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ORIGINAL PAPER

Analysis of pre- and post-operative symptoms of patients with mild trigonocephaly using several developmental and psychological tests

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Abstract
Purpose Over the past decade, we collected the cases where patients underwent decompressive cranioplasty for the treatment of mild metopic suture synostosis (mild trigonocephaly) with developmental delays. To evaluate the effectiveness of this surgery, we administered several developmental and psychological examinations to children with this condition who underwent decompressive cranioplasty.
Methods Thirty-four children (32 boys and 2 girls) who had developmental disorders with mild trigonocephaly underwent four different tests at three different time points (pre-operation, 3 and 6 months after surgery) including the: (a) Kyoto form developmental test (2001) to calculate the developmental quotient (DQ), (b) National Rehabilitation Center Sign-Significance Test (NRC S-S test) to evaluate the patients' language use and acquisition, (c) Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) to identify autistic tendencies, and (d) Japanese Child Behavior Checklist (J-CBCL) to evaluate behavioral problems. The scores were initially analyzed using analyses of variance. When significant results were observed, Tukey–Kramer multiple comparison tests were applied for further statistical evaluation.
Results Significant DQ improvements were observed, as assessed by the Kyoto form developmental test. Additionally, significant improvement in the expression of words (measured with the NRC S-S test), the scores on PARS, and some behavioral factors (measured with the J-CBCL) were observed.
Conclusions The results in this cohort suggest that decompressive cranioplasty may play an important role in supporting the improvement of developmental delays in these patients.

Keywords Craniosynostosis · Mild trigonocephaly · Development delay · Developmental test

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Introduction

Mild metopic suture synostosis (mild trigonocephaly) rarely causes clinical symptoms because it only involves very slight morphological changes in the brain. When patients with this condition exhibit symptoms, these are generally considered a result of functional abnormalities in the brain. Thus, mild trigonocephaly is not indicated for surgery [1]. A textbook on craniosynostosis suggests that surgery to remove the ridge is sufficient, if requested by the parents [2].

Since the late 1990s, we have repeatedly reported that many children with mild trigonocephaly who exhibited clinical symptoms could benefit from surgery [3–8]. However, the use of surgical interventions is not generally accepted for children with mild trigonocephaly complicated by clinical manifestations.

The clinical symptoms of mild trigonocephaly vary, including delayed language development, hyperkinesia, autistic tendencies, motor retardation, self-injurious behaviors, panic disorders, and sleep problems. We have previously evaluated the post-operative improvement of these symptoms in children based on examinations and observations performed by their parents. This method of evaluation, however, is not exempt from criticism since it is somewhat subjective. Thus, we considered it necessary to have a third party determine the pre- and post-operative conditions of the children and perform objective assessments using several psychological methods; hence, a clinical psychotherapist has been evaluating the children since October 2010. Because our previous results showed large improvements immediately after surgery, pre- and post-operative evaluations were performed using four different assessment methods with established objectivity to determine the effects of the surgical treatment. Here, we report the results of the statistical analyses of these assessments.

Methods

Patients

The study involved 34 children with mild trigonocephaly who were treated in the Okinawa Prefectural Nanbu Medical Center & Children's Medical Center between October 2010 and October 2012. If children were found to have a ridge in the central region of the forehead on inspection or palpation, they underwent three-dimensional computed tomography (3D-CT), and the diagnosis of mild trigonocephaly was confirmed when a bone ridge was observed in the frontal suture. After confirming the absence of abnormal findings in the cranium and brain by magnetic resonance imaging (MRI), we performed surgery in the children after obtaining parental consent. The age of the children was between 2 and 4 years (mean age, 3.3 years), and they included 32 boys and 2 girls. None of the children had other congenital malformations and they all appeared to be of the nonsyndromic type. The children grew normally up to 1.5 years old, and then developed clinical symptoms. Speech and behavioral regression was observed in 13 children.

The surgery was permitted by the hospital ethic committee and the psychological tests were proceeded after obtaining the consent by the parents.

