# Psychological and Neural Bases of Social Cognitive Dysfunction in Individuals with Pervasive Developmental Disorder

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## Abbreviation and Definition

| | |
|---|---|
| 3D | Three-dimensional |
| AIC | Akaike information criterion |
| AMY | Amygdala |
| ANCOVA | Analysis of covariance |
| ANOVA | Analysis of variance |
| APA | American psychiatric association |
| BA | Brodmann area |
| CARS | Childhood autism rating scale |
| CON | Controls |
| CRT | Cathode-ray tube |
| DCM | Dynamic causal modelling |
| DSM- IV-TR | Diagnostic and statistical manual of mental disorders fourth edition, text revision |
| *F* | Fisher's *F* ratio |
| FA | Flip angle |
| FG | Fusiform gyrus |
| Hz | Hertz |
| IFG | Inferior frontal gyrus |
| IQ | Intelligence quotient |

| | |
|---|---|
| *M* | Mean |
| MNI | Montreal neurological institute |
| MPFC | Medial prefrontal cortex |
| MRI | Magnetic resonance imaging |
| ms | Millisecond |
| *p* | Probability |
| PDD | Pervasive developmental disorder |
| PDD-NOS | Pervasive developmental disorder not other specified |
| *r* | Pearson product-moment correlation |
| ReML | Restricted maximum likelihood |
| RF-FAST | Radiofrequency spoiled fourier acquired steady state |
| RM | Representational Momentum |
| ROIs | Regions of interest |
| RT | Reaction time |
| *SD* | Standard deviation |
| *SE* | Standard error |
| SOA | Stimulus onset asynchrony |
| SPM | Statistical parametric mapping |
| STS | Superior temporal sulcus |

| | |
|---|---|
| *t* | Computed value of *t* test |
| TE | Echo time |
| TR | Repetition time |
| *U* | Computed value of *U* test |
| V1 | Primary visual cortex |
| WAIS-III | Wechsler adult intelligence scale-third edition |
| WAIS-R | Wechsler adult intelligence scale-revised |
| WISC-III | Wechsler intelligence scale for children-third edition |
| WISC-R | Wechsler intelligence scale for children-revised |
| $\chi^2$ | Computed value of a chi-square test |

## Abstract

Pervasive developmental disorder (PDD), including autistic disorder and Asperger's disorder, is characterized by severe abnormality in social interaction. Although facial cues, such as gaze and facial expression, play an important role in social interaction, previous studies have reported conflicting findings regarding impaired processing of gaze and facial expressions in PDD.

The research in this thesis investigated the processing of gaze direction and facial expression in individuals with PDD. Psychological and neuroimaging studies revealed that individuals with PDD demonstrated (1) impairment of reflexive joint attention triggered by emotional gaze or subliminally presented gaze, (2) impairment and an abnormal developmental trajectory of fearful face recognition, and a positive correlation between social attention and fearful face recognition, (3) reduced perception of emotional intensity in dynamic facial expressions, (4) reduced activity of social brain regions and an altered network in these regions in response to dynamic facial expressions.

The impairments found in this thesis might have a cascading effect on atypical social development in individuals with PDD, because the combination of impairment of gaze-triggered attention and reduced perception of emotional intensity in dynamic facial expressions would

lessen the chance of social interaction. These impairments might result from underlying abnormalities such as inattention to social stimuli. The psychological findings suggested that abnormal social attention lead to impaired recognition of another's emotion. The fMRI study also suggested abnormal input from the subcortical area involved in automatic face processing to the reflexive joint attention and biological motion processing systems, and some internal disorganization of these regions. These problems might derail individuals from typical developmental trajectories of social behavior.

# Chapter 1

## General introduction

## 1.1 Pervasive developmental disorder and social dysfunction

Pervasive developmental disorder (PDD) including autistic disorder and Asperger's disorder are characterized by severe abnormalities in "social interaction" and "communicative language", and by "repetitive behavior and restricted interest" (DSM-IV-TR; American Psychiatric Association [APA], 2000). In particular, qualitative impairment of social interaction distinguishes PDD from other developmental disorders. According to DSM-IV-TR (APA, 2000), the qualitative impairments of social interaction in PDD comprise (1) marked impairments in the use of multiple nonverbal behaviors, (2) failure to develop peer relationships appropriate to developmental level, (3) lack of spontaneous seeking to share enjoyment, interests, or achievements with other people, and (4) lack of social or emotional reciprocity. The earliest descriptions by two pioneers (Asperger, 1944/1991; Kanner, 1943) also noted that abnormalities of social interaction are striking in these disorders.

Some researchers have proposed that social dysfunction is fundamental to PDD, while others have hypothesized that impaired cognitive function is the fundamental cause of PDD, as with the absence of a "theory of mind" (Baron-Cohen, 1995) and dysfunctions in executive function (Ozonoff, Pennington, & Rogers, 1991). For example, Hobson (1993) proposed that

difficulty in the perception and expression of emotion contributes to a failure to establish interpersonal relationships. Previous studies have shown that emotion recognition ability positively correlates with higher-order social cognitive abilities in individuals with and without PDD (Corden, Critchley, Skuse, & Dolan, 2006; Marsh, Kozak, & Ambady, 2007; Humphreys, Minshew, Leonard, & Behrmann, 2007). Johnson (2005) proposed that an unconscious and automatic face processing system in subcortical brain regions, which enables us to detect faces and orient attention to faces, plays an important role in the development of social cognition. Some researchers have reported that social cognitive dysfunction, including joint attention, might originate from the inattention to social stimuli (e.g., Dawson, Toth, et al., 2004). Although these findings suggest that individuals with PDD have difficulty processing others' facial cues, recent experimental studies investigating the processing of facial cues such as gaze and facial expressions in PDD have reported conflicting findings as I will discuss later. In this chapter, first the processing of facial cues in typically developing individuals is briefly represented. Then, conflicting findings of impaired gaze and facial expression processing in individuals with PDD are reported, and the potential factors which can explain the conflicting findings are discussed.

## 1.2 The processing of facial cues in typically developing individuals

Gaze direction and facial expressions of emotion play crucial roles in social communication. Gaze direction provides information about the direction of others' attention (Kobayashi & Kohshima, 2001) and intention (see Becchio, Bertone, & Castiello (2008) for a review). Facial expressions indicate moment-to-moment changes in inner emotional states (Ekman & Friesen, 1976) and/or communicative intentions (Fridlund, 1997). The combination of these cues enables us to understand the adaptive value of the indicated object (Adolphs, Russell, & Tranel, 1999; Blair, 2003; Whalen et al., 2001). Considering the importance of these cues for social interaction, the ability to process facial cues rapidly confers an evolutionary advantage and would be conserved during the evolutionary process (cf. Emery, 2000).

The effective processing of these facial cues appears in early development. For example, recent experimental studies have shown that typically developing infants and adults are faster to reflexively make a saccade or to orient their attention toward a gaze-cued location than toward a non-cued location (Farroni, Massaccesi, Pividori, & Johnson, 2004; Friesen & Kingstone, 1998; Hood, Willen, & Driver, 1998), even when the cue is counter-predictive of the target location (Driver et al., 1999; Friesen,

Ristic, & Kingstone, 2004). Further, recent studies have demonstrated that a model's gaze direction transfers their motor intention to observers and interferes with the observers' incongruent actions (Becchio, Pierno, Mari, Lusher, & Castiello, 2007; Castiello, 2003). In terms of facial expression, newborn infants can imitate others' facial expressions (Meltzoff & Moore, 1977; Field, Woodson, Greenberg, & Cohen, 1982). Others' facial expressions, specifically threatening facial expressions, induce behavioral and autonomic responses, even when observers do not consciously notice them (Dimberg, Thunberg, & Elmehed, 2000; Morris, deBonis, & Dolan, 2001). Based on evidence that efficient processing of these facial cues exists in early developmental life, it appears that impaired processing of facial cues impedes the development of higher social cognitive abilities.

### 1.3 Gaze processing in PDD

Previous studies have investigated whether individuals with PDD have an impairment affecting their processing of others' gaze direction. One of the most evident features of their social impairment is a deficit in joint attention (Mundy, Sigman, & Kasari, 1994). For example, when an attending physician suddenly averts his gaze to look at environmental objects during a clinical interview, an individual with PDD fails to follow

his gaze direction (Okada, Sato, Murai, Kubota, & Toichi, 2003). However, recent studies have demonstrated that individuals with PDD can discriminate others' gaze direction (Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995; Kylliäinen & Hietanen, 2004). Children and adults with PDD can reflexively shift their attention to gaze-cued locations (Chawarska, Klin, & Volkmar, 2003; Kylliäinen & Hietanen, 2004; Okada et al., 2003; Rutherford & Krysko, 2008; Senju, Tojo, Dairoku, & Hasegawa, 2004; Swettenham, Condie, Campbell, Milne, & Coleman, 2003; Vlamings, Stauder, van Son, & Mottron, 2005; for a review see Nation and Penny (2008)), although there have also been reports of impairment (Goldberg et al., 2008; Ristic et al., 2005). In contrast to the clinical evidence for impaired joint attention, most experimental studies have found intact gaze processing in PDD.

Some recent studies provide clues for elucidating the impairment of gaze-triggered attention in individuals with PDD. First, in typically developing individuals, gaze-triggered attention orienting is enhanced by facial expressions, particularly dynamic facial expressions, (Fox, Mathews, Calder, & Yiend, 2007; Holmes, Richards, & Green, 2006; Mathews, Fox, Yiend, & Calder, 2003; Putman, Hermans, & van Honk, 2006; Tipples, 2006; Uono, Sato, Michimata, Yoshikawa, & Toichi, 2009; Uono, Sato, &

Toichi, 2009). Mundy and Sigman (1989) proposed that sharing emotion in a joint attention context induces the development of socio-emotional functions. If enhanced attention orienting by emotional gaze creates a shared emotional state between infants and caregivers when attending to objects and facilitates the association of the induced emotional state with the attended object, it might influence the development of social cognitive functions, such as empathy, and facilitate learning about the emotional value of objects. Thus, it is important to investigate whether individuals with PDD show impaired processing of emotional gaze in joint attention contexts.

Second, Sato, Okada, and Toichi (2007) revealed that, in typically developing individuals, gaze-triggered attention could occur even if the gaze cue is presented unconsciously. Experimental social psychological studies have revealed that our social interactions are full of adaptive unconscious processes (Wilson, 2002). Given that the motivation to orient attention to the other is impaired in individuals PDD at an early developmental stage (Dawson, Toth, et al., 2004), and that previous behavioral studies have reported impairment in the processing of subliminally presented facial cues in individuals with PDD (Hall, West, & Szatmari, 2007; Kamio, Wolf, & Fein, 2006), unconscious gaze-triggered

attention might be impaired in individuals with PDD. These findings suggest that it would be useful to investigate this new aspect of gaze-triggered attention orienting to understand the etiology of PDD.

### 1.4 Facial expression processing in PDD

Another line of research has examined dysfunctions of facial expression processing in individuals with PDD. Some studies have revealed that individuals with PDD are insensitive to others' facial expression. For example, in one study, individuals with PDD were more likely to categorize photographs of faces by the presence or absence of hats than by the facial expressions shown (Weeks & Hobson, 1987) and another study showed that they pay less attention to adults showing negative affects than to normal controls (Sigman, Kasari, Kwon, & Yirmiya, 1992). However, psychological studies on emotion recognition have reported contradictory findings. Several studies have demonstrated impaired facial expression recognition in PDD (Braverman, Fein, Lucci, & Waterhouse, 1989; Celani, Battacchi, & Arcidiacono, 1999), with others further suggesting that individuals with PDD are specifically impaired in recognizing fearful expressions (Ashwin, Chapman, Colle, & Baron-Cohen, 2006; Corden, Chilvers, & Skuse, 2008; Howard et al., 2000; Humphreys et al., 2007;

Pelphrey et al., 2002). By contrast, other studies have reported that individuals with PDD show no impairment in facial expression recognition (Adolphs, Sears, & Piven, 2001; Castelli, 2005; Grossman, Klin, Carter, & Volkmar, 2000).

Previous studies have also suggested potential factors that may affect emotion recognition performance. First, a participant's age might affect emotion recognition ability. Recent studies with a large number of participants have shown deficits in facial expression recognition in adults (Ashwin et al., 2006; Corden et al., 2008; Humphreys et al, 2007), but not children, with PDD (Castelli, 2005; Grossman et al., 2000). These data suggest that the ability to recognize facial expressions improves with age in normally developing individuals but not in individuals with PDD. Second, previous studies have not examined the effects of general face-processing ability on facial expression recognition. Although face-recognition ability also improves with age during childhood and adolescence in typically developing individuals (Carey, Diamond, Woods, 1980; Mondloch, Geldart, Maurer, & Le Grand, 2003), studies have shown impaired face recognition in children and adolescents with PDD (Boucher, Lewis, & Collis, 1998; Klin et al., 1999). These findings suggest that the development of face recognition leads to improved facial expression recognition in typically

developing controls but not in individuals with PDD. Third, the degree of social dysfunction in individuals with PDD may relate to deficits in facial expression recognition. In normal participants, performance in face-recognition tasks involving fearful faces correlates with higher social cognitive functions (e.g., theory of mind ability) (Corden et al., 2006; Marsh et al., 2007). Further study is needed to investigate the effect of these potential factors on emotion recognition and their relationships in PDD.

Further, although there is the ample evidence that, in typically developing individuals, dynamic presentation of facial expressions enhances various behavioral responses, such as emotion recognition (Ambadar, Schooler, & Cohn, 2005; Bould & Morris, 2008; Bould, Morris, & Wink, 2008), subjective perception (Yoshikawa & Sato, 2008), emotional experience (Sato & Yoshikawa, 2007a), and facial mimicry (Sato & Yoshikawa, 2007b), only a few studies have investigated this issue in PDD and these have not provided a clear conclusion (cf. Gepner, Deruelle, & Grynfeltt, 2001; Tardif, Lainé, Rodriguez, & Gepner, 2007). Some researchers have proposed that individuals with PDD have difficulty processing biological and low-level motion, and that this might lead to the social dysfunction found in PDD (Dakin & Frith, 2005, Kaiser & Shiffrar,

2009). Because social interactions in daily life are mainly based on dynamic facial cues, it could be a promising approach to investigate whether individuals with PDD do indeed have impaired dynamic facial expression processing.

### 1.5 The purpose of this thesis

This thesis explored gaze and facial expression processing impairments in individuals with PDD (cf. Figure 1). Chapter 2 examines gaze-triggered attention in individuals with PDD. Because previous studies found no clear impairment in this area, new factors were introduced into the gaze-cueing paradigm (cf. Uono, Sato, Toichi, 2009; Sato et al., 2007). In particular, Chapter 2 investigated whether (1) emotional expression enhances gaze-triggered attention and (2) unconsciously presented gaze cues induce gaze-triggered attention in PDD. Chapter 3 presents an investigation of emotion recognition in individuals with PDD. The experiment, which asked subjects to match emotion labels to photos of facial expressions, was conducted using a number of participants with PDD. Because previous studies reported inconsistent findings, Chapter 3 investigated how abnormal emotion recognition abilities develop. To be more precise, the effects of age, face recognition ability, and symptom severity on emotion recognition were

investigated. Chapter 4 examines the subjective perception of dynamic facial expressions. Participants were asked to match a changeable emotional face display with the last image of presented dynamic and static facial expressions. Typically developing individuals perceive the last dynamic facial expression images to be more exaggerated than the static expressions. Because social interactions in daily life are mainly based on dynamic facial cues, reduced perception of exaggeration might be found in PDD. Based on the abnormality of facial expression processing found in Chapter 3 and 4, Chapter 5 reviews and investigates the neural correlate for the processing of dynamic facial expressions. Chapter 6 summarizes the findings described throughout Chapters 2 to 5 and discusses their significance in the atypical development of social cognition. In addition, psychological and neural bases of social cognitive dysfunction in individuals with PDD are discussed.

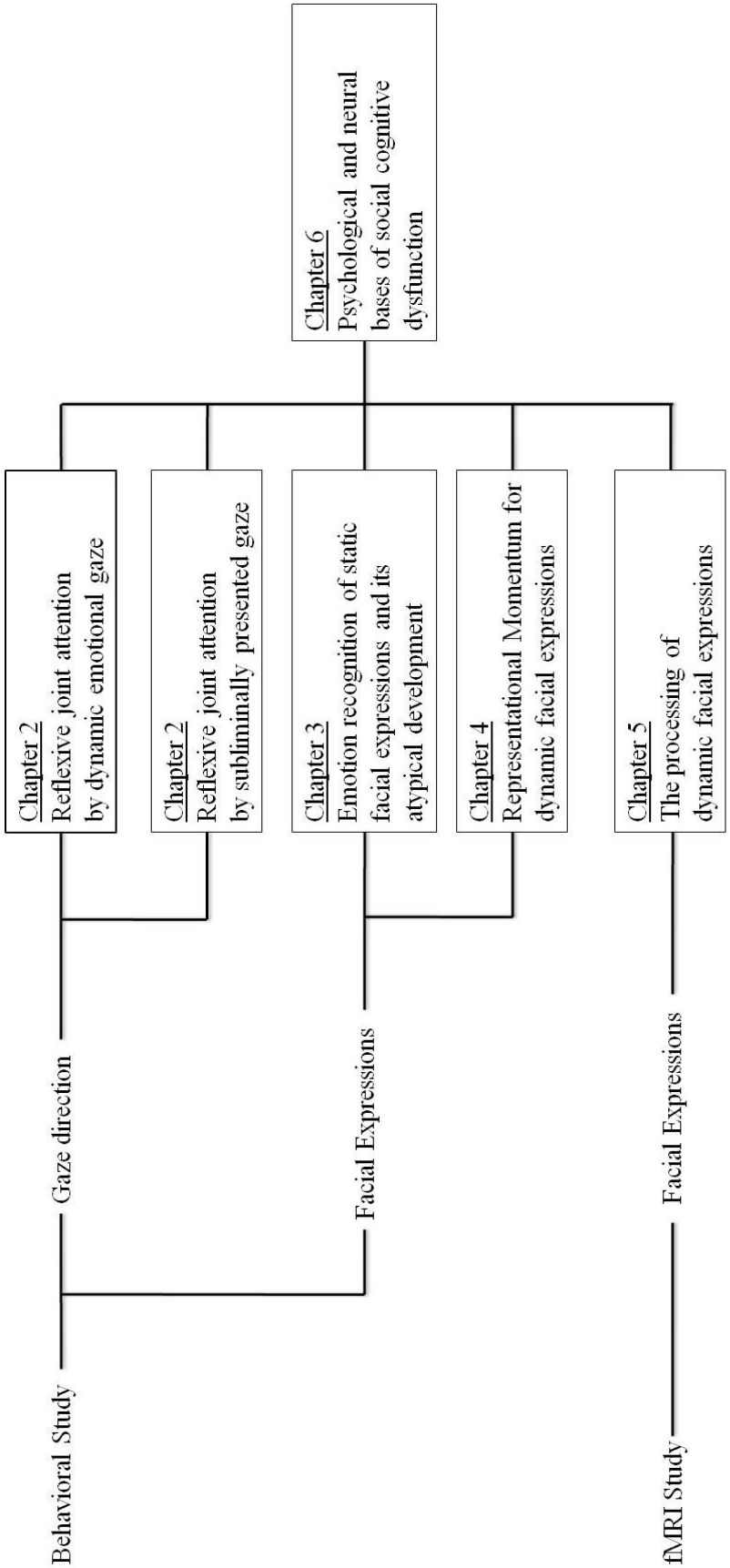


Figure 1 The structure of this thesis

# Chapter 2

## The impairment of gaze-triggered attention orienting

## 2.1 Dynamic fearful gaze does not enhance attention orienting in individuals with PDD

### 2.1.1 Introduction

One of the earliest features of these social impairments in PDD is a deficit of joint attention (Mundy, Sigman, Ungerer, & Sherman, 1986). For example, in our previous study, when the attending physician suddenly averted his or her gaze to look at environmental objects during clinical interviews, the individual with PDD did not follow the gaze direction (Okada et al., 2003).

In contrast to such clinical evidence for impaired joint attention, most experimental studies have found intact reflexive joint attention in PDD (Chawarska et al., 2003; Kylliäinen & Hietanen, 2004; Okada et al., 2003; Rutherford & Krysko, 2008; Senju et al, 2004; Swettenham et al., 2003; Vlamings et al., 2005; for a review see Nation and Penny (2008)), although there have been reports of impairment (Goldberg et al., 2008; Ristic et al., 2005). These studies applied Posner's (1980) cueing paradigm. For example, Okada et al. presented a face with left- or right-directed eyes to subjects with autism and typically developing controls, with targets appearing on the right or left side of the face. The participants were instructed that the gaze

direction did not predict where the target would appear. Nonetheless, the reaction time (RT) to detect a target was shorter for a gaze-cued (i.e., valid) location than for a gaze-uncued (i.e., invalid) location in both PDD and control groups. These results suggest that reflexive joint attention is intact in individuals with PDD.

Some researchers have pointed out the importance of an emotional component in joint attention (e.g., Mundy & Sigman, 1989). Others' emotional gaze could be important for evaluating environmental stimuli (Bayliss, Frischen, Fenske, & Tipper, 2007) and understanding the other's mental state (Shamay-Tsoory, Tibi-Elhanany, & Aharon-Peretz, 2007). Consistent with this view, recent experimental studies in normally developing individuals found that gaze-triggered attention orienting was facilitated by emotional facial expressions (Putman et al, 2006; Tipples, 2006; Uono, Sato, Toichi, 2009). For example, Uono et al. presented a dynamic emotional or neutral facial cue with left- or right-directed eyes. Participants were asked to detect a target letter. They found that a dynamic fearful gaze cue enhanced the RT difference between valid and invalid conditions compared with a dynamic neutral gaze cue.

Little is known about the effect of emotional facial expressions on reflexive joint attention in individuals with PDD. However, some evidence

suggests that the ability to process emotional gaze is impaired. For example, previous studies have reported that individuals with PDD were less likely to combine their gaze signals with emotional facial expressions in social interactions (Dawson, Hill, Spencer, Galpert, & Watson, 1990; Kasari, Sigman, Mundy, & Yirmiya, 1990). Moreover, individuals with PDD have been shown to have difficulty in understanding others' mental state from their emotional gaze (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001; Baron-Cohen, Wheelwright, & Jolliffe, 1997). Other studies have reported that individuals with PDD show impaired recognition of facial expressions of emotion; specifically fear (Corden et al., 2008; Howard et al., 2000; Humphreys et al., 2007; Pelphrey et al., 2002), although some other studies have reported intact emotion recognition among people with PDD (Adolphs et al., 2001; Castelli, 2005; Grossman et al., 2000). Neuroscience studies have revealed an atypical brain response to emotional facial expressions in individuals with PDD (Critchley et al., 2000; Ogai et al., 2003), particularly to fearful faces (Ashwin, Baron-Cohen, Wheelwright, O'Riordan, & Bullmore, 2007; Dawson, Webb, Carver, Panagiotides, & McPartland, 2004). These data suggest that individuals with PDD may show atypical patterns of joint attention when gaze is presented in combination

with emotional, particularly fearful, facial expressions.

The present study tested reflexive gaze-triggered attention orienting in individuals with PDD and an age-matched control group. The present study used dynamic fearful and neutral gaze as cues. The participants were asked to detect a peripheral target following the gaze cue. Based on previous findings, it was hypothesized that the cueing effect (i.e., the RT differences between invalid and valid cues) for a fearful gaze would be greater than that for a neutral gaze in the control group, but not in the PDD group. Additionally, it was predicted that the cueing effect of the neutral gaze would not differ between groups, but that the cueing effect of the fearful gaze would be greater in the control group than in the PDD group. Furthermore, the present study conducted exploratory analyses to test whether the results of reflexive joint attention could be accounted for by impairment in general face recognition or emotion recognition.

### 2.1.2 Methods

#### 2.1.2.1 Participants

Eleven individuals with PDD and 11 controls participated in this study. The PDD and control groups were matched for chronological age (PDD

group: 17.5 ± 6.5 years, range 9–30; control: 19.5 ± 2.2 years, range 18–26; independent t-test, $t(20) = 0.88$, $p > 0.1$) and gender (8 males and 3 females in both groups). The Verbal and Performance IQ in the PDD group was measured using the Japanese version of the WAIS-R (Shinagawa, Kobayashi, Fujita, & Maekawa, 1990) or WISC-R (Kodama, Shinagawa, & Motegi, 1982). The IQs of all of participants in the PDD group were in the normal range (Full-scale IQ: $M = 107.73$, $SD = 9.05$; Verbal IQ: $M = 107.55$, $SD = 13.06$; Performance IQ: $M = 104.55$, $SD = 10.43$).

The participants in the PDD group were diagnosed with either Asperger's disorder (8 males, 2 females) or pervasive developmental disorder not otherwise specified (PDD-NOS; 1 female) by a child psychiatrist using DSM-IV-TR (APA, 2000). According to DSM-IV-TR, PDD subtypes with a varying degree of severity are classified as PDD-NOS. In this study, one participant diagnosed as PDD-NOS had milder pathologies than those that occur in Asperger's disorder.

All were outpatients who had been referred to Kyoto University Hospital or the Faculty of Human Health Science of Kyoto University Graduate School of Medicine because of their social maladaptation. They were all free of neurological or psychiatric problems other than those associated with PDD, and none was taking any medication. The diagnosis of

PDD was based on (1) an interview; (2) information from each subject; and (3) childhood clinical records. More specifically, the diagnostic procedure in this study was as follows. First, research assistants (clinical psychologists) collected information from parents on developmental milestones (including joint attention behaviors) and episodes (e.g., how the individual with PDD behaved at school). Information about detailed observations of interactions with people (particularly non-family members) as well as repetitive behaviors, obsessive/ compulsive traits, and stereotyped behaviors, was also provided by teachers or other professionals (such as occupational counselors and mental health counselors). An expert child psychiatrist interviewed each participant in the PDD group at least three times (each on a separate day, with a between-interview interval of more than 2 weeks) before the final diagnosis was made. All participants aged 18 years and older and the parents of participants aged younger than 18 years provided written informed consent to participate in this study in accordance with the Declaration of Helsinki.

