INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) remains a complex psychiatric disorder with a prevalence rate of about 5% in children. ADHD emerges early in childhood, although typically determined in the school-age years. It has the typical characteristics of inattention, impulsivity, and hyperactivity. The disorder is one of the most common diagnoses in educational and children's mental health, particularly relevant in today's society. Usually, children diagnosed with ADHD have problems related to education, social functioning, and/or other mental illness when they reach adolescence and youth. Thus, ADHD is of high individual, as well as societal, cost to the population. Moreover, children with ADHD can develop additional problems, such as conduct disorder and mood problems. ADHD appears to make a unique contribution to key outcomes such as smoking, potentially obesity, and accidental injury in varying degrees, impairing the long term health outcomes.

Intelligence indicates the ability to learn from prior experience, to predict school and career achievement. While there are many factors that can impact a person's success in academics and their professional life, intelligence is often seen as one of the key predictors. Childhood intelligence is a powerful predictor of later adult socioeconomic success in education, occupational status, and income dimensions. Intelligence can be defined as general intelligence, such as intelligence quotient (IQ), or its two separable major facets, crystallized intelligence and fluid intelligence. A test that is often considered the best available measure of fluid intelligence is Raven's Standard Progressive Matrices (RSPM). In addition, the perceptual tasks in the Wechsler Intelligence Scale for Children (WISC-IV) can measure performance skills (performance IQ scores [PIQ]), while the verbal tasks can measure verbal IQ (VIQ). In previous studies, there were divergences in the influence of childbearing styles on children's intelligence. Several research revealed that cesarean delivery was associated with an increase of full-scale IQ (FIQ), VIQ, and PIQ compared with those born by vaginal delivery.

Original Article

Influence of Mode of Delivery on Children’s Attention Deficit Hyperactivity Disorder and Childhood Intelligence

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Objective To investigate whether differences exist in attention deficit hyperactivity disorder (ADHD) and intelligence between children born by cesarean delivery and those born by vaginal delivery.

Methods This retrospective study included singleton children that were born between January 2013 and December 2014. The Chinese version of the Conners’ Parent Rating Scale–Revised (CPRS-48) was required on the probability of psychological and behavioral problems. The China–Wechsler Intelligence Scale for Children (C-WIRS) was used for evaluation of crystallized intelligence and Raven’s Standard Progressive Matrices for evaluation of fluid intelligence.

Results A total of 10,568 valid questionnaires were obtained. CPRS-48 ADHD index and detection rate were higher in cesarean delivery group than those in vaginal delivery group. Cesarean delivery groups had a lower performance intelligence quotient score according to C-WISC.

Conclusion Children born by cesarean delivery were more likely to have a risk of ADHD and a lower performance intelligence quotient compared with those born by vaginal delivery.

Keywords Cesarean section; Attention deficit hyperactivity disorder; Intelligence.
with spontaneous vaginal delivery. However, other research showed no association between cesarean deliveries with better cognitive development in children. A recent study revealed that mode of delivery can moderate the genetics of intelligence based on an explorative genome-wide analysis. There is an urgent need for further studies that may increase our understanding of effects of delivery modes on intelligence in children.

Since the release of the family planning policy 2016, an increasing number of couples had a second child. Currently, the obstetric population in China is clinically complex, including obesity, chronic hypertension, diabetes, especially the increasing maternal age at delivery, and history of cesarean section. Therefore, the optimal mode of delivery for maternal indications is important. This might have contributed to the increase in cesarean delivery rates. Studies have reported that children born by cesarean section are associated with an increased risk of neurodevelopmental and psychiatric disorders, tending to have lower cognitive outcomes. Children with cesarean delivery births may face a delay in cognitive and motor development at 9 months; however, there are few reports about the association between delivery mode and children’s ADHD.

We have a hypothesis that mode of delivery would influence the childhood behavioral mental development, ADHD, and IQ. The current study was to examine the association between mode of delivery and childhood behavioral mental development, ADHD, and IQ.