Pre-operative symptoms and psychological tests

1. Developmental delay: All 34 children seemed to have developmental delay. We determined the developmental quotients (DQs) in several different areas including the postural-motor area, cognitive-adaptive area, language-social area, and total area using the Kyoto form developmental test [9].
2. Delayed language development: All 34 children exhibited speech impairments; i.e., 9 children did not speak any meaningful words, 19 spoke only single words, 5 could speak two-word sentences, and 1 child was able to speak three-word sentences. To analyze language development, we used the National Rehabilitation Center Sign-Significance Test (NRC S-S test) [10]. In this test, the mother kept a written record of any meaningful words that their child actually used. An examiner verified these words in the test and evaluated his/her verbal expression ability using the scoring system listed below. The points for expression ability, i.e., from "no word production" to "having a conversation," were divided as follows: 1 point for no word production, 2 points for producing 20 words or less, 3 points for producing 100 words or less, 4 points for producing over 100 words, 5 points for speaking two-word sentences, 6 points for speaking three-word sentences, and 7 points for having a conversation.
3. Autistic tendencies: Of the 34 children, 26 had some autistic symptoms, including poor eye contact, deficient play with other children, no understanding of rules, no expression of suitable words, repetitive use of language, use of gestures or pointing instead of words, preoccupation with certain objects, hand waving, and stereotyped behaviors such as rocking. To evaluate these symptoms, we used the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) [11]. PARS is an evaluation method developed by the Autism Society Japan as a rating scale that is applicable to all autism spectrum disorders including patients with high-functioning autism or Asperger syndrome. It can evaluate the severity of pervasive developmental disorders regardless of the degree of the associated hypophrenia. The mothers of all 34 children answered the questions and an examiner listened to their answers to record the scores.
4. Emotional and behavioral problems: All of the children had some emotional and behavioral problems. Specifically, 26 had hyperkinesis, 10 had motor retardation, 22 had panic disorder, 12 showed self-injurious behaviors, 16 had sleep problems, and 10 had deviated food habits. These problems were evaluated using the Japanese Child Behavior Checklist (J-CBCL). We used the J-CBCL/2-3 [12] for 2- or 3-year-old children and the J-CBCL/4-18 [13] for 4-year-old children. The checklist includes 118 questions. The responses to the questions were classified into different superordinate scoring groups including internalizing behavior scores, externalizing behavior scores, and problem behavior scores. The internalizing behavior scores were subdivided into withdrawn, anxious/neurotic, separation anxiety, and somatic complaint behaviors; the externalizing behavior scores were subdivided into aggressive/destructive behaviors, attention problems, oppositional behaviors, and delinquent behaviors; and the problem behavior scores were subdivided into developmental abnormalities, sleep/eating problems, social problems, and thought problems as subordinate concepts.

Since most of the children in this study were 2–4 years old, analyses of the J-CBCL/2-3 and J-CBCL/4-18 data were performed for all children (n=34) using four similar subordinate concepts: withdrawn, aggressive/destructive behaviors, anxious/neurotic behaviors, and attention problems. We performed analyses of the J-CBCL/2–3 data for 2- to 3-year-old children (n=21) on oppositional behaviors, separation anxiety, developmental abnormalities, and sleep/eating problems. Finally, we performed analyses of the J-CBCL/4–18 data for 4-year-old children (n=11) using other subordinate concepts including somatic complaints, social problems, thought problems, and delinquent behaviors.

T scores were obtained by determining the cumulative frequency distribution of each score (automatically produced by plotting the pre-made scoring table for each score) and were used to analyze the changes in behavior after surgery (compared to before surgery) [14].

Intracranial pressure

After reflecting back the scalp flap, a burr hole was made in the frontal region. A sensor (Camino intracranial pressure sensor, Integra Lifesciences Corporation, New Jersey, USA) was inserted extradurally to measure the intracranial pressure (ICP). pCO_2 was initially maintained at the target level of around 30 mmHg and then changed to 38–42 mmHg during the second measurement. Each measurement was continued for several minutes. In 33 children, the pCO_2 was 42 mmHg or less at the second measurement.