The neuropsychological mechanisms of face recognition and emotion recognition were investigated in all participants using the shortened version of the Benton facial recognition test (Benton, Sivan, Hamsher, Varney, & Spreen, 1994) and the emotion recognition test using six basic emotional

facial expressions (Sato et al., 2002). The data are summarized in Table 2.1. Although one participant had impaired face recognition, no significant difference in face recognition was found between groups ($t(20) = 0.86$, $p > 0.1$). The results suggested a tendency for individuals with PDD to be better able to recognize surprised faces than control subjects were ($t(20) = 2.19$, $p = 0.053$), but no significant differences between groups were found for the other emotions ($ts(20) < 0.90$, $ps > 0.1$). In summary, no significant impairments in either face or emotion recognition were found in the PDD group.

Table 2.1
Mean (with *SE*) scores of Benton facial recognition test (out of 27) and mean (with *SE*) percentages of accurate emotion recognition

| | | Benton | Facial emotion | | | | | |
|---|---|---|---|---|---|---|---|---|
| Group | | | AN | DI | FE | HA | SA | SU |
| Control | M | 23.5 | 59.1 | 40.9 | 44.3 | 97.7 | 80.7 | 94.3 |
| | SE | (0.7) | (5.9) | (6.5) | (7.4) | (1.5) | (5.4) | (2.6) |
| PDD | M | 22.4 | 61.4 | 45.5 | 34.1 | 96.6 | 87.5 | 100 |
| | SE | (0.9) | (5.9) | (6.1) | (8.9) | (1.8) | (5.3) | (0) |

AN = anger; DI = disgust; FE = fear; HA = happiness; SA = sadness; SU = surprise.

#### 2.1.2.2 Design

The experiment was constructed as a two-factorial mixed randomized-repeated design, with group (PDD or control) as the randomized factor, and emotion condition (fearful or neutral) as the repeated factor.

#### 2.1.2.3 Stimuli

I selected the cue stimuli from Ekman and Friesen (1976). Photographs of two models (1 male and 1 female) with neutral and fearful faces were selected and manipulated. The dynamic fearful expressions were created by morphing four intermediate images between the neutral (0%) and the fearful (100%) expressions in 20% steps using computer-morphing techniques (Mukaida et al., 2000) on a Windows computer.

The gaze direction was then manipulated. The irises and pupils of the eyes were cut from the original photographs and pasted to fit on the right or left side of the eyes using Photoshop 5.0 (Adobe). The irises and pupils for the intermediate photographs were fit to the position matching each transformation percentage. I cropped the photographs in an ellipse 4.6° wide and 6.2° high to exclude the hair and background.

I presented the stimuli sequentially from 0% (neutral) to 100% (original fearful) under the fearful gaze condition. The first 0% image was

presented for 300 ms, and each intermediate image were presented for 20 ms. The last 100% image remained until a response was made. Under the neutral gaze conditions, only the gaze direction was changed dynamically. A total of 42 photographs were used as dynamic gaze cue stimuli: emotion (neutral and fearful) gaze direction (four intermediate positions for right and left and an end position for right and left) person (two models), and a neutral face with straight gaze for two models. An example of the dynamic emotional expression cue is shown in Figure 2.1. The target stimulus was a letter T (1° wide and 1° high) presented 9.0° to the left or right side of the center of the screen.

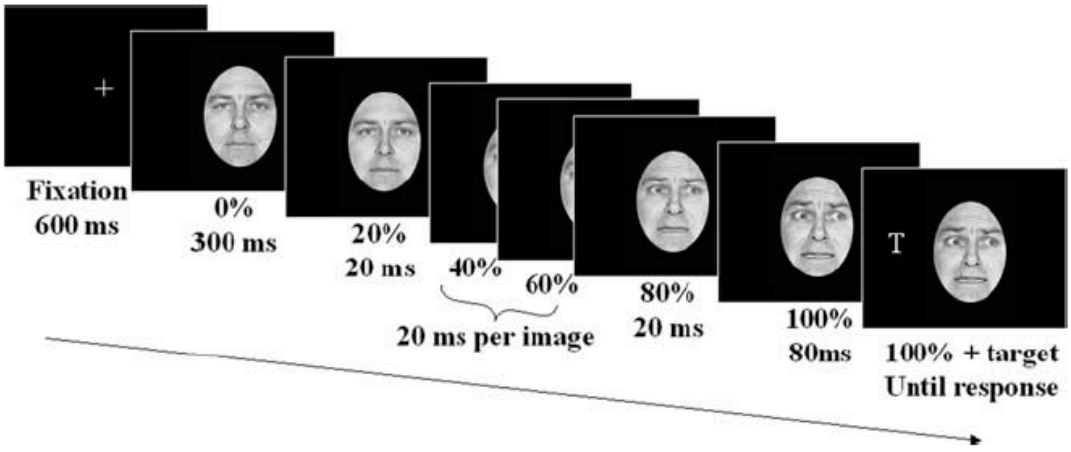


Figure 2.1 The stimulus presentation sequence under the fearful and invalid gaze condition.

#### 2.1.2.4 Apparatus

Stimulus presentation and data acquisition were controlled by Presentation® (Neurobehavioral Systems) on a Windows computer (HP xw4300 Workstation). Stimuli were presented on a 17-inch CRT monitor (Iiyama; screen resolution 1024 × 768 pixels; refresh rate 100 Hz). The distance between the monitor and the participants was fixed at approximately 57 cm using a headrest.

#### 2.1.2.5 Procedure

The sequence of stimulus presentation is shown Figure 2.1. In each trial, a fixation cross was first presented at the center of the screen for 600 ms. Subsequently, a dynamic emotional or neutral facial cue with the eyes gazing sideways (right or left) was presented at the center of the screen. After 80 ms, the target letter T appeared to the left or right side of the cue stimulus. The participants were asked to press a button as quickly as possible when a target appeared. The interval from target appearance to button response was measured in each trial. The target and cue remained on the screen until a response was made. If 1500 ms elapsed with no response, the next trial was started. The participants were told that the cues did not predict the target location and were instructed to fixate on the center of the

screen in each trial.

The experiment consisted of eight blocks of 28 trials, including 32 catch trials in which the target did not appear. Forty-eight trials were performed under each condition. The trials were presented in pseudorandom order such that the same condition appeared once in four consecutive trials. Participants were allowed to rest between blocks. Thirty practice trials preceded the experimental trials.

2.1.2.6 Data analysis

The data were analyzed using SPSS 10.0 J (SPSS Japan). Incorrect responses and responses of less than 100 ms were excluded from the RT analysis. The median RT under each condition was calculated for each participant. The RT differences between the invalid and the valid cues under facial expression conditions were calculated as a measure of the shift of attention, or the gaze cueing effect, as described in previous studies (e.g., Okada, Sato, & Toichi, 2006). First, to test the cueing effect, the RT difference under each condition was tested for the difference from zero using one-sample t-tests. Then, the RT differences were analyzed in a two-way analysis of variance (ANOVA) with emotion (fearful and neutral) as the within-participant factor and group (PDD and control) as the between-

participant factor. For significant interactions, if present, follow-up simple-effect analyses were conducted. Non-parametric Mann–Whitney U-tests were conducted to confirm the results. I further conducted an analysis of covariance (ANCOVA) using the Benton facial recognition test scores and correct scores of fearful facial expressions as covariates. A preliminary ANCOVA using participant's age as a covariate showed that the age did not affect the group emotion interaction; therefore, age was omitted in the subsequent analyses. Preliminary analyses also showed that the error rates in catch trials were small in both groups (< 8%), and no evidence of a speed-accuracy trade-off was observed; thus, I report only the RT results.

### 2.1.3 Results

The mean (with *SE*) median RTs for each condition are shown in Table 2.2. The mean (with *SE*) RT differences between the invalid and the valid conditions are shown in Figure 2.2. One-sample t-tests indicated that the cueing effects were significantly larger than zero under both emotion conditions in both groups (all $p < 0.05$).

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Table 2.2
Mean (with *SE*) median RTs for each condition in control and PDD groups

| | Control | | PDD | |
|---|---|---|---|---|
| Facial expression | Valid | Invalid | Valid | Invalid |
| Fearful | 281.3 (7.6) | 306.4 (6.1) | 291 (12.1) | 308.3 (14.4) |
| Neutral | 291.3 (5.4) | 301.8 (5.3) | 306.3 (13.3) | 322.8 (16.5) |

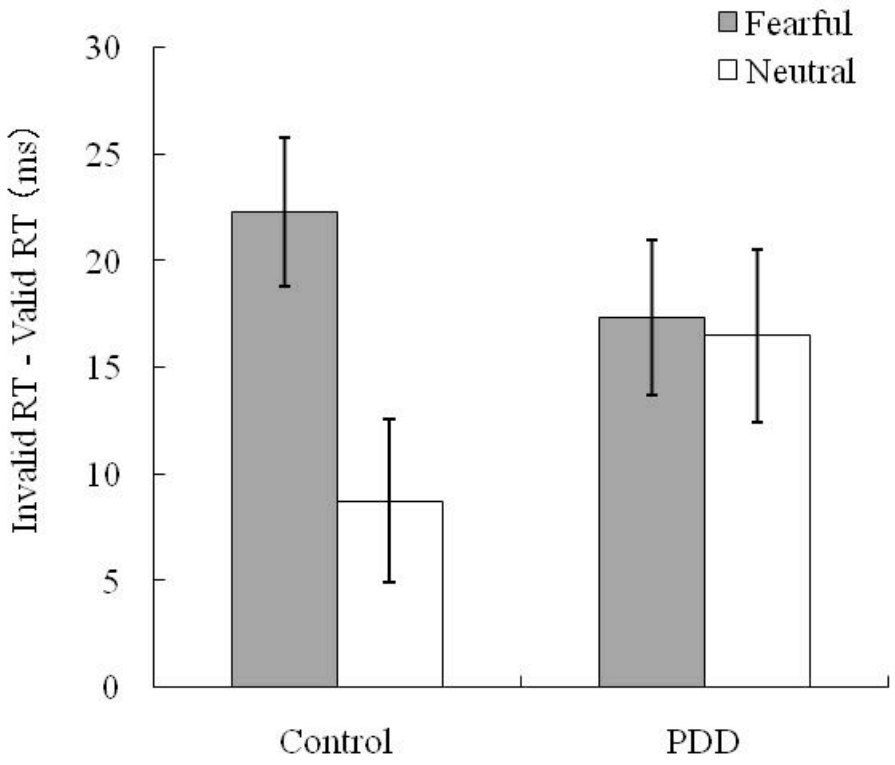


Figure 2.2 Mean (with SE) RT differences between invalid and valid gaze conditions for the Asperger and control groups. The error bars represent standard errors.

The ANOVA revealed a significant main effect of emotion ($F(1,20) = 6.54$, $p < 0.05$), and interaction of emotion by group ($F(1, 20) = 5.16$, $p < 0.05$). Simple main effect analyses revealed that the cueing effect for fearful gaze was significantly larger than that for neutral gaze in the control group ($F(1, 20) = 11.67$, $p < 0.01$), but not in the PDD group ($p > 0.1$). A further simple main effect analysis revealed that the cueing effects for fearful and neutral gaze were not significantly different between groups ($p > 0.1$). A Mann–Whitney U-test revealed that the difference between groups was marginally significant for fearful gaze ($U = 32.0$, $p = 0.06$) but not significant for neutral gaze ($U = 48.0$, $p > 0.1$).

The ANCOVA using face recognition and recognition of fearful expression as covariates showed that the interaction of emotion group remained significant ($F(1, 18) = 5.89$, $p < 0.05$). The results suggest that face recognition and recognition of fearful expression cannot account for differences in the effect of fearful gaze on attention orienting.

### 2.1.4 Discussion

Two major findings emerged from the present study. First, a significant difference in RT was found for invalid vs. valid cues, regardless of the emotion expressed by the gaze, in both the control and PDD groups.

A debate exists about the ability of individuals with PDD to orient their attention, specifically that triggered by non-social cues (e.g., Iarocci & Burack, 2004; Renner, Klinger, & Klinger, 2006). However, our results, together with those of several previous studies (e.g., Okada et al., 2003; see Nation and Penny (2008) for a review), clearly indicate that gaze-triggered orienting is not impaired in individuals with PDD.

Second, and more importantly, the RT difference (invalid minus valid) for the fearful gaze was greater than that for the neutral gaze in the control group, but not in the PDD group. The finding that a fearful gaze facilitates reflexive attention orienting in the control group is consistent with the results of previous studies (Putman et al., 2006; Tipples, 2006; Uono, Sato, Toichi, 2009). Impaired integration of emotional expression and gaze direction in the PDD group is in line with previous studies investigating social cognition (Baron-Cohen, Jolliffe, et al., 1997; Baron-Cohen et al., 2001; Baron-Cohen, Wheelwright, et al., 1997). Further, the finding of inefficient processing of a fearful gaze in the PDD group confirms previous behavioral (Corden et al., 2008; Howard et al., 2000; Humphreys et al. 2007; Pelphrey et al., 2002) and neuroscience (Ashwin et al., 2007; Dawson, Webb, et al., 2004) reports. The result of the present study extend the data on joint attention and expression processing and, to our knowledge,

provides the first evidence that a fearful gaze does not facilitate reflexive attention orienting in individuals with PDD.

Further, our results indicate that deficits in face recognition and emotion recognition do not account for this impairment. The finding that these abilities are normal in individuals with PDD is consistent with studies of emotional processing in PDD (Adolphs et al., 2001; Castelli, 2005; Grossman et al., 2000). However, some studies have reported impaired perception of facial configurations (see Behrmann, Thomas, and Humphreys (2006) for a review) or enhanced perception of facial features (see Behrmann et al. (2006) and Mottron, Dawson, Soulieres, Hubert, and Burack (2006) for reviews) in PDD. Other studies report impaired recognition of facial expressions of emotion, specifically fear, in individuals with PDD (Corden et al., 2008; Howard et al., 2000; Humphreys et al., 2007; Pelphrey et al., 2002). The sample size was small, and the possibility of impaired face recognition and emotion recognition in PDD cannot be completely ruled out. Nevertheless, these findings clearly indicate that the facilitative effect of fearful gaze on reflexive attention orienting was impaired in the PDD group, despite no clear impairment in the face or emotion recognition. Previous studies reported that individuals with PDD were less likely to combine their gaze signals with emotional

facial expressions in social interactions, although they used these signals individually as often as did people without PDD (Dawson et al., 1990; Kasari et al., 1990). Our findings, together with these previous data, suggest that individuals with PDD have difficulty in integrating emotional expressions and gaze direction rather than in processing the individual social signals.

The results partly explain the difference between clinical observations and experimental results in joint attention behavior in individuals with PDD. In real-life communication, others' emotional gaze plays an important role in evaluating attended objects (Bayliss et al., 2007) and in understanding others' mental states (Shamay-Tsoory et al., 2007). Mundy and Sigman (1989) proposed that sharing emotion in joint attention induces the development of socio-emotional functions. Given that the impairment of joint attention in PDD predicts later deficits in language skills and social communications (Charman, 2003), impaired processing of emotional gaze might underlie the deficit in more complex social and cognitive functions.

The amygdala is thought to be involved in the processing of both gaze and emotion. A recent study of patients with unilateral amygdala incision reported amygdala involvement in reflexive joint attention (Okada et al., 2008). Neuroimaging studies in subjects without PDD have indicated that

the amygdala is involved in the processing of fearful expressions (Sato, Kochiyama, Yoshikawa, Naito, & Matsumura, 2004) and that amygdala activity reflects the interaction between emotional expression and gaze direction (Sato, Yoshikawa, Kochiyama, & Matsumura, 2004). Magnetic resonance imaging (MRI) studies have reported that the amygdala shows an abnormal developmental trajectory in PDD (Nacewicz et al., 2006; Schumann et al., 2004). Neuroimaging studies reveal that the amygdala of individuals with PDD is less active in response to fearful expressions (Ashwin et al., 2007) and emotional gaze (Baron-Cohen et al., 1999) than is that in controls. Taken together, these findings suggest that a dysfunction of the amygdala in PDD that interferes with the integrative processing of gaze direction and emotion may explain the failure to elicit efficient attention orienting to a dynamic fearful gaze.

The RT for the fearful gaze condition was faster than that for the neutral gaze condition in the PDD group, regardless of cue validity (see Table 2.2). This finding was confirmed with an emotion validity ANOVA (significant main effects of emotion ($F(1, 10) = 18.95$, $p < 0.001$) and validity ($F(1, 10) = 24.13$, $p < 0.001$). This unexpected finding indicates that, in individuals with PDD, processing a fearful gaze might result in overall enhancement of visual processing, not simply selective facilitation

of joint attention, reflecting undifferentiated emotional development. Indirect evidence is available to support this interpretation. Neuroimaging studies have shown that the visual cortex is more active in individuals with PDD than in control subjects during face processing (Hubl et al., 2003) and theory of mind tasks (Castelli, Frith, Happe, & Frith, 2002). Hall, Szechtman, & Nahmias (2003) reported that the primary visual cortex is more active during an emotion perception task than during a gender discrimination task in individuals with PDD. Further studies are needed to elucidate whether this atypical processing strategy extends to reflexive joint attention.

A limitation of this study is that the present study tested only fearful gaze. In real-life communication, a happy gaze may facilitate the sharing of intention, which could also be impaired in individuals with PDD. Emotions other than fear should be examined in future research.

### 2.1.5 Summary

Although impaired joint attention is one of the core clinical features of pervasive developmental disorder including autistic disorder and Asperger's disorder, experimental studies failed to report its impairment. This discrepancy might be the result of differences between real-life and

experimental situations. The present study examined joint attention in 11 individuals with PDD and 11 age-matched controls under naturalistic conditions using a target detection paradigm with dynamic emotional gaze cues. Although both groups showed gaze-triggered attention orienting as assessed by the differences in reaction time for invalid minus valid cues, enhancement of joint attention by fearful (vs. neutral) gaze was observed in the control, but not in the PDD group. This suggests that the integration of emotion and gaze direction that elicits strong joint attention is impaired in individuals with PDD.

## 2.2 Impairment of unconscious, but not conscious, gaze-triggered attention orienting in individuals with PDD

### 2.2.1 Introduction

In contrast to obvious clinical evidence of impaired joint attention (e.g., Okada et al., 2003), several experimental studies have found a normal ability to shift attention with another's gaze reflexively in PDD (for a review see Nation & Penny, 2008). The present study investigated another potential factor explaining the discrepancy of joint attention impairments in real life and experimental settings.

Our social interactions are full of adaptive unconscious processes (Wilson, 2002). A recent study in typical developing individuals revealed that gaze-triggered attention could even occur when gaze cue was presented subliminally (Sato et al., 2007). Previous behavioral studies have demonstrated that have reported impairment in the unconscious processing of facial stimuli in individuals with PDD (Hall, et a., 2007; Kamio et al., 2006). Based on these data, it would be unconscious, rather than conscious, gaze-triggered attention shift that is impaired in PDD. Here the present study tested this hypothesis in a group of PDD and age- and gender-matched typically developing controls. The present study used the same cueing paradigm with supraliminally or subliminally presented gaze cues, as in a previous study (Sato et al., 2007).

### 2.2.2 Methods

#### 2.2.2.1 Participants

The PDD group (3 females, 9 males; mean $\pm$ *SD* age = 17.2 $\pm$ 6.3 years) consisted of 11 (2 females, 9 males) with Asperger's disorder and 1(female) with PDD-NOS, who did not satisfy all the diagnostic criteria for Asperger's disorder but exhibited mild symptoms of PDD. The diagnoses,

based on the DSM-IV-TR (APA, 2000), were made by psychiatrists with expertise in developmental disorders. Neurological and psychiatric problems other than those associated with PDD were ruled out. Participants were taking no medication. The Full-scale IQ, measured by the WAIS-R or WISC-R, of all participants in the PDD group scored in the normal range (Full-scale IQ = 106.8 ± 9.3; Verbal IQ = 106.4 ± 13.1; Performance IQ = 104.2 ± 10.0). Participants in the control group (3 females, 10 males; mean ± *SD* age = 19.7 ± 1.9 years) were matched for age and gender with the PDD group. All participants had normal or corrected-to-normal visual acuity. After the procedure and purpose of the study were explained fully and before testing, written informed consent was obtained from the participants or their parents.

#### 2.2.2.2 Experimental design

The experiment was constructed as a two-factorial mixed randomized-repeated design, with group (PDD or control) as the randomized factor, and presentation condition (subliminal or supraliminal) as the repeated factor.

#### 2.2.2.3 Apparatus

The events were controlled by SuperLab Pro 2.0 (Cedrus) and

implemented on a Windows computer (MA55J, NEC). The stimuli were presented on a 19-in. CRT monitor (GDM-F400, Sony) with a refresh rate of 100 Hz and a resolution of 1024 × 768 pixels. The participants' responses were recorded using a response box (RB-400, Cedrus).

#### 2.2.2.4 Stimuli

The gaze cues consisted of schematic faces in which the eye gaze was directed toward either the left or right. Masks were mosaic patterns that covered all of the facial features of the cue stimuli. The cues and masks subtended 6.58 vertically × 6.58 horizontally. The target was an open circle subtending 1.08 vertically × 1.08 horizontally. These stimuli consisted of a black line drawing on a white background.

#### 2.2.2.5 Procedure

The procedure was identical to that of a previous study (Sato et al., 2007). The experiments were conducted individually in a small room. The participant was seated comfortably with her/his head supported by a chin-and-forehead rest located 0.57m from the screen.

A threshold assessment session was first conducted. The stimulus onset asynchrony (SOA) between the target and mask was manipulated. To assess

the upper limit of SOA for subliminal presentation in each participant, blocks of 20 subliminal cue presentation trials, i.e., 10 each for the left and right gaze directions were prepared. In each trial, after the presentation of a fixation point, i.e., a small black ''+'' lasting 680 ms, the gaze cue was presented in the center of the monitor, after which the mask was presented in the same location. The presentation time of the mask was adjusted so that the total presentation period of the gaze cue and the mask was 200 ms. The order of gaze direction was randomized. The participant was asked to orally answer the question, ''Did you see the gaze? If so, report the direction of the gaze.'' They were also asked not to guess at answers. The participants responded either ''Yes'' or ''No,'' and in the case of the former, they then reported the gaze direction that they had seen. Starting with 10 ms, the SOA was prolonged by 10 ms increments. After the participants finished each block, the performance was investigated. If the participant correctly recognized at least 1 of the 20 stimuli, the corresponding SOA was regarded as the lower limit of conscious awareness for the cue for that participant, and an SOA 10 ms shorter than that limit was used in the trial session. The mean ($\pm$SD) SOA was as 19.2 $\times$ 10.9 and 14.7 $\times$ 7.8 ms for the PDD and control groups, respectively (two-tailed t-test, $t(23) = 1.21$, *n.s.*).

The trial session was then conducted. The participant completed a total

of 144 trials, presented in two blocks of 72. Each block contained an equal number of valid and invalid trials for each presentation condition. The order of cue validity was randomized within each block. The order of presentation condition was counterbalanced across participants. At the beginning of each block, the participant received 10 practice trials. A short break was interposed after 36 trials in each block, and a longer break was interposed after each block.

For each trial (Figure 2.3), a fixation point, i.e., a small black ‘‘+,’’ was presented for 680 ms at the center of the screen. The gaze cue was then presented at the same location. Subsequently, a target was presented in either the left or right visual field (5.08 apart from the center) until a response was made. The participant was instructed to specify as quickly as possible whether the target appeared on the left or right side of the screen by pressing the corresponding key on the switch box using the left or right index finger, respectively.

After the completion of all trials, debriefing was conducted and the participant was asked whether she/he had consciously perceived the gaze cues in the subliminal presentations. It was confirmed that none of the participants had consciously perceived the gaze cues in the subliminal presentations.

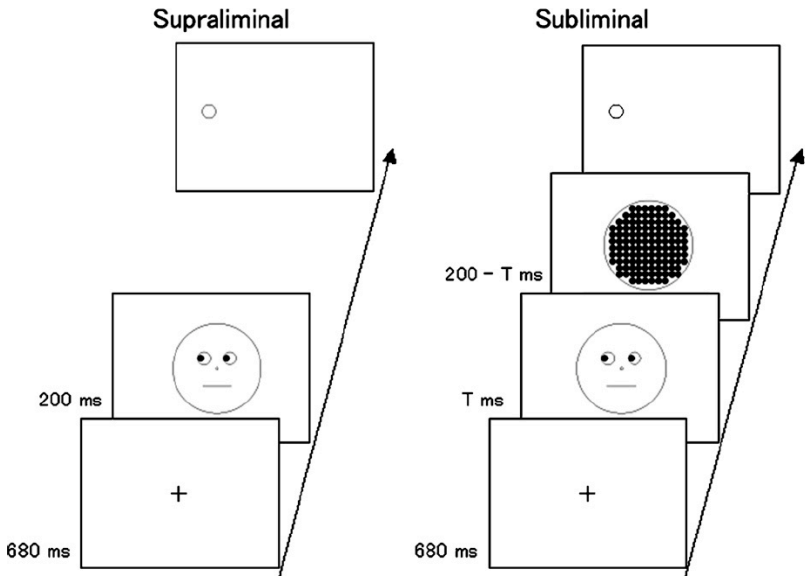


Figure 2.3 Illustrations of stimulus presentations. In the subliminal presentation, the presentation time of the gaze cue (T) was adjusted for each participant's threshold and the presentation period of the mask was also adjusted so that the total period was 200 ms.

### 2.2.2.6 Data analysis

The median correct RT under each condition was calculated for each participant. The differences in RT between valid and invalid conditions were then calculated as a measure of the gaze cueing effect as in previous studies (e.g., Okada, et al., 2006). The RT differences were analyzed using a 2 (group: PDD or control) × 2 (presentation condition: subliminal or supraliminal) ANOVA. For significant interactions, follow-up multiple comparisons were conducted for the group factor using t-tests (two-tailed)

with the Bonferroni correction. One-sample t-tests (two-tailed) were also performed to test for differences from zero with the Bonferroni correction. Preliminary analyses were conducted for error percentages. The error rates were small (<5%) and there was no evidence of a speed-accuracy trade-off phenomenon. Hence, the present study reports only the RT results.

