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Effect of corpus callosotomy on attention deficit and behavioral problems in pediatric patients with intractable epilepsy

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ABSTRACT

To evaluate the effect of corpus callosotomy (CC) on attention deficit and behavioral problems in pediatric patients with intractable epilepsy, we retrospectively investigated sequential patients who had undergone CC to control seizures. Between August 2005 and April 2010, a total of 15 patients aged between 3.1 and 17.9 years underwent CC at our institute. All the patients experienced either drop attacks or head nodding, which were considered to be therapeutic targets of CC. A standardized instrument, the Child Behavior Checklist (CBCL), was used to assess behavioral and emotional problems before and after surgery. On postoperative EEGs, 8 (53%) showed improvement and 7 (47%) showed no change in epileptiform discharges. The Attention Problems scale and total score on the CBCL significantly improved in patients whose postoperative EEGs showed improvement. In addition to amelioration of target seizures, CC can improve attention impairments in association with improvement in the postoperative EEG.

1. Introduction

Chronic uncontrolled epilepsy in children represents a significant risk for deficits in emotional, behavioral, social, cognitive, and family functioning [1,2]. Although the primary goal of epilepsy surgery is to eliminate seizures, the child's mental, behavioral, and social functioning improves once the seizures are successfully eliminated [3–5]. This phenomenon has not been clarified in past studies because the most commonly reported outcome is seizure control.

In general, corpus callosotomy (CC) is a palliative surgical procedure for patients who are not candidates for focal resective surgery despite their intractable seizures. CC best ameliorates drop attacks (tonic and atonic seizures) as well as tonic–clonic, absence, and frontal lobe complex partial seizures (CPS) [6]. The rationale underlying this procedure is based on the hypothesis that the corpus callosum is the most important pathway for interhemispheric spread of epileptiform activity [7]. With respect to the behavioral and neuropsychological effects of CC, extensive investigations have been undertaken; however, to our knowledge, no studies have yet assessed these effects with the standardized instrument for assessment of children's behavioral problems known as the Child Behavior Checklist (CBCL), developed by Achenbach [8,9].

The aim of the present study was to assess, with the CBCL, behavioral and emotional problems in children who were candidates for CC and to evaluate whether postoperative improvement in EEGs or target seizures contributed to changes in specific behavioral and emotional problems.

2. Methods

Written informed consent was obtained from the parents of all patients, according to the recommendations of the Declaration of Helsinki for investigations involving human subjects.

2.1. Patients

Between August 2005 and April 2010, a total of 15 consecutive patients aged between 3.1 and 17.9 years underwent CC to control epileptic seizures at National Center Hospital, National Center of Neurology and Psychiatry. All patients were ambulatory and had had intractable epilepsy for more than a year. Drop attacks or head nodding resulting from tonic, atonic, or CPS was observed in all patients and constituted the most disabling seizure characteristics. These characteristics were considered targets of CC. Characteristics of all patients are provided in Table 1.

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Table 1
Descriptive characteristics of patients.

Boy:girl ratio	10:5
Age at epilepsy onset	
Range	0.3–8.5 years
Median	1.8 years
Diagnosis	
Frontal lobe epilepsy	9 (60.0%)[a]
Hemispheric congenital abnormality[b]	3 (20.0%)
West or Lennox–Gastaut syndrome	3 (20.0%)
Age at surgery	
Range	3.1–17.9 years
Median	6.5 years
Duration of epilepsy prior to surgery	
Range	1.9–15.2 years
Median	4.5 years
<2 years	1 (6.7%)
2–5 years	6 (40.0%)
5–8 years	7 (46.7%)
>8 years	1 (6.7%)
Extent of corpus callosotomy	
Anterior two-thirds	7 (46.7%)
Total division	5 (33.3%)
Anterior three-fourths	2 (13.3%)
Anterior four-fifths	1 (6.7%)

[a] Number (%).
[b] Focal cortical dysplasia, polymicrogyria, and Sturge–Weber syndrome are included in hemispheric congenital abnormality.

2.2. Procedure

We retrospectively investigated all the patients. When the patients were admitted to our hospital for CC and postoperative follow-up, they underwent pre- and postoperative assessments including a developmental quotient (DQ) test, the CBCL, and interictal electroencephalography. DQ was measured using either the Kinder Infant Developmental Scale or the Enjoji Scale of Infant Analytical Development. DQ, CBCL, and interictal EEGs from the patient's last admission were used as the postoperative assessment for comparison with the preoperative one.