Surgical methods

Surgery was performed as previously described [5]. Briefly, we performed decompressive cranioplasty to increase the cranial-cavity space. Since the children had marked narrowing of the anterior cranial fossa, the following procedures were also performed in the cranial base: both the lesser and greater wings of the sphenoid were adequately removed, and the sphenoid ridge was excised to the meningo-orbital band. The sphenoid ridge was very thin with a width of 5–7 mm and intruded into the space between the frontal lobe and temporal lobe (Fig. 1). Additionally, the supraorbital margins, superolateral regions, and roofs of the orbit were dissected as one piece.

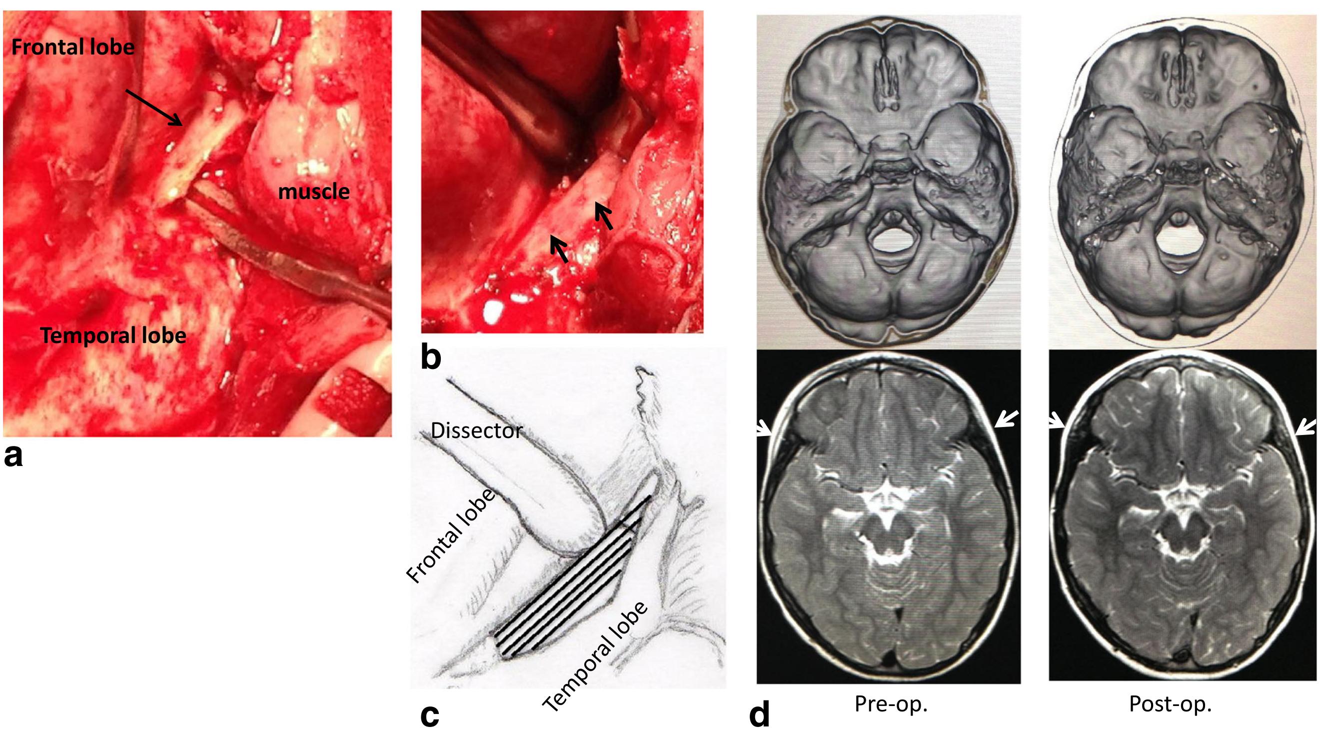

Fig. 1 Operative findings of the sphenoid ridge. **a** Images showing that the sphenoid ridge is thinner and wider (*arrow*). **b** Images showing the dura mater (*arrows*) after removing the sphenoid ridge to the orbito-meningeal band, which easily shows the width of the sphenoid ridge in these patients. **c** The *shaded area* indicates the dura matter, which was visible after the removal of the sphenoid ridge. **d** Changes of the anterior cranial fossa and frontal lobes in pre and post-operation. The post-operative 3D-CT revealed an extended anterior cranial fossa, while the expanded frontal lobes and decreased indentation of the opercular regions (*arrows*) were confirmed by post-operative MRI

Results

The patients' foreheads were enlarged in all cases after surgery. Post-operative 3D-CT revealed an extended anterior cranial fossa, while the expanded frontal lobes were confirmed by post-operative MRI (Fig. 1d).

Intracranial pressure

The mean pCO_2 and ICP of each measurement were as follows: the mean pCO_2 was 29.9 mmHg and the mean ICP was 9.6 mmHg at the first measurement, while at the second measurement, the mean pCO_2 was 37.5 mmHg and the mean ICP was 16.6 mmHg. In the second ICP measurement, the ICP was 10 mmHg or less in 2 children, 11 to 15 mmHg in 11 children, and greater than 16 mmHg in 20 children.

