Table 2 Timetable of one session

Schedule		
5 minutes	Greeting	
30 minutes	Psychoeducation on autism spectrum disorders	
10 minutes	Relaxation	
40 minutes	Work and discussion	
	<Topics>	
	Session 1 Autism spectrum disorders	Session 2 Relaxation
	Session 3 Happiness	Session 4 Comfort
	Session 5 Affection	Session 6 Anxiety
	Session 7 Anger	Session 8 Coping skills
5 minutes	Relaxation	

period of relaxation between topics (Table 2). Group therapy consists of four to five adults with ASD and two therapists. The therapist who conducts the group therapy as the leader is the certified developmental psychologist who has a PhD and over 10 years experience working with individuals with ASD. The other therapist, the sub-leader, is also a psychologist and has a Masters degree. One or two typical-development volunteers will also join the group and do the same program as the participants with ASD.

The program has two parts; one is the psychoeducation on ASD and the other is the emotion-regulation program. Materials for the psychoeducation on ASD prepared for this study will be used for learning and understanding the nature of ASD. The Cat-kit [16] will be used for the emotion-regulation program. The titles of each session are as follows: (1) the characteristics of autism; (2) relaxation 1 and happiness; (3) relaxation 2 and comfort; (4) differences from others and sadness; (5) strengths and anxiety; (6) weaknesses and coping with anxiety; (7) anger and coping methods; (8) summary: autism characteristics and conveying emotions.

During each session, participants will be asked to do some written work. For the part of psychoeducation on ASD, they will describe and present their own preferences, strengths, weaknesses, *et cetera*. In the emotion-regulation program, they will present their experience and physiological changes associated with emotion. The typical-development volunteers will also perform the same tasks. Finally, after completion of the intervention, the individuals with ASD will make out an original notebook containing descriptions of the nature of ASD and emotion-regulation learning and they will be encouraged to use this for continued study.

Randomization

Enrollment and random allocation will be performed through central registration at the University Hospital Clinical Trial Alliance Clinical Research Supporting System (UHCT ACReSS) at the University of Tokyo. A minimization method will be used with sex as the allocation factor. A third party, who is not involved in this trial, will enroll participants after examining their eligibility and informed consent. Owing to allocation concealment, the random allocation sequence will be provided by UHCT ACReSS and will not be revealed to any researchers or staff until the end of the enrollment period. As this is a single-blinded trial, all assessments will be conducted by raters without knowledge of whether the participant is in the CBT or waitlist conditions.

Statistical methods

All analyses will be performed using SPSS 20 J (SPSS Inc., Chicago, IL, USA). All data will be analyzed under the intent-to-treat principle. For the primary outcomes, independent *t*-tests will be used to compare changes in scores between the pre-assessment and post-assessment periods between the CBT group and the waitlist control group. The primary outcomes will be analyzed controlling for potential confounds (for example, age, gender, IQ, and clinical characteristics) using regression models. Secondary outcomes will be analyzed using relevant tests at each assessment, controlling for possible confounds as described above. Subgroup analyses will be performed for any possible confounds to differentiate the efficacy of CBT at follow-up.

Discussion

Expected results are that adults with ASD will be able to identify their own and understand others' mental states. We further predict that our CBT group will improve their coping skills. Furthermore, secondary symptoms, such as anxiety or depression, should reduce and adaptive behaviors should improve. The novelty of this trial lies in the utilization of CBT for improving emotion regulation among adults with ASD, in contrast with previous studies, which have included children and adolescents (up to age 16) as participants. Previous studies have also focused on the management of anxiety or anger whereas one of our study objectives is to manage the self-regulation of emotion in general. Moreover, previous studies have implemented CBT for children with ASD in addition to parental training. The current study will focus on psychoeducation regarding ASD for adult patients; that is, the current study does not include parent training as a means of the subject's understanding ASD. Thus, our design should help to determine the efficacy of CBT for adults with ASD. This CBT intervention is the first step in understanding ASD and emotion-regulation in adulthood, especially for persons diagnosed with ASD in adulthood. Our results will hopefully provide promising avenues for developing services for adults with high-functioning ASD in Japan.

Trial status

At the time of submission, 88% of the participants have been included in the trial. Of these participants, 68% have been tested at follow-up.

Abbreviations

ADOS: Autism Diagnostic Schedule; ADI-R: Autism Diagnostic Interview, Revised; AS: Asperger's syndrome; ASD: autism spectrum disorders; Cat-kit: Cognitive Affective Training Kit; CBT: cognitive-behavioral therapy; CES-D: Center for Epidemiological Studies Depression Scale; CISS: Coping Inventory for Stressful Situations; DSM-IV-TR: text revision of the diagnostic and statistical manual of mental disorders, fourth edition; GAF: Global Assessment of Functioning; IQ: intelligence quotient; LSAS: Liebowitz Social Anxiety Scale; MPMR: Motion Picture Mind-Reading task; STAI: State-trait Anxiety Inventory; SPAI: Social Phobia and Anxiety Inventory; TAS-20: 20-item Toronto Alexithymia Scale; UHCT ACReSS: University Hospital Clinical Trial Alliance Clinical Research Supporting System; WHO-QOL 26: World Health Organization Quality of Life 26-item version.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MK and YK equally contributed to the design and management of this trial and wrote most of the manuscript. HK made substantial contributions to the conception and design of this trial. KY contributed to the development of the CISS-Japanese version. YK and YK are the directors of each site and made substantial contributions to revising the design and management of this trial. All authors have read and approved the final manuscript.

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Author details

[1]Department of Psychology, Shukutoku University, 200 Daiganji-machi, Chuo-ku, Chiba-shi 260-8701, Japan. [2]Department of Child Neuropsychiatry, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. [3]Department of Child and Adolescence Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawahigashicho, Kodairashi, Tokyo 187-8553, Japan. [4]Department of Epidemiology and Environmental Health, Juntendo University Faculty of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan.

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Altered automatic face processing in individuals with high-functioning autism spectrum disorders: Evidence from visual evoked potentials

Takako Fujita [a,b], Yoko Kamio [c], Takao Yamasaki [a,*], Sawa Yasumoto [b], Shinichi Hirose [b], Shozo Tobimatsu [a]

[a] Department of Clinical Neurophysiology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Department of Pediatrics, School of Medicine, Fukuoka University, Fukuoka, Japan
[c] Department of Child and Adolescent Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan

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ABSTRACT

Individuals with autism spectrum disorders (ASDs) have different automatic responses to faces than typically developing (TD) individuals. We recorded visual evoked potentials (VEPs) in 10 individuals with high-functioning ASD (HFASD) and 10 TD individuals. Visual stimuli consisted of upright and inverted faces (fearful and neutral) and objects presented subliminally in a backward-masking paradigm. In all participants, the occipital N1 (about 100 ms) and P1 (about 120 ms) peaks were major components of the evoked response. We calculated "subliminal face effect (SFE)" scores by subtracting the N1/P1 amplitudes and latencies of the object stimuli from those of the face stimuli. In the TD group, the SFE score for the N1 amplitude was significantly higher for upright fearful faces but not neutral faces, and this score was insignificant when the stimuli were inverted. In contrast, the N1 amplitude of the HFASD subjects did not show this SFE in the upright orientation. There were no significant group differences in SFE scores for P1 amplitude, latency, or N1 latency. Our findings suggest that individuals with HFASD have altered automatic visual processing for emotional faces within the lower level of the visual cortex. This impairment could be a neural component of the disrupted social cognition observed in individuals with HFASD.

Social dysfunction is a fundamental problem in autism spectrum disorders (ASDs). Consequently, face processing in individuals with ASD has been intensively studied on both the behavioral and neurological level. A range of face processing abnormalities has been described in individuals with ASD (Behrmann et al., 2006; Berger, 2006; Dawson, Webb, & McPartland, 2005; Grelotti, Gauthier, & Schultz, 2002; Sasson, 2006; Schultz, 2005), and their relatives (Baron-Cohen & Hammer, 1997; Bölte & Poustka, 2003; Wallace, Sebastian, Pellicano, Parr, & Bailey, 2010). Some researchers have proposed face processing as a candidate for a cognitive ASD endophenotype (Dawson et al., 2002; Wallace et al., 2010; Wilson, Brock, & Palermo, 2010).

Face processing relies on a distributed, patchy network of cortical regions and subcortical structures (Atkinson & Adolphs, 2011). The core cortical regions include the inferior occipital gyri (early perception of facial features), the lateral fusiform

* Corresponding author at: Department of Clinical Neurophysiology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. Tel.: +81 92 642 5542; fax: +81 92 642 5545.
E-mail address: yamasa@neurophy.med.kyushu-u.ac.jp (T. Yamasaki).

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gyrus (perception of unique identity) and the superior temporal sulcus (perception of eye gaze, expression, and lip movement; Calder & Young, 2005). The non-conscious perception of emotional stimuli appears to involve several subcortical structures, which comprise two subsystems (Tamietto & de Gelder, 2010). One is the visually related emotion-encoding subsystem, which includes the amygdala, and the other is the non-visual emotion-encoding subsystem. These subcortical structures modulate cortical face processing (Tamietto & de Gelder, 2010). Further, these subcortical structures have been reported to be sensitive to low spatial frequency (SF) information about the emotional content of faces (Nakashima et al., 2008; Vlamings, Goffaux, & Kemner, 2009; Vuilleumier, Armony, Driver, & Dolan, 2003).

Emotionally significant stimuli, such as threat-related or social information, are first automatically processed outside of conscious awareness before being integrated with slower and more elaborative processing (Johnson, 2005). Abnormalities in automatic emotional processing are thought to be a key source of disrupted social cognition in individuals with ASD (Bailey, Braeutigam, Jousmäki, & Swithenby, 2005; Critchley et al., 2000). In accordance with this concept, our earlier behavioral study found that individuals with ASD responded to emotional faces differently than typically developing (TD) individuals, at an automatic level (Kamio, Wolf, & Fein, 2006). In contrast, ASD participants had normal performance for face tasks at a conscious level (Kamio et al., 2006a). Despite these findings, the neural basis of abnormal automatic processing of emotional faces in individuals with ASD remains uncertain.

The measurement of visual evoked potentials (VEPs) is an objective tool that has been useful in studies investigating the physiology and pathophysiology of the human visual system, including visual pathways and the visual cortex (Tobimatsu & Celesia, 2006). In particular, VEPs have high temporal resolution and are therefore suitable for the investigation of early automatic face processing. The major components evoked by conscious face stimuli are the occipital N1 (around 100 ms) and P1 (around 120 ms) peaks, and the occipito-temporal N170 (around 170 ms) peak (Bötzel, Schulze, & Stodieck, 1995; George, Evans, Fiori, Davido, & Renault, 1996). Both the N1 and P1 reflect the coarse processing of faces within the primary visual cortex (V1; Goto, Kinoe, Nakashima, & Tobimatsu, 2005; Mitsudo, Kamio, Goto, Nakashima, & Tobimatsu, 2011; Nakashima et al., 2008), whereas the N170 plays a role in processing features of faces or facial identification within the fusiform face area (FFA; Bentin, Allison, Puce, Perez, & McCarthy, 1996). When a supra-threshold face is inverted (the so-called "face inversion effect"), the N170 shows increased amplitude and delayed latency (Jacques, d'Arripe, & Rossion, 2007). This effect results from impaired integration of the features into a gestalt or holistic face representation (Young, Hellawell, & Hay, 1987). We recently reported that in healthy participants, occipital P1 amplitudes for unrecognizable (subliminal) faces are significantly larger than those for objects in the upright position (Mitsudo et al., 2011). However, P1 amplitudes for inverted faces are significantly smaller than those for upright faces. This is opposite to the face inversion effect for supra-threshold stimuli. Here, we call this phenomenon the "subliminal face effect (SFE)". Therefore, we consider that faces and objects are processed differently at the V1 level, even when the subjects are unaware of the stimuli before the face-specific processing occurs within the FFA. Taken together, changes in N1 or P1 in response to subliminal upright and inverted faces could provide an insight into the neural basis of automatic face processing in high-functioning ASD (HFASD).

In the present study, we hypothesized that individuals with HFASD have abnormal automatic processing at the V1 level (SFE in the upright or inverted orientation). To test this hypothesis, we used a 128-channel EEG system to record VEPs elicited by subliminally presented faces (fearful and neutral) and objects in the upright and inverted position. We measured the amplitudes and latencies of N1 and P1 peaks in response to these visual stimuli in HFASD and TD adults and calculated the SFE to quantify automatic face processing. We predicted that individuals with HFASD would exhibit a different pattern of V1 responses to masked subliminal faces in different orientations than TD individuals.

1. Methods

1.1. Participants

Ten individuals with HFASD (7 males and 3 females, aged 23–39 years, mean age 31.5) and 10 healthy TD control individuals (8 males and 2 females, aged 19–39 years, mean age 26.8) participated in this study. HFASD participants included four individuals with Asperger syndrome, one individual with high-functioning autism, and five individuals with pervasive developmental disorder not otherwise specified. The HFASD participants were recruited from the local Autism Society and local specialized psychiatric clinic. Diagnoses of ASD were confirmed, according to the DSM-IV-TR criteria (American Psychiatric Association, 2000), by a clinical research team that included an experienced child psychiatrist (Y.K.). ASD diagnoses were corroborated by a parental semi-structured interview that was developed and validated for Japanese populations with ASD, with a sensitivity of 0.943–0.975 and specificity of 0.929–0.956 (the PDD-Autism Society Japan Rating Scale [PARS]; Ito et al., 2012; Kamio et al., 2006b). Diagnostic agreement among the team was obtained for all participants. Although two of the 10 HFASD participants were being treated with small doses of antidepressants (1 with serotonin and noradrenalin reuptake inhibitors, 1 with quadricyclic antidepressants and selective serotonin reuptake inhibitors) at the time of participation, their symptoms were in remission and these individuals were psychologically stable. We evaluated intellectual function of the HFASD participants using the Japanese version of the Wechsler Adult Intelligence Scale-Revised. Individuals with ASD who had a full-scale IQ score lower than 85 were not included in the study.