METHODS

Participants

The procedures of our study were approved by the Qingdao Chengyang People’s Hospital (ethical approval number: no. 2012016). Written consent was obtained from the guardians of all children. All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration and later versions. The study population included children of singleton pregnancy born by vaginal delivery and cesarean section at term (gestation age 37–42 weeks) aging between January 2013 and December 2014. The following conditions were excluded; including children who were born with multiple pregnancies, low birth weight, birth defects or before 37 weeks; who received drugs for ADHD; whose natural mother with abnormal placentation recorded during antenatal care by ultrasonography or antepartum hemorrhage observed antenatally or chronic medical conditions (asthma, hypertension, epilepsy, diabetes mellitus, HIV anemia, and sickle cell disease); and whose biological parents with a history of any mental diseases. Case notes of all eligible women were reviewed and the information extracted.

Definition of delivery mode

The delivery mode was classified into two main categories: vaginal delivery, in which baby was born by the vagina; and cesarean section, which included the cesarean delivery before labor, cesarean delivery during the latent phase of labor, and cesarean delivery during the active phase of labor. The children born at term through a cesarean delivery in view of non progress of labor were defined as the cesarean delivery before labor. The latent phase of labor indicated the interval from the time point of mild regular uterine contractions to the time point of 3 cm of cervical dilatation. The active phase of labor represented the interval after the latent phase to full cervical dilatation. Because of the prolonged latent phase or prolonged active phase, the birth was moved to cesarean delivery, defined as cesarean delivery during the latent phase of labor or cesarean delivery during the active phase of labor.

Assessment of ADHD symptoms

The ADHD symptoms and behaviors were assessed in children with the Chinese version of the Conners’ Parent Rating Scale–Revised (CPRS-48). The CPRS-48 works with homogeneity reliability of 0.932 and a split-half reliability of 0.900 in evaluating symptoms and behaviors in children with ADHD. The questionnaire included 48 items rated from 0 (never) to 3 (very often). These 48 items can form six subscales to evaluate six dimensions of behavioral outcomes, including conduct problems, learning problems, psychosomatic problems, impulsive-hyperactive problems, anxiety, and ADHD index. The mean score of at least 1.5 was considered a positive symptom. The higher the score, the worse the symptom. In the present study, the CPRS-48 was independently completed by parents or guardians who lived with the children and know thoroughly their behavioral and psychological conditions. The questionnaires were excluded if they contained more than one-third of blank items, the same scores, or obvious regularity.

Evaluation of intelligence

Evaluation of crystallized intelligence

The intelligence of the children was tested by the China–Wechsler Intelligence Scale for Children (C-WISC), which was revised by Gong and Cai at Hunan Medical University. The test consists of 11 individual items, six verbal testing items (Information, Comprehend, Sorting, Arithmetic, Vocabulary, and Digit symbol), and five performance testing items (Picture Completing, Picture Arrangement, Block Pattern, Object Assembly, and Coding). Based on individual testing, the VIQ, PIQ, and FIQ were calculated progressively. The eval-
Evaluation of fluid intelligence

Fluid intelligence of the children was measured with a Chinese Primary Students mental Health Assessment System (SF/soft-C04; Beijing Normal University Technology Group, Beijing, China) produced based on RSPM by Beijing Normal University Technology Group. This test consists of 60 items divided into five series (A, B, C, D, and E), 1 point for one correct answer, each comprising 12 items.

Statistical analysis

Numerical data were summarized into means and standard deviations. Kolmogorov-Smirnov test was used to test whether the data conform to normal distribution. Statistical analysis for continuous variable was independent t-test with Welch’s correction for two-sample comparison. Chi-square was used for investigating possible associations of categorical variables with ADHD and childhood intelligence. The statistical analyses were carried out with SPSS 18.0 (SPSS Inc., Chicago, IL, USA) or GraphPad Prism 7 (GraphPad Software, Boston, MA, USA). Results with p<0.05 were considered statistically significant.