The ICP was 10 mmHg or less in 2 children, which was within the normal range. In both children, the overall clinical symptoms showed a favorable improvement, and the results of the ICP were not correlated with the level of improvement in the clinical symptoms.

Psychological evaluations

Psychological evaluation was performed before surgery, and 3 and 6 months after surgery to identify any significant post-operative changes in the scores from each assessment method. A one-way analysis of variance (ANOVA) comparing three levels of one factor was performed, with the score as the independent variable and the mean score obtained at each time point as the dependent variable. The indices showing main effects were further analyzed by multiple comparison tests using the Tukey–Kramer method. The results for each assessment method are listed below.

1. Kyoto form developmental test: All 34 children took the test. The mean DQ score was calculated at each time point for the postural-motor, cognitive-adaptive, language-social, and total areas, and then an ANOVA was performed. Main effects were observed for the cognitive-adaptive area ($p<0.001$), language-social area ($p<0.001$), and total area ($p=0.0001$). The multiple comparison tests showed that the DQ was significantly higher at both 3 and 6 months after surgery compared to the DQ before surgery. A main effect was not observed for the postural-motor area ($p=0.829$; Fig. 2). However, 6 children who had poor walking performance prior to surgery were able to walk steadily after surgery.

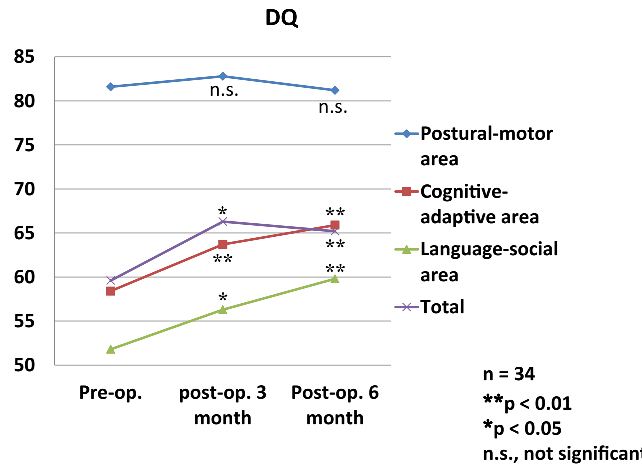

Fig. 2 Changes in patients' developmental quotients (DQs) as measured by the K-form developmental test. Note that there are statistically significant differences in the cognitive-adaptive, language-social, and total area measurements at 3 and 6 months post-operatively compared to pre-operative measurements, but the postural-motor area measurements were not significantly different

