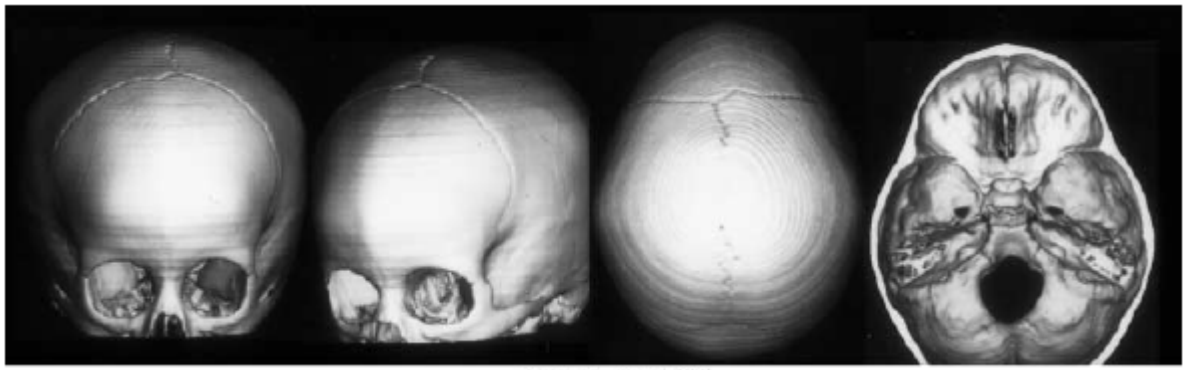
RUNNING HEAD: PSYCHOPATHOLOGY IN CHILDREN WITH TRIGONOCEPHALY?



(Source: Shimoji et al., 2002)

Psychopathology in children with trigonocephaly?

Master Thesis in Education and Developmental Psychology

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Abstract

The present study examined the prevalence of psychopathology, like ADHD- and autism-like behaviors in children diagnosed with trigonocephaly. To what extent the possible risk factors of neurobehavioral problems affected the developmental condition of the children with trigonocephaly, was also examined. In total, 47 children, 40 boys and 7 girls, and their parents, took part in this study. At time of research, their age varied from 1 up to 8 years. Contradictory to the findings of other studies, the results in general provide evidence that children with trigonocephaly of the current research sample, obtain developmental scores that do not differ from normative expectations. As far as the various risk factors are concerned, a syndromic form of trigonocephaly and a higher percentage of digital impressions seemed to predict a worse outcome with regard to internalizing and externalizing problems. The current findings however, are limited because of methodological problems and can therefore be questioned. Future research is highly recommended.

Keywords: trigonocephaly, psychopathology, ADHD, autism, neurobehavioral problems, risk factors.

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1. Introduction

1.1. What is craniosynostosis?

Craniosynostosis refers to the premature fusion during gestation of one or more of the sutures that normally separate the boney plates of the infant's skull. Open sutures allow the skull to expand as the brain grows in typically developing infants. Premature fusion of one or more sutures results in restricted growth upright to the fused suture(s). This will lead to compensatory growth in the skull's unfused boney plates, which produces an abnormal head shape (Speltz, Kapp-Simon, Cunningham, Marsh, & Dawson, 2004).

Craniosynostosis is a very uncommon condition occurring in 0.4 to 1 per 1000 children (Warschausky, Angobaldo, Kewman, Buchman, Murazko, & Azengart, 2004).

When more sutures are premature fused, this is called multiple-suture craniosynostosis. Multiple-suture fusions are often associated with several genetic syndromes. These syndromes include Apert, Crouzon, Pfeiffer, Saethre Chotzen and Carpenter and these in turn have been associated with elevated rates of mental retardation and learning disabilities (Cohen, 1991).

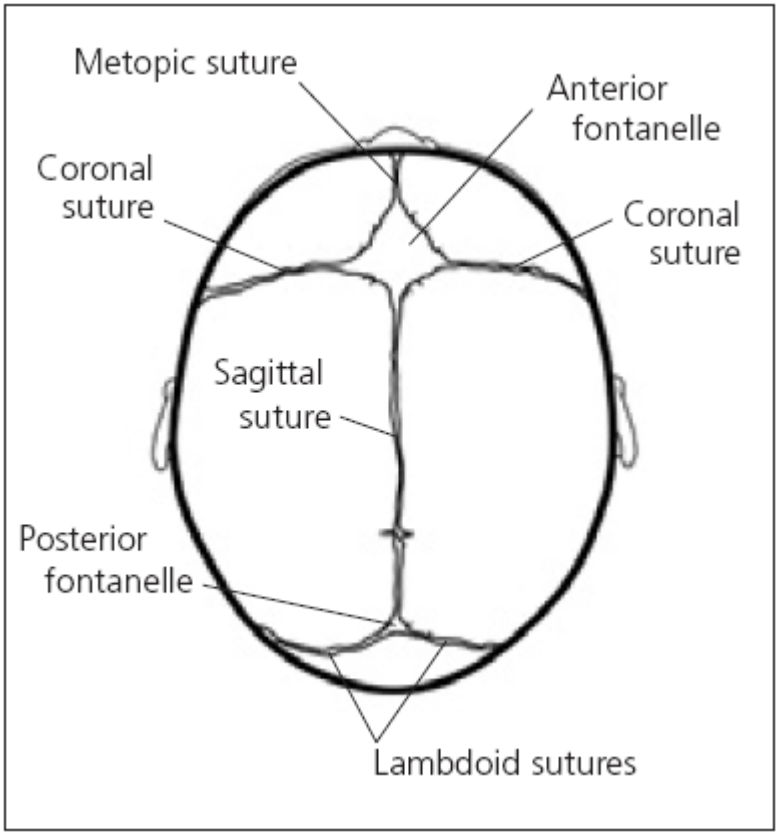

Figure 1. Fontanelles and sutures in a normal newborn skull
(source: American Family Physician; Craniosynostosis, 2005)

When only one suture is premature fused, this is called single-suture craniosynostosis. Single-suture craniosynostosis can consist of isolated fusions of the sagittal, metopic, and left or right coronal or lamboid sutures (Speltz et al., 2004). Figure 1 shows the fontanelles and different sutures in a newborn skull, with the metopic suture on top. The present study will focus on the fusion of the metopic suture in children of 1 to 8 years of age.

1.2. What is trigonocephaly?

Trigonocephaly is a form of single-suture craniosynostosis. Trigonocephaly results from a premature closure of the metopic suture, therefore this anomaly is also known as metopic synostosis. The metopic suture is located at the forehead, in front of the frontal lobes of the brain. Trigonocephaly is characterised by a triangular head shape including a forehead midline ridge and hypotelorism (abnormal closeness of the eyes). On both sides of the head frontotemporal narrowing is also present. The malformation of the forehead already starts developing from the beginning of gestation (Speltz et al., 2004). Figure 2 shows the malformation of the forehead resulting from metopic synostosis or trigonocephaly.

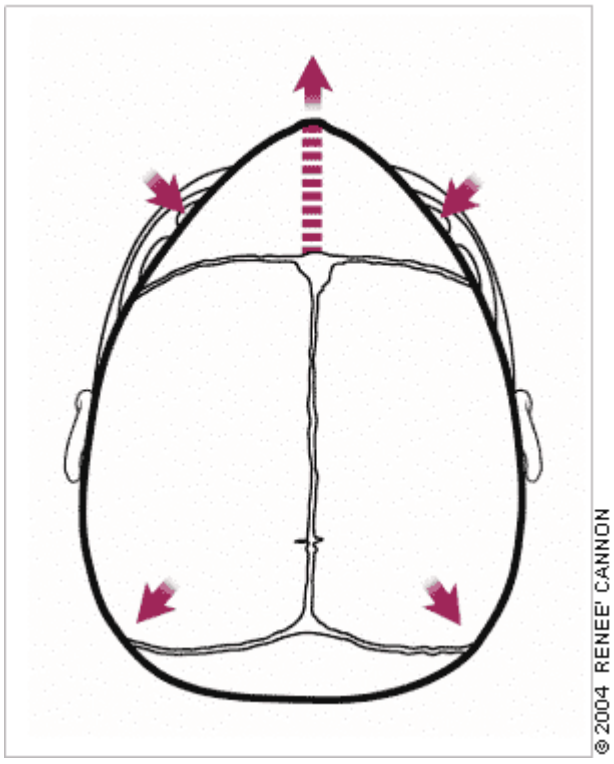

Figure 2. A triangular head shape resulting from metopic synostosis (source: American Family Physician; Craniosynostosis, 2005)

1.3. Two forms and prevalence

Two forms of trigonocephaly have been identified. Trigonocephaly can occur as an isolated malformation or as part of a syndrome. Isolated metopic suture synostosis varies from a barely noticeable ridging to a marked trigonocephaly (Sidoti, Marsh, Marty-Grames, Noetzel, 1996). The syndromic form of trigonocephaly is associated with other primary defects of morphogenesis, which means differentiation and growth of the structure of an organism or a part of an organism (Bottero, Lajeunie, Arnaud, Marchac, & Renier, 1998).

The prevalence of trigonocephaly in general is estimated at 1 in 15.000 children (Lajeunie, Le Merrer, & Renier, 1998). Males are three to four times more affected than females (Boltshauser, Ludwig, Dietrich, & Landolt, 2003). Remarkably, trigonocephaly is frequently misdiagnosed during infancy as metopic ridging without synostosis is very common. It is estimated to occur in 10-25% of normal infants and young children and has nothing to do with metopic synostosis (Cohen and McLean, 2000). Radiographs and CT scans are therefore essential in diagnosing true trigonocephaly.

Isolated trigonocephaly is a relatively rare deformity. Although numbers can vary, the incidence of an isolated metopic suture fusion is about 1 in 7000 to 1 in 70.000 live births. It is one of the less frequently identified forms of single-suture craniosynostosis. A syndromic form of trigonocephaly with additional congenital anomalies is even rarer (Sidoti et al., 1996).

1.4. Etiology

The etiology and pathogenesis of trigonocephaly are not clear. Lajeunie et al. (1998) suggest the possibility of a genetic component for this type of craniosynostosis, since concordance for trigonocephaly was observed only in monozygotic and not in dizygotic twins. Several other factors have also been implicated, including chromosomal anomalies, teratogens during gestation (e.g., nicotine and nitrosatable medications), fetal head constraint, and metabolic and hematologic disorders (Cohen 1991).

1.5. Neurobehavioral problems

There is growing evidence that trigonocephaly is associated with neurobehavioral problems, including learning disabilities and behavioral problems (Speltz et al., 2004. Kapp-Simon, Leroux, Cunningham, & Speltz, 2005). More specifically, the literature reports on cases of Attention deficit hyperactivity disorder (ADHD), autism, language disorders, mental retardation, motor disfunction etc. associated with trigonocephaly (e.g., Shimoji, Shimabukuro, Sugama, & Ochiai, 2002). However, many studies finding these associated

problems with trigonocephaly have been limited by methodological problems commonly found in studies of rare disorders. An example of these methodological problems is small sample sizes that are limiting the statistical power. Another methodological issue in many studies is the absence of clear inclusion criteria, which makes comparisons among different studies difficult (Speltz et al., 2004).