TD control subjects were local college students and members of our faculty, who were interviewed to confirm the absence of any developmental or neuropsychiatric history, and/or medical conditions. None of the control participants were currently taking medication. TD control participants were confirmed to have normal intellectual functioning via interviews,

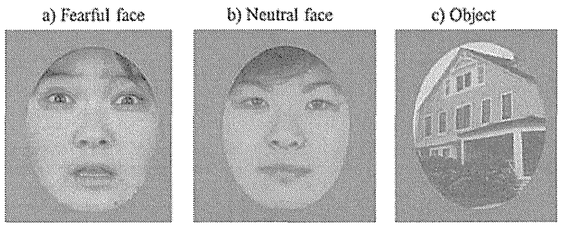

Fig. 1. Representative examples of fearful face (a), neutral face (b) and object (c) stimuli used in this study. Face stimuli are taken from the standardized Japanese and Caucasian Facial Expressions of Emotion and the Japanese and Caucasian Neutral Faces photo sets by Matsumoto and Ekman (1988). All stimuli are grayscale photographs (visual angle, 10°; mean luminance, 6 cd/m^2). The pattern mask is a 1024 × 768 pixel noise pattern.

although we did not conduct cognitive testing. All participants exhibited normal or corrected-to-normal visual acuity (>1.0), evaluated using the Landolt ring (Landolt, 1905).

1.2. Visual stimuli

The stimuli were generated by ViSaGe (Cambridge Research Systems, Cambridge, U.K.) and displayed on a gamma-corrected color monitor with a frame rate of 100 Hz (Electron22blue IV, LaCie, Tokyo, Japan). Photographs of eight fearful and eight neutral faces from 16 individuals (8 men and 8 women) were taken from Matsumoto and Ekman's (1988) standardized set of Japanese and Caucasian Facial Expressions of Emotion, and Japanese and Caucasian Neutral Faces (Fig. 1a and b). Half of the photographs were of people of Asian descent and the other half were of people of Caucasian descent. All photos were of faces viewed from the front with no hair visible. Eight different objects (e.g., house, chair) were selected as the object stimuli (Fig. 1c). Eight cartoon characters were used as the target stimuli. All pictures were grayscale photographs (visual angle, 10°; mean luminance, 6 cd/m^2). We used a 1024 × 768 pixel noise pattern generated by Adobe Photoshop 7.0 as a pattern mask.

1.3. Threshold setting

We conducted a pilot experiment to identify the sub-threshold duration at which participants would be able to determine whether the masked stimuli were faces or objects. This was done using a separate group of participants (3 HFASD and 6 TD) recruited from our volunteer pool. In this experiment, we used an ascending series of trials to prevent participants from perceiving the contents of the stimuli, as in previous studies (Mitsudo et al., 2011; Wolf, Kamio, & Fein, 2001). In each trial, masked stimuli (neutral and fearful faces, objects) were randomly presented, and participants verbally reported what they saw. In the first trial block, the stimulus presentation was 10 ms long. This duration increased in each subsequent trial block in 10 ms steps. Stimuli were presented 20–30 times in each trial block. The threshold at which participants first reported that they saw a human-like silhouette ranged between 30 and 80 ms, with a mean of 56.7 ms for the TD individuals and 56.7 ms for the HFASD individuals. Based on the results of this experiment, we set the duration of sub-threshold presentation in the current study at 20 ms.

1.4. VEP recordings

The VEP experiment was conducted in a dimly lit and electrically shielded room. Participants sat in front of the monitor at a viewing distance of 114 cm. VEPs were recorded using a Geodesic EEG system, NetAmps 200 (Electrical Geodesics [EGI], Eugene, OR). A high-density, 128-channel, HydroCel Geodesic Sensor net (EGI) was applied over the scalp of each participant. This net held each electrode in place, and distributed electrodes from the nasion to the inion and from the left to the right mastoid processes at uniform intervals. Each electrode consisted of a silver chloride carbon fiber pellet, a lead wire, a gold-plated pin, and a potassium chloride-soaked sponge. This electrode configuration effectively blocked out electrochemical noise and minimized triboelectric noise. Signals were amplified via an AC-coupled, 128-channel, high-input impedance amplifier (NetAmps 200, EGI). The analog data were digitized at a sampling rate of 500 Hz/channel. Amplified analog voltages were hardware band-pass-filtered at 0.1–200 Hz. The experimenter individually adjusted all sensors until the impedance of each electrode was less than 50 kΩ (Ferree, Luu, Russell, & Tucker, 2001). We used the vertex (Cz) electrode as a reference.

1.5. VEP tasks

Face (fearful, neutral) and object stimuli were randomly presented in six blocks composed of 150 trials with six different stimulus categories: upright fearful faces (150), inverted fearful faces (150), upright neutral faces (150), inverted neutral

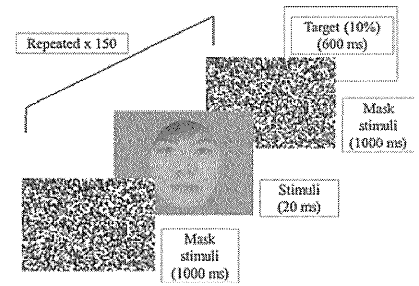

Fig. 2. Experimental procedures. The faces and objects were randomly presented for 20 ms (sub-threshold duration) in the upright or inverted orientations, followed by a 1000 ms pattern mask. The target appears in 10% of the trials in each block and is presented for 600 ms to draw the participant's attention away from the experimental stimuli.

faces (150), upright objects (150), inverted objects (150). These stimuli were presented for 20 ms followed by a pattern mask for 1000 ms. During debriefing, we confirmed that all participants were unable to recognize either the face or object stimuli. The target, which appeared in 10% of the total trials in each block, was intermixed and randomly presented for 600 ms to shift the participant's attention away from the face and object stimuli. Participants were asked to respond by pressing a button as accurately and quickly as possible when they saw the target stimulus appear on the screen (Fig. 2).

Participants were instructed to remain still and to fix their gaze on a black dot at the center of the screen. Arousal level was carefully visually monitored by an observer (T.F.) in the same room and by the EEG signal. We also recorded each participant's activity using a video camera placed outside of the room. If a participant became drowsy, he/she was alerted and provided with a brief rest period.

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

1.6. Data analysis

1.6.1. Behavioral performance

In order to confirm that participants were attending to the target stimuli, we measured the mean reaction time and correct detection rate. The group differences on these measures were evaluated using a two-way analysis of variance (ANOVA) with repeated measures (stimulus orientation × participant group).

1.6.2. VEP data

For the VEP analysis, stimulus epochs began 50 ms prior to stimulus onset and continued for 500 ms after. Epochs containing EEG deviations 50 μV greater than baseline were automatically rejected. Epochs containing blinks, horizontal or non-blink eye movements, analog to digital conversion (A/D) saturation, or obvious occipital α-activity were rejected. The electrodes surrounding the eyes were used to identify blinks and horizontal or non-blink eye movements. They were then re-referenced offline to an average of 99 channels, which represented all channels except for the channels around the eyes, ears, and neck because these channels were easily contaminated by the electric potential of muscles. Finally, in the accepted samples, 550 ms epochs were averaged in each stimulus category using Net Station software (EGI). The number of accepted samples per stimulus category across the participants was at least 120 (80%).

The major VEP components obtained for all participants in both groups were the N1 and P1 peaks, which were recorded over occipital regions (maximum at the Oz electrode). The P300 (maximum at the Pz electrode) was also evoked by the target stimulus in all participants except one HFASD female participant, who did not show the P300 component and was thus excluded from subsequent statistical analyses. Our small sample size increased the possibility of type II error. To address this, we used a two-way ANOVA with repeated measures (stimulus orientation × participant group) to examine group differences in the amplitude and latency of P300 for the target stimuli at the Pz electrode. A three-way ANOVA with repeated measures was also performed to examine the effects of stimulus type, stimulus orientation, and participant group on the amplitudes and peak latencies of the N1 and P1 components at the Oz electrode. Since our research concerns the relative impact of subliminal faces over objects on N1 and P1, SFE scores were further calculated by subtracting the N1/P1 amplitudes or latencies at the Oz electrode for object stimuli (baseline) from those for fearful or neutral face stimuli. This was done for each stimulus orientation, by group. These effects were analyzed using a three-way ANOVA with repeated measures (stimulus type × stimulus orientation × participant group). Bonferroni's correction was used for multiple comparisons. In all statistical analyses, a level of $p < 0.05$ was accepted as statistically significant.

2. Results

2.1. Intellectual function and behavioral performance in target detection

One of the ten participants in the HFASD group was excluded from further analyses because of a complete absence of P300 (see Section 1.6.2). The remaining nine participants (7 males and 2 females, aged 23–39 years, mean age 30.9) exhibited normal IQs (verbal IQ, 105.6 ± 19.1 [mean ± *SD*]; performance IQ, 104.7 ± 14.0; full-scale IQ, 105.7 ± 13.2). There were no significant effects of chronological age (*t* test: $t = -1.266$, $p = 0.22$) or sex (χ^2 test: $\chi^2 = 0.01$, $p = 1.00$) between the two groups. Neither the effect of any variable nor the two-way interaction between stimulus orientation and participant group were significant in terms of mean reaction time or correct detection rates (Tables 1 and 2). These results confirm that the participants in both groups were attentive to nearly the same degree during the experiment.

2.2. VEP responses

2.2.1. P300, N1, and P1 distribution for the TD and HFASD groups

The P300 component (maximum at Pz) was evoked when both groups viewed the target stimuli in the upright and inverted orientations. In terms of P300 amplitude and latency, there were no significant effects or interactions between stimulus orientation and participant group (Tables 1 and 2).

Grand-averaged VEP waveforms at the Oz electrode elicited by each stimulus in the upright and inverted orientations are shown in Fig. 3. In both groups, N1 (around 100 ms) and P1 (around 120 ms) were major components of the elicited waveform. Fig. 4 shows the scalp topography of N1.

2.2.2. Behaviors of N1 and P1 components

As shown in Figs. 3 and 4, the N1 and P1 components were modulated by participant group and stimulus type. The mean peak amplitudes and latencies of N1 and P1 for each stimulus are summarized for each group in Table 3. Table 4 summarizes the results of the ANOVA analysis. The N1 latency and the P1 latency and amplitude were unaffected by the stimulus conditions. However, the N1 amplitudes were modulated: there was a significant interaction effect between stimulus type, stimulus orientation, and participant group ($F(2, 34) = 7.12$, $p < 0.005$). In the TD group, we found a significantly larger N1 amplitude for fearful faces in the upright orientation compared with that for objects in the upright orientation ($p < 0.05$). This was not the case when the faces and objects were inverted. In the HFASD group, there were no significant differences in N1 amplitude among the stimuli in both the upright and inverted orientations.

2.2.3. SFE scores for upright and inverted faces

We calculated the SFE scores for the N1 and P1 peaks for each stimulus and each group (Table 5 and Fig. 5). The results of the ANOVA are summarized in Table 6. A significant 3-way interaction between stimulus type, stimulus orientation, and participant group was found for N1 amplitude only ($F(1, 17) = 9.23$, $p < 0.01$). Multiple comparisons revealed that the SFE score for upright fearful faces in the TD group was significantly greater than that for inverted fearful faces ($p < 0.05$). This finding indicates that faces, specifically fearful but not neutral faces ("emotion effect"), elicited a significantly greater N1 amplitude than objects in the TD group. The SFE was absent when the stimuli were inverted (Table 5 and Fig. 5). In contrast,

Table 1
Performance and P300 in response to the target stimuli in the TD and HFASD groups.

Groups	Stimulus orientation	Performance		P300	
		Reaction time (ms)	Correct detection rate (%)	Amplitude (μV)	Latency (ms)
TD group ($n = 10$)	Upright	446.4 ± 33.4	93.2 ± 5.5	5.5 ± 2.2	341.0 ± 61.2
	Inverted	448.9 ± 53.4	91.3 ± 7.9	5.3 ± 2.2	335.4 ± 30.2
HFASD group ($n = 9$)	Upright	443.0 ± 48.4	88.3 ± 10.2	5.0 ± 5.1	339.6 ± 53.7
	Inverted	442.8 ± 55.7	85.1 ± 9.8	4.7 ± 4.5	370.0 ± 73.8

Data are expressed as mean ± *SD*.

Table 2
Results of two-way ANOVA in performance and P300 in response to the target stimuli.

Factors	Performance				P300			
	Reaction time		Correct detection rate		Amplitude		Latency	
	F-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value
Orient	0.05	0.82	1.60	0.22	0.00	1.00	0.85	0.37
Partic	0.01	0.91	4.38	0.052	0.00	1.00	0.55	0.47
Orient × Partic	0.01	0.93	0.06	0.81	0.00	1.00	1.80	0.20

Abbreviations in this and subsequent tables: Orient, stimulus orientation (upright, inverted); Partic, participant groups (HFASD, TD).

