comparing the scores of the caregiver assistance scale with those obtained before surgery, assistance had

increased for four children (6, 7, 8 and 10) six months post-operatively (Appendix 2). In child 6 (Rasmussen encephalitis) assistance remained greater than prior to surgery, whereas child 7 recovered to maximal independence. Overall, group mean increase in the PEDI domains for functional skills and caregiver assistance was more than 20 points on the scale scores (Fig. 2B). The change between pre-surgical and 2-years post-surgical data was statistically significant ($p < 0.05$) in all domains of functional skill as well as of caregiver assistance (Table 3).

Table 3

Recovery in Functional skills and Caregiver assistance (PEDI) of 12 children. Mean ratings before and 6, 12 and 24 months after surgery averaged per subscale and compared with pre-surgical score

	Before surgery	After surgery[1]		
		6 months	12 months	24 months
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Functional skills				
Selfcare	48.53 (30.1)	57.83 (17.9)	62.97 (18.2)*	72.00 (21.1)**
Mobility	50.69 (35.6)	57.41 (35.7)	67.26 (26,1)**	73.84 (25.3)**
Social function	50.38 (33.4)	58.30 (32.2)*	70.26 (25.5)**	74.82 (23.5)**
Caregiver assistance				
Selfcare	43.63 (32.2)	48.03 (29.9)	59.77 (22.2)**	65.06 (21.0)**
Mobility	50.52 (36.1)	57.43 (31.1)*	65.91 (22.9)**	73.67 (20.5)**
Social function	52.19 (34.7)	55.10 (35.7)	64.66 (27.6)*	73.08 (21.1)**

[1]Anova for Repeated measures

Statistically significant difference (* $p < 0.05$, ** $p < 0.01$) relative to presurgical scores

Participation

Restrictions with respect to epilepsy

The mean score on the HARCES decreased significantly from 29 (range: 25-33) prior to surgery to 13 (range: 10-15) postsurgery ($p < 0.01$).

Relationships between measures.
With respect to the change between scores obtained two years after surgery to those obtained before the operation, no significant association was found between impairments (muscle tone, range of motion, muscle strength) and activities (GMFM) or functional skills (PEDI). A statistically significant correlation, however, existed on the PEDI between a decrease of caregiver assistance and an increase in functional skills: subscales self-care (r between 0.77 and 0.83, $p < 0.05$) and social functioning (r between 0.79 and 0.86, $p < 0.01$). Time of onset of epilepsy was not statistically significantly associated with functional outcome at 2 years post-surgery.

Discussion

To our knowledge, this is the first report of the outcome of hemispherectomy in children, which not only deals with seizures and motor impairments, but also focuses on changes in activities and social participation. Regarding the effects of hemispherectomy on seizure frequency this study is in agreement with previous favourable reports (Vining et al., 1996; Wyllie et al., 1998; Holthausen and Strobl, 1999; Chen et al., 2002; Devlin et al., 2003). In the two-year period following hemispherectomy, 9 out of 12 children had no seizures at all and the remaining 3 children had a reduction in seizure frequency of more than 75%.
The primary goal of epilepsy surgery is to relieve the patient of his/her epilepsy. Negative effects on function, however, make one unwilling to carry out such a drastic intervention as hemispherectomy. Based on the International Classification of Functioning Disability and Health (WHO, 2002), we present data on impairments in muscle tone, range of motion and muscle strength as well as on activities and social participation of 12 children.
At pre-surgical baseline all children had impairments. Muscle strength, range of motion and muscle tone of the arm and leg were mildly to moderately impaired on the affected side.
The different course between the arm and the leg is remarkable.

Proximally and distally in the contralateral arm, muscle tone increase was present when measured six months after hemispherectomy and assessments after 1 and 2 years showed a further increase. The increase affected the hand in particular, while muscle tone in the contralateral leg remained unchanged when measured 12 and 24 months after surgery. This increase in tone coincided with a significant decrease in muscle strength at six months after hemispherectomy and later on in the distal part of the arm, while strength in the muscles of the proximal part of arm and leg returned to preoperative values. The difference in course and degree of impairment between the upper and lower limb can be explained by several hypotheses. The upper limb and particularly the hand have become specialised to perform skilled hand movements and are more under control of the cortico-spinal pathways than the leg, while the locomotor task of the lower limbs is more under the control of the spinal neuronal circuits (Duysens and Van de Crommert, 1998; Dietz et al., 2002; Dietz, 2003). This could be a reason why the arm is more impaired than the leg after hemispherectomy. Dietz (2003) and others (Barbeau and Fung, 2001; Taub et al., 2002) suggest that the lumbosacral spinal cord contributes to the ability to walk in animals and humans. There is some indirect evidence that locomotion depends upon neuronal circuits (networks of interneurons) within the spinal cord which are thought to be a type of central pattern generator (CPG) (Dietz, 2003). Another explanation may be the following: preservation of the ability to ambulate may be due to contributions of sub-cortical regions of the nervous system. Several structures in the nervous system other than the cortex are known to support coordinated movement; these include the cerebellum and the mesencephalic locomotor region of the brain stem (Wieser et al., 1999), structures which are preserved after hemispherectomy. Thirdly, intact ipsilateral cortical pathways could be responsible for preserved locomotion. Wieser et al. (1999) described transfer of motor control of the left leg to the ipsilateral primary motor cortex in a patient with a right-sided surgical resection. He reasoned that both motor areas have the latent capacity to control motoricity bilaterally and that the ipsilateral capacity

is brought into function only after removal of the opposite hemisphere (Wieser et al., 1999). This line of reasoning does not, however, account for the fact that, apparently, transfer of motor control of the arm is less successful than that of the leg.
Holthausen et al. (1997, 1999) concluded that patients who are ambulatory prior to hemispherectomy remain so thereafter, whether the pathology was acquired or not. The present study, although on a small number of patients, corroborates and qualifies this conclusion. Children 1 to 8 (Table 1) walked before and after the hemispherectomy. These children suffered 'vascular pathology' and Rasmussen encephalitis. Children 10 and 11 were too young at the time of surgery to be ambulant; in the two-years follow-up they did not start walking. Children 9 and 12 were mentally very retarded, they walked neither before nor after surgery.

At least as important as impairments and their course is the issue of change in daily activities after hemispherectomy. A 'gold standard' reflecting 'true' change usually not being available for outcome studies, an increase of more than 10 scale points is considered to reflect a clinically relevant change (Iyer et al., 2003). The smallest change in PEDI scores during patient rehabilitation that was considered to be associated with a minimal but clinically important difference by physical therapists and other clinicians ranged from 6 to 15 points (mean =11.5, SD = 2.8) for all PEDI scales (Iyer et al., 2003). Hence, the increase of 20 points on the PEDI-scales may be taken to indicate a significant improvement in daily activities. The change in caregivers' assistance over time underscores this deduction, as the children need less assistance with self-care, mobility and social functioning.

The change on the HARCES shows indeed that freedom to participate in social life has come within reach of the children since the seizures have (largely) stopped.

On balance, impairments remain after hemispherectomy but apart from a slight deterioration in the first post-operative months they

improve to at least pre-surgical level, except for muscle strength and muscle tone in the distal part of the arm. Failing to recover of strength and tone does not, however, lead to further functional drawback. Impairments are only remotely associated with functional outcome as is underscored by the weak correlations that we found between the two. Neither the improvement in activities nor the positive changes in social participation can be understood from change in motor impairments. It is the relief from seizures that widens the scope of action for the children.

This study does not allow a detailed analysis of determinants of outcome, due to the small number of children and their heterogeneity in age, pathology and level of cognitive functioning. Differences in post-surgical outcome between children with congenital and those with acquired cerebral damage have previously been observed in the domains of general cognitive abilities and seizure freedom (Devlin el al., (2003), and in the domain of hand motor function (Holloway et al., 2000). We did not assess hand motor function with specific tests, because focus was directed to gross motor function and overall functional skills and degree of independence of the children. However, in terms of activities, outcome was poorer in the children with developmental pathology (children 10, 11 and 12) than in those with Rasmussen encephalitis and vascular pathology. It should be noted that the three patients with developmental pathology were younger than the children in both other pathology groups. Secondly, it has been suggested that children with better cognitive development prior to hemispherectomy improve more in motor function after surgery than children with weaker cognitive abilities (Devlin et al., 2003; Maehara et al., 2002). In our study three children (nos. 1, 2, 8) improved both in IQ/DI and in functional skills, but a significant relationship between level of pre-surgical intelligence and improvement in daily activities could not be found. It is obvious that these issues require further study in a larger group of patients with a longer period of follow-up.

Thirdly, time of onset of epilepsy was not associated with functional outcome. In manual muscle testing, a subjective bias can occur. We therefore compared muscle strength measurement scores as done by the neurologist and by the paediatric physical therapist. Results of neurological and physical therapy assessment of muscle strength testing using the MRC scale were found to be identical.
One might expect that the outcome of impairments in right-handed children with a right-sided hemispherectomy would be better than in right-handed children with a left-sided hemispherectomy because in the former children the dominant hemisphere was preserved. Verification of this expectation requires a larger number of children.

The present study emphasises that outcome has to be defined more extensively than in terms of seizure reduction, as discussed in a recent ILAE Commission report (Wieser et al., 2001).
Future research on the outcome of hemispherectomy should be structured according to the framework of the WHO-ICF classification, which enables one to evaluate not only impairments but also, and perhaps more importantly, activities and social participation.

Acknowledgements

We are grateful to the Phelps Stichting and the Johanna Children's Foundation for their financial support. Surgeons Prof. Dr. C.W.M. van Veelen and Dr. P.C. van Rijen operated on all patients. We thank dr. J. Pestman, department of Biostatistics, for his supervision in statistic analyses. We thank Mrs Brenda Vollers-King for correction of the English language and Mrs C. Tims-Polderman and Mrs J. Nuysink for their assistance in data-management.
We thank the Members of the Dutch Collaborative Epilepsy Surgery Programme: SEIN, Kempenhaeghe, Hans Bergerkliniek, Academic Hospitals (Utrecht, Maastricht, Amsterdam VU).

References

Barbeau H, Fung J. The role of rehabilitation in the recovery of walking in the neurological population. Curr Opin Neurol 2001;14:735-40.

Beckung E, Uvebrant P. Motor and sensory impairments in children with intractable epilepsy. Epilepsia 1993;34:924-29.

Beckung E, Uvebrant P, Hedström A, Rydenhag B. The effects of epilepsy surgery on the sensorimotor function of children. Dev Med Child Neurol 1994;36:893-901.

Beissner KL, Collins JE, Holmes H. Muscle force and range of motion as predictors of function in older adults. Phys Ther 2000;80:556-63.

Bernbeck R, Dahmen G. Kinderorthopedie. Stutgart: Georg Thieme verlag, 1983.

Bilbao A, Kennedy C, Chatterji S, Ustun B, Barquero JL, Barth JT. The ICF: Applications of the WHO model of functioning, disability and health to brain injury rehabilitation. NeuroRehabilitation 2003;18(3):239-50.

Bohannon RW, Smit MB. Interrater Reliability of a Modified Ashworth Scale of Muscle Spasticity. Phys Ther 1987;67(2):206-07.

Carpay JA, Vermeulen J, Stroink H, Brouwer OF, Peters AC, van Donselaar CA, et al. Disability due to restrictions in childhood epilepsy. Dev Med Child Neurol 1997;39(8):521-26.

Carpay JA. Childhood Epilepsy: Alternative Methods for Assessing Treatment Strategies and Outcome. (Thesis) Universiteit van Rotterdam, 1997.

Carson B, Javedan S, Freeman J, Vining EPG, Zuckerberg AL, Lauer JA, et al. Hemispherectomy: a hemidecortication approach and review of 52 cases. J of Neurosurgery 1996;84:903-11.

Chen LS, Wang N, Lin M. Seizure outcome of intractable partial epilepsy in children. Pediatric neurology 2002;26(4):282-7.

Custers JWH, van der Net J, Hoijtink H, Wassenberg-Severijnen JE, Vermeer A, Helders PJM. Discriminative validity of the Dutch Pediatric Evaluation of Disability Inventory. Arch Phys Med Rehabil 2002;83:1437-41.

Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003;126:556-66.

Dietz V, Müller R, Colombo G. Locomotor activity in spinal man: significance of afferent input from joint load receptors. Brain 2002;125:226-34.

Dietz V. Spinal cord pattern generators for locomotion. [Review]. Clin Neurophysiol 2003; 114(8):1379-89.

Duysens J, van de Crommert HWAA. Neural control of locomotion. Part 1: the central pattern generator from cats to humans. [Review]. Gait Posture 1998;7:131-141.

Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In Engel JJ, ed. Surgical treatment of the epilepsies. 2nd ed. New York: Raven Press, 1993. p. 609-21.

Feldman AB, Haley SM, Coryell J. Concurrent and construct validity of the Pediatric Evaluation of Disability Inventory. Phys Ther 1990;70:602-10.

Graveline CJ, Mikulis DJ, Crawley AP, Hwang PA. Regionalized sensorimotor plasticity after hemispherectomy fMRI evaluation. Pediatr Neurol 1998;19:337-42.

Graveline C, Hwang P, Bone G, Shikolka C, Wade S, Crawley A., Mikulis D. Evaluation of gross an fine motor functions in children with hemidecortication: Predictors of outcomes and timing of surgery. J of Child Neurology 1999;14:304-15.

Graveline C, Young N., Hwang P. Disability evaluation in children with hemidecorticectomy: Use of the activity scales for kids and the Pediatric Evaluation Disability Inventory. J of Child Neurology 2000;15:7-14.

Haley SM, Coster WJ, Ludlow LH. Pediatric Evaluation of Disability Inventory (PEDI), Boston: M.A. New England Medical Center, 1992.

Hislop HJ, Montgomery J. Daniels and Worthingham's Muscle testing Techniques of Manual Examination. Philadelphia: WB Saunders Company, 2002.

Holloway V, Gadian DG, Vargha-Khadem F, Porter DA, Boyd SG, Connoly A. The reorganization of sensorimotor function in children after hemispherectomy. A functional MRI and somatosensory evoked potential study. Brain 2000;123 Pt 12:2432-44.

Holthausen H, Strobl K, Pieper T, Teixeira VA, Oppel F. Prediction of motor function post hemispherectomy, In Tuxhorn I, Holthausen H, Boenigk. Paediatric epilepsy syndromes and their surgical treatment. London: John Libbey & Company Ltd, 1997. p. 785-98.

Holthausen H, Strobl K. Motor function before and after hemispherectomy. In: Stefan H, Andermann F, Chauval P, Shorvon SD, eds. Advances in Neurology, vol. 81 Plasticity in epilepsy: Dynamic aspects of brain function. Eds Lippincott, Williams and Wilkins, 1999. p. 201-18.

Iyer LV, Haley SM, Watkins MP, Dumas HM. Establishing minimal clinically important differences for scores on the pediatric evaluation of disability inventory for inpatient rehabilitation. Phys Ther 2003;83(10):888-98.

Maehara T, Shimizu H, Kawai K, Shigetomo R, Tamagawa K, Yamada T, et al. Postoperative development of children after hemispherectomy. Brain Dev 2002;24(3):155-60.

Medical Research Council. Aids to the investigation of peripheral nerve injuries. War memorandum 2e ed. London: HMSO, 1943.

Nichols DS, Case-Smith J. Reliability and validity of the Pediatric Evaluation of Disability Inventory. Ped Phys Ther 1996;8:15-24.

Russell DJ, Rosenbaum PL, Cadman DT. The Gross Motor Function Measure: a mean to evaluate the effects of physical therapy. Dev Med Child Neurol 1989;31:341-52.

Russell DJ, Rosenbaum PL, Avery LM, Lane M. GMFM Gross Motor Function Measure, (GMFM-66 & GMFM-88) User's Manual. Cambridge: Cambridge University Press. 2002.

Rutten GJ, Ramsey NF, van Rijen PC, Franssen H, van Veelen CW. Interhemispheric reorganization of motor hand function to the primary motor cortex predicted with functional magnetic resonance imaging and transcranial magnetic stimulation. J Child Neurol 2002; 17(4):292-7.

Scott-Lennox J, Bryant-Comstock L, Lennox R, Baker GA. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. Epilepsy Res 2001;44(1):53-63.

Spiegel TM, Spiegel JS and Paulus HE. The joint Alignment and Motion Scale; A Simple measure of Joint deformity in Patients with Rheumatoid Arthritis. The J of Rheum 1987;14:887-93.

Staudt M, Pieper T, Grodd W, Winkler P, Holthausen H, Krägeloh-Mann I. Functional MRI in a 6-year-old boy with unilateral cortical malformation: concordant representation of both hands in the unaffected hemisphere. Neuropediatrics 2001;32(3):159-61.

Staudt M, Grodd W, Gerloff C, Erb M, Stitz J, Krägeloh-Mann I. Two types of ipsilateral reorganization in congenital hemiparesis: a TMS and fMRI study. Brain 2002;125(Pt 10): 2222-37.

Steiner WA, Ryser L, Huber E. Use of the ICF model as a clinical problem-solving tool in physical therapy and rehabilitation medicine. Phys Ther 2002;82:1098-107.

Stucki G, Ewert T, Cieza A. Value and application of the ICF in rehabilitation medicine. Disabil Rehabil 2003;25:628-34.

Taub E, Gitendra U, Elbert T. New treatments in neurorehabilitation founded on basic research. Nat Rev Neurosci 2002;3:228-36.

Vining EP, Freeman JM, Pillas DJ, Uematsu S, Carson BS, Brandt J, et al. Why would you remove half a brain? The outcome of 58 children after hemispherectomy-the Johns Hopkins experience: 1968 to 1996. Pediatrics 1997;100:163-71.

Wieser HG, Henke K, Zumsteg D. Activation of the left motor cortex during left leg movements after right central resection. J Neurol Neurosurg Psychiatry 1999;67:487-91.

Wieser HG, Blume WT, Fish D, Goldensohn E, Hufnagel A, King D, et al. ILEA Commission Report. Proposol for a new classifiacation of outcome with respect to epileptic seizures following epilepsy surgery. Epilepsia 2001;42:282-86.

Wild KR von. New development of functional neurorehabilitation in neurosurgery. Acta Neurochir Suppl 2003;87:43-47.

Wyllie E, Comair YG, Kotagal P, Bulacio J, Bingaman W, Ruggieri P. Seizure outcome after epilepsy surgery in children and adolescents. Ann Neurology 1998;44:40-48.

World Health Organization (WHO) International Classification of Functioning, Disability and Health, Geneva: WHO, 2002. Available on the WHO Internet site, 2002. http://www.who.int/classification/icf.

Appendix 1

Limitations in Functional skills, as measured by PEDI (scale score) of the 12 children: pre-surgery, 6 months, 1 and 2 years post-surgery (Self-care, Mobility, Social function)

		Age	Self-care				Mobility				Social finction			
		(yr) at	Pre–	6 mo	1 yr	2 yr	Pre–	6 mo	1 yr	2 yr	Pre-	6 mo	1 yr	2 yr
Patient	Aetiology	surgery	surg	post	post	post	surg	post	post	post	surg	post	post	post
1	Vascular	4.4	62.5	63.9	69.1	74.7	67.4	85.2	89.2	94.2	53.2	56.0	62.3	66.2
2	Vascular	6.4	61.8	64.6	67.6	78.2	68.7	82.5	85.2	92.5	55.4	67.4	89.1	96.2
3	Vascular	11.1	79.0	79.0	81.4	100	100	100	100	100	96.3	100	100	100
4	SWS	7.6	54.9	54.9	59.9	71.7	63.9	59.9	79.8	89.2	53.7	53.9	59.2	70.8
5	Rasmussen	8.5	11.8	48.2	58.0	69.1	11.4	26.1	44.3	68.7	21.6	50.5	67.4	85.2
6	Rasmussen	3.0	52.4	37.0	58.6	58.6	65.0	25.4	69.1	70.1	53.7	47.3	68.4	57.2
7	Rasmussen	11.5	100	81.4	93.0	93.0	100	89.2	89.2	100	100	100	100	100
8	Rasmussen	12.1	49.6	56.2	75.9	100	49.7	11.4	82.5	79.8	70.8	56.0	100	100
9	HHE	3.9	42.9	46.7	48.9	49.6	30.6	35.9	37.1	42.4	43.1	45.0	47.3	46.2
10	Hem	0.6	39.0	38.7	42.9	48.2	32.4	30.4	35.9	40.3	40.2	38.7	47.3	53.7
11	Hem	0.3	18.7	21.4	35.1	45.2	3.2	6.1	15.2	27.3	2.1	3.1	21.6	32.5
12	Hem	1.6	11.8	33.0	38.0	47.2	0.0	20.9	33.4	42.8	0.0	14.9	30.0	39.2
Mean		5.3	48.7	53.4	61.8	69.6	49.3	47.7	63.4	70.6	49.2	52.7	66.1	70.6

Abbreviations: Age yr of surgery = age in years at the time of the operation, Hem = Hemimegalencephaly, HHE= Hemiplegia, hemi-convulsions, epilepsy syndrome, Pedi = Pediatric Evaluation of Disability Inventory, Pre-surg = before surgery, post = after surgery. Rasmussen = Rasmussen's encephalitis, SWS = Sturge-Weber syndrome, Vascular = vascular pathology.

Appendix 2

Caregiver assistance as measured by PEDI (scale score) of the 12 children pre-surgery, 6 months, 1 and 2 years post-surgery (Self-care, Mobility and Social function)

		Age	Self-care				Mobility				Social function			
		(yr) at	Pre–	6 mo	1 yr	2 yr	Pre–	6 mo	1 yr	2 yr	Pre-	6 mo	1 yr	2 yr
Patient	Aetiology	surgery	surg	post	post	post	surg	post	post	post	surg	post	post	post
1	Vascular	4.4	53.4	59	72.7	74.5	63.3	70.5	75.2	89.4	82.9	57.3	67.6	89.9
2	Vascular	6.4	57.9	63.4	62.2	75.3	65	72.7	75.2	86.4	63.3	67.6	70	78.2
3	Vascular	11.1	74.5	74.5	79.5	89.7	100	100	100	100	75.3	100	100	100
4	SWS	7.6	47.3	53.4	54.6	59	72.7	68.5	75.2	78.3	65.4	61.5	63.3	67.6
5	Rasmussen	8.5	20.1	41.1	54.6	63.4	20.3	31.9	49.8	61.8	26.6	39	53.1	67.6
6	Rasmussen	3.0	65.7	32.3	32.3	55.7	70.5	20.5	28.5	89.4	68.4	20.4	40.4	82.9
7	Rasmussen	11.5	100	89.7	100	100	100	89.4	89.4	100	100	100	100	100
8	Rasmussen	12.1	57.9	51.1	72.7	76.7	54.8	34.5	78.3	82.7	72.5	67.6	89.9	89.9
9	HHE	3.9	25.4	32.3	35	35	39	42.7	44.3	45.8	35.9	42.9	48.5	50.9
10	Hem	0.6	37.4	33.4	37.2	47.3	23	21.2	28.5	45.8	38.5	35.7	42.9	55.3
11	Hem	0.3	0	0	11.6	28.5	0	0	0	8.4	0	0	20.4	28.5
12	Hem	1.6	0	0	29.2	35.7	0	11.7	42.7	48.5	0	0	11.3	21.1
Mean		5.3	44.9	44.2	53.5	61.7	50.7	46.9	57.3	69.7	52.4	49.3	57.3	69.3

Abbreviations: Age yr of surgery = age in years at the time of the operation, Hem = Hemimegalencephaly, HHE= Hemiplegia, hemi-convulsions, epilepsy syndrome, Pedi = Pediatric Evaluation of Disability Inventory, Pre-surg = before surgery, post = after surgery. Rasmussen = Rasmussen's encephalitis, SWS = Sturge-Weber syndrome, Vascular = vascular pathology.

Chapter 3

Health-related quality of life and self-perceived competence of children assessed before and up to two years after epilepsy surgery

R. van Empelen[1*]
A. Jennekens-Schinkel[2*]
P.C. van Rijen[3*]
P.J.M. Helders[1]
O. van Nieuwenhuizen[4*]

On behalf of the Dutch Collaborative Epilepsy Surgery Programme.

1 Department of Paediatric Physical Therapy and Exercise Physiology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
NetChild, Network for Childhood Disability Research in The Netherlands
2 Department of Neuropsychology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
3 Department of Neurosurgery, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
4 Department of Child Neurology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.

* Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands.

Epilepsia 2005; 46: 258-71.

Summary

Purpose: To measure outcome of epilepsy surgery in terms of health-related quality of life and self-perceived competence of children and adolescents.
Methods: Prospective longitudinal follow-up study of 21 patients (aged 6.2 to 16.8 years). Frequency and severity of seizures and epilepsy-related restrictions, health-related quality of life and self-perceived competence were rated before and 6, 12 and 24 months after epilepsy surgery. Data were analysed non-parametrically and using ANOVA for repeated measures.
Results: Group-wise, seizure parameters had almost normalised 6 months after surgery (p′s < 0.001) and remained so. Two years after surgery, 15 patients (72%) were free of seizures. At the first post-surgical assessment, parents and children evaluated the frequency of activities as improved and that of seizures as diminished (p′s < 0.05). Parents evaluated their children as having positive emotions more frequently ($p < 0.05$). Children started to feel better about seizure variables in the second year post-surgery. Two years after surgery, children perceived themselves as being socially more competent and having greater self-worth (p′s 0.05). In the adolescent group, several aspects of self-perceived competence improved shortly after surgery (p′s < 0.05), while two years after surgery athletic competence and romance had improved (p′s < 0.05).
Conclusion: In children and adolescents, epilepsy surgery sets the stage for improvement in HrQoL and in competence to participate in social and societal domains. Most improvement occurs in the first 6 months after surgery.

Introduction

In The Netherlands, 40 children per year are presented to the Dutch Collaborative Epilepsy Surgery Programme (DuCESP) of whom 10-15 are accepted for surgery. In children, the outcome of epilepsy surgery has predominantly been measured in terms of seizure reduction and motor and cognitive impairments. Changes in the subjectively experienced burden of epilepsy are being increasingly recognised as essential outcome parameters (Baker et al., 1998; Ronen et al., 2003). In order to better advise parents and their children with medically intractable epilepsy, one has to be informed about changes in the limitations and restrictions with which the child will have to cope after surgery.

Medically intractable epilepsy has repercussions that by far transgress the medical domain. Because of their unpredictability and their behavioural manifestations, seizures signify a loss of control which, if recurring in children, may foster a feeling of uncertainty (Oostrom et al., 2000; Ferguson et al., 2000). Feelings of not being in control of one's life are likely to be reinforced both by the necessity of anti-epileptic-drug (AED)-use to prevent seizures and by the restrictions in activities of daily life that are imposed on children who are unaware of their seizures and, hence, of the cause of the restrictions. Furthermore, the behavioural concomitants of seizures may occur at school, in the playground or in other group situations, and be perceived by others, be they adults or peers. Epilepsy is different from other disorders. Healthy classmates will tend to attribute more shame to a child for having disrupted group activities because of a seizure than because of another condition (Oostrom et al., 2000). Hence, it is not surprising that the prevalence of psychosocial problems is twice as high in children with epilepsy when compared with healthy children (MacLeod et al., 2003). Children with pharmaco-resistant epilepsy belong to the segment of the epilepsy population that is characterised by manifold limitations and often maximal restrictions (WHO, 2002).

In order to gain a clear understanding of such adversities, clinimetrists designed questionnaires to assess health-related quality

of life, defined in terms of mental, physical and social functioning (Selai et al., 2000; Markand et al., 2000; Ronen et al., 2003). The concept encompasses evaluation of health, fitness, life satisfaction and well-being and is inevitably based on subjective feelings and attitudes (Bowling & Normand, 1998). Quality of life is investigated by means of generic or disease-specific questionnaires or by a dual approach. Generic instruments provide broad measures of HrQoL, irrespective of and often insensitive to the adversities brought about by the illness of the child. Disease-specific questionnaires inventory data relevant to the illness and may be too narrow. The dual approach assesses generic (WHO, 2002; Wallander et al., 2001) as well as disease-specific areas (Ronen et al., 2003; Gilliam, 2003). The How Are You (HAY) (Bruil 1999) is a well-researched questionnaire adapted to life in The Netherlands that is designed for children with epilepsy, juvenile rheumatoid diseases, asthma and diabetes mellitus, diseases with quite high prevalences in childhood. The version for children with epilepsy covers generic and epilepsy-specific areas. The items originate from interviews with children and their parents and from experts. Another strong point of the HAY is that it allows one to study the child's HrQoL as perceived by the parents but also as perceived by the child herself/himself, a perspective which until now has been under-explored (Ronen et al., 2003). Relationships between parameters of epilepsy and of HrQoL are weak, at least in studies of adults (Birbeck et al., 2002), but remain to be investigated in outcome studies of children who underwent epilepsy surgery.

As the ultimate aim of epilepsy surgery is to improve autonomy of the patient, indices of outcome may also be found in the child's perceptions of the competence with which she/he adapts. Self-perceived competence denotes the evaluations of self-worth that are part of the self-concept. The latter is defined as the body of ideas and notions that a person has about herself/himself (Harter, 1998; Thill et al., 2003). Self-perceived competence in childhood is a good predictor of later fulfilment of social roles. Children derive self-perceptions of competence particularly from motor agility and physical fitness (Skinner and Piek, 2001; Bouffard et al., 2003).

Children with motor deficits but also children with epilepsy perceive their competence as being poorer than healthy children do (Ziegler, 2002). No data exist on self-perceived competence of children who are (to be) operated on for intractable epilepsy.

The present study addresses the following question:
What is the impact of epilepsy surgery on 1) HrQoL in the perception of the children themselves and of the parents and on 2) Self-perceived competence in the opinion of the children?
The Institutional Review Board (IRE) approved the study.

Patients

Of the 52 children who underwent epilepsy surgery in the Wilhelmina Children's Hospital between 1999 and 2001, 21 (4 boys, 17 girls; 8 children [6-12 years], 13 adolescents [>12 years]) fulfilled the age requirements of the questionnaires (Harter, 1998; Bruil, 1999) and were included. Age was the only reason for exclusion. All children were living with their parents. The parents and, if over 12 years of age, the children themselves gave informed written consent. The surgical procedures consisted of temporal resection (n=10), extra-temporal resection (n=5) and hemispherectomy (n=6). Mean age at surgery was 11.2 (range 6.2 to 16.8) years. Mean age at onset of epilepsy was 5.2 (range: 6 months to 14.1) years. Mean time between onset and surgery was 5.9 (range: 1.1 to 13.6) years (Table 1A). Surgical outcome was classified using Engel's modified classification scheme (Engel, 1993). All patients used at least two AED's. Anticonvulsant medication was the same in the pre- and post-surgery period, as it is the strategy of the Dutch Collaborative Epilepsy Surgery Programme to taper off the AED's two years after surgery. Median full scale Intelligence Quotient (IQ) or equivalent was 86 (range 52-123) prior to surgery and 86 (range 53-124) 24 months after surgery (Table 1B). IQ's were determined using instruments validated for Dutch children (WISC-R and WPPSI-R or equivalent instruments [mean = 100; sd = 15]).

Table 1A

Demographic (sex, age at onset and at surgery), epilepsy data (time between onset and surgery, type of resection, aetiology)

Demographic data				**Epilepsy data**		
Nr	Sex	Age at onset of epilepsy (yrs;mo)	Age at surgery (yrs;mo)	Time between onset and surgery (yrs)	Type of resection	Aetiology
1	M	0.10	14.4	13.6	right parietal	Cortical Dysplasia
2	M	0.11	12.6	11.7	right temporal	MTS
3	M	1.7	13.11	12.4	right central	Cortical Dysplasia
4	F	14.1	16.3	2.2	right temporal	DNET
5	F	4.8	10.11	6.3	left frontal	Gangliocytoma
6	F	7.7	14.6	6.1	right parietal	Astrocytoma
7	F	6.10	10.6	3.8	right temporal	MTS
8	F	8.5	10.8	2.3	right temporal	Astrocytoma
9	F	5.1	7.9	2.8	right frontal	DNET
10	M	1.1	6.2	5.1	left temporal	MTS
11	F	8.0	12.1	4.1	left temporal	DNET
12	F	11.2	16.8	5.6	left temporal	DNET
13	F	6.2	15.1	8.1	left temporal	DNET
14	F	2.3	6.5	4.2	right temporal	Tuberous Sclerosis
15	F	6.9	11.1	4.4	right temporal	Cortical Dysplasia
16	F	0.1	6.4	5.3	right hemisphere	Vascular
17	F	1.1	11.10	10.9	left hemisphere	Vascular
18	F	0.5	7.6	7.1	left hemisphere	SWS
19	F	5.2	8.5	3.3	right hemisphere	Rasmussen
20	F	7.2	11.5	4.3	left hemisphere	Rasmussen
21	M	11.0	12.1	1.1	left hemisphere	Rasmussen

Abbreviations: F = Female, M = Male,

DNET = Dysembryoplastic NeuroEpithelioma Tumour, MTS = Mesial Temporal Sclerosis, Rasmussen = Rasmussen's encephalitis, SWS = Sturge-Weber syndrome.

Table 1B

Outcome at the four assessments (seizure classification, seizure severity, seizure-related restrictions and cognition before and 2 years after surgery of 21 children)

Outcomes of Epilepsy and of Cognition											
Nr	Seizures 2 years after surgery*	Seizure severity (HASS)**				Seizure-related restrictions (HARCES)***				Intelligence Quotient (IQ)/ Developmental Index (DI)	
		Pre	Post 6	Post 12	Post 24	Pre	Post 6	Post 12	Post 24	Pre	Post 24
1	I	37	13	13	13	23	10	10	10	85	86
2	II	33	13	13	13	33	18	10	10	107	106
3	II	36	26	30	38	18	18	21	24	100	96
4	I	31	13	13	13	28	10	10	10	99	98
5	II	35	28	27	31	30	21	15	16	63	74
6	I	18	13	13	13	15	10	10	10	123	124
7	I	31	13	13	13	23	10	10	10	94	96
8	III	34	23	23	22	33	20	10	17	121	102
9	II	38	23	13	13	32	14	14	10	71	93
10	I	28	13	13	13	16	11	10	11	90	83
11	I	28	18	17	13	22	14	10	10	106	110
12	I	39	13	13	13	30	10	10	10	85	86
13	I	33	13	13	13	25	10	10	10	114	114
14	I	33	13	13	13	18	10	10	10	83	78
15	I	33	13	13	13	33	13	10	10	89	91
16	I	34	13	13	13	33	14	10	10	60	68
17	I	32	13	13	13	32	15	10	10	52	54
18	I	34	13	13	13	23	15	10	10	54	53
19	I	37	13	13	13	23	10	10	10	67	56
20	III	35	28	27	31	30	21	15	16	67	64
21	I	34	13	13	13	33	20	10	10	69	77
	Total mean	32	15	16	17	26	14	11	11	86	86

*Engel classification (I-IV)** HASS (range 13-52; 13 = no problems)

***HARCES (range 10-40; 10 = no restrictions)

Methods

Patients were assessed using a standard protocol with fixed intervals: 1- 3 months before surgery, and 6, 12 and 24 months after surgery. Assessments took place in the outpatient departments of neurology, paediatric physical therapy and neuropsychology of the Wilhelmina Children's Hospital.

Instruments

Seizure frequency outcome was determined by the child neurologist (OvN) using Engel et al.,'s (1993) modified classification. Class I = free from seizures or residual auras, Class II = child experienced intermittent, infrequent seizures or relapsed after a significant seizure-free period and Class III = worthwhile improvement (>75% reduction in seizure frequency). Children who experienced less than 75% reduction in seizure frequency were classified as Engel Class IV.

Seizure severity as perceived by the parent or caregiver was quantified using the Hague Seizure Severity Scale (HASS) which inventories by means of four-point scales 13 ictal and postictal problems that may have been encountered in the three previous months (Carpay et al., 1997). The scale is based on the Liverpool Seizure Severity Scale (Baker, 1995; Scott-Lennox et al., 2001). The HASS is reliable in terms of test-retest stability and internal consistency (Carpay et al., 1997). Scores: 13 (no seizures) to 52 (maximal seizure severity).