RESULTS

Basic descriptive

During the study period, a total of 5,745 children were born by vaginal delivery and 4,862 children born by cesarean section (1,865 via cesarean delivery before labor, 1,930 via cesarean delivery during the latent phase of labor, and 1,067 via cesarean delivery during the active phase of labor) were enrolled. Among the issued 10,607 questionnaires, 10,568 were valid. The remaining 39 questionnaires were excluded, consisting of 4 blank responses and 35 invalid questionnaires. The participants had age ranging between 7–8 years. Basic information about the two groups is shown in Table 1. No significant differences existed in age and sex between the groups.

Comparisons of ADHD between different groups

The ADHD index in CPRS-48 was used to identify a probable diagnosis of ADHD. As shown in Table 2, the ADHD diagnosis in cesarean section group was significantly more than those in vaginal delivery group (χ²=22.81, p<0.001). The CPRS-48 subscale scores of the children in different subtypes of cesarean section groups were compared with those of vaginal delivery group (Figure 1). The children in the cesarean delivery before labor, cesarean delivery during the latent phase of labor, and cesarean delivery during the active phase of labor showed a higher ADHD index than those in vaginal delivery group (Figure 1A) (p<0.05). There was no difference in subscale scores for conduct problems (Figure 1B) and learning problems (Figure 1C) between each subtype of cesarean delivery and vaginal delivery. However, the subscale scores of cesarean delivery groups for psychosomatic (Figure 1D), impulsiveness-hyperactivity (Figure 1E), and anxiety (Figure 1F) index were significantly higher than that of the vaginal delivery group (p<0.05). More specifically, the detection rate of impulsive-hyperactive problems and anxiety in the cesarean delivery before labor group and cesarean delivery during the latent phase of labor group was higher than that in vaginal delivery group, while the detection rate of the impulsive-hyperactive problem in cesarean delivery during the active phase was higher than that in vaginal delivery group (Table 3).

Comparisons of intelligence between different groups

To further understand the influence of delivery mode on intelligence, the present study also analyzed the VIQ, PIQ, FIQ, and fluid intelligence differences. According to the results, PIQ turned out to differ significantly between the cesarean delivery before labor group and vaginal delivery group (p<0.05) (Figure 2A). On the contrary, no statistically significant differences were found in the VIQ, FIQ, and fluid intelligence according to the type of delivery (Figure 2B-D).

DISCUSSION

Children’s mental health is increasingly a public health concern. Mental health problems tend to appear in adolescence and extend throughout adulthood, with many other associated adverse effects on health and social functioning. There are many factors that affect children’s behavior problems. Cesarean section is a potential factor that may be associated with children’s mental health. This paper only discusses the influ-
ence of delivery mode on children’s ADHD, as well as intelligence. The association between delivery mode on children’s ADHD imply cesarean section has a contribution to the increase of children’s psychological disorder. Therefore it should be carefully evaluated before the implementation of cesarean section in clinical practice and should have sufficient reasons.

In order to improve the comparability between groups, we try to keep the general conditions of the vaginal and cesarean delivery groups as consistent as possible. The effect of mode of birth on children’s ADHD has been proposed, but this suggestion is still under considerable debate.27 In this study, the detection rate of ADHD in the cesarean section group was much higher than that in the vaginal delivery group, and the difference was statistically significant. This implied that cesarean section is a risk factor for ADHD in children. There is emerging evidence that babies born by caesarean section have different hormonal, physical, bacterial, and medical exposures, and that these exposures can subtly alter neonatal physiology.28 During vaginal delivery, the birth canal produces a moderate change in physical tension under the regulation of neu-

Table 3. The rate of five items in the Chinese version of the Conners’ Parent Rating Scale–Revised between vaginal delivery (VD) group and cesarean delivery (CD) group

<table>
<thead>
<tr>
<th></th>
<th>VD</th>
<th>CD-BL</th>
<th>CD-LP</th>
<th>CD-AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduct problem</td>
<td>43 (0.8)</td>
<td>15 (0.8)</td>
<td>13 (0.7)</td>
<td>10 (0.9)</td>
</tr>
<tr>
<td>Learning problem</td>
<td>112 (2.0)</td>
<td>43 (2.3)</td>
<td>44 (2.3)</td>
<td>24 (2.3)</td>
</tr>
<tr>
<td>Psychosomatic problem</td>
<td>134 (2.3)</td>
<td>46 (2.5)</td>
<td>40 (2.1)</td>
<td>17 (1.6)</td>
</tr>
<tr>
<td>Impulsive-hyperactive problem</td>
<td>141 (2.5)</td>
<td>107 (5.8)***</td>
<td>74 (3.9)***</td>
<td>41 (3.9)*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>128 (2.2)</td>
<td>61 (3.3)*</td>
<td>61 (3.2)*</td>
<td>34 (3.2)</td>
</tr>
</tbody>
</table>

