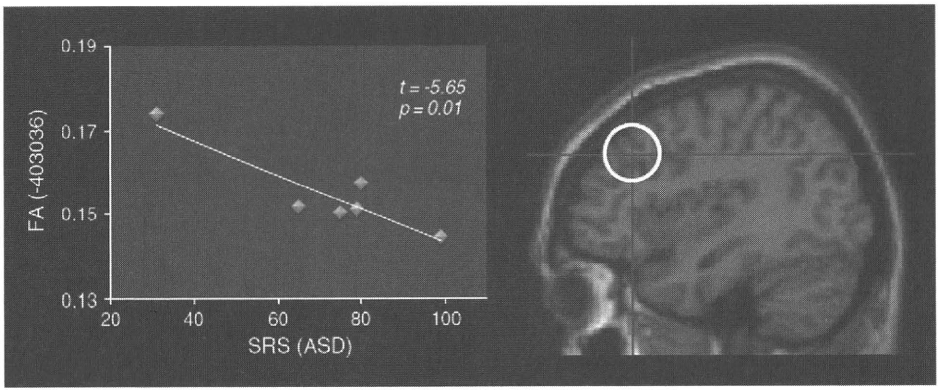


Fig. 1 – Voxels showing significant reduction of fractional anisotropy (FA) in the region around left dorsolateral prefrontal cortex (DLPFC) in the autism spectrum disorder (ASD) group compared with healthy control (HC) participants (right). Scatter plots depict the negative correlation between FA value around the left DLPFC and Social Responsiveness Scale (SRS) score in the ASD group (left).

2.2. *Correlation between DTI parameters and SRS and IQ*

The SRS scores showed significant differences between the ASD and HC groups (ASD: mean 71.5±22.7 for all participants except one with missing data; HC: mean 27.7±17.2; $t=3.9$; $P=0.004$) (Table 1). For the ASD group, there was a significant and negative correlation between the FA value in the region around DLPFC and the total SRS score ($t=-5.65$, $p=0.01$) when IQ was co-varied (Fig. 1), and the FA value was not significantly correlated with the full IQ when SRS was co-varied. No significant correlation was observed between FA or λ_1 values in the other regions and SRS or IQ in either group when controlling for them.

3. Discussion

In the present study we compared the white matter structure of autistic children with that of age- , gender-, and handedness-matched healthy control participants by assessing DTI parameters FA and λ on a voxel-based, whole brain basis. The major finding of this study was that children with ASD (11–18 years of age) showed alterations reflected in reduced FA and λ_1 values in the brain regions that play important roles in social cognition and information integration. Another major finding was that the cerebellar vermis in children with ASD showed structural alterations reflected in the increased λ_1 value. These results based on DTI measurements in developing children add to the evidence of cerebral and cerebellar white matter structural abnormalities as reported in previous functional and structural studies on ASD.

The largest cluster among the brain regions showing reduced FA and λ values was the ACC (Table 2). This finding is consistent with previous DTI studies in children and adults with ASD (Barnea-Goraly et al., 2004; Thakkar et al., 2008). The ACC is one of the regions that consistently showed structural and functional abnormalities in ASD in previous studies using MRI, positron emission tomography (Haznedar et al., 1997, 2000), and fMRI (Castelli et al., 2002; Hazlett et al., 2004; Pierce et al., 2004; Kennedy et al., 2006). The ACC is considered to be