Epilepsy-related restrictions were assessed using the Hague Restrictions in Epilepsy Scale (HARCES). The 10 items of this parent-rated scale estimate the freedom or epilepsy-related curtailment of freedom with which the child is allowed to take part in activities such as swimming, riding a bicycle, staying elsewhere overnight, and participating in physical education. Two items address overall restrictions, viz. amount of special supervision in and special arrangements for daily activities. Internal reliability (r = 0.89), and test-retest stability (r = 0.93) are good (Carpay et al., 1997). Scores

range from 10 (no restrictions) to 40 (severe restrictions).
HrQoL is inventoried by the HAY (How Are You) questionnaire, using the version for children with epilepsy and for their parents (Bruil, 1999). The children's questionnaire (HAY-C) consists of 125 items that are rated by means of four-point scales. The instrument purports to obtain the child's and parent's personal evaluation of the child's actual life by assessing both the importance attributed to activities or events and the satisfaction in the performance of these activities.

The generic part assesses the child's functioning in areas of daily life that are relevant for all children. It includes five dimensions: physical activities, cognitive tasks, social activities, general physical complaints and positive emotions. The items are rated in terms of how often the responder estimates the activities to have occurred in the past seven days. With respect to the first three dimensions the child is also asked how well he himself feels he can perform these activities (quality of execution). For four dimensions, the child also rates his feelings, i.e., how important these activities or events are for him (e.g. whether and to what degree it bothered him that he had a hard time riding a bike). The chronic illness part consists of two dimensions: concerns related to having an illness and feeling inferior because of having an illness. The epilepsy-related part refers to specific signs of epilepsy and their management and physical complaints related to epilepsy. It inventories how often the signs and/or their treatment occur and how the child feels about them. For rating his/her feelings the child is provided with visual analogs (line drawings of faces with expressions ranging from very sad to happy). Patients 17 and 18 were the two children who had an IQ < 55 and to whom the questions of the HAY about frequency and quality were read. The epilepsy version of the HAY-C is valid and reliable (Cronbach's alphas .77 to .86) (Bruil, 1999).
The parent questionnaire (HAY-P) asks the parents to rate their perception of the frequency and quality of daily activities performed by their child and to rate their own feelings related to the problems that occur for their child. The subscales are similar to those of the HAY-C. The HAY-P shows acceptable reproducibility,

supportive evidence for construct validity, and good responsiveness (Coq et al., 2000).
As outlined by the designer (Bruil, 1999), the HAY-C and HAY-P ratings are recoded so that lower scores correspond with worse evaluations, item scores are summated and averaged per subscale (range 1-4).
Self-perceived competence is measured using the Dutch adaptation of the Harter Self Perception Profile for Children (SPP-C) (Harter, 1988; Veerman et al., 1997) or the Self Perception Profile for Adolescents (SPP-A) (Wickstrom, 1995; Aasland and Diseth, 1999). Both scales assess a child's sense of competence in cognitive, social and physical domains and yield a measure of general self-worth. The SPP-C, designed for children in the age range 8-12 years, consists of 36 items distributed over five domain-specific subscales and one global self-worth subscale. The domain-specific subscales are scholastic competence, social acceptance, athletic competence, physical appearance and behavioural conduct. Adolescents (age range 12 to 18 years) fill out the SPP-A, which consists of 40 items distributed over the five domain-specific subscales of the SPP-C plus the subscales of romance and friendships. Each item of both SPP-C and SPP-A describes two children/adolescents with opposite characteristics of competence. To offset the tendency towards a socially desirable response, the responder is first asked to decide which kind of child she or he is most like: the one/child described on the right or on the left of the page. Then, the responder decides whether the description of the selected child is 'sort of true' or 'really true' for her/him. Items are scored on four-point scales (1 = low perceived competence, 4 = high perceived competence). Research has demonstrated a high internal consistency and test-retest reliability for each of the subscales (Thill et al., 2003; Schuman et al., 1999). For each subscale, sumscores are averaged. Scores in the normal population vary from 2.8 to 3.1 for the different subscales (Veerman, 1997;Veerman et al., 1997; Aasland and Diseth, 1999).

Data analysis

The HASS, HARCES and IQ scores were not normally distributed (Kolmogorov-Smirnov test), therefore change was analysed using non-parametric statistics (Wilcoxon's signed-rank test). Analysis of variance for repeated measurements (ANOVA-RM) was applied to the scores of HAY and SPP, with time (pre-, 6, 12 and 24 months post-surgery) as within-subject factor, with post hoc testing to compare between sessions, and adjusting for multiple comparison by using least significant difference (LSD).
A two-sided p-value of 0.05 or less was considered statistically significant. The SPSS software version 11.0 was used for analysis of data.

Results

Seizure frequency: Considerable seizure reduction was measured at 6 months postsurgery and this effect remained, so that two years after surgery, seizure frequency was classified as Engel class I in 10 children, class II in four and class III in one child (Table 1B).
Seizure severity (HASS) and epilepsy-related restrictions (HARCES): Median score on the HASS improved from 33 (range 18-39) before surgery to 13 (range 13-28) at six months post-surgery. The improvement was statistically significant ($p < 0.001$); the seizure severity remained stable thereafter, apart from a negative tendency in two children (# 3, 5).
On the HARCES the median score improved from 28 (range 15-33) to 13 (range 10-21) at six months post surgery. The improvement was statistically significant ($p < 0.001$); seizure-related restrictions remained stable thereafter, apart from a negative tendency in child # 3 (Table 1B).

Health-related QoL (HAY)

HAY-C (Table 2): The ratings prior to operation were compared with reference data obtained in healthy children (Bruil, 1999). The children evaluated the quality of their physical, cognitive and social activities as being statistically significantly less than normal and their physical condition bothered them more ($p's < 0.05$). Their feelings about epilepsy and its treatment were relatively poor. Postoperative assessment of the children at 6 months revealed improvement in the evaluations of both the frequency (physical activities $p < 0.05$, social activities $p < 0.01$) and the quality of their activities (physical, cognitive and social activities $p's < 0.05$). With respect to cognitive tasks the children's evaluations of frequency (not changed) and quality (sharing in the improvement) diverged. Their feelings of inferiority had diminished ($p = 0.05$). With respect to the epilepsy, the children evaluated the frequency of seizures and of epilepsy treatment as having decreased ($p < 0.05$). There was no change in how bothered they felt about physical activities and general physical condition. At 12 months, no statistically significant further change had occurred. At 24 months, however, the children felt significantly less bothered about the seizures; when compared with the data obtained prior to surgery, most of the evaluations of frequency (cognitive and social activities $p < 0.05$) and quality (cognitive and social activities $p's < 0.05$) of activities, as well as feelings about seizures ($p = 0.001$) and about epilepsy treatment ($p < 0.05$) had improved significantly. Similarly, the children evaluated the frequency of concerns and feelings of inferiority because of having a chronic illness as having decreased ($p's \leq 0.05$). No significant differences were found between children (6-12 years) and adolescents (> 12 years).

Table 2

Health-related Quality of Life (How Are you questionnaire for Children [HAY-C]). Reference data (n=134), data (averaged per sub-scale) obtained before and 6, 12 and 24 months after epilepsy surgery in 21 children who underwent epilepsy surgery and comparison between the assessments

	Healthy-Reference Group Mean (SD)	Pre-operative Mean (SD) [2]	Follow up 6 months Mean (SD)	12 months Mean (SD)	24 months Mean (SD)	Difference[1] pre-6m p	6-12m p	12-24m p	pre-24m p
Generic part									
Estimated frequency of									
Physical activities	2.60 (0.49)	2.3 (0.5)	2.9 (0.6)	2.8 (0.3)	2.8 (0.6)	0.03*	0.82	0.87	0.10
Cognitive tasks	3.07 (0.58)	2.6 (0.7)	2.8 (0.8)	3.1 (0.4)	3.4 (0.5)	0.41	0.37	0.30	0.02*
Social activities	2.37 (0.48)	2.1 (0.4)	2.6 (0.4)	2.7 (0.9)	2.9 (0.9)	0.001**	0.92	0.15	0.04*
Physical complaints	3.47 (0.51)	2.8 (0.8)	3.6 (0.4)	3.6 (0.4)	3.7 (0.4)	0.02*	0.99	0.85	0.01*
Positive emotions	3.07 (0.62)	2.8 (0.4)	3.0 (0.5)	3.2 (0.4)	3.4 (0.4)	0.45	0.35	0.31	0.04*
Estimated quality of									
Physical activities	3.91 (0.18)	3.3 (0.7)*	3.8 (0.3)	3.9 (0.2))	3.9 (0.2)	0.04*	0.23	0.99	0.08
Cognitive tasks	3.74 (0.36)	2.8 (0.9)*	3.6 (0.3)	3.6 (0.4)	3.7 (0.3)	0.02*	0.89	0.87	0.03*
Social activities	3.90 (0.23)	3.2 (0.6)*	3.8 (0.4)	3.8 (0.4)	3.9 (0.3)	0.03*	0.99	0.57	0.02*
Feeling bothered about									
Physical activities	2.52 (0.75)	1.8 (0.4)*	2.1 (0.7)	2.1 (0.8)	2.1 (0.9)	0.17	0.90	0.98	0.38
Cognitive tasks	2.18 (0.68)	2.2 (0.7)	2.1 (0.6)	2.1 (0.7)	1.9 (0.6)	0.59	0.81	0.89	0.32
Social activities	2.39 (0.62)	2.2 (0.4)	2.4 (0.5)	2.2 (0.6)	2.2 (0.6)	0.56	0.52	0.89	0.79
Physical complaints	1.90 (0.64)	1.6 (0.4)	1.7 (0.2)	1.8 (0.6)	1.8 (0.6)	0.52	0.61	0.87	0.44
Chronic Illness part									
Estimated frequency of									
Concerns		3.0 (0.7)	3.6 (0.6)	3.8 (0.3)	3.7 (0.7)	0.17	0.17	0.30	0.02*
Feelings of inferiority		3.1 (0.4)	3.7 (0.4)	3.7 (0.3)	3.8 (0.5)	0.05*	0.14	0.54	0.05*
Epilepsy part									
Estimated frequency of									
Seizures		3.0 (0.9)	3.7 (0.4)	3.9 (0.2)	3.8 (0.4)	0.03*	0.84	0.35	0.05*
Epilepsy treatment		2.5 (0.5)	3.4 (0.8)	3.4 (0.5)	3.8 (1.1)	0.03*	0.50	0.18	0.02*
Epilepsy-related complaints		2.9 (0.7)	3.4 (0.5)	3.5 (0.3)	3.5 (0.4)	0.08	0.47	0.83	0.03*
Feeling bothered about									
Physical complaints		2.1 (0.6)	2.3 (0.4)	2.3 (0.5)	2.1 (0.7)	0.46	0.84	0.19	0.82
Seizures		1.5 (0.6)	1.8 (0.6)	2.7 (0.6)	3.2 (0.8)	0.79	0.19	0.05*	0.001**
Epilepsy treatment		2.0 (0.5)	3.0 (1.1)	2.9 (0.9)	3.4 (1.2)	0.09	0.97	0.15	0.02*

[1]Anova for Repeated Measures. [2]Significance (*) in the column pertains to comparison with reference data.

Statistical significance *($p \leq 0.05$), **($p \leq 0.01$).

HAY-P (Table 3): Prior to operation, parents evaluated the frequency of social activities as significantly lower and the quality of cognitive tasks as significantly worse than the reference data (p's < 0.05). They were not unduly bothered by their children's limitations in activities or physical complaints (p's ϖ 0.05 to the disadvantage of the reference values). When comparing data obtained six months after surgery with pre-surgical ratings, significant improvements were found in the evaluations of the frequencies of physical ($p < 0.05$) and social activities ($p < 0.01$), physical complaints and positive emotions (p's < 0.05). With respect to the epilepsy, parents estimated the frequency of seizures ($p < 0.01$) and of epilepsy treatment ($p < 0.05$) as having diminished. Concerns ($p < 0.01$) and feelings about seizures ($p < 0.05$) also improved. Between 6 and 12 and between 12 and 24 months, no significant differences were found. However, when comparing the ratings at 24 months to those obtained before surgery, the parents evaluated the frequency of physical and social activities (p's < 0.01) as well as that of cognitive activities ($p < 0.05$) as having changed for the better to a statistically significant extent. They evaluated the occurrence of positive emotions as having increased considerably ($p < 0.01$). But, in the perception of the parents, the quality of the activities of their children and their own feelings about these activities had not changed to a statistically significant extent. Parents evaluated the frequencies of their children's physical complaints ($p < 0.05$), illness-related concerns, seizures (p's <0.01) and epilepsy treatment ($p < 0.05$) as having decreased.

Children versus parents: Significant positive correlations were evident between the children's and the parents' evaluations, both before and after surgery (data obtainable from first author). Children remained less positive in their feelings (Figure 1) about physical, cognitive and social activities, as well as about general physical complaints, than the parents. Quite soon after the operation, however, they became more positive than their parents about epilepsy treatment and somewhere between six and 12 months after the surgery they became more positive than their parents with regard to the seizures.

Table 3

Health-related Quality of Life (How Are you questionnaire for Parents [HAY-P]). Reference data (n = 134) data (averaged per sub-scale) obtained before and 6, 12 and 24 months after epilepsy surgery in 21 children who underwent epilepsy surgery and comparison between the assessments

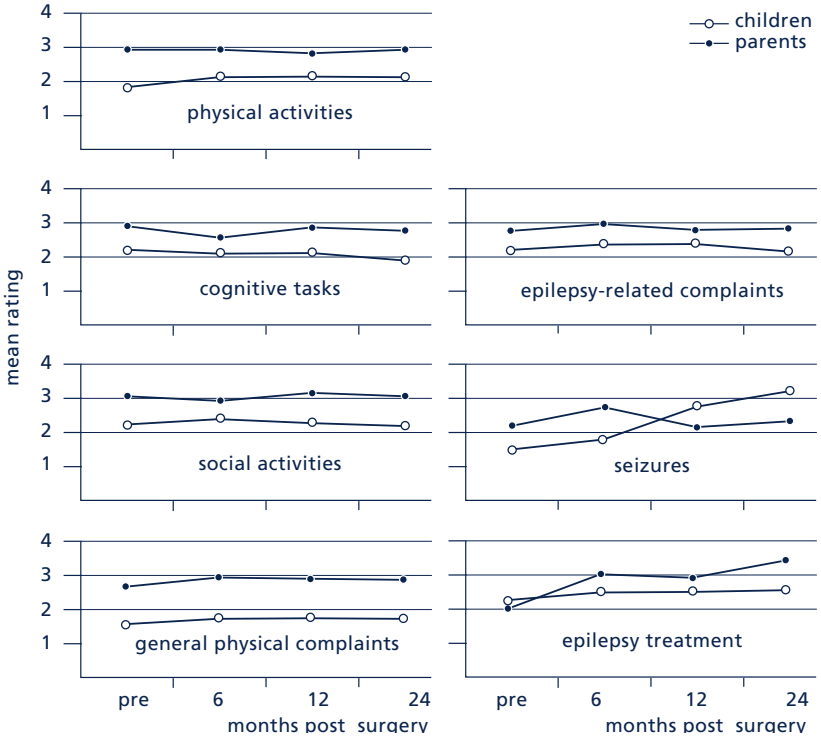
	Healthy Reference group		Follow up			Difference[1]			
	Mean (SD)	Pre-operative Mean (SD)[2]	6 months Mean (SD)	12 months Mean (SD)	24 months Mean (SD)	pre-6m p	6-12m p	12-24m p	pre-24m p
Generic part									
Estimated frequency of									
Physical activities	2.60 (0.52)	2.1 (0.3)	2.7 (0.6)	2.6 (0.6)	2.9 (0.6)	0.01*	0.63	0.06	0.007**
Cognitive tasks	3.08 (0.56)	2.5 (0.7)	3.1 (0.4)	3.0 (0.7)	3.3 (0.4)	0.09	0.64	0.21	0.03*
Social activities	2.38 (0.48)	1.8 (0.4)*	2.5 (0.5)	2.4 (0.6)	2.7 (0.6)	0.001**	0.32	0.12	0.007**
Physical complaints	3.75 (0.38)	3.3 (0.6)	3.7 (0.3)	3.5 (0.7)	3.6 (0.4)	0.02*	0.23	0.25	0.02*
Positive emotions	2.99 (0.50)	2.7 (0.6)	3.3 (0.4)	3.2 (0.6)	3.3 (0.6)	0.02*	0.55	0.33	0.005**
Estimated quality of									
Physical activities	3.96 (0.14)	3.6 (0.3)	3.8 (0.2)	3.7 (0.2)	3.9 (0.4)	0.41	0.80	0.77	0.06
Cognitive tasks	3.82 (0.31)	2.6 (0.4)*	3.5 (0.6)	3.0 (0.7)	3.1 (0.8)	0.07	0.07	0.35	0.24
Social activities	3.91 (0.27)	3.7 (0.5)	3.9 (0.3)	3.9 (0.2)	3.9 (0.4)	0.28	0.97	0.95	0.36
Feeling bothered about									
Physical activities	2.24 (0.58)	2.9 (0.8)	2.9 (0.5)	2.8 (0.4)	2.9 (0.6)	0.77	0.36	0.41	0.61
Cognitive tasks	1.98 (0.57)	2.9 (0.3)*	2.6 (0.7)	2.9 (0.3)	2.8 (0.2)	0.09	0.09	0.82	0.66
Social activities	2.03 (0.51)	3.0 (0.5)*	2.9 (0.3)	3.1 (0.4)	3.1 (0.4)	0.82	0.32	0.78	0.77
Physical complaints	2.09 (0.66)	2.7 (0.6)	3.0 (0.4)	2.9 (0.5)	2.9 (0.4)	0.26	0.83	0.93	0.73
Chronic Illness part									
Estimated frequency of									
Concerns		2.5 (0.6)	3.5 (0.4)	3.6 (0.4)	3.6 (0.4)	0.004**	0.67	0.74	0.002**
Feelings of inferiority		3.0 (0.6)	3.6 (0.3)	3.4 (0.6)	3.5 (0.4)	0.08	0.38	0.61	0.29
Epilepsy part									
Estimated frequency of									
Seizures		3.2 (0.9)	3.9 (0.3)	3.9 (0.6)	3.9 (0.5)	0.007**	0.85	0.97	0.008**
Epilepsy treatment		2.5 (0.5)	3.2 (0.5)	3.2 (0.3)	3.3 (0.4)	0.05*	0.99	0.82	0.02*
Physical complaints		3.1 (0.5)	3.7 (0.4)	3.5 (0.3)	3.6 (0.4)	0.07	0.55	0.17	0.08
Feeling bothered about									
Physical complaints		2.7 (0.2)	2.9 (0.3)	2.8 (0.5)	2.8 (0.2)	0.76	0.77	0.89	0.82
Seizures		2.1 (0.1)	2.7 (0.2)	2.2 (0.2)	2.3 (0.1)	0.02*	0.17	0.58	0.54
Epilepsy treatment		2.2 (0.2)	2.4 (0.2)	2.5 (0.3)	2.5 (0.4)	0.34	0.58	0.88	0.52

[1]Anova for Repeated Measures; [2]Significance (*) in the column pertains to comparison with reference data.

Statistical significance *($p \leq 0.05$), **($p \leq 0.01$)

Figure 1

Illustrations of difference between children and parents with respect to feelings about HrQoL



Self-perceived profile of competence of children (SPP-C) and adolescents (SPP-A) (Table 4).
Before surgery the total mean score of the eight children (SPP-C) was 3.0 (sd 0.4 range: 2.7-3.3), not different from healthy children. Adolescents (SPP-A) approached normality: total mean score = 2.9 (sd 0.3 range: 2.6-3.2); normal score is 3.0.
Six months after epilepsy surgery, the perception of competence of the children had improved significantly on the sub-scale of behavioral conduct ($p < 0.05$). In the adolescents, the perceptions on four subscales and on the total mean score for perceived competence had improved significantly (p's < 0.05). Apart from small but statistically significant decreases of children's global self-worth ($p < 0.05$) and of romance in adolescents ($p < 0.05$), no significant variations could be established at 12 months or thereafter. When comparing the ratings obtained 24 months after surgery with those beforehand, children perceived themselves as being socially more accepted; their global self-worth had increased (p's < 0.05). In adolescents, athletic competence had improved but remained below reference cut-off, while 'romance' had increased significantly (p's < 0.05). Children versus adolescents (Figure 2): Children perceived their scholastic competence more negatively than adolescents perceived theirs, both before and after surgery. But self-perceived social acceptance ameliorated in children after the first post-surgical year ($p < 0.05$) whereas it remained stable in adolescents (difference to the advantage of the children $p < 0.05$). Overall, no important discrepancies were found between the two age groups.

Table 4

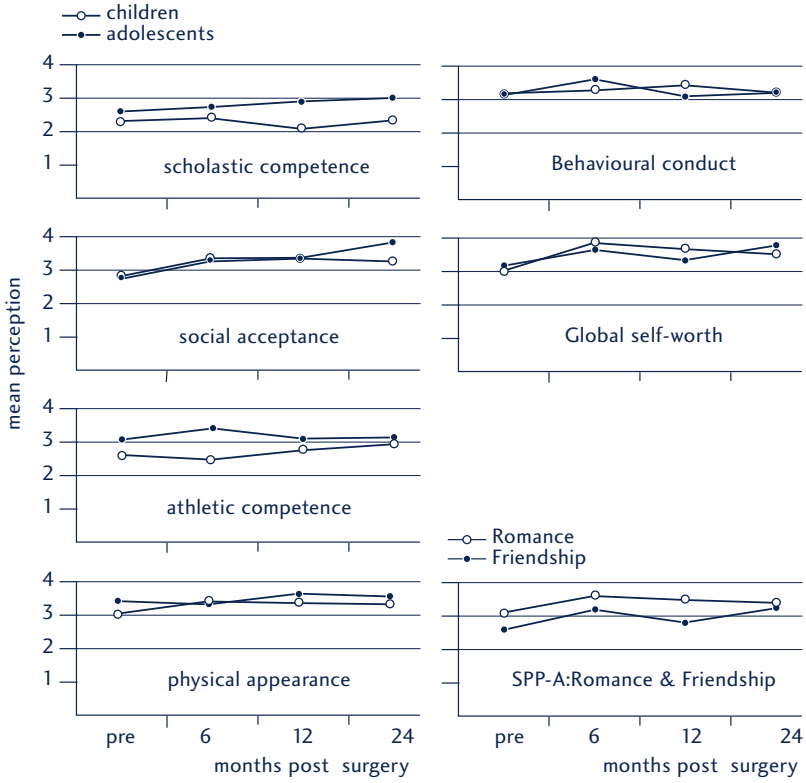
Self-perceived competence: Means (SD) and change over two years after epilepsy surgery (n=21)

	Pre-operative Mean (SD)	Follow up 6 months Mean (SD)	12 months Mean (SD)	24 months Mean (SD)	Difference[1] pre-6m p	6-12m p	12-24m p	pre-24m p
SPPC-C (n = 8)								
Total Mean Score	3.0 (0.4)	3.2 (0.2)	3.0 (0.3)	3.2 (0.1)	0.09	0.03*	0.32	0.32
Scholastic competence	2.3 (0.5)	2.4 (0.3)	2.1 (0.1)	2.3 (0.6)	0.58	0.18	0.67	0.99
Social acceptance	2.7 (0.6)	3.2 (0.3)	3.3 (0.6)	3.7 (0.5)	0.09	0.91	0.39	0.04*
Athletic competence	3.1 (0.1)	3.4 (0.1)	3.1 (0.2)	3.1 (0.3)	0.44	0.06	0.84	0.99
Physical appearance	3.4 (0.6)	3.3 (0.6)	3.6 (0.4)	3.5 (0.6)	0.42	0.18	0.74	0.42
Behavioural conduct	3.2 (0.4)	3.6 (0.5)	3.1 (0.1)	3.2 (0.1)	0.02*	0.23	0.47	0.99
Global self-worth	3.2 (0.4)	3.6 (0.4)	3.3 (0.4)	3.7 (0.3)	0.21	0.02*	0.18	0.02*
SPPC-A (n=13)								
Total Mean Score	2.9 (0.3)	3.2 (0.2)	3.2 (0.3)	3.2 (0.4)	0.04*	0.87	0.98	0.24
Scholastic competence	2.6 (0.7)	2.7 (0.4)	2.9 (0.5)	3.0 (0.3)	0.73	0.15	0.91	0.35
Social acceptance	2.8 (0.7)	3.3 (0.5)	3.3 (0.4)	3.2 (0.7)	0.09	0.85	0.63	0.28
Athletic competence	2.6 (0.6)	2.5 (0.6)	2.8 (0.7)	2.9 (0.7)	0.60	0.15	0.53	0.03*
Physical appearance	3.0 (0.6)	3.4 (0.5)	3.3 (0.5)	3.3 (0.5)	0.04*	0.20	0.89	0.18
Behavioural conduct	3.2 (0.3)	3.3 (0.4)	3.4 (0.5)	3.2 (0.5)	0.48	0.78	0.14	0.99
Global self-worth	3.0 (0.7)	3.8 (0.3)	3.6 (0.2)	3.5 (0.4)	0.04*	0.11	0.66	0.36
Romance	2.6 (0.4)	3.2 (0.6)	2.8 (0.6)	3.1 (0.5)	0.04*	0.02*	0.07	0.04*
Friendship	3.1 (0.5)	3.6 (0.3)	3.4 (0.3)	3.3 (0.6)	0.04*	0.60	0.60	0.57

[1]Anova for Repeated Measures; Statistical significance: *($p \leq 0.05$).

Figure 2

Illustrations of difference between children and adolescents on Self-Perceived Competence, difference between Romance and Friendship



Discussion

In children, outcome of surgery for drug-resistant epilepsy has been shown to be satisfactory in terms of seizure-related variables. Of the children in the present study 71% became free of seizures, a percentage that does not deviate from the outcomes of surgical procedures reported in similar patient groups (Vining et al., 1997; Kossoff et al., 2003; Berg et al., 2003; Sinclair et al., 2003; Devlin et al., 2003 Clusmann et al., 2004). However, the ultimate goal of surgery for epilepsy is to improve overall functioning and well-

being, for which reason our research focused on health-related quality of life as rated by the children themselves and their parents and on the children's self-perceived competence. To be able to interpret post-surgical change adequately, we carried out assessments both before and three times after surgery, covering a time span of two years.

Epilepsy surgery has a multi-faceted impact on HrQoL

As has been described in larger studies, drug-resistant epilepsy affects HrQoL. For various reasons the literature on HrQoL of children with epilepsy is difficult to interpret. Quality of life has been defined and operationalized in different ways. Some studies used measures of behaviour and emotional functioning, such as the Child Behavior Checklist (Huberty et al., 2000; Sabaz et al., 2003) and the Emotional Well-being Test or the Schedule for Affective Disorders (Molteno et al., 2001), while others used quality-of-life measures that were not specifically designed for children with epilepsy (Elliott et al., 2002; Sherman et al., 2002; Räty et al., 2003; Smith et al., 2004). The HAY (Bruil, 1999) has the advantages that it has been designed for children, that the items have been constructed on the basis of information provided by experts but also by children themselves, that it distinguishes not only frequency and quality of activities but also feelings with respect to both, and finally that it addresses not only generic HrQoL, but also issues of HrQoL in relation to having a chronic illness and to having epilepsy in particular, as also suggested by Smith et al., who recently attributed their failure to detect in a follow-up of one year differences between children who had been operated upon and surgical candidates to the possibility that their generic instrument had not addressed all of the illness-related experiences unique to epilepsy in children (Smith et al., 2004). Using the HAY, we can now further specify the impact of epilepsy and of epilepsy surgery.
Prior to surgery, the children (not having found significant differences between the two age groups on the HAY, we here refer to children and adolescents together as 'children') evaluated both the

quality and the frequency of their activities in physical, social and cognitive domains as worse than in the reference group of healthy children and they felt more bothered about their physical activities. Within six months after surgery, the evaluations of the children with respect to the frequency of physical and social activities improved and even normalised. The children's evaluations of the quality of their physical, social and cognitive activities, which had indeed been worse than normal before surgery, also improved significantly, over time even reaching normal values. However, the children's feelings concerning their activities remained worse than those of healthy children. The finding that the evaluations of the frequency of cognitive tasks neither decreased nor increased can be explained by the fact that school activities are regulated by class timetables. This stability emphasises the amelioration in the two remaining domains of activities: the cessation or major decrease of seizures enabled the patients to play and go out more freely than before. Their evaluations of the occurrence of positive emotions also gradually improved.

The parents

Similarly to the children, parents evaluated the frequency and quality of the activities of their children prior to surgery as worse than parents of the reference group of healthy children, although the difference was statistically significant for social activities only. Interestingly, as a group they evaluated their feelings concerning the activities of their children even more positively than the parents of the healthy children in the reference group. We cannot explain this finding, but it should be noted that the parents filled out the questionnaire during a period in which the decision to operate on the children was being made, which may have influenced their feelings. It is also possible that coping mechanisms had a moderating influence.

Overall, the parents evaluated health-related quality of life of their children as having improved after surgery. Six months after surgery this was apparent in the ameliorated or even normalised evalua-

tions of the frequency of their children's physical and social activities and their positive emotions. Thereafter, only slight improvements occurred. With respect to the quality of the activities, drastic changes were not expected because the initial evaluations – apart from the quality of cognitive activities, which remained poor but did not worsen – approached normalcy. Adding to the positive picture were the ameliorations in the evaluations of the frequency of concerns arising from having a chronic illness, whereas the increase of various activities of their children did not render the parents more concerned than before.

Children and parents

Findings with the Paediatric Evaluation of Disability Inventory (PEDI) (Empelen et al., 2004) administered to the same group of patients and their parents in the same time period showed that with cessation of seizures the children began to function more normally and that in keeping with this process caregivers withdrew help. Similar associations have been reported for other patient groups (Custers et al., 2002; Schoenmakers et al., 2004). Furthermore, both before and two years after surgery, the ratings of seizure severity (HASS) and of seizure-related restrictions (HARCES) were strongly correlated. Hence, when seizures discontinued or significantly decreased, seizure-related restrictions were relieved accordingly, a finding which corroborates previous studies in children and adults that suggest a relationship between better seizure control and improvement of quality of life (Yang et al., 1996; Kellett et al., 1997). Prior to surgery children felt less bothered with respect to physical, cognitive and social activities and to seizures than their parents felt. Two years after surgery, they still felt significantly less bothered than their parents felt about cognitive activities. At that time their feelings with respect to general physical complaints and to seizures were significantly more positive than those of the parents. Hence, although the evaluations of HrQoL of the children and their parents were not widely contrasting, because of their slightly different pitch the evaluations of both groups of respondents were

informative. Evaluations of parents and, for that matter, clinicians, although valid in themselves, are no substitute for the children's perspective (Elliott et al., 2002; Smith et al., 2004; McEwan et al., 2004).
In studies of chronic illnesses in childhood, parents usually evaluate the situation of their children more pessimistically than the children themselves, whether the latter suffer epilepsy or another chronic illness such as asthma (Bruil, 1999; Arunkumar et al., 2000; Holmbeck et al., 2002; Gordon et al., 2002; Thill et al., 2003). As the children were suffering types of epilepsy that imposed stringent restrictions on the children and were a burden for the families, we were, impressed by the fact that both parents and children evaluated HrQoL of the children with some restraint.

Epilepsy surgery has a multi-faceted impact on self-perceived competence

Children who avoid motor activities for fear of failure and peer criticism, do not have the opportunities to practise skills, which leads them to limit their social participation (Harter, 1982; Skinner and Piek, 2001). Medically intractable epilepsy and the chaperoning that it necessitates may impede the development of independence and impair social function, peer relationships and self-esteem. Using the cut-off advocated in the literature on the SPP (Wickstrom 1995; Veerman, 1997; Aasland and Diseth, 1999), we found that prior to surgery both children and adolescents perceived themselves as particularly vulnerable in their scholastic or academic competence and as being less accepted by peers, whereas adolescents also perceived themselves as being less competent athletically and in the domain of romance. However, both the children and the adolescents had surprisingly normal self-perceptions with respect to physical appearance, behavioural conduct and even global self-worth, and as far as adolescents were concerned, friendships. The children's self-perceptions of social acceptance tended to improve within the six months after surgery and gradually ameliorated thereafter, which we take to mean that, after surgery, children

learned to perceive themselves as competent to participate in most social domains. In agreement with the children's evaluations of the quality of cognitive tasks on the HAY, the instrument measuring health-related quality of life, self-perceptions of scholastic competence neither improved nor deteriorated over the two-year period of the present study. Indeed, the case histories of many children revealed learning problems at school. The slight decreases in global self-worth at 12 months after surgery may be interpreted as reflecting mild and transient awareness of difficulty in adapting to the novel opportunities.

Adolescents, whose pre-surgical self-perception profile had shown several slightly sub-normal values, improved their perceptions of competence to the largest degree in the first six months after surgery. Again, social acceptance passed the cut-off for normality, although the change was not statistically significant. Judging from the slight but statistically significant drop in the domain of romance when assessed at 12 months after surgery, adaptation to peers may not have been easy but at the end of our follow-up the adolescents seem to have found their way to a large degree. Scholastic competence remained sub-normal, although it gradually improved. As with the younger children, the case histories of the adolescents bear witness to impediment of academic learning.

As motor agility and physical fitness are important parameters for competence (Skinner and Piek, 2001), and taking into account the fact that some of the children and adolescents of the present study had a post-surgical physical impairment, we compared the self-perception profiles of those with and without physical impairment (data not shown). Adolescents rather than children with a physical impairment perceived particularly their athletic competence, as being statistically significantly worse than did adolescents who were not physically impaired. This developmentally interesting finding requires further study in larger groups of subjects.

Statistical significance versus clinical relevance and limitations of the study

Another point is how to define clinically meaningful change in research on HrQoL and self-perceived competence. Crosby et al., (2003) reviewed the issue and suggested the gold standard as the smallest difference between scores that patients perceive as beneficial. However, this measure is difficult to establish. The notion that clinically meaningful change in HrQoL results from a meaningful reduction in symptoms or from an improvement in function begs the question. One of the most commonly used anchors for establishing clinically meaningful change in longitudinal studies is the global evaluation of change (Crosby et al., 2003). However, this runs counter to the desirability to tap the multifarious aspects of HrQoL after epilepsy surgery, which was one of the reasons for choosing the HAY as an instrument. One might fear that the instrument might not be sensitive to change, but both our findings of a pattern of changes and stabilities and a responsiveness study (Coq et al., 2000) refute this fear. With respect to the SPP, the Total Mean Score did not change significantly either. It may be that persons involved in unduly severe conditions develop the tendency to evaluate their situation towards normal. However this may be, contrary to the report by Elliott et al., (2000) negative change was extremely rare both in the evaluations by children and by their parents.
The patients in our study are in many ways a very heterogeneous group. They are small in number, they differ in type of epilepsy and in type and outcome of surgery, in cognitive development as well as in age and children younger than 6 years had to be excluded because they did not fulfil the test requirements. Therefore it is not possible to generalize the results to a wider population of surgically treated children. Nor does the study allow a detailed analysis of outcome determinants.

Conclusion

Surgery not only results in a significant reduction in seizure frequency, seizure severity and normalisation of restrictions, it also sets the stage for improvement of health-related quality of life and self-perceived competence. Within six months after epilepsy surgery a pattern of improvements and stabilities is manifest. Patients and parents evaluate social functioning as improving and cognitive functioning as remaining vulnerable. The cessation or at least significant reduction of seizures widens the freedom of movement; the patients start to engage in and enjoy normal childhood/adolescence activities. Later assessments do not yield breakthroughs or major further changes.

Acknowledgements

We are grateful to the Phelps Stichting and the Johanna Children's Foundation for their financial support, to Dr. E Buskes, Julius Centre for Health Sciences and Primary Care, for his supervision of statistical analyses and to M. Peeters, M. Boonzaaijer and Dr. C. Volman, University of Utrecht, Faculty of Social Sciences, for their cooperation in this research. Surgeons Prof. Dr. C.W.M. van Veelen and Dr. P.C. van Rijen operated on all patients. We thank the Members of the Dutch Collaborative Epilepsy Surgery Programme: SEIN, Kempenhaeghe, Hans Bergerkliniek, Academic Hospitals (Utrecht, Maastricht, Amsterdam VU).

References

Aasland A, Diseth TH. Use of Selfperception Profile for adolescents as an indicator of psychosocial outcome in children with a chronic physical disorder. Eur Child Adolesc Psychiatry 1999;8:77-85.