1.6. Risk factors of neurobehavioral problems

Although few studies of trigonocephaly or single-suture craniosynostosis in general have been conducted, several risk factors of cognitive, emotional and behavioral problems in children with trigonocephaly have previously been reported. Bottero et al. (1998) found the prognosis of isolated cases of trigonocephaly to be better than the prognosis for cases with extracranial malformations, e.g. limb anomalies, ear anomalies. Children with intracranial anomalies, e.g. hydrocephalus and agenesis of the corpus callosum, also seem to have a worse final development than those without these anomalies. Bottero et al. (1998) shows the latter being a major predictor of more malign mental development. Other structural brain anomalies that have been reported among children with trigonocephaly include hypoplasia of the frontal lobes, dilated precentral sulci, frontal subdural space distention, enlarged subarachnoid cerebrospinal fluid etc. (e.g., Sidoti et al., 1996). Furthermore, Bottero et al. (1998) found that the severity of the brain anomaly also seemed to be a good predictor for the cognitive development of patients with trigonocephaly. The severity of the anomaly or phenotype is expressed in terms of the ratio of the interparietal to the intercoronal distance and can be measured through 3D CT-scan. Figure 3 shows a 3D CT-scan of the phenotype expression (ratio interparietal to intercoronal distance) of children with mild trigonocephaly and of normal children.

A study of Okkerse, Beemer, Mellenbergh, Wolters, & Heineman-de Boer (in press) reported that children with brain abnormalities like craniosynostosis have an on average lower intelligence compared to children without any brain abnormalities. Okkerse et al. (in press) also considered gender to be a risk factor of trigonocephaly. Their study revealed that craniofacial anomalies occur less frequently in girls than in boys, but girls that do have this anomaly are more severely affected, e.g. a higher frequency of syndromic diagnosis, a more severe phenotypical expression compared to boys.

ICP

IPD

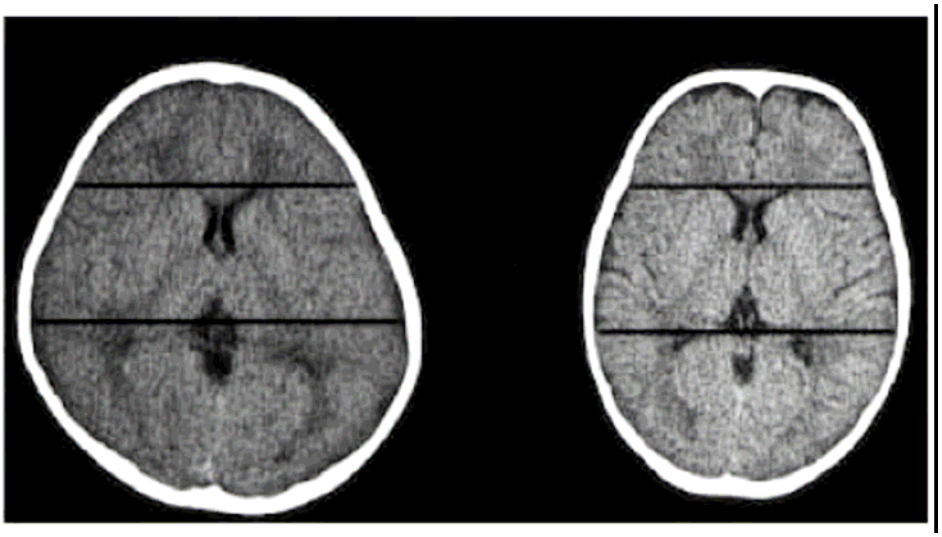

Figure 3. Left: the interparietal distance (IPD)/intercoronal distance (ICD) ratio (1.25) of children with mild trigonocephaly. Right: the interparietal distance (IPD)/intercoronal distance (ICD) ratio (1.21) of normal children (source: Shimoji et al., 2002).

The severity of digital impressions is another possible risk factor of neurobehavioral problems in children with trigonocephaly. Due to the condition of trigonocephaly there is lesser room in skull for the brain to grow. Because of this, the brain presses against the skull which could result in impressions on the skull (Shimoji & Tomiyama, 2004). Tuite, Evanson, & Chong, et al. (1996) found a relation between the severity of the digital impressions and intelligence. Figure 4 shows an X-ray of a skull with digital impressions.

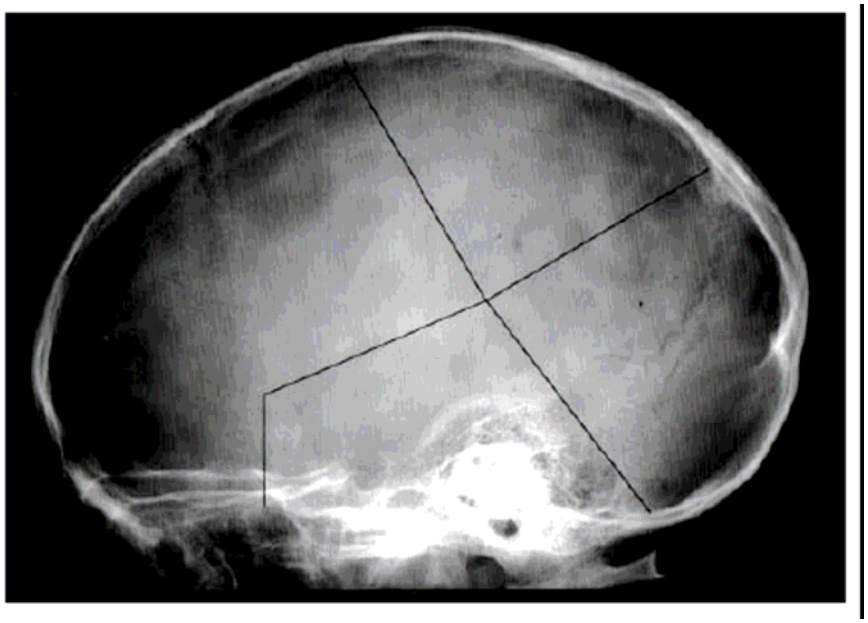

Figure 4. Digital impressions on a skull X-ray (source: Shimoji & Tomiyama, 2004)

Elevated intracranial pressure is reported to be present in mild trigonocephaly. After undergoing a decompressive surgical procedure, patients with trigonocephaly who presented with clinical symptoms such as delay in language development, hyperactivity, autistic tendencies and motor delays, showed improvement (Shimoji, Shimabukuro, Sugama, & Ochiai, 2002). Besides the condition of the brain, the family environment (e.g., social-economic status) can also be of major influence on mental development of children with trigonocephaly (Bottero et al., 1998).

1.7. Cause or correlate?

The causal relationship between this craniofacial anomaly and neurodevelopment is nevertheless uncertain, but it appears that this abnormal condition is at least a visible and early diagnosed marker for elevated risk of neurodevelopmental problems. Clinical formulations have assumed a direct, linear pathway in which suture fusion leads to brain deformation, and consequently neuropsychological impairment. Which medical factors exactly form a risk for the children's development still remains unknown. The data however, is insufficient and the theory is limited for hypothesizing any particular pathway. Whether metopic synostosis is a cause or a correlate of neuropathology remains unclear (Speltz et al., 2004).

1.8. Similarities with other disorders

There are similarities noticeable between children with trigonocephaly and children with ADHD and autism. First of all, in all three cases, the frontal lobes are affected (Speltz et al., 2004; Barkley, 1997). The frontal lobes are strongly related to executive functioning, which are commonly described as mental control processes that enable self-control and are necessary to maintain an appropriate problem solving set for the attainment of a future goal (e.g., Pennington & Ozonoff, 1996). Secondly, males are in general more affected than females in all three conditions (Boltshauser et al., 2003; Barkley, 1997). Thirdly, ADHD, autism and trigonocephaly are all associated with motor problems (Geurts, 2004; Shimoji, Shimabukuro, Sugama & Ochiai, 2002). The question is whether this is a coincidence or if trigonocephaly is also related to ADHD and autism.

To clarify the etiological pathways, there is a need to look more closely at the relation between neurobehavioral status and the severity and cortical impact of synostosis. It is also possible that the probability of psychopathology and especially, ADHD- and autism-like behaviors in children with trigonocephaly, depends in part of the co-occurrence and severity

of the risk factors of neurobehavioral problems (Speltz et al., 2004). Since only few studies have been conducted in trigonocephaly associated with psychopathology (e.g. Bottero, et al., 1998), the emphasis of the present study will be on trigonocephaly in association with psychopathology and in particular with ADHD- and autism-like behaviors.

1.9. Present study

The present study focuses on the risk factors of psychopathology in children with trigonocephaly and in particular ADHD- and autism-like behaviors. The risk factors that are included in the present study are the presence of brain anomalies like agenesis of the corpus callosum, hydrocephalus, enlarged subarachnoid cerebrospinal fluid etc.; phenotype expression (the ratio of the interparietal to the intercoronal distance); the trigonocephaly type, existence of a syndromic or nonsyndromic form; the presence of digital impressions on the skull; intracranial pressure, and social-economic status of the parents. In short, we are interested in if children with trigonocephaly are more susceptible for higher rates of psychopathology, and in particular higher rates of ADHD- and autism-like behaviors.

1.9.1. Purpose of research

The outcomes of the present study can help in the process of screening children with trigonocephaly and with increased risks for psychopathology, prematurely. Even though the direction of the relationship has not been indicated yet, the fact that there seems to be a relation between trigonocephaly and psychopathology, creates opportunities within systems of pediatric care for early detection of neurobehavioral difficulties and preventative interventions, which can influence the children's development positively (Speltz et al., 2004).

1.9.2 Main research questions and hypotheses

Three main research questions can be formulated:

1) Do children with trigonocephaly of 1 up to 8 years of age have an increased risk for psychopathology, like ADHD- and autism-like behaviors, compared to children without trigonocephaly?
2) Are children with trigonocephaly of 1 up to 8 years of age more cognitively impaired compared to children without trigonocephaly?
3) Are boys with trigonocephaly more susceptible for psychopathology, like ADHD- and autism-like behaviors, compared to girls with trigonocephaly?

Next to these three main questions, several sub questions can be formulated about to what extent the previous mentioned risk factors relate to psychopathology with ADHD- and autism-like behaviors in particular.

1) Does the presence of additional brain anomalies (e.g. hydrocephalus, agenesis of the corpus callosum, enlarged subarachnoid cerebrospinal fluid) in children with trigonocephaly predict a higher prevalence of psychopathology, like ADHD- and autism-like behaviors?
2) Does the existence of a syndromic form result in a higher prevalence of psychopathology, like ADHD- and autism-like behaviors, compared to the existence of a nonsyndromic form in children with trigonocephaly?
3) Does a more severe phenotype expression (larger ratio of the interparietal to the intercoronal distance) predict a higher prevalence of psychopathology, like ADHD- and autism-like behaviors, compared to a less severe phenotype expression in children with trigonocephaly?
4) Does a higher percentage of digital impressions on the skull in children with trigonocephaly predict a higher prevalence of psychopathology, like ADHD- and autism-like behaviors, compared to a low percentage of digital impressions?
5) Does the presence of elevated intracranial pressure result in a higher prevalence of psychopathology, like ADHD- and autism-like behaviors, in children with trigonocephaly compared to the absence of intracranial pressure?
6) Do children with trigonocephaly, from a pour social-economic background (parents with a low Social Economic Status; SES) have an increased risk for psychopathology, like ADHD- and autism-like behaviors, compared to children with trigonocephaly who are from a high social-economic background?

The present study has several expectations with regard to the outcome measures of children with trigonocephaly and their determinants of impact.

1) Children with trigonocephaly have an increased risk for psychopathology, like ADHD- and autism-like behaviors, compared to children without trigonocephaly.
2) Children with trigonocephaly are more cognitively impaired compared to children without trigonocephaly.