### 2.2.3 Results

The ANOVA for the differences in RT between validly and invalidly cued conditions (Figure 2.4) revealed a significant interaction of group × presentation condition ($F(1,23) = 5.90$, $p < .05$). The main effect of presentation condition was also significant ($F(1,23) = 38.88$, $p < .001$).

Follow-up analyses for the interaction revealed that there was a significant between-group difference in the subliminal condition ($t(23) = 3.33$, $p < .001$), which indicated a larger RT difference for the control group than for the PDD group. There was no significant between-group difference in the supraliminal condition ($t(23) = 1.34$, *n.s.*).

Bonferroni-corrected one-sample t-tests were performed to test for differences from zero. All conditions differed significantly from zero ($ts > 2.87$, $ps < .05$), with the exception of subliminal presentations to the PDD group ($t(11) = 0.92$, *n.s.*).

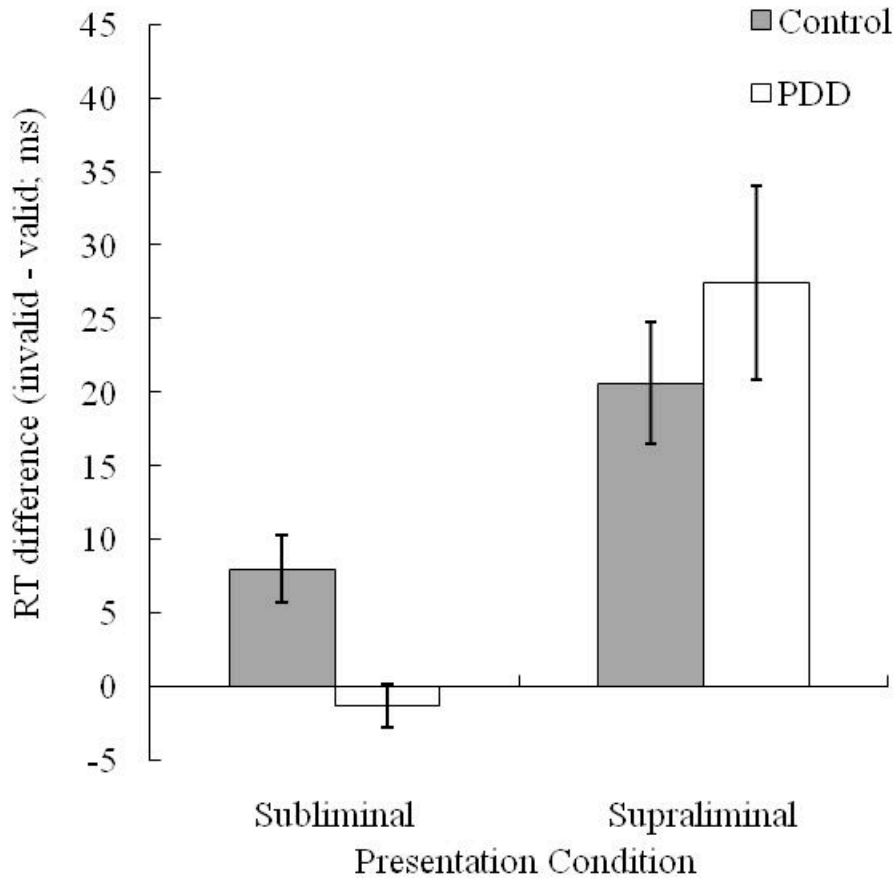


Figure 2.4 Mean (with SE) gaze cueing effect (i.e., differences in reaction time between validly and invalidly cued conditions).

### 2.2.4 Discussion

Congruent with previous studies that used the supraliminal presentation of gaze cues (Nation & Penny, 2008), I found a gaze cueing effect for both the PDD and control groups under supraliminal conditions.

These data confirm that conscious gaze-triggered attention orienting is not impaired in individuals diagnosed with PDD.

Under subliminal conditions, however, there was a gaze cueing effect in the control group, but not in the PD group. The triggering of attention orientation in participants without developmental disorders by the unconscious gaze cue is consistent with previous results (Sato et al., 2007). The impairment in the orienting response triggered by an unconscious gaze cue in individuals with PDD is a novel finding. This finding seems consistent with previous behavioral studies that have reported impairment in the unconscious processing of facial stimuli in individuals with PDD (e.g., Hall, et a., 2007). The results support the hypothesis that individuals with PDD have impaired unconscious, but not conscious, gaze-triggered attention.

The results can explain the discrepancy between previous clinical (Mundy et al., 1994) and experimental (Nation & Penny, 2008) findings on joint attention in PDD. Psychophysical studies have shown that, contrary to what intuition might suggest, humans consciously perceive only very restricted areas within the range of areas available for immediate attention (Simons & Rensink, 2005). Consistent with this notion, psychological studies have indicated that social behaviors are heavily influenced by

unconscious processing (Wilson, 2002). In particular, previous research has found that gaze-triggered attention orienting occurs unconsciously (Sato et al., 2007). Thus, individuals that exhibit typical developmental milestones have at least two mechanisms to achieve automatic joint attention: conscious processing of the gazes of others that occur within restricted attended areas and unconscious processing of the gazes of others that occur within broader unattended areas. The results indicate that individuals with PDD have access to only a single conscious mechanism for the achievement of joint attention; therefore, these individuals may fail to show joint attention in relation to individuals outside of the range of conscious attention.

The present finding of impaired unconscious gaze processing in individuals diagnosed with PDD corroborates evidence from neuroscientific literature. A neuroimaging study of typically developing participants reported the involvement of the amygdala in the unconscious processing of gaze (Whalen et al., 2004). A study of patients with unilateral amygdala incisions indicated that the amygdala is involved in gaze-triggered attention orienting (Okada et al., 2008). Considering the neural network from which the amygdala receives visual input, i.e., the subcortical pathway via the pulvinar and superior colliculus (Adolphs, 2002), it is possible that the

amygdala processes the information derived from gaze, even before conscious awareness has emerged. Postmortem histopathological (e.g., Schumann & Amaral, 2006) and neuroanatomical imaging (e.g., Schumann et al., 2004) studies have reported a pronounced abnormality of the amygdala in individuals diagnosed with PDD. Neuroimaging studies have reported that these individuals show reduced activity of the amygdala in the processing of gaze (e.g., Baron-Cohen et al., 1999). These data suggest that dysfunction of the amygdala may be the neural background of the impairment of the unconscious gaze-triggered attention orienting in individuals with PDD.

In contrast, the conscious awareness of visual stimuli is implemented in the cortical visual areas (Treisman & Kanwisher, 1998). Neuroimaging studies in normatively developing participants showed the activation of some cortical visual areas, including the superior temporal sulcus (STS) region, in response to supraliminally presented gaze (e.g., Hoffman & Haxby, 2000). A neuroimaging study in individuals with PDD also reported the activation of the STS region in the conscious processing of gaze (Baron-Cohen et al., 1999). These data suggest that the cortical pathways involved in the conscious processing of gaze are not impaired in PDD. Controversy persists about whether automatic processing can be identified

with the absence of consciousness (Tzelgov, 1997). The results indicate that automatic gaze-triggered attention consists of conscious and unconscious processes, with one dissociable from the other. It has been proposed that automatic processes could derive from either heredity or practice (Hasher & Zacks, 1979). These findings speculate that individuals with PDD may have innate impairments in the unconscious subcortical system, but can acquire, through practice, the conscious cortical system that allows joint attention.

### 2.2.5 Summary

Impairment of joint attention represents the core clinical features of pervasive developmental disorders (PDDs), including autism and Asperger's disorder. However, experimental studies reported intact gaze-triggered attention orienting in PDD. Since all previous studies employed supraliminal presentation of gaze stimuli, it was hypothesized that individuals with PDD may be impaired not in conscious but in unconscious gaze-triggered attention shift. The present study tested the hypothesis in a group of PDD (N = 12) and age- and gender-matched controls (N = 13), using a cueing paradigm with supraliminal and subliminal presentation of gaze cues. Under supraliminal conditions, the gaze cueing effect was evident in both groups. Under subliminal conditions, the PDD group, unlike

the control group, did not show the gaze cueing effect. These results indicate the impairment of unconscious, but not conscious, joint attention in individuals with PDD, which may underlie some clinical findings of social malfunction in PDD.

# Chapter 3

## The specific impairment of fearful expression recognition and its atypical development in individuals with PDD

## 3.1 Introduction

Individuals with PDD, including autism and Asperger's disorder, are characterized by a qualitative impairment of social interaction (APA, 2000). Kanner's original clinical study emphasized that individuals with autism have innately impaired affective contact with others (Kanner, 1943). Recently, Hobson (1993) proposed that the difficulty in the expression and perception of emotion contribute to a failure to establish interpersonal relationships. To elucidate the cause of social dysfunction, considerable research has focused on the ability to recognize emotion from the facial expressions of others.

However, previous studies investigating emotion recognition in PDD have reported inconsistent findings. Several studies have demonstrated impaired facial expression recognition in PDD (Braverman et al., 1989; Celani et al., 1999), with others further suggesting that individuals with PDD were specifically impaired in recognizing fearful expressions (Ashwin, et al., 2006; Corden et al., 2008; Howard et al., 2000; Humphreys et al., 2007; Pelphrey et al., 2002). However, some studies have reported that individuals with PDD showed no impairment in facial expression recognition (Adolphs et al., 2001; Castelli, 2005; Grossman et al., 2000).

These inconsistent findings regarding facial expression recognition in

PDD may be due to a number of potential factors. First, the majority of the previous studies lacked a developmental perspective for facial expression recognition in individuals with PDD. The ability to recognize faces improves with age during childhood and adolescence in typically developing individuals (for review, see Herba & Phillips, 2004), but little is known about the development of facial expression recognition in individuals with PDD. The studies described above suggest atypical development of facial expression recognition in individuals with PDD, and recent studies with a large number of participants have shown deficits in facial expression recognition in adults (Ashwin et al., 2006; Corden et al., 2008; Humphreys et al, 2007), but not children, with PDD (Castelli, 2005; Grossman et al., 2000). These data suggest that the ability to recognize facial expressions improves with age in normally developing individuals but not in individuals with PDD.

Second, previous studies did not examine the effects of general face-processing ability on facial expression recognition. Face-recognition skills are proposed to correlate with the ability to recognize fear in others (Skuse, 2003). Although face-recognition ability also improves with age during childhood and adolescence in typically developing individuals (Carey et al., 1980; Mondloch et al., 2003), studies have shown impaired face recognition

in children and adolescents with PDD (Boucher et al., 1998; Klin et al., 1999). These findings suggest that the development of face recognition leads to the improved facial expression recognition in typically developing controls but not in individuals with PDD. Previous studies have investigated the relationship between face recognition and facial expression recognition in individuals with PDD (Hefter, Manoach, & Barton 2005; Riby, Doherty-Sneddon, & Bruce, 2008), however the results are inconsistent. Hefter et al. demonstrated that participants with face-recognition deficits recognize facial expressions as well as those with normal face recognition. On the other hand, Riby et al. showed that face-recognition ability positively correlated with facial expression recognition in individuals with PDD. However, these studies did not use all six basic facial expressions, and the chronological age of participants differed between studies. Thus, further studies are needed to clarify whether atypical development of face recognition leads to deficits in the recognition of six basic facial expressions in individuals across a broader chronological age range.

Third, the degree of social dysfunction in individuals with PDD may relate to deficits in facial expression recognition. In normal participants, performance in face-recognition tasks involving fearful faces correlates

with higher social cognitive functions (e.g., theory of mind ability) (Corden et al., 2006; Marsh et al., 2007). Little evidence exists of a relationship between fear recognition and symptom severity in individuals with PDD (cf. Humphreys et al., 2007). Thus, the present study tested whether the degree of impairment in facial expression recognition positively correlates with social dysfunction in individuals with PDD.

Further, the present study investigated the relationship between fear recognition and social inattention. Previous studies have shown that the degree of the fixation to eye region affects the performance of fearful face recognition (e.g., Corden et al., 2008). Some researchers have proposed that inattention to social stimuli lead to the development of higher-order social cognition (e.g., Dawson, Toth, et al., 2004). Thus, two CARS items "relationship to people" and “visual response”, which reflects the social interest to people such as eye contact, were used.

The present study investigated facial expression recognition deficits across development in individuals with high-functioning PDD and examined the recognition of facial expressions conveying the six basic emotions. It is hypothsized that individuals with PDD would show impaired emotion recognition, particularly recognition of fearful expression. The present study also investigated the relationship between chronological age, face

recognition, and facial expression recognition. The present study tested the following model in typically developing controls and individuals with PDD using a path analysis: 1) facial expression recognition and face recognition improve with age; 2) the development of face recognition leads to the improvement of facial expression recognition. Finally, the present study tested the relationship between impaired facial expression recognition and symptom severity in individuals with PDD. Based on the evidence described above, it was hypothesized that recognition of fearful expressions would be negatively correlated with social dysfunction in individuals with PDD.

## 3.2 Methods

### 3.2.1 Participants

Participants included 28 individuals with PDD and 28 typically developing controls. The two groups (PDD and control) were matched for chronological age (PDD group: mean ± *SD* = 17.6 ±5.2, range 9-30; control: mean ± *SD* = 18.0 ± 4.0, range 9-28; independent t-test, $t(54) = 0.29$ , $p > 0.1$) and gender (PDD group: 5 females and 23 males; control: 4 females and 24 males; Fisher's exact test, $p > 0.1$). Verbal and performance IQ in the PDD group was measured using the Japanese version of the WAIS-R (Shinagawa et al. 1990), WAIS-III (Fujita, Maekawa, Dairoku, &

Yamanaka, 2006), WISC-R (Kodama et al. 1982), or WISC-III (Azuma et al. 1998). All PDD participants had IQs within the normal range (full-scale IQ: *M* = 103.3, *SD* = 13.4; verbal IQ: *M* = 105.2, *SD* = 14.7; performance IQ: *M* = 100.1, *SD* = 13.3). Participants in the PDD group were diagnosed with either Asperger's disorder (12 males, 3 females) or PDD-NOS (11 males, 2 females) by a child psychiatrist using DSM-IV-TR (APA, 2000). They were all free of neurological or psychiatric problems other than those associated with PDD, and none was taking any medication.

All participants had normal or corrected-to-normal visual acuity. All participants aged 18 years and older and the parents of participants aged younger than 18 years provided written informed consent to participate in this study in accordance with the Declaration of Helsinki.

### 3.2.2 Stimuli and Procedures

#### 3.2.2.1 Expression Recognition Task

A total of 48 photographs of facial expressions depicting six basic emotions (anger, disgust, fear, happiness, sadness, and surprise) were used as stimuli. These pictures were chosen from standardized photograph sets (Ekman & Friesen, 1976; Matsumoto & Ekman, 1988). A label-matching

paradigm previously used by Sato et al. (2002) was employed to assess participants' recognition of emotional facial expressions. Pictures of people whose faces expressed various emotions were presented on the monitor one by one in a random order. Verbal labels identifying the six basic emotions were presented next to each photograph. Participants were asked to select the label that best described the emotion shown in each photograph. They were instructed to consider all six alternatives carefully before responding. No time limits were set, and no feedback was provided about performance. Participants saw each emotional expression eight times, resulting in a total of 48 trials for each participant.

#### 3.2.2.2 Face-recognition Task

The shortened version (13 items) of the Benton Facial Recognition Test (Benton, et al., 1994) was used to investigate general face-recognition ability. This test requires matching a target face with one picture or with up to three pictures of the same person (with different orientation and lighting) presented in a six-stimulus array of faces. No time limits were set, and no feedback was provided regarding performance.

### 3.2.3 Apparatus

The events were controlled by SuperLab Pro 2.0 (Cedrus, San Pedero, CA) implemented on a Windows computer (HP xw4300 Workstation, Hewlett-Packard, Palo Alto, CA). Stimuli were presented on a 19-inch CRT monitor (HM704UC, Iiyama, Tokyo; screen resolution 1024 × 768 pixels; refresh rate 100 Hz).

### 3.2.4 Data Analysis

Data from the expression recognition task were analyzed using SPSS 10.0J (SPSS, Tokyo, Japan). Accuracy percentages were analyzed with a 2 (group) × 6 (facial emotion) repeated-measures analysis of variance (ANOVA). For significant interactions, follow-up simple effects analyses were conducted. Correlations with IQ scores were calculated for relationship between IQ and the impairment of facial expression recognition in the PDD group.

For the face-recognition task, the total number of correct responses was calculated for each participant. The mean score difference between groups was analyzed using a t-test (two-tailed). Correlations were calculated between face-recognition performance and IQ scores to test the relationship between IQ and face recognition in the PDD group.

To analyze the relationships between expression recognition, age, and

face recognition, Pearson's product-moment correlations between these variables were calculated for each group. Based on the results of ANOVA for facial expression recognition, the results from the fearful expression task were used as a measure of facial expression recognition.

Furthermore, path analyses were conducted for each group using AMOS 4.01 (SmallWaters, Chicago, IL). Maximum-likelihood estimation was employed to estimate models. To compare the overall fit of models, Akaike information criteria (AIC) were calculated. We compared the hypothesized model and the independent model (i.e., the model in which the variables are not related). For the evaluation of local fit of the models, path coefficients were tested for a difference from zero using *z*-statistics (two-tailed).

To assess the level of symptom severity in individuals with PDD, the Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1986) was administered by a psychiatrist (MT). The CARS includes 14 items assessing autism-related behavior and one item rating general impressions of autistic symptoms. Each item is rated on a scale of one to four. A higher rating indicates more severe impairment. Total scores ranged from 15 to 60. Although the CARS has factor structures, which items are included in social domain is unclear (DiLala & Rogers, 1994; Magyar & Pandolfi, 2007; Stella, Mundy, &Tuchman, 1999). Therefore, I used the

CARS items that were commonly classified in social domain in previous studies. Thus, the present study used the items “imitation,” “relationship to people,” “nonverbal communication,” “verbal communication,” “visual response,” and calculated the average score on these items. Pearson’s correlation coefficient was calculated to investigate the relationship between impaired recognition of fearful expressions and symptom severity related to social domains.

## 3.3 Results

### 3.3.1 Expression-recognition Task

The ANOVA for the accuracy percentages (Figure 3.1) revealed a significant interaction of group × facial emotion ($F(5, 270) = 4.22$, $p < 0.05$). A significant main effect of emotion ($F(5, 270) = 114.42$, $p < 0.001$) was also found. Follow-up analyses of the interaction revealed that the simple main effects of group, indicating less accurate recognition of emotional expressions in PDD subjects than in control group, were significant only for the fearful facial expressions ($p < 0.005$). No significant correlations between the accuracy of fearful expression recognition and IQs scores was found in the PDD group ($r$ = -0.07, 0.02,

and -0.22 for full-scale, verbal, and performance IQs, respectively; *p*s > 0.1).

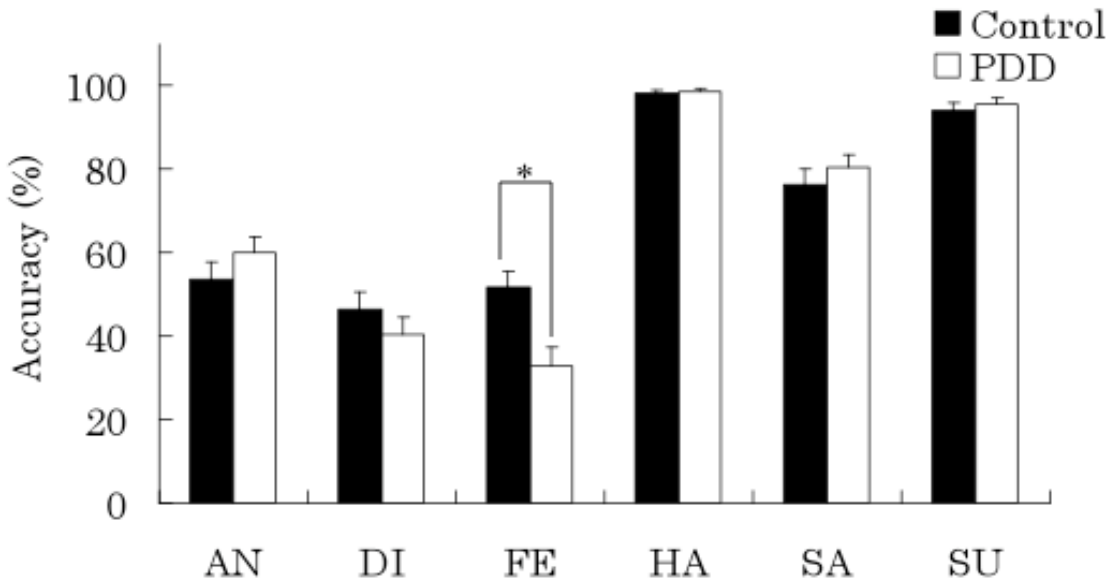


Figure 3.1 Mean (with SE) percentages of accurate facial expression recognition in typically developing controls (CON) and in individuals with PDD. An asterisk indicates a significant difference between groups ($p < 0.05$). AN = anger; DI = disgust; FE = fear; HA = happiness; SA = sadness; SU = surprise.

### 3.3.2 Face-recognition Task

Benton Facial Recognition Task performance was less accurate in the PDD group than in the control group ($M \pm SE = 22.09 \pm 2.39$ and $23.57 \pm 1.53$ for PDD and control, respectively; $t(54) = 2.95$, $p < 0.05$). The performance of all participants in both groups was above the cut-off score

(18/27; Benton et al., 1994) for impaired face recognition, except for one participant in PDD group. No significant correlations between face-recognition scores and IQ scores in the PDD group ($r$ = -0.10, -0.02, and -0.17 for full-scale, verbal, and performance IQs, respectively; $p$s > 0.1).

### 3.3.3 Relationships among Fearful Expression Recognition, Age, and Face Recognition

Fearful expression recognition showed a significant positive correlation with chronological age in the control group ($r$ = 0.51, $p$ < 0.01) but not in the PDD group ($r$ = 0.07, $p$ > 0.1) (Figure. 3.2). The correlation between face-recognition performance and chronological age showed a non-significant trend in both the control ($r$ = 0.37, $p$ < 0.1) and PDD groups ($r$ = 0.33, $p$ < 0.1) (Figure 3.3).

The correlation between fearful expression recognition and face-recognition performance was significant in the control group ($r$ = 0.53, $p$ < 0.005), but showed a non-significant trend in the PDD group ($r$ = 0.35, $p$ < 0.1) (Figure 3.4).

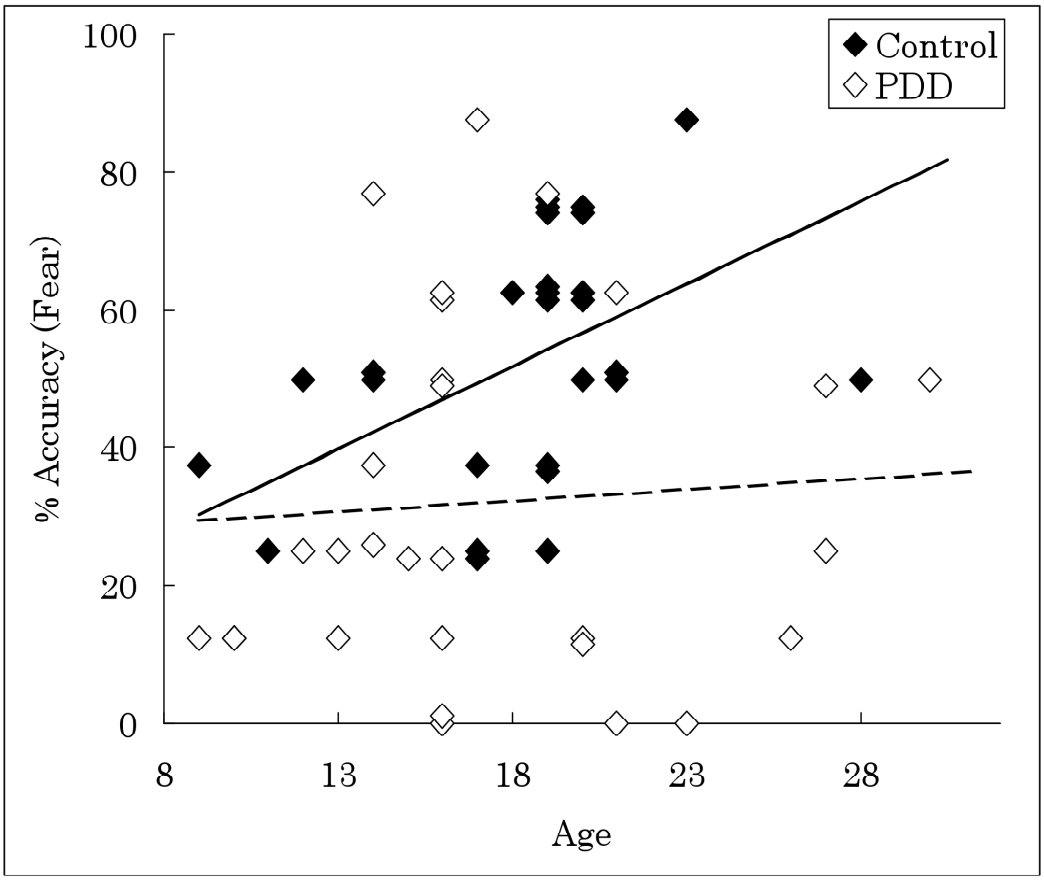


Figure 3.2 The relationships between chronological age and fearful expression recognition. The percentage of accurate fearful expression recognition is plotted against the chronological age of each participant. Black and white diamonds represent each participant in the control and PDD group, respectively. Solid and broken lines represent linear regressions in the control and PDD group, respectively.