Arunkumar, G, Wyllie E, Kotagal P, Ong HT, Gilliam F. Parent- and patient-validated content for paediatric epilepsy Quality of Life assessment. Epilepsia 2000;11:1474-84.

Baker GA. Health-related quality-of-life issues: Optimizing patient outcomes. Neurology 1995;45:S29-S34.

Baker GA, Cagnon D, McNulty P. The relationship between seizure frequency, seizure type and quality of life: findings from three European countries. Epilepsy Res 1998;30:231-40.

Berg AT, Vickrey BG, Langfitt JT, et al. Multicenter Study of Epilepsy Surgery. The multicenter study of epilepsy surgery: recruitment and selection for surgery. Epilepsia 2003;44:1425-33.

Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. Epilepsia 2002;43:535-38.

Bouffard T, Marcoux MF, Vezeau C, Bordeleau L. Changes in self-perceptions of competence and intrinsic motivation among elementary schoolchildren. Br J Educ Psychol 2003;73:171-86.

Bowling A, Normand C. Definition and measurement of outcome. In: Swash M (Ed.) Outcomes in neurological and neurosurgical disorders. Cambridge: Cambridge University Press, 1998:14-34.

Bruil J. Development of quality of life questionnaire for children with a chronic Illness. (Thesis) FSW: Universiteit Leiden, 1999.

Carpay JA, Vermeulen J, Stroink H, et al. Disability due to restrictions in childhood epilepsy. Dev Med Child Neurol 1997;39:521-6.

Clusmann H, Kral T, Gleissner U, et al. Analysis of different types of resection for pediatric patients with temporal lobe epilepsy. Neurosurgery 2004;54:847-59.

Coq le EM, Boeke AJ, Bezemer PD, Bruil J, van Eijk JT. Clinimetric properties of a parent report on their offspring's quality of life. J Clin Epidemiol 2000;53:139-46.

Crosby RD, Kolotkin RL, Williams GR. Defining clinically meaningful change in health-related quality of life. J Clin Epidemiol 2003;56:395-407.

Custers JWH, van der Net J, Hoijtink H, Wassenberg-Severijnen JE, Vermeer A, Helders PJM. Discriminative validity of the Dutch Pediatric Evaluation of Disability Inventory. Arch Phys Med Rehabil 2002;83:1437-41.

Devlin AM, Cross JH, Harkness W, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003;126:556-66.

Elliott IM, Lach L, Smith ML. Adolescent and maternal Perspectives on QoL and Neuropsychological status following epilepsy surgery. Epilepsy Behav 2000;1:406-17.

Empelen R van, Jennekens-Schinkel A, Buskens E, Helders PJM, Nieuwenhuizen O van. Functional consequences of hemispherectomy. Brain 2004;127:2071-9.

Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel JJ (ed.) Surgical treatment of the epilepsies. 2nd ed. New York: Raven Press, 1993:609-21.

Ferguson TJ, Stegge H, Eyre HL, Vollmer R, Ashbaker M. Context effects and the (mal)adaptive nature of guilt and shame in children. Genet Soc Gen Psychol Monogr 2000;126:319-45.

Gilliam F. The impact of epilepsy on subjective health status. Curr Neurol Neurosci Rep 2003;3:357-362. (Review).

Gordon KE, Dooley JM, Camfield PR, Camfield CS, MacSween J. Parents of children with epilepsy are optimistic for their children's health, but relatively pessimistic when compared with other parents. Epilepsy Behav 2002;3:262-65.

Harter S. The Perceived Competence Scale for Children. Child Develop 1982;53:87-97.

Harter S. Manual for the Self-Perception Profile for Adolescents. Denver CO: University of Denver, 1988.

Holmbeck GN, Johnson SZ, Wills KE, et al. Observed and perceived parental overprotection in relation to psychosocial adjustment in preadolescents with a physical disability: the mediational role of behavioral autonomy. J Consult Clin Psychol 2002;70:96-110.

Huberty TJ, Austin JK, Harezlak J, Dunn DW, Ambrosius WT. Informant Agreement in Behavior Ratings for Children with Epilepsy. Epilepsy Behav 2000;1:427-35.

Kellett MW, Smith DF, Baker GA, Chadwick DW. Quality of life after epilepsy surgery. J Neurol Neurosurg Psychiatry 1997;63:52-8.

Kossoff EH, Vining EP, Pillas DJ, et al. Hemispherectomy for intractable unihemispheric epilepsy etiology vs outcome. Neurology 2003;61:887-90. [Review].

MacLeod JS, Austin JK. Stigma in the lives of adolescents with epilepsy: a review of the literature. Epilepsy Behav 2003;4:112-17. [Review].

Markand ON, Salanova V, Whelihan E, Emsley CL. Health-related quality of life outcome in medically refractory epilepsy treated with anterior temporal lobectomy. Epilepsia 2000;41:749-59.

McEwan MJ, Espie CA, Metcalfe J. A systematic review of the contribution of qualitative research to the study of quality of life in children and adolescents with epilepsy. Seizure 2004;13:3-14. [Review].

Molteno G, Molteno CD, Finchilescu G, Dawes AR. Behavioural and emotional problems in children with intellectual disability attending special schools in Cape Town, South Africa. J Intellect Disabil Res 2001;45:515-20.

Oostrom KJ, Schouten A, Olthof T, Peters AC, Jennekens-Schinkel A. Negative emotions in children with newly diagnosed epilepsy. Epilepsia 2000;41:326-31.

Räty LK, Wilde Larsson BM, Soderfeldt BA. Health-related quality of life in youth: a comparison between adolescents and young adults with uncomplicated epilepsy and healthy controls. J Adolesc Health 2003;33:252-58.

Ronen GM, Streiner DL, Rosenbaum P. Health-related quality of life in childhood epilepsy: Moving beyond 'seizure control with minimal adverse effects'. Health Qual Life Outcomes 2003;1:36.

Ronen GM, Streiner DL, Rosenbaum P; Canadian Pediatric Epilepsy Network. Health-related quality of life in children with epilepsy: development and validation of self-report and parent proxy measures. Epilepsia 2003;44:598-612.

Sabaz M, Cairns D, Bleasel A, et al. The health-related quality of life of childhood epilepsy syndromes. J Paed Child Health 2003;39:690-96.

Schoenmakers MA, Gulmans VA, Gooskens RH, Helders PJ. Spina bifida at the sacral level: more than minor gait disturbances. Clin Rehabil 2004;18:178-85.

Schumann BC, Striegel-Moore RH, McMahon RP, Waclawiw MA, Morrison JA, Schreiber GB. Psychometric properties of the Self-Perception Profile for Children in a biracial cohort of adolescent girls: the NHLBI Growth and Health Study. J Pers Assess 1999;73:260-75.

Scott-Lennox J, Bryant-Comstock L, Lennox R, Baker GA. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. Epilepsy Res 2001;44:53-63.

Selai CE, Elstner K, Trimble MR. Quality of life pre and post epilepsy surgery. Epilepsy Res 2000;38:67-74.

Sherman EM, Slick DJ, Connolly MB, et al. Validity of three measures of health-related quality of life in children with intractable epilepsy. Epilepsia 2002;43:1230-38.

Sinclair DB, Aronyk KE, Snyder TJ, et al. Pediatric epilepsy surgery at the University of Alberta: 1988-2000. Pediatr Neurol 2003;29:302-11.

Skinner RA, Piek JP. Psychosocial implications of poor motor coordination in children and adolescents. Hum Mov Sci 2001;20:73-94.

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Thill AD, Holmbeck GN, Bryant FB, Nelson C, Skocic A, Uli N. Assessing the factorial invariance of Harter's self-concept measures: comparing preadolescents with and without spina bifida using child, parent, and teacher report. J Pers Assess 2003;81:111-22.

Veerman JW. De Competentiebelevingsschaal voor Kinderen: Theoretische uitgangspunten en enkele onderzoeksgegevens. Tijdschrift voor de Orthopedagogiek 1997;28:286-301.

Veerman JW, Straathof MAE, Treffers PhDA et al. Competentiebelevingsschaal voor kinderen (CBSK) Lisse: Swets Testservice 1997.

Vining EP, Freeman JM, Pillas DJ, et al. Why would you remove half a brain? The outcome of 58 children after hemispherectomy- the Johns Hopkins experience: 1968 to 1996. Pediatrics 1997;100:163-71.

Wallander JL, Schmitt M, Koot HM. Quality of Life Measurement in children and adolescents: Issues, Instruments and Applications. J Clin Psych 2001;57:571-85.

Wickstrom L. Harter's Self-Perception Profile for Adolescents: reliability, validity, and evaluation of the question format. J Pers Assess 1995;65:100-16.

W.H.O. The International Classification of Functioning, Disability and Health (2002). ICF: introduction. Geneva: World Health Organization. Available on the WHO Internet site, 2002. http://www.who.int/classification/icf.

Yang TF, Wong TT, Kwan SY, Chang KP, Lee YC & Hsu TC. Quality of life and life satisfaction in families after a child has undergone corpus callosotomy. Epilepsia 1996;37:76-80.

Ziegler RG. Behavioral and emotional correlates of epilepsy in adolescence. Epilepsy Behav 2002;3:558-60.

Chapter 4

Epilepsy surgery does not harm motor performance of children and adolescents

R. van Empelen[1*]
A. Jennekens-Schinkel[2*]
J.W. Gorter[3*]
M.J.M. Volman[4]
O. van Nieuwenhuizen[5*]
P.J.M. Helders[1]

On behalf of the Dutch Collaborative Epilepsy Surgery Programme.

1 Department of Paediatric Physical Therapy and Exercise Physiology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands. NetChild, Network for Childhood Disability Research in The Netherlands
2 Department of Neuropsychology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
3 Department of Paediatric Rehabilitation, University Medical Center –Utrecht, The Netherlands.
4 Department of General and Special Education, Utrecht University, The Netherlands.
5 Department of Child Neurology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.

* Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands.

Brain 2005; 128:1536-1545. Apr 13; [Epub ahead of print]

Summary

Purpose: The impact of epilepsy surgery on motor performance, activities of daily life (ADL) and caregiver's assistance is assessed in 37 children (age range: 0.3-15.4 years) with pharmacologically untreatable epilepsy, 17 of whom were also diagnosed as having spasticity of cerebral origin. All patients underwent epilepsy surgery between 1996 and 2001 at the Wilhelmina University Children's Hospital and were assessed using a standard protocol with fixed intervals: pre-surgery, and 6 months, 1 year and 2 years after surgery. Type of surgery was hemispherectomy (n=14), resection temporal (n=14), frontal (n=4), parietal (n=2) and central (n=2). One child underwent callosotomy.
Methods: Engel's classification was used to determine seizure outcome. Impairments were measured by means of muscle strength, range of motion and muscle tone. Motor performance of infants and children without spasticity was measured using the Movement Assessment Battery for Children (M-ABC). The Gross Motor Function Measure (GMFM-88) was used in children with spasticity, the severity of motor disability in this group being determined by means of the Gross Motor Function Classification System (GMFCS). Daily activities and caregiver's assistance were measured in all children using the Pediatric Evaluation of Disability Inventory (PEDI).
Results: Twenty-four months after surgery 74% of the children could be classified as Engel I, indicating a significant seizure reduction. Impairments revealed some decrease in muscle strength and range of motion in the group with spasticity. Scores improved statistically significantly at groups level on M-ABC and GMFM ($p's < .05$). Improvement in activities of daily life and caregiver's assistance could not be measured in children without spasticity because of the ceiling effect of the PEDI, but children with spasticity improved significantly with respect to these parameters (PEDI) ($p's < .05$).
Conclusion: Epilepsy surgery does not harm motor performance in children with or without spasticity.

Introduction

Epilepsy surgery has become a prominent intervention for children and adolescents with pharmacologically untreatable epilepsy (Wyllie et al., 1998; Graveline et al., 2000; Devlin et al., 2003). Favourable effects on seizure outcome have been reported for different types of surgery (Chen et al., 2002; Devlin et al., 2003) and psychosocial benefits of surgery have become clear (Lendt et al., 2000; Birbeck et al., 2002; Ronen et al., 2003; Ronen et al., 2003; Smith et al., 2004).

One of the criteria for resective surgery is interference of seizures with neurodevelopment (Peacock et al., 1993), but as yet there is no consensus on the outcome of this criterion. Reports on motor aspects of development after surgery are contradictory. Some researchers have described no deterioration and even an improvement in motor function, whether or not the epilepsy resulted in cessation or reduction of seizures (Beckung et al., 1994; Romanelli et al., 2001; Krsek et al., 2002). Others found motor deterioration to be a frequent complication of epilepsy surgery (Chassoux et al., 1999; Graveline et al., 1999). In order to provide children and parents with better information on the impact of surgery, there is a need for evaluation to be carried out systematically. Moreover, the impact of epilepsy surgery on activities of daily life and caregiver's assistance (and, for that matter, independence) has to be taken into account. Covering the period from prior to epilepsy surgery up to the third year after the operation, our study focuses on change in motor performance, activities of daily life and in caregiver's assistance. The taxonomy of anatomical and physiological functions, activities and social participation as offered by the International Classification of Functioning, Disability and Health (ICF) provided a useful guide for the present prospective, longitudinal study (WHO, 2002). In a previous paper (Empelen et al., 2004) we reported that impairments were only slightly associated with functional outcome after a hemispherectomy. We now report, at the individual level, a change in motor performance in two groups (children with and without spasticity) compared to reference data, and at group level, change

in functional skills and caregiver's assistance after various surgical procedures.

The fact that a subgroup of children had spasticity necessitated the use of different instruments, suitable for the assessment of motor performance. The Movement Assessment Battery for Children (M-ABC), designed to assess normal motor performance, was used for children without spasticity (Henderson & Sugden, 1992). For children with spasticity, the Gross Motor Function Measure (GMFM) was the instrument of choice (Russell et al., 2002). Classification of Gross Motor Function has been performed with the Gross Motor Function Classification System (GMFCS) (Palisano et al., 1997). Furthermore, we reasoned that seizure reduction might enhance independence and hence participation in social activities. Knowledge of the impact of epilepsy surgery on activities of daily life of children is as yet in an exploratory stage. Comparing daily functional activities in children who underwent hemispherectomy with candidates for this surgical procedure, Graveline et al. (2000) found no significant difference, although candidates for hemispherectomy tended to attain higher levels than children who had had surgery. However, our own data on hemispherectomised children suggested that after surgery, there was an improvement in the performance of daily activities and in independence (Empelen et al., 2004). In order to help solve this controversy, we describe a wider range of children in this study. The present study applies the novel concept of stratifying motor growth according to level of gross motor function (GMFCS) (Rosenbaum et al., 2002), to the changes found in the sub-group of surgically treated children with spasticity of cerebral origin. We drafted these motor growth curves using the data as described by Russell et al., (2002) on the GMFM-88 at each level of the GMFCS.

The study addresses two questions:

1) Does epilepsy surgery of children with pre-existing neurological deficit (spasticity) worsen motor impairments or harm motor performance, and what are the effects of epilepsy surgery on activities of daily life and caregiver's assistance in these children?

2) Does epilepsy surgery of children without pre-existing neuro-

logical deficit cause motor impairments, worsen or improve motor performance, and what are the effects of epilepsy surgery on activities of daily life and caregiver's assistance in these children?

Methods

Participants

Thirty-seven children (15 male, 22 female), who underwent surgery for pharmacologically untreatable epilepsy at the Wilhelmina Children's Hospital in the period 1996 to 2001, were the subjects of the present study. Median age at surgery was 8.6 years (range 0.3-15.4). Exclusion criteria were: age older than 16 years at the time of surgery and the presence of a progressive neuro-metabolic disease. Patients were assessed using a standard protocol with fixed intervals: pre-surgery, and 6 months, 1 year and 2 years after surgery. Fourteen children underwent hemispherectomy. Fourteen children underwent temporal, four frontal, two parietal and two central resection. One child underwent callosotomy. For the sake of conciseness, the demographic and illness variables are presented separately for children without spasticity (Table 1) and for children with spasticity (Table 2) together with the major motor results and the outcome with respect to seizures. Prior to surgery, 17 children had spasticity of cerebral origin, in these children gross motor function was classified with the GMFCS. (See Instruments): Level I (n = 6), Level II (n = 4), Level III (n = 2), Level IV (n = 2), Level V (n = 1); 2 children were too young to be classified. Eight of the 17 children had a non-progressive encephalopathy known as cerebral palsy (CP); the aetiologies were congenital middle cerebral artery infarction (n = 3), hemiplegia, hemiconvulsions, epilepsy syndrome (HHE) (n=1), hemimegalencephaly (n = 3) and cortical dysplasia (n = 1). The remaining 9 children with spasticity had progressive encephalopathies; the aetiologies were: Rasmussen encephalitis (n = 4), Sturge-Weber syndrome (n = 2) and cerebral tumour (n = 2). In one child a callosotomy was performed; aetiology of the epilepsy remained unclear (Table 2).

Table 1

Patients without spasticity (N = 20): demographic features (sex, ages at onset and at surgery), illness variables (type of surgery, pathology/aetiology, Engel classification), Movement ABC: raw scores and centiles (normal = > 15) pre-surgery and 6, 12 and 24 months post-surgery.

No.	Sex	Age at onset of epilepsy (yrs;mo)	Age at surgery (yrs;mo)	Surgery type	Pathology/ aetiology	Engel Classification I t/m IV	Movement ABC Total raw scores				Centiles			
							pre	6	12	24	pre	6	12	24
1	F	0.5	6.1	Temp L	Ganglioma	I	15	11.5	9	5.5	3	9	18	40
2	M	0.8	6.3	Temp L	MTS	I	9	6.5	7	2	18	32	29	79
3	F	2	6.4	Temp R	TS	I	11.5	7	7.5	3	9	29	26	65
4	F	6.5	7.11	Front R	DNET	I	13.5	3.5	4.5	5	5	50	49	45
5	F	4.5	10.0	Front L	Meningeoma	II	16.5	9.5	8	7.5	2	16	22	26
6	F	3.5	10.6	Temp R	DNET	I	28.5	26	33	27.5	1	1	1	1
7	M	1	10.6	Temp L	MTS	I	31.5	30	26	27	1	1	1	1
8	F	7	10.8	Temp L	Astrocytoma	III	15.5	13	11	16	3	6	11	2
9	M	7	11.4	Pariet L	DNET	I	11	9	4	4	11	18	54	54
10	F	6	11.5	Temp R	MTS	I	14.5	25.5	9.5	5.5	4	1	16	40
11	M	1	12.2	Front R	Dysplasia	I	10	9	7	7.5	15	18	29	26
12	F	0.5	12.2	Temp L	Glioma	II	13.5	11	12.5	11	5	11	7	11
13	M	1	12.6	Temp R	MTS	II	6	7	3.5	1.5	36	29	60	84
14	F	8	13.1	Temp L	MTS	I	11	10	7.5	5.5	11	15	26	40
15	M	11	13.9	Temp R	Glioma	I	10	7	5.5	5	15	29	40	45
16	M	1.5	13.10	Centr R	Dysplasia	I	11.5	18.5	20	15.5	9	1	1	3
17	M	1	14.4	Temp R	Dysplasia	I	7.5	8	5	4.5	26	22	45	49
18	F	3.5	14.6	Centr R	Astrocytoma	I	11	8	6.5	5	11	22	32	45
19	F	6	15.0	Temp R	DNET	I	3.5	3	2	1.5	60	65	79	84
20	F	11	15.4	Temp L	DNET	II	13.5	14	11	12.5	5	5	11	7

Abbreviations: Age (yrs;mo) at surgery = age in years and months at the time of surgery, Centr = Central resection, DNET = Dysembryoplastic NeuroEpithelioma Tumour, Front = Frontal resection, L = Left, MTS = Mesial Temporal Sclerosis, Pariet = Parietal resection, R = Right, Sex: F = Female, M = Male, Temp = Temporal resection, , TS = Tuberous Sclerosis.

Table 2

Patients with spasticity (N=17): demographic features (sex, ages at onset of epilepsy and at surgery), illness variables (type of surgery, pathology/aetiology, localisation of spasticity, Engel classification) and Gross Motor Function Classification System

Pat.	Sex	Age at onset of epilepsy (yrs;mo)	Age at surgery (yrs;mo)	Surgery type and lateralisation	Pathology/ aetiology	Localisation of spasticity	Engel Classification I t/m IV	GMFCS Pre-surgery	2 yr post-surgery
B T	F	0.5	2.11	Hemisph L	Rasmussen	Hemiplegia R	I	2	2
R S	M	2.2	3.3	Parietal L	Glioma	Hemiplegia R	I	1	1
J E	F	0.5	4.9	Hemisph R	Vas (SWS)	Hemiplegia L	I	4	4
H B	F	0.5	7.7	Hemisph L	Vas (SWS)	Hemiplegia R	I	2	2
I v B	F	5.1	8.5	Hemisph R	Rasmussen	Hemiplegia L	III	5	3
M S	F	7.11	11.5	Hemisph L	Rasmussen	Hemiplegia R	III	1	1
B B	M	4.1	11.10	Frontal R	Glioma	Hemiplegia L	II	1	1
W B	M	10.3	12.1	Hemisph L	Rasmussen	Hemiplegia R	I	1	1
D B	M	1.5	15.4	Callosotomy	No pathology	Tetraplegia	III	1	2
Children with non-progressive encephalopathy									
CGL	F	0.0	0.3	Hemisph R	Hem	Hemiplegia L	I	NA	4
Q H	F	0.0	0.8	Hemisph R	Hem	Hemiplegia L	I	NA	4
RW	M	0.4	1.6	Hemisph L	Hem	Hemiplegia R	I	3	3
E J	F	0.2	2.1	Hemisph R	Dysplasia	Hemiplegia L	I	2	2
JvdB	M	2.1	3.8	Hemisph L	HHE	Hemiplegia R	I	4	4
L D	F	1.1	4.8	Hemisph R	Vas (MCA)	Hemiplegia L	I	3	2
SdV	F	0.3	6.4	Hemisph R	Vas (MCA)	Hemiplegia L	I	2	2
C F	F	0.9	11.10	Hemisph L	Vas (MCA)	Hemiplegia R	I	1	1

Abbreviations: Age (yrs;mo) at surgery = age in years and months at the time of surgery, Frontal = Frontal resection, GMFCS = Gross Motor Function Classification System, HHE = Hemiplegia,hemiconvulsions, epilepsy syndrome, Hem = Hemimegalencephaly, Hemisph = Hemispherectomy, L = Left, MCA = congenital middle cerebral artery infarction, NA= not assessable, Rasmussen = Rasmussen encephalitis, R = Right, Sex: F = Female, M = Male, SWS = Sturge-Weber syndrome, Vas = vascular pathology.

Instruments

Seizures: Engel's Classification of Postoperative Outcome
Seizure frequency was determined using Engel et al.'s (1993) modified classification:
Class I = free from seizures or residual auras, Class II = child experienced intermittent, infrequent seizures or relapsed after a significant seizure-free period and Class III = worthwhile improvement (>75% reduction in seizure frequency). Children who experienced less than 75% reduction in seizure frequency were classified as Engel Class IV. Engel's classification was applied at 24 months after surgery by the same child neurologist (OvN).

Motor impairments

We assessed muscle strength, range of motion and muscle tone as relevant parameters.
Muscle strength of the extremities was assessed proximally and distally and scored according to the criteria for manual muscle testing, using the 6-point scale (MRC range 5-0) (Medical Research Council, 1943; Hislop and Montgomery, 2002).
Range of motion (ROM) was measured using the Joint Alignment and Motion (JAM) scale, a five-point scale of motion decrease (0 = no decrease, 1 = 1-5%, 2 = 6-25%, 3 = 26-75% and 4 = 76-100% decrease) (Spiegel et al., 1987).
Muscle Tone was assessed using the Modified Ashworth Scale (MAS) (Bohannon and Smith, 1987), a 6-point scale of tone increase (0 = no resistance, 1 = slight 'catch' when limb is moved, 1+ = slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM, 2 = resistance in whole range of movement, 3 = strong increase with decreased range of movement, 4 = limb rigidly in flexion or extension) (Bohannon and Smith, 1987).

Motor activities

Movement Assessment Battery for Children (M-ABC)
To measure the overall level of motor function and to screen for movement problems in children without spasticity, the M-ABC (Henderson and Sugden, 1992; Smits-Engelsman, 1998) was used. The M-ABC has been standardized for children from 4 to 12+ years. Children are set eight age-appropriate tasks (age band I: 4-6 years, II: 7 and 8 years, III: 9 and 10 years; IV: 11 years and older) that pertain to three domains: Manual Dexterity (3 tasks), Ball Skills (2 tasks) and Static and Dynamic Balance (3 tasks). Six-point scale values (0-5) are summed (range 0-40) and the total score is converted into an age-related centile score, which is interpreted as 'normal and good' (100th – 16th centile), 'at risk for motor problems' (15th to 6th centile) and 'impaired' (5th centile and below) (Henderson & Sugden, 1992). The lower the raw scores the better the motor function and the higher the centile score. Test-retest reliability (0.75) and inter-rater reliability (0.70- 0.89) of the Dutch version of the M-ABC are satisfactory (Smits-Engelsman, 1998).

Severity of motor disability: Gross Motor Function Classification System (GMFCS)
The GMFCS manual provides separate descriptions for four age bands: before 2nd birthday, 2nd to 4th birthday, 4th to 6th birthday, 6 to 12 years. For each age band, mobility is classified into 5 levels; the title of each level represents the highest level of mobility that a child within that level is expected to achieve. For children over the age of six years, level I is entitled: 'walks without restrictions, limitations in more advanced gross motor skills', and level V is entitled: 'self-mobility is severely limited even with the use of assisting technology' (Palisano et al., 1997). The overall reliability of the GMFCS is 0.79 and increases when tracking starts at higher ages. Inter-rater reliability is 0.93 (Wood and Rosenbaum, 2000). Validity has been reported to be excellent (Rosenbaum et al., 2002; Gorter et al., 2004).

Motor capacity in children with spasticity: Gross Motor Function Measure (GMFM)

The GMFM is a standardized clinical observational instrument designed to evaluate change in gross motor activities in children with CP. It assesses how much of an activity a child can accomplish, rather than how well the activity is performed (Russell et al., 1993; Russell et al., 2002). The 88 items of the GMFM-88 (Russell et al., 2002) are grouped into five dimensions: lying and rolling (17 items), sitting (20 items), crawling and kneeling (14 items), standing (13 items), and walking, running and jumping (24 items). The items are scored on 4-point ordinal scales (0 = cannot initiate, 1 = initiates, but completes less than 10%, 2 = partially completes item (11-99%), 3 = completes item independently). Calculated by means of the intra-class correlation coefficient, reliability values varied from 0.87 to 0.99 (Russell et al., 1993; Ketelaar et al., 2001; Russell et al., 2002). Scores: percent scores for each of the five GMFM dimensions and a total GMFM-88 percentage score. Higher scores indicate a better capacity.

Change on this instrument used to be interpreted intuitively, but we could appeal to recently published reference data for the motor development of children with CP (Russell et al., 2002; Rosenbaum et al., 2002). As in children with CP motor outcome is limited by severity of motor disability, the latter was classified by means of the GMFCS into 5 levels that are based on differences in self-initiated movement, with particular emphasis on sitting and walking (Palisano et al., 2000; Gorter et al., 2004). We compared change in children with spasticity to that in a reference group of children with spasticity caused by CP, by mapping, for every GMFCS level, the mean GMFM-88 total score on the corresponding GMFM reference value published in the GMFM manual (Russell et al. 2002: Table A 4.2, page 206).

Evaluation of activities of daily life (ADL) and caregiver's assistance: Pediatric Evaluation of Disability Inventory (PEDI)

The PEDI (Haley et al., 1992; Custers, 2001) is a structured parent's interview that assesses functional skills (capability) and

caregiver's assistance. It covers the domains of self-care (73 items), mobility (59 items) and social functioning (65 items). The scaled scores offer the opportunity to estimate skills in older children whose functional abilities lag behind those expected of 7.5-year-old healthy children (Feldman et al., 1990; Haley et al., 1992; Nichols and Case-Smith, 1996; Custers et al., 2002). We used the scaled scores. The PEDI is sensitive to changes over time. The Internal Consistency for PEDI scales has alpha scores ranging from 0.95 to 0.99 and a mean standard error of measurement of 0.09 (Haley et al., 1992; Custers, 2001). The scaled scores estimate the skill in each domain (0 = no measurable functional skill, 100 = intact functional skill; 0 = complete caregiver's assistance, 100 = no caregiver's assistance).
The smallest change in PEDI scores that is considered to be associated with a minimal, but clinically important difference in skill ranges from 6 to 15 points (mean =11.5, SD = 2.8) for all PEDI scales (Iyer et al., 2003).

All parents of the children and, if over 12 years of age, the children themselves gave informed written consent and the study was approved by the Institutional Review Board.
Motor and ADL-functions of all children were assessed by the paediatric physical therapist (RvE) who had been trained in administering and scoring the GMFM. Reliability, as assessed compared to a criterion tape after this training, was adequate (weighted Kappa > 0.80). Use of the GMFCS requires familiarity with the child and the GMFCS levels, but no formal training.

Data analysis

Changes in M-ABC, GMFM-88 and PEDI scores were analysed using the Analysis of variance (ANOVA) for repeated measures with Time (pre-, 6, 12 and 24 months post-surgery) as within-subject factor, with post hoc testing to compare sessions and adjust for multiple comparisons using least significant difference (LSD). A two-sided P-value of 0.05 or less was considered statistically

significant. The SPSS software version 11.01 was used.
The influences of variables such as age of onset of epilepsy, age at surgery, time between onset of epilepsy and surgery, aetiology, type of surgery and Engel classification on the changes in M-ABC and GMFM values compared to reference data were explored by a linear mixed model analysis (the statistical software package R version 1.8.1). Because of the small number of participants, only 2 variables could be used per item. Therefore, epilepsy surgery, e.g., was categorized into temporal resection versus non-temporal resection in the group without spasticity, and type of epilepsy surgery into hemispherectomy versus non-hemispherectomy in the group with spasticity.

Results

Seizure frequency
Table 3 shows Engel's Classification of Postoperative Outcome (Engel et al., 1993) by type of surgery. Two years after surgery, 27 children (74%) had achieved complete seizure control, five (13% children still had rare seizures and the remaining five (13%) showed a worthwhile reduction (>75%) in number of seizures.

Table 3
Seizure outcome according to type of surgery (n=37)

Seizure outcome*	Temporal resection	Frontal resection	Parietal resection	Central resection	Calloso-tomy	Hemi-spherec-tomy	Total
I	10	2	2	2	-	11	27 (74%)
II	3	2	-	-	-	-	5 (13%)
III	1	-	-	-	1	3	5 (13%)
IV	-	-	-	-	-	-	0 (0%)
Total	14	4	2	2	1	14	37 (100%)

* Engel's Classification of Postoperative Outcome (Engel et al., 1993)

Motor impairments
Range values of muscle strength, range of motion and muscle tone pre- and post-surgery are shown in the Appendix, for both the group without (n = 20) and that with spasticity (n = 17) (Appendix 1; individual data can be obtained from the first author). In the group without spasticity, two children (one child in whom the epilepsy focus was right frontal and the other right central) had a slight impairment in muscle strength (pre- and post-surgery) and muscle tone (post-surgery). In the group with spasticity, muscle strength, range of motion as well as muscle tone of the arm and leg were mildly to moderately impaired on the affected side, pre-surgery as well as post-surgery.

Motor activities: M-ABC (n=20)
Motor performance of the 20 children without spasticity is shown in both real (raw scores) and centile terms (Table 1). In 16/20 children, centile scores pre-surgery were below 16, meaning they were at risk for motor problems; 4/20 had normal scores pre-surgery and remained so at all times post-surgery. Fourteen of the 20 children attained normal centile scores at 12 and 24 months, eleven of these had been below the 16th centile pre-surgery. In 6 children, [four of them with a tumour (# 6, #8, #12 and #20)] the centile scores remained below 16 at all times. In the two children (# 11 and # 16) with some impairment, one had normal values on the M-ABC centile scores post-surgery. The mean centile scores were: pre-surgery 12.5 (SD 14.2), 6 months post-surgery 19.0 (SD 16.8), 12 months post-surgery 27.8 (SD 21.3) and 24 months post-surgery 37.3 (SD 27.5).
ANOVA for repeated measures confirmed a statistically significant change from pre-surgery to 6 months post-surgery ($p = 0.002$) and from one to two years post-surgery ($p = 0.01$).

Severity of motor disability: GMFCS (n=17)
Table 2 shows demographic and illness characteristics of 17 patients with spasticity separately for those with progressive and non-progressive encephalopathy. GMFCS levels prior to and 24 months

post-surgery are presented. Fourteen of the 17 children remained within the pre-surgery level. Two children improved (IvB from 5 to 3 and LD from 3 to 2) and one child (DB) worsened (from 1 to 2).

Motor capacity in children with spasticity: GMFM-88 (n=17)
The mean total % scores on the GMFM were: pre-surgery 53.8 (SD 36.3), 6 months post-surgery 51.2 (SD 31.6), 12 months post-surgery 62.1 (SD 29.5) and 24 months post-surgery 69.5 (SD 28.7) The ANOVA repeated measures revealed significant changes, i.e., improvements between 6 and 12 months post-surgery ($p < 0.01$) and between 12 and 24 months post-surgery ($p < 0.01$).

GMFM stratified per GMFCS level
The scores of the 17 children on the GMFM-88 were compared to the mean GMFM-88 score reported in the GMFM manual according to the GMFCS level and age. Pre-surgery, 10/17 children obtained scores that were more than 1 SD worse than their reference values, at 24 months post-surgery 6/17 children differed by more than 1 SD (three + 1SD and three - 1SD) and 16/17 children scored within 2 SD of the mean referent score at that age band and GMFCS level (Table 4).
Mixed linear model analyses showed variables such as age at onset of epilepsy, age at surgery, time between onset of epilepsy and surgery, aetiology, type of surgery, and result on Engel classification to have had no statistically significant effect on scores of M-ABC and GMFM. Time after surgery, however, had a statistically significant effect on GMFM ($p = 0.007$) and M-ABC ($p = 0.0001$).

Table 4

GMFM-88 total % score pre-surgery and 6, 12, 24 most post-surgery, in 17 children with spasticity. Age pre-surgery. GMFM score, Reference GMFM values per GMFCS level and age pre-surgery and 2 years post-surgery

Pat.	Age Pre-surgery (yrs;mo)	GMFM Pre-surgery	6 months post-surgery	12 months post-surgery	24 months post-surgery	Referent GMFM score per GMFCS level and age (pre-surgery) mean (SD)	Referent GMFM score per GMFCS level and age (2 yr post-surgery) mean (SD)
BT	2.11	72	44	68	86	61.2 (14.9)	75.8 (16.3)
RS	3.3	93	96	97	97	81.2 (13.5)	90.8 (8.6)
JE	4.9	21	26	43	50	40.4 (12.9)	36.0 (14.0)
HB	7.7	73	78	90	97	85.9 (9.5)	85.9 (9.5)
IvB	8.5	10	23	51	64	13.3 (9.4)	62.3 (13.2)
MS	11.5	100	59	83	91	96.8 (3.3)	96.8 (3.3)
BB	11.10	100	76	84	96	96.8 (3.3)	96.8 (3.3)
WB	12.1	56	57	79	87	96.8 (3.3)	96.8 (3.3)
DB	15.4	82	85	85	85	96.8 (3.3)	85.9 (9.5)
Children with non-progressive encephalopathy							
CGL	0.3	2	6	10	16	-	28.4 (9.2)
Q H	0.8	2	5	23	30	-	28.4 (9.2)
RW	1.6	8	18	26	34	37.7 (14.2)	54.3 (10.3)
E J	2.1	67	24	32	50	61.2 (14.9)	75.8 (16.3)
LD	4.8	47	67	75	83	62.0 (15.8)	85.9 (9.5)
JvdB	3.8	18	27	27	28	28.4 (9.2)	40.4 (12.9)
SdV	6.4	70	85	85	91	85.9 (9.5)	85.9 (9.5)
C F	11.10	93	95	98	98	96.8 (3.3)	96.8 (3.3)

Activities of daily life and caregiver's assistance (PEDI)

In Table 5, mean PEDI-scores are presented for children with spasticity. One child with spasticity was younger than 0.5 years of age before surgery while in another case the PEDI-forms had not been properly completed twelve months after surgery.