2.3. Grouping of patients

To determine how postoperative changes relate to CBCL and DQ, we divided the patients into those with a good outcome and those with a bad outcome on the bases of seizure outcome and EEG changes. First, patients were classified into two groups according to seizure outcome: those with favorable outcomes and those with unfavorable outcomes. In this study, a favorable outcome was defined as total cessation or ≥90% reduction in target seizures, whereas an unfavorable outcome was defined as <90% reduction or recurrence. Second, patients were classified into two other groups on the basis of postoperative improvement in EEG abnormalities. Preoperative EEGs showed bisynchronous and diffusely propagated epileptiform discharges in all patients. In this study, postoperative EEGs were considered improved when epileptiform discharges with bilateral generalization ceased or lateralized after surgery. The patients with improved EEGs were named the improved group (group I) and the patients whose EEGs did not improve were called the unimproved group (group U). We statistically analyzed the difference between the pre- and postoperative CBCLs in patients in groups I and U.

2.4. Child Behavior Checklist

The CBCL is available in two forms: a 100-item questionnaire for parents of children aged 2 or 3 years (CBCL/2–3) and a 118-item questionnaire for parents of children aged between 4 and 18 years (CBCL/4–18); the psychometric properties of the CBCL have been studied extensively [8,9]. Several CBCL items may reflect seizure semiology rather than habitual behavior. Parents were instructed not to report those symptoms that occurred only with seizures; they completed the CBCL during each admission.

The CBCL, which yields profiles of children's problems as observed by parents and other caregivers, was used to assess the behavioral and emotional problems of the patients. We used a Japanese version of the CBCL provided by previous studies [10–12]. The CBCL yields a total score, eight syndrome scale scores, and two broadband syndrome scales designated as Internalizing (withdrawn, somatic complaints, and anxious/depressed) and Externalizing (aggressive and delinquent behavior scales). Social Problems, Thought Problems, and Attention Problems are additional syndrome scales. Two of the eight syndrome scales differ between the CBCL/2–3 and the CBCL/4–18. As the CBCL/2–3 was used in two patients before surgery, their results were excluded from the analysis of the difference between pre- and postoperative syndrome scales.

The scores on the items that constitute each of the eight syndrome scales and two broadband scales and the total score were summarized (summed raw scores) and transformed into standardized scores (*t* scores) according to the norms provided in the test manual [8–12]. *t* scores were used as a dependent variable in statistical analysis. Furthermore, it was necessary to choose cutoff CBCL *t* scores to define patients as being moderately or severely disturbed. In accordance with Achenbach's suggestion [8,9], we regarded patients with syndrome scale scores of 67–70 and Internalizing and Externalizing scale scores and total scores of 60–63 as moderately disturbed, and those with syndrome scale scores ≥70 and Internalizing and Externalizing scale scores and total scores ≥63 as severely disturbed.

2.5. Statistical analyses

The *t* test was used to compare the means of postoperative DQs with those of preoperative DQs. Wilcoxon's signed-rank test was used to compare the medians of the *t* scores on the eight syndrome, Internalizing, and Externalizing scales as well as the total score before and after surgery. Statistical analysis was performed with SPSS software (SPSS Version 18.0, IBM). Differences were considered statistically significant when the *P* value was <0.05. DQs were expressed as means ± SD.

3. Results

3.1. Characteristics of patients

Ten boys and five girls were recruited for the study. The median age at epilepsy onset was 1.8 years (range: 0.3–8.5). Nine (60%) patients were diagnosed with frontal lobe epilepsy, 3 (20%) with hemispheric congenital abnormality, and 3 (20%) with West or Lennox–Gastaut syndrome. The descriptive characteristics of the patients are summarized in Table 1. The median age at surgery was 6.5 years (range: 3.1–17.9), and the median duration of epilepsy prior to surgery was 4.5 years (range: 1.9–15.2). The corpus callosum was partially divided in 10 (67%) and completely divided in 5 (33%) cases. The mean postoperative follow-up period was 0.8 ± 0.7 year (range: 0.1–2).

3.2. Seizure outcome

Target seizure outcomes are provided in Tables 2 and 3. Eleven patients (73%) showed total cessation or ≥90% reduction after surgery. With respect to other types of seizures without drop attacks or head nodding, 8 (53%) patients had tonic seizures and 4 (27%) had CPS. Postoperative cessation or ≥90% reduction was observed in 3 (38%) of the patients with tonic seizures and 3 (75%) of the patients with CPS, respectively (Table 2). Although the number of the antiepileptic drugs (AEDs) administered postoperatively was apparently small in