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Maternal age at childbirth and social development in infancy

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ABSTRACT

Difficulties in social communication are not necessarily observed only in individuals with autism spectrum disorders (ASD), and there are many subclinical cases in the general populations. Although advanced parental age at childbirth has often been considered a possible risk factor of ASD, it might contribute to poor social functioning in children, rather than to ASD itself. This study examined whether advanced maternal age at childbirth and obstetric factors were associated with atypical social development in infancy. At free health check-ups for children aged 18 months conducted in Munakata city, Japan, 1460 children (729 males) were assessed using the Japanese version of the Modified Checklist for Autism in Toddlers (M-CHAT). Adjusted odds ratio showed that children of mothers aged ≥35 years at childbirth were 2.22 (95% confidence intervals, 1.39–3.55) times more likely to fail on the M-CHAT (failing three or more items) compared with the reference group (aged ≤29). Although most mothers will have toddlers that fall in the typical range on this measure of social development, clinicians should pay more attention to early social development of children, especially for lateborn babies, and should be more sensitive to their potential needs so as to provide appropriate advice and support for their caregivers.

1. Introduction

Genetic factors are thought to be strongly associated with the etiology of autism spectrum disorders (ASD) (Bailey et al., 1995); however, the influence of other factors has been assumed, but remains controversial. Among possible contributing factors, advanced parental age at childbirth has often been considered a possible risk factor of ASD. Although past results have been inconclusive, a recent review and comprehensive meta-analysis both showed a significant association between advanced parental age and ASD (Gardener, Spiegelman, & Buka, 2009; Kolevzon, Gross, & Reichenberg, 2007).

Difficulties in social communication are core autistic symptoms, but are not necessarily observed only in individuals with ASD. The general population is now thought to be widely distributed along a continuum of severity of social impairment (Constantino et al., 2003). A recent study indicated that among children, socio-communication impairment was several times as prevalent as the triad features of ASD (Ronald, Happé, & Plomin, 2005), which underscores that there are many subclinical cases in the general population and that clinicians must become more sensitive to the potential needs of these cases.

Such recognition has raised the hypothesis that advanced parental age might contribute to poor social functioning in children, rather than to ASD or a specific psychiatric disorder itself. Weiser et al. (2008) examined 368,244 male adolescents in Israel and found that advanced parental age at childbirth was associated with poorer social functioning regarding companionships. However, this finding must be interpreted cautiously because social functioning in adolescence may be the result of long-term complex gene–environmental interactions. The best method to elucidate the association between

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advanced parental age at childbirth and poor social functioning would be an examination in early infancy; however, to our knowledge, no such study of social development in early infancy has been conducted.

Socio-communication abnormalities in ASD begin to manifest at age 1 year (Kamio, Tobimatsu, & Fukui, in press), and atypical social development at this age is identified by a lack of nonverbal reciprocal behaviors, such as socio-emotional responsiveness or joint attention. The Modified Checklist for Autism in Toddlers (M-CHAT) (Robins, Fein, Barton, & Green, 2001), which was originally developed as a 23-item parent report questionnaire that assesses early autistic symptoms, is considered to be one of the most useful tools for examining atypical social development in a large population.

The present study was conducted in Japan, where the mean maternal age at childbirth has increased from 29.3 years in 1997 to 30.7 years in 2007 (Ministry of Health, Labor and Welfare of Japan, 2009). Unlike other developed countries, concerns regarding advanced maternal age have not been thoroughly examined in Japan because Japanese local communities usually lack their own research database. The present research was conducted as a part of a community-based longitudinal study, which aimed to explore the early developmental trajectory in Japanese children.

The purpose of this study was to determine whether advanced maternal age at childbirth and other factors are associated with atypical social development in infancy as well as later ASD diagnosis.

2. Methods

Since April 2004, we have conducted a cohort study targeting children aged 18 months in Munakata city, which has a population of approximately 95,000 people and is located in central Fukuoka prefecture, Japan. A national health check-up system has been established in Japan in order to provide all children with free routine check-ups. In collaboration with check-up staff at local agencies, the check-ups conducted at 18 months of age were used as an opportunity to detect children with difficulties in social development, and detailed follow-up assessment and corresponding support programs were provided.

In the 3-year period up to March 2007, 2146 out of 2245 target children visited a local health agency for the free check-up at 18 months of age, and written informed consent to participate in our study was obtained from the caregivers of 2113 children. The protocol of this study was approved by the ethics committee of the National Center for Neurology and Psychiatry of Japan.

2.1. Retrospective data collection

We gathered available information about pre-, peri-, and neonatal complications from check-up charts transcribed from the "mother-and-baby" notebook (*boshi-techo*, in Japanese), in which mothers keep comprehensive records for the obstetrician/pediatrician. The participants of this study were 1460 children (65.0% of target children; 729 males) for whom all the information used in this study were obtained.

2.2. Evaluative procedures

2.2.1. Atypical social development at 18 months of age

Atypical social development at 18 months of age was defined as failing three or more items among the total 23 items of the M-CHAT. The M-CHAT assesses various types of social development in children aged 18–24 months (Robins et al., 2001), has been translated into many languages and is used all over the world (Robins, n.d.). The Japanese version was developed by the authors (Inada, Koyama, Inokuchi, Kuroda, & Kamio, in press) and has been used at check-ups for 18-month-old children in several Japanese communities, including Munakata. Among the total of 1460 children, 82 males (11.2%) and 55 females (7.5%) failed the criteria.

2.2.2. ASD diagnosis

The children were reassessed at a free check-up at 36 months of age and other available resources, such as referring medical professionals, were also used to identify all ASD cases. Among 1460 children, 28 children (21 males) were diagnosed as having ASD by March 2010 (at least age 4). They were diagnosed by expert consensus among the research team directed by an experienced child psychiatrist (Y.K.) according to the DSM-IV-TR criteria for pervasive developmental disorders (PDD) (American Psychiatric Association [APA], 2000), based on a detailed clinical assessment and comprehensive parental interviews on each child's developmental history. Nineteen children (67.9%) were diagnosed at age 2, while the remaining children were diagnosed at age 3. Twelve (42.9%) had developmental delay (IQ < 70) and 26 (92.9%) scored higher than the cutoff score for PDD (25.5) on the Childhood Autism Rating Scale-Tokyo Version (CARS-TV) (Kurita, Miyake, & Katsuno, 1989; Tachimori, Osada, & Kurita, 2003). Although two high-functioning (IQ ≥ 70) children scored below the CARS-TV cutoff, both of them showed significant impairment in interpersonal relationship and reciprocal communication; therefore, a diagnosis of PDD not otherwise specified (PDD-NOS) was confirmed.

2.3. Statistical analysis

For each assumed risk factor (see tables), odds ratios (ORs) and 95% confidence intervals (CIs) for ASD diagnosis and failure on the M-CHAT at age 18 months were calculated using logistic regression analysis, both before and after controlling for other factors.