3) Boys with trigonocephaly are more susceptible for psychopathology, like ADHD- and autism-like behaviors, compared to girls with trigonocephaly.

However, more impairments associated with trigonocephaly are mentioned in the literature (e.g., Okkerse et al., in press, Bottero et al., 1998). So again, several sub hypotheses concerning possible predictors of psychopathology, like ADHD- and autism-like behaviors in children with trigonocephaly, can be stated.

1) The presence of additional brain anomalies in children with trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors, compared to children with trigonocephaly without additional brain anomalies. In other words, children with these additional brain anomalies will have a worse outcome. On average they will experience more problems compared to children with trigonocephaly without additional brain anomalies.
2) The syndromic form compared to the nonsyndromic form of trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors.
3) A more severe phenotype expression (larger ratio of the interparietal to the intercoronal distance) in children with trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors, compared to children with trigonocephaly with a less severe phenotype expression. A larger ratio of the interparietal to the intercoronal distance could mean a more severe condition of trigonocephaly (Bottero, Lajeunie, & Arnaud et al., 1998).
4) More severe (a higher percentage) digital impressions will result in more psychopathology, like ADHD- and autism-like behaviors in children with trigonocephaly.
5) The presence of elevated intracranial pressure will result in more psychopathology, like ADHD- and autism-like behaviors in children with trigonocephaly.
6) It is expected that children with trigonocephaly from parents with a lower Social Economic Status (SES) will have a worse outcome compared to children from parents with a higher social economic status. Low SES children with trigonocephaly will experience more psychopathology, like ADHD- and autism like behaviors, compared to high SES children with trigonocephaly.

2. Method

2.1. Description of the sample

The subjects and their parents were recruited from the Craniofacial Center of Erasmus Medical Center Rotterdam – Sophia Children's Hospital. Inclusion criteria were (1) a diagnosis of a mild or severe form of trigonocephaly, and (2) an age between 1 and 8 years.

The parents of approximately 60 patients who met the inclusion criteria were contacted by letter and by telephone informing them about the research project. In total, 47 children and their parents participated in the study. This results in a response rate of 78.3%. The remainder 13 children were willing to participate and will be invited again for continuation research of the present study. The research period of the present study was too short, to test all 60 children at once. The parents and their children did not receive any compensation for participating in this research project.

From October 2005 to July 2006, the sample of 47 children (40 boys and 7 girls) diagnosed with trigonocephaly, were tested in Erasmus Medical Center Rotterdam – Sophia Children's Hospital. Their mean age was 4.6 years (*SD* = 2.3; range 1.10 – 8.6). Strikingly and by coincidence, it was found that ear tubes were present in 10 (37.0%) out of 27 children. For the remainder 20 children, the numbers were unknown.

The educational level of the parents varied from lower to higher education. Among the mothers, 23.4% was lower educated; 42.6% was middle educated and 34.0% was higher educated. Among the fathers, 19.1% was lower educated; 42.6% was middle educated and 38.3% was higher educated. The general educational level of the Dutch population is as follows: 34% lower education, 41% middle education, and 25% higher education (Centraal Bureau van de Statistiek (CBS), Statline, 2005). Looking at the percentage of lower and higher educated mothers and fathers, the educational level of the participating parents is considerably higher than that of the general population in the Netherlands.

2.2. Instruments

Cognitive impairments were determined through different measurements of IQ. Psychopathology in general, was measured through a questionnaire examining internalizing and externalizing problems. This questionnaire was filled out by the parents and in some cases also by their schoolteachers. ADHD- and autism-like behaviors were measured through several ADHD- and autism screening instruments/questionnaires, filled out by the parents. ADHD-like behaviors were also measured through a diagnostic interview with both parents if possible. Table 1 displays an overview of the various measurement instruments and their age ranges. Table 2 shows the number of subjects per instrument and the ages at which the test was being administered in the present study.

The presence of additional brain anomalies was determined through diagnoses of a physician. The gravity of the phenotype expression (ratio of the interparietal to the intercoronal distance) was inquired through measurement of CT-scans which were taken after birth, before their first birthday and before surgery. Whether the child has a syndromic or nonsyndromic form of trigonocephaly, has been determined through diagnoses of a physician. The presence of elevated intracranial pressure has also been determined through diagnosis of the surgeon, preoperatively. The presence and severity of digital impressions has been obtained from pre-surgical x-rays. Finally, data on Social Economic Status (SES) will be acquired from data of the educational level of the parents of the children with trigonocephaly.

Table 1

Overview of Measurement instruments and their age ranges, informants/subjects

Test domain	Instrument	Child	Parent(s)	Teacher(s)	Age (in years)
Intelligence	Mullen Scales of Early Learning (MSEL)	X			1 - 5
	WPPSI-R	X			4 – 7
	WISC-III	X			6 – 17
ADHD-screening	DISC-IV		X		6 – 18
	Disruptive Behavior Disorders (DBD)		X	X	6 - 12
Autism-screening	M-Chat		X		1-3
	Social Communication Questionnaire (SCQ)		X		4-8
Internalizing and externalizing problems	CBCL 1 ½ - 5		X	X	1 ½ - 5
	C-TRF 1 ½ - 5		X	X	1 ½ - 5
	CBCL 6 – 18		X	X	6 – 18
	TRF 6 – 18		X	X	6 – 18

Table 2.

Number of subjects per instrument, numbers of missing data and age of administration

Instrument	*n*	Missing data *n*	Age (in years)
MSEL	20	0	1 – 3
WPPSI-R	16	0	4 – 6
WISC-III	11	0	7 – 8
DISC-IV	18	0	6 – 8
DBD, rated by mother	15	2	6 – 8
DBD, rated by father	12	5	6 – 8
M-Chat	20	0	1 – 3
SCQ	24	2	4 – 8
CBCL, rated by mother	44	3	1 ½ - 8
CBCL, rated by father	38	9	1 ½ - 8
C-TRF	15	32	1 ½ - 8

2.2.1. Intelligence

Intelligence will be measured through three different IQ tests.

2.2.1.1. Mullen Scales of Early Learning (MSEL)

The Mullen Scales of Early Learning (MSEL; Mullen, 1995) measure global and motor functioning in children of 1 to 68 months of age. The MSEL consists of a Gross Motor Scale and four cognitive scales: 1) Visual Reception, 2) Fine Motor, 3) Receptive Language, and 4) Expressive Language. The Gross Motor Scale measures central motor control and mobility. The Visual Reception Scale measures a child's performance in processing visual patterns. The Fine Motor Scale tests a child's visual motor-ability. The Receptive Language Scale provides a measure of the ability to process linguistic input. Finally, the Expressive Language Scale measures a child's ability to use language productively. The four cognitive scales together form a composite score called the Early Learning Composite. This composite score provides a measure of the general cognitive factor underlying all cognitive performances. The Gross

Motor Scale can be administered from birth through 33 months and each cognitive scale covers the age range of birth through 68 months. The MSEL in this study will be used in children of 1 ½ up to 3 years of age. The MSEL consists of four scales of cognitive functioning and one motor scale. Very satisfactory internal consistency has been reported for the five Mullen Scales. The composite score demonstrate high internal reliability. The test-retest and interscorer reliability is also satisfactory to high for the five Mullen scales. Besides the high internal reliability of .91 of the MSEL, there is also good support for the construct validity of this test. Interscorer reliability varied from .91 to .99 (Mullen, 1995).

2.2.1.2. Wechsler Preschool and Primary Scale of Intelligence and Wechsler Intelligence Scale for Children (WPPSI/WISC-III)

Intelligence in the older children will be examined through the short version of the Wechsler Preschool and Primary Scale of Intelligence – Revised (WPPSI-R; Wechsler, 1997) and the short version of the Wechsler Intelligence Scale for Children – Third edition (WISC-III; Wechsler, 1992). Both tests assess general intelligence. Originally the WPPSI-R consists of 12 subtests and the WISC-III consists of 13 subtests. The WPPSI-R can be administered in children of 3 to 7 years of age and the WISC-III is developed for children of 6 to 17 years of age. In the present study the WPPSI-R will be administered in children of 4 and 6 years of age and the WISC-III will be administered in children of 7 and 8 years of age. Both the WPPSI-R and the WISC-III consists of scales of verbal and performance IQ that together form the full scale IQ. The short form of the WISC-III consists of two verbal subtests en two performance tests. We will use the verbal subtests Similarities and Vocabulary and the performance tests Picture Completion and Block Design. The verbal subtest Similarities measures logical abstract reason capacity and the verbal subtest Vocabulary measures vocabulary and the capacity to describe terms. The performance subtest Picture Completion measures the perception of details and the capacity to imagine visually. The performance test Block Design measures the recognition of patterns, visual analysis, visual orientation and visual synthesis. An intelligence score between 85 and 115 is taken as average. Acceptable reliability has been reported for the subtests of the WPPSI-R and WISC-III, .91 and .80 respectively (Wechsler, 2002).

2.2.2. ADHD-screening

2.2.2.1. Diagnostic Interview Schedule for Children (DISC-IV)

The 4th version of the Diagnostic Interview Schedule for Children (DISC-IV; Shaffer et al., 1993) will be administered to measure ADHD-like behaviors. This interview covers diagnostic criteria as specified in the Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV). The DISC-IV is organized into six diagnostic categories: 1) Anxiety Disorders, 2) Mood Disorders, 3) Disruptive Disorders, 4) Substance-use Disorders, 5) Schizophrenia, and 6) Miscellaneous Disorders. The parents will only be questioned about the disruptive module of this interview. The disruptive module consists of three scales: 1) Attention Deficit Disorder (ADHD), 2) Oppositional Defiant Disorder (ODD), and 3) Conduct Disorder (CD). Information from other diagnostic modules is not necessary in order to assign a diagnosis. The diagnostic sections assess whether the child has ever had any diagnosis presence within the past year, currently and also not currently in the past year. The questions of the DISC-IV are highly structured. Good test-retest reliability of .79 has been reported for the disruptive module of the DISC-IV (NIMH-DISC, 1998). The DISC-IV is suitable for parents with children of ages 6 to 17 and in the present study will be administered in parents of children of 6 up to 8 years of age.

2.2.2.2. Disruptive Behavior Disorders (DBD) rating scale

The paper/pencil questionnaire, the Dutch translation of the Disruptive Behavior Disorders rating scale, the Vragenlijst voor Gedrag van Kinderen (DBD; Oosterlaan, Scheres, Antrop, Roeyers, & Sergeant, 2000) will also be administered to measure behavioral problems like ADHD-like behaviors in children with trigonocephaly. The DBD consists of four scales: 1) Attention deficit, 2) Hyperactivity/impulsivity, 3) Oppositional Defiant Disorder (ODD), and 4) Conduct Disorder (CD). The DBD is meant for children of 6 – 12 years of age. In a sample of 1401 children from 6 up to 12 years of age, moderate to good reliability have been reported for the DBD. The reliability (homogeneity), expressed in Cronbach's α, of the scales Attention deficit, Hyperactivity/impulsivity, and Oppositional Defiant Disorder are around .90. The reliability of the Conduct Disorder scale is considerably lower, .60 (Oosterlaan, Scheres, Antrop, Roeyers, & Sergeant, 2000).