2. NRC S-S test: We calculated the mean score of the NRC S-S test, which was converted from the verbal expression ability of all children at each time point, and performed an ANOVA. Main effects were observed, and the results of multiple comparison tests showed that the scores at 3 and 6 months after surgery were significantly higher than the scores before surgery ($p<0.001$). These results indicate that the verbal expression abilities of the children improved at 3 and 6 months after surgery compared to their abilities before surgery (Fig. 3).
3. PARS: A main effect was observed when the mean PARS score from all children at each time

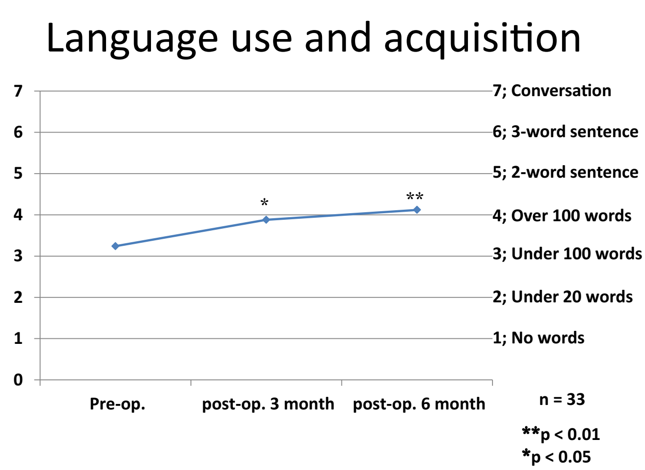

Fig. 3 Changes in language use and acquisition. Note that there is a statistically significant difference between the post-operative measurements compared to the pre-operative measurements

point was calculated and an ANOVA was performed ($p<0.001$). The results of multiple comparison tests showed that the PARS scores at 3 and 6 months after surgery were significantly lower than the scores before surgery (Fig. 4). Of the 26 children who exhibited autistic tendencies, 21 demonstrated some improvements during the clinical examinations.

4. J-CBCL When an ANOVA was performed using each T score, main effects were observed for the internalizing behavior scores of withdrawn ($p<0.0001$) and anxious/neurotic behaviors ($p<0.0048$) and for the externalizing behavior scores of aggressive/destructive behaviors ($p<0.0001$), attention problems ($p=0.017$), and oppositional behaviors ($p=0.0003$). Main effects were also identified for the problem behavior scores of sleep/eating problems ($p=0.007$) and developmental abnormalities ($p=0.003$). Multiple comparison tests demonstrated that the T scores at 3 and 6 months after surgery were significantly lower than the T scores before surgery. For the other behaviors (separation anxiety ($p=0.085$), thought problems ($p=0.569$), social problems ($p=0.933$), delinquent behaviors ($p=0.095$), and somatic complaints ($p=0.136$), the T scores tended to be decreased; but, this decrease was not statistically significant (Fig. 5).

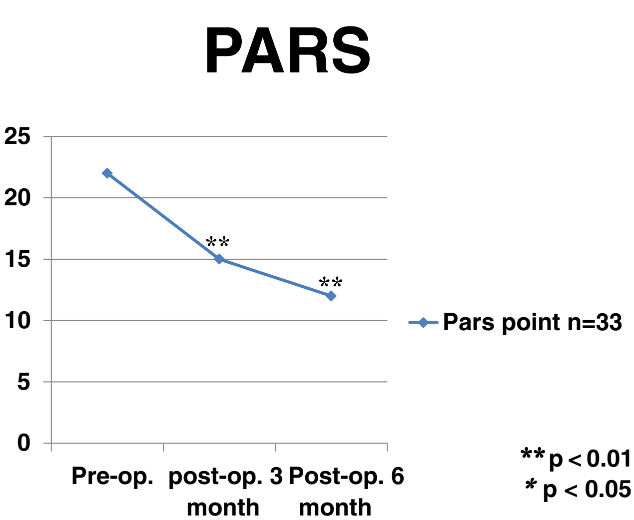

Fig. 4 Changes in the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) scores. Note that there is a statistically significant difference between the post-operative measurements compared to the pre-operative measurements

