objective

OBJECTIVES: To examine intellectual, behavioral, and emotional functioning of children who have syndromic craniosynostosis and to explore differences between diagnostic subgroups.

METHODS: A national sample of children who have syndromic craniosynostosis participated in this study. Intellectual, behavioral, and emotional outcomes were assessed by using standardized measures: Wechsler Intelligence Scale for Children, Third Edition, Child Behavior Checklist (CBCL)/6-18, Disruptive Behavior Disorder rating scale (DBD), and the National Institute of Mental Health Diagnostic Interview Schedule for Children.

RESULTS: We included 82 children (39 boys) aged 6 to 13 years who have syndromic craniosynostosis. Mean Full-Scale IQ (FSIQ) was in the normal range (M = 96.6, SD = 21.6). However, children who have syndromic craniosynostosis had a 1.9 times higher risk for developing intellectual disability (FSIQ < 85) compared with the normative population (P < .001) and had more behavioral and emotional problems compared with the normative population, including higher scores on the CBCL/6-18, DBD Total Problems (P < .001), Internalizing (P < .01), social problems (P < .001), attention problems (P < .001), and the DBD Inattention (P < .001).

Children who have Apert syndrome had lower FSIQs (M = 76.7; SD = 13.3) and children who have Muenke syndrome had more social problems (P < .01), attention problems (P < .05), and inattention problems (P < .01) than normative population and with other diagnostic subgroups.

CONCLUSIONS: Although children who have syndromic craniosynostosis have FSIQs similar to the normative population, they are at increased risk for developing intellectual disability, internalizing, social, and attention problems. Higher levels of behavioral and emotional problems were related to lower levels of intellectual functioning. Pediatrics 2014;133:e1608–e1615

WHAT’S KNOWN ON THIS SUBJECT: Children who have syndromic craniosynostosis are at risk for developing intellectual disability, behavioral and emotional problems. Study results were often based on small samples and wide age-based variation, using non-validated instruments and describing no clear inclusion and exclusion criteria.

WHAT THIS STUDY ADDS: Intellectual, behavioral, and emotional functioning is described in a national sample (N = 82) of school-aged children with syndromic craniosynostosis. Using standardized instruments, this study indicates higher risks for intellectual disability and behavioral problems mainly in children having Apert and Muenke syndromes.

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KEY WORDS: syndromic craniosynostosis, children, intellectual functioning, behavioral functioning, emotional functioning

ABBREVIATIONS

ADHD—Attention Deficit Hyperactivity Disorder

CBCL/6-18—Child Behavior Checklist for children aged 6 to 18 years

DBD—Disruptive Behavior Disorder rating scale

DISC-IV-P—Diagnostic Interview Schedule for Children for DSM-IV, parent version

DSM-IV—Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

FGFR—fibroblast growth factor receptor

FSIQ—Full-Scale Intelligence Quotient

ID—intellectual disability

WISC-III—Wechsler Intelligence Scale for Children, Third Edition

Ms Maliepaard designed the data collection instruments, performed article searches, data extraction, and statistical analyses, and drafted the initial manuscript; Dr Mathijssen coordinated medical data, participated in the interpretation of analyzed data, and critically reviewed the manuscript; Dr Oosterlaan supervised and refereed data extraction, performed and reviewed data analysis, coordinated and supervised the draft of the initial manuscript, and critically reviewed the manuscript; Dr Okkerse conceptualized and designed the study and the data collection instruments, performed and reviewed data analysis, coordinated and supervised the draft of the initial manuscript, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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(Continued on last page)
Craniosynostosis is a congenital deformity characterized by premature fusion of the cranial sutures. Craniosynostosis disorders are usually divided into two major types: non-syndromic craniosynostosis is characterized by premature fusion, usually of 1 cranial suture, and there are no other congenital malformations. In syndromic craniosynostosis, the craniosynostosis is accompanied by other anomalies such as midface retrusion, limb abnormalities, and brain anomalies. Well-known syndromes are the Apert, Crouzon, Pfeiffer, Muenke, and Saethre-Chotzen syndromes, caused by changes in the genes for fibroblast growth factor receptor (FGFR) 1, 2, and 3 and in the TWIST1 gene. If no mutation is found and 2 or more sutures are closed, the condition is referred to as complex craniosynostosis.