Due to a ceiling-effect, change in activities of daily life and caregiver's assistance in children without spasticity remained unclear (data not shown).

In children with spasticity, the statistically significant effect of Time in the ANOVA-RM indicates that self-care ($F1.36 = 4.28$, $p < .05$), mobility ($F2.44 = 6.96$, $p < .01$) and social functioning ($F1.62 = 14.92$, $p < .001$) improved at follow-up. Improvement appeared to be significant between 6 and 12 months and between 12 and 24 months post-surgery in self-care, mobility and social functioning ($p's < .05$).
Similarly, the statistically significant effect of Time with respect to caregiver's assistance indicates that assistance decreased in self-care ($F2.44 = 8.78$, $p < .001$), mobility ($F1.44 = 6.13$, $p < .01$) and social functioning ($F1.89 = 6.60$, $p < 0.01$), in other words, the children's independence increased. Improvement was statistically significant between 6 and 12 months and between 12 and 24 months post-surgery (all three dimensions $p's < .05$).

Table 5

Mean PEDI scores on functional skills and caregiver's assistance in children with spasticity (n=17), pre-surgery and 6, 12 and 24 months post-surgery.

	Pre-surgery Mean (SD)	6 m post Mean (SD)	12 m post Mean (SD)	24 m post Mean (SD)
Functional skills				
Self care	53.4 (27.3)	56.1 (20.3)	59.4 (16.7) **	66.9 (18.3) **
Mobility	58.6 (33.5)	56.9 (35.9)	64.1 (29.3) *	72.3 (25.7) **
Social function	51.8 (29.3)	54.1 (30.1)	60.7 (25.4) *	67.9 (24.9) *
Caregiver assistance				
Self care	48.9 (29.5)	48.4 (29.2)	55.8 (21.8) **	63.0 (20.5) **
Mobility	56.9 (32.8)	54.3 (33.9)	63.1 (28.3) **	74.0 (22.6) **
Social function	54.6 (30.4)	51.4 (33.4)	58.8 (25.2) *	68.5 (24.1) **

ANOVA repeated measurement: Significant effect of Time: * = p<.05 ** = p<.01

Discussion

Epilepsy surgery and motor function

Motor impairments and delays in motor development often coexist in childhood epilepsy (Beckung and Uvebrant, 1993, 1997; Carlsson et al., 2003). This is not surprising, as motor activity depends, among other factors, on the integrity of the central nervous system, as well as on mood, concentration and motivation of the child.
In terms of the WHO- International Classification of Functioning, Disability and Health (WHO, 2002), motor impairments are usually due to the underlying cause of the epilepsy, i.e., a central nervous system lesion, or to the epilepsy itself, the medication or a combination of these factors (Carlsson et al., 2003). After successful epilepsy surgery, seizure reduction may reflect a better neurological state, which may allow the children access to a more effective motor system. This may be expressed in improved motor activity (Beckung et al., 1994), a view that seems to be confirmed by the present study. Notwithstanding the remaining impairments post-surgery, especially in the group of children with spasticity, our study shows improvement of motor activity in the majority of the children, in whichever group. One should take note of the fact that most children in the group without spasticity (14/20) were classified as "normal " at 24 months follow-up, while at baseline 15/20 were classified as "at risk for motor problems". In 6 children the centile scores remained below 16 at all times. Four of these children had a tumour (Table 2 # 6, #8, #12 and #20) and three of them still had epilepsy after surgery (one with Engel 3 and two Engel 2). Two children (#7 with MTS and #16 with cortical dysplasia) had no seizures after surgery but motor activity remained retarded.
Beckung et al. (1994) reported a positive correlation between a favourable effect of surgery on seizures and improvement in motor activity. They reported on different types of surgery (i.e. hemispherectomies, lobectomies, callosotomies) in a heterogeneous group of patients (children with and without spasticity); our data are in this sense comparable with those of Beckung et al., (1994).

Factors explaining change in motor activity after epilepsy surgery

Østensjo et al., (2004) recently reported on the basis of a study of 95 children with spasticity due to CP a moderate relationship of spasticity, range of motion, selective dorsiflexion of the ankle (impairments) and gross motor function as measured with the GMFM (activities). In a study of hemispherectomised children (Empelen et al., 2004), we also found that impairments were only slightly associated with functional outcome. It is, therefore, essential to measure not only the impairments (ICF domain of anatomical and physiological functions), but also motor activity (ICF domain: activities) in relation to epilepsy surgery and to be aware of differences in impairments and activities. The Engel score, as a result of reduced seizure frequency, is not related to the difference in results in the GMFM and M-ABC values. This is not surprising, as the Engel score is just one of the many components and factors that can influence motor and ADL functioning. Overall we have to realise that impairments are not directly related to motor activity and daily functional activities.

Type of surgery, age at seizure onset, aetiology (congenital or acquired epilepsy), interval between age at seizure onset and time of surgery, age at surgery, are among the variables that have been suggested to be significant prognostic factors regarding the children's motor outcome (Graveline et al., 1999). However, although we could only explore these relationships, we found no significant influence of these variables on GMFM and M-ABC results. We were interested to find out whether motor activity would improve more in younger children and children who were operated on at a younger age than in older children, because plasticity is thought to be age-dependent (Chen R et al., 2002). We found only 'Time after surgery' to be significantly related to motor outcome.

GMFCS and GMFM

To our knowledge, this is the first study comparing motor activity in children with spasticity before and after epilepsy surgery with reference GMFM-88 scores as described in the GMFM manual by Russell et al., (2002). They described developmental values derived from assessing children with CP per GMFCS level by age. We assessed the GMFCS level pre- and post-surgery, and found changes in level scores in three children. In 14/17, the GMFCS level remained stable from prior to the last post-surgery measurement time point. Changes in GMFCS level are rare in children with CP (Rosenbaum et al., 2002). However, as in our children, GMFCS levels are also influenced by the epilepsy; therefore, changes in GMFCS level may be more likely than in the general CP-population due to improved seizure control after surgery. We compared our data, on the GMFM-88 total score for each child pre-surgery and post-surgery, with the reference data per GMFCS level. At 24 months post-surgery, 16/17 children scored within 2 SD of the expected score. Hence, the concept of GMFCS growth curves would seem to be useful when determining whether the child is performing in accordance with her/his expected growth curve of gross motor development. At least after surgery the growth curves can help to predict motor development in children with spasticity of cerebral origin. Our data suggest that children do not deteriorate in motor activity after epilepsy surgery. This finding is important, considering the uncertainties of parents and children about motor function after surgery.

Activities of daily life (ADL) and caregiver's assistance

The age ranges of the children with spasticity and of those without spasticity are quite different. This has consequences for the interpretation of PEDI-scores. In the PEDI, norm scores are based upon the assumption that healthy children of 7.5 years of age score 100% in all domains. In the children with spasticity participating in this study, the median age is 6.1 years (range 0.3-15.4). Most of

these children would, therefore, not reach a score of 100%, even without physically limitations. In the children without spasticity, the median age is 11.5 (range 6.1-15.4). It is obvious that this group approaches the 100% very closely, because most of them are older than 7.5 and they do not have, except for their epilepsy, the concrete physical limitations, which children with spasticity have. Clinically important changes in functional skills and caregiver's assistance range from 6 to 15 points (Iyer et al., 2003). In our study, in children with spasticity, scores for functional skills and caregiver's assistance on the PEDI increased from a pre-surgery: 48.9 – 58.6 to 55.8 – 63.1, two years post-surgery, indicating a clinically relevant improvement.

Limitations of the study

Our study has some intrinsic limitations. The changes in ADL-function and caregiver's assistance could not be detected in children without spasticity, due to a ceiling effect of the PEDI instrument. For measuring changes in ADL-function and independence in children aged 7.5 years and older with (severe) epilepsy and minimal physical limitations, a measuring instrument other than the PEDI should be available. The ceiling effect does not mean that there is no improvement in children without spasticity, but we were not able to measure this effectively.
The sample of children who participated in the present study is considered to be representative of the population of children with pharmacologically untreatable epilepsy who are eligible for epilepsy surgery and who have also been described in other studies (Devlin et al., 2003; Smith et al., 2004). The number of children in our study is, however, small; therefore, we have to be careful in the interpretation of the exploration of variables that may have influenced the results on GMFM and M-ABC scores. This study does not allow a detailed analysis of determinants of outcome, due to the small number of children and their heterogeneity in age, pathology and level of functioning.

Conclusion

Two years after epilepsy surgery motor function of the majority of children develops conform the expected motor development in children with and without spasticity, while impairments do not deteriorate. Caregiver's assistance decreases, indicating an increase in activities of daily functioning, in other words in the child's independence.

Acknowledgements

We are grateful to the Phelps Stichting and the Johanna Children's Foundation for their financial support; to Dr. W.R. Pestman and Dr. M. Schipper, Centre for Biostatistics, for their supervision of statistic analyses; to E. van der Steeg, MA, University Utrecht, Faculty of Social Sciences, for her assistance in this research.
The surgeons, Prof. Dr. C.W.M. van Veelen and Dr. P.C. van Rijen, operated on all patients.
We thank the Members of the Dutch Collaborative Epilepsy Surgery Programme: SEIN, Kempenhaeghe, Hans Bergerkliniek, University Hospitals (Utrecht, Maastricht, Amsterdam VU).

References

Beckung E Uvebrant P. Motor and sensory impairments in children with intractable epilepsy. Epilepsia 1993;34:924-29.

Beckung E, Uvebrant P, Hedström A, Rydenhag B. The effects of epilepsy surgery on the sensorimotor function of children. Dev Med Child Neurol 1994;36:893-901.

Beckung E, Uvebrant P. Hidden dysfunction in childhood epilepsy. Dev Med Child Neurol 1997; 39: 72-8.

Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. Epilepsia 2002;43:535-38.

Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 1987;67:206-7.

Carlsson M, Hagberg G, Olsson I. Clinical and aetiological aspects of epilepsy in children with cerebral palsy. Dev Med Child Neurol 2003;45:371-6.

Chassoux F, Devaux B, Landré E, Chodkiewicz JP, Talairach J. Chauvel P. Postoperative motor deficits and recovery after cortical resections. Adv Neurol 1999;81:189-99.

Chen LS, Wang N, Lin M. Seizure outcome of intractable partial epilepsy in children. Ped Neurol 2002;26:282-7.

Chen R, Cohen LG, Hallett M. Nervous system reorganization following injury Neuroscience 2002;111: 761-73. [Review]

Custers JWH. Pediatric Evaluation of Disability Inventory; the Dutch adaptation. [PhD thesis], Utrecht University; 2001.

Custers JWH, van der Net J, Hoijtink H, Wassenberg-Severijnen JE, Vermeer A, Helders PJM. Discriminative validity of the Dutch Pediatric Evaluation of Disability Inventory. Arch Phys Med Rehabil 2002;83:1437-41.

Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003;126:556-66.

Empelen R van, Jennekens-Schinkel A, Buskens E, Helders PJM, Nieuwenhuizen O van. Functional consequences of hemispherectomy. Brain 2004;127:2071-9.

Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel JJ, ed. Surgical Treatment of the Epilepsies. 2nd ed. New York: Raven Press; 1993. p. 609-21.

Feldman AB, Haley SM, Coryell J. Concurrent and construct validity of the Pediatric Evaluation of Disability Inventory. Phys Ther 1990;70:602-10.

Gorter JW, Rosenbaum PL, Hanna SE, Palisano RJ, Bartlett DJ, Russell DJ, et al. Limb distribution, motor impairment, and functional classification of cerebral palsy. Dev Med Child Neurol 2004;46:461-7.

Graveline C, Hwang P, Bone G, Shikolka C, Wade S, Crawley A, et al. Evaluation of gross and fine motor functions in children with hemidecortication: predictors of outcomes and timing of surgery. J Child Neurol 1999;14:304-15.

Graveline C, Young N, Hwang P. Disability evaluation in children with hemidecorticectomy: use of the activity scales for kids and the pediatric evaluation disability inventory. J Child Neurol 2000;15:7-14.

Haley SM, Coster WJ, Ludlow LH. Pediatric Evaluation of Disability Inventory (PEDI), Boston: M.A. New England Medical Center, [manual] 1992.

Henderson SE. & Sugden DA. Movement Assessment Battery for Children. London: The Psychological Corporation, [manual] 1992.

Hislop HJ, Montgomery J. Daniels and Worthingham's Muscle testing Techniques of Manual Examination. Philadelphia: WB Saunders Company, 2002.

Iyer LV, Haley SM, Watkins MP, Dumas HM. Establishing minimal clinically important differences for scores on the Pediatric Evaluation of Disability Inventory for inpatient rehabilitation. Phys Ther 2003;83:888-98.

Ketelaar M, Vermeer A, Hart H, van Petegem-van Beek E, Helders PJM. Effects of a functional therapy program on motor abilities of children with cerebral palsy. Phys Ther 2001;81:1534-45.

Krsek P, Tichy M, Belsan T, Zamecnik J, Paulas L, Faladova L, et al. Life-saving epilepsy surgery for status epilepticus caused by cortical dysplasia. Epileptic Disorders 2002;4:203-8.

Lendt M, Helmstaedter C, Kuczaty S, Schramm J, Elger CE. Behavioural disorders in children with epilepsy: Early improvement after surgery. J Neurol Neurosurg and Psychiatry 2000;69:739-44.

Medical Research Council. Aids to the investigation of peripheral nerve injuries. War memorandum 2nd ed. London: HMSO, 1943.

Nichols DS, Case-Smith J. Reliability and validity of the Pediatric Evaluation of Disability Inventory. Ped Phys Ther 1996;8:15-24.

Østensjo S, Carlberg EB, Vollestad NK. Motor impairments in young children with cerebral palsy: relationship to gross motor function and everyday activities. Dev Med Child Neurol 2004;46:580-9.

Palisano RJ, Rosenbaum PL, Walter SD, Russell DJ, Wood EP, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997;39:214-23.

Palisano RJ, Hanna SE, Rosenbaum PL, Russell DJ, Walter SD, Wood EP, et al. Validation of a model of gross motor function for children with cerebral palsy. Phys Ther 2000;80:974-85.

Peacock WJ, Comair Y, Hoffman HJ, Montes JL, Morrison G. Special considerations for epilepsy surgery in childhood. In: Engel JJ, ed. Surgical Treatment of the Epilepsies. 2nd ed. New York: Raven Press; 1993: 541-47.

Romanelli P, Weiner HL, Najjar S, Devinsky O. Bilateral resective epilepsy surgery in a child with tuberous sclerosis: case report. Neurosurg 2001;49:732-5.

Ronen GM, Streiner DL, Rosenbaum P; Canadian Pediatric Epilepsy Network. Health-related quality of life in children with epilepsy: development and validation of self-report and parent proxy measures. Epilepsia 2003;44:598-612.

Ronen GM, Streiner DL, Rosenbaum P. Health-related quality of life in childhood epilepsy: Moving beyond 'seizure control with minimal adverse effects'. Health Qual Life Outcomes 2003;1:36.

Rosenbaum PL, Walter SD, Hanna SE, Palisano RJ, Russell DJ, Raina P, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. JAMA 2002; 18:1357-63.

Russell D, Rosenbaum PL, Gowland C, Hardy S, Lane M, Plews N, et al. Manual for the Gross Motor Function Measure. (2 ed.) Hamilton, Canada: McMaster University. 1993.

Russell DJ, Rosenbaum PL, Avery LM, Lane M. GMFM Gross Motor Function Measure, (GMFM-66 & GMFM-88) User's Manual. Cambridge: Cambridge University Press; 2002.

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Smits-Engelsman BCM. Movement ABC. Nederlandse handleiding. [manual] Lisse: Swets & Zeitlinger; 1998.

Spiegel TM, Spiegel JS and Paulus HE. The joint Alignment and Motion Scale; a simple measure of joint deformity in patients with rheumatoid arthritis. J Rheumatol 1987;14:887-93.

Wood EP, Rosenbaum PL. The Gross Motor Function Classification System for cerebral palsy. Dev Med Child Neurol 2000;42:292-6.

Wyllie E, Comair YG, Kotagal P, Bulacio J, Bingaman W, Ruggieri P. Seizure outcome after epilepsy surgery in children and adolescents. Ann Neurol 1998;44:740-8.

WHO (World Health Organization) International Classification of Functioning, Disability and Health, Geneva: WHO, 2002.

Appendix 1

Muscle strength, Range of motion and Muscle Tone: median score and range pre-surgery and 6, 12 and 24 months post-surgery in children without spasticity and children with spasticity. Arm proximal and distal, Leg proximal and distal

	Muscle strength (MRC) * Median (range)				Range of motion (JAM score) * Median (range)				Muscle Tone (Ashworth scale) * Median (range)			
	pre	6 m	12m	24m	pre	6 m	12m	24m	pre	6 m	12m	24m
Without Spasticity (n= 20)												
Arm prox	5 (4-5)	5 (4-5)	5 (4-5)	5 (4-5)	0	0	0	0	0	0	0	0
Arm dist	5 (4-5)	5 (4-5)	5 (4-5)	5 (4-5)	0	0	0	0	0	0 (0-1)	0	0
Leg prox	5 (4-5)	5 (4-5)	5 (4-5)	5 (4-5)	0	0	0	0	0	0	0	0
Leg dist	5 (4-5)	5 (4-5)	5 (4-5)	5 (4-5)	0	0	0	0	0	0 (0-1)	0 (0-1)	0 (0-1)
With Spasticity (n= 17)												
Arm prox	4 (1-4)	3 (1-4)	3 (1-4)	4 (1-4)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-3)	1 (0-3)	1 (0-4)	1 (0-4)	1 (0-4)
Arm dist	3 (1-4)	3 (1-4)	3 (1-4)	3 (1-4)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)
Leg prox	4 (2-5)	4 (2-5)	4 (2-5)	4 (2-5)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-3)	1 (0-4)	1 (0-4)	1 (0-4)	1 (0-4)
Leg dist	4 (1-5)	4 (1-5)	4 (1-5)	4 (2-5)	1 (1-4)	1 (1-4)	1 (1-4)	1 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)

* Median muscle strength, range of motion and tone of the paretic side in the group with spasticity in both sides in the group without spasticity at pre-surgical baseline and 6, 12 and 24 months post-surgery. Muscle strength as MRC-score: 0-5, higher score indicates greater muscle strength (5 = normal). Range of motion as expressed in Joint Alignment and Motion (JAM) score: 0-4 (0 = normal). Tone increase as Modified Ashworth Scale Score: 0-4, higher score means greater degree of spasticity (0 = normal).

Chapter 5

Two years after the decision not to operate on children for pharmaco-resistant epilepsy: no downward course of epilepsy and motor functioning

R. van Empelen[1,*]
P.J.M. Helders[1]
P.C. van Rijen[2,*]
A. Jennekens-Schinkel[3,*]
O.van Nieuwenhuizen[4,*]

On behalf of the Dutch Collaborative Epilepsy Surgery Programme.

1 Department of Paediatric Physical Therapy and Exercise Physiology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands. NetChild, Network for Childhood Disability Research in The Netherlands.
2 Department of Neurosurgery, University Medical Center – Utrecht, The Netherlands.
3 Department of Neuropsychology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
4 Department of Child Neurology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.

* Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands.

Submitted for publication

Summary

Purpose: To study over a period of two years whether severity of epilepsy, motor functioning and epilepsy-related restrictions worsen in children with pharmaco-resistant epilepsy who are not eligible for epilepsy surgery.
Methods: Prospective longitudinal 2-year follow-up of 45 children with pharmaco-resistant epilepsy (aged 6 months to 15 years). Severity of seizures (HASS), motor impairments (muscle strength, range of motion and tone), motor development (BSID II, M-ABC, GMFM), activities of daily life (PEDI) and epilepsy-related restrictions (HARCES) were rated at baseline and at 6, 12 and 24 months thereafter. Data were analysed non-parametrically and by means of ANOVA for repeated measures and correlation and regression analysis.
Results: Seizure severity (mean score at baseline 31.35 [SD 15.6]) did not change significantly. Mean values of muscle strength, range of motion and tone were below reference norms and did not change. Motor retardation was ubiquitous but did not increase in 33 children without spasticity (BSID-II and M-ABC). Motor function of 12 children with spasticity developed (GMFM p's < 0.05; baseline 55.75 [SD 35.4], 71.82 [SD 28.4] at 24 months later), but remained poor in four/12 (>2 SD worse than reference values). In the complete group, functional skills and caregiver's assistance (PEDI) increased, but remained considerably below reference values. Restrictions (HARCES) at baseline mean 22.18 [SD 8.3] did not change significantly.
Conclusion: Of children with pharmaco-resistant epilepsy who have to do without surgical intervention and in whom no other adverse events occur, seizure severity does not progress, motor impairments do not increase, motor development does not deflect negatively and activities of daily living and restrictions do not worsen.

Introduction

Not all pharmaco-resistant seizures in childhood offer the prospect of successful surgical treatment. In The Netherlands, almost 75% of the children who are presented to the Dutch Collaborative Epilepsy Surgery Program (DuCESP) fail to fulfil the criteria for surgery and hence have to be refused this treatment. The present study followed the children who were primarily considered not eligible for surgery from the moment of presentation to DuCESP to two years thereafter, with a focus on seizure severity and on motor development of the children. We used the International Classification of Functioning, Disability and Health (ICF) (WHO, 2002; Battaglia et al., 2004) as a guide to our study, which addressed impairments (defined as a loss or abnormality in body function and structure), limitations in activities (the difficulties that the child may have when executing daily activities), and restrictions with respect to participation in social life (problems that the child experiences in social situations).

On the level of impairments, the frequent association of epilepsy with cerebral palsy is well known (Beckung and Hagberg, 2002; Østensjø et al., 2004). In children with and without spasticity, and having pharmaco-resistant epilepsy, motor development and motor impairments are not well known and have to be traced. Limitations in activities can be measured in terms of performance, caregiver's assistance, and the use of devices to perform the activities (Jette, 1994). We addressed these aspects of everyday functioning by establishing the course of functional skills and of caregiver's assistance. Parents and physicians usually impose restrictions on children with epilepsy to avoid seizure-related injuries or accidents (Carpay et al., 1997). We quantified these restrictions.

Parents fear that their children with pharmaco-resistant epilepsy, if not treated surgically, will deteriorate in terms of seizure severity, mental and motor development and epilepsy-associated impairments. Some authors consider pharmaco-resistant epilepsy not to be incompatible with positive cognitive development (Ellenberg et al., 1986), whereas others report deterioration of intelligence (Bjør-

naes et al., 2001). Cognitive development is even considered to be a major determinant of both activities and restrictions (Kennedy, 2003). Hence, we took the intelligence quotient (IQ) or developmental index (DI) into account as an index of cognitive function and we analysed at entry and 24 months later the associations of the latter with seizure severity, motor development and motor functioning and epilepsy-related restrictions.
The present study addresses the following questions: What are the impairments in terms of subjectively experienced seizure severity, the limitations in terms of motor development, and the epilepsy-related restrictions in children with pharmaco-resistant epilepsy? If they change over the two years of the follow-up, to what degree and in what direction?

Patients

Between December 1996 and 2001, 45 candidates for epilepsy surgery (19 girls, 26 boys) were considered by DuCESP not to be eligible for this treatment (Table 1). Median age of these children was 5.6 years (range 0.6-15.2). All were living with their parents. Twelve children had spasticity, eight of them due to cerebral palsy. IQ's were determined using instruments validated for Dutch children (WISC-R and WPPSI-R) (Wechsler, 1974, 1989; Bruyn et al., 1986; Steene and Bos, 1997) or equivalent instruments (mean = 100; SD = 15). In younger children, we used the mental scales of the Bayley Scales of Infant Development II (BSID-II). In these children Developmental Index scores (DI) were measured (mean = 100, SD = 15, range 50-150) (Bayley, 1993). The index of cognition (IQ/DI) was on average 62.44 (SD 17.8) at baseline, and did not change significantly (Table 2). Only 8/45 children had an IQ/DI > 80; most children (33/45) were mentally retarded (IQ/DI <70). Classification of seizure type and localization followed guidelines proposed by the International League Against Epilepsy (Commission ILAE, 1989; Eriksson and Koivikko, 1997). When entering the study, 27 children suffered from complex partial seizures, 12 from

secondary generalized seizures, three from simple partial seizures and another three from mixed seizures. The epileptogenic zone was localized in the temporal lobe in six children (right 4, left 2), in the frontal lobe in 9 children (right 6, left 3), in the occipital lobe in two children (right 1, left 1), centrally in 3 children (right 2, left 1) and in both hemispheres in 25 children. The underlying pathology as visualized by MR-imaging varied from ischemic infarction (n = 10), cortical dysplasia (n = 8), Sturge-Weber syndrome (n = 5), mesial temporal sclerosis (n = 5), multiple pathology (e.g. dual pathology, such as cyst and MTS) (n = 4), tumor cerebri (n = 4), tuberous sclerosis (n = 2), hemimegalencephaly (n = 2), Rasmussen encephalitis (n = 1), to no detectable etiology (n = 4) (Table 1). On entrance to the study, all patients were using at least two anticonvulsant drugs and were pharmaco-resistant. New drugs were prescribed during the follow-up period.

The parent(s) of the children and, if over 12 years of age, the children themselves gave informed written consent. The Institutional Review Board approved the study.

Table 1

Reasons for deciding against surgery, separately shown for the ten types of pathology as found in the 45 candidates. Entries are numbers of cases (total n=45)

Pathology	Reasons for deciding that a candidate was not eligible for surgery				
	Eloquent cortex	Multi-focal localisation or Incongruence of MRI, EEG and seizure-semiology	Infrequent seizures	Positive change in seizure severity	Re-evaluation for surgery*
Ischemic infarction	1	4	3	1	1
Cortical dysplasia	1	2	1	2	2
Sturge-Weber Syndrome			3	1	1
Multiple pathology		4			
Mesial temporal sclerosis			1	1	3
Tumor cerebri	1	1		1	1
Tuberous sclerosis		2			
Rasmussen encephalitis	1				
Hemimegalencephaly				1	1
No detectable etiology	2	1		1	
Total	6	14	8	8	9

* After closure of this study, 9 children were re-evaluated and have been accepted for surgery.

Table 2

Cognitive development, assessed at Baseline and at 6, 12 and 24 months thereafter (Full Scale Intelligence Quotient [WISC-R and WPPSI-R] or Developmental Index [BSID-II]) (n = 45)

	Baseline	6 months later	12 months later	24 months later
Mean (SD)	62.44 (17.8)	60.27 (18.1)	60.93 (17.5)	59.69 (17.9)
Median (range)	50 (38-106)	50 (36-118)	50 (40-98)	50 (40-105)

Methods

Patients were assessed in the outpatient clinic of the Wilhelmina Children's Hospital using a standard protocol with fixed intervals: baseline assessment and at 6 months, 1 year and 2 years thereafter. Following the ICF classification (WHO, 2002) we measured impairments in terms of parental ratings of seizure severity and in terms of muscle strength, range of motion and muscle tone.

Impairments

Seizure severity as perceived by the parent or caregiver's was quantified using the Hague Seizure Severity Scale (HASS), which consists of 13 items that have to be answered on a four-point scale. The items inventory problems that may have been encountered in the three previous months. The following areas are addressed: consciousness (4 items), motor symptoms (2 items), incontinence (1 item), injuries/pain (3 items) and overall seizure severity (3 items) (Carpay et al., 1997). The scale is based on the Liverpool Seizure Severity Scale (Scott-Lennox et al., 2001). It is reliable in terms of test-retest stability and internal consistency (Carpay et al., 1997). Test-retest reliability is 0.93 and internal consistency is 0.85. The scores range from 13 (no seizures) to 52 (maximal seizure severity). Muscle strength of the extremities was assessed proximally and distally and scored according to the criteria for manual muscle testing, using the 6-point MRC scale (range 5-0) (Medical Research Council, 1943; Hislop and Montgomery, 2002). Dependent on the age of the child, manual muscle testing or functional muscle testing was chosen. In children under the age of 5 years, functional muscle strength was tested in accordance with Hislop et al.'s brief course on the spectrum of muscle activity associated with each posture and movement, which showed that the skilled examiner obtains the information necessary to determine a pattern of muscular strengths and weaknesses by observing the child execute a number of developmentally appropriate movements (Hislop and Montgomery, 2002). Manual muscle testing was performed in children over

5 years of age. Despite the subjectivity of manual muscle testing, its reliability and validity are both adequate for use in clinical assessments (Hislop and Montgomery, 2002). Strength was assessed in the following muscles: flexors and abductors of the shoulders and hips (proximal), dorsal and palmar flexors in the wrists and plantar and dorsal flexors in the ankles (distal). Scores: 8 strength scores were calculated by averaging the scale values per proximal and distal and right and left muscle group.
Range of motion (ROM) was measured using the Joint Alignment and Motion (JAM) scale, a five-point scale of motion decrease (0 = no decrease, 1 = 1-5%, 2 = 6-25%, 3 = 26-75% and 4 = 76-100%). Each individual joint is scored as an estimate of the percentage of normal motion, based on the knowledge of a joint's normal ROM (Bernbeck, 1983). The examiner visually estimates whether a joint's ROM is normal or limited (Spiegel et al., 1987). Inter- and intra-reliability are reported to be high (r = 0.91 and r = 0.85) (Spiegel et al., 1987). In the upper extremities, range of flexion and abduction of the shoulders and of dorsal and palmar flexion of the wrists were determined. In the lower extremities, flexion, extension, abduction and adduction of the hips and plantar and dorsal flexion of the ankles were measured. Scores: 8 mean JAM scores were calculated by averaging the scale values of range of motion decrease proximally and distally and on the right and left.

Muscle Tone was assessed using the Modified Ashworth Scale (MAS) (Bohannon and Smith, 1987), a well known instrument consisting of a 5-point scale of tone increase (0 = no resistance, 1 = slight 'catch' when limb is moved, 2 = resistance in whole range of movement, 3 = strong increase with decreased range of movement, 4 = limb rigidly in flexion or extension). Kendall's tau correlation for inter-tester reliability was 0.85 (Bohannon and Smith, 1987). Scores: 8 mean scores were calculated by averaging the scale values of tone increase over movement directions proximally and distally and on the right and left. (0 = normal; 1 and 2 = mild, 3 = moderate and 4 = severe impairment). Within the activity domain (WHO, 2002) we applied different instruments to measure motor

development and functional possibilities, as the study group consisted of children of different ages and with and without spasticity.

Activities

Motor development in children without spasticity
Bayley Scales of Infant Development 2nd edition (BSID-II) (Bayley, 1993). The Motor scale assesses motor development of children in the age group 0 to 42 months. According to the manual, scale scores were transformed into a psychomotor developmental index (PDI) (mean 100, SD 15, range 50-150) (Bayley, 1993). The BSID-II is a valid and reliable instrument. Inter-rater and intra-rater reliability (0.75- 0.91) are satisfactory (Bayley, 1993).
Movement Assessment Battery for Children (M-ABC). The M-ABC was used to measure the overall level of motor development and to screen for movement problems (Henderson and Sugden, 1992). The M-ABC has been standardized for children aged between 4 and 12 years and older (12+). Children are set eight age-appropriate (age band I: 4- 6 years, II: 7 and 8 years, III: 9 and 10 years; IV: 11 years and older) tasks that pertain to three domains: Manual Dexterity (3 tasks), Ball Skills (2 tasks) and Static and Dynamic Balance (3 tasks). Test-retest reliability (0.75) and inter-rater reliability (0.70- 0.89) of the Dutch version of the M-ABC are satisfactory (Smits-Engelsman, 1998). Six-point scale values (0-5) are summed (range 0-40) and the total score is converted into an age-related centile score, which is interpreted as 'normal and good' (100th – 16th centile), 'at risk for motor problems' (15th to 6th centile) and 'impaired' (5th centile and below) (Henderson and Sugden, 1992). The lower the raw scores the better the motor function and the higher the centile score.

Motor development in children with spasticity
Classification of Mobility: Gross Motor Function Classification System (GMFCS).
The GMFCS manual provides separate descriptions of mobility for four age bands: before 2nd birthday, 2nd to 4th birthday, 4th to 6th

birthday, 6 to 12 years. For each age band, mobility is classified into 5 levels; the title of each level represents the highest level of mobility that a child within that level is expected to achieve. For children over the age of six years, level I is entitled: 'walks without restrictions, limitations in more advanced gross motor skills', and level V is entitled: 'self-mobility is severely limited even with the use of assisting technology' (Palisano et al., 1997). The overall reliability of the GMFCS is 0.79 and increases when tracking starts at higher ages. Inter-rater reliability is 0.93 (Wood and Rosenbaum, 2000). Validity has been reported to be excellent (Rosenbaum et al., 2002; Gorter et al., 2004)

Gross Motor Function Measure (GMFM-88). The GMFM-88 is a standardized clinical observational instrument designed to evaluate change in gross motor activities in children with cerebral palsy. It assesses how much of an activity a child can accomplish, rather than how well the activity is performed (Russell et al., 1993; Russell et al., 2002). The GMFM-88 (Russell et al., 2002) consists of 88 items grouped into five dimensions: lying and rolling (17 items), sitting (20 items), crawling and kneeling (14 items), standing (13 items), and walking, running and jumping (24 items). The items are scored on 4-point ordinal scales (0 = cannot initiate, 1 = initiates, but completes less than 10%, 2 = partially completes item (11-99%), 3 = completes item independently). Good reliability using intra-class correlation coefficient has been reported; the values varied from 0.87 to 0.99 (Russell et al., 1993; Russell et al., 2002). Score: percentage scores for each of the five GMFM dimensions and a total GMFM percentage score are calculated. Higher scores indicate better development.
Pediatric Evaluation of Disability Inventory (PEDI). The PEDI is a structured parent's interview that covers the domains of self-care (73 items), mobility (59 items) and social functioning (65 items) (Haley et al., 1992). Functional skill (capability) is measured by counting the items in which the child is perceived as having mastery and competence. Caregiver's assistance is measured by counting the daily functional activities in which the caregiver's provides

factual assistance. Although the instrument has been designed for children aged between 0.5 and 7.5 years, the scaled scores offer the opportunity to estimate skills in older children whose functional abilities lag behind those expected of 7.5-year-old healthy children (Feldman et al., 1990; Haley et al., 1992; Nichols and Case-Smith, 1996; Custers et al., 2002). The PEDI provides two types of transformed summary scores: scaled scores and normative standard scores. As the aim of the present study was to map individual change, we used the scaled scores. In children younger than 7.5 years, the standard scores allowed us also to compare with healthy peers. The PEDI is sensitive to changes with time (Iyer et al., 2003). The Internal Consistency for PEDI scales has alpha scores ranging from 0.95 to 0.99 (Haley et al., 1992; Custers et al., 2002). The scaled scores provide estimates of the level of skill (0 = no measurable functional skill, 100 = intact functional skill) and of the amount of assistance (0 = complete caregiver's assistance, 100 = no caregiver's assistance).

Epilepsy-related restrictions, or difficulties when participating in social life (WHO, 2002) due to the effects of epilepsy, were assessed using the Hague Restrictions in Childhood Epilepsy Scale (HARCES) (Carpay et al., 1997), a 10-item scale that quantifies the parent's/caregiver's perception of epilepsy-related restrictions imposed on the child to avoid seizure-related injuries or other adverse effects of seizures. The scale is reliable in terms of test-retest stability (0.93) and internal consistency (0.89) (Carpay et al., 1997). Score: 10 (no restrictions) to 40 (maximal restrictions).

Data analysis

Using SPSS (version 11.01) software, descriptive statistics were calculated, changes in seizure severity (HASS), IQ/DI values, muscle strength, muscle tone, range of motion, and restrictions (HARCES) were analyzed non-parametrically (Wilcoxon signed ranks test), changes in BSID II, M-ABC, GMFM-88 and PEDI scores were analysed by means of analysis of variance for repeated measures (ANOVA-RM) with Time (baseline, 6, 12 and 24 months

later on) as within-subject factor and with adjustment for multiple comparisons using least significant difference (LSD). The Spearman rank correlation was used to judge the strength of, e.g., the relationship of epilepsy-related (HASS, HARCES) measures with those of BSID II; M-ABC; GMFM and the relationship of IQ/DI measures with those of BSID II; M-ABC; GMFM. Using a linear regression model, we assessed the association between motor scores (BSID II; M-ABC; GMFM) and IQ/DI scores.
A two-sided P-value of 0.05 or less was considered statistically significant.

