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Improvement of language development after successful hemispherotomy

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ABSTRACT

Purpose: To investigate language development after functional hemispherotomy and to evaluate prognostic factors for (un-)favourable outcomes.

Methods: Children and adolescents who had vertical perithalamic hemispherotomy at the Medical University Wien (MUW) paediatric epilepsy centre were identified from a prospectively maintained database. Inclusion criteria were: complete clinical, neurophysiological and neuropsychological data, seizure freedom and a minimum follow-up of 12 months after surgery. The language quotients (LQ) prior to surgery and at last follow-up were calculated for each child. In addition, associations between pre- to post-surgical changes in LQ and the following variables were examined: age at epilepsy-onset, age at surgery and duration of epilepsy prior to surgery, aetiology, side of surgery, interictal EEG including sleep organization before and 12 months after surgery and antiepileptic-drug (AED) withdrawal state at last follow-up. Analyses were carried out in SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Nonparametric Wilcoxon and chi-square tests were applied, as required.

Results: Data from 28 children (14 female) were analyzed. The median age at epilepsy surgery was 64.5 months. The median follow-up after surgery was 3.0 years (±2.6 years, range 12 months to 12 years). Significant gains in LQs at last follow-up were found in 31% of the children ($p = 0.008$). Short disease duration prior to surgery, acquired pathology, lack of epileptiform EEG discharges in the contralateral hemisphere and/or normalization of EEG sleep patterns after surgery, and successful AED withdrawal were linked to favourable language outcomes.

Conclusion: Successful and early hemispherotomy results in improvement of language function in the intact hemisphere.

1. Introduction

Epilepsy has the highest incidence in the first year of life with a rate of 118 of 100,000 new patients per year [6]. These early-onset symptomatic epilepsies are often associated with multilobar or hemispheric pathology, neurological deficits and severe developmental impairment [11,12,27]. Most, if not all of these epilepsies are resistant to antiepileptic drug (AED) treatment [7,11,13]. Multilobar/hemispheric epilepsy surgery has been found to be a safe and highly effective alternative treatment option for appropriately selected children, leading to seizure freedom in up to 90% of patients after surgery [12,13,20,27,35]. In addition, cognitive, especially language abilities may improve in these patients, even after surgery in the dominant hemisphere [9,22].

However, most reports published so far on language outcomes following hemispheric surgery have concentrated on anatomic hemispherectomy [8–10,21,22,31,35]. These studies concluded that seizure freedom [8–10,16] may be a favourable predictor whereas developmental pathologies may be linked with unfavourable language outcomes. The effects of functional hemispherotomy on development have been less extensively studied and the results are inconsistent [1,24,26,27]. One possible reason for this may be that functional hemispherotomy is a comparatively new surgical

Abbreviations: LQ, language quotient; ESES, electrical status epilepticus in sleep; PMG, polymicrogyria; FCD, focal cortical dysplasia; SWS, Sturge–Weber syndrome; RE, Rasmussen encephalitis; MCD, mild cortical dysplasia.

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technique and postsurgical follow-up is therefore generally limited. In addition, most patients undergoing hemispheric surgery are infants and young children and many of them have a very low level of global and language development, making standardized neuropsychological assessment difficult [1,16]. Adequate test inventories and more extensive follow-up may be required in order to establish the full developmental impact of surgery in patients with low baseline and slow progress.

The primary aim of this study was to investigate the impact of disconnective hemispheric surgery, i.e. vertical perithalamic hemispherotomy, on long-term language development. We concentrated on language development because it is the most difficult developmental step and also the most vulnerable. Further, language impairment is associated with severe drawbacks across the lifespan.

The secondary aim was to detect additional prognostic risk factors (e.g. duration of epilepsy, age at surgery, pathological EEG pattern, etc.) linked with (un-)favourable language development.

Table 1
classification of Wieser et al. [34].

Class	
1a	Complete seizure free since surgery, no auras
1	Complete seizure free, no auras within the last evaluated year[a]
2	Only auras, no other seizures
3	1–3 seizures per year ± auras
4	4 seizure days[b] per year to 50% reduction of baseline seizure days[c]
5	<50% reduction of baseline seizure days to 100% increase of baseline seizure days ± auras
6	>100% increase of baseline seizure days ± auras

Seizure days during the first month after surgery are not counted.
[a] Seizure outcome class is determined for each year at annual intervals after surgery. Patients may change from one class to another from year to year.
[b] A seizure day is a 24 h period with one or more seizures. This may include an episode of status epilepticus.
[c] The number of baseline seizure days is calculated by determining the seizure-day frequency during the 12 months before surgery.