2.2.3. Autism-screening

2.2.3.1. Modified Checklist for Autism in Toddlers (M-Chat)

Behavioral problems will also be measured through the Dutch version of the Modified Checklist for Autism in Toddlers (M-Chat; Robins, Fein, & Barton, 1999). This paper/pencil questionnaire measures whether children between 1 and 3 years of age exhibit behavioral characteristics of autism. The M-Chat consists of 23 yes/no items. The M-chat is not a tool for diagnosing autism, but its purpose is to provide a first impression. Not all children who score high on this checklist will meet criteria for a diagnosis on the autism spectrum, but these children should be evaluated in more depth. The psychometric properties of this instrument are currently being evaluated at 18 and 24 months of age in a general population. An internal reliability of .85 has already been reported for the M-Chat. (Robins, Fein, Barton, Green, 2001).

2.2.3.2. Social Communication Questionnaire (SCQ)

The Social Communication Questionnaire (SCQ; Berument, Rutter, Lord, Pickles & Bailey, 1999) will also be used to measure autism-like behaviors. This paper/pencil questionnaire was originally developed as the Autism Screening Questionnaire by Berument et al. (1999). The items of the SCQ are dividable according to the scales of the ADI-R (Lord et al., 1994): 1) Reciprocal social interaction, 2) Communication, and 3) Restricted, repetitive, and stereotype behavior patterns. The SCQ consists of 40 yes/no items and are derived from the Autism Diagnostic Interview-Revised (ADI-R: Lord et al., 1994) and is now recognized as one of the best validated and most widely used instruments in the diagnosis of autism and related disorders. A standard cutoff score of 15 points or higher is used for differentiating between autism, autism related disorders and no autism. The SCQ was found to have good discriminative ability with respect to differentiation between PDD and non-PDD diagnoses. A cutoff score of 15 points or more gave a sensitivity of .96 and a specificity of .80 for autism versus other diagnoses (Howlin & Karpf, 2004). Moderate to good internal consistency, .84 to .93 have been found for the SCQ (Berument, Rutter, Lord, Pickles, & Bailey, 1999). The SCQ can be administered from the age of 4 and has to be filled out by the parents. Like every screening instrument, the SCQ is not suitable for making an individual diagnosis. Good reliability and validity have been reported for the SCQ (Berument, Rutter, Lord, Pickles, & Bailey, 1999).

2.2.4. Internalizing and externalizing behaviors

2.2.4.1. Child Behavior Checklist/Child-Teacher Report Form (CBCL/C-TRF)

The Dutch version of the Child Behavior Checklist for children of 1 ½ to 5 years of age (CBCL 1 ½ - 5; Achenbach, 1992) is one of the questionnaires that have to be filled out by the parents or other caregivers. The Dutch version of the Caregiver-Teacher Report Form for children of 1 ½ to 5 years of age (C-TRF 1 ½ - 5; Achenbach, 1997) will be filled out by the schoolteacher of the child. The older children themselves as well as their schoolteachers, also fill out the CBCL and C-TRF for the ages of 6 to 18 years. The CBCL and the C-TRF consist of seven scales: emotionally/reactive, anxious/depressed, somatic complaints, withdrawn, sleeping problems, attention problems and aggressive behavior. Respondents have to rate 99 item problems as *0 = not true, 1 = somewhat true*, and *2 = very true* or *often true*. Several items ask for some descriptions of the problems. For item 100, respondents are asked to write down additional problems that were not previously listed. The scales can be divided into an internalizing-, externalizing-, and total problem scale (sum of internalizing and externalizing problems). A *T*-score of 63 (90^{th} percentile) or higher is considered as a clinical score. The purpose of these questionnaires is for caregivers, schoolteachers and children to give an indication of how they function in different areas. The CBCL and C-TRF are questionnaires that focus on emotional and behavioral problems. Good test-retest reliability has been reported for both the CBCL as the C-TRF, .85 and .81 respectively (Achenbach, 1992).

2.3. Procedure

The study was approved by the Medical Ethical Commission of the Erasmus Medical Center Rotterdam. Participation occurred voluntarily; the children and their parents were able to withdraw from the study at any time.

Data were collected through paper/pencil questionnaires, test performances and medical files. The questionnaires were filled out by the parents and in some cases, also by their schoolteacher. Considering the young ages and their short attention span, relatively short test performances were chosen. The testing session lasted for approximately 2-3 hours in total.

IQ tests took place at the Erasmus Medical Center Rotterdam – Sophia Children's Hospital. The test was administered by researchers of the present study. The diagnostic interview also took place at the Erasmus Medical Center Rotterdam – Sophia Children's Hospital. When possible, the parents completed the questionnaires in the waiting room, while their child was

being tested. Due to a lack of time, some parents completed the questionnaires at home and returned them by post mail. The schoolteachers returned their questionnaires by post mail also.

2.4. Statistical methods

The present study contains a cross-sectional research design.

Different instruments, of the same kind, were chosen for the different age ranges of the subjects of the research sample. The parents and the schoolteachers of the subjects completed similar measurement instruments dependent on the age of the subjects. Subsequently, the outcomes of the measurement instruments are compared with norm groups of children without trigonocephaly, derived from the manuals.

Descriptive statistics were used to analyze both dependent, as independent variables. One-sample *t*-tests were used to assess differences in mean IQ-scores, ADHD- and autism-like behaviors, and internalizing and externalizing behaviors between the sample group versus the normal population, that served as control group. The risk factors (additional brain anomalies, syndromic or nonsyndromic forms, phenotype expression, digital impressions, intracranial pressure and SES) of psychopathology, like ADHD and autism-like behaviors, in children with trigonocephaly, were analyzed through mean comparison analyses, linear regression and one-way ANOVA. The risk factors were taken as predictor in regression analysis, to predict the dependent variables like ADHD- and autism-like behaviors and internalizing and externalizing problems. The risk factors served as factor variable in the one-way ANOVA to examine if there was a main effect of one of the risk factors on the dependent variables like ADHD- and autism-like behaviors and internalizing and externalizing problems as well. Bar charts were performed to check on the assumption of normality of the used analyses. The normal distributions were of tolerable and acceptable level.

2.5. Missing data

Between October 2005 and July 2006, collection of data was divided into two research periods. In the first research period from October 2005 until December 2005 the following variables were examined: intelligence, autistic behavior, internalizing and externalizing problems, trigonocephaly type (syndromic or nonsyndromic), phenotype expression, additional brain anomalies and SES. In the second research period from May 2006 until July 2006, variables like intelligence, ADHD- and autism-like behaviors, internalizing and externalizing problems, additional brain anomalies, trigonocephaly type, digital impressions, intracranial pressure, and SES were examined. Obviously, some variables differ in the first

and second research period. This explains the missing data for the phenotype expression in 32 children and the missing data of digital impressions in 26 children. Due to a limited period of time of the second research period, the present study did not manage to gather the variables different from the first research period and vice versa.

Some questionnaires are only available for a certain age range, e.g. the DBD, M-chat, which is also causes gaps in the data file, but can not be seen as missing data.

For the internalizing and externalizing problems, measured by the CBCL- and C-TRF, scores of the father are missing for 7 children. C-TRF scores of the schoolteacher are missing for 32 children. CBCL and C-TRF scores were missing due to (1) no return of questionnaires and (2) broken families, in which the father was not involved in parenting. Five fathers did not return the questionnaire and in two cases the father was not involved in parenting. Table 3 shows the available and missing data of both measurement instruments and risk factors of neurobehavioral problems.

Table 3.

Available and missing data per instruments and risk factors

Instrument/risk factor	No. available	No. missing
Instruments		
MSEL	20	0
WPPSI-R	16	0
WISC-III	11	0
DISC-IV	18	0
DBD mother	15	2
DBD father	12	5
M-Chat	20	0
SCQ	24	2
CBCL mother	44	3
CBCL father	40	7
C-TRF	15	32
Risk factors		
Additional brain anomalies	47	0
Phenotype expression	15	32
Type trigonocephaly	47	0
Digital impressions	21	26
Intracranial pressure	47	0
SES	47	0

Note. Number available and missing data is expressed in number of subjects. The instruments are only suitable for a certain age range, which explains not reaching the total sum of 47 subjects at all times.

3. Results

3.1. Descriptive Statistics

3.1.1. ADHD-screening

3.1.1.1. Diagnostic Interview Schedule for Children (DISC-IV)

Since the DISC-IV interview is only suitable for parents of children of 6 years of age and older, 17 interview outcomes are available. None of this 17 children corresponded fully to the DSM-IV criteria of ADHD or any of the other disruptive behavior disorders, so no diagnosis of ADHD, ODD or CD could be made.

3.1.1.2. Disruptive Behaviors Disorders (DBD)

The DBD is suitable for children between 6-12 years of age and was completed by 15 mothers and 12 fathers. Table 4 and 5 show the frequencies and percentages of the DBD outcomes rated by mother and father. One child was rated by both his parents to be in the clinical range of the Attention deficit scale, in the clinical range of the Hyperactivity/impulsivity scale and in the sub-clinical range of the CD scale. The other child, whose amount of problems also corresponded with the clinical range of the Attention Deficit scale, was only rated by his mother en not by his father. This also applies to child, whose amount of problems corresponded with the sub-clinical range of the Hyperactivity/impulsivity scale. The children, who, according to their parents, met the criteria of the (sub) clinical range of the four different scales of the DBD, were all boys.

Table 4.

Frequencies and percentages of the four DBD scales rated by mother

	Mother (n = 15)					
	Normal range		Sub-clinical range		Clinical range	
DBD scale	*n*	*Percentage*	*n*	*Percentage*	*n*	*Percentage*
Attention deficit	13	85.7	0	0	2	14.3
Hyperactivity/impulsivity	13	85.7	1	7.1	1	7.1
ODD	14	92.9	1	7.1	0	0
CD	13	85.7	2	14.3	0	0

Table 5.

Frequencies and percentages of the four DBD scales rated by father

	Father (n = 12)					
	Normal range		Sub-clinical range		Clinical range	
DBD scale	*N*	*Percentage*	*n*	*Percentage*	*n*	*Percentage*
Attention deficit	11	92.3	0	0	1	7.7
Hyperactivity/impulsivity	11	92.3	0	0	1	7.7
ODD	12	100.0	0	0	0	0
CD	11	92.3	1	7.7	0	0

The mean scores of each scale, rated by both parents, were compared with the means scores of a norm group (N = 260) of the same age range (6-8 years). Through a one-sample t-test, one significant difference was noticeable between the mean scores on the ODD scale (M = 1.25, SD = 1.42), rated by father, and the mean score of the norm group on the ODD scale (M = 3.01, SD = 3.45). Fathers had a significantly lower rating on the ODD scale ($t(11) = -4.28$, p = .001), compared to the norm group rating on the ODD scale. This difference was significant at an alpha of .05. Table 6 and 7 present an overview of descriptive statistics and p-values of each scale, of the sample and the norm group.

Table 6.

Descriptive statistics and p-values per scale for research sample (rated by mother) and norm group

	Research sample Mother (n = 15)		Norm group (N =260)		p-value
DBD scale	*M*	*SD*	*M*	*SD*	*p*
Attention deficit	4.87	6.46	3.85	4.08	.552
Hyperactivity/impulsivity	3.20	5.53	4.64	4.79	.330
ODD	2.07	2.87	3.01	3.45	.223
CD	0.47	0.92	0.57	1.29	.669

Table 7.

Descriptive statistics and *p*-values per scale for research sample (rated by father) and norm group

	Research sample Father (n = 12)		Norm group (N =260)		*p*-value
DBD scale	*M*	*SD*	*M*	*SD*	*p*
Attention deficit	4.00	5.66	3.85	4.08	.928
Hyperactivity/impulsivity	3.08	4.98	4.64	4.79	.302
ODD	1.25	1.42	3.01	3.45	.001*
CD	0.42	0.90	0.57	1.29	.567

*Note: *p < .05*

The ratings of father and mother, about their child, did not significantly differ from each other.

