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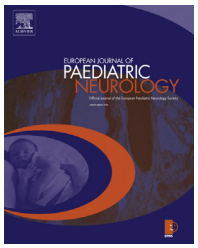

Original article

Seizure and cognitive outcomes of epilepsy surgery in infancy and early childhood

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ABSTRACT

Aims: To investigate seizure and developmental outcomes following epilepsy surgery in very young children and determine their predictive factors.
Methods: We retrospectively reviewed the clinical data, surgical variables, and outcomes of 30 children under 3 years of age that underwent resection for refractory focal epilepsy in our institution in 2001–2011.
Results: Seizure onset was in the first year of life in 27 (90%) cases and mean age at surgery was 20 months (range 5–33.6). Pathology consisted of cortical malformations in 24 (80%) cases, glioneuronal tumour and infarction with or without cortical dysplasia in three (10%) cases each. Morbidity was comparable with older paediatric cohorts. At 1–11.6 year follow-up (mean 4.1) 21 of 30 (70%) children achieved seizure freedom (Engel I), six (20%) demonstrated worthwhile improvement (Engel II/III) and three (10%) did not benefit from surgery (Engel IV). Intralobar lesionectomy more often resulted in seizure freedom than multilobar or hemispheric surgery. The abundance of non-regional interictal and ictal EEG findings did not preclude seizure freedom. Presurgical developmental impairment was established in 25 of 28 (89%) children; its severity correlated with longer epilepsy duration and determined post-operative developmental outcome. Developmental progress was established in 26 out of 28 (93%) children following surgery, showing stabilized trajectories rather than catch-up.
Conclusions: Resective surgery in very young children is safe and effective in terms of seizure control and developmental progress. Our findings underline the importance of early intervention in order to timely stop seizures and their deleterious effects on the developing brain.

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1. Introduction

Over the past decades epilepsy surgery has evolved into an established treatment option for selected paediatric candidates with symptomatic focal epilepsy.[1] However, epilepsy surgery at a very young age is still plagued by limitations of neuroimaging in clearly delineating the epileptogenic lesion.[2] Furthermore, despite the vast progress in neurosurgery, anaesthesia and intensive care, increased risks are assumed due to the limited blood volume and immature physiology of the developing brain and the extensive procedures often required to achieve seizure freedom.[3–5] Nevertheless, there is a trend in offering surgery as soon as intractability is ascertained, including the first years of life.[5–7]

This notion is driven by the high incidence of epilepsy observed in infancy[8] with one third of children developing drug resistance[9] and by the severity of epilepsy syndromes in this age group.[10] Bearing in mind the cognitive and behavioural impairment associated with early epilepsy onset,[11] longer epilepsy duration,[6] high seizure frequency,[12] continuous epileptic discharges[13] and polytherapy,[14] there is indeed a strong case for sparing children years of poor seizure control. Early epilepsy surgery is guided by reorganization and plasticity in early life[6,15] and is supported by studies showing a benefit of surgical treatment compared to pharmacotherapy in selected candidates[16] as well as the potential of successful early intervention to address both the seizure burden and the developmental delay.[6,16,17]

Currently, evidence for performing epilepsy surgery in the first years of life is encouraging but by no means comprehensive. Early surgical intervention was shown to be effective with seizure freedom achieved in 48–73% of children operated on before the age of three years in 1979–2007.[3–5,7,16–19] Furthermore, an earlier study investigating the effect of surgical treatment in children with medically refractory or successfully treated spasms, and no epileptic spasms reported that shorter epilepsy duration, higher presurgical functioning levels and seizure freedom are linked to a superior developmental outcome.[6] These observations were extended to a cohort of children under the age of 3 years, with younger age at surgery associated with improved postsurgical development.[17] However, other studies have demonstrated that the cessation of epileptic activity after early surgery is linked to sustained trajectories rather than catch-up development.[4,7,20] Overall, studies illustrating the developmental impact of epilepsy surgery in very young children are sparse and heterogeneous with regard to epilepsy substrates. They refer to surgical intervention performed over an extensive inclusion period and long before the advent of advanced imaging technology, which plays a major role in patient selection and surgical target delineation nowadays.

The purpose of our study was to investigate the outcomes of surgery for refractory epilepsy and determine predictive factors regarding seizure control and cognitive development in children under the age of 3 years that underwent resections in the Epilepsy Centre Freiburg in the last decade.

2. Patients and methods

2.1. Patient selection

We retrospectively reviewed the medical records, findings of presurgical evaluation, surgical procedures and outcomes of 30 consecutive children that underwent resective surgery for intractable structural epilepsy under the age of three years at the Epilepsy Centre, University Hospital Freiburg in 2001–2011. Patients were assessed according to a standard protocol[21,22] and were followed-up at least one year after surgery.

Presurgical evaluation was performed at the cooperating Epilepsy Centres of Heidelberg ($n = 18$), Kiel ($n = 5$), Kork ($n = 4$), and Freiburg ($n = 3$), including comprehensive medical history, full neurological examination, long-term scalp VIDEO-EEG recordings, high-resolution MRI and psychological assessment. Preoperative data was reviewed at a multidisciplinary meeting before proceeding to surgery. In some cases, interictal PET and/or SPECT were additionally performed. None of the children underwent intracranial EEG recordings.

2.2. Preoperative EEG findings

Interictal EEG was classified as encephalopathic when bilateral severe epileptic discharges with a disturbed background pattern, including hypsarrhythmia or burst suppression, were present. Interictal epileptiform discharges and ictal EEG patterns were classified either as regional, involving a single lobe or contiguous lobes, or as non-regional, including multiple lobes or even both hemispheres. In case of multiple ictal EEG patterns including diffuse and non-lateralized discharges, EEG findings were classified as non-regional.

2.3. Preoperative MRI findings

The presurgical 1.5 or 3T MRI scans of all 30 children, including T1, T2 and FLAIR sequences were retrospectively analysed, blinded to surgical outcome. In all children, MRI revealed lesions that were classified according to their extent as unilobar, multilobar, hemispheric and bilateral. Epilepsy substrates were further ascertained by histopathology.

2.4. Pre- and postoperative neurological findings

Motor functions were documented as to the presence and severity of hemiparesis and visual field deficits were clinically assessed.

2.5. Surgical procedures and seizure outcomes

All resections were performed by two neurosurgeons (J. Z., V.vV.) that applied the transsylvian keyhole or the perisylvian technique for hemispherotomy.[21,24] Histological dysplastic features were classified as suggested by Palmini.[23]

Following surgery, patients were routinely evaluated at three, six, 12 and 24 months and then yearly or at appropriate intervals in case of seizure recurrence. Seizure outcomes were portrayed according to the Engel scales[25] and only final