

ただし、患児の中には、切除手術対象となるてんかん原性の病因が認められないこともある。その際、緩和手術として、脳梁離断術や迷走神経刺激術を選択肢として有している。こうしたあらゆる選択肢を考慮して破局てんかんへの治療計画を立て、少しでも破局状況を打破すべきである。これら緩和手術など個々の術式についての発作や発達に与える影響については、さらなる継続調査によって明らかにされる見込みがある。

#### E. 結論

乳幼児破局てんかんにおいて、集学的治療により発作の改善が見込まれ、症例によっては、特に外科的加療によって発作や発達の改善が期待できる。乳幼児破局てんかんはさまざまな臨床像や病因から構成されるが、さらに調査が継続されれば、より詳細に臨床的特徴が把握され、よりよい治療選択肢が浮き彫りになる可能性があるだろう。

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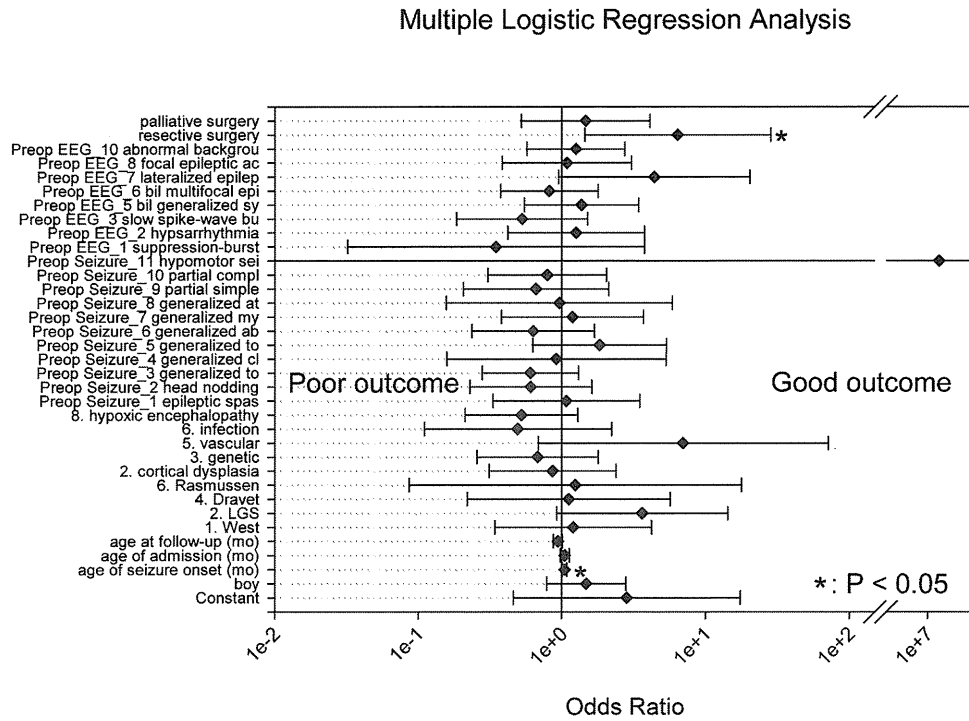
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#### H. 知的財産権の出願・登録状況

1. 特許取得  
なし
2. 実用新案登録  
なし
3. その他  
なし

図 1 : 治療 1 年後追跡調査における発作予後改善因子に関するロジスティック回帰分析



### Ⅲ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
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#### IV. 研究成果の刊行物・別冊

## 難治性てんかん外科手術：半球離断術

Hemispherotomy for intractable epilepsies



大槻 泰介

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◎大脳半球離断術は、一側大脳半球を同側の大脳基底核および対側半球より完全に離断する手術法であるが、従来の解剖学的に大脳半球を摘出する方法(大脳半球切除術)に比べ手術侵襲と合併症が少なく、乳児期における片側巨脳症(hemimegalencephaly)に対しても適応可能であり、皮質形成異常、癲癇脳回、Sturge-Weber症候群などに対する切除外科手術の適応が広がっている。

**Key word** 半球離断術、片側巨脳症、皮質形成異常、Sturge-Weber症候群

### 半球切除術から半球離断術へ

半球切除術は1920年代に悪性脳腫瘍の治療法として報告されたが、1950年代に至り乳児期からの片麻痺(infantile hemiplegia)を伴う重症てんかんの手術に適用され、発作および行動面での良好な治療結果を得た<sup>1)</sup>。しかし、半球切除後の死腔に慢性的に血腫が貯留する合併症(superficial hemosiderosis)を随伴することがわかり、死腔を減らす目的で前頭極と後頭極を離断したまま残す機能的半球切除術(functional hemispherectomy)や、灰白質のみ摘出し側脳室を覆う白質を残すhemidecorticationなどの手術法が開発された<sup>2,3)</sup>。

その後、半球切除術の適応は孔脳症、Rasmussen脳炎、Sturge-Weber症候群などの萎縮性病変に加え、広範な皮質形成異常や片側巨脳症などの肥大性病変に拡大し、また頻発するてんかん発作が発達脳に及ぼす悪影響と脳の可塑性に関する理解が進むにつれ、より発症早期の手術が推奨されるようになった<sup>2,6)</sup>。それとともに術中の出血など手術に伴う侵襲を減らすことが課題となり、1990年代以降、小開頭から一側半球を同側の基底核、視床および対側半球から離断する半球離断術(hemispherotomy)が開発された<sup>3,5,9-11)</sup>。

