**表1　社会的行動に関連するM-CHAT項目**

| 獲得月齢* | 項目 | 内容・例 |
|---|---|---|
| 8ヵ月以前 | 他児への関心 | 他の子どもに対する興味や関心があるか。 |
| | イナイイナイバー | イナイイナイバーをすると喜ぶか。 |
| | アイコンタクト | 1,2秒より長く人の目を見つめるか。 |
| | 微笑み返し | 児の顔を見たり笑いかけると、笑顔を返してくるか。 |
| | 呼名反応 | 名前を呼ばれると反応するか。 |
| 11〜12ヵ月 | ふり遊び・みたて遊び | 電話の受話器を耳にあててしゃべるまねをしたり、人形やその他のモノを使ってごっこ遊びをするか。 |
| | 要求の指さし | 欲しいモノがあるとき、指をさして要求するか。 |
| | 興味の指さし | 自分の興味のあるモノを、指をさして親に伝えようとするか（要求の指さしとは異なる）。 |
| | 模倣 | 人の動作の真似をするか。 |
| | 指さし追従 | 親が指をさした方向を見るか。 |
| | 注意喚起 | 親の注意を自分のほうに引こうとするか。 |
| 15ヵ月以降 | 共同注意 | 見て欲しいモノ（自分で組み立てた積木や描いた絵など）があるとき、それを親に見せに持ってくるか（単なる要求とは区別される）。 |
| | 視線追従 | 親が見ているモノを、一緒に見るか。 |
| | 社会的参照 | いつもと違うことがあるとき、親の顔を見て反応を確かめるか。 |

*対象児の75%が獲得した時期を示す。
Inada N, Kamio Y, & Koyama T: Developmental chronology of preverbal social behaviors in infancy using the M-CHAT: Baseline for early detection of atypical social development, Research in Autism Spectrum Disorder, 4, 605-611, 2010より一部改変して転載。

**表2　アスペルガー症候群の子どもの早期徴候**

- きょうだいとは一緒に遊ぶことはあるが、きょうだい以外の他児には興味や関心があるようには見えない（その半面、他児が持っているおもちゃには関心を持つ）。
- イナイイナイバーなどの２者関係の単純な遊びは喜ぶ。
- アイコンタクトは少ないが存在する。ただし、他者とのかかわりに統合されて使われることはあまりない。
- 大人に笑いかけてくるが、大人が笑いかけるのに対してあまり反応しない。
- ままごとやキャラクターごっこはできる。ただし、パターン化したひとり遊びか、母親と遊ぶ場合も自分で相手の役割を決めて固定してしまう傾向がある。その場のやりとりに応じて柔軟に発展させるという意味でのごっこ性は乏しい。
- 大人の指さしを見たり、自分から指さしをすることはできるが、他者との関心の共有に至らない。
- 模倣能力はある。模倣学習の能力はあるが、むしろ独学で、かなやアルファベット、ロゴマーク、機械類の操作を覚えて周囲を驚かせる。
- 親の注意をあまりひこうとしない。むしろ、ひとり遊びが好きなことが多い。

果からは、一歳六カ月という年齢で発見された子どもは必ずしも発達の遅れのある自閉症児ではなく、むしろ半数を超える子どもは、発達の遅れがなく、三歳以降に自閉症スペクトラム障害と診断されていました。こういうケースでも、確定診断のできる三歳になるのを待つよりも、親の懸念がある早い段階で療育を経験することはメリットが大きいと考えられます。もちろん、親の心情や気づきの程度に配慮すべきケースは少なくありませんので、診断を無理に押し付けるのではなく、親子の日常生活をていねいに聴取してニーズを発見し、必要な支援をすみやかに提供することを優先的に考えるのがよいでしょう。

これは、平成二十年の発達障害施策の推進に係る検討会報告書（http://www.mhlw.go.jp/shingi/2008/09/dl/s0903-7h.pdf）に挙げられている「診断前支援」、すなわち、家族が発達障害という事実に取り組む準備ができていない場合には、不用意な診断を行う前に支援をすみやかに開始できるよう取り組む、という考え方と一致するものです。

## 56 一歳から二歳までの社会的発達に注目する

アスペルガー症候群に代表される発達の遅れのない自閉症スペクトラム障害の子どもの一歳六カ月から二歳前後での行動特徴を表2に示しています。平均的な発達の子どもの社会的行動の発達（表1）と比較してご覧ください。表1は、日本語版M-CHAT項目のうち社会的行動に関連する十四項目を取り出し、一般の獲得月齢順に並べたものです。これらの行動は、アスペルガー症候群の子どもでは自閉症の子どもよりもできるものは多いけれども、頻度が著しく少ないことが特徴となります（表2）。

アスペルガーの言葉を借りれば、アスペルガー症候群の子どもたちは、高い能力も持っているのですが、そのまなざしは人に向けられていない、と言えるでしょう。この特徴は大人になっても持続し、アスペルガー症候群の人々の対人関係の困難の根底にかかわる問題と考えられています。

## おわりに

子どもは障害の有無にかかわらず、望ましい環境に恵まれれば本来の力を発揮する方向に発達していく存在です。発達障害の支援には、子どもが生活し育つ地域を基盤として、保健・医療、教育・福祉などすべてが連携できる体制を整備する必要があります。

近年、五歳という年齢に注目して健診を導入する自治体が増えていますが、これまで述べてきたように、早期発見と支援は三歳までにできることがまだまだあります。年齢が上がるにつれて、発達の問題と情緒・行動などのメンタルな問題とは区別しがたくなり、的確な診断と評価は困難になっていきます。また五歳児の実証的なデータはほとんど存在せず、どのような形の早期診断がどのような子どもに最適なのかについては、これから蓄積する必要があります。

今後、自閉症スペクトラム障害のある子どものQOLの向上とメンタルな問題の予防という観点からも、ライフステージに及ぶ支援が速やかに始まり、長く続くような地域ケアが実現することを強く期待します。

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# Determining differences in social cognition between high-functioning autistic disorder and other pervasive developmental disorders using new advanced "mind-reading" tasks

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ABSTRACT

Deficits in understanding the mental state of others ("mind-reading") have been well documented in individuals with pervasive developmental disorders (PDD). However, it is unclear whether this deficit in social cognition differs between the subgroups of PDD defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. In this study, PDD was divided into high-functioning autistic disorder (HFA) ($n = 17$) and other PDD ($n = 11$) consisting of Asperger's disorder ($n = 8$) and PDD-NOS ($n = 3$), and differences in mind-reading ability was examined between the two clinical groups and controls ($n = 50$) using a new advanced naturalistic task consisting of short scenes from a TV drama showing communication in social situations. The task was divided into visual and auditory tasks to investigate which modality was more valuable for individuals with PDD to understand the mental state of others. The results suggest that social cognition differs significantly between individuals with HFA and those with other PDD, with no difference being found between those with other PDD and controls. Neither the auditory or visual modality was found to be dominant in subjects with PDD in the mind-reading task. Taken together, complex mind-reading tasks appear to be effective for distinguishing individuals with HFA from those with other PDD.



## 1. Introduction

The term "theory of mind (ToM)", which describe the ability to attribute mental states to oneself or another person, was introduced in psychology by Premack and Woodruff (1978). Since Baron-Cohen, Leslie, and Frith (1985) first reported "deficit of ToM" in which the autistic condition is seen as a failure to attribute mental states to others, much work has been conducted on ToM in pervasive developmental disorders (PDD). The ability to understand the mental state of others, which underlies fundamental social skills, is also referred to as "mind-reading" (Baron-Cohen et al., 1985). The basic ToM test,

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usually consisting of the first and the second-order false belief tasks, is not sufficiently complex to detect deficits in adults with high-functioning PDD (HFPDD) (Bowler, 1992; Happé, 1994; Ozonoff, Pennington, & Rogers, 1991). Thus, an advanced ToM test, the Strange Situation Test, was devised by Happé (1994) in which participants are asked to provide an explanation for non-literal statements (e.g. irony or lie) made by story characters. Happé's study demonstrated that participants with PDD who passed the first and second-order false belief tasks did show specific deficits in ToM on this more complex test.