Results

Impairments

HASS: Seizure severity as perceived by parents/caregivers (Table 3): At baseline only one child had a score of 13, meaning no seizures (seizure free after change AED); most children (66%) had a score above 26, meaning moderate severity, while the score above 39 in 5 children (11%) signified very severe seizures. In the follow-up period of two years, change, if present, was not statistically significant. In 8 children HASS scores ameliorated two to 8 points, three of the children being seizure-free at 24 months. Scores worsened two to 8 points in 9 children and did not change in 28 children (62.2%).

Table 3

Seizure severity (HASS score 13-52), recorded when presented to DuCESP (Baseline) and 6, 12 and 24 months thereafter (n = 45)

	Baseline	6 months later	12 months later	24 months later
Mean (SD)	31.35 (15.6)	28.43 (13.1)	27.57 (7.1)	26.30 (8.2)
Median (range)	30 (13-42)	26 (13-42)	27 (13-41)	27 (13-40)

Motor impairments (Table 4): Group mean values of motor impairments as expressed by muscle strength, range of joint motion and muscle tone, were below reference norms and did not change significantly during follow-up. Group mean values of the 12 children with spasticity were higher on range of joint motion and muscle tone and lower on muscle strength than the values obtained in the total group. Statistically significant change during the follow-up was not found in these 12 children (data not shown). Of the 33 children without spasticity, only two had some (Leg distal 1 and 2, Arm distal 2) impairment in range of joint motion, but no impairments in muscle strength and muscle tone.

Table 4

Muscle strength (MRC score 0-5), Range of motion (JAM score 0-4), Muscle Tone (Ashworth score 0-4), recorded at Baseline and at 6, 12 and 24 months thereafter (n = 45)

	Baseline	6 months later	12 months later	24 months later
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
MRC				
Arm R proximal	4.62 (0.8)	4.62 (0.8)	4.64 (0.8)	4.64 (0.8)
Arm R distal	4.56 (0.9)	4.53 (0.9)	4.53 (0.9)	4.55 (0.9)
Arm L proximal	4.60 (0.6)	4.60 (0.6)	4.56 (0.7)	4.56 (0.7)
Arm L distal	4.56 (0.7)	4.56 (0.7)	4.49 (0.8)	4.44 (0.9)
Leg R proximal	4.76 (0.5)	4.76 (0.5)	4.76 (0.5)	4.73 (0.6)
Leg R distal	4.69 (0.5)	4.67 (0.6)	4.67 (0.7)	4.67 (0.7)
Leg L proximal	4.62 (0.5)	4.62 (0.5)	4.60 (0.6)	4.60 (0.6)
Leg L distal	4.58 (0.7)	4.58 (0.7)	4.53 (0.7)	4.47 (0.8)
JAM				
Arm R proximal	1.20 (0.6)	1.18 (0.6)	1.18 (0.6)	1.18 (0.6)
Arm R distal	1.27 (0.7)	1.27 (0.7)	1.24 (0.7)	1.25 (0.7)
Arm L proximal	1.18 (0.5)	1.18 (0.5)	1.22 (0.6)	1.24 (0.6)
Arm L distal	1.27 (0.6)	1.29 (0.7)	1.31 (0.7)	1.38 (0.7)
Leg R proximal	1.16 (0.5)	1.16 (0.5)	1.16 (0.5)	1.13 (0.4)
Leg R distal	1.38 (0.8)	1.36 (0.8)	1.33 (0.8)	1.36 (0.7)
Leg L proximal	1.18 (0.4)	1.16 (0.4)	1.20 (0.5)	1.22 (0.5)
Leg L distal	1.44 (0.8)	1.47 (0.8)	1.47 (0.8)	1.53 (0.8)
Ashworth				
Arm R proximal	1.38 (0.9)	1.36 (0.9)	1.36 (0.9)	1.42 (0.9)
Arm R distal	1.49 (1.1)	1.49 (1.1)	1.47 (1.1)	1.44 (1.1)
Arm L proximal	1.38 (0.7)	1.38 (0.7)	1.38 (0.6)	1.36 (0.6)
Arm L distal	1.53 (1.0)	1.53 (1.0)	1.56 (1.0)	1.51 (0.9)
Leg R proximal	1.29 (0.8)	1.29 (0.7)	1.27 (0.7)	1.27 (0.7)
Leg R distal	1.56 (1.0)	1.58 (0.9)	1.51 (0.9)	1.47 (0.9)
Leg L proximal	1.47 (0.8)	1.49 (0.8)	1.49 (0.8)	1.47 (0.8)
Leg L distal	1.67 (1.0)	1.60 (1.0)	1.67 (1.0)	1.58 (0.9)

Abbreviations: L = Left, R = Right, SD = Standard Deviation

Activities

Motor development (Table 5): The mean motor developmental index (BSID-II) of 13 children who were younger than 42 months and who were without spasticity was low at baseline and remained so thereafter (more than 3 SD below the mean score indicates a severe motor retardation) (Bayley, 1993). The group mean centile score of the 20 children without spasticity who were assessed with the M-ABC, was 7.15 (SD 13.0) at baseline; three children had centile scores above 15 (28, 40 and 45); all others scored below 15. Group mean centile score remained below 15 at all times. In the three children with centile scores above 15 at baseline, these remained so until 2 years later (19, 33 and 40). In two children the centile scores improved slightly from below to above 15 (16 and 19), a change that reclassified them from motorically 'at risk' to 'normal'. The GMFM administered to the 12 children with spasticity, changed statistically significantly at every follow-up assessment, when compared with the previous assessment ($p < 0.05$).

Functional skills and Caregiver's assistance (Table 5): The PEDI mean scale scores on Functional skills (self-care, mobility and social function) and Caregiver's assistance increased significantly during follow-up, but remained below the score of 100 in 33/45 children. Eighteen of these 33 children were younger than 7.5 years; for these cases, comparison with norm scores was possible. In the 15 children older than 7.5 years, scores below 100 indicate motor retardation when compared with normal development. On each occasion, the children obtained the lowest scores in the domain of Social function (Table 5). When comparing the 18 children who were younger than 7.5 years with age norms (50±20), the score on Functional skills was found to remain more than 2 SD below the norm values throughout the period of follow-up. Scores varied at baseline from 13.2 (SD 11.2) to 21.3 (SD12.1) and 24 months later from 15.5 (SD 7.7) to 25 (SD 10.4). A similar course was found for Caregiver's assistance. The PEDI scale scores were not significantly associated with IQ/DI scores and HASS or HARCES scores.

Table 5

Motor development in children without spasticity (BSID II, M-ABC). In children with spasticity: severity of motor disability (GMFCS), gross motor function (GMFM). In both groups: functional skills and caregiver's assistance (PEDI). Assessments at presentation (Baseline) and at 6, 12 and 24 months thereafter

	Baseline	6 months later	12 months later	24 months later
BSID II (PDI score) (n=13)				
Mean (SD)	53.67 (5.9)	53.67 (5.9)	54.67 (5.2)	52.57 (6.8)
Median (range)	50.00 (50-65)	50.00 (50-65)	50.00 (50-64)	50.00 (50-68)
M-ABC (centile score) (n=20)				
Mean (SD)	7.15 (13.0)	8.62 (11.9)	8.70 (13.8)	9.87 (13.7)
Median (range)	1.00 (1-45)	1.00 (1-32)	1.00 (1-54)	2.00 (1-54)
GMFCS (n=12)				
Median (range)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)
GMFM-88 (total score %) (n = 12)				
Mean (SD)	55.75 (35.4)	62.86 (32.3) *	66.82 (31.1) *	71.82 (28.4) *
Median (range)	67.00 (6-100)	73.00(7-100)	82.00 (8-100)	83.00 (13-100)
PEDI (scale scores) Mean (SD) (n=45)				
Functional Skills				
Self-care	60.76 (29.5)	64.59 (27.5) **	67.14 (27.3) **	70.02 (25.5) **
Mobility	64.43 (35.8)	71.40 (32.1) **	75.28 (29.6) **	80.19 (25.8) **
Social function	49.70 (33.2)	54.26 (30.8) **	57.57 (30.9) *	60.84 (29.4) **
Caregiver assistance				
Self-care	54.19 (38.6)	56.98 (36.1) **	61.88 (32.8) **	65.25 (30.9) **
Mobility	66.83 (38.6)	69.92 (35.2)	75.97 (28.7) **	79.29 (26.2) **
Social function	55.93 (35.7)	54.25 (35.5)	57.01 (35.8) *	61.37 (33.6) **

[1]Anova for Repeated Measures; Statistical significance: *($p \leq 0.05$), ** ($p \leq 0.01$).

Abbreviations: BSID = Bayley Scales of Infant Development; GMFCS = Gross Motor Function Classification Scale; GMFM = Gross Motor Function Measure; M-ABC = Movement Assessment Battery for Children; PDI = Psycho-motor Developmental Index; PEDI = Pediatric Evaluation of Disability Inventory; SD = standard deviation.

Participation

Epilepsy-related restrictions (Table 6): as assessed with the HARC-ES, restrictions were severe at baseline and remained so without a significant change. The child with the minimal seizure severity score also had minimal restrictions, after adaptation of AED. Moderate restrictions (score >20) were imposed on most children (68%) at all times; five children (11%) had severe restrictions (score >30) at all times. Three children had minimal restrictions at 24 months; they were free of seizures due to their new medication.
There was no significant association between HARCES and motor scores on BSID II, M-ABC and GMFM.

Table 6

Seizure-related restrictions (HARCES) assessed at initial presentation and at 6, 12 and 24 months thereafter (n=45)

	Baseline	6 months later	12 months later	24 months later
Mean (SD)	22.18 (8.3)	20.91 (7.9)	22.63 (7.7)	21.39 (6.9)
Median (range)	23 (10-38)	21 (10-38)	23 (10-39)	21 (10-38)

Correlation and association

The HASS was significantly associated with BSID-II at baseline and 24 months later (Table 7). The association between IQ/DI and motor scores on BSID II, M-ABC and GMFM was significant at baseline and at 24 months thereafter (Table 7).
The regression analysis revealed that IQ/DI explained 50% of the variance in the motor scores of the BSID-II, 26% in those of the M-ABC and 23% in those of the GMFM (Table 8).

Table 7

Spearman's rank correlations (rho) between measures of severity of epilepsy (HASS), epilepsy-related restrictions (HARCES), IQ/DI and motor score on BSID II (PDI score), M-ABC (centile score) and GMFM (total %)

	HASS		HARCES		IQ/DI	
	Baseline	24 months later	Baseline	24 months later	Baseline	24 months later
BSID II (n=13) (PDI score)	.90 **	.70 *	.40	.56	.67 *	.76 *
M-ABC (n=20) (Centile score)	.09	-.39	-.29	-.21	.48 *	.58 **
GMFM (n=12) (Total %)	.46	.22	.12	.40	.54 **	.50 **

Statistical significance: *($p \leq 0.05$), ** ($p \leq 0.01$)

Table 8

Linear regression of IQ/DI on BSID II-PDI score, M-ABC (centile score) and GMFM (total % score)

	R square	Adjusted R square	Standard error	F	p
BSID II (PDI score)	0.58	0.50	0.34	7.00	0.04 *
M-ABC (centile score)	0.30	0.26	0.11	7.71	0.01 *
GMFM (total %)	0.26	0.23	0.29	9.45	0.005 **

Statistical significance: *($p \leq 0.05$), ** ($p \leq 0.01$).

Discussion

Using a prospective longitudinal design covering two years after presentation to the Dutch Collaborative Epilepsy Surgery Program (DuCESP), we were able to study whether the decision to not operate upon children harmed the children with respect to seizure severity, motor development and epilepsy-related restrictions.

Seizure severity does not change much

The parents of 8 children perceived some decrease in seizure severity, whereas those of three children (6%) perceived their child to be seizure-free 24 months after initial contact. For studies of uncontrolled epilepsy, neither objective seizure frequency nor seizure classification (ILAE) encompasses the severity of the affliction (Carpay et al., 1997; 2002). The patients (or their parents) are authorities with regard to the effects of epilepsy on their lives (Sabaz et al., 2003; Cowan and Baker, 2004). The HASS, a 'parent-based' scale of seizure severity in children, was our instrument of choice. When writing the paper, we came across a disagreement between the child neurologist's and parent's seizure severity rating, which prompted a case-by-case check. The disagreement involved eight of the 45 children. In two, the physician considered the paroxysmal episodes to be of a psychogenic, non-epileptic nature (PNES) and in two others transient ischemic attacks were interpreted by the parents as seizures and scored accordingly on the HASS. In four other children, the child neurologist considered the seizures to be less severe than did the parents. These children were prescribed other anti-epileptic medication, which eased the urgency of surgery. This taught us to interpret the HASS with some caution, and to check whether the parents fill out the instrument with epileptic seizures or 'attacks of some sort' in mind. With improving surgical technology and skills and improved imaging techniques in the last five years, 9 patients were operated upon after the follow-up period of the present study.

Motor function in children with and without spasticity does not worsen

Follow-up studies of motor function and motor development in children with pharmaco-resistant epilepsy are lacking. Currently, studies of motor function in children with pharmaco-resistant epilepsy have been performed in children whose primary impairment was caused by cerebral palsy (CP) (Beckung and Hagberg, 2002; Østensjø et al., 2004). From the finding that children with both spasticity and epilepsy had more motor impairments than those with only spasticity, the authors deduced that epilepsy may have an adverse effect on motor function.

Our study included both children with spasticity (not only CP) and children without spasticity of widely varying age ranges. For these reasons, we examined motor function by means of different instruments. When age-related norm values were appropriate, we compared the scores with age-matched reference values. This led us to conclude that most (38/45) children had a motor retardation, defined as more than 2 SD below mean values (14,23,30). Of the seven children without a motor retardation, six had an IQ/DI above 70. As found in other studies of children with intractable epilepsy (Gordon, 2000; Bjørnaes et al., 2001), these children were also mentally retarded. It is, therefore, difficult to say whether the motor retardation was causally linked with epilepsy, with mental status or with brain damage. As previously observed for children with CP, this co-occurrence of motor retardation with epilepsy, mental retardation and brain damage prohibits causal statements (Beckung and Hagberg, 2002; Østensjø et al., 2004). The severity of mental retardation has previously been reported to be associated with the severity of motor retardation in children with CP (Beckung and Uvebrant 1997; Beckung and Hagberg, 2002). We found motor retardation of the children, whether they had spasticity or not, to be associated with their mental retardation. However, the suggestion by Kennedy (2003) of IQ/DI as a major determinant of limitations in activities cannot be derived from the data. Of course, with IQ/DI as a dependent variable and BSID II, M-ABC and GMFM as inde-

pendent variables, the same association between motor and mental retardation appears which would mean that motor scores explain the same variance in IQ/DI scores.

Parental fears after learning that their children are not eligible for surgery

Clinicians are aware of the fear in the majority of parents that development of their children with pharmaco-resistant epilepsy, if not treated by surgery, will deteriorate. Yet, the BSID II and the M-ABC showed that motor retardation in the 33 children without spasticity remained unchanged during the follow-up period of two years. Therefore, the fear of parents that children who do not qualify for epilepsy surgery will deteriorate in terms of motor development, can be refuted. When the results of the M-ABC were compared with norm reference values, i.e., with normal motor development, most (15/20) scores did, however, remain below the 15th centile. This means that the children remained 'at risk for motor problems'. In 9 of these 15 children, scores stayed below the 5th centile, i.e., in the range of impairment, which clinically indicates a severe motor delay.

In the 12 children with spasticity, the GMFM showed an increase in motor score. In order to interpret the clinical relevance of this increase, we used the recently published 'motor growth curves', which show for each level of GMFCS the change that can be expected in the GMFM-scores (Rosenbaum et al., 2002). Comparing our results with these GMFCS-anchored motor growth curves, we found that four of the 12 children remained more than 2 SD's below the motor growth curve. In the other eight children, the increase of GMFM scores remained within 2 SD below the mean of their referent curve. Therefore, the deviation from the motor growth curve did not increase in these eight children.

Functional skills do not deteriorate and caregiver's assistance does not increase

In the PEDI, scale scores are based upon the assumption that healthy children from the age of 7.5 years reach a score of 100 in all domains. Most of the children in the present study did not reach that score. Some (n=18) did not obtain the maximal score because they were younger than 7.5 years and others (n=15) because they were delayed in motor development. Nevertheless, the total group mean scale scores increased in the period of two years (e.g., Functional skills 10-15 points and Caregiver's assistance 6-12 points). Despite their pharmaco-resistant epilepsy these children developed towards greater independence, since a difference of at least six points has been reported to reflect a clinically meaningful change (Iyer et al., 2003). However, when comparing the scores of the 18 children who were younger than 7.5 years with normative referent values, the scores remained more than 2 SD below the mean reference, indicating that functional skills of these 18 children went on to lag behind normal development and that significantly more caregiver's assistance remained necessary than for healthy peers. Only 12 of the 27 children aged above 7.5 years scored 100 in all domains, which means that 15 children lagged behind normal peers with respect to functional skills and needed more than age-appropriate caregiver's assistance. Hence, although the majority of the 27 children had limitations in daily activities, compared to healthy peers, their independence did not deteriorate and caregiver's assistance did not increase during follow-up (data not shown).

Restrictions remain unchanged

The restrictions (HARCES scores) associated with the epilepsy remained unchanged during the follow-up period, meaning a continued need for support and chaperoning by parents or peers when the children participate in social life. Parents impose restrictions on their children with epilepsy to reduce the risk of seizure-related injuries and they are often advised to do so by their physicians.

Activities like bathing, swimming, climbing and riding a bike are often restricted (Carpay et al., 1997; 2002). Epidemiological studies assessing the risks of seizures in a population of children with epilepsy are, however, rare, and so this advice is hardly evidence-based (Broek van den et al., 2004). Accidents and injuries are slightly more frequent among adults with epilepsy than in the general population. This risk is probably highest in patients with symptomatic epilepsy and frequent seizures, in whom associated handicaps carry additional risks (Tomson et al., 2004). Hence, parents are in fact left to set their own standards of acceptable risks and make their own judgments about associated restrictions.
The children of the present study are not comparable with a group of surgically treated children, as there were significant reasons for not performing surgery. It would seem to be challenging, however, to determine whether a group of 52 children who underwent epilepsy surgery and who have been followed with identical instruments and during the same time interval of two years (Empelen et al., 2005), show similar trends as reported for the present group not eligible for surgery.
In the surgery group the HASS and HARCES scores changed significantly, as one might expect; whereas in the group of children who were not eligible for surgery the mean scores did not change significantly. The outcomes with respect to severity of epilepsy and restrictions imposed by epilepsy were, therefore, positive in the surgically treated children, whereas neither parameters worsened in those who were not eligible for surgery. IQ/DI values did not change significantly in either group. In the current literature, we only find one study - by Smith et al., (2004) - in which a group of surgically treated children is compared with a control group of children with medically pharmaco-resistant seizures. The children were examined at comparable times, with a pre-surgical examination in the former group (Smith et al., 2004). The purpose was to evaluate the impact of surgery on cognitive, psychosocial, and family function. The IQ's remained stable in both groups. Smith et al. (2004) argue that the lack of an effect of seizure outcome on IQ suggests that the pre-existing abnormal neural substrate, rather

than the seizures themselves, underlies the cognitive deficits. In our surgery group the M-ABC centile mean score and the GMFM-88 total % score changed significantly. In the group not eligible for surgery, the M-ABC mean score did not change significantly, although the total % scores on the GMFM-88 did change significantly. When we compare the results on the GMFM-88 with reference values in children with cerebral palsy by using the GMFCS levels, in the surgery group 16/17 children scored post-surgery within 2 SD of the mean referent score. In the group not eligible for surgery, 4/12 children remained more than 2 SD below the referent values.

Conclusion

The notion that children with severe epilepsy who are found not to be eligible for surgical intervention will deteriorate in terms of mental and motor status and epilepsy-associated restrictions, is not confirmed by our results. The children remained more or less at their previous level and their functioning did not worsen during a time span of two years. This finding seems of utmost importance to clinicians, when confronted by parents who ask what will happen if their child is found not to be eligible for epilepsy surgery.

Acknowledgements

We are grateful to the Phelps Stichting and the Johanna Children's Foundation for their financial support; to Dr. W.R. Pestman, Center for Biostatistics, for his supervision of statistical analyses. E van der Steeg, MA, M Peters, MA and Dr. C. Volman, University Utrecht, Faculty of Social Sciences, for their assistance in this research. We thank Mrs Brenda Vollers-King for correction of the English language and Mrs C. Tims-Polderman and Mrs J. Nuysink for their assistance in data-management. We thank the Members of the Dutch Collaborative Epilepsy Surgery Program for their cooperation: SEIN, Kempenhaeghe, Hans Bergerkliniek, Academic Hospitals (Utrecht, Maastricht, Amsterdam VU).

References

Battaglia M, Russo E, Bolla A, et al. International Classification of Functioning, Disability and Health in a cohort of children with cognitive, motor, and complex disabilities. Dev Med Child Neurol 2004;46:98-106.

Bayley N. Manual for the Bayley scales of Infant Development, 2nd edition. San Antonio: Psychological Corporation, TX, 1993.

Beckung E, Uvebrant P. Hidden dysfunction in childhood epilepsy. Dev Med Child Neurol 1997;39:72-8.

Beckung E, Hagberg G. Neuroimpairments, activity limitations, and participation restrictions in children with cerebral palsy. Dev Med Child Neurol 2002;44:309-16.

Bernbeck R, Dahmen G. Kinderorthopedie. Stuttgart: Georg Thieme Verlag, 1983.

Bjørnaes H, Stabell K, Henriksen O, Loyning Y. The effects of refractory epilepsy on intellectual functioning in children and adults. A longitudinal study. Seizure 2001;10:250-9.

Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 1987;67:206-7.

Broek M van den, Beghi E; RESt-1 Group. Accidents in patients with epilepsy: types, circumstances, and complications: a European cohort study. Epilepsia 2004;45:667-72.

Bruyn EEJ de, Vander Steene G, Haasen PP van. Wechsler Intelligence Scale for Children – Revised (WISC-R). Nederlandstalige uitgave en verantwoording. Lisse: Swets & Zeitlinger 1986.

Carpay JA, Vermeulen J, Stroink H, et al. Disability due to restrictions in childhood epilepsy. Dev Med Child Neurol 1997;39:521-6.

Carpay JA, Vermeulen J, Stroink H, et al. Parent-reported subjective complaints in children using antiepileptic drugs: what do they mean? Epilepsy Behav 2002;3:322-9.

Commission on Classification and Terminology of the International League Against Epilpesy. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989;30:389-99.

Cowan J, Baker GA. A review of subjective impact measures for use with children and adolescents with epilepsy. Qual Life Res 2004;13:1435-43.

Custers JWH, van der Net J, Hoijtink H, Wassenberg-Severijnen JE, Vermeer A, Helders PJM. Discriminative validity of the Dutch Pediatric Evaluation of Disability Inventory. Arch Phys Med Rehabil 2002;83:1437-41.

Ellenberg JH, Hirtz DG, Nelson KB. Do seizures in children cause intellectual deterioration? N Engl J Med 1986;314:1085-8.

Empelen R van, Jennekens-Schinkel A, Gorter JW, Nieuwenhuizen O van, Helders PJM. Epilepsy surgery does not harm motor performance of children and adolescents. Brain 2005; 128:1536-45, 2005; Apr 13; [Epub ahead of print]

Eriksson KJ, Koivikko MJ. Prevalence, classification, and severity of epilepsy and epileptic syndromes in children. Epilepsia 1997;38:1275-82.

Feldman AB, Haley SM, Coryell J. Concurrent and construct validity of the Pediatric Evaluation of Disability Inventory. Phys Ther 1990;70:602-10.

Gordon N. Cognitive functions and epileptic activity. Seizure 2000;9:184-8. [Review].

Gorter JW, Rosenbaum PL, Hanna SE, et al. Limb distribution, motor impairment, and functional classification of cerebral palsy. Dev Med Child Neurol 2004;46:461-7.

Haley SM, Coster WJ, Ludlow LH. Pediatric Evaluation of Disability Inventory (PEDI), Boston: M.A. New England Medical Center, [manual] 1992.

Henderson SE, Sugden DA. Movement Assessment Battery for Children. London: The Psychological Corporation, [manual] 1992.

Hislop HJ, Montgomery J. Daniels and Worthingham's Muscle testing Techniques of Manual Examination. Philadelphia: WB Saunders Company, 2002.

Iyer LV, Haley SM, Watkins MP, Dumas HM. Establishing minimal clinically important differences for scores on the Pediatric Evaluation of Disability Inventory for inpatient rehabilitation. Phys Ther 2003;83:888-98.

Jette AM. Physical disablement concepts for physical therapy research and practice. Phys Ther 1994;74:380-6.

Kennedy C. Functioning and disability associated with mental disorders: the evolution since ICIDH. Disabil Rehabil 2003;25:611-9.

Medical Research Council. Aids to the investigation of peripheral nerve injuries. War memorandum 2nd ed. London: HMSO, 1943.

Nichols DS, Case-Smith J. Reliability and validity of the Pediatric Evaluation of Disability Inventory. Ped Phys Ther 1996;8:15-24.

Østensjo S, Carlberg EB, Vollestad NK. Motor impairments in young children with cerebral palsy: relationship to gross motor function and everyday activities. Dev Med Child Neurol 2004;46: 580-9.

Palisano RJ, Rosenbaum PL, Walter SD, Russell DJ, Wood EP, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997;39:214-23.

Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. JAMA 2002;18:1357-63.

Russell D, Rosenbaum PL, Gowland C, et al. Manual for the Gross Motor Function Measure. (2 ed.) Hamilton, Canada: McMaster University. 1993.

Russell DJ, Rosenbaum PL, Avery LM, Lane M. GMFM Gross Motor Function Measure, (GMFM-66 & GMFM-88) User's Manual. Cambridge: Cambridge University Press; 2002.

Sabaz M, Lawson JA, Cairns DR, Duchowny MS, Resnick TJ, Dean PM, Bye AM. Validation of the quality of life in childhood epilepsy questionnaire in American epilepsy patients. Epilepsy Behav 2003;4:680-91.

Scott-Lennox J, Bryant-Comstock L, Lennox R, Baker GA. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. Epilepsy Res 2001;44:53-63.

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Smits-Engelsman BCM. Movement ABC. Nederlandse handleiding. Lisse: Swets & Zeitlinger; 1998.

Spiegel TM, Spiegel JS and Paulus HE. The joint Alignment and Motion Scale; a simple measure of joint deformity in patients with rheumatoid arthritis. J Rheumatol 1987;14:887-93.

Steene G van der, Bos A. WPPSI-R, Wechsler Preschool and Primary Scale of Intelligence. Vlaams-Nederlandse aanpassing. Handleiding voorlopige versie. Lisse: Swets & Zeitlinger 1997.

Tomson T, Beghi E, Sundqvist A, Johannessen SI. Medical risks in epilepsy: a review with focus on physical injuries, mortality, traffic accidents and their prevention. Epilepsy Res 2004;60:1-16. [Review]

W.H.O. The International Classification of Functioning, Disability and Health (2002). ICF: introduction. Geneva: World Health Organization. Available on the WHO Internet site, 2002.http://www.who.int/classifiction/icf.

Wechsler D. WISC-R. Wechsler Intelligence Scale for Children – Revised. New York: The Psychological Corporation 1974.

Wechsler D. Manual for the Wechsler Preschool and Primary Scale of Intelligence – Revised (WPPSI-R). New York: The Psychological Corporation 1989.

Wood EP, Rosenbaum PL. The Gross Motor Function Classification System for cerebral palsy. Dev Med Child Neurol 2000;42:292-6.

Chapter 6

Two years after the decision not to operate on children for pharmaco-resistant epilepsy: quality of life and self-perceived competence remain poor

R. van Empelen[1*]
P.J.M. Helders[1]
P.C. van Rijen[2*]
A. Jennekens-Schinkel[3*]
O. van Nieuwenhuizen[4*]

On behalf of the Dutch Collaborative Epilepsy Surgery Programme.

1 Department of Paediatric Physical Therapy and Exercise Physiology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands. NetChild, Network for Childhood Disability Research in The Netherlands.
2 Department of Neurosurgery, University Medical Center – Utrecht, The Netherlands.
3 Department of Neuropsychology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.
4 Department of Child Neurology, University Medical Center – Wilhelmina Children's Hospital, Utrecht, The Netherlands.

* Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands..

Submitted for publication

Summary

Purpose: To study the course of health-related quality of life (HrQoL) and self-perceived competence of children with pharmacoresistant epilepsy once the decision has been taken that they are not eligible for epilepsy surgery.
Methods: Prospective longitudinal 2 years follow-up of 20 patients aged 6 years to 15 years. Severity of seizures (HASS), epilepsy-related restrictions (HARCES), HrQoL and self-perceived competence were rated at baseline and 6, 12 and 24 months later. Data were analysed by ANOVA for repeated measures and correlation analysis.
Results: HrQoL: Group-wise, parents and children evaluated the frequency of social activities as significantly less than normal ($p < 0.05$) at baseline and during follow-up. Parents rated the frequency of physical and cognitive activities significantly below normal (p's < 0.05) at 24 months follow-up. Children with epilepsy had significantly more physical complaints than the reference group ($p < 0.05$) on entry into the study and complaints increased during follow-up. Parents of those with epilepsy found their children had more physical complaints than did the parents of healthy children ($p < 0.05$). Children with epilepsy had feelings of inferiority and were concerned about their epilepsy; with respect to their activities and the quality of activities the children with epilepsy felt similar to those of the reference group.
Self-perceived competence: epileptic children evaluated their scholastic and athletic competence and behavioral conduct as less than those of a healthy reference group, and when followed up adolescents perceived themselves in almost all domains as having less competence than a healthy reference group.
Conclusion: In children with severe epilepsy who were not eligible for epilepsy surgery, health-related quality of life and competence remained below normal. Perceived frequencies of physical complaints, seizures and epilepsy-related treatment worsened during the follow-up period, but most feelings about activities and quality of activities did not change.

Introduction

The focus of the present study is on children who have pharmaco-resistant epileptic seizures and who are not eligible for surgery. Parents and children themselves pin their hopes on epilepsy surgery and are greatly disappointed when they learn of the experts' decision to refrain from epilepsy surgery. Many parents fear that the epilepsy process will cause a gradual decline in their child's development and they anticipate a worsening of their child's quality of life. The present two-year follow-up was undertaken in order to answer these recognizable emotions. Its aim was to see whether health-related quality of life (HrQoL) and self-perceived competence deteriorate in children who were not eligible for surgery. Within the framework of the International Classification of Functioning, Disability and Health (ICF) (WHO, 2002), both aspects pertain to restrictions of participation in social life. A companion paper (chapter 5) inventoried the three levels of the ICF i.e., impairments (seizure severity and motor function), limitations in daily activities and epilepsy-related restrictions of a group of 45 children. The 20 patients of the present study is a subgroup of these 45 children who were old enough (> 6 years) to fill out the questionnaires with respect to HrQoL and self-perceived competence. The follow-up covers the period from the moment of presentation (baseline) to the Dutch Collaborative Epilepsy Surgery Program (DuCESP) to two years thereafter, with re-assessments at 6, 12 and 24 months. In the health care of children with chronic medical conditions for which a total cure is not expected, such as some types of epilepsy, HrQoL is an important outcome measure. Seizures impede the development of independence, peer relationships, self-esteem, mood and cognition, which has negative impact on HrQoL (Hoare et al., 2000; Smith et al., 2004; McEwan et al., 2004). Due to their unpredictability and unwanted behavioral manifestations, epileptic seizures are experienced as a loss of control, which, if recurring, may foster a feeling of uncertainty and, all too often, a fear of failure and of peer criticism in the children and adolescents (Oostrom et al., 2000, Ferguson et al., 2000). When uncertainty drives chil-

dren and adolescents to avoid social activities, this in turn limits opportunities to practise skills and to participate socially, which, again, trims down their feeling of self-worth and competence (Harter 1987; Skinner et al., 2001). Self-worth and competence have not yet been investigated in children with pharmaco-resistant epilepsy. We took the intelligence quotient (IQ) or developmental index (DI) into account as an index of cognitive function and we analysed at entry and 24 months later the associations of the latter with health-related quality of life and competence.
The present study addresses the following questions:
How do children, who were found not to be eligible for surgery, perceive their competence and health-related quality of life at baseline and later on? How do parents perceive the health-related quality of life of their children? What are the relationships between seizure severity, seizure-related restrictions, competence and health-related quality of life? What are the relationships of IQ/DI with health-related quality of life and competence?

Patients

Between 1996 and 2001, 45 candidates for epilepsy surgery (19 girls, 26 boys) were considered by DuCESP not to be eligible for this treatment during the period of this follow-up. Twenty of these 45 children fulfilled the age requirements (6.2 years to 15.4 years) for the application of the parental health-related quality of life questionnaire. Thirteen of these 20 children met the cognitive conditions to allow them to complete the questionnaires themselves. Intellligence quotients (IQ) were determined using instruments validated for Dutch children (WISC-R and WPPSI-R) (mean = 100; SD = 15) (Wechsler, 1974, 1989; Bruyn et al., 1986; Steene and Bos, 1997). Demographic and clinical characteristics of the children are summarised in Table 1.
All patients used at least two anti-convulsant drugs. If appropriate, medication was changed during the follow-up period.

The parents of all children and, if over 12 years of age, the children themselves gave informed written consent. The Institutional Review Board approved the study.

Table 1

Demographic and clinical characteristics of 20 children who were not eligible for surgery

Patient no.	Sex	Age at onset of epilepsy (yrs;mo)	Type of seizures	Age at baseline (yrs;mo)	Aetiology	IQ/DI Base-line	IQ/DI 2 yrs later	Reasons not to elect for surgery
1	M	4.7	CP	7.11	Multiple pathology	50	50	Multifocal localisation
2	F	0.1	CP	6.9	Multiple pathology	67	69	Multifocal localisation
3	F	5.7	SG	15.4	Cortical dysplasia	50	50	Multifocal localisation
4	M	1.1	MS	8.9	Multiple pathology	50	50	Multifocal localisation
5	M	5.0	MS	15.2	Multiple pathology	50	50	Multifocal localisation
6	F	1.1	PG	15.1	Cortical dysplasia	77	74	Multifocal localisation
7	M	3.8	SG	10.3	Multiple pathology	50	50	Multifocal localisation
8	F	0.5	SG	6.6	Cerebral tumour	50	58	Multifocal localisation
9	M	2.7	CP	6.2	Cortical dysplasia	50	50	Multifocal localisation
10	F	4.10	SP	6.10	No aetiology	106	98	Eloquent zone
11	M	1.8	CP	15.6	Cerebral tumour	93	91	Eloquent zone
12	F	2.0	CP	8.8	No etiology	68	60	Eloquent zone
13	M	0.4	CP	6.3	Tuberous sclerosis	83	80	Eloquent zone
14	F	9.3	CP	15.5	Cerebral tumour	85	91	Positive change in seizure severity
15	M	0.9	CP	9.10	Cyst	86	97	Positive change in seizure severity
16	M	6.1	SP	7.7	MTS	90	81	Infrequent seizures
17	F	7.10	SP	8.5	Cerebral tumour	89	74	Under analysis
18	F	7.6	CP	14.3	MTS	93	95	Under analysis
19	F	6.10	SP	11.9	MTS	67	78	Under analysis
20	F	13.6	PG	15.4	Rasmussen	75	74	Under analysis

Abbreviations: DI = Developmental Index, F = Female, IQ = full scale Intelligence Quotient, M = Male, Type of Seizures: CP= Complex partial, MS= Mixed Seizures, SP = Simple Partial, PG= Primary Generalised, SG = Secondary Generalised; Aetiology: MTS = Mesial Temporal Sclerosis, Multiple pathology = co-existence of different pathologies, Rasmussen = Rasmussen's encephalitis, yrs;mo = years, months

Methods

Patients were assessed in the outpatient clinic of the Wilhelmina Children's Hospital using a standard protocol with fixed intervals: baseline assessment and 6 months, 1 year and 2 years thereafter. Seizure severity as perceived by the parent or caregiver was quantified using the Hague Seizure Severity Scale (HASS), which consists of 13 items that have to be answered on a four-point scale. The scale inventories problems that may have been encountered in the three previous months. The following areas are addressed: consciousness (4 items), motor symptoms (2 items), incontinence (1 item), injuries/pain (3 items) and overall seizure severity (3 items) (Carpay, 1997). The scale is based on the Liverpool Seizure Severity Scale (Scott-Lennox et al., 2001). It is reliable in terms of test-retest stability (0.93) and internal consistency (0.85) (Carpay, 1997). The scores range from 13 (no seizures) to 52 (maximal seizure severity).
Epilepsy-related restrictions, or difficulties when participating in social life due to the effects of epilepsy, were assessed using the Hague Restrictions in Childhood Epilepsy Scale (HARCES) (Carpay, 1997), a 10-item scale that quantifies the parent's/caregiver's perception of epilepsy-related restrictions imposed on the child to avoid seizure-related injuries or other adverse effects of seizures. The scale is reliable in terms of test-retest stability (0.93) and internal consistency (0.89) (Carpay, 1997).
Scores range from 10 (no restrictions) to 40 (maximal restrictions).