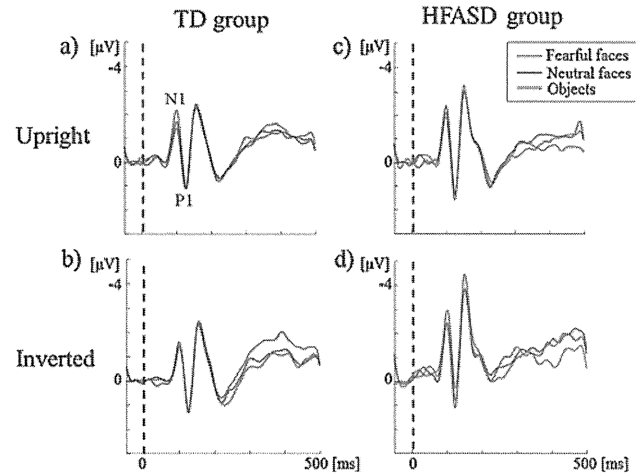

Fig. 3. Grand-averaged VEP waveforms at the Oz electrode in response to each stimulus in the TD ($n = 10$) (a, b) and HFASD ($n = 9$) (c, d) groups. In both groups, the stimulus (in both orientations) elicited the negative component at approximately 100 ms (N1) and the following positive peak at about 120 ms (P1) after stimulus onset.

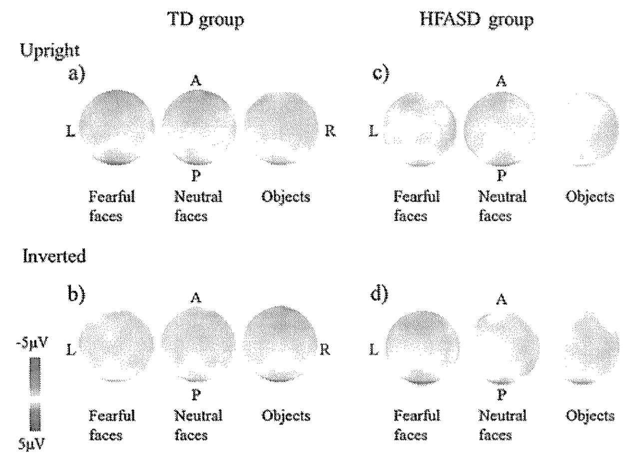

Fig. 4. Grand-averaged scalp topography of the N1 component in the TD ($n = 10$) (at 100 ms) (a, b) and HFASD ($n = 9$) groups (at 100 ms) (c, d). The N1 components were predominant over the occipital regions (maximal at the Oz electrode) when participants in both groups viewed stimuli in both the upright (a, c) and inverted (b, d) orientations. There are substantial differences in the scalp topography between the two groups depending on stimulus type and orientation. L: left, R: right, A: anterior, P: posterior.

the SFE score of the N1 amplitude in the HFASD group did not differ between upright or inverted fearful and neutral faces, indicating the absence of SFE for upright and inverted faces in this group. Between the two groups, the SFE score of the N1 amplitude for fearful faces was significantly larger in the TD group compared with that of the HFASD group in the upright condition ($p < 0.05$) but not the inverted condition (Table 5 and Fig. 5).

Table 3
Peak amplitudes and latencies of N1 and P1 (mean ± *SD*) at the Oz electrode in the TD and HFASD groups.

Stimulus		N1		P1	
		Amplitude (μV)	Latency (ms)	Amplitude (μV)	Latency (ms)
(a) TD group (n = 10)					
Upright	Fearful	2.5 ± 0.7*	99.6 ± 6.3	1.6 ± 2.3	127.0 ± 5.2
	Neutral	2.1 ± 0.9	99.2 ± 7.7	1.7 ± 1.8	127.4 ± 5.9
	Object	1.8 ± 0.7	98.6 ± 9.3	1.7 ± 1.8	126.6 ± 6.4
Inverted	Fearful	2.0 ± 0.7	99.4 ± 9.3	1.7 ± 1.7	127.2 ± 5.7
	Neutral	2.0 ± 1.0	99.4 ± 10.1	1.8 ± 1.7	126.8 ± 5.8
	Object	2.1 ± 0.9	99.8 ± 7.9	1.8 ± 1.8	125.6 ± 6.6
(b) HFASD group (n = 9)					
Upright	Fearful	2.0 ± 1.9	97.6 ± 6.8	1.6 ± 1.5	124.0 ± 3.7
	Neutral	2.3 ± 2.0	98.4 ± 5.1	1.6 ± 1.9	124.0 ± 4.1
	Object	2.2 ± 2.1	97.3 ± 5.7	1.9 ± 2.2	123.0 ± 4.1
Inverted	Fearful	2.9 ± 2.7	98.4 ± 6.2	0.5 ± 1.5	124.0 ± 3.5
	Neutral	2.4 ± 2.6	97.8 ± 6.1	0.9 ± 1.1	124.0 ± 2.8
	Object	2.3 ± 2.5	96.0 ± 5.1	1.3 ± 1.5	122.0 ± 3.5

* Upright fearful face vs. Upright object, $p < 0.05$.

Table 4
Results of three-way ANOVA in N1 and P1.

Factors	N1				P1			
	Amplitude		Latency		Amplitude		Latency	
	F-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value
Stim	1.51	0.24	3.19	0.054	1.99	0.15	5.56	**<0.01**
Orient	0.44	0.52	0.00	0.98	1.54	0.23	3.94	0.06
Partic	0.51	0.48	0.28	0.60	0.31	0.59	2.03	0.17
Stim × Orient	0.56	0.58	0.18	0.84	0.27	0.77	2.06	0.14
Stim × Partic	0.11	0.90	1.87	0.17	1.09	0.35	0.09	0.91
Orient × Partic	1.62	0.22	0.60	0.45	2.66	0.12	0.20	0.66
Stim × Orient × Partic	7.12	**<0.005**	1.64	0.21	0.33	0.72	0.04	0.96

Abbreviations in this and subsequent tables: Stim, stimulus types (neutral faces, feareful faces, objects).
Bold values indicate significance.

Table 5
"Face effect" scores for N1 and P1 (mean ± *SD*) in the TD and HFASD groups.

Stimuli		N1		P1	
		Amplitude (μV)	Latency (ms)	Amplitude (μV)	Latency (ms)
(a) TD group (n = 10)					
Upright	Fearful faces minus Objects	0.8 ± 0.6*, #	1.0 ± 4.8	0.1 ± 1.0	0.4 ± 2.3
	Neutral faces minus Objects	0.3 ± 1.0	0.6 ± 3.1	0.0 ± 0.9	0.8 ± 2.1
Inverted	Fearful faces minus Objects	−0.1 ± 0.6	−0.4 ± 2.6	0.1 ± 0.8	1.6 ± 1.8
	Neutral faces minus Objects	−0.1 ± 0.6	−0.4 ± 3.1	0.0 ± 0.5	1.2 ± 2.1
(b) HFASD group (n = 9)					
Upright	Fearful faces minus Objects	−0.2 ± 1.0	0.2 ± 1.9	0.0 ± 1.0	1.1 ± 2.7
	Neutral faces minus Objects	0.1 ± 0.7	1.1 ± 1.5	−0.2 ± 1.1	1.1 ± 2.7
Inverted	Fearful faces minus Objects	0.6 ± 1.2	1.8 ± 3.5	0.7 ± 1.6	2.0 ± 2.0
	Neutral faces minus Objects	0.1 ± 0.5	2.0 ± 2.4	0.3 ± 1.1	1.8 ± 2.1

* Upright fearful faces minus Objects vs. Inverted fearful faces minus Objects, $p < 0.05$.
\# TD groups vs. HFASD group, $p < 0.05$.
See also Fig. 5.

P1 amplitude, P1 latency, and N1 latency revealed no significant SFE for either fearful or neutral faces in either stimulus orientation and in either group.

3. Discussion

In the present study, we measured VEPs in response to masked subliminal faces and objects to investigate the early stages of visual processing underlying automatic or implicit face processing in adults with HFASD. Our results show that the face stimuli evoked two major occipital components (N1 and P1) in adults with and without ASD, even though the masked faces

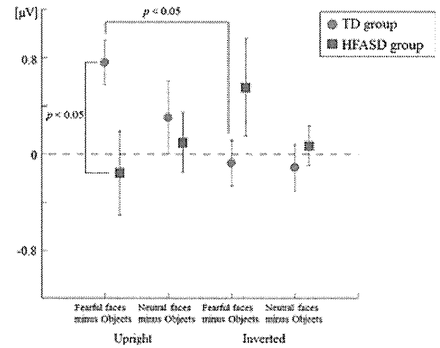

Fig. 5. Differences in N1 amplitude for faces relative to objects between the TD ($n = 10$) (red filled circle) and HFASD ($n = 9$) (blue filled square) groups. In the TD group, the N1 amplitude for fearful faces relative to objects in the upright orientation was significantly larger than that in the inverted orientation ($p < 0.05$) and that of the HFASD group in the upright orientation ($p < 0.05$). Results are shown ± SEM. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 6
Results of three-way ANOVA in "Face effect" score for N1 and P1.

Factors	N1				P1			
	Amplitude		Latency		Amplitude		Latency	
	F-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value	*F*-value	*p*-Value
Stim	1.23	0.28	0.02	0.90	0.85	0.37	0.03	0.87
Orient	0.32	0.58	0.01	0.91	0.22	0.65	1.61	0.22
Partic	0.11	0.74	3.56	0.08	2.14	0.16	0.13	0.72
Stim × Orient	0.91	0.35	0.92	0.35	0.37	0.55	3.01	0.10
Stim × Partic	0.11	0.75	0.18	0.67	0.15	0.70	0.03	0.87
Orient × Partic	5.69	**<0.05**	1.42	0.25	0.26	0.62	0.05	0.82
Stim × Orient × Partic	9.23	**<0.01**	2.64	0.12	0.48	0.50	0.03	0.88

Bold values indicate significance.

were not consciously perceived. Consistent with our prediction, the SFE was not found in the early visual processing of adults with HFASD, whereas the SFE was observed in TD adults. More specifically, TD adults exhibited enhanced neural activity in response to fearful faces presented at sub-threshold compared with objects ("emotion effect"), reflected in the earliest VEP component (N1). To our knowledge, this is the first neurophysiological evidence for altered early visual processing of briefly perceived emotional faces in individuals with ASD, consistent with the findings reported in behavioral studies (Hall, West, & Szatmari, 2007; Kamio et al., 2006a).

The observed group difference in the N1 response pattern cannot be explained by attention levels, since the target detection task revealed that adults with HFASD did not differ from TD adults in either behavioral performance or P300 responses to the target stimuli. Therefore, we suggest that the distinct neural response observed in the V1 of TD adults was specific to perception of fearful faces in our study.

3.1. "Subliminal face effect" in TD

The TD group demonstrated a fearful face-specific SFE under the upright condition. This can be explained by the effect of low SF information on faces. Itier and Taylor (2004) proposed that low-level spatial information is critical in discriminating faces from objects. For instance, images of fearful faces with a low SF elicited a larger P1 relative to neutral faces with a low SF, while this emotional effect was not observed in high SF faces (Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005). In humans, visual images containing low and high SF information are processed by distinct neural channels. The magnocellular channel is responsible for processing low SF (holistic) information (Tobimatsu & Celesia, 2006). Therefore, the observed increase in N1 in response to upright fearful faces in TD adults may reflect activation of the magnocellular system within the V1. This system may work to enable the rapid identification of upright fearful faces.

It is possible that subcortical fast face processing contributed to the observed alterations in the N1 in our study because the upright SFE was specific to fearful faces ("emotion effect"). The subcortical system involved in the non-conscious perception of emotional stimuli is known to interact with cortical areas (Tamietto & de Gelder, 2010). For example, the amygdala response to emotional stimuli (in particular, low SF stimuli) has been found to arise automatically, without explicit attention or awareness (Jiang & He, 2006; Morris, Ohman, & Dolan, 1999; Whalen et al., 1998; Vuilleumier et al., 2003). A magnetoencephalographic study demonstrated that early-latency neural networks, including the amygdala (just after 100 ms), might be sensitive to fearful faces (Streit et al., 2003). Therefore, rapid processing within the subcortical pathways may also have contributed to the differential response to fearful faces at the V1 level in TD adults.

Unfortunately, we could not replicate the SFE in neutral faces (Mitsudo et al., 2011). This was probably caused by a slight difference in the face stimuli (they were trimmed to remove the hairline) and the differences between study populations. Since the holistic processing of faces relies on low SF information, our findings partly support the idea that low SF facilitates fearful face perception.

3.2. Lack of the "subliminal face effect" in HFASD

In the present study, HFASD adults exhibited no signs of SFE, as reflected by the unaltered N1 for stimuli of different types and orientations. Since the TD group did not show upright SFE for neutral faces, we suggest that at least emotional face information conveyed by low SF is impaired in HFASD. Correspondingly, neuropsychological studies have demonstrated impaired low SF processing in people with ASD. Compared with control participants, children with ASD performed better when given high rather than low SF information during a face-matching task (Deruelle, Rondan, Gepner, & Tardif, 2004). Another neuropsychological study compared emotional recognition between adult individuals with Asperger syndrome and normal controls by manipulating the SF content of emotional faces (Kätsyri, Saalasti, Tiippana, von Wendt, & Sams, 2008). Given images with a very low SF, the participants with Asperger syndrome were less accurate than controls in recognizing facial emotions, but this was not the case when given non-filtered stimuli (Kätsyri et al., 2008). Further, several psychological and physiological studies using magnocellular stimuli (such as motion stimuli) have found deficient magnocellular function in people with ASD (Spencer et al., 2000; Sutherland & Crewther, 2010). Therefore, V1 magnocellular function (related to low SF processing) may be impaired in adults with HFASD. Alternatively, it is possible that the lack of SFE in the N1 amplitude in our HFASD participants was caused by impaired amygdala function, because the amygdala is sensitive to emotional stimuli (particularly low SF stimuli; Vuilleumier et al., 2003). Adolphs, Sears, and Piven (2001) investigated the recognition of emotional and social information, primarily from faces, in autism. They found that the behavioral data of subjects with autism showed atypical social evaluations from faces similar to neurological subjects with focal amygdala damage (Adolphs et al., 2001). In functional magnetic resonance imaging (fMRI) studies, individuals with ASD showed decreased amygdala activity while making mental inferences from eyes and faces (Ashwin, Baron-Cohen, Wheelwright, O'Riordan, & Bullmore, 2007; Baron-Cohen et al., 2000). Another fMRI study reported reduced activation in the amygdala, pulvinar, and superior colliculi as well as in the fusiform gyrus while HFASD adults processed briefly presented (23.4 ms) masked fearful faces (Kleinhans et al., 2011). Several studies have suggested that individuals with ASD have decreased cortico-subcortical (Bookheimer, Wang, Scott, Sigman, & Dapretto, 2008) and cortico-cortical (Bird, Catmur, Silani, Frith, & Frith, 2006; Koshino et al., 2008) connectivity during face processing. Our results may be interpreted as reflecting this insufficient circuitry, which could affect the rapid, automatic, or implicit aspects of cortical and subcortical face processing in people with ASD.