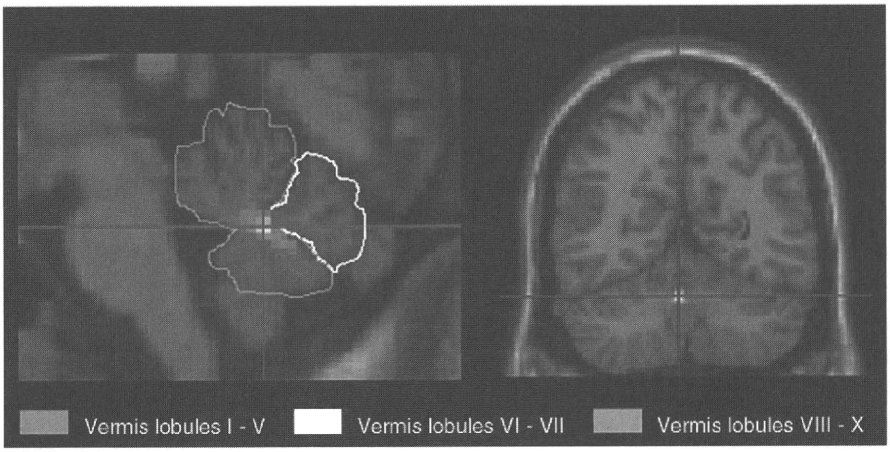


Fig. 2 – Sagittal and coronal views of increased λ_1 values in the cerebellar vermis lobules for the autism spectrum disorder (ASD) group compared with healthy control (HC) participants, particularly in the white matter regions between the fastigium and parts of vermis lobules V (orange) and VIII (green), which are near lobules VI and VII (white), respectively.

Table 1 – Participant characteristics.

	Diagnosis	Chronological age	Sex, M/F (6:1)	IQ			CARS-TV score	PARS score	SRS score
Autism spectrum disorder (ASD), $n=7$				VIQ	PIQ	FIQ		($n=6$)	($n=6$)
A1	HFA	11 y1 m	M	89	92	89	38.5	45	–
A2	ASP	12 y0 m	M	103	106	104	27.5	25	80
A3	HFA	12 y3 m	M	97	86	91	37.5	43	75
A4	ASP	12 y11 m	M	100	100	100	29	13	31
A5	ASP	14 y6 m	F	95	82	88	36.5	24	65
A6	ASP	16 y7 m	M	81	94	86	39.5	–	99
A7	HFA	18 y5 m	M	91	92	91	31	23	79
Mean		13.96±2.68 y		93.7±7.41	93.14±8.07	92.71±6.68	34.21±4.91	28.8±12.53	71.5±22.71
Healthy controls (HC), $n=7$						Estimated IQ			($n=7$)
H1		10 y9 m	M			112			22
H2		11 y7 m	M			118			53
H3		11 y10 m	M			124			42
H4		12 y0 m	M			97			39
H5		13 y6 m	F			121			6
H6		15 y3 m	M			124			20
H7		18 y7 m	M			119			12
Mean		13.36±2.74 y				116.43±9.50			27.71±17.23
t-test		n.s.				$t=5.40$, $p=0.0001$			$t=3.86$, $p=0.004$
χ^2 test			n.s.						

Groups were matched for age, gender and right-handedness. For the estimation of intelligence, the ASD group was administered the Japanese version of the WISC-III or WAIS-III, and the HC group was administered short forms of the Japanese version of the WISC-III or WAIS-III, both of which consist of two subtests (Information and Picture Completion), depending on their age at the time of testing. HFA=High-functioning autism spectrum disorder; ASP=Asperger's disorder; IQ=intelligence quotient; VIQ=verbal IQ; PIQ=performance IQ; FIQ=full IQ; CARS-TV=Childhood Autism Rating Scale-Tokyo version; PARS=Pervasive Developmental Disorders Autism Society Japan Rating Scale; SRS=Social Responsiveness Scale; M=Male; F=Female; n.s.=not significant; y=year; m=month.

associated with social cognitive processes such as self-reflection, empathy and making inferences about others' thoughts (Eisenberger and Lieberman, 2004; Jackson et al., 2005; Amodio and Frith, 2006). A recently evolved neuronal population in the ACC, the von Economo neurons (VENs), is postulated to serve in socioemotional and higher-order

Table 2 – Brain regions showing significantly high FA or λ_1 values in HC versus ASD and ASD versus HC.