Characteristics of syndromic craniosynostosis are shown in Table 1.

Few studies have investigated intellectual, behavioral, and emotional functioning in children who have syndromic craniosynostosis. Table 2 provides details on these studies. Overall, these pioneering studies reported divergent outcomes on intellectual functioning of children who have well-known syndromes. In Apert syndrome, mean Full Scale IQ (FSIQ) scores were found to vary between 62.0 and 93.8 (range, 10–115). FSIQs of children who have Crouzon and Pfeiffer syndrome ranged from not testable to 115, but the majority of these children have FSIQs within the average range (90–110). Mean FSIQs of patients who have Muenke and Saethre-Chotzen syndrome ranged from 50 to 120. No published studies were found on intellectual functioning in children who have complex craniosynostosis.

Studies on behavioral and emotional functioning reported higher rates of social and attention problems in children who have Apert, Muenke, and Crouzon syndrome compared with the normative population. There are no published studies on behavioral and emotional functioning of children who have Pfeiffer syndrome, Saethre-Chotzen syndrome, or complex craniosynostosis.

A great variety of measures have been used to assess intellectual, behavioral, and emotional functioning, hindering comparison of results between studies. Furthermore, studies have used small samples, the ages of the participants differed widely between studies, and no clear inclusion and exclusion criteria were described. Finally, in some studies non-validated instruments were used to assess intellectual, behavioral, and emotional functioning.

Clearly the field is in need of studies with larger sample sizes, employing clear inclusion and exclusion criteria and using psychometrically sound instruments to assess intellectual, behavioral, and emotional functioning. The aim of the current study is to describe intellectual, behavioral, and emotional functioning in a national sample of children who have syndromic craniosynostosis, using well-validated instruments. We hypothesized that children who have syndromic craniosynostosis will have lower FSIQs and more behavioral and emotional problems compared with the normative population. Specifically, we expected parents to report more internalizing, externalizing, social, and attention problems. Furthermore, we explored the effects of syndromic craniosynostosis subgroups on intellectual, behavioral, and emotional functioning. Studies report a 3 to 7 times higher prevalence of behavioral and emotional problems in children who have intellectual disability (ID) than in children who have normal intelligence. Therefore, we also explored behavioral and emotional problems separately for children who have and who do not have ID.