HrQoL was inventoried by the HAY (How Are You) questionnaires for children and parents, using the version for children with epilepsy (Bruil, 1999). The children's questionnaire (HAY-C) consists of 125 items that are rated by means of four-point scales. The instrument purports to obtain the child's personal evaluation of her/his actual life by assessing both the importance that the child attributes to activities or events and the satisfaction by her/his performance of these activities.
The generic part assesses the child's functioning in areas of daily

life that are relevant for all children. It includes five dimensions: physical activities, cognitive tasks, social activities, general physical complaints and positive emotions. The items are rated in terms of how often the child estimates the activities to have occurred in the past seven days. With respect to physical activities, cognitive tasks and social activities, the child/adolescent (henceforth responder) is also asked how well she/he feels she/he can execute these activities (quality of execution). For four dimensions (physical, cognitive and social activities, and physical complaints), the responder also rates her/his feelings, i.e., how important these activities or events are for her/him (e.g. whether and to what degree it bothered her/him that she/he had a hard time riding a bike). The chronic illness part consists of two dimensions: concerns related to having an illness and feeling inferior because of having an illness. The epilepsy-related part refers to specific signs of epilepsy and their management and physical complaints related to epilepsy. It inventories how often the signs and/or their treatment occur and how the responder feels about them. As an aid to rating his/her feelings, the responder is provided with visual analogs (line drawings of faces with expressions ranging from very sad to happy). The epilepsy version of the HAY-C is valid and reliable (Crombach's alphas 0.77 to 0.86) (Bruil, 1999).

The parent questionnaire (HAY-P) asks the parents to rate their perception of the frequency and quality of daily activities performed by their child and to rate their own feelings related to the problems that occur for their child. The subscales are similar to those of the HAY-C. The HAY-P has acceptable reproducibility, supportive evidence for construct validity, and good responsiveness (Coq et al., 2000). As outlined by the designer (Bruil, 1999), the HAY-C and HAY-P ratings are recoded so that lower scores correspond with worse evaluations, item scores are summated and averaged per subscale (range 1-4).

Perceived competence was measured using the Dutch adaptation of the Harter Self Perception Profile for Children (SPP-C) (Harter, 1988, Veerman 1997, Veerman et al., 1997) or the Self Perception Profile for Adolescents (SPP-A) (Wickstrom 1995, Aasland and

Diseth, 1999). The scales assess a child's or adolescent's sense of competence in cognitive, social and physical domains and yield a measure of general self-worth. The SPP-C, designed for children in the age range 8-12 years, consists of 36 items distributed over five domain-specific subscales and one global self-worth subscale. The domain-specific subscales are scholastic competence, social acceptance, athletic competence, physical appearance and behavioral conduct. Adolescents (age range 12 to 18 years) fill out the SPP-A, which consists of 40 items distributed over the five subscales of the SPP-C plus the subscales of romance and friendships. Each item of both SPP-C and SPP-A describes two protagonists with opposite characteristics of competence. To offset the tendency towards a socially desirable response, the responder is first asked to decide which kind of protagonist he or she is most like. Then, the responder decides whether the characterisation of the protagonist of her/his choice is 'sort of true' or 'really true' for her/him. Items are scored on four-point scales (1 = low perceived competence, 4 = high perceived competence). Research has demonstrated a high internal consistency and test-retest reliability for each of the subscales (Thill et al., 2003, Shumann et al., 1999). For each subscale, sum scores are averaged. Scores in the normal population vary from 2.8 to 3.1 for the different subscales (Veerman, 1997, Wickstrom 1995, Aasland and Diseth, 1999).

Data analysis

Using SPSS (version 11.01) software, descriptive statistics were calculated, changes in health-related quality of life and self-perceived competence were analysed by means of analysis of variance for repeated measures (ANOVA-RM) with Time (baseline, 6, 12 and 24 months later on) as within-subject factor and with adjustment for multiple comparisons using least significant difference (LSD). The Spearman rank correlation was used to judge the strength of the relationship of epilepsy-related (HASS, HARCES) measures with those of health-related quality-of-life (HAY) and self-perceived competence (SPPC) and between IQ/DI and health-related quality-

of-life (HAY) and self-perceived competence (SPPC).
A two-sided *p*-value of 0.05 or less was considered statistically significant.

Results

At the level of impairments, seizures were perceived by parents/caregivers (HASS) as moderately severe, but change, if present in the follow-up period of two years, was not statistically significant (Table 2).
At the level of epilepsy-related restrictions, the parents/caregivers found these to be severe at baseline but did not rate them as changing significantly with time (HARCES) (Table 2).

Table 2

Seizure severity (HASS score range 13-52), and epilepsy-related restrictions (HARCES score range 10-40) recorded when presented to DuCESP (Baseline) and 6, 12 and 24 months thereafter (n = 20)

	Baseline	6 months later	12 months later	24 months later
HASS				
Mean (SD)	29.2 (7.2)	28.2 (8.0)	28.6 (6.5)	28.8 (6.9)
Median (range)	29 (16-42)	29 (15-42)	29 (15-39)	29 (15-40)
HARCES				
Mean (SD)	22.2 (8.5)	21.2 (7.7)	23.0 (7.3)	23.4 (7.4)
Median (SD)	23 (13-38)	22 (13-38)	23 (12-39)	24 (12-39)

On the HAY (HrQoL) generic part, parents and children evaluated the frequency of social activities as statistically significantly less than normal at baseline and also later ($p < 0.05$). Parents also found the frequency of physical and cognitive activities to be significantly below normal values ($p's < 0.05$); the estimated frequency of physical activities was significantly decreased at 24 months follow-up (Tables 3 and 4). Children had significantly more physical complaints compared to normal values at baseline ($p < 0.05$). Parents of those with epilepsy also found their children to have more physical complaints than did the parents of healthy

children ($p < 0.05$). With respect to the epilepsy-specific scales of the HAY, children but not their parents evaluated the frequency of seizures as to increase. Children and parents rated epilepsy-related complaints as severe. Children had many concerns and feelings of inferiority. However, they rated the frequency and quality of their activities similar to the reference group and this did not change.

With respect to self-perceived competence (SPP-C) children perceived themselves as having less than normal competence in scholastic and athletic domains and in behavioral conduct (<3). Not at the start but during the follow-up period, adolescents perceived themselves as having less than normal competence in 8/9 subscales (<3) (Table 5).

Relationships of epilepsy parameters (HASS and HARCES) and of cognition (IQ/DI) with HrQoL (HAY-C, HAY-P) (Table 6)
A negative but not strong relationship was found between seizure severity (HASS) and HAY-C, and between epilepsy-related restrictions (HARCES) and HAY-C. Not one correlation between HASS and HAY-C and between HARCES and HAY-C was statistically significant, either at baseline or 24 months later.
Similarly, not one correlation between IQ/DI and HAY-C was statistically significant.
Relationships of epilepsy parameters (HASS and HARCES) and of cognition (IQ/DI) with Perceived competence (SPP-C/SPP-A) (Table 6). At baseline, significant negative correlations were found between seizure severity (HASS) and both School performance (SPP-C/SPP-A) ($r = -.75$, $p<0.05$) and Athletic competence (SPP-C/SPP-A) ($r = -.79$, $p<0.05$). Twenty-four months after entry into the study, epilepsy-related restrictions (HARCES) were statistically significantly related to Physical appearance ($r = -.80$), Behavioral conduct ($r = -.77$), Global self-worth (SPP-C/SPP-A) ($r = -.89$) ($p's < 0.05$).
At entry, the correlation of IQ/DI with global self-worth (SPP-C/SPP-A) was significant and 24 months later with social acceptance (SPP-C/SPP-A) (Table 6).

Table 3

Health-related Quality of Life (How Are you questionnaire for Parents [HAY-P]). Reference data (n = 134) data (averaged per sub-scale) obtained at baseline and after 6, 12 and 24 months in 20 children who were candidates for epilepsy surgery and comparison between the assessments

	Healthy		Follow up			Sign. Difference[1]
	Reference Group	Baseline	6 months	12 months	24 months	at follow-up
	Mean (SD)	Mean (SD)[2]	Mean (SD)	Mean (SD)	Mean (SD)	p value
Generic part						
Estimated frequency of						
Physical activities	2.60 (0.52)	2.5 (0.5)	2.5 (0.5)	2.3 (0.5)	2.2 (0.5)	0-24m 0.01 *
Cognitive tasks	3.08 (0.56)	2.4 (0.8) *	2.5 (0.8)	2.5 (0.8)	2.5 (0.8)	-
Social activities	2.38 (0.48)	2.0 (0.4) *	2.1 (0.7)	2.2 (0.6)	1.9 (0.5)	-
Physical complaints	2.75 (0.38)	2.3 (0.5) *	2.4 (0.4)	2.5 (0.4)	2.5 (0.6)	-
Positive emotions	2.99 (0.50)	2.9 (0.5)	2.9 (06)	2.9 (0.4)	2.8 (0.4)	-
Estimated quality of						
Physical activities	3.47 (0.38)	3.4 (0.6)	3.3 (0.7)	3.1 (0.9)	3.1 (0.9)	-
Cognitive tasks	3.11 (0.44)	2.9 (0.9)	2.6 (0.8)	2.8 (0.9)	2.7 (0.8)	0-6m 0.05 *
Social activities	3.35 (0.44)	2.5 (0.6)*	2.4 (0.8)	2.4 (0.8)	2.5 (0.7)	-
Feeling bothered about						
Physical activities	2.56 (0.69)	2.9 (0.5)	2.9 (0.7)	2.9 (0.6)	2.9 (0.7)	-
Cognitive tasks	2.34 (0.58)	2.1 (0.7)	2.1 (0.8)	2.1 (0.5)	2.4 (0.7)	-
Social activities	2.29 (0.58)	2.2 (0.6)	2.1 (0.6)	2.1 (0.4)	2.1 (0.5)	-
Physical complaints	2.51 (0.54)	2.0 (0.4) *	2.2 (0.5)	2.1 (0.4)	2.4 (0.4)	-
Chronic Illness part						
Estimated frequency of						
Concerns		2.7 (0.6)	2.7 (0.6)	2.7 (0.6)	2.9 (0.7)	-
Feelings of inferiority		2.2 (0.4)	2.2 (0.4)	2.1 (0.5)	2.2 (0.5)	-
Epilepsy part						
Estimated frequency of						
Seizures		3.1 (0.6)	2.8 (0.6)	2.5 (0.5)	2.8 (0.7)	-
Epilepsy treatment		2.8 (0.4)	3.1 (0.8)	2.9 (0.4)	2.8 (0.6)	-
Epilepsy-related complaints		1.8 (0.3)	2.0 (0.4)	1.9 (0.4)	2.1 (0.7)	-
Feeling bothered about						
Physical complaints		2.3 (0.5)	2.6 (0.5)	2.4 (0.5)	2.3 (0.5)	-
Seizures		3.0 (0.7)	2.9 (0.6)	2.8 (0.7)	2.9 (0.6)	-
Epilepsy treatment		2.9 (0.6)	2.5 (0.7)	2.5 (0.8)	2.4 (0.8)	-

[1]Anova for Repeated Measures. [2]Significance (*) in the column pertains to comparison with reference data.

Statistical significance *($p \leq 0.05$), **($p \leq 0.01$).

Table 4

Health-related Quality of Life ('How Are you' questionnaire for Children [HAY-C]). Reference data (n=134), data (averaged per sub-scale) obtained at baseline and after 6, 12 and 24 months in 13 children who were candidates for epilepsy surgery and comparison between the assessments

	Healthy Reference Group Mean (SD)	Base- line Mean (SD) [2]	Follow up 6 months Mean (SD)	12 months Mean (SD)	24 months Mean (SD)	Sign. Difference[1] at follow-up p value
Generic part						
Estimated frequency of						
Physical activities	2.60 (0.49)	2.4 (0.7)	2.4 (0.6)	2.3 (0.6)	2.3 (0.6)	-
Cognitive tasks	3.07 (0.58)	2.7 (0.6)	2.7 (0.6)	2.8 (0.6)	2.8 (0.6)	-
Social activities	2.37 (0.48)	1.9 (0.7) *	1.9 (0.5)	1.9 (0.5)	2.0 (0.5)	-
Physical complaints	3.47 (0.51)	1.5 (0.4) **	1.7 (0.5)	1.4 (0.3)	1.3 (0.3)	6-12m 0.02*
Positive emotions	3.07 (0.62)	2.4 (0.7) *	2.5 (0.8)	2.7 (0.7)	2.5 (0.8)	-
Estimated quality of						
Physical activities	3.91 (0.18)	3.7 (0.4)	3.7 (0.4)	3.8 (0.4)	3.7 (0.5)	-
Cognitive tasks	3.74 (0.36)	3.4 (0.5)	3.5 (0.4)	3.6 (0.2)	3.3 (0.7)	-
Social activities	3.90 (0.23)	3.7 (0.5)	3.6 (0.5)	3.7 (0.5)	3.6 (0.5)	-
Feeling bothered about						
Physical activities	2.52 (0.75)	2.6 (0.7)	2.5 (0.7)	2.8 (0.7)	2.7 (0.8)	-
Cognitive tasks	2.18 (0.68)	2.4 (0.5)	2.4 (0.4)	2.4 (0.6)	2.4 (0.6)	-
Social activities	2.39 (0.62)	2.6 (0.7)	2.7 (0.7)	2.7 (0.6)	2.7 (0.7)	-
Physical complaints	1.90 (0.64)	1.3 (0.8) *	1.9 (0.8)	1.9 (0.8)	1.9 (0.5)	0-6m 0.02*
Chronic Illness part						
Estimated frequency of						
Concerns		1.6 (0.5)	1.4 (0.3)	1.4 (0.7)	1.5 (0.7)	-
Feelings of inferiority		1.6 (0.6)	1.5 (0.6)	1.3 (0.4)	1.4 (0.3)	-
Epilepsy part						
Estimated frequency of						
Seizures		2.1 (0.8)	1.8 (0.7)	1.5 (0.6)	1.8 (0.8)	0-24m 0.01*
Epilepsy treatment		2.1 (0.4)	2.0 (0.3)	1.8 (0.3)	1.9 (0.2)	6-12m 0.04*
Epilepsy-related complaints		1.9 (0.6)	1.8 (0.7)	1.8 (0.7)	1.9 (0.7)	-
Feeling bothered about						
Physical complaints		2.3 (0.5)	2.6 (0.5)	2.4 (0.5)	2.3 (0.5)	-
Seizures		3.0 (0.7)	2.9 (0.6)	2.8 (0.7)	2.9 (0.6)	-
Epilepsy treatment		2.9 (0.6)	2.5 (0.7)	2.5 (0.8)	2.4 (0.8)	-

[1]Anova for Repeated Measures. [2] Significance (*) in the column pertains to comparison with reference data.

Statistical significance *($p \leq 0.05$), **($p \leq 0.01$).

Table 5

Self-perceived competence (SPP-C; SPP-A): Means (SD) and change over two years (n=13)

	Baseline	Follow up			Sign.Difference[1]
		6 months	12 months	24 months	at follow-up
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p
SPP-C (n = 6)					
Total Mean Score	2.8 (0.4)	2.7 (0.5)	3.0 (0.4)	2.9 (0.4)	6-12m 0.02*
Scholastic competence	2.2 (0.6)	2.4 (0.5)	2.5 (0.5)	2.4 (0.5)	-
Social acceptance	2.8 (0.9)	3.0 (0.8)	2.8 (0.9)	3.1 (0.6)	-
Athletic competence	2.9 (0.3)	2.7 (0.2)	3.2 (0.3)	2.9 (0.4)	6-12m 0.01*
					12-24m 0.05*
Physical appearance	3.2 (0.7)	2.7 (0.9)	3.5 (0.5)	3.1 (0.6)	6-12m 0.05*
Behavioral conduct	2.7 (0.7)	2.4 (0.6)	2.8 (0.6)	2.7 (0.7)	-
Global self-worth	3.2 (0.3)	2.8 (0.7)	3.2 (0.4)	3.3 (0.4)	-
SPP-A (n=7)					
Total Mean Score	2.8 (0.3)	2.7 (0.4)	2.7 (0.3)	2.7 (0.4)	-
Scholastic competence	2.7 (0.8)	2.4 (0.8)	2.5 (0.7)	2.6 (0.8)	-
Social acceptance	2.9 (0.5)	2.6 (0.5)	2.8 (0.4)	2.7 (0.4)	-
Athletic competence	2.3 (0.6)	2.4 (0.4)	2.5 (0.6)	2.5 (0.7)	-
Physical appearance	2.8 (0.6)	3.0 (0.3)	2.9 (0.6)	2.8 (0.2)	-
Behavioral conduct	3.0 (0.3)	2.8 (0.3)	2.9 (0.5)	2.7 (0.2)	-
Global self-worth	3.0 (0.7)	3.1 (0.9)	3.0 (0.9)	2.6 (0.9)	-
Romance	2.7 (0.5)	2.5 (0.6)	2.6 (0.5)	2.6 (0.7)	-
Friendship	3.2 (0.6)	2.9 (0.7)	2.6 (0.4)	3.0 (0.3)	-

[1]Anova for Repeated Measures; Statistical significance: *($p \leq 0.05$).

Table 6

Correlations (Spearman rho) of measures of severity of epilepsy (HASS), of epilepsy-related restrictions (HARCES) and of IQ/DI with Health-related Quality of Life (HAY-C) and self-perceived competence (SPP-C/SPP-A) at baseline and 24 months later (n=13).

	HASS		HARCES		IQ/DI	
	base	24m	base	24m	base	24m
HAY:						
Generic part						
Estimated frequency of						
Physical activities	- .24	- .10	- .06	- .01	.19	.19
Cognitive tasks	- .46	- .06	- .54	- .47	.51	.31
Social activities	- .17	- .08	- .34	- .36	.45	.20
Physical complaints	- .35	- .20	- .29	- .42	.18	.13
Positive emotions	- .08	- .09	- .46	- .29	.04	.04
Estimated quality of						
Physical activities	- .51	- .37	- .33	- .19	- .21	- .26
Cognitive tasks	- .52	- .39	- .30	- .44	.06	- .21
Social activities	-. 35	- .15	- .25	- .23	-. 07	- .18
Chronic Illness part						
Estimated frequency of						
Concerns	- .31	- .10	- .19	- .23	.21	- .55
Feelings of inferiority	- .01	- .05	- .18	- .17	- .18	- .34
Epilepsy part						
Estimated frequency of						
Seizures	- .25	- .33	- .05	- .14	- .24	.12
Epilepsy treatment	- .58	- .35	- .53	- .35	.57	.63
Physical complaints	- .26	- .15	- .20	- .27	- .44	.36
Generic part						
Feeling bothered about						
Physical activities	- .08	- .06	- .36	- .21	- .09	.07
Cognitive tasks	- .26	- .48	- .17	- .45	.12	.29
Social activities	- .19	- .25	- .34	- .38	.47	.32
Physical complaints	- .12	- .23	- .13	- .19	.06	.01
Epilepsy part						
Feeling bothered about						
Physical complaints	- .12	- .09	-.34	- .18	.08	.22
Seizures	- .03	- .09	- .25	- .17	- .47	.63
Epilepsy treatment	- .12	- .20	- .06	- .13	- .33	.46
SPP-C/SPP-A:						
Total competence	- .34	-. 31	- .24	- .58	.71	.61
School performance	- .75 *	- .68	- .50	- .31	.55	.27
Social acceptance	- .63	- .44	- .29	- .40	.25	.88 *
Athletic competence	- .79 *	- .60	- .58	- .60	.59	.50
Physical appearance	.05	- .20	- .65	- .80 *	.64	.44
Behavioral conduct	.21	- .40	- .46	- .77 *	.25	.67
Global self-worth	- .61	- .23	- .23	- .89 *	.80 *	.50
Romance	- .40	- .44	- .41	- .48	.55	.51
Friendship	- .50	- .48	- .42	- .52	.61	.55

Abbreviations: base = baseline, DI = Developmental Index, IQ = Intelligence Quotient, m = months, SPP-C = Self-perceived competence Children, SPP-A = Self-perceived competence Adolescents

Statistical significance: *($p \leq 0.05$).

Discussion

In many cases, the decision to refrain from performing epilepsy surgery in a child with pharmaco-resistant epilepsy means a disappointment for the child and her/his parents and for the parents the fear of undue cognitive and social deterioration. In the long run, social, educational and socio-economical outcomes of childhood epilepsy indeed appear to be poor, particularly if the epilepsy is symptomatic (Sillanpää et al., 2004; Wakamoto et al., 2000). Using a time-window of two years after presentation to the Dutch Collaborative Epilepsy Surgery Program (DuCESP), we studied HrQoL and self-perceived competence in children with pharmaco-resistant epilepsy who were not eligible for epilepsy surgery. The purpose of the study is to find out whether an undue negative course starts immediately after the decision not to operate.

Epilepsy, HrQoL and self-perceived competence

Epilepsy can have a profound impact on psychosocial function, HrQoL and perceived competence. Epilepsy impedes the development of independence and impairs social function, peer relationships, self-esteem, mood and cognition (Hoare et al., 2000; Smith et al., 2004; McEwan et al., 2004). Knowledge of these impacts of epilepsy is obtained from parents or caregivers. The perceptions of the children themselves have yet to be inventoried (McEwan et al., 2004).

In our study, children and parents perceived HrQoL to be less than normal, especially with respect to social activities. Children with ongoing epilepsy were less frequently involved in social activities than healthy peers. Moreover, parents perceived the quality of the social activities of their children to be less than normal, as is described in other studies about children with epilepsy (Camfield and Camfield 2003; Räty et al., 2003). Epilepsy-related complaints increased during the follow-up and frequencies of activities remained less than normal.

As described earlier, children and adolescents living with epilepsy

are more at risk of developing behavioral and school-related problems (Räty et al., 2003). The children in the present study perceived themselves as being less competent in scholastic and athletic domains and in behavioral conduct, when compared to normal values. The adolescents perceived themselves as having less than normal competence in the majority of relevant domains.
When comparing children and adolescents, the lower perceived self-worth of the latter group is in accordance with findings from other studies (Räty et al., 2003). The adolescents feel themselves less competent than and less accepted by peers, which is important because support and acceptance by peers is extremely important in this age group. Athletic competence and social acceptance are supposed to be the major contributors to self-worth in adolescents (Harter, 1987). The combination of a self-perceived poor level of athletic competence and poor social acceptance in adolescents may, therefore, be major contributors to low self-worth in these adolescents with pharmaco-resistant epilepsy. The inventory and, if possible, treatment of social functioning may be more important for later social equilibrium than just measuring seizure severity and assuring seizure control (Berg et al., 2004).

Relationships between seizure severity and HrQoL are not always clear, as found in studies of adults. Some studies described a significant relationship of HrQoL with seizure frequency and severity (Malmgren et al., 1997; Markand et al., 2000; Birbeck et al., 2002). Other studies were not able to show a statistically significant correlation between HrQoL and seizure severity (Baker 1998; Johnson et al., 2004). In our study no significant relationship between parameters of epilepsy (HASS and HARCES) and HrQoL could be detected, either at entry to the study or at 24 months follow-up. In the studies with a significant relation between improvement of HrQoL and decreased seizure severity, patients were seizure-free, but in patients where seizures remain this relation is not found to be significant, as in our children. Perceived competence, however, showed a significant negative correlation with epilepsy-related restrictions, at least when Physical appearance, Behavioral conduct

and Global self-worth were evaluated. Children and adolescents who have severe epilepsy-related restrictions consider themselves to be less competent. This finding is of importance, as large epidemiological studies revealed lasting risks with respect to social outcome (Sillanpää et al., 2004; Javala et al., 2004). The consequences of having pharmaco-resistant epilepsy and epilepsy-related restrictions have a negative impact on the self-worth of the children and will also exert an influence on development. If individuals perceive themselves as being physically competent, they will continue to participate in physical activities. If, however, they perceive themselves as physically incompetent, they will restrict their participation (Skinner and Piek, 2001).

The children of the present study cannot be considered comparable to a group of surgically treated children, as there were significant reasons for not performing surgery. It would, however, be a challenge to determine whether a group of 21 children of a similar age who underwent epilepsy surgery and who have been followed with identical instruments during the same time interval of two years (Empelen et al., 2005), show similar trends as reported for the group that was not eligible for surgery. The 21 children (4 boys, 17 girls; aged 6.2 to 15.4 years) were all derived from 52 children who underwent epilepsy surgery in the Wilhelmina Children's Hospital between 1996 and 2001, and who met the requirements for the health-related quality of life questionnaire and the self-perceived competence profiles used in the present study (Empelen et al., 2005).

In the surgically treated group, parents evaluated their children as having positive emotions more frequently after surgery, while in the evaluations of both children and parents the frequency of social activities in the post-surgical period was not different from that in healthy children. Children started to feel better about seizure variables in the second post-surgical year.
In the group of children who were not eligible for surgery, parents and children evaluated the frequency of social activities as

significantly less than normal at baseline and during follow-up; parents also found the frequency of physical and cognitive activities still to be significantly below normal at 24 months follow-up. Children and parents scored a high level of epilepsy-related complaints. Children had many concerns and feelings of inferiority; the degree to which they were bothered about activities and about the quality of activities did not change and both were not significantly worse than into normal children.

Children in the surgically treated group perceived themselves as being socially more competent and having greater self-worth (p's 0.05) than before the operation. In the adolescent group, several aspects of self-perceived competence improved shortly after surgery (p's < 0.05), while two years after surgery athletic competence and romance had improved significantly (p's < 0.05).
In the group not eligible for surgery, children perceived themselves as having less scholastic and athletic competence and poorer behavioral conduct compared to normal values; adolescents perceived themselves as having less competence in 8/9 domains compared to normal values during the follow-up period.
Elliot and colleagues also described an increase in self-esteem and self-confidence after surgery in adolescents (2000), but this was not confirmed for younger children (Smith et al., 2004). Parents whose children underwent epilepsy surgery reported that they were able to promote a higher level of independence in the family than parents of children who did not undergo this procedure (Elliot et al., 2000; Smith et al., 2004).

Participation

Children not eligible for surgery evaluate their HrQoL and competence as being less than reference (norm) values, during the follow-up of two years change was not established. The study appears to take the edge off the fear of significant worsening when surgery is not feasible. After two years parents perceived their children as to engage less in physical activities than at the start of the study.

After two years, children perceived the frequency of their seizures as to have increased.

Acknowledgement

We are grateful to the Phelps Stichting and the Johanna Children's Foundation for their financial support; to W.R. Pestman, PhD (Center for Biostatistics) for his supervision of statistical analyses, to E. van der Steeg, MA, M. Peters, MA and M.J.M. Volman, PhD (University Utrecht, Faculty of Social Sciences) for their assistance in this research. We thank Mrs Brenda Vollers-King for correction of the English language and Mrs C. Tims-Polderman and Mrs J. Nuysink for their assistance in data-management.
We thank the Members of the Dutch Collaborative Epilepsy Surgery Program for their cooperation: SEIN, Kempenhaeghe, Hans Bergerkliniek, Academic Hospitals (Utrecht, Maastricht, Amsterdam VU).

References

Aasland A, Diseth TH. Use of Selfperception Profile for adolescents as an indicator of psychosocial outcome in children with a chronic physical disorder. Eur Child Adolesc Psychiatry 1999;8:77-85.

Baker GA, Cagnon D, McNulty P. The relationship between seizure frequency, seizure type and quality of life: findings from three European countries. Epilepsy Res 1998;30:231-40.

Berg AT, Smith SN, Frobish D, Beckerman B, Levy SR, Testa FM, Shinnar S. Longitudinal assessment of adaptive behavior in infants and young children with newly diagnosed epilepsy: influences of etiology, syndrome, and seizure control. Pediatrics 2004;114:645-50.

Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. Epilepsia 2002;43:535-8.

Bruil J. Development of quality of life questionnaire for children with a chronic Illness. (Thesis) FSW: Universiteit Leiden, 1999.

Bruyn EEJ de, Vander Steene G, Haasen PP van. Wechsler Intelligence Scale for Children – Revised (WISC-R). Nederlandstalige uitgave en verantwoording. Lisse: Swets & Zeitlinger 1986.

Camfield P, Camfield C. Childhood epilepsy: what is the evidence for what we think and what we do? J Child Neurol 2003;18:272-87. [Review].

Carpay JA, Vermeulen J, Stroink H, et al. Disability due to restrictions in childhood epilepsy. Dev Med Child Neurol 1997;39:521-6.

Coq le EM, Boeke AJ, Bezemer PD, Bruil J, van Eijk JT. Clinimetric properties of a parent report on their offspring's quality of life. J Clin Epidemiol 2000;53:139-46.

Elliott IM, Lach L, Smith ML. Adolescent and Maternal Perspectives of Quality of Life and Neuropsychological Status Following Epilepsy Surgery. Epilepsy Behav 2000;1:406-17.

Empelen R van, Jennekens-Schinkel A, Rijen PC van, Helders PJM, Nieuwenhuizen O van. Health-related quality of life and self-perceived competence of children assessed before and up to two years after epilepsy surgery. Epilepsia 2005;46:1-14.

Ferguson TJ, Stegge H, Eyre HL, Vollmer R, Ashbaker M. Context effects and the (mal)adaptive nature of guilt and shame in children. Genet Soc Gen Psychol Monogr 2000;126:319-45.

Harter S. Manual for the Self-Perception Profile for Adolescents. Denver CO: University of Denver, 1988.

Hoare P, Mann H, Dunn S. Parental perception of the quality of life among children with epilepsy or diabetes with a new assessment questionnaire. Qual Life Res 2000;9:637-44.

Jalava M, Sillanpaa M, Camfield C, Camfield P. Social adjustment and competence 35 years after onset of childhood epilepsy: a prospective controlled study. Epilepsia 1997;38:708-15.

Johnson EK, Jones JE, Seidenberg M, Hermann BP. The relative impact of anxiety, depression, and clinical seizure features on health-related quality of life in epilepsy. Epilepsia 2004;45:544-50.

McEwan MJ, Espie CA, Metcalfe J. A systematic review of the contribution of qualitative research to the study of quality of life in children and adolescents with epilepsy. Seizure 2004;13:3-14. [Review].

Malmgren K, Sullivan M, Ekstedt G, Kullberg G, Kumlien E. Health-related quality of life after epilepsy surgery: a Swedish multicenter study. Epilepsia 1997;38:830-8.

Markand ON, Salanova V, Whelihan E, Emsley CL. Health-related quality of life outcome in medically refractory epilepsy treated with anterior temporal lobectomy. Epilepsia 2000;41:749-59.

Oostrom KJ, Schouten A, Olthof T, Peters AC, Jennekens-Schinkel A. Negative emotions in children with newly diagnosed epilepsy. Epilepsia 2000;41:326-31.

Räty LK, Wilde Larsson BM, Soderfeldt BA. Health-related quality of life in youth: a comparison between adolescents and young adults with uncomplicated epilepsy and healthy controls. J Adolesc Health 2003;33:252-8.

Schumann BC, Striegel-Moore RH, McMahon RP, Waclawiw MA, Morrison JA, Schreiber GB. Psychometric properties of the Self-Perception Profile for Children in a biracial cohort of adolescent girls: the NHLBI Growth and Health Study. J Pers Assess 1999;73:260-75.

Scott-Lennox J, Bryant-Comstock L, Lennox R, Baker GA. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. Epilepsy Res 2001;44:53-63.

Sillanpää M, Haataja L, Shinnar S. Perceived impact of childhood-onset epilepsy on quality of life as an adult. Epilepsia 2004;45:971-7.

Skinner RA, Piek JP. Psychosocial implications of poor motor coordination in children and adolescents. Hum Mov Sci 2001;20:73-94.

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Steene G van der, Bos A. WPPSI-R, Wechsler Preschool and Primary Scale of Intelligence. Vlaams-Nederlandse aanpassing. Handleiding voorlopige versie. Lisse: Swets & Zeitlinger 1997.

Thill AD, Holmbeck GN, Bryant FB, Nelson C, Skocic A, Uli N. Assessing the factorial invariance of Harter's self-concept measures: comparing preadolescents with and without spina bifida using child, parent, and teacher report. J Pers Assess 2003;81:111-22.

Veerman JW. De Competentiebelevingsschaal voor Kinderen: Theoretische uitgangspunten en enkele onderzoeksgegevens. Tijdschrift voor de Orthopedagogiek 1997;28:286-301.

Veerman JW, Straathof MAE, Treffers PhDA et al. Competentiebelevingsschaal voor kinderen (CBSK) Lisse: Swets Testservice 1997.

Wakamoto H, Nagao H, Hayashi M, Morimoto T. Long-term medical, educational, and social prognoses of childhood-onset epilepsy: a population-based study in a rural district of Japan. Brain Dev 2000;22:246-55.

Wechsler D. WISC-R. Wechsler Intelligence Scale for Children – Revised. New York: The Psychological Corporation 1974.

Wechsler D. Manual for the Wechsler Preschool and Primary Scale of Intelligence – Revised (WPPSI-R). New York: The Psychological Corporation 1989.

Wickstrom L. Harter's Self-Perception Profile for Adolescents: reliability, validity, and evaluation of the question format. J Pers Assess 1995;65:100-16.

W.H.O. The International Classification of Functioning, Disability and Health (2002). ICF: introduction. Geneva: World Health Organization. Available on the WHO Internet site, 2002. http://www.who.int/classification/icf

Chapter 7

Summary, general discussion and conclusions

Summary

The main aim of this thesis is to gain greater insight into the health-related consequences of epilepsy surgery and of not being eligible for surgery. In a prospective longitudinal design, we studied all children referred to the Dutch Collaborative Epilepsy Surgery Programme (DuCESP) between 1996 and 2001. Some 40 patients per year were referred by neurologists, paediatric neurologists and epileptologists working at epilepsy centres and secondary and tertiary institutions of health care all over the country. After careful screening, about 10-15 children per year can be operated, but not all intractable seizures in childhood can be treated successfully by surgical intervention. In The Netherlands, almost 75% of the children who are presented to DuCESP do not fulfil the criteria for surgery and are, therefore, not offered this treatment. Reasons for not being eligible for surgery include multifocal localisation or localisation of the epileptogenic zone in an eloquent cerebral area.
The International Classification of Functioning, Disability and Health (ICF) provided the framework for studying health-related consequences of epilepsy surgery (WHO, 2002). The ICF distinguishes three levels of human functioning, i.e., body function and structure, activities and participation in social life, and by defining disability at each level, as impairment, activity limitation or participation restriction.
Covering the period from prior to epilepsy surgery up to two years after the operation, our study focuses on 1) Impairments: measured as change in seizure frequency and severity, and effects on muscle strength, range of motion and muscle tone, 2) Limitations in activities, assessed in terms of motor functioning and self-care, mobility and social function. 3) For the level of participation, epilepsy-related restrictions were assessed. In addition we measured the course of health-related quality of life (HrQoL) and self-perceived competence.
Patients were assessed using a standard protocol with fixed intervals: 1- 3 months before surgery, and 6 months, 1 year and 2 years after surgery.