半球離断術は、①頭頂部から側脳室に達し垂直

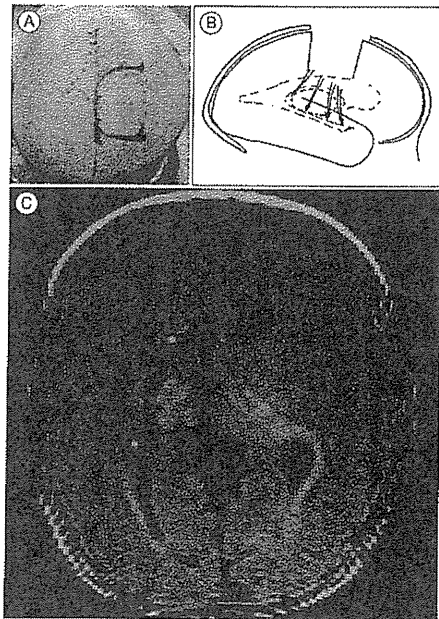


図1 片側巨脳症に対する半球離断術(Delalande法)

A:皮切, B:cortical windowよりの視床外側離断の模式図, C:術後MRI水平断, 大脳皮質が視床および基底核より離断されている。

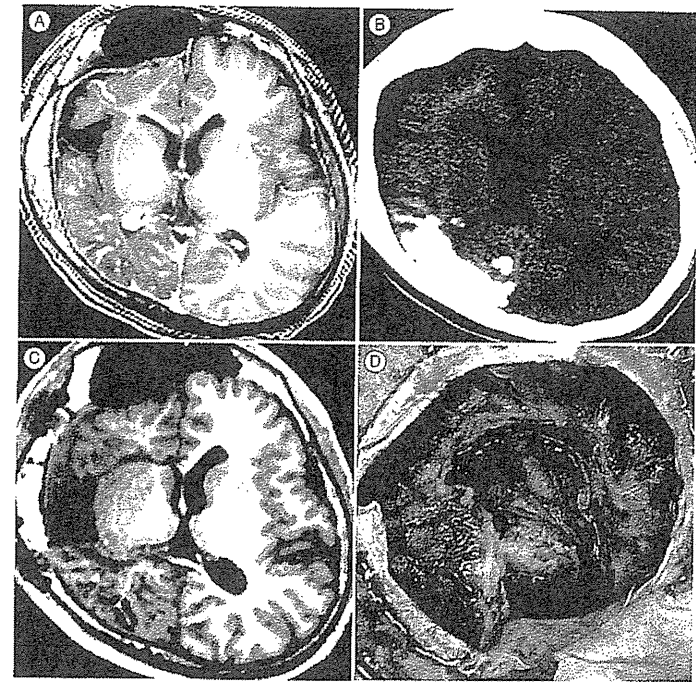


図2 Sturge-Weber症候群に対する半球離断術(Peri-insular hemispherotomy)

A:術前MRI, B:術前CT, C:術後MRI, D:術中写真

島周囲を切断し大脳半球を基底核・視床より切り離した後、経側脳室的に脳梁を離断する。

方向に視床・基底核周囲を切断するDelalandeの方法<sup>9)</sup>(図1)と、②側方から島に達し島周囲を切断するPeri-insular hemispherotomy<sup>10,11)</sup>(図2)が代表的である。半球離断術の効果は、手術侵襲が少ないほかは半球切除術との差はないとされ<sup>3)</sup>、半球離断術の導入により、乳児期においても片側巨脳症などの高リスクの手術を少ない出血量で安全に行うことが可能となった。

### 半球離断術の適応

半球離断術の適応は一側大脳半球全域に及ぶてんかん原性病変を有する難治てんかん症例で、発作により日常生活、知的機能、あるいは発達に障害をきたし、病変に起因する片麻痺や半盲などの神経症状がすでに明らかになっているか、または進行性の増悪が不可避と予測される場合である。

① 片側巨脳症……片側巨脳症は生後早期より重症のてんかん性脳症を呈し、乳幼児期に半球離断術が必要となることが多い<sup>3,6)</sup>。その場合、出血のリスクが少なく脳梁周囲の形成異常への対応が容易なDelalande法が有用である。

② 皮質形成異常……一側性に広範な皮質形成異常は、病変が限局し片麻痺が明瞭でない場合には段階的な皮質切除や多葉離断も可能であるが<sup>4)</sup>、最終的には半球離断が選択される可能性が高い。

③ 癲癇脳回……周産期の血管障害や外傷による孔脳症と片麻痺を伴う難治性てんかんは半球離断術のよい適応である。術前より手指の運動と足関節の背屈の障害を認める場合、術後一過性に片麻痺が増悪しても、1カ月程度で術前の状態に回復する。癲癇の消失に伴い、運動障害が改善する場合もある<sup>6,8)</sup>。