3.1.2. Autism-screening

3.1.2.1. Modified Checklist for Autism in Toddlers (M-Chat)

The M-Chat is meant for children between 1 and 3 years of age. Outcomes were available for 20 children of this age range. 2 (10%) out of 20 children were screened positive for autism by their parents.

3.1.2.2. Social Communication Questionnaire (SCQ)

The SCQ is suitable for children from 4 years of age. Outcomes were available for 24 children. The majority, 19 (79.2%) out of 24 children scored below the critical cutoff point of 15. according to their parents. 5 (20.8%) out of 24 children scored equally or above the cutoff point of 15, which corresponds to a clinical range. Four of the children who scored above the cutoff point, were boys. Table 8 shows the frequencies and percentages of the SCQ outcomes.

Table 8.

Frequencies and percentages of SCQ scores

	SCQ	
Score	*n*	*percentage*
< 15 (normal range)	19	79.2
> 15 (clinical range)	5	20.8
Total	24	100.0

The mean score of the research sample (n = 24) was compared to the mean score of an autism reference group (N = 71), using a one-sample t-test. The mean score of the research sample (M = 7.46, SD = 5.82), differed significantly of the mean score of the autism reference group (M = 18.30, SD = 6.60). The research sample, children with trigonocephaly, scored significantly lower on the SCQ, compared to the reference group, which consisted of children with autism (t(-9.21) = 23, p = .000). In Table 9 the descriptive statistics and p-values are presented for the mean SCQ score of the research sample and the autism reference group.

Table 9.

Descriptive statistics and p-values of research sample and autism reference group

	Research sample (n = 24)		Autism reference group (N = 71)		p-value
SCQ	*M*	*SD*	*M*	*SD*	*p*
Score	7.46	5.82	18.30	6.60	.000*

*Note. *p<.05*

3.1.3. Internalizing and externalizing behaviors

3.1.3.1. Child Behavior Checklist/Child-Teacher Report Form (CBCL/C-TRF)

Raw scores were transformed into T-scores. A T-score above 63 is considered as a clinical score. Only the three main scales, Internalizing-, Externalizing-, and Total problems, were analyzed. CBCL outcomes were obtained from 44 mothers, 38 fathers, and C-TRF outcomes were obtained from 15 schoolteachers. The mothers reported a mean T-score of 49.8 (SD = 10.8) on the Internalizing problem scale; a mean T-score of 49.0 (SD = 11.0) on the Externalizing problem scale; and a mean T-score of 49.8 (SD = 8.7) on the Total problem scale. The fathers reported slightly lower mean T-scores, compared to the mothers: 47.2 (SD = 10.6) on the Internalizing problem scale; 46.0 (SD = 9.5) on the Externalizing problem scale; and 46.0 (SD = 10.8) on the Total problem scale. The 15 schoolteachers reported a mean T-score of 51.3 (SD = 11.2) on the Internalizing problem scale; a mean T-score of 49.7 (SD = 10.5) on the Externalizing problem scale; and a mean T-score of 50.4 (SD = 11.1) on the Total problem scale. Table 10 shows the descriptive statistics of the CBCL and C-TRF outcomes rated by mother, father and schoolteacher.

Table 10.

Descriptive statistics of CBCL/C-TRF outcomes rated by mother, father and schoolteacher

	Mother (n = 44)		Father (n = 38)		Schoolteacher (n =15)	
CBCL scale	*M*	*SD*	*M*	*SD*	*M*	*SD*
Internalizing problems	49.8	10.8	47.2	10.6	51.3	11.2
Externalizing problems	49.0	11.0	46.0	9.5	49.7	10.5
Total problems	49.8	8.7	46.0	10.8	50.4	11.1

Note. Descriptive statistics in T-scores

A one-sample *t*-test did not reveal any significant differences between the mean CBCL scores of the mothers and the mean *T*-score of 50 (*SD* = 10) of the normal population.

Comparing mean CBCL scores of the fathers with the mean *T*-score of 50 (*SD* = 10) of the normal population, by using a one-sample *t*-test, resulted in two significant differences. The mean CBCL outcomes of the fathers, on the Externalizing problem scale ($t(37) = -2.61$, $p = .013$) and Total problem scale ($t(37) = -2.31$, $p = .026$), were significantly lower, compared to the mean *T*-score of 50 of the normal population.

A one-sample *t*-test did not reveal any significant differences by comparing the mean C-TRF outcomes to the mean *T*-score of 50, of the normal population. Table 11 shows the descriptive statistics of the CBCL and C-TRF *T*-scores rated by mother, father and schoolteacher and the accompanying *p*-values.

Table 11.

Descriptive statistics CBCL/C-TRF outcomes and *p*-values

	CBCL/C-TRF scale						
		Internalizing problems		Externalizing problems		Total problems	
Informant	*n*	*M* (*SD*)	*p*	*M* (*SD*)	*p*	*M* (*SD*)	*p*
Mother	44	49.8 (10.8)	.889	49.0 (11.0)	.550	49.8 (8.7)	.863
Father	38	47.7 (10.6)	.110	46.0 (9.5)	.013*	46.0 (10.8)	.026*
Schoolteacher	15	51.3 (11.2)	.669	49.7 (10.5)	.904	50.4 (11.1)	.891

Note. p-values are based on mean comparisons between research sample and normal population

**p<.05*

3.1.4. Intelligence

IQ-scores were available for all 47 subjects. Three IQ-tests were used to obtain IQ-scores. Table 12 presents an overview of the numbers of subjects per IQ-test and the age ranges at which the test was administered.

Table 12.

Frequencies, percentages of numbers of subjects and their age ranges

IQ-test	*n*	*Percentage*	*Age (years)*
MSEL	20	42.56	1 – 3
WPPSI-R	16	34.04	4 – 6
WISC-III	11	23.40	7 – 8
Total	47	100.00	

The mean IQ-score was 104.04 (*SD* = 25.11). Through a one sample *t*-test, the IQ-scores of the trigonocephaly sample were compared to the mean IQ-score of 100 (*SD* = 15) of the normal population. The mean IQ-score of the subjects did not significant differ from the mean IQ-score of the normal population ($t(46) = 1.01$, $p = .275$) at an alpha of .05. 10.6% ($n = 5$) of the children scored more than two standard deviations below the mean (IQ-score < 70). An IQ-score below 70 is considered as mental retardation according to the DSM-IV criteria. 14.9% ($n = 7$) of the children scored one standard deviation below the mean (IQ score < 85). The majority, 40.5% ($n = 19$) of the children scored between 85 and 115 which, according to the DSM-criteria, is considered as an average IQ-score. 34.0% ($n = 16$) of the children scored one or more standard deviations above the mean (IQ-score > 115). Table 13 shows the frequencies and percentages of the IQ-scores.

Table 13.

Frequencies and percentages of IQ-scores

	IQ	
Score	*n*	*Percentage*
< 70	5	10.6
< 85	7	14.9
85 – 115	19	40.5
> 115	16	34.0
Total	47	100.0

3.1.5. Risk factors

None of the 47 subjects appeared to have any brain anomalies. Out of the 47 children, 15 children (31.91%) were diagnosed with a syndromic form of trigonocephaly. Among the children with a syndromic form of trigonocephaly, there was only one girl.

Data about the phenotype expression, measured by the ratio of the interparietal to the intercoronal distance, was available for 15 children. Two of them were girls. Their mean ratio was 1.33 (*SD* = 0.06, *range* = 1.28 - 1.44). Shimoji et al. (2002) found a mean ratio of 1.21 (*SD* = 0.03) for normal children (*n* = 35). A one-sample *t*-test did reveal a significant difference between the mean phenotype expression of the research sample and the mean phenotype expression of the normal children ($t(14) = 7.62$, $p < .001$). The research sample had an on average higher ratio of phenotype expression compared to the mean ratio of phenotype expression of the normal group of children, mentioned by Shimoji et al. (2002). Table 14 presents the descriptive statistics of the phenotype expression of the research sample and the normal group of children.

Table 14.

Descriptive statistics of research sample and normal children, and *p*-value

	Reference group				
	Research sample (*n* = 15)		Normal children (*n* = 35)		*p*-value
	M	*SD*	*M*	*SD*	*p*
Phenotype expression	1.33	0.06	1.21	0.03	.000*

Note: Reference group from Shimoji et al. (2002)

**p<.001*

Data of digital impressions were available for 21 (46.8%) out of 47 children. The mean percentage of digital impressions was 8.34% (*SD* = 17.63, *range* = 0 - 82.02). The 21 children, of whom data on digital impressions were available, consisted of 3 girls (*M* = 8.67, *SD* = 6.58) and 18 boys (*M* = 4.20, *SD* = 6.41).

Among the 47 children, 5 (10.64%) were having elevated intracranial pressure, of which 2 were girls and 3 were boys. Table 15 shows the frequencies, percentages and available descriptive statistics of these risk factors of neurobehavioral problems in children with trigonocephaly.

Table 15.

Frequencies, percentages and descriptive statistics of risk factors

	Research sample (*n* = 47)				Reference group normal children (*n* =35)		
Variable	*n*	*Percentage*	*M*	*SD*	*M*	*SD*	*p-value*
Brain anomalies							
Present	0	0					
Not present	47	100.0					
Type trigonocephaly							
Syndromic	15	31.91					
Nonsyndromic	32	68.09					
Phenotype expression			1.33	0.06	1.21	.003	.000*
Digital impressions			8.34	17.63			
Intracranial pressure							
Present	5	10.64					
Not present	42	89.36					

*Note. *p<.001*

3.2. Gender Differences Dependent Variables

3.2.1. Behavioral problems measured by DBD

Fathers reported on average more ODD problems in boys (*M* = 1.5, *SD* = 1.43), compared to girls (*M* = 0.00, *SD* = 0.00). This effect was significant (*t*(1) = -3.31, *p* = .009). Again, it should be mentioned that only 12 DBD ratings of father were available, which consisted of 2 girls and 10 boys. Mothers did not significantly discriminate in their ratings between boys and girls.

3.2.2. Autism-like behaviors measured by SCQ

Comparison of means did not reveal any significant differences. Boys (n = 21) and girls (n =3) did not significantly differ in their scores on the SCQ, rated by their parents.

3.2.3. Internalizing and externalizing behaviors measured by CBCL/C-TRF

Parents reported no significant difference in the amount of internalizing and externalizing problems between boys and girls. Schoolteachers however, reported on average more internalizing problems for girls, compared to boys. This effect was significant ($t(13) = 2.27$, $p = .041$) at an alpha of .05. It should be noted that there were only ratings available of 15 schoolteachers, who in total, rated 2 girls and 13 boys.

3.2.4. Intelligence

Girls (n = 7, M = 111.86, SD = 13.95) had an on average higher IQ-score compared to boys (n = 40, M = 102.68, SD = 26.47). This difference was not significant ($t(45) = .891$, $p = .378$) at an alpha of .05.

3.3. One-Way ANOVA and Regression Analysis

Not all variables will be included into the regression and ANOVA analysis. Brain anomalies were not found to be present in the current sample, and will therefore be excluded. Regression analysis was performed on continues independent variables like phenotype expression and digital impressions and One-way ANOVA was performed on categorical independent variables like trigonocephaly type, intracranial pressure and SES. As far as regression analysis is concerned, an R^2 of .10 is considered as small, .30 as moderate, and .50 as large (Aron & Aron, 2003).