3.3. Clinical implications of abnormal automatic face processing in people with HFASD

Interestingly, the effect of subliminal fearful faces on the N1 in the control adults in our study disappeared when the faces were inverted. That this phenomenon occurred during non-conscious face perception is consistent with psychophysical (Zhou, Zhang, Liu, Yang, & Qu, 2010) and event-related potential (Mitsudo et al., 2011) findings. Mitsudo et al. (2011) reported an increased early P1 response that was present for upright faces but not for objects. This difference between stimuli disappeared when the stimuli were inverted (Mitsudo et al., 2011). In another study, the conventional behavioral face inversion effect was reflected in the N170 component (occipitotemporal region) with an increase in amplitude and a delayed latency (Jacques et al., 2007). This effect was not present in the N1/P1 components (early occipital region) (Mitsudo et al., 2011). Thus, the response patterns between the subliminal upright and inverted faces i.e., the SFE, in this and previous studies (Mitsudo et al., 2011) are clearly different from the conventional supra-threshold face inversion effect.

There have been many reports showing a lack of or a reduced explicit supra-threshold face inversion effect in adults with HFASD (Dawson et al., 2002; Gauthier, Klaiman, & Schultz, 2009; Hobson, Ouston, & Lee, 1988; Joseph & Tanaka, 2003; Lahaie et al., 2006; Langdell, 1978; Webb et al., 2012). However, to our knowledge, we are the first to report a lack of early occipital sensitivity to face inversion in subliminal faces in people with ASD. Although the underlying neural mechanisms remain controversial, our findings support the notion that individuals with ASD have altered subcortical face processing. Recently, Bookheimer et al. (2008) investigated the neural basis of inverted face processing in ASD by using fMRI with a face matching task, though they used supra-threshold face stimuli. They found significant differences in brain activation between ASD and TD groups in the prefrontal cortex and the amygdala, and not in the FFA (Bookheimer et al., 2008). These findings may converge with our neurophysiological findings to imply the presence of an altered subcortical pathway in people with ASD, resulting in altered face processing.

3.4. Methodological limitations

Our sample size was small, considering the heterogeneity of autism. Thus, a much larger sample size will be needed to better understand how face processing varies amongst individuals with HFASD. ANOVA is a relatively robust analysis tool, even for a small sample size. Therefore, we believe that the lack of SFE in individuals with HFASD truly reflects underlying pathophysiology. The intellectual function of the control participants was not assessed by cognitive testing, and was not matched between those in the HFASD and TD groups. To what degree the difference in intellectual function between the two groups affected the VEP findings is unclear. For the purpose of clinical diagnoses, we did not use standard tools such as the Autism Diagnostic Interview – Revised or the Autism Diagnostic Observation Schedule because the Japanese versions of these tests were not available at the time. Instead, we used a widely used scale (PARS) with high sensitivity and high specificity in Japanese populations to identify individuals with ASD (Kamio et al., 2006b).

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Qualitative analyses of verbal fluency in adolescents and young adults with high-functioning autism spectrum disorder

Eiko Inokuchi, Yoko Kamio *

Department of Child and Adolescent Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8553, Japan

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ABSTRACT

Systematic qualitative analyses of verbal fluency might aid our understanding of the characteristic cognitive processes in individuals with autism spectrum disorder (ASD). In this study, we compared through qualitative and quantitative analyses performance on letter fluency (LF), category fluency (CF), and action fluency (AF) in adolescents and young adults with high-functioning autism spectrum disorders (HFASD) with that of an age-, gender-, and IQ-matched control group. Quantitative analyses revealed significantly fewer correct responses on category and action fluency and significantly more intrusions on category fluency in individuals with HFASD than in control participants. Qualitative analyses revealed significantly fewer semantic clusters and significantly more phonemic clusters during action fluency in individuals with HFASD compared to control participants. With respect to action fluency, the number of correct responses and clusters were related to verbal IQ for individuals with HFASD but not for control participants. We discuss these results in terms of abnormalities in semantic/phonemic strategy choice, cognitive flexibility, and generativity in ASD.

1. Introduction

Autism spectrum disorder (ASD) is one of the neurodevelopmental disorders characterized by social and communication deficits and repetitive/stereotyped behavior. Evidence suggests that higher-order brain dysfunctions, including executive dysfunction, in ASD might be attributable to atypical neural development of the frontal lobe, possibly starting early in life and persisting over a long period (Ben Bashat et al., 2007; Carper & Courchesne, 2000; Courchesne, Campbell, & Solso, 2011; Hazlett et al., 2011; Noriuchi et al., 2010). Executive dysfunction in ASD involves aspects of planning and monitoring, the inhibition of prepotent behaviors (Hughes, Russell, & Robbins, 1994; Ozonoff, Pennington, & Rogers, 1991; Prior & Hoffmann, 1990), cognitive flexibility (Hughes et al., 1994; Ozonoff & Jensen, 1999; Ozonoff et al., 1991), and generativity (Lopez, Lincoln, Ozonoff, & Lai, 2005; Turner, 1997) among other functions.

Verbal fluency tests are widely used to assess executive function, especially cognitive flexibility and generativity (Tröster et al., 1998; Troyer, Moscovitch, & Winocur, 1997; Troyer, Moscovitch, Winocur, Alexander, & Stuss, 1998). The three kinds of verbal fluency tests are letter fluency (LF), category fluency (CF), and action fluency (AF). LF requires a search for words beginning with a particular letter to inhibit recall by semantic association (Crowford, Parker, & McKinlay, 1992); CF requires a search for words belonging to a particular semantic category; and AF requires generation of verbs in the

* Corresponding author. Tel.: +81 42 341 2711; fax: +81 42 346 1978.
E-mail address: kamio@ncnp.go.jp (Y. Kamio).

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absence of prompting stimuli (Piatt, Fields, Paolo, Koller, & Tröster, 1999). The latter test is considered more sensitive to executive function than the LF or CF tests (Woods et al., 2005; Woods, Weinborn, Posada, & O'Grady, 2007).

Previous research on verbal fluency in individuals with autism appears somewhat inconsistent. As for LF, some studies have reported that children and adults with ASD can produce as many words as verbal ability-matched controls using the letters F, A, and S (Barnard, Muldoon, Hasan, O'Brien, & Stewart, 2008; Minshew, Goldstein, Muenz, & Payton, 1992; Minshew, Goldstein, & Siegel, 1995; Rumsey & Hamburger, 1988). However, Spek, Schatorjé, Scholte, and van Berckelaer-Onnes (2009) have found that adults with high-functioning autism spectrum disorder (HFASD) performed worse than controls using the letter M. As for CF, some studies demonstrated that children and adults with ASD generated fewer correct responses than verbal ability-matched controls (Dichter, Lam, Turner-Brown, Holtzclaw, & Bodfish, 2009; Minshew et al., 1992; Spek et al., 2009), whereas other studies reported that they produced as many words as their controls using the "animal" category (Dunn, Gomes, & Sebastian, 1996; Minshew et al., 1995). However, Dunn et al. (1996) found that children with ASD produced fewer prototypical nouns than did control children. To our knowledge, there have been no studies reporting on ASD and AF.

To explore the cognitive processes underlying verbal fluency, Troyer et al. (1997) focused on clustering and switching. They defined clustering as the ability to generate words in a certain semantic or phonemic subcategory, which is considered more efficient for word generation than a disorganized search. They defined switching as the ability to shift from one cluster to another to avoid slowing down (Troyer et al., 1997). Clustering in terms of cluster size (i.e., the number of words within one cluster) reflects word storage (Abwender, Swan, Bowerman, & Connolly, 2001; Raskin, Sliwinski, & Borod, 1992; Troyer et al., 1997). Switching in terms of the number of clusters reflects cognitive flexibility (Abwender et al., 2001; Tröster et al., 1998; Troyer et al., 1997, 1998). In a study on LF and CF in children with HFASD, Turner (1999) suggested that the poorer performance of these children relative to control children might be attributable to a failure to use phonemic or semantic strategies to improve performance, rather than an inability to produce multiple responses per se. On the other hand, Spek et al. (2009) found that adults with HFASD exhibited significantly impaired performance on both LF and CF tasks. They reasoned that because these adults and their verbal ability-matched controls exhibited similar frequency of clustering or switching during LF and CF, their poorer performance on verbal fluency tests was not attributed to insufficient use of strategies or to difficulties switching between strategies, but rather to the relatively low processing speed found in adults with HFASD.

Currently, insufficient evidence exists to draw any conclusions about the utility of verbal fluency tests for individuals with ASD. However, systematic qualitative analyses of verbal fluency might contribute to our current understanding of the characteristic cognitive processes in individuals with ASD. Therefore, the aim of this study was to determine whether adolescents and young adults with HFASD exhibit impaired performance on the LF, CF, and AF verbal fluency tests, and if they do, to determine which test is more sensitive and whether the atypical cognitive strategies identified, such as clustering or switching, are associated with such impairments in these individuals. Here we conducted LF, CF, and AF tests, determined cluster-related indices, and compared conventional quantitative scores (e.g., number of total responses or errors) between adolescents and young adults with HFASD and control participants matched by gender, age, verbal IQ (VIQ), performance IQ (PIQ), and full scale IQ. We also examined the relationship between verbal fluency performance and age or IQ to explore possible developmental plasticity and compensation.

2. Material and methods

2.1. Participants

We recruited participants from psychiatric clinics and local schools. Both authors, who are experienced child psychiatrists, diagnosed participants in the HFASD group (n = 30; 8 with autistic disorder, 14 with Asperger's disorder, 8 with pervasive developmental disorder-not otherwise specified) based on clinical information according to the DSM-IV-TR (American Psychiatric Association, 2000). We confirmed that control participants (n = 18) had no history of head injury, neurological disorder, or severe psychiatric disorder, although two control participants were diagnosed with social anxiety disorder, two with generalized anxiety disorder, one with an adjustment disorder, and one with a manic episode that had occurred 3 years earlier but was in remission at the time of participation. Diagnostic agreement was obtained for all participants (n = 48).

Some participants were receiving medication, although the amount was small (14/30 participants with HFASD, specifically 4 atypical antipsychotics, 6 selective serotonin reuptake inhibitors, 4 mood stabilizers; and 10/18 control participants, specifically 2 atypical antipsychotics, 5 selective serotonin reuptake inhibitors, and 3 mood stabilizers). The proportion of participants taking medication did not significantly differ between the two groups (χ^2 test). The mental conditions of all participants were stable at the time of participation. All participants had sufficient verbal and cognitive abilities as measured by the Japanese version of the WAIS-R, with no significant group differences (full scale IQ: t = .59; VIQ: t = .40; PIQ: t = .74). The gender ratio (5:1) was identical and mean chronological age (CA) did not significantly differ between groups (t = 1.23) (Table 1).

The protocol of this study was approved by the Ethics Committee of the National Center of Neurology and Psychiatry, Japan and was performed in accordance with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from the parent of each minor participant and each adult participant.

Table 1
Demographic characteristics of participants.

Parameter		HFASD (n = 30)	Control (n = 18)
Age (years)	Mean (SD)	19.2 (2.6)	20.1 ± 2.0
	Range	16:00–25:11	16:01–24:03
Gender	M: F	25:5	15:3
Verbal IQ	Mean (SD)	101.9 (13.9)	103.5 (12.4)
	Range	76–134	80–121
Performance IQ	Mean (SD)	96.4 (14.0)	99.6 (15.5)
	Range	72–128	78–134
Full scale IQ	Mean (SD)	99.6 (12.8)	101.9 (13.9)
	Range	74–121	78–126

Note: IQ: intelligence quotient; HFASD: high-functioning autism spectrum disorder.
None of the parameters exhibited significant group differences.

2.2. Task

Letter fluency (LF): For words beginning with the Japanese syllables "a", "ka", and "shi" (Ito, Hatta, Ito, Kogure, & Watanabe, 2004), participants were asked to generate as many words as possible within 60 s. The mean number of correct responses by healthy Japanese adolescents and adults (aged 18–30 years) was 11.2 (SD 3.5), 12.6 (3.0), and 10.3 (3.5), respectively (Ito et al., 2004).

Category fluency (CF): For words in the "animal", "sport", and "vehicle" categories, participants were asked to generate as many words as possible within 60 s. The mean number of correct responses by Japanese healthy adults aged 18–30 years for "animal" was 18.0 (SD 3.6), and that for "sport" was 16.1 (3.6) (Ito et al., 2004). To our knowledge, the Japanese reference value for "vehicle" in adults has not been reported, but we chose this category expecting it would generate a sufficient number of related words from participants with ASD. We considered that if they produced too few words due to poor vocabulary, true qualitative analysis would be impossible.