Brain region	L/R	MNI coordinates						t-value	Cluster size
		FA			λ_1				
		X	Y	Z	X	Y	Z		
HC>ASD									
Dorsolateral prefrontal cortex (DLPFC)	L	−40	30	36				14.29	4
Posterior superior temporal sulcus (pSTS)/temporo-parietal junction (TPJ)	L				−52	−66	40	11.97	4
Temporal pole (TP)	R	48	6	−16				12.19	6
Amygdala	R	28	−4	−12				13.86	16
Anterior cingulate cortex (ACC)	R				16	32	28	15.74	44
	–	0	10	44				14.59	28
Anterior corpus callosum (aCC)	–	0	16	16				13.57	21
	L	−14	24	14				12.49	12
Superior longitudinal fasciculus (SLF)	R	32	−6	28				12.56	5
Occipitofrontal fasciculus (OFF)	R	22	−4	34				11.24	4
ASD>HC									
Cerebellar vermis lobules	L				−4	−58	−26	22.64	69

$P<0.05$, Family Wise Error (FWE).
HC=Healthy control; ASD=Autism spectrum disorder; L=left; R=right; MNI=Montreal. Neurological Institute; FA=Fractional anisotropy; λ=Lambda.

cognitive processing (Nimchinsky et al., 1999). Simms et al. (2009) reported alterations in the density of VENs in the ACC in autism. Taken together with previously reported findings using various approaches, our present findings also indicate maldevelopment of the ACC in ASD.

The posterior STS/TPJ and TP/amygdala, around which reduced FA and λ_1 values in ASD were found in our study and previous DTI studies (Barnea-Goraly et al., 2004; Lee et al., 2007; Cheung et al., 2009), are also implicated in socioemotional processes such as theory of mind function and social perception through face or human action (Adolphs, 2001; Siegal and Varley, 2002; Dolan and Vuilleumier, 2003; Frith and Frith, 2003, 2006; Morris et al., 2005; Fitzgerald et al., 2006; Olson et al., 2007; Saarela and Hari, 2008; Hall et al., 2009). It has been reported that individuals with ASD show less activation of the STS during tasks involving mental attribution to moving geometric figures (Castelli et al., 2002), biological motion cues (Pelphrey and Carter, 2008), and human speech perception (Gervais et al., 2004). In addition, less activation of the amygdala/TP in response to faces (Baron-Cohen et al., 1999; Critchley et al., 2000; Wang et al., 2004; Williams et al., 2006; Ashwin et al., 2007) has been documented in ASD compared to control participants.

In addition, we found reduced FA around the DLPFC, which concurs with the findings of other DTI studies in ASD (Sundaram et al., 2008; Thakkar et al., 2008; Cheung et al., 2009; Ke et al., 2009; Pardini et al., 2009; Pugliese et al., 2009; Sahyoun et al., 2010). The DLPFC has been found to interact with posterior association areas such as STS and to manipulate cognitive representation of socioemotional processes (Taylor and Fragopanagos, 2005; Yurgelun-Todd and Killgore, 2006; Weissman et al., 2008). Our finding is consistent with the fMRI finding indicating abnormal connectivity among the DLPFC, medial PFC, and posterior association areas (Wicker et al., 2008). Furthermore, we found a significant association between FA around the DLPFC and degree of social impairment as measured by the SRS in the ASD group even when IQ was co-varied (Fig. 1), indicating that the more severe the social impairment, the more altered the DLPFC structure. Given our findings, structural alteration of the DLPFC might be an index of social impairment in ASD. The finding might be influenced by the age range of our participants restricted to childhood. There are some indications that prefrontal activity is pronounced during late childhood (Monk et al., 2003; Yurgelun-Todd and Killgore, 2006; Blakemore, 2008). For example, when attention was unconstrained for emotionally engaging face stimuli, children (9–17 years of age) showed greater activation of the prefrontal cortex relative to adults (25–36 years of age) (Monk et al., 2003). Similarly, Yurgelun-Todd and Killgore reported that activity within the prefrontal cortex during fear perception was significantly and positively correlated with age (8–15 years). Therefore, our present data support the concept that efficient connectivity of the prefrontal region during late childhood is specifically important for appropriate social responsiveness.