3.3.1. Ttrigonocephaly type as factor variable and DBD scores as dependent variable

The current study was interested in if the type of trigonocephaly (syndromic/nonsyndromic) made any difference in the DBD scores, rated by both mother and father. Analysis was performed on the four DBD scales, with trigonocephaly type as factor variable, by using a one-way ANOVA. Analysis of the four DBD scale scores, rated by mother, did not reveal any significant main effects of trigonocephaly type: Attention deficit ($F_{1,14} = 1.67$, $p = .299$), Hyperactivity/impulsivity ($F_{1,14} = 2.43$, $p = .143$), Oppositional Defiant Disorder ($F_{1,14} = .473$, $p = .504$), and Conduct Disorder ($F_{1,14} = 2.89$, $p = .113$).

Analysis of the four DBD scale scores, rated by father, did not reveal any significant main effects of trigonocephaly type either: Attention deficit ($F_{1,11}$ = 4.45, p = .061), Hyperactivity/impulsivity ($F_{1,11}$ = 3.42, p = .093), Oppositional Defiant Disorder ($F_{1,11}$ = .171, p = .688), and Conduct Disorder ($F_{1,11}$ = 2.97, p = .116). Apparently, the type of trigonocephaly did not make any difference in DBD scores, rated by both parents. Table 16 displays the descriptive statistics per trigonocephaly type and per DBD scale, rated by mother and father.

Table 16.

Descriptive statistics per trigonocephaly type and per DBD scale rated by mother and father

	Trigonocephaly type			
DBD scale	*Nonsyndromic*		*Syndromic*	
Mother (n = 15)	*M*	*SD*	*M*	*SD*
Attention deficit	3.60	5.32	7.40	8.38
Hyperactivity/impulsivity	1.70	3.74	6.20	7.66
ODD	1.70	3.27	2.80	1.92
CD	0.20	0.42	1.00	1.41
Father (n = 12)				
Attention deficit	1.88	2.59	8.25	8.10
Hyperactivity/impulsivity	1.38	1.77	6.50	7.77
ODD	1.13	1.55	1.50	1.29
CD	0.13	0.35	1.00	1.41

3.3.2. Trigonocephaly type as factor variable and SCQ scores as dependent variable

By using a one-way ANOVA, it was investigated if the type of trigonocephaly (syndromic/nonsyndromic) made any difference in SCQ score. By taking the trigonocephaly type as factor variable and SCQ scores as dependent variable, this did not lead to a significant main effect of trigonocephaly type ($F_{1,23}$ = 3.17, p = .089). Table 17 displays the descriptive statistics of the SCQ scores per trigonocephaly type.

Table 17.

Descriptive statistics of SCQ scores per trigonocephaly type

	Trigonocephaly type			
	Nonsyndromic		*Syndromic*	
	M	*SD*	*M*	*SD*
SCQ score (*n* = 24)	6.42	5.57	11.40	5.55

3.3.3. Trigonocephaly type as factor variable and CBCL/C-TRF scores as dependent variable

Once more a one-way ANOVA was used to examine if the type of trigonocephaly (syndromic/nonsyndromic) made a difference in CBCL and C-TRF scores. The CBCL and C-TRF scores were analyzed per informant and per scale: Internalizing problem scale, Externalizing problem scale, and Total problem scale.

When the trigonocephaly type was taken as factor variable and the CBCL scale scores, rated by mother, as dependent variable, it did result in one significant main effect of trigonocephaly type on the Total problem scale ($F_{1,43} = 7.39$, $p = .010$). For the other two scales, trigonocephaly type did not make any difference: Internalizing problem scale ($F_{1,43} = 2.44$, $p = .126$) and Externalizing problem scale ($F_{1,43} = 2.72$, $p = .107$).

When the trigonocephaly type was taken as factor variable and the CBCL scale scores, rated by father, as dependent variable, it revealed two significant main effects of trigonocephaly type on the Externalizing problem scale ($F_{1,37} = 7.58$, $p = .009$) and the Total problem scale ($F_{1,37} = 11.24$, $p = .002$). Trigonocephaly type did not make any difference for the Internalizing problem scale ($F_{1,37} = 3.41$, $p = .073$). The results of the CBCL, rated by mother and father, are displayed in Table 18.

Table 18.

Descriptive statistics of CBCL/C-TRF scores per trigonocephaly type

	Trigonocephaly type			
CBCL scale	*Nonsyndromic*		*Syndromic*	
Mother (n = 44)	*M*	*SD*	*M*	*SD*
Internalizing problems	48.07	11.58	53.43	8.01
Externalizing problems	47.17	12.27	52.93	6.40
Total problems	47.50	8.47	54.64	7.27
Father (n = 38)				
Internalizing problems	45.22	9.89	52.00	11.15
Externalizing problems	43.48	8.71	52.09	8.84
Total problems	42.63	9.44	54.09	9.85

When the C-TRF scale scores, rated by the schoolteacher were taken as dependent variable and trigonocephaly type as factor variable, it did not lead to any significant main effects of trigonocephaly type: Internalizing problem scale ($F_{1,14}$ = 1.71, p = .214), Externalizing problem scale ($F_{1,14}$ = .004, p = .954), and Total problem scale ($F_{1,14}$ = 2.26, p = .157). The results are displayed in Table 19.

Table 19.

Descriptive statistics of C-TRF scores per trigonocephaly type

	Trigonocephaly type			
C-TRF scale	*Nonsyndromic*		*Syndromic*	
Schoolteacher (n = 15)				
Internalizing problems	49.42	11.12	52.00	11.15
Externalizing problems	43.48	8.71	52.09	8.84
Total problems	48.33	11.32	54.09	9.85

3.3.4. Phenotype expression as predictor and CBCL scores as dependent variable

Data on phenotype expression was only available for 15 subjects. For these 15 subjects, there was no information available, obtained by the DBD, SCQ and C-TRF. That is why regression analysis could only be performed with CBCL scores, since these scores were available for almost every subject.

Regression analysis with phenotype expression as predictor and CBCL scores as dependent variable, did not lead to any significant results. The results are displayed in Table 20.

Table 20.

Regression analysis of phenotype expression on CBCL scores, rated by mother and father

	Predictor phenotype expression			
CBCL scale	*Beta*	*R*	R^2	*p*
Mother (*n* = 44)				
Internalizing problems	.094	.094	.009	.748
Externalizing problems	.288	.288	.083	.318
Total problems	.171	.171	.029	.559
Father (*n* = 38)				
Internalizing problems	-.363	.363	.132	.273
Externalizing problems	-.260	.260	.068	.440
Total problems	-.366	.336	.134	.268

3.3.5. Digital impressions as predictor and DBD scores as dependent variable

Regression analysis did not reveal any significant effects between the scores on the four scales of the DBD, rated by mother, and the digital impressions. Evidently, the R^2 of the digital impressions on the DBD scores of mother, are considerably low.

Regression analysis of the digital impressions on the DBD scores, rated by father, did not reveal any significant effects either. Again, the R^2's of the digital impressions on the DBD scores, rated by father, are rather low. The results, rated by both parents, are displayed in Table 21.

Table 21.

Regression analysis of digital impressions on DBD scores, rated by mother and father

	Predictor digital impressions			
DBD Scale	*Beta*	*R*	*R²*	*p*
Mother (*n* = 15)				
Attention deficit	.065	.065	.004	.832
Hyperactivity/Impulsivity	-.285	.285	.081	.345
ODD	.131	.131	.017	.670
CD	-.250	.250	.062	.410
Father (*n* = 12)				
Attention deficit	.197	.197	.039	.539
Hyperactivity/Impulsivity	-.142	.142	.020	.660
ODD	.079	.079	.006	.808
CD	.016	.016	.000	.962

3.3.6. Digital impressions as predictor and SCQ scores as dependent variable

With a R^2 of .130, the regression analysis of the digital impressions on the SCQ scores, rated by both parents, did not resulted in a significant effect ($F_{1,18} = 2.55$, $p = .129$).

3.3.7. Digital impressions as predictor and CBCL/C-TRF scores as dependent variable

Regression analysis was performed on the CBCL and C-TRF scores, with digital impressions as predictor. The CBCL-scores, rated by mother and father, were separately analyzed. The CBCL-scores were analyzed per informant and per scale, the Internalizing, Externalizing and Total problem scale. Regression analysis of the digital impressions on the three CBCL scales, rated by mother and father, did not lead to any significant effects. Table 22 displays the results of this regressions analysis.

Table 22.

Regression analysis of digital impressions on CBCL scores rated by mother and father

	Predictor digital impressions			
CBCL scale	*Beta*	*R*	*R²*	*p*
Mother (*n* = 44)				
Internalizing problems	.271	.271	.073	.262
Externalizing problems	-.032	.032	.001	.897
Total problems	.006	.006	.000	.979
Father (*n* = 38)				
Internalizing problems	.249	.249	.062	.335
Externalizing problems	.015	.015	.000	.955
Total problems	.125	.125	.016	.633

Performing regression analysis on the C-TRF scores rated by the schoolteacher, with digital impressions as predictor, ended up in two significant results. By taking the internalizing problems as dependent variable and the digital impressions as predictor, this resulted in a R^2 of .592 ($F_{1,9} = 11.59$, $p = .009$). This relation is positive and indicates that a higher percentage of digital impressions are associated with more internalizing problems in the child, according to ratings of the schoolteacher. Regression analysis on the C-TRF total problems, with digital impressions as predictor, revealed also a significant effect. This resulted in a R^2 of .591 (($F_{1,9} = 11.55$, $p = .009$). Thus, a higher percentage of digital impressions are again associated with more Total problems in a child, according to ratings of the schoolteacher. In Table 23, the results of regression analysis on the C-TRF scores, with digital impressions as predictor, are displayed.

Table 23.

Regression analysis of digital impressions on C-TRF scores rated by schoolteacher

	Predictor digital impressions			
CBCL scale	*Beta*	*R*	*R²*	*p*
Schoolteacher (*n* =9)				
Internalizing problems	.769	.769	.592	.009*
Externalizing problems	.378	.378	.143	.282
Total problems	.769	.769	.591	.009*

*Note. *p<.05*

3.3.8. Intracranial pressure as factor variable and DBD scores as dependent variable

The question was whether the presence of elevated intracranial pressure (ICP) would make a difference in DBD scores, rated by both parents. The presence or absence of ICP did lead to any significant main effects of ICP on the DBD scale scores, rated by mother: Attention deficit ($F_{1,14}$ = .437, p = .520), Hyperactivity/impulsivity ($F_{1,14}$ = .006, p = .938), Oppositional Defiant Disorder ($F_{1,14}$ = .084, p = .776), and Conduct Disorder ($F_{1,14}$ = .770, p = .396).

The presence or absence of ICP did also not reveal any significant main effects of ICP on the DBD scale scores rated by father: Attention deficit ($F_{1,11}$ = .287, p = .604), Hyperactivity/impulsivity ($F_{1,11}$ = .395, p = .544), Oppositional Defiant Disorder ($F_{1,11}$ = .830, p = .384), and Conduct Disorder ($F_{1,11}$ = .217, p = .651). The accompanying descriptive statistics of ICP on DBD scores, rated by mother and father, are displayed in Table 24.

Table 24.