Many advanced ToM studies were subsequently conducted with adults with HFPDD in order to investigate subtle deficits of "mind-reading" ability. The Eyes Test was created for adults with HFPDD as a mind-reading task that uses information from the visual modality alone (Baron-Cohen, Wheelwright, & Jolliffe, 1997; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). In the task, participants are shown photographs in which only the areas of the eyes are cut out from a person's face, and they are asked to identify the person's mental state. Researchers have revealed that individuals with PDD provide less correct justifications of mental state than controls, indicating that the Eyes Test is highly accurate in measuring mind-reading ability. However, in the real world, in order to integrate all of the information which people express, we look not only at the eyes of others, but also at their facial expressions, body language, posture and so forth. Moreover, we do not look at a static face and body in the real world, but at a moving face and body. Thus, a task that presents dynamic information in both the visual and auditory modality, such as video, was deemed to be more realistic and was expected to measure the ability to understand others' mental states in daily life. Accordingly, Heavey, Phillips, Baron-Cohen, and Rutter (2000) developed the "Awkward Moments Test" which uses scenes taken from TV programs and commercials and Roeyers, Buysee, Ponnet, and Pichal (2001) devised the "Empathic Accuracy Task" which uses recordings of real communicative interactions. In their studies, participants viewed moving images (video) and tried to determine the mental states of the characters. Participants with PDD provided less correct justifications of mental state than typically developing subjects.

More recently, a question has been raised about which of the auditory and visual modality is more valuable for adults with PDD to understand the mental state of others. A task that extends the abovementioned advanced tasks into the auditory modality was created by Rutherford, Baron-Cohen, and Wheelwright (2002), and a study employing this task with adults with Asperger's disorder (AS) and high-functioning autistic disorder (HFA) revealed that both groups had difficulty extracting mental state information from vocalizations (Golan, Baron-Cohen, Hill, & Rutherford, 2007). In addition, use of the Cambridge "Mind-Reading" (CAM) Face-Voice Battery in adults with AS to test their cognition of 20 complex emotions and mental states from faces or voices (Golan, Baron-Cohen, & Hill, 2006) showed that although the participants showed deficits in social cognition when relying on either facial or vocal information alone, they could understand others' mental state better from the voices than from the faces. Given this finding among individuals with AS, one of the objectives of the present study is to identify which modality—visual (facial expression, gesture and posture) or auditory (pitch, intonation and tone of speech)—is more valuable for adults with PDD to understand the complex emotions of others.

Most recent studies using the advanced mind-reading tasks with moving stimuli have treated adults with PDD as one group. Some earlier studies, however, investigated the difference in mind-reading ability between the subgroups of PDD, especially between HFA and AS, but still today it is unclear whether in fact the two disorders differ in degree of impairment of mind-reading ability (Dahleger & Trillingsgaard, 1996; Ozonoff, Rogers, & Pennington, 1991; Ozonoff, South, & Miller, 2000; Zaitai, Durkin, & Pratt, 2003). A recent study that compared the subgroups of HFA and AS with typically developing adults was conducted by Spek, Scholte, and Van Berckelaer-Onnes (2010), who used the Eyes Test (Baron-Cohen et al., 1997), the Faux Pas Recognition Test (Stone, Baron-Cohen, & Knight, 1998) and the Strange Stories Test (Happé, 1994). The findings suggested that there was no significant difference in mind reading ability between individuals with HFA and AS on any of the tasks. However, since Spek et al. did not employ the CAM or moving images in their mind-reading task, it remains to be determined whether mind-reading ability differs on a more complex, moving mind-reading task between the PDD subgroups.

Thus, the second objective of the present study was to clarify whether any differences exist in mind-reading ability between HFA, a typical PDD, and other PDD consisting of AS and pervasive developmental disorder not otherwise specified (PDD-NOS). We hypothesized that individuals with HFA would show greater deficits in mind-reading ability than those with other PDD.

## 2. Methods

### 2.1. Participants

The clinical group comprised 28 male adolescents and adults with PDD (mean age 24.5 years, SD = 7.7 years, range = 16–45 years). Participants were recruited from a private child psychiatric clinic specializing in PDD or a research volunteer pool of the PDD research group at the National Institute of Mental Health. All participants were diagnosed by experienced child psychiatrists. The diagnostic process was conducted by a team of one child psychiatrist and one or two clinical psychologists. The psychiatrist interviewed the parents about their child's developmental history and daily behaviors. In parallel, in another room, the clinical psychologist observed the social behavior and communication of each participant during the IQ test and in conversation which included questions about daily life, their community and interpersonal relationships. Based on the data obtained, the participants were diagnosed according to the established criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) (APA, 2000): 17 were diagnosed with HFA (showing qualitative impairment in social interaction, qualitative impairment in communication, and restricted repetitive and stereotyped patterns of behavior, interests, and activities), and 11 were diagnosed with other PDD, which combined 8 participants with

**Table 1**
Descriptive characteristic of participants.

| | HFA[a] ($n = 17$) | | | Other PDD[b] ($n = 11$) | | | Control ($n = 50$) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Range | Mean | SD | Range | Mean | SD | Range |
| Chronological age | 24.2 | 8.5 | 16–45 | 25.0 | 6.6 | 17–35 | 19.3 | 1.7 | 18–22 |
| Full Scale IQ | 103.2 | 13.5 | 87–132 | 108.2 | 9.7 | 88–119 | | | |
| Verbal IQ | 103.9 | 14.5 | 80–136 | 109.4 | 10.1 | 83–120 | | | |
| Performance IQ | 100.3 | 16.7 | 72–126 | 106.5 | 16.4 | 66–127 | | | |
| AQ[c] | 33.3 | 6.5 | 24–44 | 33.6 | 6.3 | 28–44 | | | |

[a] High-functioning autistic disorder.
[b] Pervasive developmental disorders.
[c] Autism Spectrum Quotient.

AS and 3 participants with PDD-NOS (showing atypical autistic symptoms that are relatively mild and do not meet the diagnostic criteria of the main symptoms of Autistic disorder). Also, 14 participants were tested using the Wechsler Adult Intelligence Scale Reversed (WAIS-R), 3 were tested using the WAIS-Third Edition (WAIS-III), and 11 were tested using the Wechsler Intelligence Scale for Children-Third Edition (WISC-III) (Wechsler, 1981, 1991, 1997). The characteristics of the participants with PDD are shown in Table 1. All participants had a full intelligence quotient (FIQ) of at least 85. In addition, all participants except one were administered the Autism Spectrum Quotient (AQ)-Japanese version (Wakabayashi, Baron-Cohen, Wheelwright, & Tojo, 2005). No significant differences in FIQ ($t = 1.1$, $p = .30$), the verbal intelligence quotient (VIQ) ($t = 1.1$, $p = .29$), the performance intelligence quotient (PIQ) ($t = 1.0$, $p = .35$) and AQ ($t = .18$, $p = .90$) scores were found between the HFA group and other PDD group. The participants had no other psychological diagnosis.

The control group consisted of 50 male students recruited from the University of Chiba (mean age 19.3 years, SD = 1.74). They were no administered IQ tests, but on the basis of their grade level it was assumed that they had normal intelligence.

Written informed consent to participate in the study was obtained in advance from all participants and from their parents when the participants were minors (<20 years of age), and the study protocol was approved by the Ethics Committee of the National Institute of Neurology and Psychiatry.