Action fluency (AF): Following the protocol of Piatt et al. (1999), participants were asked to generate words describing what people do without using the same word with different endings, such as eat, eating, and eaten. The mean number of correct responses by healthy adults aged 22–66 years was 18.2 (Woods et al., 2005), but no Japanese norm has been reported.

Each task was administered with instructions to refrain from repeating words and saying proper nouns. Before each trial, participants practiced LF ("sa") and CF ("fruit") tasks to confirm that they understood the instructions. We examined each participant individually. Order of the LF, CF, and AF tests was counterbalanced among participants.

2.3. Scoring

2.3.1. Quantitative analyses

We counted the number of total responses, correct responses, and errors for LF, CF, and AF, respectively. We classified errors into perseverations and intrusions. If there were any proper nouns among intrusions, we counted the number of proper nouns.

2.3.2. Qualitative analyses

A semantic cluster was defined as a group of successively generated words belonging to the same semantic subcategory (Raskin et al., 1992; Troyer et al., 1997). The subcategory exemplars under the animal category were "pet", "farm animal", "bird", "carnivorous", "insect", or "fish". In cases of AF, a group of words expressing "gross motor" (e.g., stand up, walk, or jump), "vital activities" (e.g., sleep or wake up), and "prosocial behaviors" (e.g., help or encourage) were treated as subcategories. A phonemic cluster was defined (as per Troyer et al.'s studies) as a group of successively generated words beginning with the same two syllables (e.g., a/sa/hi [meaning "rising sun"] and a/sa/ga/o [meaning "morning glory"]). Although clusters were defined as two or more related words (Abwender et al., 2001; Koren, Kofman, & Berger, 2005), in the present study we counted cluster size starting with the first word but not the second word in a cluster. We used the number of clusters as a measure of cognitive flexibility, in accordance with Koren et al. (2005).

3. Results

3.1. Quantitative analyses

3.1.1. LF

We observed no significant group differences in the mean number of total responses, correct responses, perseverations, intrusions, or proper nouns when "a", "ka", and "shi" trials were combined (Table 2). However, for separately compared trials, the HFASD group generated significantly more intrusions in the "ka" trial than did the control group ($U = 203.0$, $p < 0.05$, $r = .37$) with a moderate-sized between-group difference.

Table 2
Results of quantitative analyses on letter fluency of the HFASD and control groups.

Quantitative index	HFASD	Control	p
Total			
Total responses	30.53 ± 11.93	32.78 ± 8.37	
Correct responses	28.77 ± 11.94	32.11 ± 8.22	
Perseverations	0.16 ± 0.59	0.056 ± 0.23	
Intrusions	1.63 ± 3.06	0.61 ± 1.14	
Proper nouns	1.40 ± 2.85	0.50 ± 1.04	
"a" trial			
Total responses	9.63 ± 4.01	11.05 ± 3.68	
Correct responses	8.83 ± 3.80	10.61 ± 3.63	
Perseverations	0.033 ± 0.18	0.055 ± 0.23	
Intrusions	0.76 ± 1.25	0.38 ± 0.77	
"ka" trial			
Total responses	11.36 ± 4.64	12.05 ± 3.47	
Correct responses	10.80 ± 4.58	12.00 ± 3.48	
Perseverations	0.10 ± 0.40	0	
Intrusions	0.46 ± 0.93	0.055 ± 0.23	*
"shi" trial			
Total responses	9.56 ± 4.38	9.66 ± 2.93	
Correct responses	9.13 ± 4.71	9.50 ± 2.74	
Perseverations	0.033 ± 0.18	0	
Intrusions	0.40 ± 1.45	0.16 ± 0.38	

Note: HFASD: high-functioning autism spectrum disorder.
*$p < 0.05$.

3.1.2. CF

The HFASD group generated significantly fewer total responses and correct responses, and more intrusions than did the control group in combined "animal", "sport", and "vehicle" trials with moderate effect size ($U = 173.5$, $p < .05$, $r = .38$; $U = 158.5$, $p < 0.05$, $r = 0.43$; $U = 183.0$, $p < 0.05$, $r = 0.43$, respectively; Table 3).

For each trial, the HFASD group produced significantly fewer correct responses for "animal" and "sport", and tended to generate significantly fewer responses for "vehicle" ($U = 174.0$, $p < 0.05$, $r = 0.38$; $U = 173.5$, $p < 0.05$, $r = 0.38$; $U = 183.5$, $p = 0.058$, respectively) than did the control group. The HFASD group had significantly more intrusions for "sport" and "vehicle" than did the control group ($U = 202.5$, $p < 0.05$, $r = 0.37$; $U = 176.5$, $p < 0.05$, $r = 0.37$, respectively).

Table 3
Results of quantitative analyses on category fluency of the HFASD and control groups.

Quantitative index	HFASD	Control	p
Total			
Total responses	42.40 ± 14.07	48.44 ± 8.61	*
Correct responses	41.07 ± 13.2	48.05 ± 8.41	*
Perseverations	0.30 ± 0.65	0.33 ± 0.59	
Intrusions	1.03 ± 1.93	0.056 ± 0.23	*
Proper nouns	0.30 ± 0.93	0	
"animal" trial			
Total responses	17.66 ± 6.99	20.50 ± 4.90	*
Correct responses	17.46 ± 7.07	20.33 ± 4.86	*
Perseverations	0.10 ± 0.40	0.16 ± 0.51	
Intrusions	0.10 ± 0.54	0	
"sport" trial			
Total responses	13.26 ± 4.92	15.22 ± 3.38	†
Correct responses	12.80 ± 4.71	15.00 ± 3.41	*
Perseverations	0.066 ± 0.25	0.16 ± 0.38	
Intrusions	0.40 ± 0.67	0.055 ± 0.23	*
"vehicle" trial			
Total responses	11.45 ± 3.61	12.72 ± 3.26	
Correct responses	10.80 ± 3.21	12.72 ± 3.26	†
Perseverations	0.13 ± 0.40	0	
Intrusions	0.53 ± 0.97	0	*

Note: HFASD: high-functioning autism spectrum disorder.
*$p < 0.05$, †$p < 0.1$.

Table 4
Results of quantitative analyses on action fluency of the HFASD and control groups.

	HFASD	Control	p
Quantitative index			
Total responses	14.90 ± 6.63	17.22 ± 4.31	0.069
Correct responses	12.53 ± 6.69	16.56 ± 4.23	*
Perseverations	0.13 ± 0.35	0.28 ± 0.46	
Intrusions	2.23 ± 4.60	0.39 ± 0.7	

Note: HFASD: high-functioning autism spectrum disorder.
$^*p < 0.05$.

3.1.3. AF

The HFASD group generated significantly fewer total correct responses ($U = 150.0$, $p < 0.05$, $r = 0.33$) compared to the control group, with a moderate effect size (Table 4). Total responses tended to be fewer in the HFASD group than in the control group ($U = 185.0$, $p = 0.069$).

The mean number of correct responses by the control group for each trial was almost comparable to those reported in previous studies (Ito et al., 2004; Mitrushina, Boone, Razani, & D'Elia, 2005; Woods et al., 2005).

3.1.4. Relationship between number of correct responses and age, VIQ, or PIQ

To investigate whether underlying cognitive processes differed between the two participant groups, we conducted forced entry regression with age, VIQ, and PIQ as predictor variables and the number of correct responses as a criterion variable. For AF, VIQ was a significant predictor of the number of correct responses in the HFASD group ($R^2 = 0.22$, $p < 0.05$), whereas no such relationship was found in the control group. For LF and CF, neither age nor VIQ or PIQ in either group was significantly correlated with the number of correct responses.

3.2. Qualitative analyses: mean cluster size and number of clusters (Table 5)

We analyzed mean cluster size and number of clusters using a two-way ANOVA with a between-subject factor, Group (HFASD and control) and a within-subject factor, Strategy (semantic and phonemic), for each of the three verbal fluency tests.

3.2.1. LF

Neither mean cluster size nor number of clusters differed significantly between the groups. The number of semantic clusters in the HFASD group tended to be significantly fewer than that in the control group ($U = 187.5$, $p = 0.069$).

Table 5
Results of qualitative analyses of the HFASD and control groups.

Qualitative index	HFASD	Control	p
Letter fluency			
Mean cluster size			
Semantic	2.03 ± 1.11	1.97 ± 0.75	
Phonemic	1.97 ± 1.14	1.75 ± 1.03	
Number of clusters			
Semantic	1.66 ± 1.22	2.17 ± 1.36	0.069
Phonemic	2.75 ± 2.31	2.20 ± 2.47	
Category fluency			
Mean cluster size			
Semantic	2.68 ± 0.75	2.46 ± 0.64	
Phonemic	1.82 ± 0.66	1.83 ± 0.64	
Number of clusters			
Semantic	9.38 ± 4.15	11.46 ± 4.44	
Phonemic	2.02 ± 1.36	2.03 ± 0.94	
Action fluency			
Mean cluster size			
Semantic	2.68 ± 1.03	2.70 ± 0.45	
Phonemic	0.90 ± 1.08	0.44 ± 0.88	
Number of clusters			
Semantic	2.98 ± 1.53	4.28 ± 1.53	*
Phonemic	0.50 ± 0.62	0.20 ± 0.48	*

Note: HFASD: high-functioning autism spectrum disorder.
$^*p < 0.05$.

3.2.2. CF

Neither mean cluster size nor number of clusters differed significantly between the groups.

3.2.3. AF

Although we found no significant group differences for mean cluster size, the number of both semantic and phonemic clusters significantly differed by group. The HFASD group had significantly fewer semantic clusters and significantly more phonemic clusters than the control group ($U = 174.5$, $p < 0.05$, $r = 0.40$; $U = 181.0$, $p < 0.05$, $r = 0.26$, respectively).

3.2.4. Relationship between number of clusters and age, VIQ, or PIQ

To investigate the association between switching and age, VIQ, or PIQ for each group, we calculated Spearman's rank correlation coefficient for LF, CF, and AF, respectively. A significant correlation was found only between the total number of clusters for AF and VIQ in the HFASD group ($\rho = 0.50$, $p < 0.01$).

4. Discussion

To our knowledge, this study is the first to examine AF in individuals with ASD, specifically HFASD, and to identify both quantitative and qualitative abnormalities. Our main finding was that, among three types of verbal fluency tests, AF most discriminated adolescents and young adults with HFASD from matched controls using qualitative as well as conventional quantitative analyses. That is, during AF, adolescents and young adults with HFASD in our study produced fewer correct responses and used a different strategy for switching from one cluster to another compared to control participants. On the other hand, only number of correct responses and intrusions differed significantly between the two groups for CF, while we found no significant group differences for LF.

A small number of clusters is considered to reflect deficits of cognitive flexibility (Abwender et al., 2001; Reverberi, Laiacona, & Capitani, 2006; Tröster et al., 1998; Troyer et al., 1997, 1998). We observed a smaller number of semantic clusters for AF in individuals with HFASD, which is consistent with the previous study of Boucher (1988) in which children with HFASD failed at word generation without category cues. In our study, because LF and CF instructions contained cues, participants of both groups appeared similarly to depend on a phonemic strategy for LF and a semantic strategy for CF. On the other hand, AF involved word generation without cues. These differing test requirements might explain why AF was the most sensitive in discriminating individuals with HFASD from control participants in our study.

For AF, individuals with HFASD produced significantly more phonemic clusters than control participants. This relatively enhanced phonemic strategy appears to compensate for diminished semantic processing (Fein et al., 1996; Kamio, Robins, Kelley, Swainson, & Fein, 2007; Minshew & Goldstein, 2001; Rumsey & Hamburger, 1988; Toichi & Kamio, 2003). Further, the total number of clusters produced by those with HFASD was significantly correlated with VIQ, although we found no correlation for control participants. Similarly, the number of correct responses produced by those with HFASD was significantly correlated with VIQ, and we found no correlation for control participants. This overall overdependence on VIQ while individuals with HFASD were performing the AF task appears to reflect atypical cognitive processes underlying word generation without cues in ASD.

As for response number during LF, our results are consistent with those of most previous studies (Barnard et al., 2008; Minshew et al., 1992, 1995; Rumsey & Hamburger, 1988). As for the response numbers during CF, our results are also in line with most previous studies (Dichter et al., 2009; Minshew et al., 1992; Spek et al., 2009). Moreover, we found a discrepancy between quantitative and qualitative analyses for CF which is also consistent with the study by Spek et al. (2009) in which adults with HFASD produced fewer responses but exhibited unimpaired switching from one semantic cluster to another. Although Spek et al. (2009) concluded that the fluency deficits of the participants with HFASD could not be attributed to insufficient use of strategies or to difficulties in switching between strategies, our results based on three verbal fluency tests provide evidence that atypical use of switching in adults with HFASD underlies fluency deficits.

Finally, participants with HFASD generated significantly more intrusions in our study, whereas control participants rarely did so. One explanation is that those with HFASD have difficulty inhibiting inappropriate responses in the current context (Hughes et al., 1994; Ozonoff et al., 1991; Prior & Hoffmann, 1990). For example, intrusions occurred in the "sports" trial, including "muscle training", "horse racing", or "Japanese chess". Among the intrusions, only the HFASD group generated proper nouns during CF, suggesting that this group failed to use an appropriate semantic strategy. In a case study of proper name hypermnesia in an autistic "savant" subject, Mottron, Belleville, and Stip (1996) proposed that their subject memorized lists of proper names without using semantic strategies and instead relying on the items' non- hierarchical surface characteristics.

5. Conclusions

This study demonstrated that adolescents and young adults with HFASD had poor performance on the CF and AF tests. In particular, AF testing seemed most sensitive to abnormalities in semantic/phonemic strategy choice, cognitive flexibility, and generativity in ASD. However, we need more evidence about AF to draw any conclusion about its specificity to ASD. Because previous verbal fluency studies reported that girls generated more phonemic clusters and showed greater cognitive flexibility than boys (Abwender et al., 2001; Koren et al., 2005), further research is needed to explore sex differences and developmental changes in verbal fluency in individuals with ASD.

