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Developmental outcome after surgery in focal cortical dysplasia patients with early-onset epilepsy

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Summary The purpose of this study was to investigate the developmental outcome after surgery for early-onset epilepsy in patients with focal cortical dysplasia (FCD). Among 108 patients with histopathologically confirmed FCD operated between 1985 and 2008, we selected 17 patients with epilepsy onset up to 3 years of age.

Development was evaluated by the developmental quotient or intelligence quotient (DQ-IQ) and mental age was measured by the Mother-Child Counseling baby test or the Tanaka-Binet scale of intelligence. Postsurgical development outcome was evaluated by the changes in DQ-IQ and mental age as well as rate of increase in mental age (RIMA) after surgery. RIMA was calculated as the increase in mental age per chronological year (months/year; normal average rate: 12 months/year).

Age at epilepsy onset of 17 patients ranged from 15 days to 36 months (mean ± SD, 11.0 ± 10.0 months). Age at surgery ranged from 18 to 145 months (75.1 ± 32.4 months). Evaluation just before surgery showed that 13 of 17 (76.4%) patients had DQ-IQ below 70. Ten patients (58.8%) were seizure-free throughout the postsurgical follow-up period. After surgery, DQ-IQ was maintained within 10 points of the presurgical level in 13 patients (76.4%), and increased by more than 10 points in one patient (5.9%). After surgery, RIMA in patients with Engel's class I (7.5 ± 3.8) was higher than patients with Engel's class II—IV (2.6 ± 3.4) (unpaired *t*-test with Welch's correction, $t = 2.99$, df = 15, $p = 0.0092$). RIMA was particularly low in two patients with spasm. In four patients with presurgical DQ-IQ < 70, seizure-free after surgery and without spasm, DQ-IQ did not increase but RIMA improved from 3.6 ± 2.8 before surgery to 6.9 ± 2.5 months/year after

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surgery. RIMA became better from 2 years after surgery. In four patients with presurgical DQ-IQ ≥ 70 and no spasm, two showed the same or higher RIMA than normal average after surgery.
In 58.8% of FCD patients with early onset epilepsy, epilepsy surgery effectively controlled seizures, and in 82.3% of patients, epilepsy surgery preserved or improved development. Residual seizures after surgery and lower DQ-IQ before surgery might be potential risk factors for poor development after surgery. In patients of Engel's class I with lower presurgical DQ-IQ, catch-up increase in mental age was observed after two years following surgery.

Introduction

Focal cortical dysplasia (FCD) was first described in 1971 as 'neuropathology with epilepsy' (Taylor et al., 1971). It is characterized by disorganization of the cerebral cortex, including cortical architectural abnormalities, immature cells, giant neurons, dysmorphic neurons, and balloon cells (Palmini et al., 2004). The embryologic and epileptogenic mechanisms of FCD are not well known (Sisodiya et al., 2009). FCD has been reported to be the etiology in 20—25% of patients with intractable focal epilepsy (Kuzniecky et al., 1993; Tassi et al., 2002; Fauser et al., 2006), and epileptic seizures are poorly controlled by antiepileptic drugs. Epilepsy surgery resulted in complete seizure control in 40—65% of the patients (Tassi et al., 2002; Krsek et al., 2009; Widdess-Walsh et al., 2005).

Regarding the outcome of developmental quotient or intelligence quotient (DQ-IQ) after epilepsy surgery, several studies reported increases in DQ-IQ in patients with early-onset epilepsy who underwent epilepsies surgery in infancy (Wyllie, 1996; Lortie et al., 2002; Loddenkemper et al., 2007). However some studies reported that the majority of patients do not show any significant improvement of DQ-IQ after epilepsy surgery if seizure occurred more than several years (Jonas et al., 2005; Freitag and Tuxhorn, 2005; Argenzio et al., 2011). In this study, we evaluated the developmental outcome after epilepsy surgery in FCD patients with early-onset epilepsy, not only by the evolution of conventional DQ-IQ but also by the evolution of mental age as a trial.

Patients and methods

Patients

We retrospectively evaluated the medical records of 813 patients who underwent epilepsy surgery at the National Epilepsy Center between 1985 and 2008, and found 108 patients with a diagnosis of FCD confirmed by histopathology (Fig. 1). To investigate the post-surgical developmental outcome in pediatric FCD patients with childhood onset epilepsy, we adopted the following exclusion criteria: (1) presence of comorbidity affecting development (one patient with hydrocephalus after surgery, one with Chiari malformation, and one with a history of head trauma); (2) lack of developmental evaluation at two years after surgery (15 patients); (3) more than one surgery (three patients); and (4) age at epilepsy onset ≧15 years (ten patients). Consequently, 77 pediatric patients were identified. To evaluate the developmental outcome in patients with very young onset, we further selected patients who had earlier epilepsy onset using the following inclusion criteria (1) onset of epilepsy ≦3 years of age; (2) age of surgery ≦13 years; (3) evaluation of development by specific psychological tests for children before and after surgery. Eventually 17 patients were studied (Fig. 1).

Classification of subgroups

To analyze the effects of multiple factors affecting developmental outcome after surgery, we classified patients into four subgroups by potential determinants of developmental outcome; namely, seizure outcome, presurgical developmental levels, and presence of spasms (Fig. 2). First, the 17 patients were classified by postsurgical seizure outcome. Seven patients with Engel's class II—IV were classified as group 4 (Patients 11-17). Among ten patients with Engel's class I, four patients with presurgical DQ-IQ ≧ 70 were classified as group 3 (Patients 7-10), and the remaining six patients with presurgical DQ-IQ < 70 were further divided into a group with spasm (group 2; Patients 5 and 6) and a group without spasm (group 1; Patients 1-4).

Pre-surgical evaluation

All patients had poor seizure control despite using more than three antiepileptic drugs. All underwent pre-surgical evaluations including surface electroencephalography (EEG)-video monitoring, brain magnetic resonance imaging, computed tomography, and single-photon emission computed tomography. Seizures were classified as 'daily' if they occurred everyday for at least three months prior to surgery.

Seizure outcome and histopathology after surgery

Seizure outcome was classified using Engel's classification (Engel et al., 1993). Histopathology was classified according to Palmini's classification (Palmini et al., 2004).

Psychological evaluation

Cognitive function was assessed by neuropsychologists. The psychological tests were selected according to the developmental level and chronological age. The