### METHODS

**Patient Population**

This study used a consecutive sample of all children aged 6 to 13 years who have Apert syndrome (S252W, S252F and P253R FGFR2 mutations), Crouzon/Pfeiffer syndrome (defined as non-Apert FGFR2 mutations), Muenke syndrome (P250R FGFR3 mutation), Saethre-Chotzen syndrome (TWIST1 mutation or deletion), or complex craniosynostosis referred to the Dutch Craniofacial Centre at the Erasmus MC-Sophia Children’s Hospital (a tertiary-care university hospital) in Rotterdam, The Netherlands. This center is responsible for medical care of...
<table>
<thead>
<tr>
<th>Study</th>
<th>Craniosynostosis Type</th>
<th>N/n</th>
<th>Age Range (y)</th>
<th>Assessment Instruments</th>
<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flapper et al (2009)</td>
<td>Crouzon</td>
<td>n = 16</td>
<td>16 to 39</td>
<td>WISC, WAIS</td>
<td>Crouzon</td>
<td>IQ range 90–110, 80–90, 70–80, &lt;70, not tested</td>
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<td></td>
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<td>Muenke</td>
<td>IQ range 90–110, 70–80, &lt;70</td>
</tr>
<tr>
<td>Yacubian-Fernandez (2007)</td>
<td>Crouzon</td>
<td>n = 11</td>
<td>1,4 to 13</td>
<td>WISC-III, WAIS</td>
<td>Mean IQ 84.2 (range, 66–102)</td>
<td>WISC-III is not suitable for administration to children under the age of 6 years.</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td>Crouzon: mean IQ 92 (range, 62–116)</td>
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<td></td>
<td></td>
<td>Saethre-Chotzen: mean IQ 86 (range, 49–104)</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Witkop: mean IQ 93</td>
<td></td>
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<tr>
<td>Shipster et al (2002)</td>
<td>Apert</td>
<td>N = 10</td>
<td>4 to 6</td>
<td>British Ability scale II</td>
<td>Mean IQ 93.8 (range, 77–115)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean performance IQ 95 (range, 88–107)</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>n = 15 had IQ &lt;70, 7/15 having S252W mutation</td>
<td></td>
</tr>
<tr>
<td>Lajeunie et al (1989)</td>
<td>Apert</td>
<td>N = 36</td>
<td>Not reported</td>
<td>Not reported</td>
<td>More social dysfunction and behavioral problems in children who had the craniofacial correction after age 4 years compared with those operated on before 4 years of age</td>
<td></td>
</tr>
<tr>
<td>Renier et al (1996)</td>
<td>Apert</td>
<td>N = 38</td>
<td>3 to 28</td>
<td>WPPSI</td>
<td>Mean IQ 62 (range, 10–114)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>32% IQ &gt;70, 68% IQ &lt;70</td>
<td></td>
</tr>
<tr>
<td>Sarimski et al (2001)</td>
<td>Apert</td>
<td>N = 25</td>
<td>5–17</td>
<td>CBCL/6-18 interview: Kinder-DIPS</td>
<td>n = 14 within clinical range on Social Problems n = 10 within clinical range on Attention Problems IQ estimated by parents and teacher</td>
<td></td>
</tr>
<tr>
<td>Escobar et al (2009)</td>
<td>Muenke</td>
<td>N = 2, twins</td>
<td>7</td>
<td>Not reported</td>
<td>n = 2 diagnosed with ADHD n = 1 diagnosed with PDD</td>
<td></td>
</tr>
<tr>
<td>Pertschuk (1987)</td>
<td>Syndromic craniosynostosis</td>
<td>Not reported</td>
<td>6–13</td>
<td>Semi-structured interview</td>
<td>More social dysfunction and behavioral problems in children who had the craniofacial correction after age 4 years compared with those operated on before 4 years of age</td>
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</table>
all children who have syndromic craniosynostosis born in the Netherlands. Children who were known to suffer from other genetically determined syndromes were excluded from the study. The Erasmus MC Medical Ethical Review Board approved the study (MEC-2005-273) and parents as well as children older than 11 years signed informed consent.

**Measures**

**Intellectual Functioning**

To estimate children’s FSIQ, we used a 4-subtest short form of the Dutch version of the third edition of the Wechsler Intelligence Scale for Children (WISC-III), a standardized test that measures intellectual functioning in children aged 6 to 16 years. Subtest scores were converted into composite scores that were used to calculate FSIQ, which correlates highly \((r = 0.90\) range) with FSIQ. Following the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR, American Psychiatric Association [APA], 2000), children who have either borderline intellectual functioning (defined as a FSIQ of 71–84) or mental retardation (FSIQ <71) were defined as intellectually disabled (ID).25

**Behavioral and Emotional Functioning**

Two parent-rated questionnaires and 1 diagnostic interview administered to the parents (usually the mother) were used to assess children’s behavioral and emotional functioning. The Child Behavior Checklist for ages 6 to 18 years (CBCL/6-18) was used to assess the child’s behavioral and emotional functioning.26 The CBCL/6-18 is a widely used questionnaire and consists of 120 items assessing behavioral, emotional, and other problems. Responses are recorded on a 3-point scale. To test our hypothesis that children who have syndromic craniosynostosis have more internalizing, externalizing, social, and attention problems than the normative population, we used the CBCL/6-18 scales Total Problems, Internalizing, Externalizing, Social Problems, and Attention Problems. To assess symptoms of Attention Deficit Hyperactivity Disorder (ADHD) in more detail, the Inattention and Hyperactivity/Impulsivity scales of the Dutch version of the 42-item Disruptive Behavior Disorder rating scale (DBD) was used. Responses on this scale were recorded on a 4-point rating scale.27,29. Higher scores on the scales derived from both questionnaires indicate greater intensity of problems. T-scores were computed from raw scores; higher scores on the syndrome scales indicate greater severity of problems. Adequate psychometric properties for this rating scale have been established.25