And in children not eligible for surgery we followed the same procedure, with the same focus but without surgery, with baseline assessments and the same frequency of follow-up.
In fact, we followed two groups. One comprised 52 children who underwent epilepsy surgery between 1996 and 2001 at the Wilhelmina University Children's Hospital. The other group consisted of 45 children who were not eligible for epilepsy surgery between 1996 and 2001.
Surgical outcomes in terms of seizure frequency were assessed using Engel et al.'s (1993) modified classification. Class I = free of seizures or residual auras, Class II = fewer than 3 seizures per year, after a significant seizure-free period and Class III = noticeable improvement, i.e., more than 75% reduction in seizure frequency. The outcome in children who experience less than 75% reduction in seizure frequency is classified as Engel Class IV.
Seizure severity as perceived by the parent or caregiver was quantified using the Hague Seizure Severity Scale (HASS), an inventory of 13 ictal and postictal problems that may have been encountered in the previous three months (Carpay et al., 1997).
We assessed muscle strength, range of motion and muscle tone as relevant parameters for motor impairments. In the activity level of the ICF we studied motor performance using the following instruments: Motor scale of the Bayley Scales of Infant Development 2nd edition (BSID-II) (Bayley, 1993), the Movement Assessment Battery for Children (M-ABC) (Hendersen & Sugden, 1992) in children without spasticity. And in children with spasticity, the Gross Motor Function Measure (GMFM-88) and the Gross Motor Function Classification System (GMFCS) were useful for comparing the results with reference scores for children with cerebral palsy (Russell et al., 2002; Rosenbaum et al., 2002).
In addition to motor performance, we were interested in daily activities and participation of the children before and after surgery. We used the Pediatric Evaluation of Disability Inventory (PEDI) as a functional assessment to gauge activities of daily life (Haley et al., 1992). The PEDI is a structured parent's interview that covers the domains of self-care (73 items), mobility (59 items) and social

functioning (65 items). Limitations in activities can be measured in terms of performance, caregiver's assistance, and the use of devices to perform the activities. Participation problems were assessed in terms of epilepsy-related restrictions and quantified by means of the Hague Restrictions in Childhood Epilepsy Scale (HARCES) (Carpay, 1997).

In addition to impairments, limitations and restrictions we assessed health-related quality of life and self-percieved competence.
For health-related quality of life we used the How Are You (HAY) questionnaire. The HAY is a questionnaire adapted to life in The Netherlands and designed for children with epilepsy. This version for children with epilepsy covers generic and epilepsy-specific areas (Bruil, 1999).
Perceived competence was measured using the Dutch adaptation of the Harter Self Perception Profile for Children (SPP-C) or the Self Perception Profile for Adolescents (SPP-A). The scales assess a child's or adolescent's sense of competence in cognitive, social and physical domains and yield a measure of general self-worth (Harter, 1988; Veerman et al., 1997).

Chapter 1 presents an introduction to refractory epilepsy and the research programme about health-related consequences of epilepsy surgery describing its various effects as well describing its effects in terms of seizure outcome. We used the International Classification of Functioning, Disability and Health (ICF) model, designed by the WHO (WHO, 2002), to study the effects of epilepsy surgery.

In chapter 2, we report the investigation into the degree to which seizure severity, motor impairments, motor activities and aspects of social participation exist prior to hemispherectomy and change thereafter in 12 children. The score on the HASS (seizure severity) showed an almost maximum improvement immediately after surgery and remained so for the subsequent 2 years. For seizure frequency we scored 9 children with Engel I and 3 children with Engel III score.

Motor impairments: after hemispherectomy muscle strength and muscle tone on the side of the body contralateral to the hemispherectomy, which were already decreased preoperatively, decreased even further in the first six months after surgery, but returned to pre-surgical baseline thereafter, except for the distal part of the arm. Motor activities: mean GMFM increase was 20% after two years, while mean PEDI-increase was even more than 20 scale-points. In nearly all children HARCES scores (epilepsy-related restrictions) had normalized in the two years after surgery.

Chapter 3 describes the frequency and severity of seizures and epilepsy-related restrictions, health-related quality of life and self-perceived competence in 21 patients (aged 6.2 to 16.8 years) before and 6, 12 and 24 months after epilepsy surgery. Prior to surgery, the children's evaluations of both the quality and frequency of their activities in physical, social and cognitive domains was worse than that of the reference group of healthy children; they also felt more bothered about their physical activities. Considerable seizure reduction was measured 6 months post-surgery and this effect remained, so that two years after surgery, 15 patients (72%) were free of seizures (Engel I). Median score on the HASS (seizure severity) improved from 33 before surgery to 13 post-surgery. Parents and children evaluated health-related quality of life in activities as having improved. The children's evaluations of the quality of their physical, social and cognitive activities, improved significantly, over time even reaching normal values. However, the children's feelings concerning their activities remained worse than those of healthy children. Parents more frequently evaluated their children as having positive emotions.

The children's self-perceptions of social acceptance tended to improve within the six months after surgery and gradually ameliorated thereafter, which we take to mean that, after surgery, children learned to perceive themselves as being competent to participate in most social domains. In agreement with the children's evaluations of the quality of cognitive tasks on the HAY, self-perceptions of

scholastic competence neither improved nor deteriorated over the two-year period of the present study.
Two years after surgery, children perceived themselves as being socially more competent and as having greater self-worth. In the adolescent group, several aspects of self-perceived competence improved shortly after surgery, while two years after surgery athletic competence and romance had improved.
On the HARCES (epilepsy-related restrictions), the median score improved from 28 pre-surgery to 13 post-surgery, a significant improvement, which means that the children having much more freedom and fewer restrictions after surgery.

Chapter 4 presents the study of the impact of epilepsy surgery on motor performance, activities of daily life (ADL) and caregiver's assistance in 37 children and adolescents (age range: 0.1-15.4 years) with pharmacologically untreatable epilepsy, 17 of whom were also diagnosed as having spasticity of cerebral origin. Fourteen children underwent hemispherectomy, fourteen underwent temporal, four frontal, two parietal and two central resection. One child underwent callosotomy. Motor performance of infants and children without spasticity was measured using the Movement Assessment Battery for Children (M-ABC). The Gross Motor Function Measure (GMFM-88) was used in children with spasticity, the severity of motor disability in this group being determined by means of the Gross Motor Function Classification System (GMFCS). Scores improved post-surgery statistically significantly at group level on M-ABC and GMFM. At 24 months post-surgery, 16/17 children with spasticity scored less than 2 SD from the mean reference score that was appropriate for their age and GMFCS level. These children also improved significantly with respect to ADL-function and caregiver's assistance (PEDI). Improvement in activities of daily life and caregiver's assistance could not be measured in children without spasticity because of the ceiling effect of the PEDI.
We concluded that two years after epilepsy surgery, motor function of the majority of children develops in accordance with the expected motor development in children with and without spasticity,

while impairments do not deteriorate, except for the impairments in the distal part of the arm after hemispherectomy.

Chapter 5 reports on the study, carried out over a period of two years, into whether severity of epilepsy, motor functioning and epilepsy-related restrictions worsened in 45 children with pharmaco-resistant epilepsy (aged 6 months to 15 years), who were not eligible for epilepsy surgery. All data were rated at baseline and at 6, 12 and 24 months thereafter. Seizure severity, mean score at baseline 31 (range 13-52), did not change significantly during follow-up. Mean values of muscle strength, range of motion and tone were below reference norms and did not change. Motor retardation was ubiquitous but did not increase in 33 children without spasticity (BSID-II and M-ABC). Motor function of 12 children with spasticity did develop (GMFM total score baseline 55% to 71% at 24 months later), but remained poor in four/12 (>2 SD worse than reference values). In the group as a whole, functional skills and Caregiver's assistance (PEDI) increased, but remained considerably below reference values. Restrictions (HARCES) at baseline, mean 22 (range 10-40), did not change significantly.
In conclusion we can say that in these children seizure severity does not progress, motor impairments do not increase, motor development does not deflect negatively and activities of daily living and restrictions do not worsen.

In chapter 6, we report on the course, over a period of 2 years, of health-related quality of life (HrQoL) and self-perceived competence in 20 children (aged 6 years to 15 years) with pharmaco-resistant epilepsy once the decision had been taken that they were not eligible for epilepsy surgery. Parents and children evaluated the frequency of social activities as being significantly less than normal at baseline and during follow-up. Children with epilepsy had significantly more physical complaints than the reference group on entry into the study and complaints increased during follow-up. Parents of those with epilepsy found their children had significantly more physical complaints than did the parents of healthy

children. Children with epilepsy had feelings of inferiority and were concerned about their epilepsy; with respect to their activities and the quality of activities the children with epilepsy felt similar to those of the reference group.
Self-perceived competence: epileptic children evaluated their scholastic and athletic competence and behavioral conduct as being less than those of a healthy reference group, and when followed up, adolescents perceived themselves in almost all domains as having less competence than a healthy reference group.
In conclusion we can say that in children with severe epilepsy who were not eligible for epilepsy surgery, health-related quality of life and competence remained below normal. Perceived frequencies of physical complaints, seizures and epilepsy-related treatment worsened during the follow-up period, but most feelings about activities and quality of activities did not change.

Chapter 7 consists of a summary, the general discussion and conclusions as well as recommendations for future research.

General discussion

A prospective longitudinal design with a baseline assessment and three follow-up assessments was used. The baseline assessment was performed prior to surgery for those whose epilepsy was surgically treated. Following the children who were rejected for surgery, we used the same longitudinal design in order to determine whether this group of children shows trends similar to those reported for the surgery group. The follow-up covering two years enabled us to evaluate change. Furthermore, reference data provided the opportunity to compare the children with a relevant population. The reader should not consider the data obtained on children who could not be operated on as control data, as there were significant reasons for not performing surgery. The findings do increase knowledge with respect to the course of the disabilities of children with refractory epilepsy.
The study is representative for The Netherlands, because nationwide, secondary and tertiary institutions of health care refer to the Dutch Collaborative Epilepsy Surgery Programme (DuCESP), within which experts of the epilepsy centres conjointly evaluate the feasibility of epilepsy surgery for every referral.

Clinical relevance of this study

Surgically treated children
The impressive improvement in seizure reduction following surgery is in accordance with or even better than previous favourable reports (Vining et al., 1997; Wyllie et al., 1998; Holthausen and Strobl, 1999; Carter Snead, 2001; Chen et al., 2002; Kloss et al., 2002; Lendt et al., 2002; Devlin et al., 2003). Motor impairments, if present before surgery, remain after surgery. Nevertheless, motor activities improve (Chapter 2 and 4). Following hemispherectomy, the motor impairments in children are increased in the first 6 months post-surgery, and remained so later on in the distal part of the hemiparetic arm, while impairments in the leg were at the same level as pre-surgery. This information is very relevant for the

parents and children, who must be made aware of this prior to surgery. In hemispherectomised children and in children with extratemporal resections, motor impairments are only slightly associated with functional outcome. Most children with temporal resections are free from motor impairments prior to epilepsy surgery and do not develop these impairments thereafter. Yet, motor functioning of these children improves after surgery. We feel that this is an important new piece of knowledge: in the children who underwent epilepsy surgery, motor impairments, i.e., defects at the level of the anatomical / structural features, were only loosely associated with functional outcome! In this respect, the children who underwent epilepsy surgery are no different from children with other medical conditions, as revealed in recent studies on disability research in children with haemophilia (Schoenmakers et al., 2001), osteogenesis imperfecta (Engelbert et al., 2004) and spina bifida (Schoenmakers et al., 2004).
After surgery parents decrease their caregiver's assistance and children find themselves more independent. This change for the better, effected in the daily conduct of caregivers and in that of the children themselves, is reflected in the improvement on the Hague Restrictions in Childhood Epilepsy Scale (HARCES). We feel that this information is one of the major outcomes of the present study and of great clinical relevance.
These improvements in daily functioning and in functional independence are associated with relief from seizures or at least improvement in seizure severity, as measured with the Hague Seizure Severity Scale (HASS) (Carpay, 1997). Hence, we feel safe in concluding that daily functioning gets a chance to improve in children after reducing the seizures.

With respect to health-related quality of life, we distinguished between the evaluations of the children themselves and those of their parents. Overall, both the children and their parents evaluated health-related quality of life as having improved after surgery. Postoperative assessment of the children at 6 months revealed improvement in the evaluations of both the frequency and the quality

of their activities (physical, cognitive and social activities). At 12 months, no further change, which was statistically significant, had occurred. At 24 months, however, the children felt significantly less bothered about the seizures when compared with the data obtained prior to surgery. Our explanation of these results are as follows: not having seizures made it possible to improve on activities in the first 6 months after surgery, but the fear of seizures was still there. After 24 months of seizure freedom, the fear for seizures has petered out. Cessation or major decrease of seizures enables the children to play and go out more freely than before.

With respect to competence, children perceived themselves as being socially more competent and having greater self-worth. Adolescents, whose pre-surgical self-perception profile was sub-normal in the subscales of social acceptance and athletic competence, improved their perceptions of their competence after surgery. Together with improvement in social acceptance, the children and adolescents showed greater participation in peer contacts. Adolescence is a critical period for identity formation and self-definition; chronic illness can disturb the natural attainment of developmental milestones by complicating peer interaction and self-identification and by delaying independence (Snead et al., 2004). Improvement in the feelings of competence and greater participation in peer contacts is an essential effect of not having seizures after epilepsy surgery. To be free of having seizures is essential for most adolescents.
One has to realise to define the patient's and family's goals for the epilepsy surgery, not only in terms of seizure control, but also in terms of quality of life and competence expectations (Carter Snead, 2001).

Effects of not being eligible for epilepsy surgery
It is a clinical impression that, when epilepsy is refractory and children are not eligible for epilepsy surgery, parents fear that their children will deteriorate in terms of seizure severity, development and epilepsy-associated impairments. Following these children over the same period and with the same methods as those who un-

derwent surgery, taught us that seizure severity does not progress, motor impairments do not increase, motor development does not deflect negatively and activities of daily living and restrictions do not worsen. However, health-related quality of life and competence remain below normal and epilepsy-related restrictions, severe at baseline, remain without a significant change.
It is reassuring for the parents that, if other things remain constant, it is not likely that their children will experience increased impairments or deterioration in motor function. The parents must, however, be warned that although motor functioning will probably not deteriorate, they must expect that their children's health-related quality of life and self-perceived competence may remain poor, especially in adolescence, if proper measures are not taken.
This remaining poor health-related quality of life demands research into psychosocial interventions in adolescents with epilepsy (Snead et al., 2004). Snead and colleagues offered a structured psycho-educational group intervention to adolescents with epilepsy and their parents. Participants were introduced to a variety of cognitive-behavioural strategies, and were encouraged to share their own experiences with epilepsy. Feedback from adolescent and parent participants indicated that the intervention was relevant to their needs, helped them better understand their epilepsy, and allowed an opportunity for positive peer support. Also, post-intervention outcome measurement indicated an overall positive trend for quality of life improvement in the adolescents (Snead et al., 2004).

Contextual factors

The decrease of the seizure severity, by succesfull epilepsy surgery, is a pivotal change when one tries to understand the improvement in the ICF-levels of activities and participation. Not having seizures seems to be the outstanding factor in the improvements in activities and participation, because seizures are the only factor on the ICF level of impairments that really changed after epilepsy surgery. Nevertheless, improvement in functioning may have been caused by other factors as well. Within the ICF, disability and

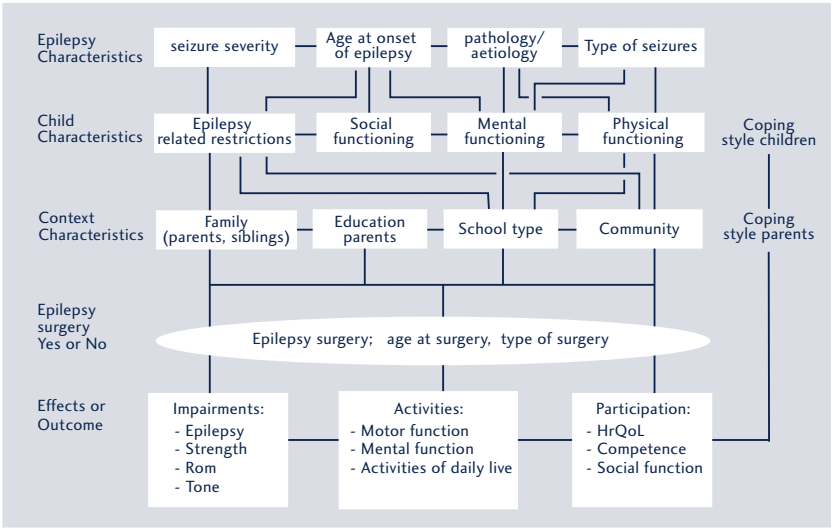
functioning are viewed as outcomes of interactions between health conditions and contextual factors. Contextual factors are external environmental factors (for example, social attitudes, architectural characteristics, legal and social structures) and internal personal factors which include gender, age, coping styles, social background, education, past and current experience, overall behaviour pattern, character and other factors that influence how disability is experienced by the individual (WHO, 2002). The environment is mentioned as a facilitator or barrier for both capacity and performance of actions and tasks in daily living. Contextual factors and expectation of parents and teachers can also play an important role in the functioning of the child (Stanton, 1999; Smith et al., 2004; Shore et al., 2004) and should be a subject of study in subsequent research.
Managing children with epilepsy is difficult, because seizures are unpredictable and often associated with a stigma. A brief, global instrument that measures the psychosocial impact of paediatric epilepsy on the family was not available at the start of our study. Camfield and colleagues developed an 11-item scale for parents' use to evaluate the influence of epilepsy on the major aspects of their family and child's life: the Impact of Pediatric Epilepsy Scale (IPES), which assesses the impact on academic achievement, participation in activities, health, relationships with family and with peers and siblings, social activities, self-esteem, and the caregiver's hopes for their child's future (Camfield et al., 2001).

In any case, the positive and negative influences on outcome are complex, as figure 1 illustrates. This figure tries to make these influences explicit by distinguishing the Epilepsy characteristics, Child characteristics and Context characteristics, by specifying relevant factors per level and by suggesting relationships (lines). It was beyond the scope of the present study to cover all influences; the epilepsy characteristics and child characteristics are the influences that we inventoried and analysed. The context characteristics have been inventoried but await analysis in future studies, because the relatively small number of patients and the large number of

variables restricted statistical options. The coping style of children and parents, the possible effect of which is acknowledged but requires a new study. In our study the accent was on the effects of epilepsy surgery on the 3 levels of the ICF model: Impairments, Activities and Participation (Figure 1). Associations have to be studied in larger groups to analyse the relation between the different aspects.

Figure 1

Possible relations between factors contributing to development in children with refractory epilepsy



Strengths and weaknesses of the study

The condition that all children who were presented to the Dutch Collaborative Epilepsy Surgery Programme were included over a period of 5 years and were followed for a period of two years, enabled one to gain knowledge on effects of epilepsy surgery over and above change in seizure patterns in children in The Netherlands. The strengths of this study include a prospective longitudinal approach, and the evaluation of the impact of epilepsy surgery on motor function, within the framework of three different domains of

the ICF. Not only the effects on seizures and motor impairments, but also those on motor activities and social participation, together with HrQoL and self-perceived competence are important factors to be reported. In this way we obtain information from our own assessments and from the children and parents themselves, with information about participation in their own situation. It is essential to be able to compare with referent data on motor development in children with and without spasticity, therefore we have used different motor assessments.

Non-randomised studies, such as the present one, provide potentially biased information about the effect of interventions. We do not know exactly what motor function and development could be in these children without epilepsy surgery. In the opinion of our team, a randomised controlled trial, with children who are not be operated or have to wait for surgery, would not be ethical.

This study does not allow a detailed analysis of determinants of outcome, due to the small number of children and their heterogeneity with regard to age, pathology and level of cognitive functioning. Also, relations between factors have to be studied in larger groups; for example: what is the influence of context factors like community and school situation and what kind of influence has coping style of children and parents on social participation and development. The PEDI is the only instrument used that addresses the domain of the environment by including questions about the context of activities and participation of the child, but is limited in its age range (Haley et al., 1992).

Effects on ADL-function and independence could not be measured in all children, due to the ceiling effect of the PEDI. To be able to measure limitations in ADL-function and independence in children aged 7.5 years upwards, with severe epilepsy and minimal physical impairments, an instrument other than the PEDI should be developed. It was not possible to assess HrQoL (HAY questionnaire) and self-perceived competence in children younger than 6 years, because they did not fulfil the test requirements, such as being able to read and understand the questions. Hence, information on this subject is derived from only part of the group.

Implications of this study

Although motor impairments, if present, remain, motor activities and social participation improve and HrQoL increases after epilepsy surgery. This is, together with reduction of seizures, the most important outcome of this study with respect to children who had medically refractive epilepsy. When clinicians are aware of the importance of the levels of functioning that go beyond the level of physical functions and their impairments, they will be more inclined to extend their assessment of the children and to measure not only seizure frequency but also activities, participation and HrQoL. A disease-related HrQoL questionnaire (like the HAY questionnaire) for children with epilepsy has an advantage over a general HrQoL questionnaire, because many aspects of quality of life are related to the seizures. The HAY offers the opportunity to gather the complementary evaluations of the parents and of the children. With respect to quality of life, the evaluations of the parents and children are essential and perhaps more material than the opinions of their physicians.

Not being eligible for epilepsy surgery implies that HrQoL of the children and parents remains poor or may even worsen. Especially in adolescents ongoing seizures can lead to psychosocial problems (Snead et al., 2004).

If possible, early surgical intervention is generally recommended to prevent further detrimental seizure effects, but the optimal age at which epilepsy surgery should be performed is still unclear (Kloss et al., 2002; Lendt et al., 2002; Devlin et al., 2003). We could not prove age of onset of epilepsy, age of surgery, or even illness duration as being determining factors for motor development or motor function. The present finding of no age effect might support the suggestion by Kloss and colleagues that early surgery should be considered, when possible, in infants and young children.

Conclusions

- After hemispherectomy, decrease of seizure frequency and severity widens the scope of motor and social functioning, which overrides the effects of remaining motor impairments (especially in the distal part of the arm).

- Over two years after epilepsy surgery, the majority of children improved significantly in motor performance, together with a decrease in seizure severity.

- When stratified by severity of motor disability (GMFCS levels), most children with spasticity followed a course on the 'motor growth curve' almost identical to reference children who had cerebral palsy but had not undergone surgery for intractable epilepsy.

- Activities of daily life improved and caregiver's assistance diminished significantly after epilepsy surgery in children with spasticity. This effect could not be measured in children without spasticity, because of the ceiling effect of the instrument.

- In children and adolescents, epilepsy surgery sets the stage for improvement in health-related quality of life (HrQoL) and in competence to participate in social and societal domains. But this relation could also be interpreted the other way around: more participation in social life gives a better HrQoL.

- In children with pharmaco-resistant epilepsy who have to do without surgical intervention and in whom no other adverse events occur, seizure severity does not progress, motor impairments do not increase, motor development does not deflect negatively and activities of daily living and restrictions do not worsen. But health-related quality of life and competence remained less than normal.

- The study appears to take the edge off the fear of significant worsening when surgery is not feasible.

Recommendations for future research

1 A larger cohort study is needed to measure the influences of variables such as age of onset of epilepsy, age at surgery, time between onset of epilepsy and surgery, aetiology (congenital or acquired), type of surgery and Engel classification on motor function and development. There is also a need to measure other factors like coping style of children and parents, and environmental and other personal factors. This study might possibly be performed within an European multi-centred research programme.

2 The present study emphasises that outcome has to be defined more extensively than simply in terms of seizure reduction, as discussed in a recent ILAE Commission report (Wieser *et al.,* 2001). It is recommended that future research on the outcome of epilepsy surgery should be structured according to the framework of the WHO-ICF classification, which enables one to evaluate not only impairments but also, and perhaps more importantly, activities and social participation. As contextual factors also play an important role in the functioning of the child, this also has to be a matter for future research.

3 A greater age range is essential for several instruments: other instruments on functional assessments (instead of the PEDI) and HrQoL have to be developed for future use in research on consequences of epilepsy.

4. A follow-up study of five years or longer is essential to measure the consequences of epilepsy and of epilepsy surgery in the ongoing development of children.

References

Bayley N. Manual for the Bayley scales of Infant Development, 2nd edition. San Antonio: Psychological Corporation, TX, 1993.

Bruil J. Development of quality of life questionnaire for children with a chronic illness. (Thesis) Universiteit Leiden. (FSW) 1999.

Camfield C, Breau L, Camfield P. Impact of pediatric epilepsy on the family: a new scale for clinical and research use. Epilepsia 2001;42:104-12.

Carpay JA, Vermeulen J, Stroink H, Brouwer OF, Peters AC, van Donselaar CA, Aldenkamp AP, Arts WF. Disability due to restrictions in childhood epilepsy. Dev Med Child Neurol 1997;39:521-6.

Carpay JA. Childhood Epilepsy: Alternative Methods for Assessing Treatment Strategies and Outcome. (Thesis) Universiteit van Rotterdam, 1997.

Carter Snead O 3rd. Surgical treatment of medically refractory epilepsy in childhood. Brain Dev 2001;23:199-207. [Review].

Chen LS, Wang N, Lin M. Seizure outcome of intractable partial epilepsy in children. Ped Neurol 2002;26:282-7.

Devlin AM, Cross JH, Harkness W, Chong WK, Harding B, Vargha-Khadem F, et al. Clinical outcomes of hemispherectomy for epilepsy in childhood and adolescence. Brain 2003;126:556-566.

Engel JJ, Van Ness PC, Rasmussen TB, Ojemann LM. Outcome with respect to epileptic seizures. In: Engel JJ, ed. Surgical Treatment of the Epilepsies. 2nd ed. New York: Raven Press; 1993. p. 609–21.

Engelbert RH, Uiterwaal CS, Gerver WJ, van der Net JJ, Pruijs HE, Helders PJ. Osteogenesis imperfecta in childhood: impairment and disability. A prospective study with 4-year follow-up. Arch Phys Med Rehabil 2004;85:772-8.

Haley SM, Coster WJ, Ludlow LH. Pediatric Evaluation of Disability Inventory (PEDI), Boston: M.A. New England Medical Center, [manual] 1992.

Harter S. Manual for the Self-Perception Profile for Adolescents. Denver CO: University of Denver, [manual] 1988.

Henderson SE, Sugden DA. Movement Assessment Battery for Children. London: The Psychological Corporation, [manual] 1992.

Holthausen H, Strobl K. Motor function before and after hemispherectomy. In: Stefan H, Andermann F, Chauval P, Shorvon SD, eds. Advances in Neurology, vol. 81 Plasticity in epilepsy: Dynamic aspects of brain function. Eds Lippincott, Williams and Wilkins, 1999, pp. 201-18.

Kloss S, Pieper T, Pannek H, Holthausen H, Tuxhorn I. Epilepsy surgery in children with focal cortical dysplasia (FCD): results of long-term seizure outcome. Neuropediatrics 2002;33:21-6.

Lendt M, Gleissner U, Helmstaedter C, Sassen R, Clusmann H, Elger CE. Neuropsychological outcome in children after frontal lobe epilepsy surgery. Epilepsy and behavior 2002;3:51-9.

Russell DJ, Rosenbaum PL, Avery LM, Lane M. GMFM Gross Motor Function Measure, (GMFM-66 & GMFM-88) User's Manual. Cambridge: Cambridge University Press. 2002.

Rosenbaum PL, Walter SD, Hanna SE, Palisano RJ, Russell DJ, Raina P, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. JAMA 2002; 18:1357-63.

Schoenmakers MA, Gulmans VA, Helders PJ, van den Berg HM. Motor performance and disability in Dutch children with haemophilia: a comparison with their healthy peers. Haemophilia 2001;7:293-8.

Schoenmakers MA, Uiterwaal CSPM, Gooskens RHJM, Gorter JW, Helders PJM. Determinants of functional independence and quality of life in children with myelomeningocele: a physical therapy perspective. Dev Med Child Neurol 2004;46:31.

Shore CP, Austin JK, Dunn DW. Maternal adaptation to a child's epilepsy. Epilepsy Behav 2004;5:557-68.

Smith ML, Elliott IM, Lach L. Cognitive, psychosocial, and family function one year after pediatric epilepsy surgery. Epilepsia 2004;45:650-60.

Snead K, Ackerson J, Bailey K, Schmitt MM, Madan-Swain A, Martin RC. Taking charge of epilepsy: the development of a structured psychoeducational group intervention for adolescents with epilepsy and their parents. Epilepsy Behav 2004;5:547-56.

Stanton BR. Does family functioning affect outcome in children with neurological disorders? Pediatr Rehabil 1999;3:193-9. [Review].

Veerman JW, Straathof MAE, Treffers PhDA et al. Competentiebelevingsschaal voor kinderen (CBSK) Lisse: Swets Testservice 1997.

Vining EP, Freeman JM, Pillas DJ, Uematsu S, Carson BS, Brandt J, Boatman D, Pulsifer MB, Zuckerberg A. Why would you remove half a brain? The outcome of 58 children after hemispherectomy - the Johns Hopkins experience: 1968 to 1996. Pediatrics 1997;100:163-71.

W.H.O. The International Classification of Functioning, Disability and Health (2002). ICF: introduction. Geneva: World Health Organization. Available on the WHO Internet site, 2002. http://www.who.int/classification/icf.

Wyllie E, Comair YG, Kotagal P, Bulacio J, Bingaman W, Ruggieri P. Seizure outcome after epilepsy surgery in children and adolescents. Annals of Neurology 1998;44:740-8.

Nederlandse Samenvatting

Effecten van epilepsiechirurgie op de kinderleeftijd - motorische functie, gezondheidsgerelateerde kwaliteit van leven en competentie beleving

Samenvatting

Het doel van dit proefschrift is om inzicht te krijgen, in de gevolgen van epilepsiechirurgie, voor de motoriek, het dagelijkse functioneren en de kwaliteit van leven van de geopereerde kinderen. Door middel van een prospectieve longitudinale studie onderzochten we kinderen en jongeren voor en na epilepsiechirurgie, die geopereerd werden tussen 1996 en 2001 en met een follow-up van twee jaar.

De Landelijke Werkgroep voor Epilepsiechirurgie, die bestaat uit vertegenwoordigers van de verschillende epilepsiecentra en academische ziekenhuizen, behandelt de aanmeldingen voor epilepsiechirurgie. Per jaar worden gemiddeld 40 kinderen bij de landelijke werkgroep aangemeld voor epilepsiechirurgie. Niet al deze kinderen werden geopereerd. Er zijn diverse redenen om af te zien van operatie, zoals multifocale lokalisatie van de epilepsie, of lokalisatie van de epileptische haard in een hersengebied dat betrokken is bij de ondersteuning van een essentiële functie (een zogeheten eloquente zone).

Van de aangeboden kinderen/jongeren werden 10-15 kinderen/jongeren per jaar geopereerd. Aan de hand van het door de Wereldgezondheidsraad ontwikkelde internationale classificatiemodel van het menselijke functioneren (ICF) evalueerden we functioneren en welzijn van deze kinderen. De ICF ordent de gevolgen van ziekten of aandoeningen op drie niveaus: 1) stoornissen in anatomische en fysiologische eigenschappen van het organisme, 2) beperkingen in activiteiten, 3) restricties in participatie in het maatschappelijke leven.

Voor en na epilepsiechirurgie onderzochten wij:

ad 1) op het niveau van de stoornissen: aanvalsfrequentie en aanvalsernst van de epilepsie en stoornissen in kracht, mobiliteit en tonus,

ad 2) op het niveau van de activiteiten en de beperkingen hierin: motorische ontwikkeling, activiteiten van het dagelijks leven en mate van hulpverlening door ouders bij deze activiteiten,

ad 3) op het niveau van de participatie de aan epilepsie gerelateerde beperkingen van de kinderen. Daarnaast onderzochten we de gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving van de kinderen.

Wij maakten gebruik van een standaard protocol met vaste meetmomenten: 1-3 maanden voor de operatie, 6, 12 en 24 maanden na de chirurgie.

We onderzochten ook de kinderen die niet geopereerd konden worden. Hierbij volgden we dezelfde procedure, namelijk een basismeting en 3 vervolgmetingen 6, 12 en 24 maanden daarna, gericht op de stoornissen, beperkingen, restricties, kwaliteit van leven en competentiebeleving zonder operatie. Ons onderzoek betrof dus twee groepen: 52 kinderen die epilepsiechirurgie hebben gekregen tussen 1996 en 2001 in het Wilhelmina Kinderziekenhuis/UMCU en 45 kinderen die aangemeld zijn bij de Landelijke Werkgroep voor Epilepsiechirurgie, maar niet geopereerd konden worden tussen 1996 en 2001.

De frequentie van epileptische aanvallen werd vastgelegd met de zogeheten Engel classificatie (Engel et al., 1993): I = geen aanvallen of aura's, II = minder dan drie aanvallen per jaar, na een lange periode van aanvalsvrijheid, III = meer dan 75% vermindering van de aanvalsfrequentie, IV = minder dan 75% vermindering van de aanvalsfrequentie. De ouders scoorden de aanvalsernst op een vragenlijst genaamd "Haagse schaal voor de ernst van epileptische aanvallen"; de lijst bestaat uit 13 vragen over de aanvallen in de drie maanden voorafgaand aan het meetmoment (Carpay et al., 1997). Kracht, mobiliteit en tonus werden getest als relevante parameters voor stoornissen.

Op het ICF- niveau van de activiteiten testten we de motorische ontwikkeling met de volgende motometrische instrumenten: Bayley Scales of Infant Development 2e editie (BSID-II), en Movement Assessment Battery for Children (M-ABC). Bij kinderen met spasticiteit gebruikten we de Gross Motor Function Measure (GMFM-88); het niveau van het grof-motorische functioneren scoorden we met het Gross Motor Function Classification System (GMFCS).

Door de resultaten van de GMFM-88 in samenhang te brengen met de score op de GMFCS, beoogden wij de motorische score van kinderen met spasticiteit te vergelijken met passende referentiewaarden voor kinderen met een cerebrale parese (Russell et al., 2002; Rosenbaum et al., 2002).
Voor de dagelijkse activiteiten en de mate van hulpverlening door de ouders gebruikten we de Pediatric Evaluation of Disability Inventory (PEDI), een gestructureerde vragenlijst voor ouders. De lijst bevat items in de domeinen: zelfverzorging (73 items), ambulantie (59 items) en sociaal functioneren (65 items). Beperkingen in de dagelijkse activiteiten leidden we af uit de mate van hulp die gegeven moest worden.
Participatieproblemen maten we aan de hand van aan de epilepsie gebonden beperkingen, met behulp van de "Haagse schaal voor beperkingen bij kinderen met epilepsie" (HARCES) (Carpay et al., 1997).
Tevens maten we de gezondheidsgerelateerde kwaliteit van leven met de How Are You (Hoe gaat het) vragenlijsten voor ouders en kinderen. Deze lijsten zijn in Nederland ontwikkeld voor kinderen met epilepsie; ze bevatten algemene ("generieke") vragen over de kwaliteit van het leven maar ook specifieke vragen, dat wil zeggen vragen die rechtstreeks betrokken zijn op het leven met epilepsie (Bruil 1999).

De competentiebeleving, dat wil zeggen de beleving van het eigen cognitieve, sociale en fysieke functioneren en de mate van algehele zelfwaardering, onderzochten we met de Nederlandse versies van de Harter-schalen voor de competentiebeleving van Kinderen (CBSK) en Adolescenten (CBSA).

In hoofdstuk 1 schreven we een introductie over medicamenteus onbehandelbare epilepsie, over ons onderzoeksprogramma en over de kadering daarvan in het door de Wereldgezondheidsorganisatie uitgewerkte model, genaamd International Classification of Functioning, Disability and Health (ICF) (WHO, 2002). Dit model werd uitgewerkt en met voorbeelden geïllustreerd en maakt het mogelijk

stoornissen in anatomische en fysiologische structuren, activiteiten en participatie weer te geven, eventueel gekoppeld aan interne en externe factoren.

In hoofdstuk 2 beschreven we bij twaalf kinderen de ernst van de epileptische aanvallen, de motorische stoornissen, motorische activiteiten en aspecten van sociale participatie voorafgaand aan hemisferectomie, en hoe dit postoperatief veranderde. De score op de HASS (ernst van epilepsie) liet al een vrijwel maximale verbetering zien in de eerste maanden na de operatie, en deze verbetering bleef tijdens de follow-up. De aanvalsfrequentie verbeterde sterk, 9 kinderen hadden een Engel I score en 3 kinderen een Engel III score na 2 jaar follow-up. De motorische stoornissen die al aanwezig waren voor de hemisferectomie, verergerden in de eerste 6 maanden postoperatief, maar verbeterden weer tot de preoperatieve waarden, behalve voor de handstoornissen. Op het gebied van de motorische activiteiten maten we 2 jaar na de operatie op de GMFM een toename van 20% en in de verschillende onderdelen van de PEDI zelfs meer dan 20 punten. Van bijna alle kinderen normaliseerden de scores voor de aan epilepsie gerelateerde beperkingen. De verbetering op activiteiten niveau kan niet verklaard worden vanuit verbetering in de motorische stoornissen, maar lijkt het resultaat van het bevrijd zijn van de aanvallen.