### 2.2. Instruments

#### 2.2.1. Visual and auditory tasks

We administered the Motion Picture Mind-Reading (MPMR) Task, which was originally designed to measure individual differences among adults in the general population (Wakabayashi & Katsumata, in press). The MPMR consists of short clips from the TV drama "*Shiroi Kyotou*" (Kobayashi, 1978), which was famous in the 1970s but would not be well known to the younger participants in this study. The storyline concerns malpractice at a famous medical school in Japan. The drama was edited into clips using DVRaptor software (Canopus Company, Japan). The length of each of the 41 scenes ranged from 3 s to 11 s (mean 5.2 s). The MPMR Task thus contained more realistic material than the ToM tasks used in previous studies because it contained scenes from dramatized real life. Moreover, the content was highly complex, including many non-literal scenes with incongruent dialogue and mental states conveying, for example, characters who were lying or being ironic. The participants were asked to understand the hidden intent, masked behind incongruent visual information (facial expression, gesture and posture) and auditory information (the non-literal aspects of speech of pitch, intonation and tone).

In order to identify whether the visual or auditory modality was more valuable for adults with PDD to understand the complex mental states of others, we modified the 41 clips of the MPMR to create one visual task and one corresponding auditory task for each clip. For the visual task, the sound was edited out of each scene. For the auditory task, no picture was displayed on the PC monitor and only the auditory stimuli composed of segments of the one character's speech was heard (see Fig. 1). In each of the visual and auditory trials, participants had to decide whether a label appearing on the PC monitor described the character's mental state (intent) appropriately or not. Of the 41 clips, 27 were labeled correctly and 14 incorrectly (Table 2).

#### 2.2.2. Autism Spectrum Quotient-Japanese version (AQ-Japanese version)

The AQ is a self-report questionnaire which measures the degree to which any adult of normal IQ possesses traits related to the autism spectrum (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). The AQ-Japanese version (Wakabayashi et al., 2005) was used in this study.

### 2.3. Procedure

The participants were tested individually in a quiet room at the clinic or university. Both the visual and auditory task stimuli were presented to the participants while were wearing headphones. The clinical groups viewed the stimuli on a 13.3-in. monitor of a laptop computer running Windows XP (Dynabook SS MX/190DR, Toshiba), while the control group viewed them on a 17-in. PC monitor (Dimension XP 4400, Dell). The participants' response to each item was recorded by computer. Each task began with the message "To start, press the space key". After 1 s, the stimuli were presented in either the visual or


**Fig. 1.** Example of the test stimuli used in the visual task without auditory information (Scene 1, Feigning). In the auditory task which presented the dialogue, "Um, I just feel like seeing you, big brother" there was no picture of the character displayed on the screen. In each of the visual and auditory trials, participants had to decide whether the label appearing on the screen described the character's mental state (intent) appropriately or not.

auditory modality scene accompanied by the word or phrase describing a mental state. The participant was asked to judge whether the word or phrase presented on the screen described the person in each scene appropriately or not. To record their judgment, they pressed the F key to which was attached a small label saying "appropriate" or the J key to which was attached the label "inappropriate". One second after participants pressed a key, a message appeared saying "Next scene, press the space key", and as a participant pressed it, the next trial started. The presentation order of the 41 clips was randomized for each participant.

Participants completed one practice trial for one visual and one auditory task before the experiment started. The order of the visual and auditory tasks was counterbalanced. Throughout the entire test, a task requiring the participants to determine the camera angle from which a photo was taken was inserted between the Visual tasks and the Auditory tasks to serve as interference stimuli.

## 3. Results

### *3.1. Comparison of groups by diagnosis*

Accuracy rate was determined by two-way repeated measures ANOVA. The main effect of Group was significant: the HFA group had a lower accuracy rate than the other PDD and control groups. The main effect of Task was also significant in all three groups. The interaction between Group and Task was not significant ($F(2,75) = 0.2$, $P = 0.80$).

The accuracy rate for each task modality is shown in Fig. 2. ANOVA revealed significant main effects for Task ($F(1,75) = 19.0$, $P < 0.01$) and Group ($F(2.75) = 7.9$, $P < 0.01$). The accuracy rate was higher on the visual task than on the auditory task in all groups. The interaction between Task and Group was not significant ($F(2,75) = 0.2$, $P = 0.80$). Results of Bonferroni multiple-comparison tests showed that the accuracy rate of the HFA group was lower than that of the control group ($P < 0.01$) and the other PDD group ($P < 0.05$). No significant difference was found between the other PDD and control groups.

### *3.2. Within-group comparisons of accuracy rate*

No correlations were found for the HFA group and other PDD group with respect to the accuracy rates on the visual task and auditory task, and FIQ, VIQ, PIQ and AQ scores.

### *3.3. Between-group comparisons of accuracy rate*

The accuracy rates on the visual task and auditory task (41 items each) were compared between the HFA, other PDD, and control groups using Fisher's exact test. As shown in Table 2, significant differences were observed for some items on the Visual and Auditory task.

## 4. Discussion

This study investigated differences in mind-reading performance among PDD subgroups by using advanced mind-reading tasks comprised of clips from a TV drama that included social context in the form of another character appearing and

**Table 2**
Accuracy rate for determining the character's mental state among the three subgroups of PDD.

| Scene | Duration (s) | Word/phase shown on screen | Visual | | | | Auditory | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | HFA[a] ($n$ = 17) | Other PDD[b] ($n$ = 11) | Control ($n$ = 50) | $p$ | HFA ($n$ = 17) | Other PDD ($n$ = 11) | Control ($n$ = 50) | $p$ |
| 1 | 3 | Feigning | 53 | 64 | 72 | .35 | 94 | 82 | 82 | .47 |
| 2 | 3 | **Respectful** | 35 | 73 | 82 | .00** | 65 | 64 | 76 | .54 |
| 3 | 6 | Sarcastic | 71 | 73 | 82 | .55 | 59 | 55 | 52 | .89 |
| 4 | 7 | Ironic | 82 | 100 | 88 | .36 | 71 | 46 | 46 | .20 |
| 5 | 6 | **Pleased** | 30 | 64 | 48 | .19 | 38 | 30 | 14 | .10 |
| 6 | 3 | Disbelieving | 65 | 82 | 60 | .39 | 65 | 82 | 70 | .62 |
| 7 | 4 | **Convinced** | 47 | 73 | 80 | .03* | 82 | 91 | 92 | .52 |
| 8 | 9 | **Confident** | 35 | 55 | 74 | .01* | 29 | 55 | 70 | .01* |
| 9 | 6 | Bluffing | 82 | 82 | 72 | .61 | 77 | 82 | 82 | .88 |
| 10 | 3 | Ingratiating | 65 | 64 | 62 | .98 | 71 | 80 | 74 | .87 |
| 11 | 6 | Astonished | 88 | 82 | 74 | .45 | 71 | 73 | 48 | .13 |
| 12 | 3 | Feigning | 82 | 91 | 76 | .51 | 63 | 100 | 76 | .08 |
| 13 | 4 | Pretending not to want | 77 | 82 | 64 | .39 | 12 | 27 | 28 | .39 |
| 14 | 9 | Ironic | 77 | 90 | 86 | .56 | 65 | 73 | 72 | .84 |
| 15 | 9 | Sarcastic | 59 | 73 | 92 | .01* | 53 | 55 | 66 | .56 |
| 16 | 4 | Playing down | 82 | 82 | 58 | .10 | 53 | 91 | 86 | .01* |
| 17 | 5 | Coercive | 65 | 73 | 68 | .91 | 56 | 64 | 88 | .01* |
| 18 | 9 | **Worried** | 82 | 100 | 82 | .31 | 65 | 46 | 62 | .55 |
| 19 | 6 | Lying | 41 | 64 | 72 | .07 | 71 | 55 | 72 | .52 |
| 20 | 4 | Ironic | 88 | 64 | 74 | .30 | 59 | 64 | 84 | .07 |
| 21 | 4 | Guilty | 41 | 91 | 86 | .00** | 41 | 91 | 62 | .03* |
| 22 | 3 | Sarcastic | 41 | 64 | 64 | .24 | 47 | 82 | 68 | .14 |
| 23 | 9 | Ingratiating | 41 | 64 | 52 | .50 | 81 | 91 | 88 | .72 |
| 24 | 3 | **Appreciative** | 29 | 91 | 84 | .00** | 35 | 73 | 62 | .09 |
| 25 | 4 | Feigning | 53 | 73 | 82 | .60 | 88 | 82 | 88 | .85 |
| 26 | 5 | **Wondering** | 77 | 64 | 82 | .40 | 18 | 36 | 50 | .06 |
| 27 | 9 | **Praising** | 24 | 27 | 46 | .18 | 29 | 36 | 38 | .82 |
| 28 | 3 | Angry | 82 | 73 | 90 | .29 | 59 | 73 | 86 | .06 |
| 29 | 5 | **Mocking** | 24 | 18 | 30 | .68 | 12 | 10 | 32 | .13 |
| 30 | 3 | **Disappointed** | 77 | 46 | 68 | .22 | 47 | 55 | 60 | .64 |
| 31 | 11 | Figuring someone out | 41 | 91 | 46 | .02* | 53 | 82 | 68 | .27 |
| 32 | 4 | **Unsure how to react** | 47 | 55 | 78 | .04* | 35 | 36 | 48 | .58 |
| 33 | 3 | Employing tactics | 82 | 73 | 86 | .56 | 69 | 100 | 78 | .14 |
| 34 | 7 | Flattering | 82 | 82 | 92 | .43 | 59 | 55 | 40 | .34 |
| 35 | 7 | Teasing | 65 | 73 | 46 | .16 | 77 | 64 | 70 | .76 |
| 36 | 6 | **Apologetic** | 77 | 73 | 96 | .02* | 29 | 72 | 78 | .00** |
| 37 | 5 | Covering up Embarrassed | 71 | 100 | 82 | .14 | 53 | 64 | 68 | .54 |
| 38 | 7 | **Not liking** | 65 | 73 | 86 | .14 | 41 | 36 | 58 | .28 |
| 39 | 5 | Modest | 88 | 91 | 92 | .90 | 71 | 90 | 84 | .36 |
| 40 | 7 | Sarcastic | 77 | 46 | 56 | .21 | 59 | 73 | 78 | .31 |
| 41 | 9 | **Ashamed** | 31 | 36 | 62 | .05* | 47 | 80 | 86 | .00** |