The Dutch version of the National Institute of Mental Health Diagnostic Interview Schedule for Children, parent version (DISC-IV-P) was used to establish DSM-IV-TR diagnoses of anxiety disorders and ADHD, using the modules Social Phobia, Separation Anxiety Disorder, Generalized Anxiety Disorder, and Attention-Deficit Hyperactivity Disorder.25,31–33

**Statistical Analyses**

Eighty-two children (39 boys and 43 girls, median age 8.9 years, range 6–13 years) participated in the study (response rate 85%). Ten children were diagnosed with Apert syndrome, 23 children with Crouzon/Pfeiffer syndrome, 13 children with Muenke syndrome, and 14 children with Saethre-Chotzen syndrome. Twenty-two children suffered from complex craniosynostosis. FSIQ scores were available for 76 children; six children were unable to complete any subtest of the WISC-III owing to task incoherence and study dropout. For 67 children complete data were available for the CBCL/6-18, DBD, and DISC-IV-P. Data were missing owing to not completing DBD questionnaires and time constraints for the DISC-IV-P.

Data were analyzed by using PASW statistics 17.0 for Windows (SPSS, Inc, Chicago, IL). Welch’s \(t\) test was used to assess differences in FSIQ and differences on the CBCL/6-18 and DBD scales between the craniosynostosis group and normative data. Effect sizes (Cohen’s \(d\) were calculated to quantify the magnitude of group differences, with effect sizes of 0.2
to 0.5 considered small, effect sizes of 0.5 to 0.8 considered medium, and effect sizes of 0.8 and higher considered large.\textsuperscript{35} Spearman’s \(\rho\) and Pearson correlation coefficients were calculated to measure the association between FSIQ and measures of behavioral and emotional problems, including: (1) the presence or absence of Social Phobia, Separation Anxiety Disorder, Generalized Anxiety Disorder, and ADHD as assessed with the DISC-IV, and (2) scores on both the CBCL/6-18 and DBD. Odds ratios (ORs) and accompanying 95\% confidence intervals (CIs) were calculated to compare behavioral and emotional functioning of children who had FSIQs <85 and >85 in the syndromic craniosynostosis group.

Exploratory analyses tested possible differences between syndromic craniosynostosis subgroups. These analyses used analysis of covariance, with age and FSIQ entered as covariates with post-hoc Tukey tests to compare differences between syndromic craniosynostosis subgroups. In all analyses \(\alpha\) was set at 0.05.

**RESULTS**

**Intellectual Functioning**

Mean FSIQ in children who have syndromic craniosynostosis was 96.6 (SD = 21.6; range, 49–141) and did not differ significantly from mean FSIQ in the normative group (M = 100; SD = 15). However, exploratory analysis comparing syndromic craniosynostosis subgroups on FSIQ revealed that children who have Apert syndrome had significantly lower scores (M = 76.7; SD = 13.3) compared with the normative population and the other syndromic subgroups (Table 3). Children who have Apert syndrome (\(P < .01\)) and Muenke syndrome (\(P < .05\)) had a higher chance of being diagnosed with ID than children who have Crouzon syndrome, Saethre-Chotzen syndrome, or complex craniosynostosis. Of the 6 children who have Apert syndrome, 4 children were diagnosed with ID.

**Behavioral and Emotional Functioning**

Compared with normative data, children who have syndromic craniosynostosis obtained higher scores on the CBCL/6-18 scales Total Problems, Internalizing, Social Problems, and Attention Problems, but not on the Externalizing scale. The syndromic craniosynostosis group also had higher scores on the DBD Inattention scale compared with the normative sample, but did not differ on the DBD Hyperactivity/Impulsivity scale (Table 4). Compared with the normative sample, the proportion of children who have a DISC-IV-P derived diagnosis of ADHD-any type and ADHD-hyperactive-impulsive type was higher in children who have syndromic craniosynostosis, with accompanying ORs of 2.05 (95\% CI, 1.22–2.87) and 7.16 (95\% CI, 5.62–9.27), respectively (Table 5).