Descriptive statistics of ICP on DBD scores rated by mother and father

	Intracranial pressure			
DBD scale	*No ICP*		*ICP*	
Mother (n = 15)	*M*	*SD*	*M*	*SD*
Attention deficit	5.31	6.85	2.00	1.41
Hyperactivity/impulsivity	3.15	5.80	3.50	4.95
ODD	2.15	3.02	1.50	2.12
CD	0.38	0.87	1.00	1.41
Father (n = 12)				
Attention deficit	4.27	5.85	1.00	0.00
Hyperactivity/impulsivity	3.36	5.12	0.00	0.00
ODD	1.36	1.43	0.00	0.00
CD	0.45	0.93	0.00	0.00

3.3.9. Intracranial pressure as factor variable and SCQ scores as dependent variable

A one-way ANOVA did not reveal any significant main effects of ICP on SCQ scores ($F_{1,23}$ = .061, p = .808). The presence or absence of ICP did not make any difference for the SCQ scores. Table 25 shows the descriptive statistics of ICP on SCQ scores.

Table 25.

Descriptive statistics of ICP on SCQ scores

	SCQ (n = 24)	
Intracranial pressure	*M*	*SD*
No ICP	7.57	6.15
ICP	6.67	3.21

3.3.10. Intracranial pressure as factor variable and CBCL scores as dependent variable

No significant main effect of ICP was found on the three CBCL scale scores, rated by mother: Internalizing problem scale ($F_{1,43}$ = .614, p = .438), Externalizing problem scale ($F_{1,43}$ = .007, p = .932), and the Total problem scale ($F_{1,43}$ = .414, p = .524).

No significant main effect of ICP was found either on the three CBCL scale scores, rated by father: Internalizing problem scale ($F_{1,37}$ = 2.62, p = .115), Externalizing problem scale ($F_{1,37}$

= 2.72, p = .108), and the Total problem scale ($F_{1,37}$ = 1.43, p = .240). Thus, the presence or absence of ICP did not make any difference for the CBCL scores, rated by mother and father. Table 26 shows the descriptive statistics of ICP on CBCL outcomes rated by both mother and father.

Table 26.

Descriptive statistics of ICP on CBCL scores rated by mother and father

	Intracranial pressure			
CBCL scale	*No ICP*		*ICP*	
Mother (n = 44)	*M*	*SD*	*M*	*SD*
Internalizing problems	50.23	11.07	46.20	8.17
Externalizing problems	48.95	10.05	49.40	18.58
Total problems	50.08	8.29	47.40	12.40
Father (n = 38)				
Internalizing problems	48.24	10.69	40.20	7.29
Externalizing problems	46.94	9.15	39.60	10.21
Total problems	46.76	10.88	40.60	9.53

3.3.11. Social Economic Status as factor variable and DBD scores as dependent variable

Social Economic Status (SES) was measured by the educational level of the parents. Their educational levels were divided into lower, middle, and higher education.

The scores and educational levels of the parents were separately analyzed through a one-way ANOVA. It was expected that the educational level of the parents would make a difference in DBD scores. Analysis did not reveal any significant main effects of the educational level of mother on DBD scores, rated by mother: Attention deficit ($F_{1,14}$ = .395, p = .682), Hyperactivity/Impulsivity ($F_{1,14}$ = .401, p = .678), Oppositional Defiant Disorder ($F_{1,14}$ = .118, p = .890), and Conduct Disorder ($F_{1,14}$ = .079, p = .925).

There were also no significant main effects found of the educational level of father on DBD scores, rated by father: Attention deficit ($F_{1,11}$ = .437, p = .659), Hyperactivity/impulsivity ($F_{1,11}$ = .667, p = .537), Oppositional Defiant Disorder ($F_{1,11}$ = 1.04, p = .373), and Conduct Disorder ($F_{1,11}$ = .547, p = .597).

The descriptive statistics of educational level of both parents on DBD scores, rated by mother and father, are presented in Table 27.

Table 27.

Descriptive statistics of educational level of mother and father on DBD scores rated by mother and father

	Educational level					
DBD scale	*Low*		*Middle*		*High*	
Mother (*n* = 15)	*M*	*SD*	*M*	*SD*	*M*	*SD*
Attention deficit	6.14	5.30	2.00	2.00	4.80	9.63
Hyperactivity/impulsivity	3.43	4.61	0.67	0.58	4.40	8.26
ODD	2.14	3.67	1.33	2.31	2.40	2.30
CD	0.43	0.79	0.33	0.58	0.60	1.34
Father (*n* =12)						
Attention deficit	1.33	1.15	4.40	3.05	5.50	9.68
Hyperactivity/impulsivity	1.67	2.08	2.00	1.58	5.50	8.54
ODD	1.33	1.53	0.60	1.34	2.00	1.41
CD	0.00	0.00	0.40	0.55	0.75	1.50

3.3.12. Social Economic Status as factor variable and SCQ scores as dependent variable

A one-way ANOVA did not reveal any significant main effects of educational level of mother ($F_{1,23} = 1.80$, $p = .189$) and father ($F_{1,23} = 1.50$, $p = .246$), on SCQ scores. The descriptive statistics of the educational levels of the parents, on SCQ scores, are displayed in Table 28.

Table 28.

Descriptive statistics of educational level on SCQ scores

	Educational level											
	Mother						Father					
	Low		*Middle*		*High*		*Low*		*Middle*		*High*	
SCQ	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Scores (*n*= 24)	10.38	5.13	6.88	6.22	5.13	5.49	11.0	5.24	7.36	6.12	5.38	5.32

3.3.13. Social Economic Status as factor variable and CBCL scores as dependent variable

A one-way ANOVA did not reveal any significant main effects of the different educational levels of mother, on CBCL scores, rated by mother: Internalizing problem scale ($F_{1,43} = .338$, $p = .715$), Externalizing problem scale ($F_{1,43} = 2.71$, $p = .0.78$), and the Total problem scale ($F_{1,43} = .628$, $p = .539$).

Performing analysis on the CBCL scores, rated by father and the different educational levels of father, did not reveal any significant main effects of educational level either: Internalizing problem scale ($F_{1,37} = 2.29$, $p = .116$), Externalizing problem scale ($F_{1,37} = .442$, $p = .646$), and the Total problem scale ($F_{1,37} = 1.33$, $p = .277$).

The accompanying descriptive statistics are presented in Table 29.

Table 29.

Descriptive statistics of educational level on CBCL scores rated by mother and father

	Educational level					
	Low		*Middle*		*High*	
CBCL scale	*M*	*SD*	*M*	*SD*	*M*	*SD*
Mother ($n = 44$)						
Internalizing problems	48.00	17.12	51.26	7.40	49.07	9.60
Externalizing problems	42.30	14.25	51.79	9.40	49.93	9.23
Total problems	48.50	8.30	51.47	6.70	48.47	11.12
Father ($n = 38$)						
Internalizing problems	41.20	12.17	50.72	10.69	44.93	8.99
Externalizing problems	44.00	10.49	47.50	8.56	44.80	10.57
Total problems	41.60	11.78	48.83	9.19	43.93	12.01

Note. One-way ANOVA on educational level of mother, on CBCL scores, rated by mother.

One-way ANOVA on educational level of father, on CBCL scores, rated by father.

4. Discussion

4.1. In general

The present study studied 47 children with trigonocephaly of 1 up to 8 years of age by screening them for psychopathology, with ADHD- and autism-like behaviors in particular. Cognitive impairment was also looked at, by measuring IQ-scores. In general, the results of this study provide evidence that children with trigonocephaly in the age of 1 up to 8 years, obtain developmental scores that do not differ from normative expectations. These results are contradictory to the findings of e.g. Bottero et al. (1998), and Sidoti et al. (1996).

The hypotheses of this study will be separately discussed below.

4.2. Main hypotheses

4.2.1. Children with trigonocephaly of 1 up to 8 years of age, have an increased risk for psychopathology, like ADHD- and autism-like behaviors, compared to children without trigonocephaly

First of all, as far as ADHD-behaviors are concerned, the outcomes of the DISC-IV interview did not indicate any diagnoses of Attention Deficit Hyperactivity Disorder, Oppositional Defiant Disorder or Conduct Disorder in the 17 children whose parent(s) were interviewed. Secondly, Disruptive Behavior Disorders (DBD) scores, measuring Attention deficit, Hyperactivity/impulsivity, Oppositional Defiant Disorder and Conduct disorder, were not able to discriminate significantly between children with trigonocephaly and children without trigonocephaly. Yet, one significant difference was found between ratings of the fathers on the ODD scale and the ODD scores of the norm group. Fathers of children with trigonocephaly rated their children significantly lower on the ODD scale compared to the norm group, which is contradictory to the stated hypothesis.

With regard to autism-like behaviors, no norm data was available for the normal population, so the SCQ scores were compared to an autism reference group. Children with trigonocephaly scored significantly lower on the SCQ, rated by their parents, compared to the children with autism of the reference group. Once again, this finding does not correspond with the first hypothesis. According to the hypothesis, one would expect children with trigonocephaly to score around the same level as children with autism of the reference group.

Finally, psychopathology in general was measured through the Internalizing, Externalizing and Total problem scale of the CBCL and C-TRF. The parents and the schoolteachers served as informants. The scores on the three CBCL scales, rated by the mothers, did not reveal any significant differences compared to the normal population. So according to the mothers of the subjects of the present study, their children do not display more internalizing and externalizing problems compared to the normal population. As far as the CBCL scores, rated by the fathers are concerned, they gave their children significantly lower ratings on the Externalizing, and Total problem scale, compared to the normal population. So according to the fathers of the subjects, their children displayed fewer Externalizing and Total problems compared to the normal population. The few C-TRF data available did also not discriminate significantly between the children with trigonocephaly and the normal population, based on internalizing and externalizing problems.

In summary, children with trigonocephaly of 1 up to 8 years of age do not seem to have an increased risk for psychopathology, like ADHD- and autism-like behaviors, based on the current findings. It even appears that whenever a significant result was reached, children with trigonocephaly seem to score better, according to their parents, compared to the normal population. A possible factor of influence is the relatively young age of the children in the current research sample. When they reach puberty and adolescence, their parents' role will perhaps become less influential and negative environmental influences and live events can become more of a risk factor for psychopathology. Adolescence is often associated with elevated levels of sensation-seeking, reckless and risk-taking behaviors, as well as changes in anxiety and harm-avoidance. This age-period becomes critically vulnerable with respect to lack of impulse control and development of addictive behavior, due to the development of brain circuits underlying motivation and decision-making (Adriani & Laviola, 2004). The increasing exposure to major live events in early adolescence and at the same time physical, cognitive and psychosocial changes, associated with pubertal onset can heighten chronic stress levels. The risk of developing psychological, behavioral, and somatic disorders increases, because stress contributes to negative affect in young adolescents. Stress and stress reactivity are therefore considered to play a role in the development of psychopathology in this critical period (Schneider, Nicolson, Berk et al., 2006). Moreover, Sidoti et al. (1996) did find, in their follow-up study, cognitive and behavioral abnormalities to be present in a significant number of patients with trigonocephaly. The age of their sample ranged from 6 months to 22 years. The incidence of cognitive and behavioral problems became even more dramatic, when the preschool-aged children of their study were eliminated.

The family structure has also been associated with the development of psychopathology in adolescence. Single parent households and complex stepfamilies (father and mother are not biologically related to the child) appear to be a risk for behavioral or affective disorders than intact families (Cuffe, McKeown, Addy, & Garirison, 2005). Information about family structure of the current research sample was not explicitly gathered. Since family structure can change over time it can become a risk factor of the development of psychopathology in these children with trigonocephaly.