Conflicts of interest

The authors declare that they have no conflict of interest.

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第107回日本精神神経学会学術総会

シンポジウム

小・中学校におけるエビデンスにもとづく学校精神保健の課題

神尾 陽子, 森脇 愛子, 井口 英子, 稲田 尚子,
武井 麗子, 黒田 美保, 中鉢 貴行, 高橋 秀俊
(国立精神・神経医療研究センター精神保健研究所児童・思春期精神保健研究部)

成人期の精神障害の約半数は児童期に初発症状があったとされ，児童期の精神障害／症状への早期介入はQOLを長く高く維持するのに重要であることが以前よりも認識されてきた．しかしながら，児童期のどのような精神症状が後の精神障害を予測しうるのか，すなわち早期介入のターゲットとすべき精神症状は何なのかについてはまだ十分にわかっていない．最近，通常学級に在籍する小学生を対象として私たちが地域ベースで行った疫学研究から，平均知能を持ちながら自閉症スペクトラム障害（ASD）の診断のある子どもは合併精神医学的障害または閾下の精神症状を高率に有することが明らかとなり，さらに通常学級に在籍する小中学生を対象とした質問紙による全国調査から，自閉症症状／特性の高い子どもは臨床レベルの情緒や行動の問題を高率に有し，その割合が年齢に無関係に高いことが明らかになった．多数存在するASD診断閾下の子どもにおいても，ASD診断の有無にかかわらず，メンタルヘルスの問題を高率に持ちやすい．自閉症症状／特性の高い子どもではメンタルヘルスの問題が自然回復しにくい可能性がある．子どものメンタルヘルスという観点からは，発達面のスクリーニングを行い，発達／教育支援のニーズを把握すると同時に，就学前からメンタルチェックをする機会を設け，特に自閉症症状／特性の高い子どもについては，就学後は学校精神保健の枠組みで定期的なチェックをすることが後の精神障害の予防につながるものと考えられる．精神医学的ニーズを早期に発見するためには，毎日の学校現場での観察を通した子どものメンタルヘルスについての深い理解と，それを家族や医療などのメンタルヘルス専門家と共有できる校内でのサポート体制が重要と考えられる．そのような学校精神保健システムにサポートされた学校教育はさまざまなニーズを持った子どもとその家族に柔軟に対応でき，ひいては良好なQOLが期待できるものと思われる．

＜索引用語：情緒障害，行動障害，自閉症，児童期，合併＞

はじめに

子どもが示す不安や恐怖などの情緒の問題，または多動や攻撃などの行為の問題は，治療を必要とする精神医学的問題の可能性があるにもかかわらず，いまだに「問題児」，あるいは親のしつけの問題，などの誤解やスティグマを受け，治療へのアクセスが遅れることは稀ではない．大規模な前向き研究からは，幼児期の情緒や行動の障害が，成人期の不安や気分の障害または行動の病理とある程度連続することが示されている[1]．また大規模な後ろ向き研究からも，成人期の不安や気分の障害などの約半数が児童期になんらかの精神症状を初発していたことが報告されている[10]．しかしながら，児童期の精神病理の長期経過は環境の影響を大きく受けるため，当然のことであるが直線的に予測できるものではなく[7]，児童期のどのような精神症状が後の精神障害を予測しうるのか，すなわち，どの精神症状を早期介入のターゲットとすべきであるかはまだ十分にわかっていない．

一方，児童期早期に発症する発達障害は，発症

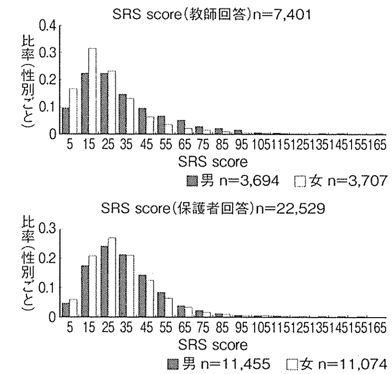

図1　一般児童における自閉症症状／特性の分布
教師回答は，142小学校，69中学校の計2,769学級の担任教師が回答した．対象児童生徒は，学級内で一定数をあらかじめ決められた一定のルールで選び，その選択は恣意的でない．保護者回答は，148小学校，71中学校の児童生徒87,548人の保護者に依頼し，回収できた25,779人（回収率29.4%）中欠損のない22,529人の回答のみを解析対象とした．

年齢が低いこと，生涯にわたって持続するために早期介入がきわめて重要な症候群である．なかでも，自閉症スペクトラム障害（autism spectrum disorders：ASD，DSM-IV-TRでは広汎性発達障害に概当）は近年高い有病率が報告されており，「ありふれた疾患（common disease）」とみなされる．しかしながら，その大部分を占める，平均知能を有する高機能ASD者の多くが，社会的機能が悪いにもかかわらず，未診断，未治療であることがわかってきた[6,11]．高機能ASD児の多くは未診断のまま成人し，合併精神障害を併発して初めて精神科を受診する[5]．その合併精神障害の存在はQOLを低下させる要因の1つとなっているが[6]，高機能ASD児者の多くは未診断であることから，精神医学的ニーズの実態はまだ明らかになっていない[14]．

近年，教育現場では，特別支援教育の視点から，通常学級に在籍する，ASDや注意欠如・多動性障害（attention-deficit/hyperactivity disorder：ADHD）などの発達障害の特徴を有し，教育上の特別なニーズの高い児童生徒に対する取り組みが熱心にすすめられている．最近，教育上の特別なニーズが高い子どもは学習だけでなく，メンタルヘルスに関連したニーズもまた高いということを示すわが国でのエビデンスが得られた．東京多摩地区の小学校通常学級に在籍する児童を対象として行った疫学研究[8]，そして全国の小・中学校通常学級に在籍する大規模児童集団を対象として行った質問紙調査[9]の結果を紹介し，学校精神保健の観点から課題と今後必要と考えられる取り組みを提案する．

Ⅰ．通常学級に在籍する一般児童における自閉症症状の分布

小・中学校通常学級に在籍する児童生徒を対象とした全国調査の結果，回収された教師および保護者回答データを，図1に示した（それぞれ解析した人数は7,401人，22,529人）．横軸に，教師あるいは保護者が回答した65項目からなる対人応答性尺度（social responsiveness scale：SRS）[2]で測った自閉症症状／特性の程度を示しており，縦軸に，その人数比率を男女別に示している．一般児童における自閉症症状／特性の分布は，やや左（低得点）に偏っており，男児は女児よりも右寄り，すなわち高得点側に分布することがわかる．SRSは国内外で十分に妥当性が検証されており，極端に高得点であればASD診断の疑いが高い[9]（図2）．SRSで測定された自閉症特性はなめらかに分布していて，ASD群とそうでない群との間に重複はあっても明らかなギャップがみられず，使用する恣意的なカットオフによって有病率が大きく変動することが理解される．韓国の疫学研究が報告した2.6%という最新で最大のASDの有病率[11]を著者らの日本のサンプルと重ねると，男児81点，女児73点というカットオフに相当する．しかしながら，カットオフ閾下に多数の軽度の自閉症的特性を有するケースが存在することに注意されたい（図2）．

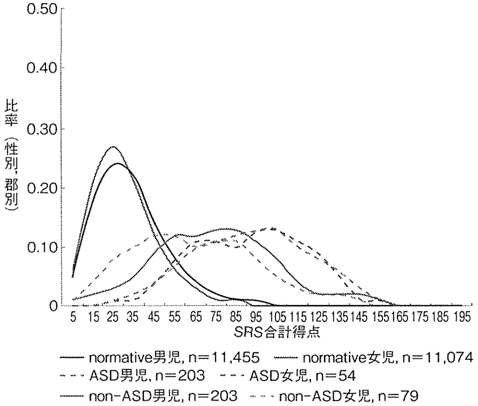

図 2　一般児童，ASD 児，非 ASD 児の SRS 合計得点の分布
全国サンプル（normative sample），ASD と診断された臨床サンプル，ASD 以外の診断がなされた臨床サンプルの子どもの SRS 合計得点について，男女別に人数分布を比率で示している．60 点以上 100 点以下は，必ずしも ASD の診断がなされるとは限らないが，様々な症状を持ち，中程度から軽度の対人的困難を呈する子どもたちで構成されている．

Ⅱ．一般児童における ASD に合併する精神医学的障害

平均知能の ASD 児には，どのような種類の精神障害をどのくらいの頻度で合併しているのかを明らかにするために，東京都小平市内の 3 小学校の通常学級に在籍する児童 1,374 人（当該地域の 14.9%）を対象に疫学研究を行った．保護者の同意を得て本研究に参加した 775 人（56.4%）から，教師回答の質問紙による 2 段階スクリーニングによって，ASD が疑われる 37 人の陽性者と，陰性者から無作為に抽出した児童のうち，同意が得られた計 41 人（陽性 22 人，陰性 19 人）が親子の診断面接に参加した．面接に参加した 22 人の陽性ケースは非参加の陽性ケース 15 人と性比では変わらなかったが，算数の学習と対人コミュニケーションにより困難を有する群であった．

ADI-R，ADOS，PDD-AS，K-SADS-PL の診断評価尺度を用いた面接の結果，DSM-IV-TR に従い，7 人が ASD の診断基準に合致した（自閉性障害（n=1），アスペルガー障害（n=1），特定不能の広汎性発達障害（Pervasive Developmental Disorder-Not Otherwise Specified：PDD-NOS）（n=5））．図 3 に，黒いバーで示したのは，ASD と診断された児童の合併精神障害の頻度（%）である．診断基準の半数に相当する症状があり，機能障害を呈している場合は閾下診断とし[3]，閾上，閾下を含めてカウントした結果をドットのバーで示した．ASD 児の 72%が 1 つ以上の DSM-IV-TR 診断を有していた．閾下診断も含めると ASD 児全員がなんらかの診断を有した．情緒の問題（不安障害または恐怖症に相当）と，行動の問題（注意または行動の問題に相当）は，児童期の精神病理の大きな 2 つのカテゴリーであるが，いずれも 43%にみられた．含まれる下位診断は図 3 に示す通りである．高頻度の合併精神障害とその種類のパターンは，知的障害も含む ASD 児の合併精神障害を調べた英国の大規模疫学研究[14]の結果ときわめて近似した．私たちの結果では，閾下診断も含めてカウントすると，サブクリニカルの水準以上の不安や恐怖症状を呈した ASD 児は 71%にも達することが明らかになった．この臨床的な意味づけは，今後長期経過をフォローすることで明らかになるであろう．

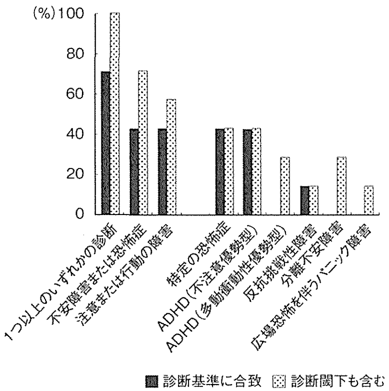

図 3　小平地域の ASD 児にみられる合併精神障害（リンク）
不安障害または恐怖症のカテゴリーは，情緒の問題（internalizing disorder とも呼ばれる）に相当する．注意または行動の障害のカテゴリーは，行動の問題（externalizing disorder とも呼ばれる）に相当する．

以上は，ASD 児の合併精神障害の実態を疫学的アプローチで明らかにしたわが国で最初の研究である．平均知能の ASD 児は不安障害や恐怖症から，ADHD や反抗挑戦性障害まで，多様な精神医学的ニーズを有することがわかった．サンプル数が小さい点が限界点であるが，厳密な診断手続きで地域の ASD 児を把握しており，その有病率の推定は 1.6%と近年の疫学研究と一致しており，結果は地域に住む平均知能の ASD 児の実態をかなり正確に反映するものと考えられる．

Ⅲ．一般児童生徒のメンタルヘルスと自閉症的特性

子どもの全般的なメンタルヘルスの予測には，情緒面や行動面の問題の量的把握に有用とされる，子どもの強さと困難さアンケート（strengths and difficulties questionnaire：SDQ）[1]を，自閉症的特性の予測には前述の SRS を用いて，前述の全国調査の一部として小中学生 25,075 人についての保護者回答をもとにそれらの関連を調べた[12]．図 4 に，自閉症的特性の程度の異なる 3 群（Probable ASD, Possible ASD, Unlikely ASD）のそれぞれにおけるメンタルヘルスの程度を，情緒の問題と行為の問題に分けて，SDQ 得点にもとづく臨床域，境界域，定型域の 3 分類の割合で示した．ASD が疑われる ASD-probable 群の子どもの情緒面は，男児の 53%，女児の 42%が臨床域に入り，境界域も含めると男児の 67%，女児の 62%がなんらかの支援ニーズを有すると推測される．行動面では，男児の 33%，女児の 25%が臨床域に入り，境界域も含めると男児の 48%，女児の 46%がなんらかの支援ニーズを有すると推測される．またこの群において情緒，行為以外の不注意・多動性，仲間関係を含む全般的なメンタルヘルスの臨床レベルの問題は 77%にみられた．自閉症的特性の軽度な群，特性がほとんどみられない群と比べると，どの領域のメンタルヘルスについても，問題を有する割合は有意に高かった（$ps<.001$）．