Exploratory analysis comparing the syndromic craniosynostosis subgroups on behavioral and emotional functioning showed that children who have Muenke syndrome obtained higher ratings on the CBCL/6-18 scales Social Problems and Attention Problems as well as on the DBD scales Inattention and Hyperactivity/Impulsivity compared with other syndromic craniosynostosis subgroups. No subgroup differences were found on any of the DISC-IV-P derived DSM-IV-TR diagnoses (Table 6).

**DISCUSSION**

The current study investigated intellectual, behavioral, and emotional functioning in a large national sample of children who have syndromic craniosynostosis aged between 6 and 13 years. We used standardized, validated, and reliable...
Da Costa and colleagues found significantly lower FSIQs (FSIQ = 83.1; SD, 21.9) in a group of 13 children who have syndromic craniosynostosis compared with the normative population.9 Those results contrast with our study that obtained FSIQs in the normal range. One possible explanation for these discrepant findings is the higher percentage of children who have Apert syndrome (23%) included in the study of Da Costa compared with our study (8%), because Apert syndrome has been found to be associated with lower FSIQs.8,20 Flapper and colleagues reported FSIQs of more than 1 SD below the normative mean in 32% of their patients who have Crouzon/Pfeiffer (n = 16). However, that study used a highly selected sample of patients referred to the hospital.12 Noetzel and colleagues described intellectual functioning in children who have syndromic craniosynostosis and found FSIQs >90 in 71% of the 24 children in their sample, a percentage comparable to the finding of the current study with 63.2% of the children who have syndromic craniosynostosis obtaining FSIQs in the normal range. Those results contrast with our study, in which the sole exception of the small group of children who have Apert syndrome who obtained FSIQs in the normal range was not predictive of intellectual functioning in our study, with the sole exception of the small group of children who have Apert syndrome who obtained FSIQs in the normal range.

**TABLE 6** Behavioral and Emotional Problems According to Syndromic Craniosynostosis Subtypes

<table>
<thead>
<tr>
<th>Behavioral and Emotional Problems</th>
<th>Apert (n = 6)</th>
<th>Crouzon/Pfeiffer (n = 22)</th>
<th>Muenke (n = 13)</th>
<th>Saethre-Chotzen (n = 13)</th>
<th>Complex (n = 20)</th>
<th>Pairwise Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>CBCL/6-18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total problems</td>
<td>58.1</td>
<td>15.7</td>
<td>55.1</td>
<td>13.4</td>
<td>64.8</td>
<td>12.1</td>
</tr>
<tr>
<td>Internalizing</td>
<td>52.3</td>
<td>12.7</td>
<td>57.3</td>
<td>15.2</td>
<td>65.4</td>
<td>12.3</td>
</tr>
<tr>
<td>Externalizing</td>
<td>52.9</td>
<td>14.8</td>
<td>51.1</td>
<td>11.8</td>
<td>53.6</td>
<td>13.9</td>
</tr>
<tr>
<td>Social problems</td>
<td>62.7</td>
<td>10.3</td>
<td>57.5</td>
<td>12.9</td>
<td>69.5</td>
<td>12.6</td>
</tr>
<tr>
<td>Attention problems</td>
<td>67.7</td>
<td>11.6</td>
<td>53.6</td>
<td>13.0</td>
<td>67.2</td>
<td>10.9</td>
</tr>
<tr>
<td>BDDB</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inattention</td>
<td>58.4</td>
<td>11.6</td>
<td>52.5</td>
<td>10.0</td>
<td>66.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Hyperactivity/impulsivity</td>
<td>50.6</td>
<td>6.5</td>
<td>51.4</td>
<td>10.5</td>
<td>59.2</td>
<td>6.9</td>
</tr>
</tbody>
</table>

A, Apert; C/P, Crouzon/Pfeiffer; M, Muenke; S-C, Saethre-Chotzen; C, Complex. Results provided in T-scores. Pairwise comparisons: overall α set at .05.