#### ④ Rasmussen脳炎, Sturge-Weber症候群

Rasmussen 脳炎や Sturge-Weber 症候群は、持続性部分てんかん(epilepsia partialis continua)などでてんかん発作が頻発し発達障害・知的障害が進行する場合、てんかん性脳機能障害を最小限に抑えるために早期の手術が勧められる。Sturge-Weber 症候群では血管腫の切除のみでも効果があるとされるが<sup>1)</sup>、Rasmussen 脳炎の場合には半球切除が不可避である<sup>2)</sup>。いまだ片麻痺などの神経障害が完成しない段階での手術時期の判断は難しいが、小児期には脳の可塑性が高く術後の運動・言語障害の回復が期待できる<sup>3)</sup>。

#### 著者の手術

##### 1. Delalande's approach(垂直法)

仰臥位にて頭部は正中位でやや前屈、頭頂部の一部冠状縫合にかかる横 3.5 cm×縦 6 cm ほどの開頭から横 2 cm×縦 4 cm ほどの皮質を切除し、側脳室体部を開放する(cortical window の作成)。ついで側脳室内側壁を一部吸引し脳梁上面に達し、傍脳梁動脈を前後に迫ることで経側脳室的に脳梁を全離断する。その際、前方は梁下野皮質および直回を吸引除去し、前交通動脈と Heubner 動脈を露出、後方はガレン大静脈を確認し視床枕後方で脳弓を切断する。つぎに、側脳室下角の位置を確認し、視床外側部の白質(正中から外側約 2 cm, thalamostriate sulcus が目安)、側脳室体部より側脳室下角に達する切断面をおく。海馬の上面を確認しつつ下角前端に達し、扁桃体を吸引除去した後、前交通動脈-前角-下角を結ぶ面で前頭葉を離断する。離断の途中、くも膜越しに嗅神経および中大脳動脈本幹が確認される。

##### 2. Peri-insular approach(水平法)

仰臥位で頭部を水平に傾け、クエスチョンマーク型皮切で前頭・側頭・頭頂開頭をおき、弁蓋部皮質を吸引除去して島回全体を露出、ついで前側頭葉切除を行い扁桃体と海馬を摘出し、海馬采脳弓移行部で脳弓を切断する。さらに、島周囲を側脳室に添って切断し、側脳室三角部および側脳室体部を開放した後、側脳室内側壁を一部吸引し脳梁上面に達し脳梁を全周にわたり離断する。その際前方は前大脳動脈を避け、前交通動脈を確認す

る。最後に、前頭葉を島の前縁で離断し、蝶形骨縁に沿って梁下野に達する。島皮質は吸引除去する。Peri-insular approach は癲癇脳回などの萎縮性病変の場合は容易であるが、片側巨脳症など肥大型病変の場合は出血が多く適さない。

#### 手術予後・合併症

周産期の血管障害や外傷による孔脳症と片麻痺を伴う難治性てんかんは、術後 70~80% の症例で発作消失が期待できる<sup>3,6,8)</sup>。半側巨脳症など形成異常の手術予後は他の病因より劣るとされるが<sup>6)</sup>、その原因として、病変が基底核・視床などにも及ぶことが指摘されている<sup>3)</sup>。

術後の片麻痺の増悪に関しては、上肢では指折りなど手指の巧緻運動障害、下肢では足のタッピングなど足関節における背屈障害が目安となり、術前よりこれらの運動障害を認める場合には、成人においても半球離断術の影響は術前の状態にまで回復可能である。言語機能に関しては 2~3 歳までは対側脳に移動するといわれているが、年長児でもある程度の改善は期待できる<sup>1)</sup>。

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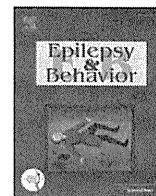
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## Effect of corpus callosotomy on attention deficit and behavioral problems in pediatric patients with intractable epilepsy

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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.

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### 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%) <sup>a</sup>
Hemispheric congenital abnormality <sup>b</sup>	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%)

<sup>a</sup> Number (%).

<sup>b</sup> 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  $\geq 90\%$  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  $\geq 70$  and Internalizing and Externalizing scale scores and total scores  $\geq 63$  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  $\pm$  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  $0.8 \pm 0.7$  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  $\geq 90\%$  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  $\geq 90\%$  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

**Table 2**  
Association of development (DQ) and intelligence (IQ) quotients with seizure outcome and postoperative findings.

		n (%)	DQ (n) IQ (n)		
			Pre	Post	
Target seizure outcome (n = 15)	Total cessation/ ≥90% reduction	11 (73.3%)	35.4 ± 19.4 (8) 37.8 ± 21.1 (4)	33.3 ± 17.4 (8) 39.0 ± 22.2 (4)	NS NS
	≤90% reduction/ stable/ recurrence	4 (26.7%)	34.0 ± 2.6 (3) NA	29.7 ± 4.2 (3) NA	
Other seizure outcome Tonic seizures (n = 8)	Total cessation/ ≥90% reduction	3	NA	NA	
	≤90% reduction/ stable	5	NA	NA	
Complex partial seizures (n = 4)	Total cessation/ ≥90% reduction	3	NA	NA	
	≤90% reduction/ stable	1	NA	NA	
Postoperative EEG (n = 15)	Normalization or lateralization of discharge (group I)	8 (53.3%)	34.2 ± 17.0 (6) 45.3 ± 17.9 (3)	35.5 ± 21.2 (6) 47.3 ± 18.0 (3)	NS
	No change in epileptic discharge (group U)	7 (46.7%)	36.1 ± 17.4 (5) 47.0 ± 38.7 (3)	30.6 ± 16.6 (5) 49.7 ± 37.1 (3)	NS

6 of 15 patients (Table 3), substantial reduction was obtained in only 3 (patients 2, 3, and 5).