これらの結果からわかることは，小学校通常学級に，自閉症的特性が強く，診断を受ければ ASD 診断に該当するか，あるいは診断閾下に該当する子どもが多く存在し，大多数は未診断である．さらに，これらの子どもたちは，自閉的症状だけでなく，それとは独立した情緒面や行動面のメンタルヘルスの問題も高率に抱えている可能性が示された．ASD 診断の可能性は低くなるが，自閉症的特性のやや高い閾下群も，情緒面や行動面での境界域以上の問題を有し，支援ニーズが高いことは注目すべきである（図 4）．ASD があることはリスク要因であるが，診断にかかわらず，自閉症的特性が強いケースでは日常の丁寧な行動観察が重要となることが示唆される．

次に，精神医学的障害の予防的観点から，このような自閉症的特性が高く，教育的ニーズを有すると同時にメンタル面での支援ニーズを要する子

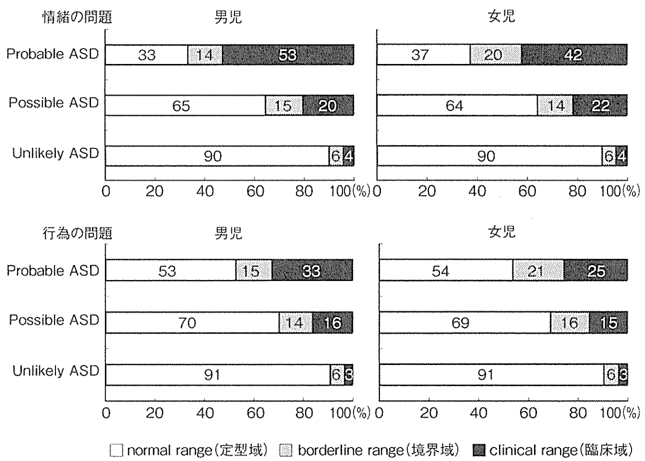

図4 一般児童における自閉症症状／特性と情緒や行為の問題の合併

自閉症的特性の程度によって分類した3群（T得点の60，75点をカットオフとする），probable ASD群（n＝607），possible ASD群（n＝3,061），unlikely ASD群（n＝21,407）別に，子どもの強さと困難さアンケート（Strengths and Difficulties Questionnaire：SDQ）の2つの下位尺度，「情緒の問題」，「行為の問題」の程度に分けて男女別に示している．SDQの分類区分には，対象全体の約80%に相当するnormal range（定型域），それより得点の高い約10%に相当するborderline range（境界域），そして最も高得点の約10%に相当するclinical range（臨床域）に分ける一般的な分類法に従った[1]．

どもたちへの介入時期についても，示唆的なエビデンスが得られた[13]．自閉症的特性の程度の異なる3群における情緒と行為の問題の割合が，各年齢区分（小学校低学年，小学校高学年，中学校）でどのくらいで，年齢による違いがあるのかについて調べた．その結果，一般に年齢が上がると問題が低くなる傾向がみられたのに対して，ASD-probable群のみは年齢に無関係に問題の割合が高く，年齢による変化がみられなかったのである．このことから，自閉的特性の高い子どもでは，通常は成長に伴い期待できるメンタルヘルスの自然回復が生じにくく，問題の慢性化傾向が高い可能性が考えられる．したがって，このような子どもたちに対しては自然回復を期待して問題を一時的なものとみなし，単に経過を観察するといった対応ではなく，メンタルな問題に気づけばニーズに応じた早期介入を検討する必要がある．

Ⅳ．学校精神保健の今後の課題

本研究によって，通常学級の児童生徒に連続的にみられる自閉症症状／特性は，情緒や行為などのメンタルヘルスの問題と密接に関連すること（因果関係ではなく）が明らかになった．ASD診断のある子どもはもちろんであるが，それよりはるかに多数存在する診断閾下の子どもにおいても，メンタルヘルスの問題を高率に持ちやすい．さらに，ASD診断の有無にかかわらず，自閉症症状／特性の高い子どもではメンタルヘルスの問題が自然回復しにくい可能性がある．ASDまたは閾下の子どものメンタルヘルスという観点からは，就学前から発達面のスクリーニングを行い，発達／教育支援のニーズを把握すると同時に，メンタルチェックをする機会を設け，就学後は学校精神保健の枠組みで定期的なチェックをすることが後の精神障害の予防につながるものと考えられる．精神医学的ニーズを早期に発見するためには，毎日の学校現場での観察を通した子どものメンタルヘルスについての理解と，それを家族や医療などのメンタルヘルス専門家と共有できる校内でのサポート体制が重要と考えられ，子どもと家族に一貫して提供される多領域連携が可能な学校精神保健システムの構築が必要と考えられる．

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Issues of School Mental Health in Japan : Evidence from Studies Based in Primary/Secondary Schools

Yoko KAMIO, Aiko MORIWAKI, Eiko INOKUCHI, Naoko INADA, Reiko TAKEI, Miho KURODA, Takayuki NAKAHACHI, Hidetoshi TAKAHASHI

Department of Child and Adolescent Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry

Recent studies have shown that early intervention for psychiatric disorders and symptoms in children will improve their QOL in adulthood. Although more than half of all adults suffering from psychiatric disorders experienced psychiatric symptoms when they were children, it remains unclear whether psychiatric symptoms in childhood can predict later psychiatric disorders. In other words, which symptoms should be targeted for early intervention? Our recent small-sized epidemiological study on primary school children in mainstream classes demonstrated that children with autism spectrum disorders (ASD) but with normal intelligence are likely to have comorbid psychiatric or subthreshold disorders. Another large-sized national survey of children in mainstream classes aged 6-15 years supported the above finding : children with autistic symptoms and/or traits are likely to have emotional or conduct difficulties at the clinical level, and the frequency of difficulties does not decline with age. Importantly, this finding is true for many children with subthreshold ASD symptoms, and suggests that natural recovery is unlikely in children with autistic symptoms and/or traits. From the viewpoint of maintaining and improving mental health in children, developmental screening to assist in understanding the developmental and educational needs of children should be administered along with starting comprehensive mental assessment at the preschool age. At school age, mental health should be regularly assessed, particularly in children with risk factors such as ASD or other developmental disorders, as this approach will help to prevent the later development of psychiatric disorders. The following are needed to increase the awareness of psychiatric needs in children : deep understanding of a child's mental health through everyday behavioral observation during school activities ; and a school support system to facilitate communication between teachers and other mental health professionals. Individual education supported by such a mental health system can deal with the needs of children and their families, resulting in a higher QOL.

<Authors'abstract>

<**Key words** : emotional disorder, behavior disorder, autism, childhood, comorbidity>

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自閉症スペクトラム研究　第10巻

我が国の小・中学校通常学級に在籍する一般児童・生徒における自閉症的行動特性と合併精神症状との関連

森脇　愛子（国立精神・神経医療研究センター精神保健研究所 児童・思春期精神保健研究部）
神尾　陽子（国立精神・神経医療研究センター精神保健研究所 児童・思春期精神保健研究部）

Associations between Autistic Traits and Psychiatric Issues and Japanese School Children and Adolescents

Aiko Moriwaki (*National Center of Neurology and Psychiatry, National Institute of Mental Health*)
Yoko Kamio (*National Center of Neurology and Psychiatry, National Institute of Mental Health*)

■要旨：近年の研究報告では，自閉症的行動特性は一般母集団内でなめらかな連続分布を示し，知的水準や自閉症スペクトラム（ASD）の診断に関わらずその特性を多く持つ群では，情緒や行為面のいわゆる精神症状の合併によって適応が悪いことが指摘されている。本研究では，全国の小・中学校通常学級の一般児童・生徒を対象とした大規模調査を行い，自閉症的行動特性と合併精神症状との関連について検討した。標準化の完了した質問紙に対する24,728名分の保護者回答について解析した結果，自閉症的行動特性の程度と情緒・行為の各問題には有意な相関関係があり，自閉症的行動特性を多く持つ群ほど精神医学的症状の合併する割合が高いことが示された。またASD診断閾下となるような軽微な特性を持つ子どもの場合にも精神症状の合併リスクが高いことから，学校現場において教育的支援のみならずメンタルケアのニーズが高い実態が明らかとなった。

■キーワード：自閉症的行動特性，合併精神症状，情緒・行為の問題，一般児童・生徒，メンタルケア

Ⅰ．背景と目的

特別支援教育（文部科学省初等中等教育局特別支援教育課，2006）によって，通常学級における自閉症スペクトラム障害（Autism Spectrum Disorder：以下ASD）の子どもに対する個々の特性とニーズに応じた支援が広がっている。しかし近年，ASDの子どもの問題は対人・コミュニケーション・常同的・限局的な行動だけに限らず，うつや不安といった情緒面，あるいは反社会的／非社会的な行動面の，いわゆる精神症状の合併が多いことが報告されている（Simonoff et al., 2008；神尾ら，2011；Kamio et al., 2013）。このことは知的障害を伴わないASDや臨床診断の閾下となるような軽症例においても同様に見られ，情緒や行動面の合併症状によってASD単独発症例よりも適応が悪くなる場合が指摘されている（Kanne et al., 2009；神尾，2012；Kamio et al., 2013）。

しかし，このようなASDと合併精神症状に関する調査研究は，これまでクリニック受診児を対象とした報告はあるものの，地域ベースの研究は英国の報告（Simonoff et al., 2008）を除いて存在しない。情緒・行動面がASD児の適応に大きな影響を与えると考えられるにも関わらず，一般母集団を対象とした実態はほとんど分かっておらず，予防的観点からその把握は必要不可欠と考えられる。

さらに，近年の我が国の一般小中学生を母集団とした大規模疫学調査（Kamio et al., 2012）の結果では，ASD診断可能性が高い上位約2%の子どもの下に，診断はつかないが閾下レベルの自閉症的行動特性を多く持つ子どもも多数存在することが明らかにされており（図1），ASD診断の有無に関わらず，自閉症的行動特性の程度と情緒・行動などの合併精神症状との関連について調べることも重要である。

本研究は，我が国の小・中学校通常学級に在籍する一般児童・生徒の保護者に質問紙調査を実施し，自閉症的行動特性の程度と情緒・行動面の合併精神症状との関連について明らかにすることを目的とする。

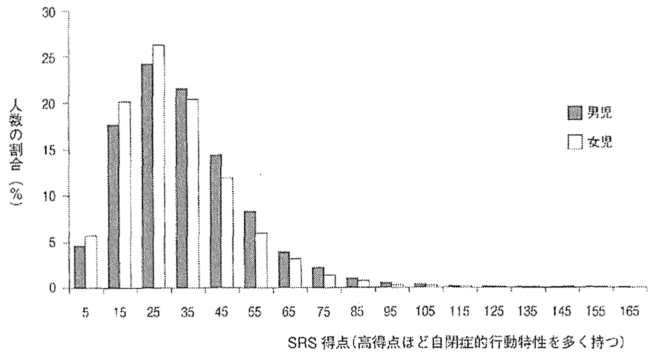

図1　我が国の一般小中学生母集団内における自閉症的行動特性の程度の分布（保護者回答 N=24,728）

Ⅱ. 方　法

1. 研究協力者

厚生労働省および文部科学省の協力のもと，各都道府県ないし市町村教育委員会を通して研究協力校を募ったところ，北海道・東北・関東甲信越・中部・関西・四国中国・九州ブロックのすべてから，小学校148校，および中学校71校，計219校が調査に参加した。各学校の通常学級に在籍する小学1年～中学3年生の児童・生徒87,548名の保護者に学校から依頼文書と質問票一式を配布し，回答を依頼した。質問票への回答は保護者の自由意志とし，調査事務局への返送をもって同意と見なした。質問票は無記名とし，個人情報に十分に配慮した。なお本研究の手続きは，国立精神・神経センター（現NCNP）の倫理審査委員会の承認を得た計画に沿って実施された。

2009年12月～2010年4月末日までの調査期間中に，25,779名分（29.7%）の質問票を回収し，そのうち性別・学年のいずれかに欠損があった者，また各質問紙尺度のうち1割以上の欠損項目がある者は除外した（各質問紙尺度において1割未満の欠損項目がある場合は性別の当該項目中央値によって補完して解析対象に加えた）ところ，全体の28.2%にあたる24,728名（男児12,567名，女児12,161名）分を有効回答として解析の対象とした。

2. 質問紙尺度

(1)対人応答性尺度（Social Responsiveness Scale：SRS）日本語版

4～18歳の子どもの日常生活で観察される行動特性を保護者または教師が評価することができる質問紙である（Constantino & Todd, 2000）。全65項目は5つの下位尺度（社会的気づき：Social Awareness，社会認知：Social Cognition，社会的コミュニケーション：Social Communication，社会的動機づけ：Social Motivation，自閉的常同性：Autistic Mannerism）に分類されており，ASDに特徴的な双方向的な対人相互作用に関連する行動に，常同反復的行動パターンを加えた諸徴候をカバーしている。SRS日本語版は原著者と原出版社の承諾を得て，国立精神・神経センター（現NCNP）と名古屋大学グループによって翻訳され，逆翻訳の手続きを経て作成された。項目の一部を表1に示す。これらの項目には4件法（あてはまらない～ほとんどいつもあてはまる）で回答がなされ，合計得点（範囲0～195点）が算出される。SRS日本語版の信頼性・妥当性は確認されており（神尾ら，2009；Kamio et al., 2012），我が国の一般母集団内でも米国原版同様にSRS合計得点は一元的な連続分布を示すことが確認されていることから（Constantino et al., 2003；Kamio et al., 2012），知的発達とは独立した自閉症的行動特性の定量的評価に適しているとされる。またASD診断が疑われる子どもたちのスクリーニング・ツールとしての臨床的有用性も高い（Kamio et al., 2012）。本研究においては，原版マニュアルに従い，男女別T得点の60，75で3群（SRS-3群）に分け，T得点＞75（男児：N＝302，女児：N＝296，高得点から2.4%）をASD診断が強く疑われるASD-Probable群，その下60≦T得点≦75（男児：N＝1,496，女児：N＝1,508，各12%）を診断閾下となるような軽微な特性を持つASD-Possible群，そしてT＜60となる症状をほとんどもたない大多数のASD-Unlikely群（男児：N＝10,769，女児：N＝10,357，各85%）として，後の分析に使用した。