A prospective, long-term, longitudinal study is necessary to determine the incidence of potential cognitive and/or behavioral disturbances in the current research sample more accurately. Other potential risk factors of psychopathology in adolescence, like major live event, family structure, stress and stress reactivity, should be taken into account.

4.2.2. Children with trigonocephaly of 1 up to 8 years of age are more cognitively impaired compared to children without trigonocephaly

Cognitive impairment was measured using IQ-scores. Children with trigonocephaly of 1 up to 8 years of age did not have a lower IQ-score compared to the normal population. In fact, the subjects had an on average higher IQ-score (104.04), compared to the IQ-score of the normal population (100). This difference however, did not reach any significance. Nevertheless, this hypothesis can not be confirmed based on IQ-scores of the current research sample.

4.2.3. Boys with trigonocephaly are more susceptible for psychopathology, like ADHD- and autism-like behaviors, compared to girls with trigonocephaly

The majority of the present sample consisted of boys (40:7). According to the literature, males in general are more affected when it comes down to ADHD- and autism-like behaviors, compared to girls (Barkley, 1997). Fathers reported on average more ODD problems in boys, compared to girls. Although this difference was significant, only 12 DBD ratings of father were available for no more than 2 girls and 10 boys. Therefore, this finding should be carefully interpreted. Mothers did not discriminate between boys and girls in their DBD ratings.

Boys and girls did also not significantly differ in their SCQ scores, rated by their parents. This finding suggests that boys with trigonocephaly are not more susceptible for autism-like behaviors, compared to girls with trigonocephaly, based on the SCQ. However, it should be taken into account that only 3 girls were compared against 21 boys, and interpretations should again be carefully made.

Once again, parents reported no significant differences between boys and girls with regard to internalizing and externalizing problems, measured by the CBCL. Schoolteachers however, reported on average more internalizing problems for girls on the C-TRF, compared to boys. It should be noted that there were only ratings available of 15 schoolteachers, who in total, rated 2 girls and 13 boys.

In summary, the hypothesis can not be completely confirmed nor rejected. The results did not provide any convincing evidence for boys with trigonocephaly being more susceptible for ADHD- and autism-like behaviors and internalizing and externalizing problems compared to girls with trigonocephaly. Although fathers reported significantly more ODD problems in boys, compared to girls, the number of girls was undermanned in the present research sample, which possibly caused a distorted image. This also applies to the finding that girls with trigonocephaly are more susceptible for internalizing problems compared to boys with trigonocephaly, rated by the schoolteachers. On the other hand, these gender differences are also present in the normal population: boys are diagnosed more frequently with ODD than girls (Jackson & King, 2004) and girls in general, are more vulnerable for internalizing problems compared to boys (Leadbeater, Kuperminc, Blatt, & Hertzog, 1999).

Moreover, as far as the DBD and C-TRF instruments are concerned, only a small amount of data was available, this also could affect the results. Therefore, the two significant differences found between boys and girls, should still be carefully interpreted and future research is required to examine these gender differences more closely when more data is available.

4.3. Sub hypotheses

4.3.1. The presence of additional brain anomalies in children with trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors, compared to children with trigonocephaly without additional brain anomalies.

This hypothesis can not be confirmed nor rejected since in none of the children of the current research sample additional brain anomalies were present. Future research is recommended to investigate this hypothesis once more.

4.3.2. The syndromic form compared to the nonsyndromic form of trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors

The presence of a syndromic form of trigonocephaly did not result in more behavioral problems, like ADHD, measured by the DBD. The type of trigonocephaly did also not make any difference for autism-like behaviors measured by the SCQ.

The presence of a syndromic form however, did make a difference for the Total problem scale of the CBCL rated by the mother. Mothers ascribed significantly more internalizing and externalizing problems to children with a syndromic form of trigonocephaly compared to children with a nonsyndromic form. Nevertheless, the scores on the Total problem scale of the children with a syndromic form, rated by mother, are still within the normal range. The CBCL scores rated by the fathers did also significantly differentiate between a syndromic and nonsyndromic form of trigonocephaly. Fathers ascribed significantly more externalizing and total problems to children with a syndromic form of trigonocephaly compared to children with a nonsyndromic form.

In summary, the results did not show any evidence for more ADHD- and autism-like behaviors in children with a syndromic form of trigonocephaly. A possible explanation is the small amount of data available on ADHD- and autism-like behaviors. Future research will have to investigate this. Psychopathology in general, measured by internalizing and externalizing behaviors, was, in some cases, more evident in children with a syndromic form of trigonocephaly. This finding suggests a worse outcome for children with a syndromic form of trigonocephaly, compared to children with a nonsyndromic form, which is consistent with the literature. Cohen (1991) found the syndromic form of trigonocephaly to be associated with elevated rates of mental retardation and learning disabilities, since the syndromic form is often associated with additional anomalies. Thus, this hypothesis can partially be confirmed.

4.3.3. A more severe phenotype expression (larger ratio of the interparietal to the intercoronal distance) in children with trigonocephaly will result in more psychopathology, like ADHD- and autism-like behaviors, compared to children with trigonocephaly with a less severe phenotype expression

Merely few data of phenotype expression were available. The children of whose phenotype expression was determined only had CBCL data available. Possibly because of that, results did not show any effects of the severity of phenotype expression on psychopathology. A larger ratio of the interparietal to the intercoronal distance did not seem to cause more

psychopathology in children with trigonocephaly. This hypothesis should therefore be rejected.

4.3.4. More severe (a higher percentage) digital impressions will result in more psychopathology, like ADHD- and autism-like behaviors in children with trigonocephaly

Based on the findings, this hypothesis can partially be confirmed. A higher percentage of digital impressions did not result in more psychopathology, like ADHD- and autism-like behaviors in the children with trigonocephaly, reported by both parents. As far as the ratings of the schoolteachers are concerned, regression analysis revealed a significant effect between the dependent variables internalizing and total problems of the C-TRF and the predictor digital impressions. This relation was positive and indicates that a higher percentage of digital impressions are associated with more internalizing and total problems in the child, according to ratings of the schoolteacher. It should be mentioned however, that considerably less data was available of the schoolteacher compared to the amount of data available of both parents for the CBCL. Besides that, data on digital impressions were only available for 21 children Therefore it should be questioned whether these significant results are really reliable. On the other hand, the ratings of different informants of social, emotional or behavior problems are often discrepant. In virtually every method of clinical assessment that researchers and practitioners use to assess abnormal behavior in youths, informant discrepancies have been found. Unfortunately, there is no single measure or method of assessing psychopathology in children that provides a definitive standard to measure which children are experiencing a given set of problems or disorders. Moreover, there is a need to incorporate information from multiple informants to assess psychopathology in juveniles. Nevertheless, even when different informants observe a child's behavior in similar context or situations, they still have different motivations for providing ratings of children and have different perceptions or thresholds of what constitutes abnormal behavior in a certain child. Regrettably, research had generally failed to explain the discrepancies of informants (De Los Reyes & Kazdin, 2005). Future research is recommended to investigate this hypothesis more precisely when more data of digital impressions and of the dependent variables are acquired, to at least check on the reliability of the significant results found.

4.3.5. The presence of elevated intracranial pressure will result in more psychopathology, like ADHD- and autism-like behaviors in children with trigonocephaly

The presence of elevated intracranial pressure did not resulted in more psychopathology, like ADHD- and autism-like behaviors. The presence and absence of intracranial pressure did not differentiate between the amounts of problems, reported by the parents. A possible explanation for rejecting the hypothesis is that surgery creates more room for the brains to grow together with decreasing intracranial pressure, which could possibly prevent future developmental problems. Shimoji, Shimabukuro, Sugama, & Ochiai, (2002) found that patients with trigonocephaly who presented with clinical symptoms such as delay in language development, hyperactivity, autistic tendencies and motor delays, showed improvement after undergoing a decompressive surgical procedure.

4.3.6. Low SES children with trigonocephaly will experience more psychopathology, like ADHD- and autism like behaviors, compared to high SES children with trigonocephaly

Low SES children, children whose parents were lower educated, did not display more psychopathology, like ADHD- autism-like behaviors compared to higher SES children, children whose parents were higher educated. According to the current results, this hypothesis can not be confirmed. Possibly, the three educational levels of the parents did not differ strong enough, to really influence the child's development in negative way.

4.4. Summary

The present study was not able to find much satisfactory and convincing evidence for children with trigonocephaly to have worse outcomes on psychopathology compared to normal children without trigonocephaly, referring to the main hypotheses. Fathers even reported less Oppositional Defiant Disorder (ODD) behaviors in their children with trigonocephaly, compared to normal children. As far as gender differences are concerned, boys displayed, according to their fathers, more ODD behaviors compared to girls. Schoolteachers reported for girls with trigonocephaly, more internalizing problems, compared to boys with trigonocephaly. However, the number of girls was undermanned in the present research sample (40:7) and even more in comparing boys and girls in DBD and C-TRF scores, respectively 10:2 and 13:2. For that reason, these findings should be carefully interpreted and future research is required to investigate these gender differences more accurately.

As far as the risk factors for neurobehavioral problems are concerned, present study found that children with a syndromic form of trigonocephaly seem to have a worse outcome with

respect to internalizing and externalizing problems, compared to children with a nonsyndromic form of trigonocephaly. This finding corresponds with the literature (e.g. Cohen, 1991). Another finding was that a higher percentage of digital impressions predict more internalizing and total problems, measured by the C-TRF, rated by the schoolteachers. This significant result could be related to informant discrepancies, but considering the small amount of data available, future research is recommended to check on the reliability of current findings.

4.5. Limitations

Although a few significant results have been found, these have to be carefully interpreted, since the present study had to cope with methodological problems, which are commonly found in studies of rare disorders.

First of all, the small sample size of 47 participating children and their parents were limiting the statistical power. Moreover, the majority of instruments were not suitable for all the different ages, the sample consisted of. As a consequence, only small numbers out of 47 children could, for instance, be analyzed on ADHD- and autism-like behaviors. Besides that, many data was missing as well, which reduces the statistical power even more. As mentioned before, the gender distribution was not equally divided in the present study which could cause a distorted image as far as gender differences are concerned. Considering the small sample size, many missing data, and an unequally divided gender distribution, the question arises whether the significant results of present study are really reliable. Because of that, it could be that possible existing differences and effects could not be proven by present study. Future research, containing a larger sample size, more complete data sets and equally divided (gender) distributions, is required to be able to answer the formulated research questions of present study more precisely and reliable.

Short versions of the WPPSI-R (Wechsler, 1997) and WISC-III (Wechsler, 1992), consisting of four subtest, were used to measure IQ in the subjects of 4 up to 8 years of age. Although short IQ-tests are permitted to use for scientific research, it is questionable whether the IQ-scores are reliable since it only concerns 20 children whose IQ is measured by the WPPSI-R and WISC-III. Not administering the complete version of the two IQ-tests could possibly cause a distorted image of the IQ-scores, considering the small number of children. Future research is recommended to administer the short version of an IQ-test in a larger sample size or to administer the complete version of an IQ-test.

Afterwards, it appeared that a testing session of approximately 2-3 hours was too long for the children to handle. In many children, their attention decreased throughout the test session. Presumably, the drop in attention, affected the results. In future research the testing session should be of a shorter period of time or should be distributed over several days.

Another limitation of this study is the absence of a tangible control group that matches the current research sample. Comparisons between the children with trigonocephaly and normal children were mostly based on norm data of test manuals. Use of a tangible and matched control group is the only definite way to compare the developmental progression of children with trigonocephaly with normal children.

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