3.3. Postoperative EEG changes

In 8 (53%) patients, epileptiform discharges either ceased or lateralized (group I), whereas in 7 (47%) patients, there were no changes on the postoperative interictal EEG (group U) (Tables 2 and 3). In 2 patients in group I, bisynchronous and diffusely propagated epileptiform discharges ceased after surgery. Target seizure outcome was favorable in all patients (100%) in group I and in 3 patients (43%) in group U.

3.4. Developmental quotient

Pre- and postoperative DQs of the patients in the favorable outcome group/group I/group U were 35.4 ± 19.4/34.2 ± 17.0/36.1 ± 17.4 and 33.3 ± 17.4/35.5 ± 21.2/30.6 ± 16.6, respectively. In the present study, comparison between pre- and postoperative DQs of each group showed no statistical differences (Table 2). A favorable outcome with respect to target seizures did not improve DQ during the observation period or postoperative EEGs.

3.5. Outcome of behavioral and emotional problems as assessed with the Child Behavior Checklist

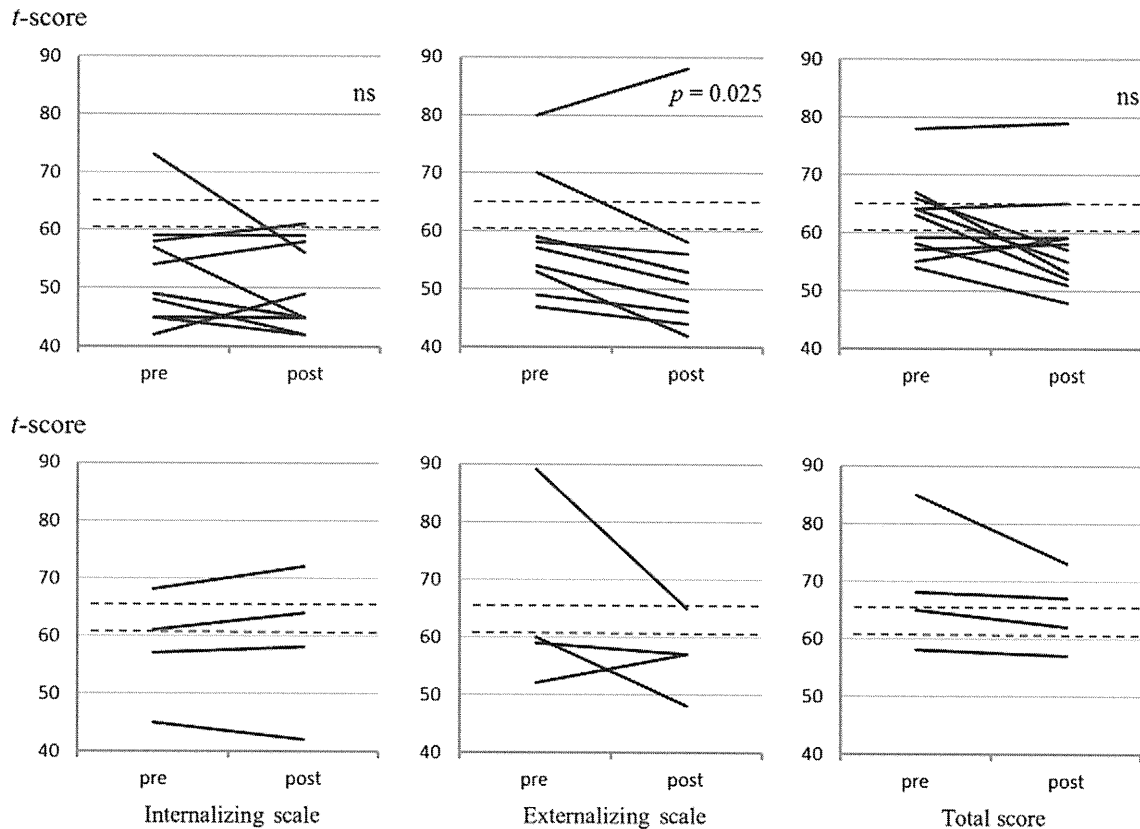
The postoperative Externalizing, Delinquent Behavior, and Thought Problems *t* scores for patients with a favorable outcome differed significantly from those before surgery (Figs. 1 and 2B). Comparison of the pre- and postoperative Attention Problems scores showed no statistical differences (Fig. 2B). Pre- and postoperative Internalizing, Externalizing, and total *t* scores in groups I and U are illustrated in Fig. 3, and *t* scores for the eight syndrome scales, in Fig. 4. Total ( $P=0.028$ ), Attention Problems ( $P=0.028$ ), and Delinquent Behavior ( $P=0.042$ ) scores for the patients in group I showed a statistically significant decrease after CC, and Externalizing ( $P=0.041$ ) and Delinquent Behavior ( $P=0.043$ ) scores for patients in group U significantly decreased. The postoperative decrease in the Delinquent Behavior score for patients in group I and in the Externalizing and Delinquent Behavior scores for patients in group U were found to be clinically unimportant and have no significant impact, as these patients were considered undisturbed before surgery. We identified the postoperative decrease in the total and Attention Problems scores for patients in group I as the most clinically important findings.