*Note*: Words/phrases not appropriate to the scene are shown in bold italics. Items shown in yellow highlight are under chance level of the control group. Fisher's exact test, *$p < .05$, **$p < .01$.
[a] High-functioning autistic disorder.
[b] Pervasive developmental disorders.

background scenery being visible. According to Adolphs, Sears, and Piven (2001) and Golan et al. (2006), compared to recognizing general emotions, it is difficult for adults with PDD to recognize the intentions and emotions underlying facial expressions that do not correspond with speech. All of the task items in the present study were designed to assess participants' understanding of hidden emotions and mental states that do not concord with the language heard, and these items were thus expected to present some difficulty for adults with PDD. While differences were observed between the HFA group and control group and between the HFA group and other PDD group, no differences were observed between the other PDD group and control group. This finding suggests that a close relationship exists between cognitive ability, which is closely connected with social communication such as mind-reading ability, and the behavioral characteristics of PDD as laid out in the DSM diagnostic criteria. These findings replicate those of previous ToM research studies which showed that the differential abilities in ToM may help to distinguish AS from autism (Ozonoff, Rogers, et al., 1991; Zaitai et al., 2003).

As to differences in mind-reading ability between the subgroups of PDD, Spek et al. (2010) previously reported no such difference between subjects with HFA and AS. The contradictory results of our study and theirs might be due to the different format of the tasks used. More specifically, the tasks used in their study might not be able to detect the subtle differences in mind-reading performance between the HFA and AS subgroups. Golan et al.'s (2006) comparative study of individuals with AS and those with typical development which used the CAM reported significant differences in performance on both the

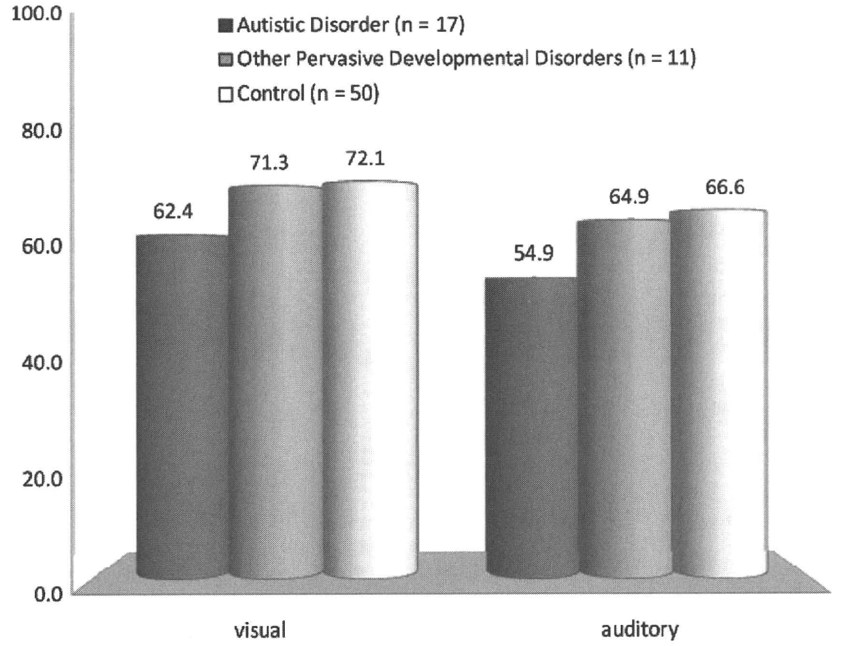


Fig. 2. Mean accuracy rate on the visual and auditory tasks for each group.

visual and auditory tasks, findings which do not accord with those of the present study. The reason for the discrepancy might be attributable to the inclusion of social context in the MPMR clips, where, for example, two characters can appear together on screen or background scenery can be visible. Also the participants' response method differed between the two studies: while Golan et al. (2006) asked participants to select a word from 4 alternatives to describe an appropriate mental state matching facial expression and voice, we asked them to judge whether a word describing a mental state was appropriate or not to the scene.

The present finding that individuals with other PDD showed accuracy rates close to those of the control group suggests that adults with other PDD might understand other people's minds to some extent. However, in everyday life, their social communication is often not successful, which could suggest that even though they may understand other people's mental states, they might experience difficulties responding to them. Moreover, previous studies have shown that individuals with PDD rely on strategies different from those of the general population when trying to understand others' thoughts and emotions (Baron-Cohen et al., 1999; Castelli, Frith, Happé, & Frith 2002; Happé et al., 1996). Future studies of the brain by, for example, functional magnetic resonance imaging might reveal the difference in strategies adopted by individuals with other PDD and controls.

The present study found no correlation between FIQ, VIQ and PIQ scores and task performance in the HFA and other PDD groups. A previous study by Happé (1995) showed that VIQ score was correlated with mind-reading ability, whereas in the present study there was no such relation between VIQ score and performance. This is because all participants had an IQ $\geq$80, and therefore differences in VIQ score were small among the PDD subgroups. Moreover, there was no correlation between AQ score and task performance. A high AQ score indicates serious symptoms of autism, alongside which lower mind-reading task performance would be expected. The finding therefore suggests that mind-reading ability might be associated with symptom profiles that are in accordance with the diagnostic criteria of DSM-IV-TR, rather than degrees of autism as assessed by AQ scores.