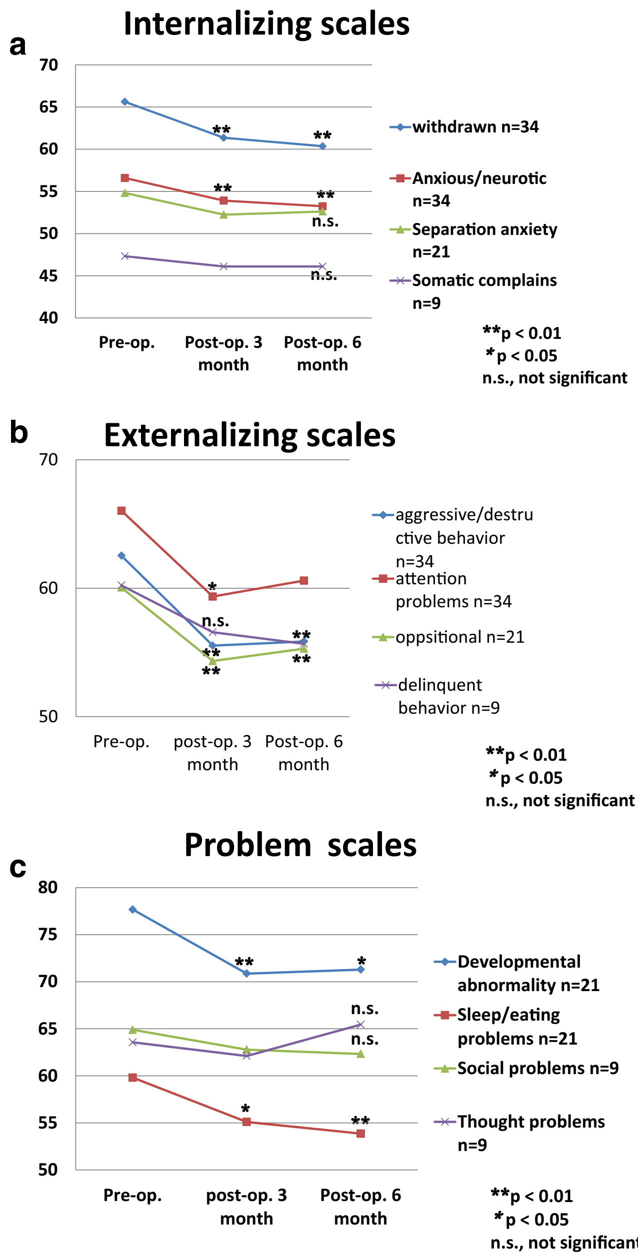

Fig. 5 Changes Japanese Child Behavior Checklist (J-CBCL). **a** Changes in internalizing behavior scores. Note that the changes in the scores for withdrawn and anxious/neurotic behaviors between the pre-operative and post-operative measurements are statistically significant, but those for separation anxiety and somatic complaints are not. **b** Changes in externalizing behavior scores. Note that changes in the scores for aggressive/destructive behaviors between the pre-operative and post-operative measurements are statistically significant, as are those for oppositional and attention problems (3 months post-operative), while the pre-operative and post-operative scores for delinquent behavior are not significantly different. **c** Changes in problematic behavior scores. Note that the changes in the scores for developmental and sleep/eating behaviors between the pre-operative and post-operative measurements are statistically significant, but those for social thought are not

Symptoms observed before surgery including hyperkinesia, motor retardation, panic disorders, self-injurious behaviors, and sleep problems were improved or absent after surgery. Of the ten children with deviated food habits, eight showed improvements after surgery.