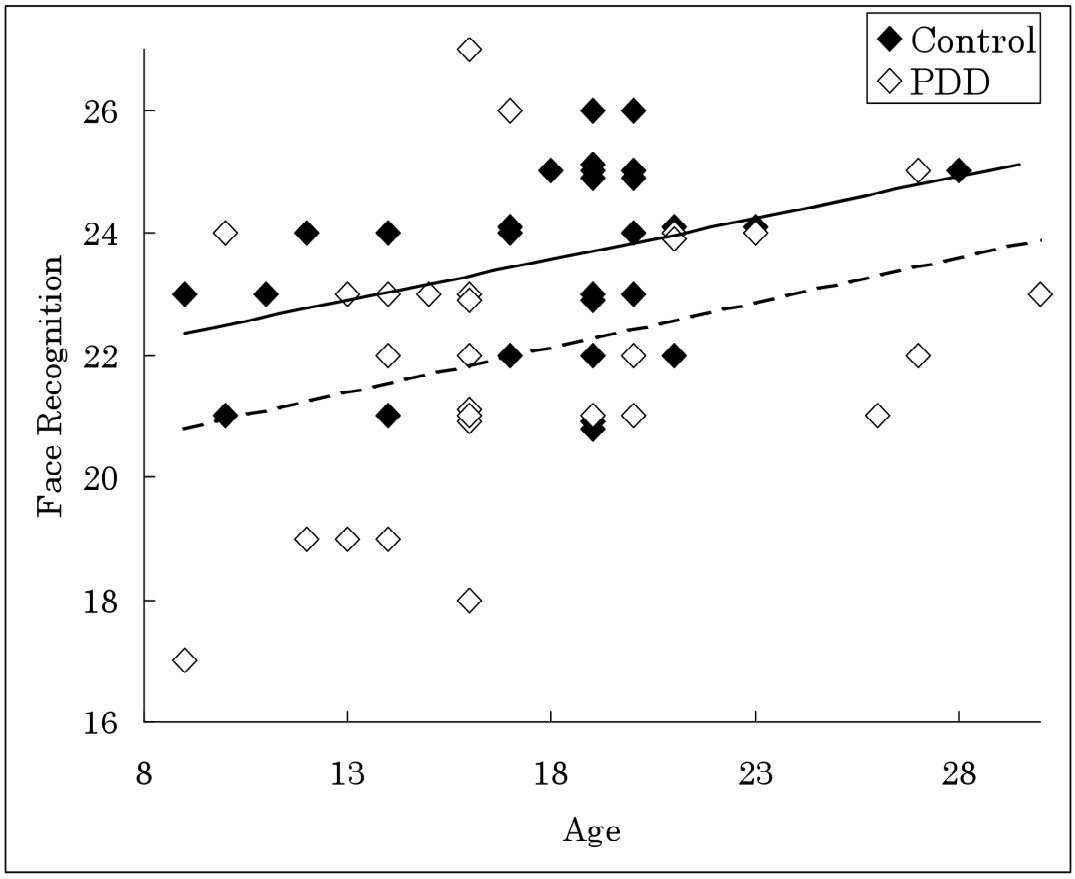


Figure 3.3 The relationships between chronological age and face recognition. The face-recognition task score is plotted against the chronological age of each participant. Black and white diamonds represent each participant in the control and PDD group, respectively. Solid and broken lines represent linear regressions in the control and PDD group, respectively.

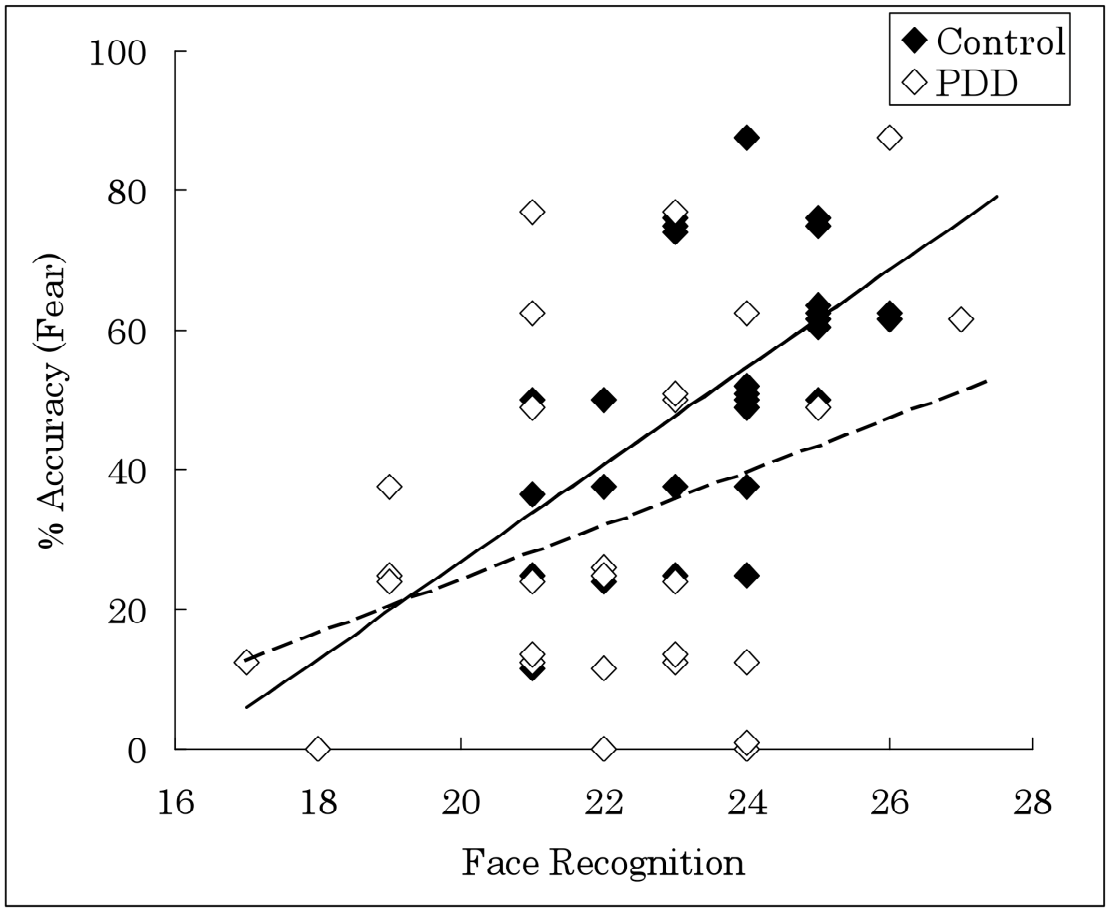


Figure 3.4 The relationships between fearful expression recognition and face recognition. The percentage of accurate fearful expression recognition is plotted against the score in the face-recognition task. Black and white diamonds represent each participant in the control and PDD group, respectively. Solid and broken lines represent linear regressions in the control and PDD group, respectively.

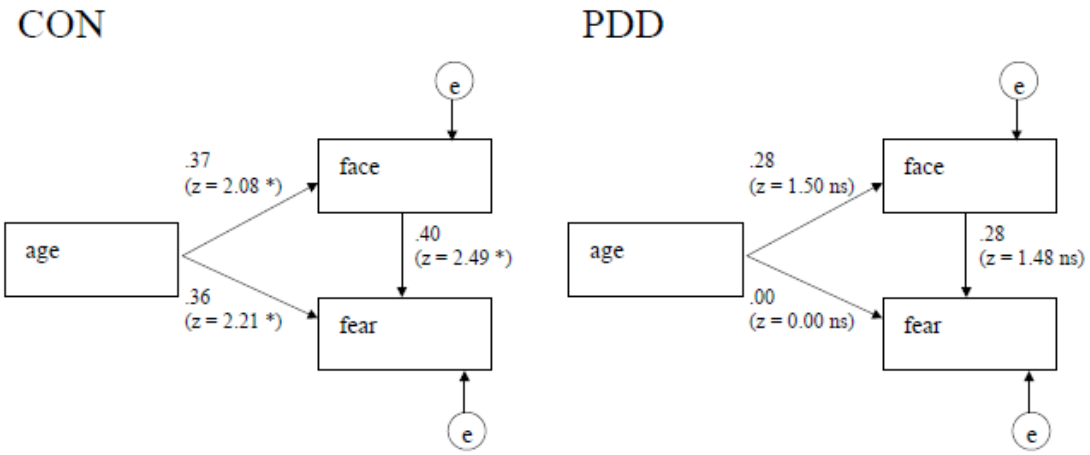


Figure 3.5 The hypothesized model for the development of fearful face recognition. Face recognition and fearful expression recognition improve with age, and the development of face recognition improves fearful face recognition. The hypothesized model shows better an overall fit compared to the independent model in typically developing controls (Left) but not in individuals with PDD (Right). Asterisks indicate a significant local fit of the hypothesized model ($p < 0.05$).

Path analyses were conducted for each group to further examine the relationships among these variables. Based on the previous results in typically developing participants, the analyzed model assumed that age has positive effects on recognition of emotional expressions, both directly and indirectly via the development of face recognition. The hypothesized model is presented in Figure 3.5.

For the control group, the hypothesized model showed a better overall fit compared to the independent model (AIC = 12.00 and 32.05, respectively). Tests of local fit confirmed that all paths in the hypothesized

model were significant (from age to expression recognition, from age to face recognition, and from face recognition to expression recognition; $z$ = 2.21, 2.08, and 2.49, respectively, all $p$s < 0.05).

For the PDD group, the independent model showed a better overall fit compared to the hypothesized model (AIC = 10.71 and 12.00, respectively). To further confirm the relationships among variables, the present study tested the local fit of the hypothesized model in the PDD group. The results showed that no paths in the hypothesized model reached significance (from age to expression recognition, from age to face recognition, and from face recognition to expression recognition; $z$ = 0.00, 1.50, and 1.48, respectively, all $p$s > 0.1).

### 3.3.4. The Relationship between Impaired Fearful Expression Recognition and Symptom Severity

The CARS scores in PDD group ranged from 18 to 25.5. The average score of four items used as indices of social dysfunction ranged from 1.13 to 2.

Correlation analyses revealed that fearful expression recognition in the PDD group was negatively and significantly correlated with social dysfunction ($r$ = -0.51, $p$ < 0.005). Thus, individuals with PDD who showed

worse recognition of fearful expressions had more severe symptoms in social domains (Figure 3.6). Even when the influence of chronological age, verbal IQ, and performance IQ were factored out, the correlation remained significant ($r$ = -0.57, $p$ < 0.005).

The CARS items used in the present study include "relationship to people" and “visual response” which reflects the social interest to people such as eye contact. Some previous studies have shown that the degree of the fixation to eye region affects the performance of fearful face recognition (e.g., Corden et al., 2008). Further, some researchers have proposed that inattention to social stimuli lead to the development of higher-order social cognition (e.g., Dawson, Toth, et al., 2004). When only these two items were used, the relationship between fearful expression recognition and social dysfunction remains significant ($r$ = -0.40, $p$ < .05).

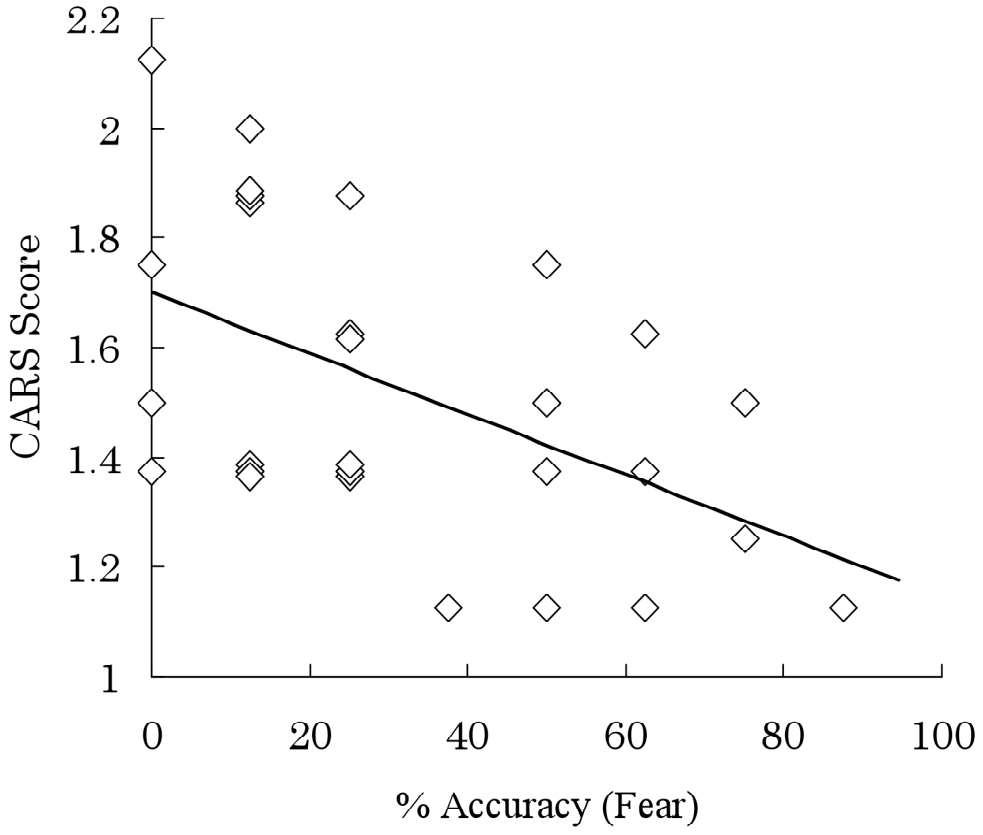


Figure 3.6 The relationship between the percentage of accurate fearful expression recognition and the degree of social dysfunction evaluated using the CARS. Severe social dysfunction predicts the poor recognition of fearful expressions in individuals with PDD.

### 3.4 Discussion

The present study revealed that individuals with PDD were less accurate in recognizing fearful facial expressions than were typically developing controls. This finding was not the result of differences in general intellectual abilities, as recognition of fearful facial expressions was not significantly correlated with IQ measures. Consistent with the present study, recent studies have shown impaired facial expression recognition, particularly of fearful faces in subjects with PDD (Ashwin et al., 2006; Corden et al., 2008; Humphreys et al., 2007). Although some reports have documented general impairment of facial expression recognition, the findings suggest that individuals with PDD have a greater tendency to show impaired fearful expression recognition compared to other facial expressions.

The results also show that the ability to recognize fearful facial expressions improves with age in typically developing controls but not in PDD subjects; hence, the impairment of fearful face recognition in the PDD group manifested in adult subjects. Consistent with these data, recent studies have shown impaired fearful face recognition in adults (Ashwin et al., 2006; Corden et al., 2008; Humphreys et al., 2007), but not in children with PDD (Castelli, 2005; Grossman et al., 2000). These findings suggest

that age-dependent effects on facial expression recognition may underlie previous inconsistent findings related to impaired fearful face recognition in individuals with PDD. However, these findings do not imply normal emotion processing in children with PDD. For example, Dawson, Webb, et al. (2004) demonstrated that children with PDD aged 3 to 5 years show atypical brain responses to fearful faces, suggesting that individuals with PDD have impaired fearful face processing during childhood. Developmental psychology studies have shown that the accurate recognition of fearful expressions emerges later than that for other emotions, except for disgust, even in typically developing children (Holder & Kirkpatrick, 1991; Vicari, et al., 2000). Based on these findings, the paradigm used here, i.e., matching facial photographs with the appropriate verbal label, may be less sensitive to group differences in fearful expression recognition in childhood.

Based on the result that the ability of fearful expression recognition does not improve with age in PDD group independent of face recognition skill, deficits in emotion processing may play an important role in impaired fearful expression recognition. Some groups have proposed that emotional reactions in response to the facial expressions of others are useful for accurate facial expressions recognition (e.g., Adolphs, 2002). Consistent with this theory, studies have suggested that a callous–unemotional trait

(e.g., lack of empathy) specifically relates to impaired fearful face recognition (see Marsh & Blair, 2008 for a review). Minio-Paluello, Baron-Cohen, Avenanti, Walsh, and Aglioti (2009) found that individuals with PDD do not show empathetic bodily responses, and McIntosh, Reichmann-Decker, Winkelman, and Wilbarger (2006) reported that individuals with PDD do not exhibit spontaneous facial mimicry of other people's emotional expressions. Taken together, these findings suggest that deficits in emotional responses may hamper the development of facial expression recognition, particularly recognition of fearful faces, in individuals with PDD.

The path analysis revealed that face-recognition ability improves with age in controls but not in PDD subjects. Furthermore, typically developing controls, but not individuals with PDD, showed a significant positive relationship between face recognition and fearful expression recognition. Hefter et al. (2005) showed that face-recognition performance does not positively correlate with facial expression recognition in individuals with PDD, and previous studies have shown that face recognition (see Maurer, Le Grand, & Mondloch (2002) for a review) and facial expression recognition (Calder, Young, Keane, & Dean, 2000; Durand, Gallay, Seigneuric, Robichon, & Baudouin, 2007) rely on facial configuration

processing in typically developing individuals. The detection of subtle changes in facial configuration (e.g., in the eye region) is required to discriminate between fearful and surprised faces (Ekman, 2003; Skuse, 2003). These findings suggest that the development of perceptual face processing facilitates fearful expression recognition in typically developing controls but not in individuals with PDD.

Finally, the result showed that the degree of the impairment of fearful expression recognition was positively correlated with that of social dysfunction in individuals with PDD. In line with the result, previous studies have shown that the accurate recognition of fearful faces positively correlates with social cognitive abilities in typically developing individuals (Corden et al., 2006; Marsh et al., 2007). The CARS items used in the present study include "relationship to people" and “visual response” which reflects the social interest to people such as eye contact. When only these two items were used, the relationship between fearful expression recognition and social dysfunction remains significant. Some studies suggested that the information of fearful expressions are extracted from the eye region effectively (e.g. Smith, Cottrell, Gosselin, & Schyns, 2005). Thus, these findings speculate that social disinterest to other’s face contaminate the development of facial expression recognition in individuals

with PDD.

A potential neural substrate for impaired recognition of fearful expressions in individuals with PDD is the amygdala. Previous neuropsychological studies have demonstrated that the amygdala plays an important role in fearful expression recognition (e.g., Sato et al., 2002). A recent functional magnetic resonance imaging (fMRI) study reported that the amygdala showed less activation to fearful faces in individuals with PDD (Ashwin et al., 2006). Furthermore, in line with the finding that fear recognition improves with age in controls but not in individuals with PDD, structural magnetic resonance imaging studies have found that amygdala volume increases from childhood to adulthood in normal controls, but not in individuals with PDD (Schumann et al., 2004; Nacewicz et al., 2006). These data suggest that abnormal amygdala development may contribute to impaired fearful expression recognition in individuals with PDD.

The fusiform gyrus, a region that shows face-specific responses (e.g., Kanwisher, McDermott, & Chun, 1997), is a possible candidate for the abnormal development of face-recognition skills in PDD. Some neuroimaging studies have found that individuals with PDD show less fusiform gyrus activation to face stimuli (Schultz et al., 2000; Pierce, Müller, Ambrose, Allen, & Courchesne 2001). Consistent with the finding

that face-recognition ability increases with age in normal subjects, studies have demonstrated that the fusiform gyrus shows increasing face-specific activity across development (Aylward et al., 2005; Golarai et al., 2007). Furthermore, fMRI studies have suggested that the fusiform gyrus shows less activation to emotional facial expressions in individuals with PDD (Hall et al., 2003; Wang, Dapretto, Hariri, Sigman, & Bookheimer 2004). These results indicate that abnormal development of the functional integrity of the fusiform gyrus may play an important role for not only face recognition, but also facial expression recognition in individuals with PDD.

Some limitations of the present study should be noted. First, no time limits for stimulus presentation and subject responses were set. In the real world, rapid understanding of other people's emotions is critical for undertaking appropriate behaviors. More rapid stimulus presentation in the facial expression recognition task might result in impaired recognition of other emotional facial expressions in individuals with PDD. Second, face recognition and facial expression recognition in younger participants should be investigated further, as social dysfunction in PDD appears in the first year of life (Osterling, Dawson, & Munson, 2002; Ozonoff et al., 2010).

## 3.5 Summary

Difficulty in the expression and percept ion of emotion is proposed to result in a failure to establish interpersonal relationships in individuals with pervasive developmental disorder (PDD), including autism and Asperger's disorder. Although a number of studies have examined facial expression recognition in PDD, results have been inconsistent. Furthermore, no studies have investigated the influence of age, perceptual abilities, and PDD subtypes on facial expression recognition. Subjects were 28 individuals with milder PDD subtypes (Asperger's disorder or PDD-NOS) and 28 age- and gender -matched typically developing controls. The present study investigated the relationship between impaired facial expression recognition in PDD and chronological age, face recognition, and symptom severity. Among six emotions, the recognition of fearful faces was specifically impaired in the PDD group, as was face recognition in general. Age had positive effects on fearful expression recognition directly and indirectly via the development of face recognition in controls but not in PDD subjects. Furthermore, fearful expression recognition was related to the severity of PDD symptoms. In conclusion, individuals with PDD show an atypical development of facial emotion recognition. Moreover, impaired fearful expression recognition is closely related to social dysfunction in the real world.

# Chapter 4

# The Impairment of Representational Momentum for Dynamic Facial Expressions

## 4.1 Introduction

Individuals with PDD have difficulty with social interaction, including communication via emotional facial expressions (APA, 2000). Over the last two decades, many experimental studies have investigated this issue using static faces as stimuli, but results have been contradictory. For example, some studies showed that individuals with PDD had a normal ability to discriminate (e.g., Adolphs et al., 2001) and recognize (e.g., Castelli, 2005) the facial expressions of others. Other studies reported that these individuals were impaired in the recognition of facial expressions, particularly facial expressions of a fearful emotional state (e.g., Corden et al., 2008).

Social interactions in daily life are mainly based on dynamic facial cues. Consistent with this notion, some studies in typically developing subjects have reported that dynamic facial expressions enhance various types of processing, including expression perception (Yoshikawa & Sato, 2008), emotion recognition (Bould et al., 2008) and emotional experience (Sato & Yoshikawa, 2007a), compared to static facial expressions. Use of dynamic, relative to static, face stimuli may provide ecologically valid evidence on the facial expression processing in individuals with PDD.

A few previous studies have explored the recognition of dynamic facial

expressions in individuals with PDD. Gepner et al. (2001) investigated this issue using dynamic, strobe flash and static presentations. Although individuals with PDD were as able as typically developing controls to recognize dynamic and static facial expressions, strobe flash presentation improved recognition of facial expression compared with static presentation in typically developing controls but not in individuals with PDD. Tardif et al. (2007) demonstrated that slow dynamic presentation of facial expressions improved emotion recognition in individuals with PDD, although these participants were less able than were controls to recognize dynamic and static facial expressions. Previous studies therefore suggest differences in performance between individuals with PDD and normal controls in the recognition of dynamic facial expression. However, these data also suggest that the recognition of dynamic facial expressions is enhanced compared to that of static expressions in individuals with PDD. Thus, findings on the recognition of static and dynamic facial expressions in PDD are inconsistent. In order to clarify facial emotion processing impairments specific to PDD, it is necessary to examine each component of the dynamic facial expression recognition process.

Little is known, however, about earlier perceptual processing for dynamic facial expressions in individuals with PDD. A recent study of

typically developing participants (Yoshikawa & Sato, 2008) identified the representational momentum (RM) for dynamic facial expression. RM describes a phenomenon in which the final position of a moving object shifts in the direction of the observed movement in the perceiver's mind (Freyd & Finke, 1984; Hubbard, 1990). This effect has also been reported in the transformation of object shape (e.g., Kelly & Freyd, 1987). Thus, Yoshikawa and Sato found that participants perceived the last image presented during the dynamic facial expression in an exaggerated form. They suggested that the RM for dynamic facial expressions is an adaptive mechanism for detecting subtle changes in another's facial expression. Identifying the reasons individuals with PDD find it difficult to communicate with others via emotional facial expressions would require clarification of whether this mechanism that perceives dynamic facial expressions to be exaggerated is impaired in these individuals.

### 4.2. Experiment 1

The present study investigated RM for dynamic facial expressions among individuals with high-functioning PDD and age-matched typically developing controls, using a paradigm set out in a previous study (Yoshikawa & Sato, 2008). Briefly, dynamic and static images of facial

expressions were presented, and participants were asked to match the changeable emotional face display with the perceived last image of dynamic facial expression and static facial expression stimuli. Based on the clinical observation that individuals with PDD find it difficult to communicate with others via emotional facial expressions, the present study tested hypothesis that typically developing controls but not individuals with PDD would perceive the last image in the dynamic facial expression to be more exaggerated than the last static facial expression

### 4.2.1 Methods

#### 4.2.1.1 Participants

Participants included 13 individuals with PDD and 13 typically developing controls. The two groups (PDD and control) were matched for chronological age (PDD group: $M$ = 19.0 years, $SD$ = 5.7; control: $M$ = 19.8 years, $SD$ = 2.7; independent t-test, $t(24) = 0.44$, $p > 0.1$) and gender (PDD group: 12 males, 1 female; control: 12 males, 1 female). Verbal and performance IQ in the PDD group was measured using the Japanese version of the WAIS-R (Shinagawa et al. 1990), WAIS-III (Fujita et al., 2006), WISC-R (Kodama et al., 1982), or WISC-III (Azuma et al., 1998). All

participants with PDD had IQs within the normal range (Fullscale IQ: *M* = 101.8, *SD* = 12.9; Verbal IQ: *M* = 104.4, *SD* = 15.5; Performance IQ: *M* = 98.3, *SD* = 10.6). Participants in the PDD group were diagnosed with either Asperger's disorder (4 males, 1 female) or PDD-NOS (8 males) by a child psychiatrist using DSM-IV-TR (APA, 2000). They were all free of neurological or psychiatric problems other than those associated with PDD, and none was taking any medication. All participants aged 18 years and older and the parents of participants aged younger than 18 years provided written informed consent to participate in this study in accordance with the Declaration of Helsinki.

#### 4.2.1.2 Design

The experiment was constructed as a three-factorial mixed randomized-repeated design, with group (PDD or control) as the randomized factor, and presentation condition (dynamic or static) and emotion condition (fearful or happy) as the repeated factor.