2. Methods

This study was approved by the Medical University of Vienna Clinical Research Ethics Board. Written informed consent was obtained from all patients and/or caregivers in accordance with the standards of the Declaration of Helsinki.

Prospectively collected data from a longitudinal observational electronic database containing the medical records of all paediatric patients who had presurgical evaluation and epilepsy surgery at the study clinic were screened. Data from all patients who fulfilled the following criteria were analyzed: (1) presurgical evaluation and vertical perithalamic hemispherotomy performed at the study centre; (2) age <18 years at surgery; (3) complete presurgical and follow-up data for at least 12 months after surgery, including complete language developmental data, and (4) seizure freedom after surgery (outcome class 1a [34]).

Presurgical evaluation followed a standardized protocol [13] including neurological, ophthalmologic, and neuropsychological assessment as well as intensive video EEG monitoring, FDG-PET and high-resolution MRI. All surgeries were performed by one neurosurgeon (T.C.) using the same technique, i.e. vertical perithalamic hemispherotomy introduced by Delalande in 1992 [12,13]. Histopathology was classified by one of the authors (AM) according to the ILAE criteria [4,25]. Post-operative follow-up visits were scheduled at 3 months after surgery and then once per year after surgery. Post-operative follow-up examinations included thorough neurologic, psychological, psychiatric and neuro-ophthalmologic assessment as well as 48 h-EEG-Video Monitoring and MRI. Seizure outcome was classified according to the ILAE criteria [34] (Table 1), because the classification proposed by Wieser is based on annual data evaluation and therefore overcomes several disadvantages of the widely used Engel outcome classification [14].

Neuropsychological tests were performed during the presurgical evaluation process (baseline) and at all scheduled follow-up visits after surgery. The tests administered depended on the age of the patient and date of assessment. Language skills were assessed using Denver Scales II [15] in severely handicapped children and the German versions of the Wechsler Intelligence Scales (HAWIWA, HAWIK and HAWIE) [33] in all other patients. We extracted the scores of the subtests vocabulary, description of concept, finding communalities and general knowledge and on this basis the language quotient (LQ) was calculated for each patient in order to make results comparable within and between patients. LQ was defined as that portion of the developmental age divided by chronological language age all multiplied by 100 [17,18]. The maximum quotient is 100, LQ ≥ 85 stands for normal development, a value between 84 and 71 refers to mild to moderate delay whereas a score of 70 or below indicates severe delay [17,18,23]. LQs prior to surgery were compared with those obtained at the last follow-up visit after surgery (minimum 12 months, longest observation 12 years). To explore clinical predictors of language outcome after surgery, possible associations between the pre-/post-operative changes in LQ within the following clinical parameters were evaluated as shown in Table 2.

The patient cohort was divided according to above-mentioned parameters into two subgroups (details of the subgroups are defined in Table 2). The LQ for each subgroup was then assessed according to the above-mentioned parameters, once prior to surgery, and once at the last follow-up visit. Using statistical analysis (described below), we then calculated the change in LQ following surgery within the two subgroups (pre- to post-operative) of each parameter and compared the changes in LQ between the subgroups.

2.1. Statistical analysis

For statistical analysis of continuous data the nonparametric Wilcoxon test was used. To identify associations between categorical data (group comparison) the chi-square test was used. Data were analyzed with SPSS WIN 20.0 software (SPSS Inc., Chicago, IL, USA). The minimum coincidence level to prove the significant differences of our results was $p < 0.05$.

3. Results

3.1. Description of the study group and patient characteristics

Since 1999 a total of 245 children had epilepsy surgery at our centre: 42 patients had vertical perithalamic hemispherotomies. We included 28 patients (14 girls), 14 did not meet the inclusion criteria: five patients were excluded because of incomplete follow-up data (two of them also were not seizure free). Four patients were excluded because of follow-up periods shorter than 12 months (one of them was also not seizure free). Three patients were excluded because they were older than 18 years of age at surgery. One additional patient was excluded because of ongoing seizures after surgery. One further patient was excluded because the child died on the fourth day following surgery due to brain oedema.

The median age (Table 3) at seizure onset was 13.5 months ± 30.9 months. The reason for the variability was the ranging from one to 112.0 months. In 46.4% of the patients (13/28) the seizure onset was before the age of 12 months. The median age at