Reduced FA was also observed around the SLF and OFF in the present study, confirming the findings of previous studies (Pugliese et al., 2009). The SLF contains long association fibers connecting all the lobes, and the OFF connects the occipital and frontal regions of the brain. In addition, reduced FA was also observed around the aCC, which is important for connecting prefrontal regions (Witelson, 1989; Huang et al., 2005). This finding concurs with previous DTI studies in ASD (Alexander et al., 2007; Thakkar et al., 2008). The finding of disorganization of these commissural and association fibers in autistic children may support the cortical underconnectivity hypothesis of ASD (Belmonte et al., 2004; Geschwind and Levitt, 2007; Müller, 2007).

Another major finding of the present study was the significantly increased λ_1 in the cerebellar white matter regions between the fastigium and parts of vermis lobules V and VIII, which are near lobules VI and VII, respectively. To date, the most consistent pathologic finding in ASD is a decreased number of Purkinje cells in the cerebellum vermis or hemisphere (Bauman and Kemper, 1985; Courchesne, 1997; Bailey et al., 1998). In MRI studies, cerebellum vermis lobules VI and VII have been consistently reported to be smaller in individuals with ASD than in typically developing children, adolescents, and adults (Courchesne et al., 1988, 1994, 2001; Ciesielski et al., 1997; Carper and Courchesne, 2000; Kaufmann et al., 2003). It has been shown that the volume of vermis lobules VI and VII is related to stereotyped behaviors (Pierce and Courchesne, 2001) and attention-orienting deficits (Harris et al., 1999; Townsend et al., 1999), which are often found in individuals with ASD. Recent mouse knockout studies showed that the loss of Ca^{2+}-dependent activator protein for secretion 2 (CAPS2) function resulted in several cerebellar morphologic abnormalities such as fewer branched dendrites on Purkinje cells and increased granule cell death in vermis lobules VI and VII as well as autistic-like behavioral phenotypes (Sadakata et al., 2007a,b). Given these findings, lobules VI and VII might have been expected to show structural abnormalities in our DTI analysis. Unexpectedly, our whole-brain λ analysis detected structural alterations in neighboring vermis regions (V and VIII). The reason for this is unclear; however, we speculate that the neural connections with neighboring lobules V and VIII might develop excessively to compensate for possible functional abnormalities in lobules VI and VII. Additional studies are necessary to confirm this speculation.

The implications of the present study are as follows. First, our participants were relatively homogenous in that all were high functioning, and both groups were well matched with respect to age, gender, and handedness, indicating successful differentiation of the two groups. Second, our whole-brain analysis of multiple DTI parameters (FA, λ_1, λ_2, and λ_3) revealed structural alterations and also demonstrated a brain–behavior relationship in ASD, which has not been reported previously. Potential study limitations include the fact that the neural mechanism in ASD could not be clearly explained by the alteration in DTI parameters because the physiologic meanings of FA and λ are unclear, sample size was small, and IQs were not group-matched.

Behavioral symptoms of ASD manifest early in life and develop under interaction between genetic and environmental factors, resulting in diverse clinical manifestations. To explore the diverse developmental trajectories in ASD in the future, a database of brain structure and their relationship to behavioral phenotypes should be established from infancy and through childhood, adolescence, and adulthood. Whether the brain alterations identified in the present study are specific to autism or common to other developmental disorders is another issue that warrants investigation.