Regarding test items that showed significant differences in accuracy rate between the three groups, the HFA group had lower accuracy on most of the visual and auditory tasks than the other PDD and control groups. Contrary to expectation, the accuracy rate of the HFA group for some items was under the chance level (50%) of the control group, and the other PDD group showed a higher accuracy rate than the control group on several items, including "figuring someone out" on the visual task and "guilty" on the auditory task. Moreover, the HFA group showed a higher accuracy rate than the control group on a few items. We suspect that some emotions and mental states are relatively easier for adults with PDD to understand, based on their previous experiences. This remains a subject for further investigation.

With respect to the objective of determining whether there exist differences in the mind-reading performance according to whether the visual or auditory modality is used, we found no such differences. These findings are contrary to those of Golan et al. (2006) who found that males with AS perform better on the auditory task than on the visual task, which suggests that there may be no difference in understanding of others' mind by modality. The reason for this may be attributable to the complexity of the tasks and language used, or cultural differences between the two experimental settings. In general, Japanese people make less obvious facial expressions than Western people, and as such, cultural differences might have produced differences in the results.

A limitation of this study is that the group of PDD participants was small, as then was the two subgroups. Therefore, future study should involve a larger number of participants. In addition, the profiles of the control group participants lacked important information. For example, no accurate IQ information was available, although because the average IQ of the PDD group participants was higher than 100 and no correlation was found between IQ and mind-reading performance, the influence of IQ appears to be limited. In future studies, the IQ, age and education level of the control group should be matched to those of the PDD group. Moreover, the participants in this study were all male. Given that gender differences on mind-reading tasks have been reported (Baron-Cohen, Wheelwright, Skinner, et al., 2001; Baron-Cohen, 2003; Golan et al., 2006; Rutherford et al., 2002; Wakabayashi & Katsumata, in press), future work should include female participants. Finally, the tasks used in this study were created from clips from a TV drama, which resulted in somewhat uncontrolled categories of emotions. Thus, future use of controlled categories of emotions to examine performance differences among groups divided by diagnosis should contribute to identifying those emotions and mental states that are relatively easier for adults with HFA to recognize.

## 5. Conclusions

Using the new visual and auditory tasks, this study compared the performance of subgroups of PDD divided according to DSM-IV-TR diagnostic criteria in order to clarify the difference in mind-reading abilities among the subgroups. The results demonstrated that on both the visual and auditory tasks, individuals with HFA experienced the greatest difficulty in understanding the complicated emotions and mental states of others. In contrast, the results suggest that the mind-reading abilities of adults with AS and PDD-NOS did not differ much from those without PDD. Taken together, complex mind-reading tasks appear to be effective for distinguishing individuals with HFA from those with AS or PDD-NOS. Clinically, adults with HFA who are not able to understand easily others' thoughts and emotions will likely encounter problems in social relationships. Individuals with AS or PDD-NOS will likewise experience such problems, but for different reasons: although they might well be able to understand others' emotions and thoughts, they will likely have difficulty knowing how to adapt their own social behavior. The support offered to individuals of different PDD subgroups may need to be differentiated accordingly.

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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.

**Table 1**
Associated factors for ASD diagnosis ($n = 1460$).

| | ASD diagnosis, *n* (%) | | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| | Affected | Unaffected | | |
| Sex of child (male, *n* = 729) | 21 (2.9%) | 7 (1.0%) | 3.07 (1.30–7.26)* | 3.01 (1.27–7.15)* |
| Maternal age at childbirth | | | | |
| 29 years or younger (*n* = 661) | 9 (1.4%) | | 1 | 1 |
| 30–34 years (*n* = 556) | 12 (2.2%) | | 1.60 (0.67–3.82) | 1.54 (0.64–3.74) |
| 35 years or older (*n* = 243) | 7 (2.9%) | | 2.15 (0.79–5.83) | 2.14 (0.76–5.98) |
| Prenatal factors | | | | |
| Maternal smoking (*n* = 147) | 2 (1.4%) | 26 (2.0%) | 0.68 (0.16–2.91) | 0.75 (0.17–3.32) |
| Maternal drinking (*n* = 119) | 1 (0.8%) | 27 (2.0%) | 0.41 (0.06–3.06) | 0.38 (0.05–2.89) |
| Toxemia (*n* = 113) | 2 (1.8%) | 26 (1.9%) | 0.92 (0.21–3.91) | 0.90 (0.21–3.94) |
| Threatened abortion/premature labor (*n* = 165) | 1 (0.6%) | 27 (2.1%) | 0.29 (0.04–2.12) | 0.28 (0.04–2.09) |
| Other trouble/abnormality (*n* = 101) | 3 (3.0%) | 25 (1.8%) | 1.63 (0.48–5.51) | 1.70 (0.49–5.87) |
| Perinatal or neonatal factors | | | | |
| Delivery by caesarean section (*n* = 188) | 4 (2.1%) | 24 (1.9%) | 1.13 (0.39–3.29) | 1.30 (0.42–4.04) |
| Vacuum extraction (*n* = 122) | 4 (3.3%) | 24 (1.8%) | 1.86 (0.63–5.44) | 1.84 (0.60–5.68) |
| Oxytocic use (*n* = 95) | 2 (2.1%) | 26 (1.9%) | 1.11 (0.26–4.74) | 1.05 (0.23–4.73) |
| Birth weight less than 2500 g (*n* = 113) | 1 (0.9%) | 27 (2.0%) | 0.44 (0.06–3.24) | 0.38 (0.05–3.02) |
| Icterus neonatorum (*n* = 268) | 7 (2.6%) | 21 (1.8%) | 1.50 (0.63–3.55) | 1.62 (0.66–3.96) |
| Other abnormality with baby (*n* = 104) | 2 (1.9%) | 26 (1.9%) | 1.00 (0.23–4.29) | 0.96 (0.22–4.23) |

ASD, autism spectrum disorders; OR, odds ratio; CI, confidence interval.
* $p < .05$.

All tests were two-tailed and statistical significance was set at $p < .05$. All statistical analyses were performed using SPSS 18.0J for Windows.

## 3. Results

As shown in Table 1, no significant association was observed between maternal age at childbirth and ASD diagnosis.

In line with the findings of previous epidemiological studies (Fombonne, 2003), a significant association was observed between male sex of child and ASD diagnosis. The association remained even when other factors were controlled for; male children were 3.01 (95% CI, 1.27–7.15) times more likely to have an ASD diagnosis than females. The associations between other factors and ASD diagnosis were not significant.

**Table 2**
Factors associated with failure on the M-CHAT at 18 months of age ($n = 1,460$).

| | Failure on the M-CHAT, *n* (%) | | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|---|
| | Affected | Unaffected | | |
| Sex of child (male, *n* = 729) | 82 (11.2%) | 55 (7.5%) | 1.56 (1.09–2.23)* | 1.52 (1.06–2.18)* |
| Maternal age at childbirth | | | | |
| 29 years or younger (*n* = 661) | 50 (7.6%) | | 1 | 1 |
| 30–34 years (*n* = 556) | 50 (9.0%) | | 1.21 (0.80–1.82) | 1.20 (0.79–1.83) |
| 35 years or older (*n* = 243) | 37 (15.2%) | | 2.19 (1.39–3.45)* | 2.22 (1.39–3.55)* |
| Prenatal factors | | | | |
| Maternal smoking (*n* = 147) | 13 (8.8%) | 124 (9.4%) | 0.93 (0.51–1.69) | 0.99 (0.53–1.83) |
| Maternal drinking (*n* = 119) | 16 (13.4%) | 121 (9.0%) | 1.57 (0.90–2.74) | 1.69 (0.95–3.02)† |
| Toxemia (*n* = 113) | 8 (07.1%) | 129 (9.6%) | 0.72 (0.34–1.51) | 0.61 (0.29–1.29) |
| Threatened abortion/premature labor (*n* = 165) | 20 (12.1%) | 117 (9.0%) | 1.39 (0.84–2.30) | 1.38 (0.82–2.31) |
| Other trouble/abnormality (*n* = 101) | 10 (9.9%) | 127 (9.3%) | 1.07 (0.54–2.10) | 1.00 (0.50–2.00) |
| Perinatal or neonatal factors | | | | |
| Delivery by caesarean section (*n* = 188) | 21 (11.2%) | 116 (9.1%) | 1.25 (0.77–2.05) | 1.12 (0.66–1.92) |
| Vacuum extraction (*n* = 122) | 16 (13.1%) | 121 (9.0%) | 1.52 (0.87–2.65) | 1.60 (0.89–2.88) |
| Oxytocic use (*n* = 95) | 11 (11.6%) | 126 (9.2%) | 1.29 (0.67–2.48) | 1.50 (0.76–2.97) |
| Birth weight less than 2500 g (*n* = 113) | 15 (13.3%) | 122 (9.1%) | 1.54 (0.87–2.73) | 1.39 (0.75–2.61) |
| Icterus neonatorum (*n* = 268) | 23 (8.6%) | 114 (9.6%) | 0.89 (0.56–1.42) | 0.77 (0.47–1.25) |
| Other abnormality with baby (*n* = 104) | 11 (10.6%) | 126 (9.3%) | 1.15 (0.60–2.21) | 1.04 (0.53–2.04) |