表1　SRS日本語版項目の一部

下位尺度	項目例
対人的気づき	人が何を考え，感じているかに気づいている。
対人認知	人の声の調子や表情の変化に気づき，適切に対応する。
対人コミュニケーション	物事を文字通りにとりすぎて，会話の意味が理解できない。
対人的動機づけ	強いられないと集団活動または社交的なイベントに参加しない。
自閉的常同症	ストレスがかかると，奇妙なほど頑固で融通のきかない行動パターンが見られる。

(2)子どもの強さと困難さアンケート（Strength and Difficulties Questionnaire：SDQ）保護者評価用日本語版

4～16歳の子どもの日常行動の評価によって，情緒や行動面のいわゆる精神症状を把握する質問紙として英国で開発された（Goodman, 1997）。全25項目について3件法（あてはまらない，ややあてはまる，あてはまる）で回答するが，非常に少ない項目で簡便にスクリーニングできることから欧米諸国をはじめ多くの国々で注目され，使用されている。英国原版および日本語を含む約60か国語版はSDQウェブサイト（http://www.sdqinfo.org）から無料でダウンロードできる。保護者評価用の日本語版は，信頼性および妥当性が確認されている（Matsuishi et al., 2008；Moriwaki et al., in submission）。

SDQは5つの下位尺度（各下位尺度は5項目から成る）から構成されているが，そのうち本研究では「情緒の問題（Emotional Symptoms）」および「行為の問題（Conduct Problem）」の2下位尺度を用いた。これらの2下位尺度は児童期の精神医学的障害の2大カテゴリーである内向性症状と外向性症状を反映する項目が選定されている（Goodman,1994）。また，100項目以上の質問によってより詳細なアセスメントに使用される「子どもの行動チェックリスト（Child Behavior Checklist：CBCL）」（Achenbach et al., 1991；井澗ら，2001）と，SDQの2つの下位尺度の関連性を調べると，情緒の問題は内向性症状を，行為の問題は外向性症状をそれぞれ弁別的に評価できることも確認されている（Klasen et al., 2000；Janssens & Deboutte, 2010；Moriwaki et al., in submission）。

逆転項目を処理して，情緒の問題と行為の問題の各下位尺度得点（各0~10点）をそれぞれ算出したのち，性別・学年帯別に設定されたカットオフ（Moriwaki et al., in submission）を用いて，臨床レベルを示す3群を次のように定めた。高得点から約10%を臨床域（情緒：男児N＝765，女児N＝903，行為：男児N＝910，女児N＝560），その下約10%を境界域（情緒：男児N＝624，女児N＝750，行為：男児N＝1,031，女児N＝791），残り80%を定型域（情緒：男児N＝11,178，女児N＝10,508，行為：男児N＝10,626，女児N＝10,810）として，この分類を後の分析に用いた。

3. 分析方法

解析の前処理として各尺度の1割未満の欠損項目には性別ごとの該当項目中央値で補完した上で，SRS得点およびSDQ下位尺度得点をそれぞれ算出した。SRS得点およびSDQ各得点には性の効果が見られたことから，以下の解析はいずれも性別に分析することとした。SRS-3群別に，情緒・行為の各得点平均と標準偏差を求め，SRS-3群間に差が見られるかどうかをクラスカル・ウォリス法により比較した。

まず，SRS得点とSDQの情緒の問題および行為の問題の各下位尺度得点との関連性を調べるためにSpearmanの順位相関係数を算出した。また，算出された相関係数は差の検定を行い，SRS得点が情緒の問題／行為の問題のどちらとより強い関連を示すかを比較した。

次に，SRS-3群別に情緒や行為の問題が合併する（症状が臨床域・境界域にある）人数の割合を調べ，

表2　男女別，SRS-3 群別の情緒の問題・行為の問題得点の平均（標準偏差）

	男児（N＝12,567）				女児（N＝12,161）			
	ASD-Unlikely（N＝10,769）	ASD-Possible（N＝1,496）	ASD-Probable（N＝302）	$\chi^2_{(2)}$	ASD-Unlikely（N＝10,357）	ASD-Possible（N＝1,508）	ASD-Probable（N＝296）	$\chi^2_{(2)}$
情緒の問題	1.06(1.42)	2.57(2.04)	4.23(2.39)	17493.23*	1.23(1.15)	2.78(2.13)	4.27(2.51)	15417.98*
行為の問題	1.72(1.43)	2.97(1.85)	3.90(2.24)	14838.81*	1.53(1.28)	2.62(1.67)	3.33(2.02)	16897.97*

KW 検定　*$p < 0.001$

表3　性別，SRS-3 群別における情緒の問題・行為の問題の合併の割合（%）と残差

		情緒の問題			行為の問題		
		定型域 %（残差）	境界域 %（残差）	臨床域 %（残差）	定型域 %（残差）	境界域 %（残差）	臨床域 %（残差）
男児	ASD-Probable（N＝302）	37.7(−26.7)	13.9(4.9)	48.3(31.1)	47.0(−18.8)	13.6(5.5)	39.4(20.9)
	ASD-Possible（N＝1,496）	70.6(−25.2)	11.6(13.3)	17.8(20.8)	64.2(−22.0)	15.2(11.4)	20.6(19.0)
	ASD-Unlikely（N＝10,769）	92.9(35.0)	3.8(−14.4)	3.3(−32.9)	88.4(28.5)	7.1(−12.9)	4.5(−26.7)
女児	ASD-Probable（N＝296）	39.9(−24.0)	17.6(9.3)	42.6(23.1)	58.4(−17.3)	16.6(8.7)	25.0(15.6)
	ASD-Possible（N＝1,508）	65.6(−25.3)	12.7(11.8)	21.7(22.5)	72.2(−22.3)	14.3(12.7)	13.5(18.3)
	ASD-Unlikely（N＝10,357）	90.8(33.9)	4.9(−14.9)	4.3(−30.9)	92.2(28.2)	5.1(−15.7)	2.7(−23.7)

*残差はいずれも $p < 0.001$

その割合が自閉症的行動特性の程度に応じて偏りがあるかどうかを χ^2 検定によって比較した。さらに合併がある場合には，情緒か行為のいずれか一方の症状のみか，あるいは情緒と行為の両症状を合併するのか，そのパターンについて SRS-3 群を比較した。データの統計的解析は SPSS17.0 for Windows を用いた。

Ⅲ．結　果

1．記述統計

男女別に，SRS-3 群における情緒の問題および行為の問題の各下位尺度得点の平均と標準偏差を算出し，3 群間を比較した結果を示した（表 2）。男女いずれにおいても，SRS-3 群において情緒の問題，行為の問題の各得点は 0.1%水準で有意に差があった。

2．SRS 得点と SDQ 各得点の相関

SRS 得点と情緒の問題および行為の問題の各得点との相関を調べたところ，情緒の問題にやや強い有意な相関（男児 ρ ＝0.43，女児 ρ ＝0.40，ps<0.001），行為の問題においてもやや強い相関（男児 ρ ＝0.38，女児 ρ ＝0.35，ps<0.001）が見られた。SRS 得点と情緒の問題，SRS 得点と行為の問題のそれぞれの相関係数（ρ）の差の検定を行うと，男女とも情緒の問題が行為の問題よりも 1% 水準で有意に相関が強いことが明らかになった（男児 z＝4.76，女児 z＝3.90，ps<0.01）。

3．SRS-3 群における情緒の問題・行為の問題を合併する割合とその比較

情緒の問題や行為の問題が，臨床域・境界域となる人数の割合を男女別，SRS-3 群別に算出した（表 3）。自閉症的行動特性の程度に応じてその合併の割合に偏りがあるかどうかを調べるために χ^2 検定を行ったところ，男女とも情緒・行為の問題を合併する割合は SRS-3 群によって有意に異なった（情緒の問題：男児 $\chi^2_{(4)}$＝1707.08，女児 $\chi^2_{(4)}$＝1391.35，ps < 0.001，行為の問題：男児 $\chi^2_{(4)}$＝11157.91，女児 $\chi^2_{(4)}$＝913.93，ps<0.001）。残差分析の結果から，男女とも，ASD-Probable 群および ASD-Possible 群においては，情緒・行為の問題が臨床域ないし境界域となる割合が顕著に多く，ASD-Unlikely 群のみ情緒・行為のどちらの症状でも合併の割合が明らかに少ないことが示された。

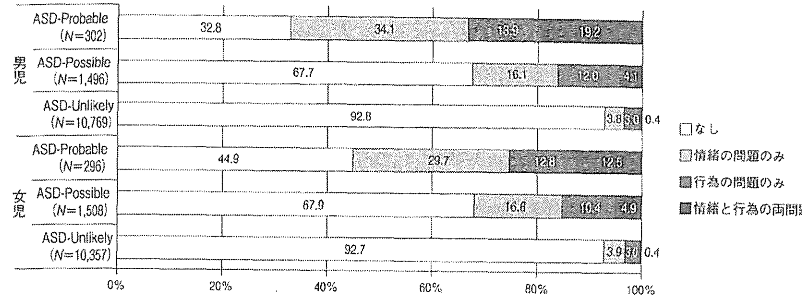

図 2　性別，SRS-3 群別における情緒の問題・行為の問題の合併パターン

4．SRS-3 群における情緒の問題・行為の問題の合併パターン

メンタルケアの必要なレベルにある精神症状を合併する場合，情緒面あるいは行為面のいずれかが単独で出現するのか，あるいは両方の問題が共に出現するのか，その合併パターンを明らかにし，それらのパターンが自閉症的行動特性の程度に応じて異なるかを検討した（図 2）。

情緒・行為面における何らかの症状がある割合は ASD-Unlikely 群では男女とも 8% 未満であった。しかし ASD-Possible 群では男児 28.1%，女児 27.2%，ASD-Probable 群では男児 48.0% に，女児 42.5% に，情緒・行為のいずれかの合併，あるいは両方の症状の合併が見られた。特に，ASD-Probable 群では情緒と行為の両症状を合併する割合が男児 19.2%，女児 12.5% と高く，自閉症的行動特性を多く持つ子どもの合併パターンが他群とは異なる傾向があることが示唆された。また，情緒ないし行為の問題のうちどちらか一方を合併する場合は，情緒の問題の方が，より割合が高いことも示された。

Ⅳ．考　察

本研究では，全国の通常学級に在籍する一般児童・生徒母集団を対象として，標準化された保護者評価の質問紙を用いた大規模調査を行い，自閉症的行動特性の程度と情緒・行為の問題のいわゆる合併精神症状との関連について検討を行った。

合併する情緒の問題は，ASD 診断が疑われる ASD-Probable 群では約半数に，行為の問題は約 4 割強にメンタルケアの必要なレベルの合併症状が認められた。この値は Siminoff（2008）による ASD 診断のある子どもを対象とした調査において，DSM-Ⅳの情緒障害カテゴリーに含まれる不安障害，恐怖症，気分障害の診断がつく割合 44.4%，反抗挑戦性障害か行為障害の診断がつく合計の割合 30.9% とも近い。また，ASD 診断閾下となるような自閉症的行動特性をやや持っている ASD-Possible 群においても，情緒の問題は約 2 割に，行為の問題は 1 割～2 割の子どもに顕著な症状が見られることが明らかになった。このように，自閉症的行動特性を多く持つ子どもほど，より高率に，より困難な程度の精神症状を合併することが，SRS 得点と情緒・行動の問題得点の相関からも裏付けられた。

さらに，自閉症的行動特性を多く持つ群の場合には，情緒・行為面の両方の症状を合併する可能性が高いことから，適応に大きな影響をもたらすと懸念される。そのため，適切に支援・対応するためには，ASD の行動特性を持つ子どもに対して，いかなる合併症状があるか，またそれらの程度について

のアセスメントが必要不可欠となるだろう。本研究では情緒・行為面の評価に簡便なスクリーニング評価尺度を用いているため，それぞれの得点と臨床診断が直接的に結びつくということではない。本研究のようなスクリーニングを通して症状があると推測される児童・生徒に対しては，より詳細な評価や臨床診断による合併症状の特性把握を可能にする評価体制を見直すことも重要である。

米国の調査データ（Kessler et al., 2005）では，人口の2人に1人が，生涯のうち何らかの精神障害に罹患し，特にこれまで成人の疾患と考えられてきたうつ病や不安障害の約半数が14歳までの児童期に初発することが分かっている。児童・思春期におけるメンタルヘルスとその予防の重要性は極めて大きい。本研究結果において，診断の有無に関わらず自閉症的行動特性を持つ児童・生徒は，精神症状合併のハイリスク群であることが示唆された。これらのことから，学校教育現場における学習面や生活面の特別支援のみならず，情緒や行為の問題に対する的確なニーズ把握とともに，必要な場合にはメンタルケアが可能となる教育と医療の連携体制の構築が必要であると言えるだろう。本研究は我が国の一般児童・生徒母集団を対象とした地域ベースの大規模調査を実施したことによって，児童・思春期の実態把握とともに，今後の支援の在り方を検討する上で重要なエビデンスとなると考えられる。

さらに，横断調査だけではなく子どもたちのメンタルヘルスのリスクが予後の適応や生活の質(QOL)にどのような影響を及ぼすのか，またそれらに自閉症的行動特性の程度が関連するのか等，発達的観点を踏まえた前向きの縦断研究が課題である。そして，これらのメンタル・リスクを予防する，あるいは乗り越えるための有効な支援方法についても検討する必要があると考える。

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