4. Experimental procedures

4.1. Participants

Children with ASD and HC children were recruited from local schools and the community by advertisement and were enrolled in the study. The ASD group ($n=7$) consisted of children diagnosed with high-functioning ASD. The HC group ($n=7$) was selected to be matched for age, gender and right-handedness (Table 1). Diagnosis of ASD, which had been made by independent clinicians in the community, was confirmed according to DSM-IV-TR criteria (American Psychiatric Association, 2000) by our research team, which included an experienced child psychiatrist (Y. K.). To corroborate the ASD diagnosis, autistic symptom severity was evaluated using the Childhood Autism Rating Scale-Tokyo version (CARS, Schopler et al., 1988; Japanese translated and adapted version [CARS-TV], Kurita et al., 1989), and all participants with ASD were confirmed to score higher than the cutoff score of 25.5 for pervasive developmental disorders (PDD) (Tachimori et al., 2003). In addition, in semistructured interviews, the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS), which has been validated for the Japanese PDD population (Adachi et al., 2006; Kamio et al., 2006) was completed for all participants except one in the ASD group; all six scored higher than the cutoff score of 9 for PDD (Table 1). Participants in the HC group were confirmed to have no history of neurologic or psychiatric disorder according to interviews with their parents.

Intellectual function of the participants with ASD was evaluated using the Japanese version of the Wechsler Intelligence Scale for Children-Third Edition (WISC-III, Wechsler, 1991; Japanese translated and adapted version, Azuma et al., 1998) or the Japanese version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III, Wechsler, 1997; Japanese translated and adapted version, Fujita et al., 2006), whereas that of the HC group was estimated using the short form of the Japanese version of the WISC-III (Inada and Kamio, in press) or the short form of the Japanese version of the WAIS-III (Dairoku et al., 2009), both of which consist of two subtests, Information and Picture Completion (Table 1).

All participants and their parents provided informed consent to participate in the study. The study protocol was approved by the Research Ethics Committee of the National Center of Neurology and Psychiatry, Japan.

4.2. Assessment of social responsiveness

To measure the degree of social responsiveness of our participants, the Japanese version of the SRS (Constantino et al., 2000; Kamio et al., 2009) was completed by parents. The SRS is a 65-item questionnaire that was developed to assess social impairment observed in autism. Completed by a parent or teacher in 15 to 20 min, the SRS provides a clear picture of a child's social awareness, social information processing, reciprocal social communication, social anxiety/avoidance, and autistic preoccupations and traits. These items form a single measure of autistic traits rather than distinct scores associated with specific symptom domains (Constantino et al., 2000, 2004; Constantino and Todd, 2005), and can quantify social impairments across the entire child population including both clinical and nonclinical populations (Constantino and Todd, 2003). Total SRS raw scores range from 0 (corresponding to high social competence) to 195 (corresponding to significant social impairment as observed in severe autism). Scores between 60 and 80 are associated with mild forms of autism (Constantino and Todd, 2005).

4.3. Magnetic resonance imaging

Magnetic resonance images were obtained using a 3.0 T MRI device (Achieva Series Quasar Dual 3.0 T; Philips Medical Systems, Best, Netherlands) and an 8-channel head array coil for parallel imaging (SENSE). Single-shot echo planar DTI was performed using a twice refocused, spin echo sequence with the following sequence parameters: repetition time/echo time=7420/88 ms; motion probing gradient 32 axes (b value 800 [s/mm^2]: 32; b value 0 [s/mm^2]: 1); 128×128 matrix; 1.8×1.8 mm in-plane resolution; 60 slices; 2 mm (0 mm gap) slice thickness; scan duration 5′33.5″.