The findings indicate that children who have ID were significantly higher in the syndromic craniosynostosis group than in the normative population, with 30% of the children who have syndromic craniosynostosis classifying as ID, compared with 15.9% in the normative population. Our study is the first to investigate intellectual functioning in a large group of children who have syndromic craniosynostosis. The results suggest that syndromic craniosynostosis is associated with intellectual impairment, with children in the syndromic craniosynostosis group having significantly lower FSIQs (FSIQ = 83.1; SD, 21.9) compared to children in the normative population. These findings highlight the need for early intervention and support for children with syndromic craniosynostosis.
significantly lower FSIQs (mean FSIQ, 76.7) than the normative population. Several other studies also reported lower than average FSIQs in their samples of patients who have Apert syndrome: Yacubian et al reported a mean FSIQ of 74, \( n = 18 \); Da Costa in their study described a mean FSIQ of 70, \( n = 3 \); and Renier reported a mean FSIQ of 62, \( n = 38 \). Only in the study of Shipster and colleagues\(^6\) was a mean FSIQ of children who have Apert syndrome reported of \( 93.8 \), \( n = 10 \). However, that study used the British Ability Scale to assess intellectual functioning, which is known to put less demand on attention and fine motor skills compared with the Wechsler scales used in other studies.\(^1\)

Children who have syndromic craniosynostosis obtained higher parent ratings of social problems, attention problems, and internalizing problems compared with normative data. In addition, a higher prevalence of ADHD-any type and ADHD-hyperactive-impulsive type was found in our study group. We also found that behavioral and emotional problems were particularly evident in children who have lower intellectual functioning, as children who have ID obtained higher scores on the CBCL Total Problems, Internalizing and Externalizing scales than children who do not have ID. This is in line with other studies in children who have ID, showing that the proportion of behavioral and emotional problems is up to 2 to 3 times higher in children who have ID than those who do not have ID (FSIQ <85).\(^37\)

Parents of children who have Muenke syndrome reported higher levels of behavioral and emotional problems than parents of children who have other syndromic subtypes, including higher rates of inattention and social problems. Behavioral and emotional problems of children who have Crouzon/Pfeiffer syndrome, Saethre-Chotzen syndrome, and complex craniosynostosis were comparable to the normative population. Other studies also report more social problems and attention problems in children who have syndromic craniosynostosis, especially in children who have Apert syndrome.\(^10,16,18,38\) Escobar described ADHD in 2 children who have Muenke syndrome, a twin pair, although both children had severe developmental delay.\(^19\) Importantly, most of these previous studies, however, did not use standardized measures to assess behavioral and emotional problems or failed to report on the type of measures used. The reason for the higher rates of behavioral problems in children who have syndromic craniosynostosis and children who have ID and Muenke syndrome in particular is not known.

Despite the unique sample size of our study, statistical power was limited to test differences between syndromic craniosynostosis subgroups owing to the low incidence of children diagnosed with syndromic craniosynostosis subtypes. Strengths of this study included the use of a consecutive sample of children who have syndromic craniosynostosis. Our study had a favorable response rate of 85%. Furthermore, children who have syndromic craniosynostosis were compared with normative data derived from very large representative samples. In contrast to previous studies, the current study used clear inclusion and exclusion criteria and standardized and well-validated instruments. We argue that future studies should use clear inclusion and exclusion criteria and standardized measures. This would contribute to a firm base of empirical evidence on functioning of children who have syndromic craniosynostosis, allowing clinicians to inform parents of the prospects for their children and to guide interventions.

**CONCLUSIONS**

The current study demonstrates that the mean IQ of children who have syndromic craniosynostosis is comparable to the normative population; however, these children run twice the risk for having ID. Children who have Apert syndrome were found to differ from other syndromic subgroups: children who have Apert syndrome were found to have the lowest FSIQs and the highest risk for developing ID or of craniosynostosis subgroups. Children who have syndromic craniosynostosis and children who have Muenke syndrome in particular were found to have higher risk for developing behavioral and emotional problems than the general population.

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Intellectual, Behavioral, and Emotional Functioning in Children With Syndromic Craniosynostosis
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