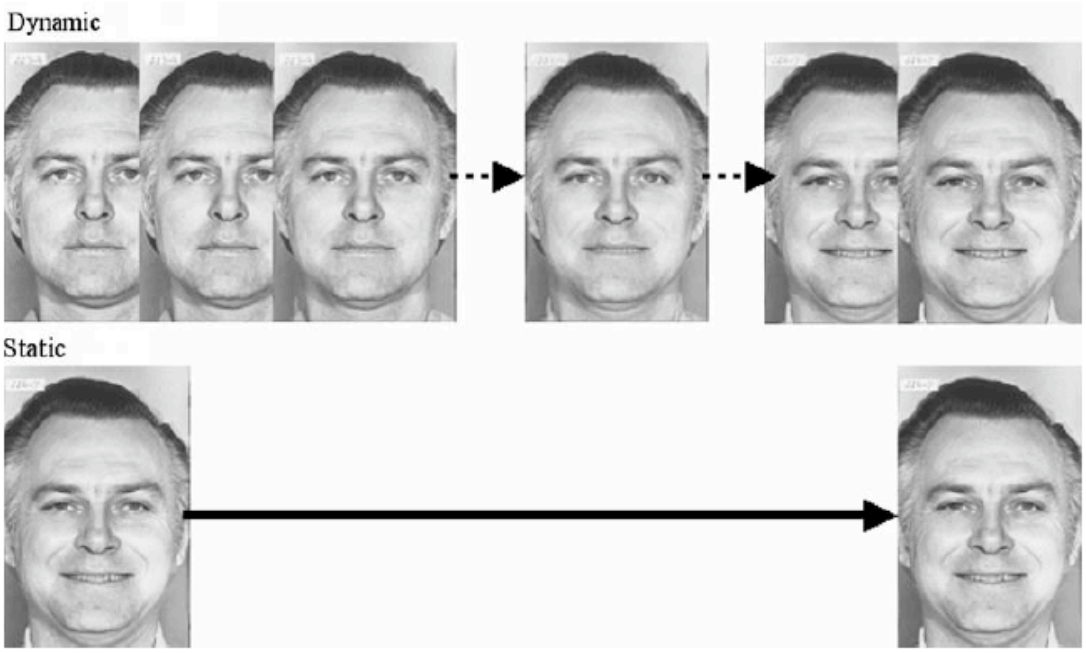


Figure 4.1 Examples of the morphing image sequence for dynamic facial expression of emotion

4.2.1.3 Stimuli

From a set of facial images (Ekman & Friesen, 1976), I selected one neutral expression slide and two emotional expression (fearful and happy) slides for each of four actors (two men and two women). Computer-morphing techniques (Mukaida et al., 2000) were used to produce images that were intermediate between the neutral expression and each of the two emotional expressions in 4% steps. I produced dynamic facial expression stimuli that changed from 4% emotional expression to a maximum of 80% of the full emotional expression. I presented a total of 20 image frames in

succession, i.e., the first image (4% of the full emotional expression image), 18 intermediate images (from 8 to 76%, in 4% steps), and the final image (80%). Figure 4.1 shows the first image, some intermediate images, and the final image of a dynamic stimulus. Stimuli duration was 200 ms (10 ms/frame). In the static condition, emotional expressions (at 80%) were presented for 200 ms.

#### 4.2.1.4 Apparatus

Stimulus presentation and data acquisition were controlled using a program written in Visual C++ 5.0 (Microsoft) on a Windows computer (HP xw4300 Workstation). Stimuli were presented on a 17-inch CRT monitor (Iiyama; screen resolution 1,024 × 768 pixels; refresh rate 100 Hz). The distance between the monitor and participants was fixed at approximately 57 cm using a headrest.

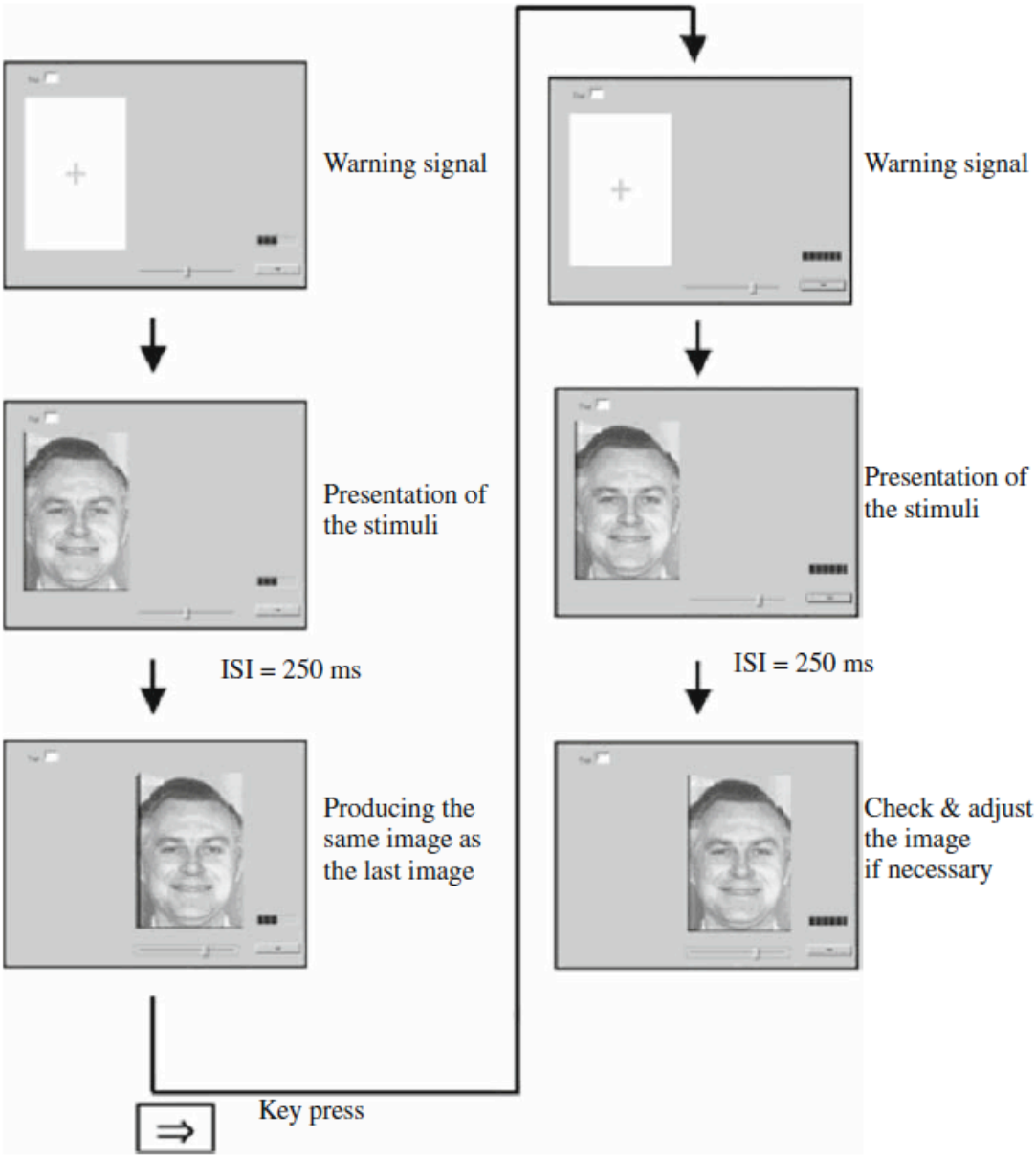


Figure 4.2 The trial sequence

4.2.1.5 Procedure

Figure 4.2 shows the trial sequence. On the monitor, the left window was used for stimulus presentation and the right window was used for participant responses. Visual angles of the stimulus and response windows were 11.1° × 7.8°, respectively. In each trial, a dynamic or static stimulus was presented in the stimulus window, and 250 ms later, an initial face image was presented in the response window. Participants were instructed to match the image in the response window exactly with the last image shown in the dynamic or static stimulus by using the mouse to drag a slider to the left or right. This procedure enabled us to obtain participants' perceptual images more precisely than the typical RM paradigm in which participants need to select, from a limited number of prepared images, one that they think best matches their perceptual image. The face shown in the initial image in the response window had an emotional expression with 70, 80, or 90% intensity. Slider scales had one of three predefined ranges, each of which had a 100% range of emotional intensity (i.e., 20–120, 30–130, or 40–140%). These slider scale ranges varied randomly across trials, and slider ranges were not visible to participants. After a participant selected an image, he or she clicked the button, and the image in the response window disappeared. Then, the stimulus was presented again in the left window, and

250 ms later, the image chosen by the participant appeared in the response window. If the participant thought the images matched, he or she clicked the button on the display and went on to the next trial; if not, the participant could modify the image until it matched. This second exposure was introduced to avoid a potential problem with participants' responding too slowly upon the first exposure to maintain their perceptual images, which may decay over time. A total of 32 trials (8 trials per condition) were performed in blocks, and the order of trials was counterbalanced across participants. Before starting the experiment, each participant was given several practice trials and allowed to practice image manipulation using the mouse to move the slider.

#### 4.2.1.6 Data analysis

Data were analyzed using SPSS 10.0J (SPSS Japan). For each participant, the average intensity of selected images was calculated for each condition and analyzed with a 2 (group) × 2 (presentation) × 2 (emotion) repeated measures ANOVA. If any significant interaction was observed, a follow-up simple effect analysis was conducted.

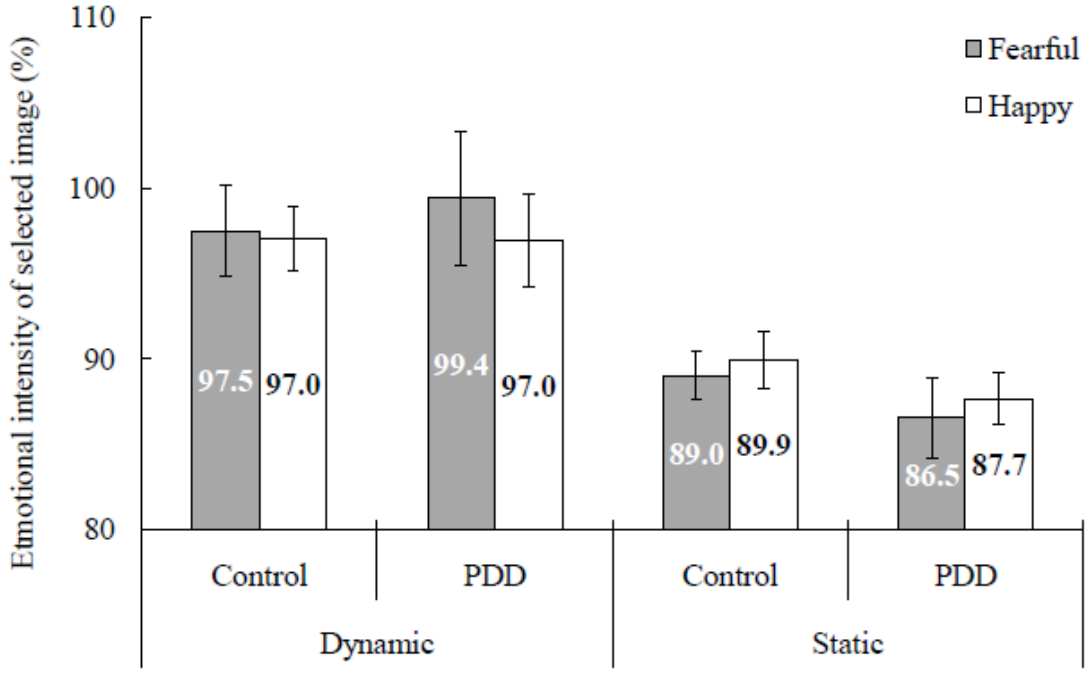


Figure 4.3 The mean percentage (with SE) of selected images in each condition.

### 4.2.2 Results

The ANOVA revealed a significant main effect of presentation condition ($F(1,24) = 28.82$, $p < 0.01$), indicating that the selected images had a higher emotional intensity in the dynamic facial expression condition than in the static condition (see Figure 4.3). The confirmation analysis verified that both PDD and control groups perceived the last dynamic facial expression image to be more exaggerated than the static facial expression (PDD group: $F(1, 24) = 19.88$, $p < 0.01$; control group: $F(1, 24) = 9.97$, $p <$

0.01). No other significant main effect or interactions were observed (emotion: $F(1, 24) = 0.03$, $p = 0.87$; emotion × presentation: $F(1, 24) = 2.56$, $p = 0.12$; group × emotion: $F(1, 24) = 0.11$, $p = 0.74$; group × presentation: $F(1, 24) = 0.88$, $p = 0.36$; group × emotion × presentation: $F(1, 24) = 0.51$, $p = 0.48$).

### 4.2.3 Discussion

The results showed that typically developing controls perceived the last image of dynamic facial expression to be more exaggerated than a static stimulus. This indicates that dynamic presentation of a facial expression elicits RM. These results for the control group support previous findings (Yoshikawa & Sato 2008).

More importantly, the results show that individuals with PDD also perceived dynamic facial expressions to be exaggerated; this is the first study to show that dynamic presentation of a facial expression induces RM among individuals with PDD, just as it does among typically developing controls. The results are consistent with those of previous studies investigating the processing of dynamic facial expressions in PDD populations. Gepner et al. (2001) have found relatively good recognition of facial expressions in dynamic presentation conditions among individuals

with PDD, although overall recognition of facial expressions in individuals with PDD is worse relative to controls. Also, Tardif et al. (2007) have shown that slow, dynamic presentation of facial expressions benefits facial expression recognition in individuals with PDD, although these participants were less able than controls to recognize dynamic and static facial expressions. These findings seem to support the results of the present study, indicating that dynamic presentation enhances the processing of facial expressions. Furthermore, the present study showed that individuals with PDD appeared to have a subjective perception of the intensity of dynamic facial expression that was comparable to that of typically developing controls, and that the extent to which dynamic presentation enhanced subjective perception was indistinguishable between individuals with and those without PDD. Taken together, the results appear to indicate that individuals with PDD have an intact ability to process dynamic information from facial cues, at least on a perceptual level.

### 4.3 Experiment 2

Experiment 2 investigated the effects of emotional intensity on the RM for dynamic facial expressions. Recent studies regarding emotion recognition in typically developing individuals have reliably demonstrated

the effect of dynamic presentation on recognition performance of subtle facial expressions (Ambadar et al., 2005; Bould & Morris, 2008; Bould et al., 2008), though dynamic presentation can't be very effective in recognition performance of relatively intense emotional facial expressions (Gepner et al., 2001; Tardiff et al., 2007). Therefore, it might be possible that dynamic presentation of subtle facial expressions clearly revealed impairment of the RM in the PDD group. The present study tested hypothesis that the degree of the RM of the control group was larger than that of the PDD group in subtle facial expression condition.

### 4.3.1 Methods

#### 4.3.1.1 Participants

Participants included 12 individuals with PDD and 12 typically developing controls. The two groups (PDD and control) were matched for chronological age (PDD group: $M$ = 22.3 years, $SD$ = 6.9; control: $M$ = 20.7 years, $SD$ = 1.4; independent t-test, $t(22) = 0.83$ , $p > 0.1$,) and gender (PDD group: 10 males, 2 female; control: 8 males, 4 female; $\chi^2(1, N = 24) = 0.89$, $p > 0.1$). Verbal and performance IQ in the PDD group was measured using the Japanese version of the WAIS or the WISC. All participants with PDD

had IQs within the normal range (Full scale IQ: *M* = 112.4, *SD* = 10.1; Verbal IQ: *M* = 112.9 *SD* = 10.7; Performance IQ: *M* = 110.4, *SD* = 13.1), except that the IQs for two participants were not available. Participants in the PDD group were diagnosed with either Asperger's disorder (4 males) or PDD-NOS (6males, 2 females) by a child psychiatrist using DSM-IV-TR (APA, 2000). They were all free of neurological or psychiatric problems other than those associated with PDD, and none was taking any medication. All participants aged 18 years and older and the parents of participants aged younger than 18 years provided written informed consent to participate in this study in accordance with the Declaration of Helsinki.

4.3.1.2 Stimuli

From a set of facial images (Ekman & Friesen, 1976), we selected one neutral expression slide and two emotional expression (fearful and happy) slides for each of four actors (two men and two women). We used computer-morphing techniques (Mukaida et al., 2000) to produce images that were intermediate between the neutral expression and each of the two emotional expressions in 4% steps. We produced dynamic facial expression stimuli that changed from 4% emotional expression to a maximum of 52%, 80%, and 108% of the original emotional expression in 4% steps. We

presented a total of 14, 20, and 26 image frames in succession in 52%, 80%, and 108% condition, respectively (e.g., in 52% condition, the first image, 12 intermediate images (from 8 to 48%, in 4% steps), and the final image). In dynamic condition, each flame was presented for 10 ms. Thus, the total presentation time is 140 ms, 200 ms, and 260 ms in 52%, 80%, and 108% condition, respectively. Figure 4.4 shows the last image of a dynamic stimulus in each condition. In static conditions, the last frame of dynamic facial expressions was presented. The total presentation time is the same as those of dynamic facial expression conditions corresponding with the intensity.

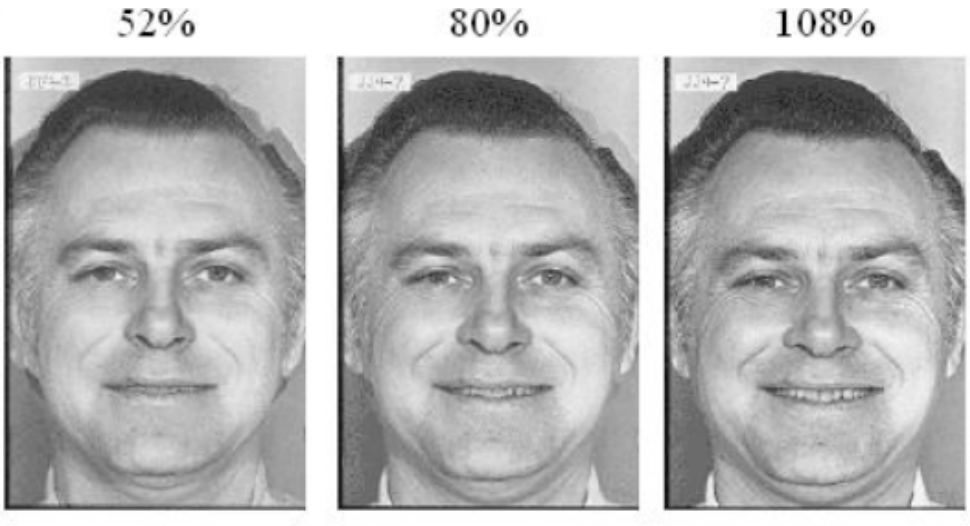


Figure 4.4 The last image of dynamic facial expressions in each intensity condition.

#### 4.3.1.3 Design

The experiment was constructed as a three-factorial mixed randomized-repeated design, with group (ASD or control) as the randomized factor, and presentation condition (dynamic or static) and intensity (52 %, 80 %, or 108 %) as the repeated factor.

#### 4.3.1.4 Apparatus

The apparatus was the same as in Experiment 1

#### 4.3.1.5 Procedure

The procedure was the same as in Experiment 1. However, there are some exceptions. First, facial expressions with 52%, 80%, and 108% intensity were presented at randomized order. Second, the face shown in the initial image in the response window had an emotional expression with -10, 0, +10% intensity of the presented stimuli (e.g., in 52% condition, 42%, 52%, or 62%). Slider scales had one of three predefined ranges, each of which had a 80% range of emotional intensity (e.g., in 52% condition, 2–82, 12–92, or 22–102%). These slider scale ranges varied randomly across trials, and slider ranges were not visible to participants. A total of 48 trials (8 trials per condition) were performed in blocks, and the order of trials was

counterbalanced across participants.

#### 4.3.1.6 Data analysis

Data were analyzed using SPSS 10.0J (SPSS Japan). For each participant, the mean intensity of responded images was calculated for each condition. Then, the ratio between the intensity of responded and presented images was calculated for each condition. The ratios were analyzed with a 2 (group) × 2 (presentation) × 3 (intensity) repeated measures analysis of variance (ANOVA). To test our predictions, follow-up simple interaction analyses and simple-simple main effect analyses were conducted (cf. Kirk, 1995).

### 4.3.2 Results

The ratios between the intensity of responded and presented images were calculated (Figure 4.5) and subjected to the group × presentation × intensity ANOVA. Most important, the results revealed a significant three-way interaction ($F(2,44) = 5.19$, $p < 0.05$). Besides, the results revealed a main effect of presentation ($F(1,22) = 33.21$, $p < 0.05$) , indicating that the participants perceived more exaggerated images in dynamic than in static conditions. A main effect of intensity ($F(2,44) = 13.99$, $p < 0.05$) and an

interaction between intensity and presentation ($F(2,44) = 3.61$, $p < 0.05$) were also significant. The interaction between group and presentation was marginally significant ($F(1,22) = 3.13$, $p < 0.10$). Other main effect or interactions did not reach significance ($Fs < 2.30$, $ps > 0.10$).

As follow-up analyses for the three-way interaction, simple interaction analysis was conducted for each intensity condition. The results revealed that the simple interactions between group and presentation condition were significant in 52% intensity condition ($F(1,66) = 12.03$, $p < 0.05$), but not in 80% and 108% intensity conditions ($F(1,66) = 0.03$, $p > 0.10$; $F(1,66) = 0.10$, $p > 0.10$, respectively). Follow-up simple-simple main effect analysis of group in 52% intensity condition revealed that typically developing controls perceived more exaggerated images than individuals with ASD did in the dynamic condition ($F(1,132) = 6.27$, $p < 0.05$), but not in the static condition ($F(1,132) = 0.72$, $p > 0.10$).

To confirm the main effect of presentation, which could replicate the previous findings (Yoshikawa & Sato, 2008), follow-up analysis was conducted in each group and intensity. For the control group, the simple-simple main effects of presentation were significant in all intensity conditions (52%: $F(1,66) = 38.18$, $p < 0.05$; 80%: $F(1,66) = 4.04$, $p < 0.05$; 108%: $F(1,66) = 7.90$, $p < 0.05$). Also for the ASD group, the simple-simple

main effects of presentation were significant or marginally significant in all intensity conditions (52%: $F(1,66) = 3.13$, $p < 0.1$; 80%: $F(1,66) = 3.73$, $p < 0.05$; 108%: $F(1,66) = 6.75$, $p < 0.05$). In sum, the results indicated that both control and ASD groups perceived the last dynamic facial expression images to be more exaggerated than the static expressions in all intensity conditions.

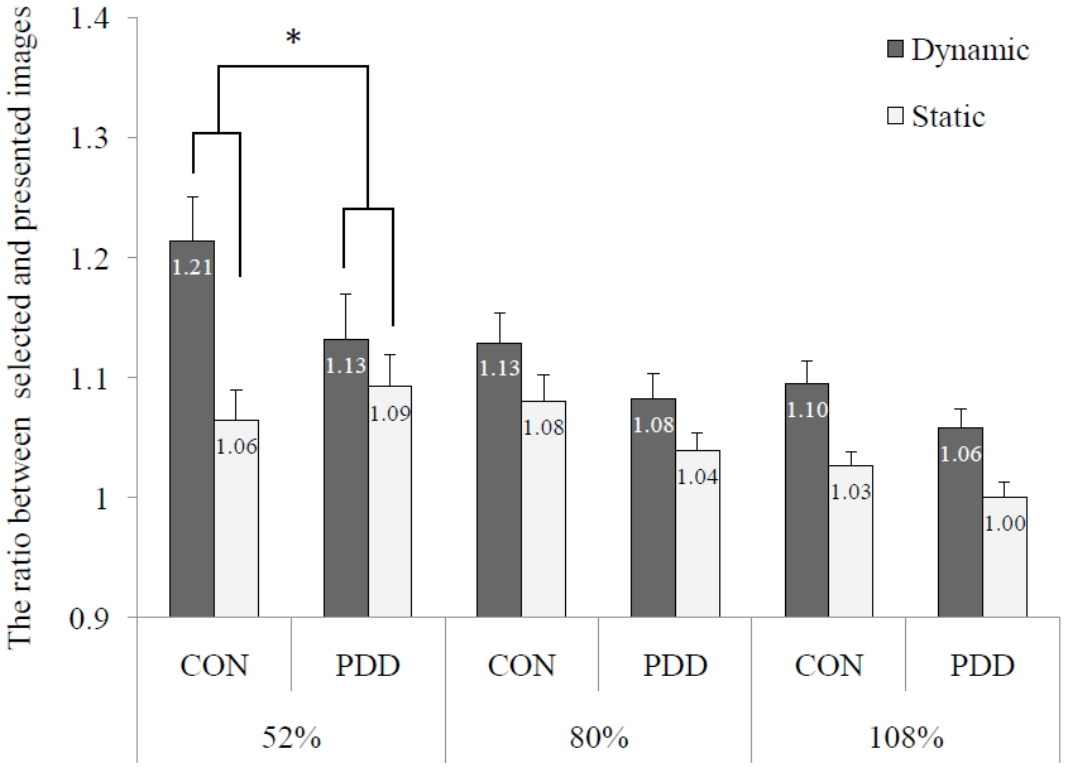


Figure 4.5 The mean ratio between the intensity of responded and presented images in each condition. The asterisk represents the interaction between group and presentation, indicating the reduced RM for subtle dynamic facial expressions in ASD. Error bars show the SE.

### 4.3.3 Discussion

The results show that individuals with PDD perceive the last image in the dynamic facial expression to be more exaggerated than the static facial expression when they observe relatively strong emotional facial expressions. Consistent with the results of experiment 1 and previous studies (Gepner et al., 2001; Tardiff et al., 2007), the results suggest that dynamic presentation enhances facial expressions processing in individuals with PDD.

However, when subtle emotional facial expressions were presented, dynamic presentation of a facial expression induced the RM in typically developing individuals, but not in individuals with PDD. Further, typically developing controls perceived as more exaggerated form than individuals with PDD in dynamic condition, but not in static condition. These results suggest that perceived emotional intensity of dynamic facial expressions is different between individuals with and without PDD. It might be possible that reduced perception of the emotional intensity in PDD leads to difficulty in detecting subtle changes in another's facial expression and in rapidly inducing adaptive behavioral responses (cf. Section 1 in Chapter 2).