4.4. Image analysis

To correct for image distortion owing to eddy current, diffusion-weighted (DW) images obtained at a b value of 800 s/mm^2 were first coregistered with the diffusion-unweighted image at $b=0$ s/mm^2 using software of the MRI system. For each participant, voxel-wise calculation of DTI and subsequent mapping of diffusivity were performed using in-house software running on Interaction Data Language (IDL) ver. 6.1 (ITT Visual Information Solutions, Boulder, CO). Using 32 DW images ($b=800$ s/mm^2) and one diffusion-unweighted image ($b=0$ s/mm^2), a 3×3 DTI was obtained for each voxel, from which three eigenvalues, λ_1, λ_2, and λ_3, were calculated; FA was calculated from the eigenvalues. In addition, for group analyses (HC vs. ASD, ASD vs. HA), the FA, λ_1, λ_2, and λ_3 maps for each participant were analyzed separately using Statistical Parametric Mapping (SPM)2 software (http://www.fil.ion.ucl.uk/spm/software/spm2/). Maps were spatially normalized to the Montreal Neurological Institute (MNI) T2 template and smoothed using a Gaussian filter of 6 mm full width at half maximum. Random-effect analyses were thresholded for FA, λ_1, λ_2, and λ_3 values between the ASD and the HC groups at $P<0.05$, Family Wise Error (FWE), with an extent threshold of three voxels.

4.5. Correlational analysis

For each of the ASD and HC groups, a multivariate regression method (SPSS v17.0) was used for correlation analysis between the DTI parameters and the scores of SRS and IQ ($p<0.05$). The DTI parameters were those of averaged FA and λ values in the spherical region of interest (ROI; radius, 5 mm), the center of which was the peak voxel in each cluster showing significant difference.

Acknowledgments

This work was supported by the Research Institute of Science and Technology for Society, Japan Science and Technology Agency as well as the Japan Foundation for Neuroscience and Mental Health.

We gratefully acknowledge the participation of the children in this study and the support of their families. We thank N. Inada and Y. Miyanaga for data collection, Dr. A. Senoo for providing the software for analysis, and Drs. Y. Moriguchi and H. Fukui for helpful discussions.

REFERENCES

Adachi, J., Yukihiro, R., Inoue, M., Uchiyama, T., Kamio, Y., Kurita, H., Sugiyama, T., Tsujii, M., Ichikawa, H., 2006. Reliability and Validity of the Pervasive Developmental Disorder (PDD)-Autism Society Japan Rating Scale (PARS): a behavior checklist for children with PDDs. Rinsyo Seishin Igaku (Jpn. J. Clin. Psychiatr.) 11, 1591–1599 (in Japanese).

Adolphs, R., 2001. The neurobiology of social cognition. Curr. Opin. Neurobiol. 11, 231–239.

Alexander, A.L., Lee, J.E., Lazar, M., Boudos, R., DuBray, M.B., Oakes, T.R., Miller, J.N., Lu, J., Jeong, E.K., McMahon, W.M., Bigler, E.D., Lainhart, J.E., 2007. Diffusion tensor imaging of the corpus callosum in autism. Neuroimage 34, 61–73.

American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association, Washington DC.

Amodio, D.M., Frith, C.D., 2006. Meeting of minds: the medial frontal cortex and social cognition. Nat. Rev. Neurosci. 7, 268–277.

Ashwin, C., Baron-Cohen, S., Wheelwright, S., O'Riordan, M., Bullmore, E.T., 2007. Differential activation of the amygdala and the "social brain" during fearful face-processing in Asperger syndrome. Neuropsychologia 45, 2–14.

Azuma, H., Ueno, K., Fujita, K., Maekawa, H., Ishikuma, T., Sano, H., 1998. Japanese Wechsler Intelligence Scale for Children, 3rd ed. Nihon Bunka Kagakusha, Tokyo (in Japanese).

Bailey, A., Luthert, P., Dean, A., Harding, B., Janota, I., Montgomery, M., Rutter, M., Lantos, P., 1998. A clinicopathological study of autism. Brain 121, 889–905.

Barnea-Goraly, N., Kwon, H., Menon, V., Eliez, S., Lotspeich, L., Reiss, A.L., 2004. White matter structure in autism: preliminary evidence from diffusion tensor imaging. Biol. Psychiatry 55, 323–326.