In hoofdstuk 3 beschreven we de frequentie en ernst van de epilepsie aanvallen, in combinatie met de beperkingen door de aanvallen, de gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving bij 21 kinderen (leeftijd 6,2 tot 16,8 jaar) voor en na chirurgie. Voor de operatie vonden de kinderen de kwaliteit en de frequentie van hun fysieke, sociale en cognitieve activiteiten minder dan een gezonde referentiegroep, en de kinderen voelden zich meer gehinderd in hun fysieke activiteiten.
Zes maanden na de operatie maten we een aanzienlijke verbetering in de aanvalsfrequentie; dit effect bleef in de verdere postoperatieve periode. Vijftien van de 21 kinderen (72%) bleken epilepsievrij na de operatie (Engel I score) en op de HASS (ernst

van de epilepsie) was de mediaan score verbeterd van 33 preoperatief naar 13 (de laagst mogelijke score).
De ouders en de kinderen evalueerden ten aanzien van verschillende activiteiten de kwaliteit van leven als verbeterd. De kinderen evalueerden hun fysieke, sociale en cognitieve activiteiten nu zelfs met normale waardes. Hun gevoel over hun activiteiten bleef echter minder positief dan bij gezonde kinderen, terwijl de ouders toch vonden dat hun kinderen vaker positieve emoties hadden na de operatie. De kinderen tendeerden zes maanden na operatie tot de perceptie van verbetering in hun sociale acceptatie. Hun zelfwaardering verbeterde in dit opzicht daarna nog verder, wat betekende dat de kinderen zich na de operatie meer competent voelden in sociale participatie. Net als hun waardering op de HAY van de kwaliteit van hun cognitieve taken, verbeterde noch verslechterde de perceptie van de leercompetentie op de CBSK/CBSA in de 2 jaar follow-up. Bij de adolescenten verbeterde kort na de operatie de evaluatie van verschillende aspecten van competentie, maar pas 2 jaar na de operatie verbeterde de perceptie van de eigen competentie in het aangaan van vriendschappelijke relaties. Op de schaal voor beperkingen ten gevolge van de epilepsie (HARCES) verbeterde de mediaan score significant van 28 preoperatief naar 13 postoperatief, wat betekende dat de kinderen na de operatie veel meer vrijheid en minder beperkingen hadden. Epilepsiechirurgie resulteerde dus niet alleen in een significante vermindering van de aanvallen en vermindering van de beperkingen, maar liet ook een duidelijke verbetering zien in de gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving van de kinderen.

In hoofdstuk 4 beschreven we het resultaat van diverse vormen van epilepsiechirurgie op de motoriek, de dagelijkse activiteiten en de mate van hulp die ouders verleenden. Dit werd onderzocht bij 37 kinderen die in leeftijd voor de operatie varieerden van 0,1 tot 15,4 jaar. Zeventien van deze kinderen hadden naast de medicamenteus onbehandelbare epilepsie tevens spasticiteit van cerebrale oorsprong. De operaties betroffen bij 14 kinderen een hemisfer-

ectomie, bij 14 kinderen een temporale resectie, bij 4 kinderen een frontale resectie, bij 12 kinderen een pariëtale resectie, bij 2 kinderen een centrale resectie en één kind kreeg een callosotomie. Op groepsniveau scoorden we een significante verbetering op de M-ABC en de GMFM-88. Bij 16 van de 17 kinderen lag de score op de GMFM-88 binnen 2 standaard deviaties van de gemiddelde score, zoals beschreven bij een referentiegroep van kinderen die vergelijkbare niveaus hadden op de GMFCS. De kinderen met spasticiteit verbeterden ook significant in de dagelijkse activiteiten en de mate van hulpverlening zoals gemeten met de PEDI. Deze verbetering op de PEDI kon niet worden gemeten bij de kinderen zonder spasticiteit wegens het plafondeffect binnen de test.
We concluderen dat er geen toename was van de motorische stoornissen, behalve aan de distale arm na een hemisferectomie, en dat de meerderheid van de kinderen met medicamenteus onbehandelbare epilepsie verbeterde op de motorisch scores in de twee jaar na de epilepsiechirurgie. De kinderen met spasticitiet ontwikkelden qua motoriek conform de referentiewaarden van kinderen met cerebrale parese.

In hoofdstuk 5 beschreven we 45 kinderen met medicamenteus onbehandelbare epilepsie die niet geopereerd konden worden (leeftijd 6 maanden tot 15 jaar) met de vraagstelling of de epilepsie, het motorische functioneren en de beperkingen ten gevolge van de epilepsie verergerden. Voor de ernst van de epilepsie werd in de eerste meting een gemiddelde relatief hoge score van 31 (range 13-52) gevonden; deze score liet geen verandering zien op de volgende meetmomenten.
Spierkracht, mobiliteit en tonus waren licht onder de normale waarden en veranderden niet nadien. De bij aanvang vastgestelde motorische ontwikkelingsachterstand van 33 kinderen zonder spasticiteit nam niet toe bij vervolgmetingen met de BSID II en de M-ABC test. De gemiddelde totaal-motorische score op de GMFM-88 van 12 kinderen met spasticiteit verbeterde van 55% bij de eerste meting naar 71% bij meting 24 maanden later. Maar de score bleef bij 4 van de 12 kinderen meer dan 2 SD onder de refe-

rentiewaarden die hoorden bij hun GMFCS score.
In de totale groep verbeterden de scores op de functionele vaardigheden en de mate van hulpverlening, maar de scores bleven onder de referentiewaarden voor de leeftijd.
De gemiddelde beperkingen score op de HARCES, bij de eerste meting 22 (range 10-40), veranderde niet in de vervolgmetingen.
Concluderend: bij de voor epilepsiechirurgie afgewezen kinderen nemen de ernst van de epilepsie en de mate van motorische stoornissen niet toe; de motorische ontwikkelingsscore en de dagelijkse activiteiten verminderen niet en de beperkingen ten gevolge van de epilepsie blijven gelijk.

In hoofdstuk 6 beschreven we van 20 kinderen uit de groep van 45 kinderen met medicamenteus onbehandelbare epilepsie die niet geopereerd konden worden (leeftijd 6 tot 15 jaar) de gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving. De ouders en de kinderen scoorden zowel bij eerste meting als bij de vervolgmetingen de frequentie van sociale activiteiten als significant lager dan normaal. De kinderen hadden significant meer fysieke klachten dan een gezonde referentiegroep bij de eerste meting. Deze klachten namen toe gedurende de follow-up. De ouders van de kinderen met epilepsie vonden dat de kinderen significant meer fysieke klachten hadden dan ouders van gezonde kinderen. De kinderen met epilepsie hadden minderwaardigheidsgevoelens en waren bezorgd over hun epilepsie, maar ze voelden zich met betrekking tot hun activiteiten en de kwaliteit van hun activiteiten niet anders dan gezonde kinderen. De bij zichzelf waargenomen competentie op de gebieden van school, sport en het eigen gedrag scoorden kinderen met epilepsie minder dan gezonde leeftijdsgenoten, de adolescenten scoorden in de follow-up de eigen competentie in vrijwel alle domeinen lager dan gezonde leeftijdsgenoten.
We concluderen dat bij kinderen met medicamenteus onbehandelbare epilepsie, die niet geopereerd konden worden, de kwaliteit van leven en de competentiebeleving minder dan normaal blijft. De evaluaties ten aanzien van de frequentie van fysieke klachten,

het aantal aanvallen en de negatieve gevoelens over de epilepsie-medicatie werden negatiever in de follow-up periode, terwijl de gevoelens over hun activiteiten en de kwaliteit van hun activiteiten niet veranderden.

In hoofdstuk 7 beschreven we de samenvatting, de algemene discussie, conclusies en aanbevelingen voor verder onderzoek.

Conclusies

- Na hemisferectomie verminderen ernst en frequentie van aanvallen. Deze vermindering van de effecten van de epilepsie geeft mogelijkheden voor verbetering van motorisch en sociaal functioneren en deze verbeteringen overheersen de effecten van de blijvende stoornissen (met name aan de arm distaal).

- Bij de meerderheid van de kinderen, met preoperatief medicamenteus onbehandelbare epilepsie, verbetert niet alleen de epilepsie postoperatief, maar ook de motorische score laat een significante verbetering zien in de twee jaar na de epilepsiechirurgie.

- Men beoordeelt de motorische ontwikkeling van kinderen met spasticiteit, van cerebrale oorsprong, pas goed wanneer men deze afzet tegen die van een referentiegroep van kinderen met cerebrale parese, met het vergelijkbare niveau van grof motorische functie op de GMFCS. In de door ons onderzoek bestreken periode, volgden de meeste kinderen die epilepsiechirurgie ondergingen, de referentie waarden voor motorische ontwikkeling, passend bij hun GMFCS niveau.

- De dagelijkse activiteiten en de mate van hulpverlening door de ouders verbeteren na de epilepsiechirurgie significant bij kinderen met spasticiteit. Het plafondeffect van de PEDI verhinderde de vaststelling van overeenkomstige effecten bij kinderen zonder spasticiteit.

- Epilepsiechirurgie opent de mogelijkheid voor verbetering van de gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving, zodat beter geparticipeerd kan worden in het sociale leven. Dit door de epilepsiechirurgie geopende verband kan ook andersom worden geïnterpreteerd: kinderen die meer participeren in het sociale leven hebben een betere kwaliteit van leven.

- Aanvalsernst en motorische stoornissen nemen bij de kinderen met medicamenteus onbehandelbare epilepsie die niet geopereerd konden worden en die geen andere beschadigende gebeurtenissen ondergingen, niet noodzakelijk toe. De motorische ontwikkeling van deze kinderen wordt niet *per se* geremd en de aan epilepsie gerelateerde beperkingen nemen niet noodzakelijk toe. De gezondheidsgerelateerde kwaliteit van leven en de competentiebeleving blijven echter minder dan normaal en laten geen verandering zien.

- Deze studie toont aan dat geopereerde kinderen, sommigen ondanks blijvende motorische stoornissen, in activiteiten en participatie vooruitgaan. Ze neemt bij ouders van kinderen met niet chirurgisch behandelbare epilepsie kinderen de angst voor ernstige achteruitgang in aanvallen en ontwikkeling weg.

Aanbevelingen voor verder onderzoek

1 Om de invloed van de variabelen waaronder leeftijd bij het begin van de epilepsie, leeftijd bij de operatie, tijd tussen het ontstaan van de epilepsie en de operatie, etiologie (aangeboren of verworven), type operatie en de Engel score; op de motoriek en ontwikkeling te kunnen onderzoeken, dient een grotere onderzoekgroep samengesteld te worden. Dit geldt ook voor vaststelling van effecten van andere factoren, zoals coping stijl van kinderen en ouders, omgevingsfactoren en persoonlijke factoren. Een onderzoekprogramma in Europees verband is hiervoor noodzakelijk.

2 Deze studie laat zien dat de gevolgen van epilepsiechirurgie meer inhouden dan aanvalsreductie, zoals ook eerder bediscussieerd werd in een commissie van de ILEA (Wieser *et al.,* 2001). Verder onderzoek naar de gevolgen van epilepsiechirurgie zou gestructureerd moeten worden volgens het kader van het ICF model van de Wereldgezondheidsraad, wat stimuleert om niet alleen stoornissen te onderzoeken, maar ook activiteiten en sociale participatie. Ook de omgevingsfactoren en persoonlijke factoren dienen in vervolgonderzoek betrokken te worden.

3 Voor verschillende instrumenten is een groter leeftijdsbereik essentieel, daarom zullen andere instrumenten ontwikkeld en gebruikt moeten worden, gericht op functionele vaardigheden (in plaats van de PEDI) en kwaliteit van leven bij kinderen en jongeren na epilepsiechirurgie.

4 Langere follow-up, bijvoorbeeld van 5 of 10 jaar, is van belang om de gevolgen van epilepsiechirurgie op langere termijn te kunnen meten.

Dankwoord

Het is er toch van gekomen een proefschrift te schrijven. Mede door de stimulans van velen, die ik graag hierbij wil bedanken.

Promotor, Prof. dr. O. van Nieuwenhuizen, beste Onno, toen we in september 1998, bij het ICNA congres (Slovenië), rond het meer van Bled liepen bespraken we de opzet van dit proefschrift, wat kon worden geschreven naar aanleiding van de follow-up van de kinderen met epilepsie. Onno, je bent een inspirerende en positieve leider van de afdeling kinderneurologie. Je humor en gave van het presenteren blijven voor mij altijd een voorbeeld. Ik ben blij dat je mijn promotor wilde zijn.

Promotor, Prof. dr. P.J.M. Helders, beste Paul, vanaf 1979 naar aanleiding van het congres: "Het kind in de fysiotherapie", werken we al samen, eerst aan een opleiding tot kinderfysiotherapeut, met een start in 1984. Later koos je vooral voor de wetenschappelijke kant van ons vakgebied. Hierin heb je een leidende rol en ben je voor velen en voor mij een inspirator. Ik ben dankbaar dat je me gesteund hebt in de afronding van dit onderzoek en het schrijven van de artikelen.

Copromotor, dr. A. Jennekens-Schinkel, beste Aag, vanaf de start van het onderzoek ben je mijn begeleider en heb je me gecoached in het doen van wetenschappelijk onderzoek en het beschrijven ervan. Je bent een zeer conscentieuze en vriendelijke dame, die altijd gaat voor het beste. Hierdoor is het gelukt hele mooie publicaties te maken, wat we onder andere bij jullie thuis hebben gevierd met een Brain Breakfast, door jou georganiseerd samen met je man prof. dr. Frans Jennekens.

Het dinsdagochtend overleg om 8.00 uur tezamen met dr. Aag Jennekens-Schinkel, prof. dr. Onno van Nieuwenhuizen, prof. dr. Paul Helders en incidenteel aangevuld met dr. Peter van Rijen (neurochirurg) en dr. Jan-Willem Gorter (kinderrevalidatiearts), heeft een

geweldige input gegeven bij het beschrijven van de gegevens en de resultaten van het onderzoek. Ik ben jullie dankbaar voor alle stimulans en de vele correcties.

Ik wil alle kinderen/jongeren en hun ouders hartelijk danken voor het meedoen aan dit follow-up onderzoek. Zonder hun inzet en bereidheid tot invullen van alle vragenlijsten en steeds weer laten zien hoe het met hen ging, was dit onderzoek niet mogelijk geweest. Ook de medewerking bij het op video vastleggen van de vorderingen van diverse kinderen, of het opsturen van foto's maakte het mogelijk ook aan anderen te laten zien hoe het gaat na de operatie. Alle deelnemers en verwijzers van de landelijke werkgroep voor epilepsiechirurgie wil ik bedanken voor het insturen van de kinderen.

Mijn belangstelling voor de kinderneurologie werd al gewekt door de colleges van dr. Jan Blom, van het herseninstituut in Amsterdam en dr. J.P. Schadé, tijdens mijn opleiding tot fysiotherapeut te Amsterdam. Daarna werd de kennis gevoed in het St. Radboudziekenhuis (UMC St. Radboud), aanvankelijk door de samenwerking met de neuropediaters (later kinderneurologen) dr. Nan Krijgsman, prof. dr. Jan Rotteveel en dr. Reinier Mullaart en later binnen het IKNC met prof. dr. Fons Gabreels en prof. dr. Willy Renier.
Bij mijn overgang naar Utrecht, mocht ik samenwerken met prof. dr. Cobus Willemse, prof. dr. Onno van Nieuwenhuizen, prof. dr. Boudewijn Peters, dr. Rob Gooskens, prof. dr. Marjo van de Knaap en dr. Cees Braun. Via de kinderneurologie ontstond mijn belangstelling voor de epilepsiechirurgie. Aangezien het UMCU/WKZ door de minister werd aangewezen als het universitair centrum voor deze vorm van chirurgie, kwamen alle patiënten uit Nederland naar Utrecht.

De neurochirurgen prof. dr. Cees van Veelen, dr. Peter van Rijen en drs. Peter Gosselaar ben ik dankbaar voor het vertrouwen dat zij in mij stelden bij dit follow-up onderzoek van de door hen geopereerde kinderen. Het zijn en blijven prachtige prestaties om deze

operaties te kunnen doen, die zo'n goed resultaat hebben. De coördinator van de epilepsiechirurgie en secretaresse van de afdeling neurochirurgie, mw. Els van Wijk wil ik hartelijk danken voor alle informatie die ze me steeds stuurde van de kinderen die aangemeld werden bij de landelijke werkgroep voor epilepsiechirurgie.

Als extra inspiratiebron voor het doen van wetenschappelijk onderzoek gelden de bezoeken aan de internationale kinderneurologiecongressen: ICNA en EPNS en de EACD congressen met betrekking tot het onderzoek naar "childhood disability" en de gevolgen van aandoeningen en ziekten.

De collega's binnen de afdeling kinderfysiotherapie, dr. Janjaap van der Net, dr. Raoul Engelbert, dr. Jan Custers, dr. Tim Takken, dr. Marja Schoenmakers, Rian Eijsermans, drs. Femke Kooijmans, Patrick van der Torre, drs. Marco van Brussel, drs. Lianne Verhagen en de revalidatiearts dr. Jan-Willem Gorter, ben ik dankbaar voor de jarenlange samenwerking en wetenschappelijke discussies. Tevens dank ik de secretaresses Sonja Raaff, Carla van Rooyen en Annemieke Apeldoorn voor hun enthousiaste ondersteuning bij alle werkzaamheden. En met name Carla voor het adressenbestand en alle uitnodigingen en brieven.

Ook de samenwerking met de medewerkers op de afdeling Dolfijn en de afdeling neuropsychologie: dr. Aag Jennekens-Schinkel, drs. Monique Schooneveld, Anke van der Avoort, dr. Kim Oostrom, dr. Anneke Schouten en de secretaresse Lilli Loois-Scheper zijn van groot nut geweest voor dit onderzoek. Inmiddels is onze samenwerking tot groot genoegen uitgebreid met drs. Martine van de Velden, drs. Liesbeth Vos en drs. Joost Meekes.

Het Johanna Kinderfonds en de Phelps Stichting ben ik dankbaar voor hun financiële bijdrage aan dit onderzoek, zodat er drie jaar gedeeltelijk vervanging mogelijk was voor mijn klinische taak, door collega's Maartje Wormgoor en Myrthe Bunt. Ook de sponsors van het proefschrift dank ik voor hun financiële bijdrage.

Mw. Carla Tims en Jacqueline Nuysink dank ik voor hun medewerking bij de opzet van het datamanagement bij de start van de studie. Carla, dat ik later ook nog steeds bij je aan mocht kloppen heeft mij erg geholpen bij de statistische verwerking van alle gegevens. Hiervoor wil ook de statistici dr. Joop Pestman en dr. Maria Schipper van de afdeling Biostatistiek hartelijk danken. Jullie inloopspreekuur voor advies met betrekking tot de statistiek is voor menig onderzoeker een geweldige service.

De collegialiteit van dr. Marja Schoenmakers en de samenwerking bij de programma's: Data Builder en Data Entry, hebben enorm geholpen en gaven ons beiden inzicht in het gebruik van deze invoerprogramma's voor onze statistische analyses. De samen gemaakte syntaxen hebben goed gewerkt, zelfs toen we overgingen naar Windows XP. Marja je bent mijn onvolprezen tandemmaatje; de opvang van de patiëntenzorg en de begeleiding van mijn vervangsters maakte het mogelijk dat ik door kon werken aan mijn onderzoek. Dat je ook nog het hele manuscript wilde nalopen op foutjes was fantastisch.

Jacqueline Nuysink, waardeer ik al jaren als collega en (mede) coördinator van congressen in de kinderfysiotherapie, dat je zelf een universitaire studie fysiotherapie bent gaan doen is een logisch gevolg van je capaciteiten.

Marja en Jacqueline, ik ben blij en trots dat jullie mijn paranimfen willen zijn, zie het als waardering voor jullie betekenis voor mij.

De ex-studenten en inmiddels afgestudeerde pedagogen, drs. Marieke Boonzaaijer, drs. Esther van der Steeg en drs. Mariel Peters en hun begeleider dr. Chiel Volman ben ik dankbaar voor hun medewerking aan delen van het onderzoek.

De taalkundige correctie van het Engels werden snel en efficiënt uitgevoerd door Mw. Brenda Vollers-King, hierdoor kreeg ik nooit opmerkingen over het Engels van de tijdschriften, waarvoor ik haar zeer dankbaar ben.

Onze familie, vrienden en buren wil ik danken voor de belangstelling en het medeleven tijdens het onderzoek en de schrijffase. Ik denk hierbij speciaal aan mr. Hein van Dijk (†) en Hannes van Dijk-Windemuller, met wie we menig glaasje hebben gedronken en met wie we graag discussieerden "over het leven".
Zonder vriendschappen houd je dit intensieve leven niet vol. De jaarlijkse Hemelvaart/ Pinkstervakantie met Truuske & Robert, Yke & George zijn een heerlijke ontspanning en inmiddels uitgebreid met samen wintersporten. Ook onze jarenlange vriendschappen met drs. Berteke & drs. Bruno van Erp-Taalman Kip-Overes, dr. Willem Putman & drs. Joke Putman-Versteegh, drs. Arrie van Veen & drs. Lex Raadgever en Ineke & drs. Feike de Vries zijn van veel betekenis voor mij en Afra.
Dr. Pepijn van Empelen, zoals verwacht heb je onze "promotiestrijd" al lang gewonnen, je promotie op zo'n jonge leeftijd is een geweldige prestatie, graag wil ik je samen met je vriendin drs. Nicole van Kesteren, je tweelingzus Xavière van Empelen en haar vriend Remco Ruisz betrekken bij dit promotiefeest.

Mijn ontspanning beleef ik de laatste jaren op de donderdagavond bij de inspanning die ik moet leveren tijdens de "spinning lessen" door Peter van Leeuwen van Better Bodies. Graag wil ik mijn "spinningmaten" en Peter heel hartelijk danken voor de plezierige en sportieve bezigheid. Ook onze nieuwe hond Tess, gaf de nodige afleiding en ontspanning tijdens het schrijfjaar.

Onze kinderen, Simone & Boudewijn, Margot en Rogier hebben altijd een centrale rol in ons leven gespeeld. Ook al leek het wel eens dat ik meer oog had voor de boeken, kan ik hen zeggen dat ik genoot van hun opgroeien en verworven zelfstandigheid. Het is geweldig om dit feest samen met jullie te mogen vieren.

Lieve Afra, ook na meer dan 30 jaar huwelijk ben je van grote betekenis voor mij, zonder je steun en stimulans had ik deze studie en het schrijven nooit afgerond. Dankbaar ben ik voor alle jaren, die we samen mochten beleven en nog zullen genieten. Deze promotie is ook een kroon op jouw werk en toewijding.

Curriculum Vitae

De auteur is op 5 november 1950 geboren te Amsterdam. Na de afronding van de middelbare school in 1967, volgde hij in 4 jaar de opleiding tot fysiotherapeut aan de Academie voor Fysiotherapie Amsterdam. Na de militaire dienstplicht als sportinstructeur te hebben vervuld van 1971 tot 1973, ging hij werken bij de Johanna Stichting (kinderrevalidatiecentrum) te Arnhem tot 1977. Alhier werd gestart met rolstoelbasketbaltraining als uitbreiding van de ISVA, in samenwerking met dr. A. Klapwijk. In deze periode werd de studie MO-A pedagogiek aan de universiteit van Nijmegen afgerond. Na de kinderrevalidatie werd hij teamhoofd kinderfysiotherapie in het St. Radboudziekenhuis te Nijmegen (hoofd: GM.Worm) van 1977 – 1989. Aansluitend aan de MO-A pedagogiek werd in deze periode de studie MO-B pedagogiek gevolgd en afgerond in 1980.

Vanaf 1979 was hij betrokken bij de ontwikkeling van de opleiding kinderfysiotherapie te Utrecht en vanaf de start in 1984 tot 1996 verbonden als coördinator en docent aan deze opleiding. De opleiding kinderfysiotherapie werd gevolgd van 1984-1987.

Bij de overgang van de afdeling kinderneurologie van het AZU naar het Wilhelmina Kinderziekenhuis (WKZ) in 1989, kwam hij in dienst van het WKZ (hoofd: Prof. dr. PJM. Helders). Tien jaar lang werden de werkzaamheden ingevuld op een dubbellocatie: C5 kinderneurologie en WKZ stad en vanaf 1999 in het nieuwe UMCU/WKZ op de Uithof.

In 1997 werd een studiebezoek gebracht aan het University College Hospital te Londen bij dr. Ann Stewart, in verband met de studie naar de betrouwbaarheid van het tonusonderzoek bij kinderen.

In het collegejaar 1995-1996 werd het doctoraal Pedagogiek afgerond aan de Universiteit Utrecht (opleider prof. dr. A.Vermeer).

Aansluitend aan dit doctoraal examen werd gestart met de opzet van een follow-up studie van kinderen die geopereerd werden wegens hun epilepsie binnen het UMC Utrecht/Wilhelmina Kinderziekenhuis. Bij de aanstelling van prof. dr. O. van Nieuwenhuizen als hoogleraar kinderneurologie met het aandachtsgebied van de epilepsiechirurgie bij kinderen, werd de studie officieel gestart, welke nu in 2005 wordt afgerond met dit proefschrift.

Inmiddels werd op verschillende internationale congressen verslag gedaan van dit onderzoek: 1999 EPNS te Nice (Fr.); 2001 EPNS Baden-Baden (D); 2002 ICNA Peking (China); 2003 EACD Oslo (N); 2004 EACD Edinburgh (Sc); 2005 EPNS Gotenburg (S).

De auteur is in 1972 getrouwd met Afra van Empelen-Stein en kregen samen drie kinderen: Simone, Margot en Rogier, die allen inmiddels volwassen zijn. De oudste dochter Simone trouwde in 2004 met Boudewijn de Vries.

List of publications

Rotteveel JJ, Mullaart RA, Weemaes CM, van Empelen R. Plasmapheresis in 2 children with Guillain-Barre syndrome. Tijdschr Kindergeneeskunde 1983;51:57-62.

Empelen R van. Sensorimotor training in children with motor retardation. Tijdschr Kindergeneeskunde 1983;51:138-43.

Smeitink J, Hamel BC, van Empelen R, de Vries JD, Monnens LA. Prune-belly syndrome: experiences with 9 patients. Ned Tijdschr Geneeskunde 1987;131:489-93.

Empelen R van. Meetmethoden gericht op de kwaliteit van de motoriek van kinderen. Ned Tijdschr voor Fysiotherapie 1992;102:184-88.

Empelen R van, Schoenmakers MAGC, Net J. van der, Helders PJM. Tonusonderzoek bij kinderen. Objectivering door gebruik van een meetinstrument. Fysiopraxis 1994;3:20-23.

Empelen R van, Kruitwagen CLJJ, Engelbert RHH, Custers JWH, Kuijer Y,Helders PJM,Vermeer A. Tonusonderzoek van Amiel-Tison voor kinderen van 0 t/m 5 jaar. Een betrouwbaarheidsonderzoek. Ned Tijdschr voor Fysiotherapie 1997;107:65-69.

Uppelschoten MA, Empelen R van. Loopstoornissen na Musculus Tibialis Posterior transpositie bij cerebrale bewegingsstoornis. Fysiopraxis 1997;6: 4-9.

Engelbert RHH, Graaf Y van der, Empelen R van et al. Osteogenesis Imperfecta in Childhood: Impairment and Disability. Pediatrics 1997;99:1-7.

Empelen R van, Schoenmakers MAGC, van der Zee DC. Biofeedbacktraining ter verbetering van anale incontinentie na traumatische ruptuur van de sfincter ani. Fysiopraxis 1998;4:11-14.

Engelbert RHH, Empelen van R, Scheurer N, Helders PJM, Nieuwenhuizen van O. Influence of infant-walkers on motor development: mimicking spastic diplegia? Eur J Paediatr Neurol 1999;3:273-5.

Empelen R van, Jennekens-Schinkel A, Buskens E, Helders PJM, Nieuwenhuizen O van. Functional consequences of hemispherectomy. Brain 2004;127:2071-9.

Empelen R van, Jennekens-Schinkel A, Rijen PC van, Helders PJM, Nieuwenhuizen O van. Health-related quality of life and self-perceived competence of children before up till two years after epilepsy-surgery. Epilepsia 2005;46:258-71.

Empelen R van, Jennekens-Schinkel A, Gorter JW, Volman MJM, Nieuwenhuizen O van, Helders PJM. Epilepsy surgery does not harm motor performance of children and adolescents. Brain 2005; 128:1536-45, 2005;Apr 13; [Epub ahead of print]

Books

Empelen R van. Sensomotorische training. Lochem: de Tijdstroom, 1980.

Empelen R van. Effectiviteit van sensomotorische training. Lochem: de Tijdstroom, 1981.

Empelen R van. Tonusonderzoek bij Kinderen, Houten: Bohn Stafleu van Loghum, 1996.

Empelen R van, Nijhuis van Sande R, Hartman A. (red). Kinderfysiotherapie, Maarssen: Reed Elsevier Gezondheidszorg, 2000.

Chapters in books

Empelen R van. Meedoen is winnen, enkele aspecten van de sensomotorische training, In: Meer begrip voor Buitenbeentjes, Lochem: de Tijdstroom, 1979. (p.70-77).

Empelen R van. Motorische diagnostiek en behandeling van ADHD kinderen. In: Buitelaar JK. Diagnostiek en behandeling van ADHD. Stichting Onderwijs en Voorlichting, 1993. (p.77-90).

Nieuwenhuizen O van, Empelen R van, Janssen FE. Onbehandelbare aanvallen en dan? In: Dertig jaar Kinderneurologie Liber amicorum prof. dr. F.J.M. Gabreëls Nijmegen, Vantilt, 2000 (p. 37-42).

Essink M, Empelen R van, Brugman-Boezeman ATM. Faeces – Obstipatie en Incontinentieproblemen In: Empelen R van, Nijhuis van der Sanden R, Hartman A. (red). Kinderfysiotherapie, Maarssen, Elsevier Gezondheidszorg, 2000 (p.563-571).

Empelen R van, Nijhuis van der Sanden R. Wijze van werken in de Kinderfysiotherapie. In: Empelen R van, Nijhuis van Sande R, Hartman A. (red). Kinderfysiotherapie, Maarssen, Elsevier Gezondheidszorg, 2000 (p.21-29).

Abstracts

Empelen R van, Helders PJM. Dislocation and subluxation of the hipjoint in children with cerebral palsy, using a standing device. ICNA 13-18 september 1998, Ljubljana.Slovenië.
In: Brain & Development vol.20(6), 1998, 410-411.

Oostenbroek H, Roermund van PM, Engelbert RHH, Empelen R van. Correction of limb discrepancy in 35 children with the Ilizarov method. European Pediatric Orthopedic Society, Madrid, 1-4-1998.

Empelen R van, Engelbert RHH, Helders PJM, Veelen van C, en Nieuwenhuizen van O. Functional limitation and motor function in children after epilepsy-surgery. 3 rd EPNS Congress Nice (Fr) 7-10 november 1999. In: European Journal of Paediatric Neurology 1999;

Empelen R van, Boonzaaijer M, Nuysink J, Veelen CWM van, Rijen PC van, Nieuwenhuizen O van.Improvement in motor function and Quality of Life after Epilepsy Surgery. EPNS congres 2001: Baden-Baden. In: European Journal of Paediatric Neurology 2001; O127, A63.

Empelen R van. ‘‘Kinderen na verwijdering van 1 hemisfeer: motorische functioneren in relatie tot kwaliteit van leven.’’ In: Keypoint, jaargang 25, nr.2, juli 2001.

Boonzaaijer M, Empelen R van, Jennekens-Schinkel A, Volman C, Veelen CWM van, Rijen PC van, Nieuwenhuizen O van. The Effects of Epilepsy-surgery on the Quality-of-Life of Children. Joint Congress of ICNA and AOCNA, 20-25 september 2002, Beijing, China. In: Brain and Development, WS-2-5, 2002;24:383-384

AB E, Marja Schoenmaker MAGC, Empelen R van, Aart J. Klijn JA, Jong TPVM de. Dynamics ultrasound of the Pelvic floor. Eur. Society for Pediatric Urology, Budapest, Hongarije12-04-2002.

Révész T, Gooskens R, Nievelstein RJ, Nikkels P, Kort G de, Lo T, Isselt J van, Empelen R van, Pruijs J, Dik P, Jansen M. Multifocal kaposiform haemangio-endothelioma, whose patient is she anyway? 14th International Workshop on vascular anomalies, Nijmegen, The Netherlands 26-29 juni. 2002

Nieuwenhuizen O van. Jennekens-Schinkel A, Empelen R van. Epilepsy surgery in mentally retarded patients with refractory epilepsy. 4th Annual International Clinical Symposium Kempenhaeghe: "Epilepsy and Sleep Update @Kempenhaeghe.nl" Heeze,12 april 2002.

Empelen R van, Oosterom I, Rijen PC van, Helders PJM, Nieuwenhuizen O van. Functionele hemisferectomie wegens onbehandelbare epilepsie. Kinderfysiotherapie, tijdschrift van de NVFK, december 2003, jaargang 15, nr 39, p 10-13.

Empelen R van, Peeters M, Volman MJM, Jennekens-Schinkel A, van Rijen PC van, Nieuwenhuizen O van. Health-Related Quality of Life and Perceived Competence in children and adolescents before and after epilepsy surgery. EACD Congress, Oslo 2-4 october 2003. In: Developmental Medicine & Child Neurology, Supplement no. 97 October 2003 Vol.45, pag. 29

Peeters M, Empelen R van, Volman MJM, Jennekens-Schinkel A, van Rijen PC van, Nieuwenhuizen O van. Gezondheidsgerelateerde kwaliteit van leven en competentiebeleving bij kinderen en adolescenten voor en na epilepsie chirurgie. NVFK congres, Den Haag 8-11-2003.

Steeg E van der, Empelen R. van, Volman MJM, Jennekens-Schinkel A, Rijen PC van, Nieuwenhuizen O. van. Motoriek en functionele mogelijkheden bij kinderen voor en na epilepsiechirurgie. NVFK congres, Den Haag 8-11-2003.

Empelen R van, Peeters M, Steeg E van der, Volman MJM, Jennekens-Schinkel A, van Rijen PC van, Nieuwenhuizen O van. Motoriek, functionele mogelijkheden, kwaliteit van leven en competentiebeleving bij kinderen voor en na epilepsie chirurgie. Amy Schenk symposium, Utrecht 14-11-2003.

Empelen R van, Peeters M, Volman MJM, Jennekens-Schinkel A, van Rijen PC van, Nieuwenhuizen O van. Health-Related Quality of Life and Perceived Competence in children and adolescents before and after epilepsy surgery. EACD Congress, Oslo, 2-4 October 2003. In: Developmental Medicine & Child Neurology, Supplement no. 97 October 2003 Vol.45, pag. 29

Empelen R van, Jennekens-Schinkel A, Steeg E van der, Rijen PC van, Helders PJM, Nieuwenhuizen O van. Motor function, ADL and functional independence in children before and after epilepsy surgery. EACD Congress, Edinburgh, 7-9 October 2004. In: Developmental Medicine & Child Neurology, Supplement no100 October 2004 Vol.46, pag.22-23.

Empelen R van, Jennekens-Schinkel A, Rijen PC van, Helders PJM, Nieuwenhuizen O van. Epilepsy surgery does not harm motor performance of children and adolescents. EPNS Congress, Gotenburg, 14-17 September 2005. In: European Journal of Paediatric Neurology 2005;

Nieuwenhuizen O van, Empelen R van, Jennekens-Schinkel A, Rijen PC van, Helders PJM. Functional consequences of hemispherectomy. EPNS Congress, Gotenburg, 14-17 September 2005. In: European Journal of Paediatric Neurology 2005;