## 4.4 General discussion

The present study showed that dynamic presentation of a facial expression induce the RM in typically developing individuals but not in individuals with PDD when they observed subtle facial expressions. In this section, the potential explanations for the finding were discussed.

First, emotional processing impairment might deteriorate the RM when subtle facial expressions were used as stimuli. Previous studies have demonstrated that dynamic presentation of a facial expression enhances emotional reactions (Sato & Yoshikawa, 2007a, 2007b) and subjective emotion perception (Yoshikawa & Sato, 2008). Some researchers have proposed that emotional responses to facial expressions are useful for the processing of facial expressions (e.g., Adolphs, 2002). Recent fMRI studies (e.g., Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004) suggests that the amygdala which is involved in emotional processing (e.g., Sato, Yoshikawa, et al., 2004b; Sato, Kochiyama, & Yoshikawa, 2010) moderate the activity in the fusiform gyrus which relates to the visual analysis and/or the subjective perception of faces (e.g., for a review, see Haxby, Hoffman, & Gobbini, 2000). These findings suggest that higher emotional arousal enhance subjective perception of dynamic facial expressions than that of static facial expressions in typically developing individuals. In contrast, a behavioral study has reported that, when an experimenter showed either

distressed or neutral facial and vocal expressions dynamically, individuals with PDD did not show higher autonomic and behavioral responses to distressed than to neutral expressions (Corona, Dissanayake, Arbelle, Wellington, & Sigman, 1998). Previous studies have reported flattered affect (Yirmiya, Kasari, Sigman, & Mundy, 1989) and structural and functional abnormalities of the amygdala (Schumann & Amaral, 2006; Nacewicz et al., 2006). However, further studies are needed to clarify abnormalities in emotional processing to dynamic and static facial expressions in PDD and its relationship to emotion perception, because the literature is devoid of a definitive study in PDD.

Second, impairment of low-level/biological motion processing might lead to the dysfunction of the RM for dynamic facial expressions. Some behavioral studies have demonstrated that individuals with PDD have impairments in their perception of dynamic point-light displays describing human actions (Blake, Turner, Smoski, Pozdol, & Stone, 2003), specifically emotional actions (Moore, Hobson, & Lee 1997; Hubert et al., 2007). In reviewing the behavioral and neuroscientific studies, some researchers proposed that individuals with PDD are impaired in their perception of human actions and this impairment appears to be related to the dysfunction of the STS (Dakin & Frith, 2005; Kaiser & Shiffrar, 2009). For example, a

previous neuroimaging study has shown that biological motion activates the STS in the typically developing controls, but not in the PDD group (Freitag et al., 2008; Herrington et al., 2007). Researchers have also speculated that the neural mechanism for RM includes an interaction between the dorsal and ventral visual stream including the medial temporal lobe (MT) and the superior temporal sulcus (STS) (Kourtzi & Kanwisher 2000; Senior et al. 2000). It might be possible that the effect of impaired motion processing on the RM is clear in subtle dynamic facial expression condition.

Third, the prediction of other's facial change might be impaired in individuals with PDD. The processing of motion information enables us to predict what will ensue. Previous studies have demonstrated that the RM is affected by some factors, such as the gravity rule (see Hubbard (2005) for a review). Based on the evidence, Hubbard has proposed that the purpose of the RM might be to predict the location of the target on the basis of the movement information, and the RM is useful to gap the bridge between perception and action. In terms of biological motion, a recent study have demonstrated that the RM for rotating head of a perceived agent is enhanced when the gaze direction of a perceived agent is congruent with the agent's head motion (Hudson, Liu, & Jellema, 2009). The results suggest that the prediction of other's motion is important issue for inducing the RM.

Previous studies have shown that individuals with PDD have difficulty in understanding other's motor intentions (Becchio et al., 2007; Pierno, Mari, Glover, Georgiou, & Castiello, 2006). These findings suggest that individuals with PDD might not automatically make a prediction of other's facial change, because subtle dynamic facial expressions provide insufficient motion cues.

These explanations are not mutually exclusive. The impairment of emotional and perceptual processing might underlie the difficulty of predicting other's facial change. Some researchers have proposed that basic emotional and perceptual impairments lead to higher social cognitive dysfunction (e.g., Behrmann et al., 2006; Hobson, 1989). Further studies are needed to elucidate how these factors contribute to impairment of the RM for dynamic facial expressions.

### 4.5 Summary

Individuals with PDD have difficulty with social communication via emotional facial expressions, but behavioral studies involving static images have reported inconsistent findings about emotion recognition. The present study investigated whether dynamic presentation of facial expression would enhance subjective perception of expressed emotion in individuals with

PDD and age- and gender- matched typically developing controls. Dynamic and static emotional (fearful and happy) expressions were presented. Participants were asked to match a changeable emotional face display with the last image of the presented dynamic and static stimuli. In experiment 1, the results showed that both groups perceived the last image of dynamic facial expression with relatively strong emotion to be more emotionally exaggerated than the static facial expression. This finding suggests that dynamic presentation enhances the perceptual processing of facial expressions in individuals with PDD. However, the results of experiment 2 revealed that typically developing controls perceived as more exaggerated form than individuals with PDD in dynamic but not in static condition when they observed subtle emotional facial expressions. These results suggest that subjective perception of the emotional intensity of dynamic facial expressions is different between typically and atypically developing individuals. It might be possible that this dysfunction lead to difficulty in detecting subtle changes in another's facial expression and in rapidly inducing adaptive behavioral responses.

# Chapter 5

# Altered social brain network for the processing of dynamic facial expressions

## 5.1 Introduction

Individuals with PDD, including autism and Asperger's disorder, are characterized primarily by qualitative impairments of social interaction (APA, 2000). One of the most evident features of their social impairments is the deficit in communication via emotional facial expressions (Hobson, 1993). Some studies have reported that individuals with PDD are insensitive to other's facial expression. For example, several previous behavioral studies have reported that the individuals with PDD exhibited less attention (Sigman et al., 1992), weak emotional behaviors (Corona et al., 1998), and reduced and/or inappropriate facial reactions (Yirmiya, Kasari, Sigman, & Mundy, 1989) in response to facial expressions of other individuals compared to typically developing individuals.

Several neuroimaging studies have tested the neural substrates of impaired facial expression processing in PDD and have reported inconsistent findings. Almost all of such studies used the photos of emotional facial expressions as stimuli, and found that individuals with PDD showed abnormal activity in some brain regions, including the posterior superior temporal sulcus (STS) and adjacent regions (Baron-Cohen et al., 1999; Critchley et al., 2000; Ashwin et al., 2007), the posterior fusiform gyrus (FG) (Critchley et al., 2000; Hall et al., 2003;

Piggot et al., 2004; Wang et al., 2004; Dalton et al., 2005; Deeley et al., 2007), the amygdala (AMY) (Baron-Cohen et al., 1999; Critchley et al., 2000; Dalton et al., 2005; Ashwin et al., 2007), and the inferior frontal gyrus (IFG) (Hall et al., 2003; Ogai et al., 2003; Dapretto et al., 2006). Ample neuroimaging and neuropsychological evidence in typically developing individuals suggest that all of these brain regions are related to social activities, such as the visual analysis of dynamic aspects of faces for the STS (Allison, Puce, & McCarthy, 2000), the visual analysis of invariant aspects of faces and/or the subjective perception of faces for the FG (Haxby et al., 2000), the emotional processing for the AMY (Calder, Lawrence, & Young, 2001), and the motor mimicry for the IFG (Iacoboni, 2005). Based on these findings, these regions have been called as "social brain" regions (Brothers, 1990; Emery & Perrett, 2000; Adolphs, 2003; Frith, 2007; Blakemore, 2008; Pelphrey & Carter, 2008). Hence, the findings in individuals with PDD appear to be reasonable to account for their impaired emotional expression processing. Hence, the findings in individuals with PDD appear to be reasonable to account for their impaired emotional expression processing. However, it must be noted that different studies have reported abnormalities in different parts in the social brain network, and the results appear to be largely controversial. Furthermore, it remains

unknown whether the neural substrates of impaired expression processing in PDD could be identified in abnormal activity of any specific brain regions in the social brain network and/or in altered networking patters between the regions, which has been suggested in other lines of PDD research (cf. Belmonte et al., 2004; however, see Welchew et al., 2005).

Dynamic facial expressions are natural and powerful cues in daily social interactions. Behavioral studies in typically developing participants have indicated that dynamic facial expressions, as compared with static expressions, induce more evident psychological activities, such as perception (Yoshikawa & Sato, 2008), emotional experience (e.g., Sato & Yoshikawa, 2007a), and facial mimicry (e.g., Sato & Yoshikawa, 2007b). Consistent with these data, some neuroimaging studies in typically developing participants have shown that the social brain regions were more active when viewing dynamic facial expressions compared with static facial expressions (Kilts, Egan, Gideon, Ely, & Hoffman, 2003; LaBar, Crupain, Voyvodic, & McCarthy, 2003; Sato, Kochiyama, et al., 2004; Schultz & Pilz, 2009; Trautmann, Fehr, & Herrmann, 2009). The regions included the STS (Kilts et al., 2003; LaBar et al., 2003; Sato, Kochiyama, et al., 2004; Schultz & Pilz, 2009; Trautmann et al., 2009), the FG (Kilts et al., 2003; LaBar et al., 2003; Sato, Kochiyama, et al., 2004), the AMY (LaBar et al.,

2003; Sato et al., 2004a; Trautmann, et al., 2009), and the IFG (LaBar et al., 2003; Sato, Kochiyama, et al., 2004; Trautmann, et al., 2009).

Nevertheless, few studies investigated the brain activity in response to dynamic facial expressions in individuals with PDD. Some behavioral studies have demonstrated impairments in emotional expression processing using dynamic facial expression stimuli in individuals with PDD (see Chapter 2 and 4). In typically developing individuals, dynamic facial expressions enhance behavioral (Yoshikawa & Sato, 2008; Sato & Yoshikawa, 2007a, 2007b) and brain response in typically developing controls (Sato et al., 2004a). Based on these finding, it appears to be reasonable to expect that neuroimaging studies with using dynamic facial expressions would clearly depict the abnormal brain activity in individuals with PDD. Exceptionally, Pelphrey, Morris, McCarthy, and Labar (2007) have tested this issue. The researchers presented dynamic and static emotional facial expressions of anger and fear to a group of PDD and age- and gender-matched typically developing controls. They found that some of the social brain regions, including the STS, FG, and AMY, show the reduced activity for dynamic versus static facial expressions for the PDD than control groups. The data suggest that the dynamic, compared to static, facial expressions allow to totally illustrate the neural substrates of

impaired facial expression processing in PDD. However, the study did not show clear difference in the activity of IFG between groups. The IFG have been considered to compose a mirror neuron system, which is involved in understanding other's intention and imitating other's action (Gallese, Keysers, & Rizzolatti, 2004; Rizzolatti, Fogassi, & Gallese, 2001). Researchers have proposed that the IFG is one of the most important neural underpinnings in PDD (Williams, Whiten, Suddendorf, & Perrett, 2001), because individuals with PDD show the difficulty with these functions. Therefore, it is critical issue to investigate whether the IFG activate in response to dynamic facial expressions in PDD.

Furthermore, the functional network patterns across the social brain regions in response to dynamic facial expressions remains unknown in individuals with PDD, as well as in typically developing individuals. A previous study has tested the functional connectivity in the typically developing control and PDD groups using dynamic facial expression stimuli, and found some common and some different functional connections between the brain regions in these groups (Wicker et al., 2008). However, because that study has focused on the effect of tasks, comparing emotion versus age recognition, the functional network for the processing of dynamic facial expressions per se remains to be tested. One of the most important

components of such network would be the STS, which has been shown to conduct the visual analysis of dynamic facial expressions (Allison et al., 2000; Emery & Perrett, 2000). Monkey anatomical studies have indicated that the STS is directly connected with the AMY (Iwai & Yukie, 1987) and IFG (Schmahmann et al., 2007), which are shown to both relate to social activities (Calder et al., 2001; Iacoboni, 2005) and are connected to each other (Avendano, Price, & Amaral, 1983). Based on these data, it was hypothesized that the observation of dynamic versus static facial expressions would enhance the functional connectivity between the STS, AMY, and IFG in typically developing individuals. In line with this idea, a previous study proposed that the STS-AMY-IFG connections might be relevant in the social impairments in PDD (Williams et al., 2001). Therefore, it was hypothesized that some alteration would be found in such functional neural network in individuals with PDD.

In the present fMRI study, we examined the brain activity in a group of high-functioning PDD and age- and gender-matched typically developing controls while they viewed dynamic and static facial expressions (cf. Figure 5.1). We used dynamic facial expression stimuli, which have been shown to activate the social brain network, including the IFG, in a previous study (Sato, Kochiyama, et al., 2004). We prepared facial expressions of both

negative (fearful) and positive (happy) emotional valences. By comparing the dynamic versus static facial expression conditions, we identified the brain regions involved in the processing of dynamic facial expressions. Furthermore, to investigate the functional connectivity, we conducted dynamic causal modelling (DCM) for the brain activity in response to dynamic versus static facial expressions.

## 5.2 Methods

### 5.2.1 Participants

The PDD group (1 female, 11 males; mean ± *SD* age = 27.5 ± 7.6 years) consisted of * (1 female, 7 males) with Asperger's disorder and * (4 male) with PDD not otherwise specified (PDD-NOS), who did not satisfy all the diagnostic criteria for Asperger's disorder but exhibited mild symptoms of PDD. The diagnoses, based on the DSM-IV-TR (American Psychiatric Association, 2000), were made by psychiatrists with expertise in developmental disorders. Neurological and psychiatric problems other than those associated with PDD were ruled out. Participants were taking no medication. Although an additional male candidate actually participated, his data were not analyzed due to large motion artifacts (see Image analysis).

Participants in the control group (1 females, 12 males; mean ± *SD* age = 24.3 ± 3.4) were matched for age and gender with the PDD group. They were recruited through advertisements and participated in the experiment as volunteers and had no neurological or psychiatric problems.

All participants had normal or corrected-to-normal visual acuity. All participants gave informed consent to participate in the study, which was conducted in accord with institutional ethical provisions and the Declaration of Helsinki.

### 5.2.2 Experimental design

The experiment involved a three-factorial mixed randomized-repeated design, with group (PDD, control) as the randomized factor, with presentation condition (dynamic, static) and emotion (fear, happiness) as the repeated factors.

### 5.2.3 Stimuli

The stimuli were almost identical with those used in a previous study (Sato et al., 2004a). The raw materials were grayscale photographs of eight individuals' faces chosen from a standard set (Ekman & Friesen, 1976) depicting fearful, happy, and neutral expressions. For all subjects, none of

these faces were familiar. For the dynamic expressions stimuli, computer animation clips of emotional facial expressions were made from these photos. First, between the neutral (0%) and emotional (100%) expressions, 24 intermediate images in 4% steps were created using computer morphing software (Mukaida et al., 2000) implemented on a computer running Linux. Figure 5.1 shows an example of the stimulus sequence. Next, to create a moving clip, a total of 26 images (i.e., one neutral image, 24 intermediate images, and the final emotion's image) were presented in succession. Each image was presented for 40 ms, and the first and last images were additionally presented for 230 ms; thus each animation clips lasted for 1500 ms. This presentation speed has been found to sufficiently reflect natural changes in the dynamic facial expressions of fear and happiness (Sato and Yoshikawa, 2004b). For the static expression stimuli, the expressions that correspond to the final images in the dynamic expression condition were presented. These faces were presented for 1500 ms.

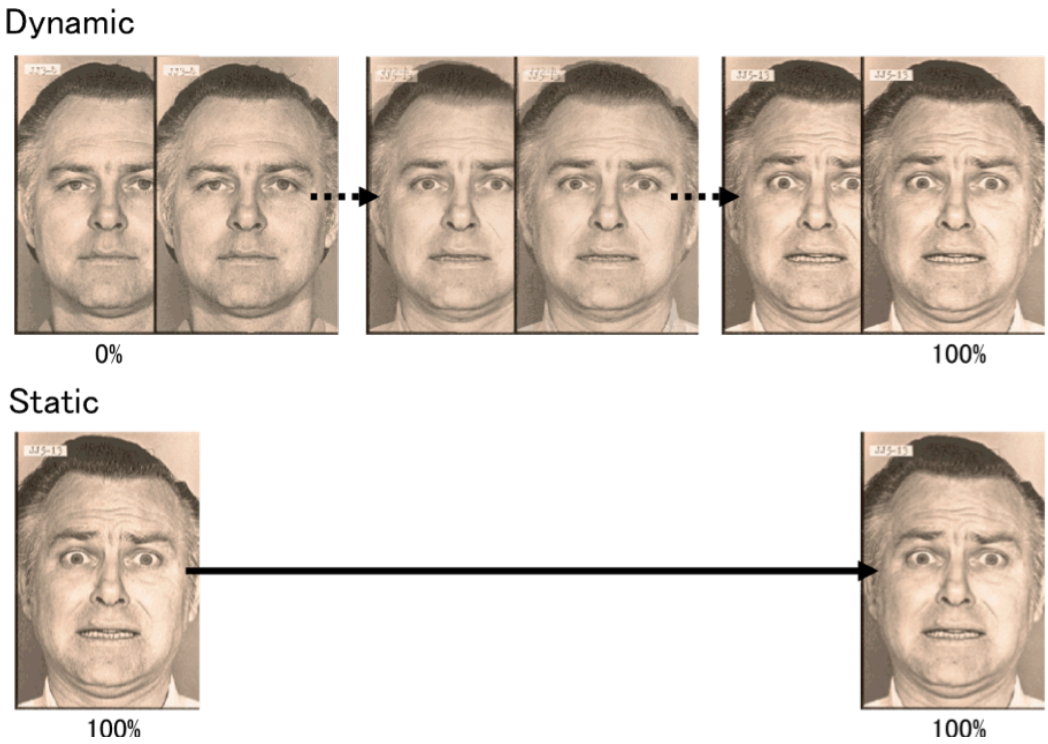


Figure 5.1 Illustrations of stimulus presentations in the dynamic (upper) and static facial expressions (lower).

### 5.2.4 Presentation apparatus

The events were controlled by Presentation software version 10.0 (Neurobehavioral System) implemented on a Windows computer. The stimuli were projected from a liquid crystal projector (DLA-G150CL, Victor) to a mirror that was positioned in a scanner in front of the subjects.

In the present visual condition, the stimuli subtended a visual angle of about 15.0˚ vertical x 10.0° horizontal.

5.2.5 Procedure

The scan session consisted of twelve 18 sec epochs with twelve 18 sec rest periods (a blank screen was presented) interleaved. Each of the four stimulus conditions (dynamic fear, dynamic happiness, static fear, and static happiness) was presented in different epochs within each scan. The order of epochs within each run was pseudorandomized. The order of stimuli within each epoch was randomized.

In each epoch, eight trials were performed. In each trial, a fixation point (the picture with a small “+” in a gray color on a white background and of the same size as the stimulus) was presented at the center of the screen for 1500 ms. Then, the stimulus was presented for 1500 ms. The subjects were instructed to maintain the center of the screen until the face had disappeared and to specify the gender of the presented face by pressing one of the two buttons with their forefingers after the face had disappeared. This task ensured the subjects' attention to stimuli and also did not require explicit recognition or categorization of emotional expressions. Post-hoc debriefing confirmed that the subjects were not aware that investigation of emotional variables was the purpose of the experiment.

### 5.2.6 MRI acquisition

Image scanning was performed on a 3 T scanning system (MAGNETOM Trio A, Tim System, Siemens) using a standard radio frequency head coil for signal transmission and reception. A forehead pad was used to stabilize the head position. The functional images consisted of 50 consecutive slices parallel to the anterior-posterior commissure plane, covering the whole brain. A T2*-weighted gradient echo-planar imaging sequence was used with the following parameters: TR/TE = 3000/60 msec; FA = 90°; matrix size = 64 × 64; voxel size = 3 × 3 × 3 mm. After the acquisition of functional images, a T1 anatomical image was also obtained using a 3D RF-FAST sequence (TR/TE = 12/4.5 ms; FA = 20°; matrix size = 256 × 256; voxel dimension = 1 × 1 × 1 mm) after the functional image acquisition.

### 5.2.7 Image analysis

#### 5.2.7.1 Preprocessing

Image preprocessing and regional brain activity analyses were performed using the statistical parametric mapping package SPM5

(http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB Version 7 (Mathworks Inc.). First, to correct for head movements, functional images of each run were realigned using the first scan as a reference. Because an initial candidate for the PDD group showed large motion artifacts (> 3 mm), and thus the data from this subject were not analyzed further. Data from all subjects reported here showed small motion correction (< 2 mm). Then, T1 anatomical images were coregistered to the first scan in the functional images. Following this, the coregistered T1 anatomical images were normalized to a standard T1 template image as defined by the Montreal Neurological Institute (MNI) involving linear and non-linear three-dimensional transformations (Friston, Ashburner, et al., 1995; Ashburner & Friston, 1999). The parameters from this normalization process were then applied to each of the functional image. Finally, these spatial normalized functional images were resampled to a voxel size of 2 x 2 x 2 and smoothed with an isotopic Gaussian kernel (8 mm) to compensate for anatomic variability among subjects.

5.2.7.2 Regional brain activity analysis

Random effects analyses were used to search for significantly activated voxels that displayed interesting effects. First, we performed a single-

subject analysis (Friston, Holmes, et al., 1995; Worsley & Friston, 1995). The task-related neural activities for each condition were modeled with a box-car function, convoluted with a canonical hemodynamic response function. A high-pass filter composed of a discrete cosine basis function, with a cut-off period of 128, was used to eliminate the artifactual low-frequency trend. Serial autocorrelation, assuming a first-order autoregressive model, was estimated from the pooled active voxels with a restricted maximum likelihood (ReML) procedure and was used to whiten the data and the design matrix (Friston et al., 2002). To reduce the motion-related artifacts, realign parameters were included into the model.

Planned contrast was thereafter performed. First, the simple main effect of presentation condition, contrasting between dynamic and static presentations, was tested for each group. For these analyses, correction was conducted for the entire brain volume. Next, our prediction of the interaction between group and presentation condition was tested. For the analysis of the interaction, which we had our specific predictions, the regions of interest (ROIs) were selected using 6 mm radius spheres on the activation foci in the analysis for the control group (cf. Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2007). We confirmed that all ROIs overlapped with the activation foci in previous studies (e.g., Pelphrey et al., 2007).

Other areas were corrected for the entire brain volume. Finally, as the exploratory analyses, other interactions related to the factor of group were analyzed. For these analyses, the flexible factorial model was generated to create a random effect SPM{T}. The model included group, presentation condition, and emotion as factors of interest, and subject as a factor of no interest. Significantly activated voxels were identified if they reached the extent threshold of $p < .05$ corrected for multiple comparisons, with height threshold of $p < .01$ (uncorrected).

5.2.7.3 Functional connectivity analysis

To analyze the modulation of effective connectivity between the brain regions, we conducted DCM in SPM8 (http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB Version 7 (Mathworks Inc.). First, we modeled single-subject analyses using identical procedures with the above regional brain activity analyses but with following non-task specific regressors: visual input (i.e., all experimental conditions), dynamic presentation, and emotion (fear versus happiness, which were coded as 1 verses –1). The regressors of emotion were included as the effects of no-interest. For each subject, the effect of interest activity was extracted from the regions of interest (ROIs) defined as 4-mm radius spheres. ROIs included the primary

visual cortex (V1; x = 22, y = –84, z = -4), STS (x = 52, y = –62, z = 0), AMY (x = 28, y = –8, z = -12), and IFG (x = 56, y = 28, z = 10) in the right hemispheres. These ROIs were selected based on our hypothesis as described in the Introduction. The coordinates of the latter three regions were defined based on the results of presentation condition effect (dynamic versus static) in regional brain activity analysis for the control group. The coordinate of the primary visual cortex was derived from the strongest activation focus in response to all stimulus presentations compared to the rest in the control group in the search region of the primary visual cortex, which was defined by the cytoarchitectonic map derived from the data of human postmortem brains using the Anatomy Toolbox Version 1.5 (Eickhoff et al., 2005). For the primary visual cortex, the identical activation focus was shown in the PDD group using the same procedure. The ROIs were restricted to the right hemisphere, firstly because some ROIs showed significant activity only in the right hemisphere.

Then, the hypothesized model was constructed for each subject. In the model, the visual input was modeled as an input into V1. The bi-directional (feedforward and feedback) intrinsic connections were constructed between the V1 and STS, STS and AMY, STS and IFG, and AMY and IFG. The effect of dynamic presentation was modeled to modulate all of these bi-

directional connections. The modulatory effects for the connections were subjected to one-sample t-tests (one-tailed) to test for differences from zero for each group. The results were considered significant at $p < .05$.

## 5.3 Results

### 5.3.1 Behavioral performance

Performance on the dummy gender discrimination was good ($M \pm SD$ %correct = 98.3 ± 3.7 and 93.7 ± 15.1 for control and PDD groups, respectively). A 3-way analysis of variance (ANOVA) with group, presentation condition, and emotion as factors for the percentages of correct responses showed no significant differences ($ps > .1$) except that the interaction between group and emotion reached magical significance ($F(1,23) = 3.79$, $p < .1$). The ANOVA for the reaction times of correct responses only showed a significant main effect of presentation condition, indicating longer reaction times for dynamic than for static presentations ($F(1,23) = 13.96$, $p < .005$). In summary, the results of behavioral performance revealed no significant effects related to the factor of group.

### 5.3.2 Regional brain activity: Effect of presentation condition in each group

The simple main effect of presentation condition was tested for each group (Table 5.1; Figure 5.2).

For the control group, the results showed almost the same pattern with those of a previous study (Sato et al., 2004a). Broad ranges of bilateral posterior regions, which included the activation foci of the inferior occipital gyri, middle temporal gyri, and fusiform gyri were detected significantly. Significant bilateral activities of the inferior frontal gyri and amygdala were also observed. In addition, there was a modest activation cluster in the bilateral dorsomedial prefrontal cortices, which reached marginal significance in the extent threshold ($p < .1$, corrected).