Discussion

It was thought that mild trigonocephaly rarely causes clinical symptoms because it results in only minor morphological changes in the brain. Symptoms exhibited by patients with this condition are generally considered to be due to functional impairments in the brain [1,2]. Since the early 1990s, however, some studies have described clinical manifestations, including cognitive disorders, in patients with mild trigonocephaly [15]. We have also reported improvements in the various clinical symptoms of children with mild trigonocephaly after surgery [3–8]. Since some children with mild trigonocephaly exhibit severe mental retardation, it is difficult to assume that mild trigonocephaly causes all of their symptoms. However, the symptoms are improved in many children after surgery, which may be attributable to the surgical intervention [5]. As of 2008, more than 300 children at one medical center have undergone surgery. The Ministry of Health, Labour, and Welfare in Japan conducted a prospective multi-center study for early metopic suture synostosis and the final report indicated that many patients demonstrated significant improvements in their clinical symptoms at 6 months and 1 year after surgery [8]. The evaluation method used in this study, however, was a subjective assessment performed by the mothers, which lacked objectivity. In the present study, we used suitable objective methods in which we had a third-party clinical psychotherapist evaluate the children. The 4 psychological tests used in this study employed rating scales to produce numerical scores. Thus, we calculated the mean scores of all children and performed a double statistical analysis consisting of ANOVAs to determine the presence/absence of main effects, and multiple comparison tests by the Tukey–Kramer method to identify specific changes.

The Kyoto form developmental test is commonly used in Japan for assessing pre-school children and establishes the DQ by evaluating children during play to determine their general development. Similar tests are performed in other countries, which include some differences. For the children involved in this study, the mean DQs of the cognitive-adaptive, language-social, and total areas were significantly higher compared to their respective pre-operative DQs. All of the children in this study had intellectual disabilities with a DQ of 70 or less. A study reported that the DQs of children with intellectual impairments tended to decrease over time [16]; similarly, our previous study showed a tendency for the intellectual disability level to decrease over time [3]. In addition, the children in this study had pervasive developmental disorder. There is a study reporting that the DQ does not significantly change over time in children with pervasive developmental disorder [17]. As in these cases, the DQs of children with intellectual impairment or pervasive development disorder generally tend to decrease or remain stable over time. In the present study, however, a statistically significant improvement in the post-operative DQ was observed even though the children had intellectual disabilities and pervasive developmental disorders before surgery. While no statistically significant changes in DQ were observed in the postural-motor area, the children's movement clinically improved after surgery, leading to increases in the quality of their daily lives.

All of the children in our study had delayed development in verbal expression and this ability was evaluated using the NRC S-S test. In this test, cards and equipment are used to determine the language ability of 0- to 6-year-old children who are in the stage of verbal development. The test encompasses both listening and speaking. It was revised in 1989 to the current version [10]; however, the validity of the test was investigated in healthy children [18]. All of the children who participated in this study were determined to have delayed verbal development compared to healthy children. The status of language acquisition was expressed as a score, and the results showed significant increases in scores at 3 and 6 months after surgery compared to the scores before surgery. We have repeatedly reported that the most impressive improvement after surgery was verbal expression. Although the cohort used here consisting of 33 children is small, it seems to be of considerable significance because the present study objectively demonstrated the improvement of verbal expression, thus, confirming our previous observations.

Many of the children in this study had autistic symptoms, which were considered as clinical manifestations originating from the frontal lobe. We used the PARS to determine symptom changes before and after surgery. PARS is a revised version of the childhood autism rating scale (CARS) [19] and was developed as an easy assessment method that could be carried out during patients' everyday movements in order to understand the behaviors of children with pervasive developmental disorders. The evaluation items were selected by 8 child psychiatrists and child clinical developmental psychologists specializing in autism and pervasive developmental disorder who had more than 10 years of experience [11]. The test is composed of 57 questions covering 6 areas: personal relationships, communication, obsession, stereotyped behaviors, difficulty, and hypersensitivity. The test is performed by interviewing the parent(s) of a child. Questions 1 to 34 are for young children. The reliability and validity of PARS were previously investigated and the test attained a certain level of credibility [20,21]. The cut-off point for young children is 9 points. If a child has 9 points or more, he/she is suspected to have pervasive developmental disorder.