**Table 3**  
Pre- and postoperative characteristics of all the patients.

Patient	Seizure type	DQ (IQ)		Age at surgery (years)	Extent of callosotomy	Frequency of targeted seizures		Number of medications	
		Pre	Post			Pre	Post	Pre	Post
1	DA	32	22	5.3	Anterior 3/4	Daily	None	4	4
2	DA, tonic	(65)	(65)	6.5	Anterior 2/3	Daily	90% reduction	3	2
3	DA, tonic	62	51	5.8	Total	Daily	None	4	3
4	HN, tonic	35	25	6.1	Anterior 2/3	Weekly	None, recurrence	3	2
5	DA, CPS	29	37	7.0	Total	Daily	None	4	2
6	HN, CPS	36 (36)	31 (47)	7.1	Anterior 2/3	Daily	50–90% reduction	4	4
7	HN, CPS	63	55	6.3	Anterior 2/3	Daily	None	3	3
8	HN, tonic	15	9	7.4	Anterior 4/5	Daily	90% reduction	5	5
9	HN, tonic	22	32	3.1	Total	Daily	None	3	3
10	HN, tonic	31	33	4.4	Total	Daily	50–90% reduction	3	3
11	DA	(90)	(88)	12.6	Anterior 3/4	Daily	<50% reduction	3	3
12	DA, CPS	15	13	5.8	Total	Daily	None	4	3
13	DA, tonic	(41)	(48)	13.7	Anterior 2/3	Daily	None	3	3
14	DA	45 (30)	47 (29)	9.1	Anterior 2/3	Daily	None	2	2
15	HN, tonic	(15)	(14)	17.9	Anterior 2/3	Daily	None	5	4

Note. Patients 1–3, 5, 9, and 12–14 are in the group of patients whose EEGs improved after surgery. DA, drop attack; HN, head nodding; CPS, complex partial seizures.





**Fig. 1.** Line graphs illustrating the comparison between pre- and postoperative Internalizing, Externalizing, and total *t* scores for the patients with a favorable outcome ( $n=11$ , upper row) and those with an unfavorable outcome ( $n=4$ , lower row). The two dashed lines in each graph represent cutoff points classifying patients as undisturbed (lower), moderately disturbed (middle), and severely disturbed (upper). There was a statistically significant ( $P=0.025$ ) decrease in Externalizing scores for the patients with a favorable outcome. ns, not significant.