Failure on the M-CHAT is defined as failing three or more items among the total 23 items. M-CHAT, Modified Checklist for Autism in Toddlers; OR, odds ratio; CI, confidence interval.
† $p < .10$.
* $p < .05$.

Table 2 shows the associations between each factor and failure on the M-CHAT at age 18 months. A significant association was observed between maternal age at childbirth even after controlling for other factors. Children of mothers in the oldest age group (≥35 years at childbirth) were 2.22 (95% CI, 1.39–3.55) times more likely to fail the M-CHAT compared with the reference group (mothers aged ≤29 years at childbirth).

A significant association was observed between male sex of child and failure on the M-CHAT; when other factors were controlled for, male children were 1.52 (95% CI, 1.06–2.18) times more likely to fail the M-CHAT than females. The associations between other factors and failure on the M-CHAT were not significant.

## 4. Discussion

To our knowledge, this is the first study to examine whether advanced maternal age is associated with not only the development of ASD, but also atypical social development in infancy. Although a recent review and comprehensive meta-analysis both showed a significant association between advanced maternal age at childbirth and later ASD diagnosis of the child (Gardener et al., 2009; Kolevzon et al., 2007), no association was identified in this study, likely due to the relatively small ASD sample size. Because the previous Japanese study based on a large clinical sample suggested significant elevation of maternal age at childbirth for ASD children (Koyama, Miyake, & Kurita, 2007), replication would be required with a larger epidemiological sample. Although the sample size was not large enough to calculate final ASD prevalence at this stage, 28 cases among 1460 children (1.92%) is similar to recent estimates of the prevalence of ASD in Europe (Baird et al., 2006) and Japan (Kawamura, Takahashi, & Ishii, 2008), thus suggesting that few undetected cases would remain. Future extension of cohort would provide more reliable figures and steady findings.

The most important finding of this study was that advanced maternal age at childbirth was significantly associated with atypical social development at 18 months of age regardless of adjustment for other factors. Of course, older mothers might report social developmental problems more on the M-CHAT, which may have enhanced the association; however, the current finding confirms that of Weiser et al. (2008), who reported that advanced parental age at birth is associated with poorer social functioning in adolescence. The percentage of children who failed the M-CHAT is comparable to the percentage of male adolescents with low social functioning (18.7%, 68,685/368,244) (Weiser et al., 2008), although the different aspects of social function assessed in both studies may prevent a direct comparison.

Failure on the M-CHAT at 18 months is not specific to ASD children (Inada et al., in press; Kleinman et al., 2008) but can involve various conditions. However, some children who failed the M-CHAT at 18 months of age might be relatively vulnerable to develop serious social dysfunction and/or maladaptation later. Although the developmental trajectory varies, and optimal outcomes have been reported even in children with ASD (Sutera et al., 2007), longer-term monitoring is required. Social dysfunction is not necessarily disorder-specific, but can be found in various neuropsychiatric disorders throughout life with age-dependent manifestations (Kamio et al., in press). In addition, harmful maturational events for early brain development might result in insufficiently organized neural circuitry, which would affect higher-order processing, including social function.

Although the etiological mechanism underlying the relationship between advanced maternal age at childbirth and atypical early social development in children is quite complex and remains unclear, a small portion of the relationship could be explained by increased risk of chromosomal abnormalities in ova of increased age or unstable tri-nucleotide repeats (Kolevzon et al., 2007). However, simple explanation seems unrealistic because other physical factors among older pregnant women may be involved in increasing the risk of atypical social development of a child, and/or because many unknown genetic or psychosocial factors that result in late marriage or pregnancy might exist. To clarify the complex nature-nurture mystery regarding the association between maternal age at childbirth and the child's social development, future research should include physical and psychosocial assessments of parents (Constantino & Todd, 2005; Hurley, Losh, Parlier, Reznick, & Piven, 2007).

This study did not examine paternal age at childbirth, although maternal and paternal ages are usually correlated. The previous studies that examined the association between parental age at childbirth and ASD diagnosis did not necessarily adjust for paternal or maternal age and vice versa, and findings were inconsistent in the studies that controlled for the other parental age (Gardener et al., 2009). Further evidence should be accumulated in order to clarify this issue.

The effect of obstetric factors were all negative in this study; however, due to infrequent occurrence and/or incomplete information, we could not examine some index factors used in the previous studies (e.g. maternal prenatal medication use) (Gardener et al., 2009; Kolevzon et al., 2007). Therefore, a conclusion cannot be made regarding the influence of each obstetrical factor on the development of atypical social development in infancy, and more thorough examination will be necessary in order to illustrate a whole picture.

In conclusion, this community-based epidemiological study, of which few have been conducted in Japan, is the first to demonstrate a significant association between advanced maternal age at childbirth and atypical social development of the child at 18 months in the general population. 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. However, the findings of this study require future replication because the above-mentioned limitations may have confounded the results. Such future research should elucidate the etiological explanation for the association.

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# Top-down and bottom-up visual information processing of non-social stimuli in high-functioning autism spectrum disorder

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ABSTRACT

Individuals with high-functioning autism spectrum disorder (HF-ASD) often show superior performance in simple visual tasks, despite difficulties in the perception of socially important information such as facial expression. The neural basis of visual perception abnormalities associated with HF-ASD is currently unclear. We sought to elucidate the functioning of bottom-up and top-down visual information processing in HF-ASD using event-related potentials (ERPs). Eleven adults with HF-ASD and 11 age-matched normal controls (NC) participated in this study. Visual ERPs were recorded using 128-channel EEG. The P1 and P300 were recorded in response to target stimuli. Visual mismatch negativity (vMMN) potentials were obtained by subtracting responses to standard from those to deviant stimuli. Behaviorally, individuals with HF-ASD showed faster target detection than NCs. However, vMMN amplitude and latency were the same between the two groups. In contrast, P1 and P300 amplitudes were significantly decreased in HF-ASD compared with NCs. In addition, P300 latency was significantly delayed in HF-ASD. Individuals with HF-ASD exhibit altered visual information processing. Intact bottom-up attention (vMMN) may contribute to their superior simple visual task performance in spite of abnormal low-level (P1) and top-down (P300) visual information processing.