For the PDD group, bilateral posterior regions were detected significantly with similar activation foci with those in the control group, although the visual inspections suggests that their cluster sizes were relatively small. There was no other significant activation; specifically no activation was found in the inferior frontal gyrus and dorsomedial prefrontal cortex. There was a small activation cluster including the right amygdala, but it did not reach significance in the extent threshold ($p > .1$, corrected).

**Table 5.1** Brain regions showing significant activation in response to dynamic versus static facial expressions in the control (left) and PDD groups (right). The coordinates of activation foci in MNI system and their T-values are shown.

| Brain region | BA | Control | | | | PDD | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Coordinates | | | T-value | Coordinates | | | T-value |
| | | x | y | z | | x | y | z | |
| R. middle occipital gyrus | 19 | 34 | −84 | 8 | 7.12 | 46 | −78 | 0 | 6.35 |
| R. middle temporal gyrus | 37 | 52 | −62 | 0 | 17.60 | 52 | −64 | −2 | 9.29 |
| R. middle temporal gyrus | 21 | 50 | −36 | 6 | 6.05 | 48 | −48 | 6 | 6.21 |
| R. middle temporal gyrus | 37 | 40 | −60 | −12 | 6.92 | | | | |
| R. temporal pole | 38 | 54 | 6 | −12 | 3.42 | | | | |
| R. supra marginal gyrus | 48 | 54 | −28 | 28 | 5.75 | 60 | −24 | 38 | 3.92 |
| R. precentral gyrus | 6 | 40 | −2 | 50 | 4.59 | 48 | −6 | 46 | 3.42 |
| R. inferiror frontal gyrus | 45 | 56 | 28 | 10 | 4.47 | | | | |
| R. middle frontal gyrus | 9 | 52 | 8 | 36 | 4.59 | 46 | 8 | 36 | 3.73 |
| R. medial superior frontal gyrus | 10 | 6 | 64 | 22 | 4.50 | | | | |
| R. hippocampus | – | 32 | −10 | −16 | 4.27 | | | | |
| R. amygdala | – | 28 | −8 | −12 | 4.54 | | | | |
| L. middle occipital gyrus | 19 | −48 | −78 | 0 | 13.45 | −52 | −72 | 2 | 9.28 |
| L. middle temporal gyrus | 21 | −56 | −50 | 10 | 6.62 | −58 | −54 | 2 | 4.55 |
| L. middle temporal gyrus | 22 | −52 | −18 | 0 | 3.19 | | | | |
| L. superior temporal gyrus | 42 | −62 | −32 | 20 | 3.52 | | | | |
| L. fusiform gyrus | 37 | −42 | −58 | −16 | 4.86 | | | | |
| L. supra marginal gyrus | 48 | −46 | −32 | 22 | 4.07 | | | | |
| L. medial superior frontal gyrus | 10 | −14 | 50 | 18 | 4.76 | | | | |
| L. amygdala | – | −26 | −6 | −16 | 4.65 | | | | |

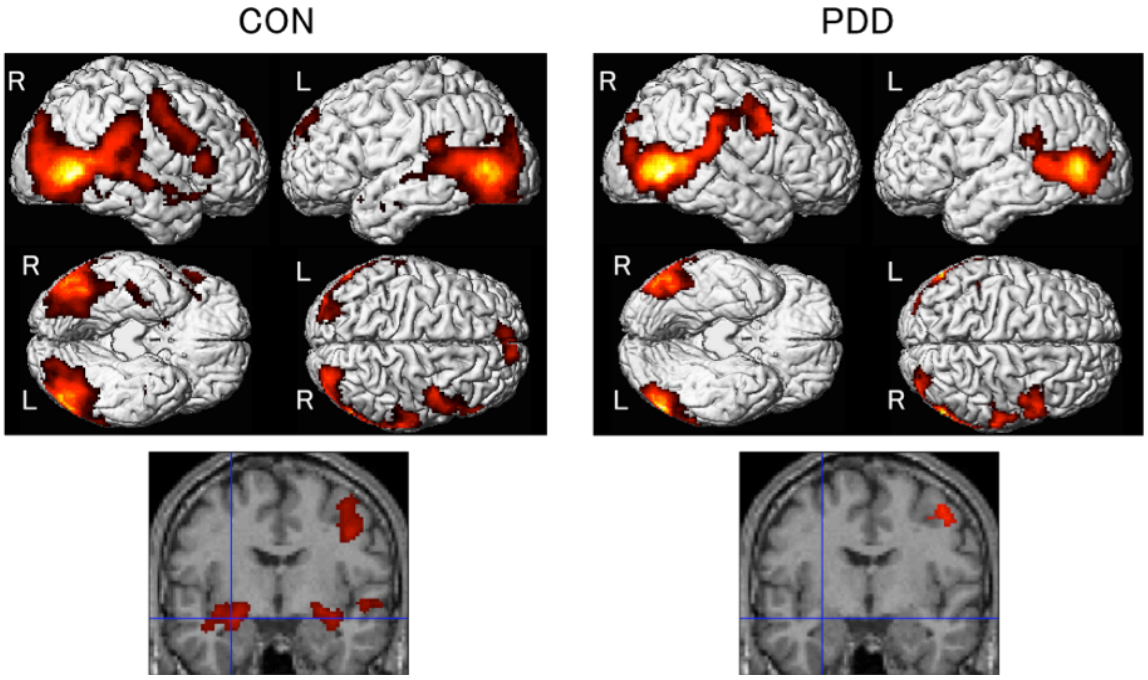


Figure 5.2 Statistical parametric maps showing brain regions activated in response to dynamic versus static facial expressions in the control (left) and PDD group (right). The areas of activation are rendered on spatially normalized brains (upper) and overlaid on the normalized anatomical MRI of one of the participants involved in this study at the coronal section showing amygdala activity (lower). L = Left hemisphere; R = Right hemisphere.

### 5.3.3 Regional brain activity: Interaction between group and presentation condition

A planned contrast of the interaction between group and presentation condition, specifically testing the higher activity for dynamic versus static expressions for the control than PDD groups, revealed significant activation in several brain regions that were detected in the above analyses for the control group (Table 5.2; Figure 5.3). Bilateral posterior regions, including the activation foci of the inferior occipital gyri, middle temporal gyri, and fusiform gyri were detected significantly. Significant bilateral activities of the inferior frontal gyri and dorsomedial prefrontal cortices were also observed. There was also a significant activation in the left amygdala.

### 5.3.4 Regional brain activity: Other effects

The present study conducted exploratory analyses for other interactions related to the group factor. For the interaction between group and emotion, a significant activation cluster was found in the bilateral precuneus (the strongest focus: x-18 y-50 z48, $T$ = 5.14), suggesting relatively high activity for happy expressions in the PDD group compared to the control group. For the 3-way interaction, a significant activation cluster was found in the right cingulated gyrus (the strongest focus: x22 y–

4 z38; $T$ = 4.94), suggesting relatively high activity for static happy expressions in the PDD group and for dynamic happy expressions in the control group compared to other conditions. However, the strongest activation foci of these clusters were in the white matters, and visual inspections of effect sizes suggested that these significant results were strongly related to deactivations in other conditions. Hence, these results were not discussed further here. There was no other significant activity.

**Table 5.2** Brain regions showing significant interaction between group and presentation condition. The coordinates of activation foci in MNI system and their T-values are shown.

| Brain region | BA | Coordinates | | | T-value |
|---|---|---|---|---|---|
| | | x | y | z | |
| R. inferior occipital gyrus | 19 | 42 | −78 | −16 | 3.04 |
| R. inferior temporal gyrus | 19 | 48 | −70 | −8 | 3.79 |
| R. middle temporal gyrus | 37 | 52 | −62 | 0 | 5.08 |
| R. middle temporal gyrus | 21 | 48 | −36 | 4 | 3.84 |
| R. fusiform gyrus | 37 | 40 | −58 | −14 | 3.00 |
| R. inferiror frontal gyrus | 45 | 48 | 26 | 8 | 3.06 |
| R. medial superior frontal gyrus | 10 | 8 | 66 | 20 | 3.87 |
| L. lingual gyrus | 18 | −16 | −86 | −12 | 3.55 |
| L. inferior occipital gyrus | 18 | −30 | −88 | −22 | 4.27 |
| L. middle occipital gyrus | 19 | −48 | −80 | 0 | 5.42 |
| L. fusiform gyrus | 37 | −42 | −60 | −16 | 3.08 |
| L. medial superior frontal gyrus | 10 | −14 | 50 | 18 | 4.33 |
| L. amygdala | – | −28 | −4 | −18 | 2.89 |

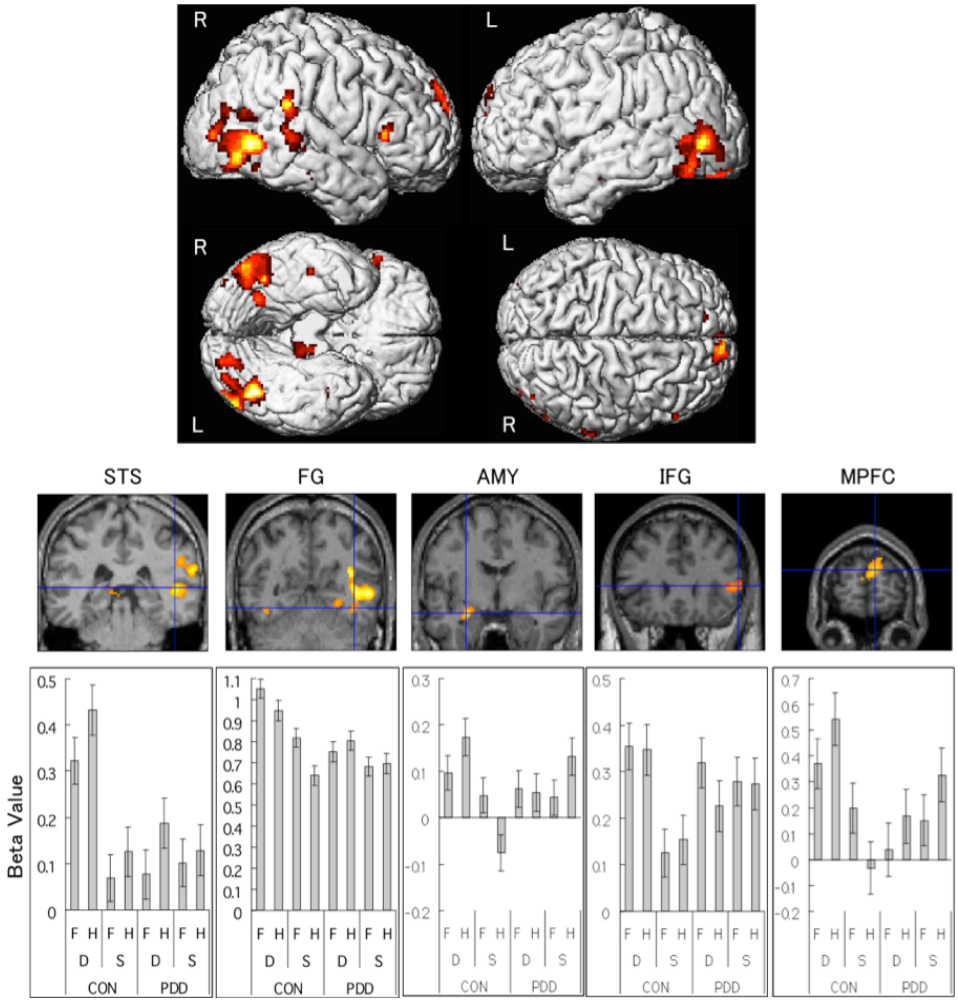


Figure 5.3 Brain activities for the interaction between group and presentation condition, specifically testing the higher activity for dynamic versus static expressions for the control than PDD groups. Upper) Statistical parametric maps rendered on spatially normalized brains. L = Left hemisphere; R = Right hemisphere. Middle) Statistical parametric maps of representative brain regions overlaid on the normalized anatomical MRI of one of the participants involved in this study. STS = superior temporal sulcus; FG = fusiform gyrus; AMY = amygdala; IFG = inferior frontal gyrus; MPFC = medial prefrontal cortex. Lower) Mean beta values (with SE) of brain regions corresponding to the above overlaid MRIs. The data were extracted at the sites of peak. F = fear; H = happiness; D = dynamic; S = static; CON = control.

5.3.5 Functional connectivity

For the control group, the one-sample t-tests showed that facilitative modulatory effects of dynamic presentation were significant for all bi-directional connections between the V1 and STS, STS and AMY, STS and IFG, and AMY and IFG (*ps* < .05; Figure 5.4 left).

For the PDD group, as in the case of the control groups, facilitative modulatory effects of dynamic presentation were significant for almost all connections between the regions (t-test, *ps* < .05); however, the effects did not reach significance for the connections from the STS to IFG and from the AMY to IFG (*ps* > .1; Figure 5.4 right).

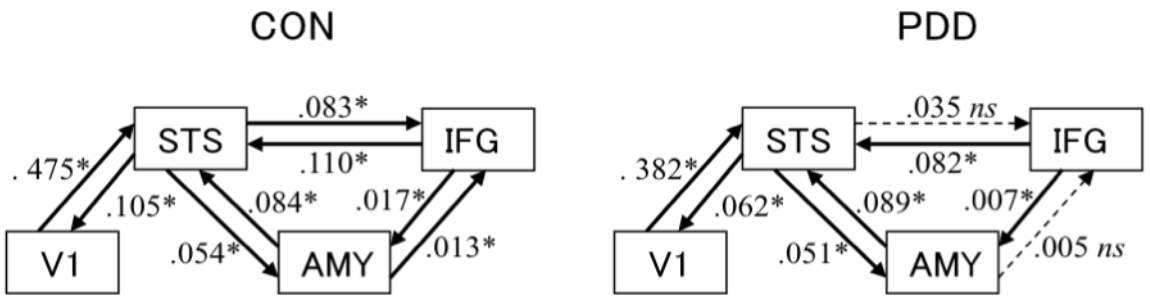


Figure 5.4 Dynamic causal models in the control (left) and PDD group (right). Solid and dotted lines indicate significant and non-significant modulatory effects of dynamic presentation, respectively. V1 = primary visual cortex. STS = superior temporal sulcus; AMY = amygdala; IFG = inferior frontal gyrus.

## 5.4 Discussion

### 5.4.1 Regional Brain Activity

The results in the control group showed that the observation of dynamic, compared to static, facial expressions of fear and happiness highly activated distributed brain regions, including the STS, FG, AMY, IFG, and MPFC. The activities in the STS, FG, AMY, and IFG are consistent with those of a previous study using same dynamic and static facial expression stimuli (Sato et al., 2004a) and some other studies (e.g., LaBar et al., 2003). The MPFC has also been shown to be active for the dynamic facial expression processing in some previous studies (Kilts et al., 2003; LaBar et al., 2003). All of these brain regions have been proposed to constitute the social brain network (Adolphs, 2003; Brothers, 1990). These results confirm that dynamic versus static facial expressions are appropriate conditions to activate the social brain network in typically developing subjects.

More importantly, the results of group comparisons showed that these social brain regions were less activated in response to dynamic versus static facial expressions in the PDD group compared to the control group. The reduced activities of the STS, FG, and AMY in individuals with PDD while

perceiving dynamic versus static facial expressions confirm the results of a previous study (Pelphrey et al., 2007), extending that this is the case for positive, as well as negative, valenced expressions. The group difference in the activities of IFG and MPFC have not been reported in the previous study (Pelphrey et al., 2007), and hence, the current study represents the first to provide evidence that the functional abnormalities in the IFG and MPFC are related to the impaired processing of dynamic facial expression in PDD. Some methodological differences may account for the disparity in the results. For example, the dynamic facial expression stimuli in the present study showed more rapid changes compared to those in (Pelphrey et al., 2007) (i.e., taking 1040 versus 1500 ms to change from neutral to full-blown emotional expressions). A previous behavioral study has reported that the changing speed in dynamic facial expressions have influence on the naturalness recognition of facial expressions (Sato & Yoshikawa, 2004), and the fitted functions obtained in that study suggest that the speed in this study was more preferable to implement natural dynamic facial expressions. Some other methodological differences between the present study and (Pelphrey et al., 2007) may also be relevant, such as the image acquisition conditions (3 versus 1.5 T scanners; cf. Scarabino et al., 2007) and image analyses (classical versus empirical Bayesian approaches for covariance

component estimation; cf. Friston et al., 2002). Because several anatomical studies have also reported the macroscopic and/or microscopic abnormalities in several of these social brain regions, specifically in the STS (Boddaert et al., 2004; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006; Levitt et al., 2003), FG (Kwon, Ow, Pedatella, Lotspeich, & Reiss, 2004; Van Kooten et al., 2008), AMY (Schumann & Amaral, 2006; Nacewicz et al., 2006), IFG (Hadjikhani et al., 2006; Levitt et al., 2003), and MPFC (Hyde, Samson, Evans, &, Mottron, 2010; Hadjikhani et al., 2006), it appears plausible that these regions show abnormal activity in PDD. Because the dynamic facial expressions are natural media for social interactions, our results suggest that the reduced activities of these social brain regions are related to the real-life impairment in communication via facial expressions in PDD.

The STS has been shown to be involved in visual analyses of dynamic or changeable aspects of faces in previous neuroimaging studies with typically developing participants (e.g., Hoffman & Haxby, 2000; Puce, Allison, Bentin, Gore, & McCarthy, 1998; Wheaton, Thompson, Syngeniotis, Abbott, & Puce 2004; for reviews, see Allison et al. (2000) and Haxby et al. (2000)). A previous neuroimaging study has also shown that biological motion activated the STS in the typically developing controls but not in the

PDD group (Freitag et al., 2008). In line with these data, some behavioral studies have reported that individuals with PDD have impairments in the perception of biological motions (Moore et al., 1997; Blake et al., 2003; Hubert et al., 2007). In reviewing the behavioral and neuroscientific studies, Dakin and Frith (2005) proposed that the individuals with PDD are impaired in the perception of human actions and this impairment appears to be related to the dysfunction of the STS. Together with these data, our results suggest that the reduced activity of the STS could be involved in the impaired visual analysis of dynamic aspects in emotional facial expressions in PDD.

In contrast with the functional role of the STS, the FG has been shown to relate to the visual analysis of invariant aspects of faces and/or the subjective perception of faces in typically developing participants (e.g., Hoffman & Haxby, 2000; Tong, Nakayama, Vaughan, & Kanwisher, 1998; for a review, see Haxby, et al., 2000). Consistent with the present results, a previous neuroimaging study have shown that dynamic facial expressions more activated the FG than static facial expressions in typically developing individuals but not in individuals with PDD (Pelphrey et al., 2007). These findings suggested that this enhanced activation of the FG relate with the enhanced subjective perception of dynamic facial expressions. A recent

behavioral study in typically developing individuals has reported that the perception of the last images in dynamic facial expressions was more exaggerated than those of static facial expressions (Yoshikawa & Sato, 2008). Furthermore, behavioral studies with the participants with PDD have shown that, although these participants also showed such exaggerated last-image perception for dynamic facial expressions, their exaggerated perception were restricted to dynamic facial expressions with intense emotion (see Chapter 4). Collectively, it is speculated that the reduced activity of the FG found in the present study may be related such altered face perception while viewing dynamic facial expressions in PDD.

The AMY has been shown to be involved in emotional processing while viewing dynamic facial expressions in typically developing participants (Sato et al., 2010; Sato et al., 2004a). A previous neuroimaging study have reported that the amygdala activity changed depending on the intensity of emotional facial expression photos in the typically developing controls but not in the PDD groups, suggesting the abnormal emotional processing in the amygdala of individuals with PDD (Ashwin et al., 2007). Several animal lesion studies have also indicated that the amygdala damage induced abnormal emotional reactions in response to emotional expressions of other individuals (e.g., Emery et al., 2001), which have been proposed to

be analogous to socio-emotional impairments in PDD (Bachevalier, 1996). In line with these neuroscientific data, a previous behavioral study has reported that, when an experimenter showed either distressed or neutral facial and vocal expressions dynamically, individuals with PDD did not show higher autonomic and behavioral responses to distressed than to neutral expressions, although typically developing controls showed such responses (Corona et al., 1998). The results of the present study, combined with these data, suggest that the reduced amygdala activity may be involved in the impaired emotional reactions to dynamic facial expressions in PDD.

With regard to the IFG, some previous neuroimaging studies in typically developing participants have reported that this regions was more activated not only when participants passively observed dynamic versus static facial actions (Buccino et al., 2001; Buccino et al., 2004; LaBar et al., 2003; Sato et al., 2004a; Trautmann et al., 2009), but also when participants imitated the facial expressions while viewing the dynamic facial expressions stimuli than when they passively viewed the stimuli (Lee, Josephs, Dolan, & Critchley, 2006; Leslie, Johnson-Frey, & Grafton, 2004). Such result is consistent with the theories that the IFG constitutes the "mirror neuron" system (Gallese et a., 2004; Rizzolatti et al., 2001). Single-unit recording studies in monkeys have revealed that specific

neurons in the ventral premotor cortex discharge both when the monkey observes experimenters performing specific hand actions and when it executes those actions; these neurons have been named mirror neurons (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). Because the IFG has been suggested to be a human homologue of monkey ventral premotor cortex (Rizzolatti & Arbib, 1998), it would be reasonable to posit that this regions contains mirror neurons, which can match the observation and executions of facial expressions and enable us to imitate other's facial expression. Based on the neuroscientific evidence, together with behavioral data indicating the abnormal mimicking in individuals with PDD (e.g., Hobson & Lee, 1999; for a review, see Smith and Bryson, 1994), Williams et al. (2001) proposed that the dysfunction of the IFG might be related to PDD. In line with these empirical and theoretical studies, recent neuroimaging (Dapretto et al., 2006) and magnetoencephalographic studies (Nishitani, Avikainen, & Hari, 2004) have indicated that the mimicking of facial actions while viewing static facial stimuli less activated the IFG in the PDD group compared to controls. Together with these data, our results suggest that the abnormal activity in the IFG in response to dynamic facial expressions is related to deficits in automatic facial mimicry in PDD.

It is interesting to note that visual inspections of the IFG activation patterns in the PDD group (Figure 5.3) indicate that these subjects showed high, not less, IFG activity for both dynamic and static facial expressions, compared to the activity for static facial expressions in the controls. Consistent with these data, some previous behavioral studies have reported that individuals with PDD did not lack facial reactions for emotional facial expressions of other individuals, but showed the facial expressions in different ways compared to typically developing individuals (McIntosh et al., 2006; Tardif et al., 2007; Yirmiya et al., 1989). Collectively, the results of the present study suggests that the individuals with PDD may activate the mirror neuron system in the IFG in altered patterns, which then could produce abnormal facial mimicry, during social interactions via facial expressions.

The MPFC has been shown to be activated when participants read mental states of other individuals (i.e., mentalize or make theory of mind; e.g., Gallagher et al., 2000; for a review, see Frith and Frith (2003)). The mentalizing ability has been proposed to be one of the specific characteristics in human evolution (Tomasello, Carpenter, Call, Behne, & Moll 2005), and to be one of the core social deficits in PDD (Baron-Cohen, Leslie, & Frith, 1985). The reduced activity of the MPFC in mentalizing

tasks in individuals with PDD, compared to typically developing individuals, has also been shown in a previous neuroimaging study (Castelli et al., 2002). Collectively, the results that this region was activated in response to dynamic facial expressions in the control group suggest that in typically developing individuals automatically try to read others' mental states in real life social interactions. Furthermore, our results of the group difference in the activity of this region suggest that such automatic mind reading is relatively weak in PDD.

The results of the present study showed that cortical activities in response to dynamic versus static facial expressions in the control group and their differences with the PDD group were more evident in the right, compared with the left, hemispheres. The result in typically developing participants is consistent with a previous neuroimaging studies investigating the observation of same dynamic facial expression stimuli (Sato et al., 2004a) and confirms the traditional proposal of the right hemispheric dominance in emotional communication (for a review, see Heller, Nitschke, and Miller (1998)). The result in individuals with PDD appears to be in line with those of previous neuropsychological studies indicating that the patients with acquired right hemispheric damages showed social impairments similar with PDD (Happe, Brownell, & Winner,

1999) and that individuals with PDD showed poor performance in some assessments for the right hemispheric cognitive functioning (Gunter, Ghaziuddin, & Ellis, 2002). The results of the present study extend these findings, suggesting that the reduced activity in the right hemisphere is related to the impaired facial expression processing in PDD.

### 5.4.2 Functional connectivity

The results for the DCM in the control group showed that the observation of dynamic, compared to static, facial expressions of fear and happiness enhanced functional connectivity between the primary visual cortex and STS, STS and AMY, STS and IFG, and AMY and IFG. To our knowledge, this is the first evidence that the dynamic facial expressions enhance not only the regional brain activity but also the functional connectivity between the regions. As a potentially relevant finding, a previous neuroimaging study has reported that the activity of the IFG while conducting facial imitation in response to dynamic facial stimuli was enhanced by the emotional, compared to ingestive, expressions in the faces (Lee et al., 2006). We speculate that such emotional modulation on IFG activity while viewing dynamic facial expressions could be elicited through the enhanced functional connectivity from AMY to IFG.

The present study provide behavioral implications that the observation of dynamic facial expressions enhances not only the behavioral/cognitive components (e.g., emotion elicitation and facial mimicry), but also the interactions between these components (e.g., emotional modulation for facial mimicry and facial mimicry modulation on emotion). Some researchers have long theoretically argued the possibilities of such interactions between behavioral/cognitive components for the facial expression processing (e.g., Nietzsche, 1881/1997; Lipps, 1903). There has also been supportive empirical data that the visual recognition of dynamic bodily actions was modulated by the emotional content of the actions (Chouchourelou, Matsuka, Harber, & Shiffrar, 2006). Together with these data, our results suggest that, in typically developing individuals, the observation of dynamic facial expressions not only enhances the regional activity of social brain regions, but also the interaction between these regions.