Since many of the children in this study had autistic tendencies, the PARS was used for evaluation. The mean score was significantly decreased after surgery, indicating decreases in the autistic tendencies of the children. There is a study reporting that PARS scores do not significantly change over time in children with pervasive developmental disorder [22]. It is interesting that significant decreases in the scores were observed in the children in this study after surgery, although their scores did not reach the normal level of 8 points. This result may support our long-term observations of post-operative attenuation of autistic tendencies.

The children in this study had emotional and behavior problems including hyperkinesia, autistic tendencies, motor retardation, panic disorders, self-injurious behaviors, sleep problems, and deviated eating habits. We used the CBCL for pre- and post-operative evaluation of these symptoms. CBCL is a checklist developed by Achenbach [14] to comprehensively evaluate emotions and behaviors in children. In this study, we used the Japanese version of the CBCL [12,13]. The J-CBCL is composed of 118 questions, which are answered by the child's parent (s). The results can be divided into internalizing behavior scores (2- and 3-year-olds: separation anxiety, withdrawn, and anxious/neurotic behavior; 4- to 18-year-olds: withdrawn, somatic complaints, and anxious/depression behavior), externalizing behavior scores (2- and 3-year-olds: aggressive/destructive behaviors, attention problems, and oppositional behaviors; 4- to 18-year-olds: delinquent behaviors and aggressive behaviors), and problem behavior scores (2- and 3-year-olds: developmental abnormalities and sleep/eating problems; 4- to 18-year-olds: social, thought, and attention problems).

The ANOVA results revealed main effects for the internalizing scores of withdrawn and anxious/neurotic behaviors; externalizing scores of aggressive behaviors, attention problems, and oppositional behaviors; and problem scores of sleep/eating problems and developmental abnormalities. Multiple comparison tests showed that T scores were significantly lower at 3 and 6 months after surgery than the scores before surgery. The statistically significant improvements in the T scores of these subordinate concepts suggest extensive amelioration of actions and emotion in the children after surgery.

In this study, 16 children had sleeping problems. Of these 16 children, 6 experienced sudden waking and crying, i.e., night terrors. The sleeping problems, including night terrors, were reduced or absent after surgery. Further research is needed to determine whether an increase in ICP is involved in the mechanism(s) underlying these sleeping problems.

Deviated eating habits were observed in 10 children before surgery. After surgery, 8 children showed improvements in these habits. We plan to examine the mechanism(s) underlying this unexplainable problem further, as this issue is observed in clinical settings.

The results showing post-operative improvements, as assessed by four different evaluation methods, may suggest that the clinical symptoms of children with mild trigonocephaly significantly improved after surgery.

The main focus of this study is to examine the changes noted immediately after surgery, and the results of a long-term follow-up are under analysis.

A possible explanation for why surgery would lead to such improvements in clinical symptoms includes decreased ICP by aggressive decompressive cranioplasty [6] and enlargement of the frontal lobe attributable to the expansion of the anterior cranial fossa due to formation of the cranial base by aggressive excision of the sphenoid bone. In particular, the removal of sphenoid ridges intruding into the opercular regions may be essential for enlarging the frontal lobe (Fig. 1). We observed that extremely wide bilateral sphenoid ridges were intruding into the opercular region in the early phase and had previously reported that it was important to remove them [7]. Recently, functional MRI studies have demonstrated that blood flow in the opercular region of the brain is reduced in children with autism, and have noted that that the function of mirror neurons may be decreased [23,24]. Moreover, an MRI study reported decreased grey matter volume in the opercular region in children with high-functioning autism [25].

Our procedure involving aggressive removal from the lateral bone of the opercular region to the sphenoid ridge may lead to decompression of the opercular region (Fig. 1d), which in turn, may contribute to the improvement of symptoms in children with autistic tendencies.

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