## 1. Introduction

Autism spectrum disorder (ASD) is a developmental neuropsychiatric disorder characterized by deficits in socialization, communication, and repetitive/stereotyped behaviors. Over the past several decades, extensive studies using various genetic, neurobiological, cognitive and behavioral approaches have sought a single explanation for the heterogeneous manifestations of ASD, but no consensus on the etiology of ASD has emerged (Happé & Frith, 2006). Although there are prominent symptoms of ASD within the social domain, several researchers have proposed that abnormalities also exist in basic (lower level) sensory processing as well as attention and cortical (higher level) processing (Dakin & Frith, 2005; Mottron & Burack, 2001; Tuchman & Rapin, 2006). Indeed, a number of studies have shown atypical performance of

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individuals with ASD in a wide range of perceptual tasks (e.g. for a review, Mottron, Dawson, & Soulières, 2009). In terms of research findings in the visual modality, evidence emerging over the past few decades has indicated that ASD is associated with both unique abilities and unique deficits in higher level visual processing (Dakin & Frith, 2005). For instance, individuals with ASD generally perform well on the Wechsler Intelligence Scale for Children (WISC) Block Design test (Shah & Frith, 1983; Shah & Frith, 1993), the embedded figures test (Jolliffe & Baron-Cohen, 1997), visual search (Plaisted, O'Riordan, & Baron-Cohen, 1998), and copying impossible figures (Mottron, Burack, Stauder, & Robaey, 1999). In contrast, their performance tends to be poor for detecting biological motion (Blake, Turner, Smoski, Pozdol, & Stone, 2003), integrating rapid visual motion (Gepner & Mastre, 2002), and perceiving coherent motion (Spencer, O'Brien, Riggs, Baraddick, Atkinson, & Wattam-Bell, 2002). These findings have often been interpreted from the viewpoint of local vs. global processing (Frith, 1989; Happé, 1999; Mottron & Burack, 2001; Plaisted, 2001). One persuasive theoretical account to explain the range of abilities and deficits characterizing ASD is "weak central coherence" (WCC). This theory proposes that the bias toward detail-focused, local processing over global processing results in a failure to extract global form/meaning (Happé & Frith, 2006). Alternatively, the concept of top-down and bottom-up attention may be related to the peculiar visual task performance of individuals with ASD. At present a conclusive explanation remains unclear due to the limited time resolution of the psychobehavioral techniques used so far.

Visual sensory information is first processed at a low level, with information flowing from the retina to the primary visual cortex (V1). The information then passes into a higher level of neural processing. It is well known that the P1 (i.e. the first positive peak from the stimulus onset) reflects the lower level visual information processing stage (i.e. V1 or earlier; for a review, Tobimatsu & Celesia, 2006). Previous studies have suggested that lower level visual information processing may be affected in ASD, because affected individuals exhibit a decreased and delayed P1 (Boeschoten, Kenemans, Engeland, & Kemner, 2007; Hoeksma, Kemner, Verbaten, & van Engeland, 2004; Hoeksma, Kemner, Kenemans, & van Engeland, 2006; Itier and Taylor, 2002, 2004; O'Conner, Hamm, & Krik, 2005; Taylor, Edmonds, McCarthy, & Allison, 2001; Webb et al., in press). Alternatively, selective attention may be involved. Selective attention is the process whereby a subset of the input is selected preferentially for further processing and has two major aspects: bottom-up attention and top-down attention. Bottom-up attention is elicited or driven by the properties of stimuli automatically whereas top-down attention refers to a volitional focusing of attention on a location and/or an object based on current behavioral goals (Ciaramelli, Grady, & Moscovitch, 2008). These streams can operate in parallel but bottom-up attention occurs more quickly than top-down attention (e.g. Treisman, Vieira, & Hayes, 1992). Event-related potentials (ERPs), which have the benefit of a very high-temporal resolution (in the order of milliseconds), are an appropriate technique for recording electrophysiological signals from the scalp. ERPs allow us to temporally characterize human sensory information processing. Two specific components of the ERP, the visual mismatch negativity (vMMN) and the visual P300, are candidates for biomarkers of bottom-up and top-down attention, respectively (Maekawa, Goto, Kinukawa, Taniwaki, Kanba, & Tobimatsu, 2005; Maekawa, Tobimatsu, Ogata, Onitsuka, & Kanba, 2009). To the best of our knowledge, there have been no ERP studies focusing on the bottom-up and top-down attention in ASD. Therefore, the aim of this study was to characterize visual information processing in high-functioning ASD (HF-ASD) individuals and to determine whether or not bottom-up and/or top-down attention is affected by the disorder. To this end, we measured early visual ERP components including the P1 and P300, as well as the vMMN.

## 2. Methods

### *2.1. Participants*

Eleven individuals with HF-ASD (eight males and three females, aged 18–40 years, mean age 28.0), and 11 healthy controls (HCs) matched for chronological age (CA) and sex (four males and seven females, aged 20–38 years, mean age 28.9) participated in the study. The HF-ASD group included six individuals with Asperger's disorder, three individuals with autistic disorder, and three individuals with a pervasive developmental disorder not otherwise specified (PDD-NOS). The HF-ASD participants were diagnosed by a research team including a general psychiatrist experienced in the field (T.M.), an experienced child psychiatrist (Y.K.), and a licensed clinical psychologist (N.I.) according to the DSM-IV-TR criteria (APA, 2000) based on clinical interviews with participants and/or parents using semi-structured interviews validated for Japanese PDD populations (Kamio et al., 2006; Tani, Yukihiro, & Tsujii, 2009). Diagnostic agreement among the team was obtained for all participants. The NC participants (NC group) were recruited from the general public, and their NC status was confirmed by interviews. The intellectual function of HF-ASD participants was evaluated using the Japanese versions of the Wechsler Adult Intelligence Scale (WAIS-R or WAIS-III).

Informed consent was obtained from all participants. The experimental procedures were approved by the ethics committee of the Graduate School of Medical Sciences, Kyushu University.

### *2.2. Visual stimuli and procedures*

Visual stimuli, apparatus, procedures, and EEG recordings except for the EEG machine were the same as in our earlier studies of healthy adults (Maekawa et al., 2005, 2009).

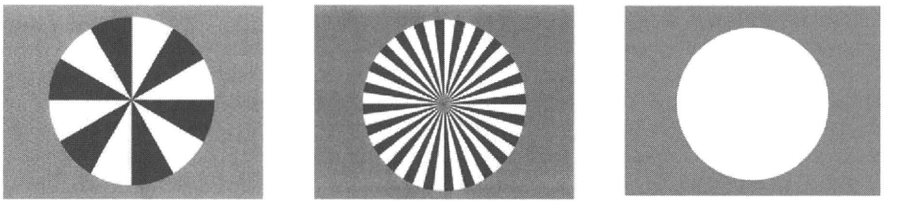


**Fig. 1.** Three stimulus types used in the present study; six-vane circular black–white windmill pattern stimulus (A), 24-vane stimulus (B), and unpatterned white circle stimulus (C). The two windmill pattern stimuli were adopted as standard or deviant stimuli (their probabilities were changed between sessions each other) and the white circle was always used as the target stimulus. Probabilities of standard, deviant, and target stimuli were 8:1:1, respectively.

Circular black–white windmill patterns with 90% contrast were presented on a 20-inch CRT monitor and controlled using a ViSaGe graphics board (Cambridge Research Systems, UK). The visual stimulus subtended 5.8° of visual angle in diameter at a viewing distance of 114 cm. Participants were seated comfortably in a semi-dark room. The participants were instructed to focus on a story delivered binaurally through earphones while looking at the center of the monitor and to press a button with their right thumb as soon as they recognized a target stimulus on the monitor. Between the stimulus runs, they were asked to fill out a questionnaire about the context of the story that they had heard.

Standard, deviant, and target stimuli were presented in a random order for 200 ms on the computer monitor (Fig. 1). The inter-stimulus interval (ISI) was 800 ms. Stimulus probabilities were 80% (standard), 10% (deviant), and 10% (target).

ERP recordings were composed of two sessions. One session had a windmill pattern with six vanes as the standard, 24 vanes as the deviant, and a non-patterned white circle as the target stimulus. In the other session, a six-vane windmill pattern was adopted as the deviant and a 24-vane pattern as the standard stimulus. The target stimulus was the same in both sessions.