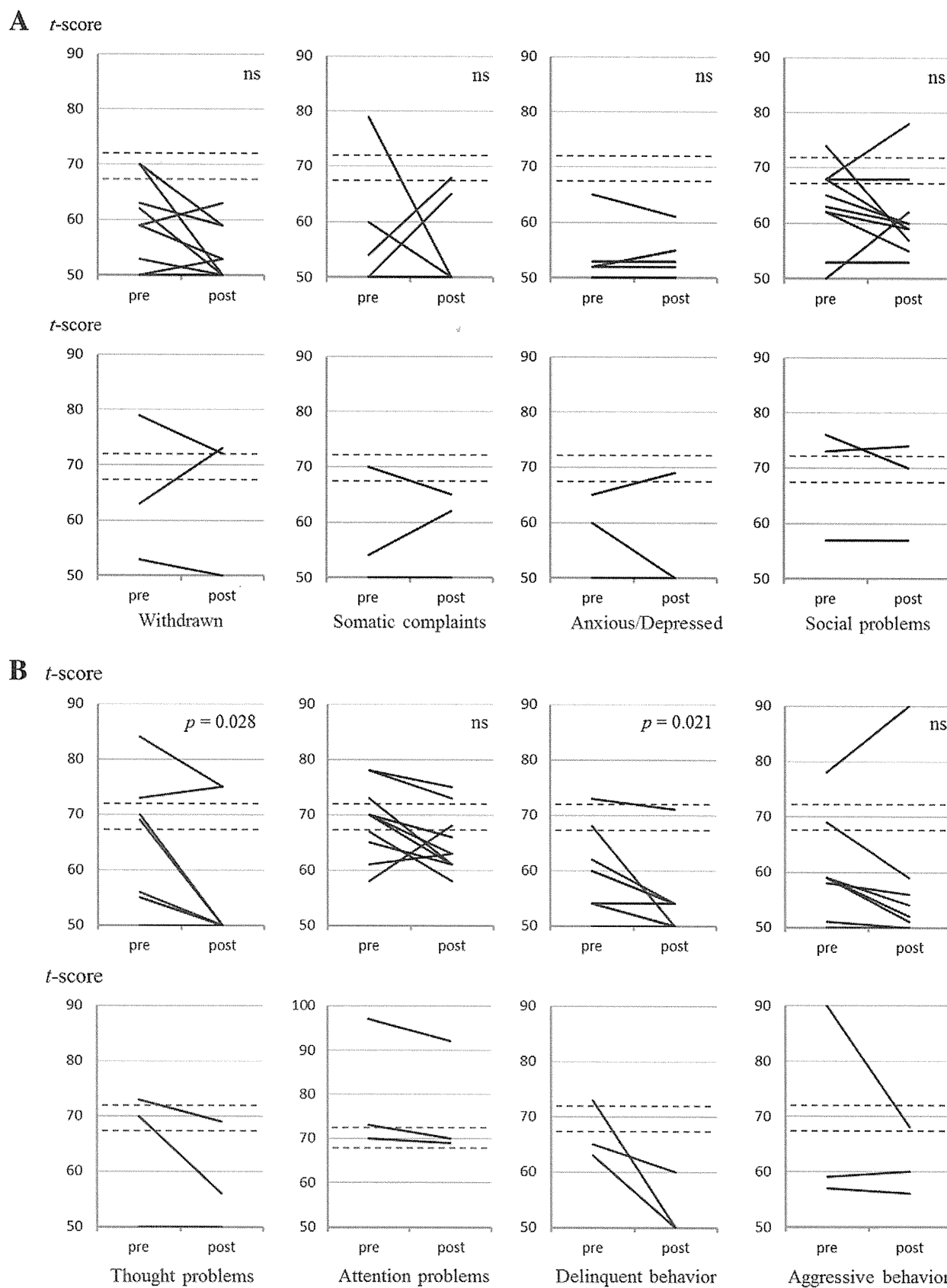
#### 4. Discussion

In this study, we assessed, with the CBCL, behavioral and emotional problems in children who were candidates for CC and evaluated whether favorable target seizure outcome or improvement in postoperative interictal EEG were associated with changes in specific behavioral and emotional problems. A comparison between the pre- and postoperative Attention Problems scale *t* scores for patients with a favorable outcome showed no statistical differences (Fig. 2B). On the other hand, improvement in the postoperative EEG was significantly associated with decreases in Attention Problems and total *t* scores (Figs. 3 and 4B). Therefore, we consider that this finding will play an important role in improving attention deficit and behavioral problems.

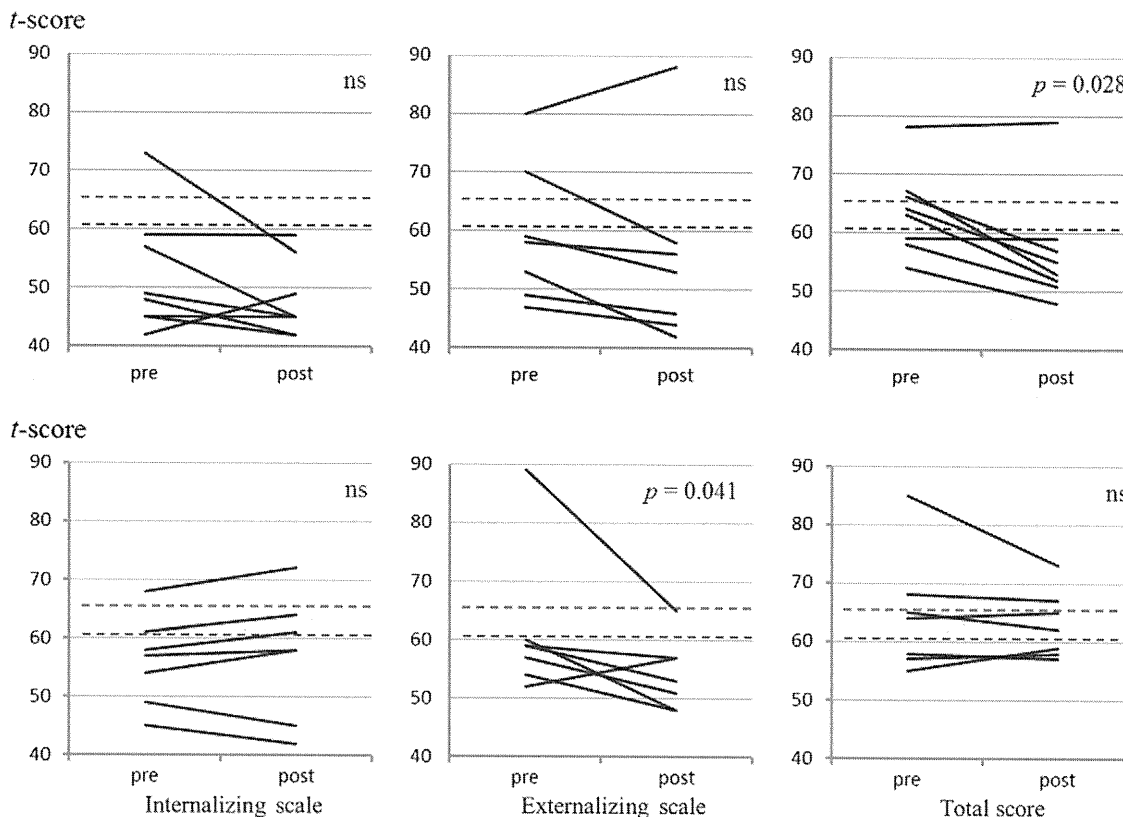
Behavioral or cognitive dysfunction is frequently observed in patients with intractable epilepsy. Several studies have described attention problems as frequent behavioral problems in these patients. Dunn et al. [13] reported that 37% of children with epilepsy had scores above the clinical cutoff for the CBCL Attention Problems scale. Davies et al. [14] found that 12% of children with uncomplicated epilepsy had attention-deficit/hyperactivity disorders according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. The presence of marked cognitive or behavioral symptoms is an important factor in the institutionalization of individuals with epilepsy. Such symptoms need to be assessed carefully with validated neuropsychological tests. Achenbach's CBCL is the instrument most frequently used to assess behavioral adjustment in children with epilepsy [10]. Although several items included in the CBCL may reflect seizure semiology rather than habitual behavior, Gleissner et al. concluded that the CBCL is a valid assessment tool in children with epilepsy [15]. We used a Japanese version of the CBCL in this study.