More interestingly, our results in the PDD group revealed that the lack of enhanced connectivity from STS and AMY to IFG in response to dynamic, compared to static facial expressions. This is also, to our knowledge, the first evidence for the altered functional connectivity for the processing of dynamic facial expressions in PDD. Consistent with our finding, the

functional disconnectivity in PDD has been theoretically proposed in some previous studies (e.g., Brock, Brown, Boucher, & Rippon, 2002). There have been several previous studies that reported the reduced functional connectivity in individuals with PDD while engaging in some social tasks, such as expression recognition (Welchew et al., 2005; Wicker et al., 2008), face perception (Bird, Catmur, Silani, Frith, & Frith, 2006; Kleinhans et al., 2008), mentalizing (Castelli et al., 2002), as well as in some other non-social cognitive tasks (Just, Cherkassky, Keller, Kana, & Minshew, 2007; Just, Cherkassky, Keller, & Minshew 2004; Koshino et al., 2005, 2008; Villalobos, Mizuno, Dahl, Kemmotsu, & Muller, 2005). The results of the present study extend the literature indicating that the functional disconnectivity is also shown in the social brain network during the processing of dynamic facial expressions. The present study specifically showed that the altered pattern is in the input connections to the IFG from STS and AMY.

Related data have been reported in a previous anatomical imaging study (Barnea-Goraly et al., 2004). In that study, the researchers used diffusion tensor imaging to investigate the disruption of white matter structures in PDD. They found that the individuals with PDD, compared to typically developing controls, showed reduction in fractional anisotropy

values, which reflect micro-structural features of the white matter tracts such as fiber diameter and density, in and adjacent to the some brain regions, including the STS, AMY, and IFG. The findings of abnormal functional connectivity between the social brain regions in PDD may be, at least partially, accounted for by such abnormal anatomical connectivity.

### 5.4.2 Implications, limitations, and future directions

The results that the dynamic versus static facial expressions clearly depicted the group differences in the activities of the several social brain regions have practical, as well as theoretical, implications for experimental studies in PDD. Several previous behavioral, as well as neuroscientific, studies have used static stimuli of emotional facial expressions to investigate the abnormality in emotional expression processing in PDD, and accumulated inconsistent findings. Based on the results of the present study, it is proposed that dynamic presentation of emotional facial expressions is more appropriate than static presentation to reveal the abnormality in the communication via emotional facial expressions in PDD. Consistent with this idea, some pioneering behavioral studies have shown that dynamic presentations of facial stimuli revealed the abnormal behavioral patterns in social interactions in PDD, which have not found using static presentations.

For example, the finding of Chapter 2 have reported that the experiments using dynamic facial expression stimuli revealed the facilitative effect of emotional expression on automatic gaze-triggered attention orienting in typically developing individuals and its impairment in individuals with PDD, although previous studies have not clearly demonstrated the dysfunction of gaze-triggered attention orienting (see review for Nation and Penny (2007), but see Ristic et al., (2005)). Further studies using dynamic facial expression stimuli would more evidently reveal cognitive mechanisms and their neural substrates underlying the social impairments in PDD.

The results of functional connectivity also provide some implications. For example, it is interesting to note that the PDD group did not enhanced input to IFG from STS and AMY, but showed enhanced output from IFG to STS and AMY. The results suggest that the top-down processing is relatively intact in individuals with PDD. Previous studies have proposed that the IFG is involved in the imitation of other's action (e.g., Dapretto et al., 2006; Williams et al., 2001). Some psychological studies have demonstrated that the imitation of other's facial expression plays an important role for emotion recognition (Niedenthal, Brauer, Halberstadt, & Innes-Ker, 2001; Oberman, Winkielman, & Ramachandran, 2007). Previous

neuroimaging studies in typically developing individuals suggest that the motor learning enhance neural processes during the observation of the same action (Calvo-Merino, Grèzes, Glaser, Passingham, & Haggard, 2005, 2006). Tardif et al. (2007) reported that slowing-down presentation of dynamic facial expressions induce facial imitation and enhance the performance of emotion recognition in individuals with PDD. Although it remains unknown about the causal relationship between imitation and recognition of facial expressions, this evidence suggests that the imitation of other's facial expressions might be helpful to understand other's emotion in individuals with PDD.

Some limitations to this study should be acknowledged. First, our PDD group included only individuals with high-functioning PDD. Gepner (2004) suggested the possibility that the processing of dynamic visual information may be more impaired in individuals with low- than high-functioning PDD. It may be possible that the more strong or widespread brain abnormality may be found in individuals with PDD, which may be confounded with general intellectual and/or language problems. Further research is needed to determine whether the results can be extended to individuals with lower-functioning PDD.

Second, the present study tested only fearful and happy facial

expressions. Hence, the effect of dynamic presentations on other emotions in individuals with PDD remains unknown. The observation of dynamic facial expressions of other emotions may reveal abnormal activities in other brain regions in PDD. For example, some previous neuroimaging in typically developing participants have reported that the observation of dynamic and/or static disgusted facial expression activated the brain regions that were not shown in the present study (e.g., Wicker et al., 2003; for a review, see Calder et al. (2001)). A previous neuroimaging study with PDD participants has shown that the observation of disgusted facial expression photos less activated the basal ganglia and insula in the PDD group compared to controls (Ogai et al., 2003), although such group difference was not evident in another study (Deeley et al., 2007). These data suggest the possibility that the dynamic versus static facial expressions of disgust may provide clear evidence regarding the abnormal activity in these brain regions in PDD. This kind of exploration with dynamic facial expression stimuli of other emotions appears to be promising to provide new insights in the neural substrates of impaired facial expression processing in PDD.

Third, the present study did not record eye movement during observing dynamic and static facial expressions, though some studies suggest that the

abnormal fixation pattern to faces reduced the FG activity in individuals with PDD (cf. Dalton et al., 2005). However, our results demonstrated that the FG and other brain region of individuals with PDD activated to static facial expression at the same extent with those of typically developing controls. Furthermore, participants were asked to maintain a fixation placed between the eyes (the center of the screen). Some studies (Hadjikhani et al., 2004; Pierce, Haist, Sedaghat, & Courchesne, 2004) using the same instruction with the present study has also found that the FG normally activated in response to faces in individuals with PDD. These findings might role out the possibility that the abnormal fixation pattern to faces explain less brain activation in individuals with PDD.

**5.5 Summary**

Impairment of the communication via emotional facial expressions represents the core clinical features of pervasive developmental disorders (PDD), including autism and Asperger's disorder, and its neural substrate remains controversial. Although dynamic facial expressions constitute natural media of daily communication, little is known about the alterations in the regional brain activities and their functional couplings for the processing of dynamic facial expressions in PDD. Dynamic and static facial

expressions of fear and happiness were presented to a group of high-functioning PDD (N=12) and age- and gender-matched typically developing controls (N=13) and depicted the brain activity by using functional magnetic resonance imaging (fMRI). Regional brain activity analyses for the interaction between group and presentation condition, specifically testing the higher activity for dynamic versus static expressions for the control than PDD groups, revealed higher activation in several brain regions, inducing the superior temporal gyrus (STS), fusiform gyrus, amygdala (AMY), inferior frontal gyrus (IFG), and medial prefrontal cortex. Dynamic causal modelling analyses revealed that, for the control group, all of the bi-directional connections between the primary visual cortex and STS, STS and AMY, STS and IFG, and AMY and IFG were enhanced in response to dynamic, compared to static, facial expressions. For the PDD group, similar connectivity patterns but with the lack of enhanced connections from STS to IFG and AMY to IFG were found. These results suggest that reduced regional activities and the functional disconnectivity of the social brain network underlie the impairment in real life communication via emotional facial expressions in PDD.

# Chapter 6

## General discussion

## 6.1 Summary of new findings

The results revealed a gaze and facial expression processing impairment in individuals with PDD. The findings in Chapters 2 to 5 can be summarized as follows.

In Section 1 of Chapter 2, the results revealed that an enhancement of gaze-triggered attention orienting by a dynamic fearful gaze was observed in the control group but not in the PDD group, though both groups showed attention orienting by neutral gaze cues. This suggests that the integration of emotion and gaze direction that elicits strong joint attention is impaired in individuals with PDD. In Section 2 of Chapter 2, it was found that, unlike the control group, the PDD group did not show attention orienting by subliminally presented gaze cues. The results indicate that unconscious processing of facial cues is impaired in PDD.

In Chapter 3, recognition of fearful faces was found to be specifically impaired in the PDD group, as was face recognition in general. Age had positive effects on fearful expression recognition, both directly and indirectly via the development of improved face recognition in controls but not in PDD subjects. Furthermore, fearful expression recognition was related to the severity of PDD symptoms. The results reveal that individuals with PDD show atypical development of facial emotion recognition and that

impaired fearful expression recognition is closely related to social dysfunction in the real world.

In Chapter 4, the results showed that individuals with PDD did not perceive the last image in a dynamic facial expression to be more exaggerated than a static facial expression when ambiguous emotional expressions were used as stimuli. The result suggests that the perceived emotional intensity of dynamic facial expression differs between typically and atypically developing individuals.

In Chapter 5, consistent with the finding in the above chapter, the results revealed reduced regional activities of the social brain network and an altered network in these regions for processing dynamic facial expressions. A dysfunction in the processing of dynamic face information might underlie the impairment in real life communication via emotional facial expressions in PDD.

Based on these new findings, in the next section, I discuss the psychological and neural bases of social dysfunction in PDD (cf. Figure 6). The impairments found in this thesis might have a cascading effect on atypical social development in individuals with PDD, because the impairment of gaze-triggered attention and the reduced perception of emotional intensity in dynamic facial expressions lessen the chances of

social interaction. These impairments might have underlying abnormalities such as inattention to social stimuli. The psychological finding suggests that abnormal social attention leads to impaired recognition of other's emotion. The fMRI study also suggests abnormal input from the subcortical area involved in automatic face processing to reflexive joint attention and the biological motion processing system, as well as internal disorganization of these regions. These problems might derail individuals from typical developmental trajectories of social behavior.

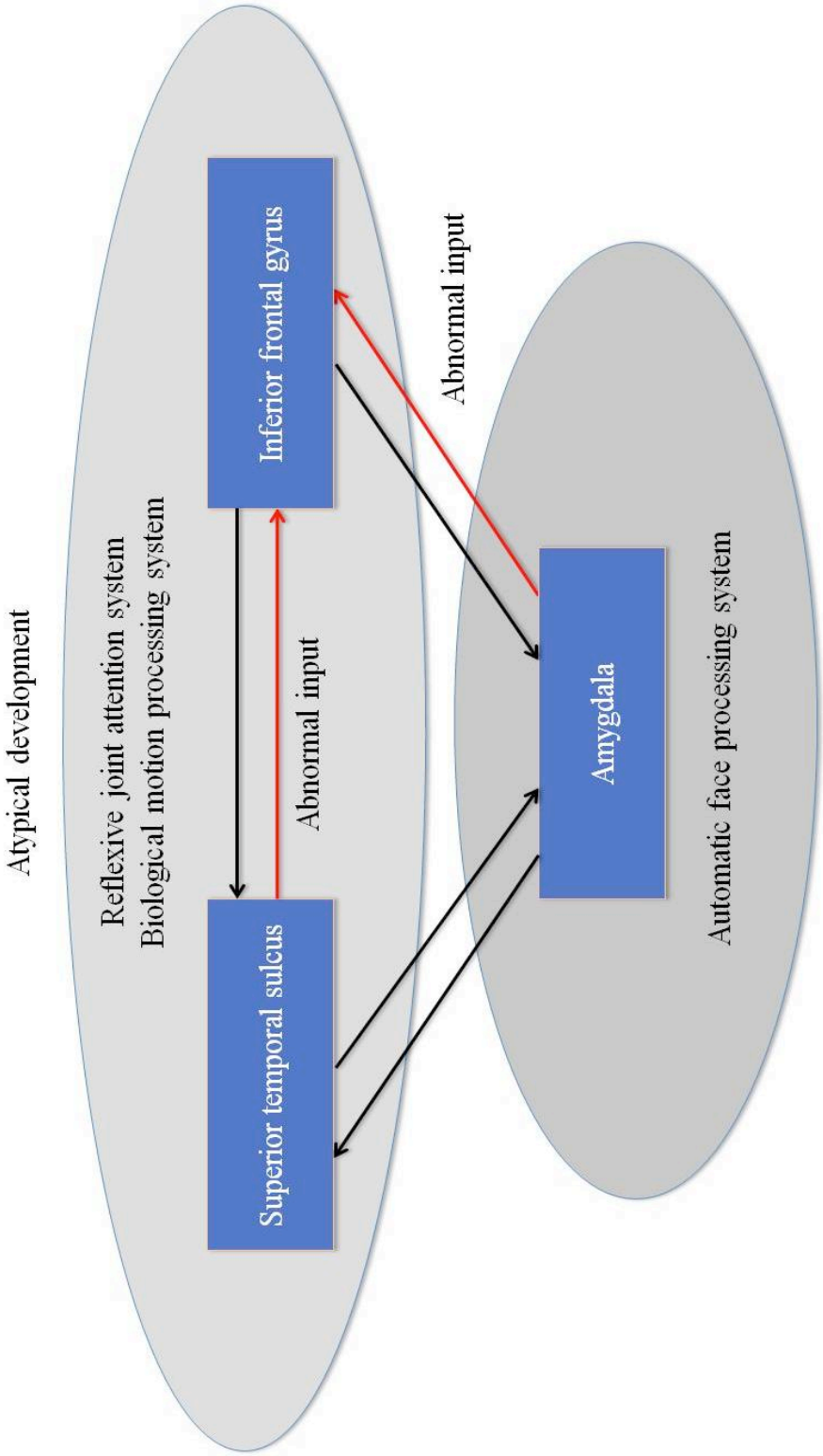


Figure 6 Psychological and neural bases of social cognitive dysfunction in individuals with PDD.

## 6.2 Psychological basis of the social dysfunction in PDD

The finding that individuals with PDD show impairments in emotional and unconscious joint attention and dynamic facial expression processing has important implications for understanding the developmental mechanisms of social dysfunction.

One of the earliest features of social impairment to emerge in PDD is a deficit of joint attention (Mundy et al., 1986) and impairment of joint attention predicts later deficits in language skills and social communications (Charman, 2003). In contrast with growing evidence that individuals with PDD have no impairment of gaze-triggered attention orienting, individuals with PDD did not show an enhancement of attention orienting by dynamic fearful gaze (see Chapter 2). This suggests that the integration of emotion and gaze direction is impaired in individuals with PDD (see also Akechi et al., 2009, 2010). Previous studies in typically developing infants have demonstrated that emotional gaze toward objects enhances the attention system (Hoehl, Wiese, & Striano, 2008; Hoehl & Striano, 2010). If enhanced attention orienting by emotional gaze creates a shared emotional state to attended objects between infants and caregivers, and facilitates the association of an induced emotional state with the attended object, this modulating effect might influence the development of

social cognitive functions, such as empathy, and facilitate learning of the emotional value of objects. Mundy and Sigman (1989) proposed that sharing emotion in joint attention induces the development of socio-emotional functions. Although there is a lack of evidence in younger individuals, impaired integration of gaze and emotion is one candidate for the cause of atypical social development in PDD.

More importantly, individuals with PDD did not show attention orienting to subliminally presented gaze cues (see Chapter 2). Previous behavioral studies have also reported impaired processing of subliminally presented facial expression in individuals with PDD (Hall et al., 2007; Kamio et al., 2006). These findings indicate that unconscious processing of facial cues is impaired in PDD. Psychophysical studies have shown that humans consciously perceive only very restricted areas within the range of areas available for immediate attention (Simons & Rensink, 2005). Consistent with this notion, social interactions are heavily influenced by unconscious processing (Wilson, 2002). Because another's gaze is not always within our conscious attention, individuals with PDD might also fail to show joint attention in relation to individuals outside of the range of conscious attention. Reduced unconscious joint attention would have a cascading effect on the atypical development of social cognition in PDD.

Individuals with PDD also showed impaired dynamic facial expression processing. It might be possible that reduced perception of the emotional intensity of dynamic facial expressions leads to difficulty in detecting subtle changes in another's facial expression and in rapidly inducing adaptive behavioral responses (see Chapter 2 and 4). The results suggest that individuals with PDD show an impairment of biological motion processing in terms of emotional, perceptual, and predictive processing. A recent behavioral study has demonstrated that individuals with PDD have impairments in their perception of dynamic point-light displays describing human actions (Blake et al., 2003). Further, a recent study demonstrated that toddlers with PDD failed to recognize point-light displays of biological motion (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009). These finding suggest that impairment of motion/biological motion processing exists in early developmental life. Some researchers have proposed that detection of biological motion is one of the precursors to developing a theory of mind (Baron-Cohen, 1995; Frith & Frith, 1999). Perlman, Vander Wyk, and Pelphrey (2010) proposed that in early life the biological motion detection system allows us to use knowledge about others' actions and intentions. Atypical subjective perception of dynamic facial expressions might deprive individuals with PDD of understanding in relation to others' emotional

intentions and actions.

It is conceivable that atypical joint attention and biological motion processing in PDD play an important part in determining social cognitive development. However, there might be underlying abnormalities relating to this issue. Some researchers have proposed that an innate impairment of the subcortical face processing system, which enables us to detect faces and orient our attention to faces, impedes the development of social interaction in PDD (Johnson, 2005; Senju & Johnson, 2009). In line with this theory, a prospective study found that 12-month-old infants with high-risk for PDD showed reduced fixation on others' faces (Ozonoff et al., 2010). These findings suggest that difficulty in automatic face processing exists in early developmental life. Consistent with these findings, the result in Chapter 2 shows an impairment of attention orienting by subliminally presented gaze cues in PDD, and the result in Chapter 3 suggests that individuals with atypical attention to others in daily life show more severe impairment of fearful expression recognition. The findings of Chapters 2 to 4 might also be interpreted in this context. The results in these chapters showed that individuals with PDD have difficulty with face recognition, emotion recognition, and dynamic facial expression processing. It seems that innate impairment of the subcortical face processing system deprives them of the

chance to process facial cues.

### 6.3 Neural basis of social dysfunction in PDD

The results in Chapter 5 revealed reduced regional activities in the social brain network, including STS, FG, AMY, IFG, and MPFC, for the processing of dynamic facial expressions. Anatomical studies have also reported structural abnormalities in these regions (STS: Boddaert et al., 2004; Hadjikhani et al., 2006; Levitt et al., 2003, FG: Kwon et al., 2004; Van Kooten et al., 2008, AMY: Schumann & Amaral, 2006; Nacewicz et al., 2006, IFG: Hadjikhani et al., 2006; Levitt et al., 2003, and MPFC: Hyde et al., 2010; Hadjikhani et al., 2006). Furthermore, DCM analysis revealed a lack of enhanced connectivity from STS and AMY to IFG in response to dynamic, as compared to static, facial expressions.

The evidence of altered brain networks in PDD supports the developmental psychological model described above. The STS has been shown to be involved in visual analyses of dynamic or changeable aspects of faces (gaze and facial expressions) (e.g., for reviews, see Allison et al. (2000) and Haxby et al. (2000)). The IFG have been proposed to be involved in the understanding of others' actions and intentions (e.g., Gallese et al., 2004). The lack of enhanced connectivity between STS and

IFG is consistent with the theory that, in early life, the biological motion processing systems allow us to use knowledge about others' actions and intentions (Perlman et al., 2010), and leads to the development of a theory of mind (Frith & Frith, 1999). The lack of enhanced connectivity between STS and IFG for processing dynamic facial expressions might reflect a difficulty in understanding others' emotional intentions and actions from biological motion. Furthermore, recent studies have demonstrated that STS and IFG activate during gaze-triggered attention orienting (Sato, Kochiyama, Uono, & Yoshikawa 2009; Tipper, Handy, Giesbrecht, & Kingstone, 2008; Grosbras, Laired, & Paus, 2005; however, see Hietanen, Nummenmaa, Nyman, Parkkola, & Hamalainen, 2006). The atypical connectivity between STS and IFG might relate to an impairment of reflexive joint attention in PDD, specifically when gaze and facial expression change dynamically.

The altered connectivity between AMY and IFG might relate to an impairment of early input of facial information into frontal regions. Consistent with this, previous studies have demonstrated that in PDD the AMY is structurally and functionally impaired (e.g., Schumann & Amaral, 2006; see Baron-Cohen et al., 2000 for a review). Some researchers have proposed that innate impairment of the subcortical face processing system,

including the AMY, leads to deterioration of the neural and psychological development of social interaction in PDD (Johnson, 2005; Senju & Johnson, 2009). As described above, it has been proposed that the IFG are involved in reflexive joint attention and in understanding others' intentions from their biological motion (e.g., Gallese et al., 2004; Sato et al., 2009). Abnormal input to the reflexive joint attention and biological motion processing system, including the IFG, which is impaired in PDD (see Chapter 2 and 4), might derail an individual from a typical trajectory of neural and psychological development with regard to social cognition.

### 6.4 Implications for intervention and for mutual understanding

The new findings have some implications for clinical interventions in PDD. The results of this series of experiments indicate that impairment occurs in the bottom-up/unconscious processes, not in the top-down/conscious processes. The fMRI results showed neural abnormalities in bottom-up connections (e.g., from amygdala to IFG) but not in top-down connections (e.g., from IFG to amygdala). The behavioral results of Chapter 2 revealed that individuals with PDD had an impairment of conscious, but not unconscious, gaze triggered orienting. The results of Chapter 3 revealed that individuals with normal attention to social stimuli show more accurate

emotion recognition. In line with these findings, some previous studies have reported that the instruction to intentionally control fixation improved behavioral and brain responses to social tasks in individuals with PDD (Perlman, Hudac, Pegors, Minshew, & Pelphrey, in press; Senju et al., 2009). A clinical study using cognitive behavioral therapy has also reported that rule-based training improves emotion recognition, theory of mind ability, and problem solving in individuals with PDD (Stichter et al., 2010). Some studies of intervention programs suggest that attention-grabbing stimuli are useful to orient attention and lead to improved social cognitive skills (cf. Golan et al., 2010; Tanaka et al., 2010). Together with these findings, the results suggest that top-down/conscious regulation can be an effective tool for improving social cognitive skills in individuals with PDD.

Knowledge of the psychological and neural bases of social impairments in PDD reported in this thesis could improve understanding between individuals with and without PDD. If individuals with PDD and those around them, such as caregivers, teachers, and friends, understand the fundamental nature of the social impairment found in PDD, this could reduce the stressfulness of their daily social interactions. Such an improvement in social interaction would heighten their quality of life and reduce secondary problems, such as social withdrawal, in individuals with

PDD. In addition to interventions solely relating to individuals with PDD, improving mutual understanding between individuals with and without PDD might provide a shorter route to improving social adaptation in individuals with PDD. I hope that the scientific knowledge I have set out here can help improve social adaptation in individuals with PDD.

### 6.5 Future directions

This thesis revealed impairments of reflexive joint attention and of biological motion processing in adolescents and adults with PDD. These impairments might play crucial roles in the atypical development of social cognition. However, there is little evidence of these impairments in infants with PDD. Recently, a number of prospective studies have demonstrated that infants at high risk for PDD show reduced attention to social stimuli (Ozonoff et al., 2010), impaired biological motion processing (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009), and reduced joint attention (Rozga et al., in press). Further prospective and longitudinal studies are needed to elucidate the fundamental causes of social dysfunction and the relationships between the impairments described above. Such studies could enable us to depict the atypical developmental trajectory of social cognition in PDD.

It might also be promising to investigate whether the impairments

described above are shared across subgroups in PDD, because the present study focused on the high-end spectrum of PDD. It has recently been reported that these subgroups show different behavioral profiles in some research areas (cf. Kaiser & Shiffrar, 2009). Comparison across subgroups would provide crucial information for distinguishing fundamental and secondary problems of social cognitive dysfunction and for differentiating these subgroups clearly.

Unfortunately, there is currently no suitable research environment in Japan to conduct such a prospective, longitudinal and group-comparison study. The creation of a research environment for investigating these issues as soon as possible is called for.

### 6.6 Conclusion

The results in this thesis reveal that individuals with PDD show impaired gaze triggered attention orienting and dynamic facial expression processing. These basic functions play important roles in the typical and atypical development of social cognition. There might be a further abnormality underlying these dysfunctions, such as inattention to social stimuli. The fMRI study suggests that reduced activity of social brain regions and an altered network between these regions manifests in

dysfunction of gaze triggered attention orienting and dynamic facial expression processing. Abnormal input to reflexive joint attention and biological motion processing systems and their internal dysfunction might derail the typical developmental trajectory of social behavior. However, there is little evidence of this atypical developmental trajectory in PDD. Further studies are needed to investigate this issue longitudinally in infants at high-risk for PDD. The development of research would allow us to determine appropriate interventions to help these individuals attain a more typical developmental trajectory.

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# Publications related to this dissertation

This dissertation is based on the following published papers. In particular, Chapter 2 is revisions of [3][5]. Chapter 4 is the revision of [4]. Chapter 3 and 5, and a part of Chapter 4 are in submission.

[1] Uono, S., Sato, W., Michimata, C., Yoshikawa, S., & Toichi, M. (2009). Facilitation of gaze-triggered attention orienting by a fearful expression and its relationship to anxiety. *Psychologia: An International Journal of Psychological Sciences, 52*, 188–197.

[2] Uono, S., Sato, W., & Toichi, M. (2009). Dynamic fearful expressions enhance gaze-triggered attention orienting in high and low anxiety individuals. *Social Behavior and Personality: An international journal, 37*, 1313–1326.

[3] Uono, S., Sato, W., & Toichi, M. (2009). Dynamic fearful gaze does not enhance attention orienting in individuals with Asperger's disorder. *Brain and Cognition, 71*, 229–233.

[4] Uono, S., Sato, W., & Toichi, M. (2010). Brief report: Representational momentum for dynamic facial expressions in pervasive developmental disorder. *Journal of Autism and Developmental Disorders, 40*, 371–377.

[5] Sato, W., Uono, S., Okada, T., & Toichi, M. (2010). Impairment of unconscious, but not conscious, gaze-triggered attention orienting in Asperger's disorder. *Research in Autism Spectrum Disorders, 4*, 782–786.