### *2.3. ERP recordings*

ERPs were recorded from 128 scalp sites referenced to Cz, using a high-density electroencephalography (EEG) system. EEG data were analyzed using a dense array EEG workstation (Net Station, Electrical Geodesics, Inc., USA). All 128 electrodes were attached with a sensor net (Net Station, Electrical Geodesics, Inc., USA). The impedances of all electrodes were maintained below 50 kΩ. EEG was continuously digitized at 500 Hz per channel and stored on a computer hard disk using a 0.05–200 Hz on-line filter. EEG data were filtered off-line with a bandpass of 0.5–30 Hz. Digital codes synchronized to the stimulus onset were also stored. At the end of the experiments, EEG epochs of 600-ms duration (100 ms pre-stimulus, 500 ms post-stimulus) associated with each stimulus type were extracted from the continuous record. Epochs contaminated by electro-oculograms, blinks, or muscle artifacts exceeding an artifact rejection threshold of $\pm 70\ \mu V$ were discarded automatically. Artifact-free epochs were then segregated by stimulus codes and averaged for each subject. The amplitudes of the ERPs were measured relative to a 100-ms pre-stimulus baseline. The grand average across all subjects in each stimulus condition was also computed. To compare our findings with those of previous studies (Maekawa et al., 2005, 2009), a re-reference was applied using the average of the two electrodes beside the nose (electrodes 126 and 127). Eye movements and blinks were measured from bipolar electrodes placed above and below the eyes (right, electrodes 14 and 126; left, electrodes 21 and 127).

### *2.4. Data analysis*

#### *2.4.1. Behavioral performance*

To characterize degree of attention, the accuracy of participants' answers to questions about the story was evaluated. Questionnaires consisted of 40 questions, for example "What was the name of the hero?" or "How many persons participated in the operation?" In addition, reaction time (RT) and accuracy for the target stimuli were also measured as indices of participants' task performance.

#### *2.4.2. ERP data*

Difference waveforms were constructed by subtracting the waveforms in response to the standard stimuli from that to the deviants. Topographic distributions were inspected to verify that the vMMN was at its maximum at the Oz electrode, where the vMMN is typically largest. vMMN amplitude was calculated for each participant 150–350 ms from the stimulus onset. Lower level information processing was assessed using the P1, N1, P2, and N2 components at Oz. Top-down attention was evaluated by the P300 for the target stimulus at Pz. The amplitudes of major components for each stimulus were measured relative to baseline. Peak latencies and amplitudes were then compared between HF-ASD and NC groups using Student's *t*-tests.

## 3. Results

Although the behavioral performance of all participants was successfully measured, EEG data from two participants in each group were excluded from the ERP analyses because of excessive artifacts in their ERP recordings. Following these exclusions, there were nine participants in each group. Although the gender ratio appeared to be quite different between the two groups (i.e. female to male ratio in HF-ASD was 7:2 and that in NC was 4:5), there were no significant between-group differences in sex ratio (Fisher's exact test, $P = 0.33$), or CA (unpaired $t$-test, $P = 0.29$).

The HF-ASD participants exhibited IQ within the normal range (mean verbal IQ, $102.8 \pm 14.3$, range 90–125; mean performance IQ, $108.9 \pm 13.9$, range 91–136; mean full scale IQ, $107.0 \pm 14.5$, range 91–134). The information subscale of the WAIS-R or WAIS-III was adopted to estimate intellectual functioning. No significant difference was found between the two groups on this subscale ($12 \pm 3.7$ vs. $13.6 \pm 1.9$, respectively).

### 3.1. Performance data

There was no significant difference in mean accuracy rate for questions related to the story context between the HF-ASD and NC groups (97.0% vs. 96.9%, respectively), confirming that both groups cooperated successfully and paid a high level of attention to the story. There was no significant difference in target stimulus detection accuracy between the two groups ($92.5\% \pm 6.3\%$ vs. $92.1\% \pm 4.7\%$, respectively). However, the HF-ASD group showed significantly shorter RTs than the NC group ($374.2 \pm 36.6$ vs. $410.4 \pm 40.6$ ms, respectively. $P < 0.05$).

### 3.2. ERPs

Grand averaged waveforms of ERPs in response to each stimulus are shown in Fig. 2. A positive (P1)–negative (N1)–positive (P2) deflection was elicited equally by each stimulus type and was maximal at Oz (see Fig. 2A). Peak amplitudes and latencies of the P1, N1, P2, N2, and P300 in response to each stimulus type are summarized in Table 1. P1 amplitude in response to standard and deviant stimuli in the HF-ASD group was significantly smaller than in NCs (for standard, $t(16) = -2.47$, $P < 0.05$; for deviant stimuli, $t(16) = -2.79$, $P = 0.013$). However, there was no significant difference in P1

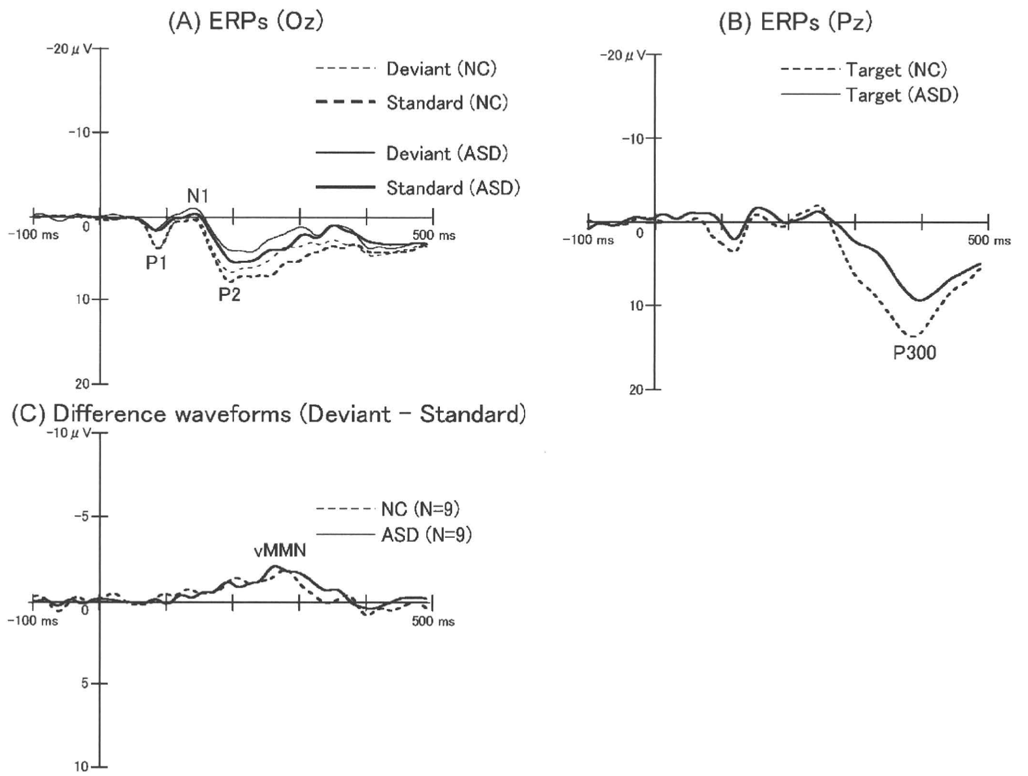


**Fig. 2.** Grand averaged waveforms of ERPs in each group. (A) Waveforms for standard stimuli (NC, thick dotted line; ASD, thick solid line) and for deviant stimuli (NC, thin dot line; ASD, thin solid line) at Oz. (B) Waveforms for target stimuli at Pz (NC, dotted line; ASD, solid line). While P300 latencies did not show any significant differences between the two groups, P300 amplitudes in ASD were significantly smaller than those of the NC group ($P < 0.05$). (C) Difference waveforms from responses to standard stimuli relative to responses to deviant stimuli at Oz (NC, dotted line; ASD, solid line). There were no statistically significant differences in the mean peak latency and amplitude of vMMN between the two groups.