Assessment of the conventional seizure and neuropsychological outcomes is usually problematic because CC is a palliative surgical procedure and candidates for CC have not only severe drug-resistant seizures, but also significant functional and psychological impairments. Although extensive investigations of the behavioral and neuropsychological efficacy of CC have been undertaken, two studies have specifically investigated the quality of life of the candidates. Yang et al. [16] surveyed the families of 25 children who underwent CC and found that 19 (76%) were satisfied with the surgical result and 18 (72%) were satisfied with their family's quality of life. With respect to specific behavioral changes, 11 (44%) improved in hyperactivity, attention span, and social skills [16]. Gillam et al. [17] conducted a similar study with parents of 17 children who underwent CC. Improved alertness and responsiveness were noted, and 15 families (88%) reported satisfaction and recommended the surgery [17]. In 11 patients (73%) in the present study, CC resulted in favorable outcomes with respect to drop attacks and head nodding, similar to the results of previous studies (Table 3) [18,19]. In addition, patients with improved postoperative EEGs showed significant improvement in their attention deficits.

Furthermore, total cessation or lateralization of preoperative EEG abnormalities such as bilateral generalization was achieved after surgery in 8 (53%) of the patients. The corpus callosum has been thought to be a major pathway for the spread of epileptiform discharges from one hemisphere to the other for bilateral generalization [7]. Several qualitative studies have partly supported the view that CC significantly reduces bilaterally synchronous generalized epileptiform discharges [20,21]. In addition, CC reduces preoperative epileptiform discharges in both hemispheres, suggesting a facilitatory role played by callosal neurons, which enables the asymmetric epileptogenic



**Fig. 2.** Line graphs illustrating the comparison between pre- and postoperative *t* scores on CBCL/4–18 syndrome scales for the patients with a favorable outcome ( $n = 10$ , upper row) and those with an unfavorable outcome ( $n = 3$ , lower row). The two dashed lines in each graph represent cutoff points classifying the patients as undisturbed (lower), moderately disturbed (middle), and severely disturbed (upper). There were statistically significant ( $P = 0.028$  and  $0.021$ , respectively) decreases in the Thought Problems and Delinquent Behavior scale scores for patients with a favorable outcome. As two patients had been assessed with the CBCL/2–3 before surgery, their results were excluded from analysis of the difference between pre- and postoperative syndrome scale scores. ns, not significant.



**Fig. 3.** Line graphs illustrating the comparison between pre- and postoperative Internalizing, Externalizing, and total *t* scores for the patients in group I ( $n = 8$ , upper row) and group U ( $n = 7$ , lower row) by Wilcoxon's signed-rank test. The two dashed lines in each graph represent cutoff points classifying the patients as undisturbed (lower), moderately disturbed (middle), and severely disturbed (upper). There were statistically significant increases in total score in group I ( $P = 0.028$ ) and Externalizing score in group U ( $P = 0.041$ ), although the postoperative decrease in the Externalizing score in group U is not considered clinically important because these patients were nearly undisturbed before surgery. ns, not significant.

susceptible state of both hemispheres to develop bisynchronous and bisymmetric discharges [22]. Although even total CC need not result in complete abolition of bilaterally synchronous interictal epileptiform discharges, seizures have been completely suppressed with normalization of the EEG in some cases [23,24]. In two of our patients, bisynchronous and diffusely propagated epileptiform discharges actually ceased after surgery.

Several authors have reported impairment of attention, motor dexterity, and perceptual processing in association with the occurrence of spike-wave complexes [25,26]. In the present study, we found Attention Problems scores in group I, that is, patients in whom epileptiform discharges ceased or lateralized, to decrease significantly after surgery. Therefore, we clarified that attention deficits significantly ameliorated after CC, which might be associated with cessation or lateralization of the bisynchronous and diffuse epileptiform discharges.

An advantage of the present study was the use of a standardized assessment procedure. There were, however, several limitations. The first was our small and heterogeneous sample, and the second was the considerable variation in observation periods after surgery. In this study, we recruited children who had been ambulatory at surgery, as attention deficits and behavioral problems are more likely to be significant for ambulatory patients and their families than for nonambulatory patients. Furthermore, the single-center experience and retrospective study design did not necessarily allow us to include DQ, CBCL, and interictal EEG in the samples at the same points after surgery.

Finally, continuous use of AEDs is an important factor in cognitive function. If children who are seizure free can reduce or discontinue

their medication, the effects of CC on aspects of cognitive function may emerge. As CC is a palliative surgical option and candidates may continue to experience seizures to some degree after surgery, they must continue to take AEDs as usual.

The main goal of CC is to palliate the severity of seizures rather than eradicate them. Clinical studies thus far have indicated that generalized seizures with falls are the seizures particularly likely to respond to this procedure. In addition to reduction in seizure frequency and severity, recent studies have indicated improvements in behavior and parental satisfaction, which support the findings of the present study. Therefore, we believe that CC can not only reduce target seizures, but also improve attention impairment.