Values are presented as number (%). *p<0.05; **p<0.01; ***p<0.001. CD-BL, cesarean delivery before labor; CD-LP, cesarean delivery during the latent phase of labor; CD-AP, cesarean delivery during the active phase of labor.
rohumoral fluids, and the fetal body, chest, abdomen, and fetal head are squeezed rhythmically. Babies born by cesarean section are usually delivered quickly and passively in a short period. Therefore, this delivery mode can lead to different levels of neurohumoral fluids, and may cause behavioral problems. Our result was consistent with another Swedish sibling-matched study, which found that birth by cesarean section was associated with a higher risk of ADHD.

It has been reported that elective cesarean section affected child psychology and behavior, including inattention, hyperactivity/impulsivity, social problems, and executive dysfunction. Especially, the inattention problem in the elective cesarean section group was worse, representing a higher Swanson, Nolan, and Pelham rating scale IV–Parent Form inattention score compared with the vaginal delivery group. In this study, the inattention of the children was embodied in impulsive-hyperactive problems and anxiety. Notably, this study revealed that the emergency cesarean section moved from the prolonged latent phase or active phase caused more impulsive-hyperactive problem and anxiety in children than vaginal delivery. These findings indicate that children delivered by cesarean section are more likely to show ADHD symptoms, especially hyperactivity/impulsiveness, and anxiety.

An investigation of the impact of the two different modes of delivery on neuropsychological development found that cesarean section hinders verbal development, nonverbal development, global development, and general intelligence in twin births, that shows, cesarean delivery may be a possible risk factor for neuropsychological development and intelligence in twin births. This study further investigated the impact of the
two different modes of delivery on the intelligence of school-age children. The results indicated that the PIQ, not the VIQ, FIQ, or fluid IQ, was different between three kinds of cesarean section and vaginal birth. This clue can be found in a study by Curran et al., which found an association between delivery mode and school performance. Curran et al. assessed the school performance in Swedish adolescents with 1,036,424 children born by unassisted vaginal delivery and 42,107 by elective cesarean section and found poor school performance was observed more in adolescents in cesarean-section birth. The method of delivery may moderate the genetic disposition (rs705670 on chromosome 9) of PIQ in children. The rs705670 on chromosome 9 for PIQ, LINC01502, have recently been implicated in several neuropsychiatric disorders where IQ is affected, such as ADHD. Therefore, the mode of delivery might influence PIQ of children.

The current investigation has several limitations and strengths. There is the potential for residual confounding in this study, because of unavailability of some data, such as maternal stress, marital discord, history of breastfeeding, and other sociocultural factors. Another limitation is the absence of information on genetic factors, which have been theorized to play a role in ADHD and IQ development. Finally, this study lacked information about paternal age, comorbidities, and behavioural factors that could also contribute to offspring ADHD and IQ.

In conclusion, our results indicate that the mode of delivery might have effects on ADHD and intelligence in children. The presented findings increased the understanding of the effects of various modes of delivery on children’s mental health outcomes and prompt the need for further studies.

Availability of Data and Material
The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Min Xu, Xinxin Ji. Data curation: Min Xu. Investigation: Xuemei Yu, Benjie Fan, Guimei Li, Xinxin Ji. Methodology: Min Xu, Xinxin Ji. Software: Min Xu, Xuemei Yu, Benjie Fan. Validation: Min Xu, Xinxin Ji. Visualization: Xuemei Yu, Benjie Fan, Guimei Li, Xinxin Ji. Writing—original draft: Min Xu. Writing—review & editing: all authors.

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