## 5. Conclusion

The present study indicates that CC significantly improved preoperative epileptiform discharges, implicated in the improvement of attention impairments. CC is a palliative procedure for cases of intractable epilepsy not amenable to focal resective surgery, and it can improve attention deficit and behavioral problems in association with improvement in diffusely propagated interictal epileptiform discharges.

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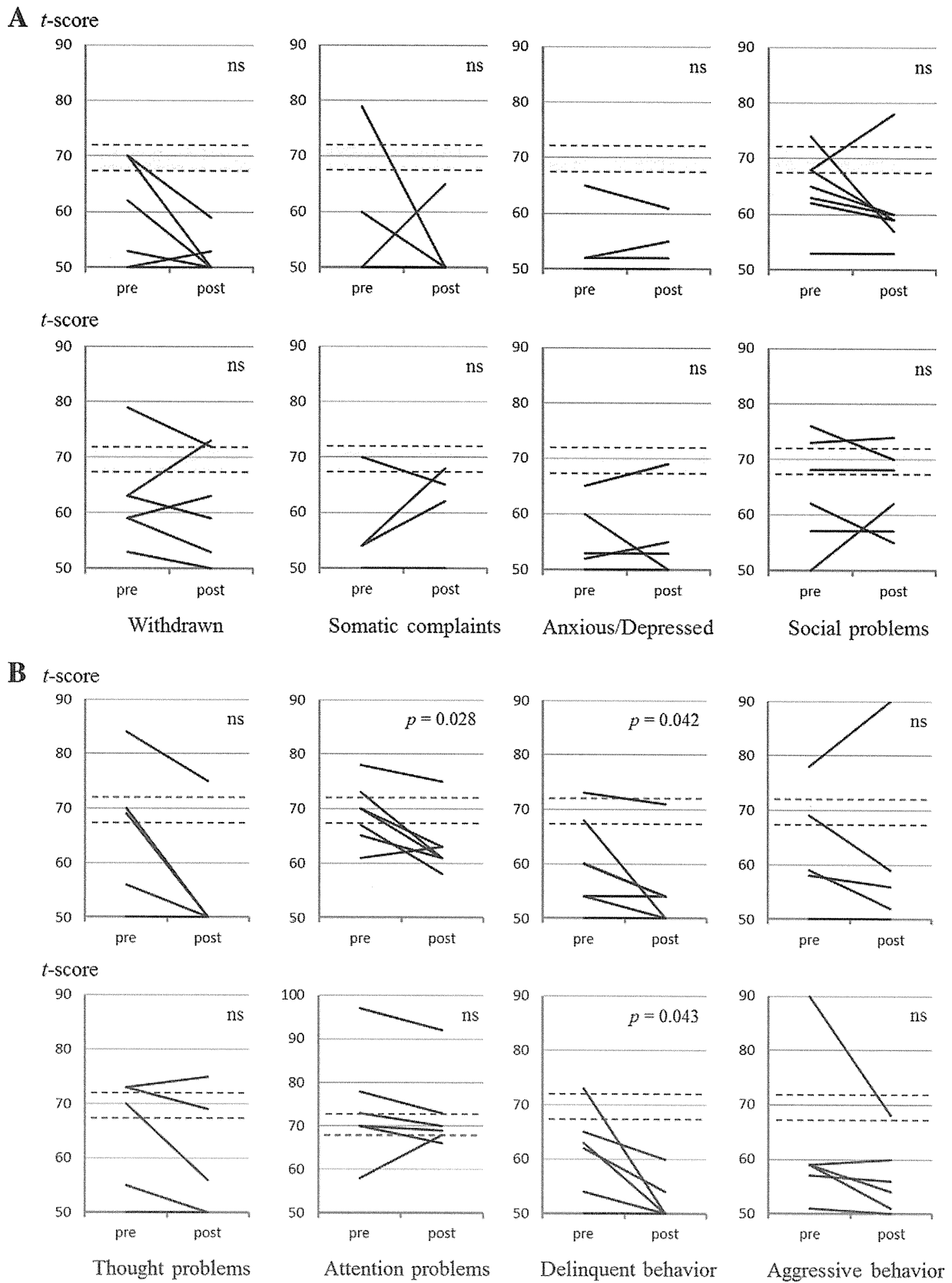


Fig. 4. Line graphs illustrating the comparison between pre- and postoperative CBCL/4–18 syndrome scale *t* scores for patients in group I ( $n = 7$ , upper row) and group U ( $n = 6$ , lower row) by Wilcoxon's signed-rank test. The two dashed lines in each graph represent cutoff points classifying patients as undisturbed (lower), moderately disturbed (middle), and severely disturbed (upper) scores. There were statistically significant decreases in the Attention Problems score in group I ( $P = 0.028$ ) and the Delinquent Behavior scores in groups I and U ( $P = 0.042$  and  $0.043$ , respectively), although the postoperative decrease in the Delinquent Behavior score in both groups is not considered clinically important as these patients were nearly undisturbed before surgery. As two patients had been assessed with the CBC/2–3 before surgery, their results were excluded from analysis of the difference between pre- and postoperative syndrome scales. ns, not significant.