Baron-Cohen, S., Ring, H.A., Wheelwright, S., Bullmore, E.T., Brammer, M.J., Simmons, A., Willams, S.C., 1999. Social intelligence in the normal and autistic brain: an fMRI study. Eur. J. Neurosci. 11, 1891–1898.

Basser, P.J., Pierpaoli, C., 1996. Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. J. Magn. Reson. B 111, 209–219.

Bauman, M.L., Kemper, T.L., 1985. Histoanatomic observations of the brain in early infantile autism. Neurology 35, 866–874.

Belmonte, M.K., Allen, G., Beckel-Mitchener, A., Boulanger, L.M., Carper, R.A., Webb, S.J., 2004. Autism and abnormal development of brain connectivity. J. Neurosci. 24, 9228–9231.

Blakemore, S.J., 2008. The social brain in adolescence. Nat. Rev. 9, 267–277.

Boddaert, N., Chabane, N., Gervais, H., Good, C.D., Bourgeois, M., Plumet, M.H., Barthélémy, C., Mouren, M.C., Artiges, E., Samson, Y., Brunelle, F., Frackowiak, R.S., Zilbovicius, M., 2004. Superior temporal sulcus anatomical abnormalities in childhood autism: a voxel-based morphometry MRI study. Neuroimage 23, 364–369.

Carper, R.A., Courchesne, E., 2000. Inverse correlation between frontal lobe and cerebellum size in children with autism. Brain 123, 836–844.

Castelli, F., Frith, C., Happe, F., Frith, U., 2002. Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. Brain 125, 1839–1849.

Cheung, C., Chua, S.E., Cheung, V., Khong, P.L., Tai, K.S., Wong, T.K., Ho, T.P., McAlonan, G.M., 2009. White matter fractional anisotropy differences and correlates of diagnostic symptoms in autism. J. Child Psychol. Psychiatry 50, 1102–1112.

Ciesielski, K., Harris, R., Hart, B., Pabst, H., 1997. Cerebellar hypoplasia and frontal lobe cognitive deficits in disorders of early childhood. Neuropsychologia 35, 643–655.

Constantino, J.N., Todd, R.D., 2003. Autistic traits in the general population: a twin study. Arch. Gen. Psychiatry 60, 524–530.

Constantino, J.N., Todd, R.D., 2005. Intergenerational transmission of subthreshold autistic traits in the general population. Biol. Psychiatry 57, 655–660.

Constantino, J.N., Przybeck, T., Friesen, D., Todd, R.D., 2000. Reciprocal social behavior in children with and without pervasive develop mental disorders. J. Dev. Behav. Pediatr. 21, 2–11.

Constantino, J.N., Gruber, C.P., Davis, S., Hayes, S., Passanante, N., Przybeck, T., 2004. The factor structure of autistic traits. J. Child Psychol. Psychiatry 45, 719–726.

Courchesne, E., 1997. Brainstem, cerebellar and limbic neuroanatomical abnormalities in autism. Curr. Opin. Neurobiol. 7, 269–278.

Courchesne, E., Yeung-Courchesne, R., Press, G.A., Hesselink, J.R., Jernigan, T.L., 1988. Hypoplasia of cerebellar vermal lobules VI and VII in autism. N Engl J. Med. 318, 1349–1354.

Courchesne, E., Saitoh, O., Yeung-Courchesne, R., Press, G.A., Lincoln, A.J., Haas, R.H., Schreibman, L., 1994. Abnormality of cerebellar vermian lobules VI and VII in patients with infantile autism: identification of hypoplastic and hyperplastic subgroups with MR imaging. AJR Am. J. Roentgenol. 162, 123–130.

Courchesne, E., Karns, C., Davis, H.R., Ziccardi, R., Carper, R., Tigue, Z., Pierce, K., Moses, P., Chisum, H.J., Lord, C., Lincoln, A.J., Pizzo, S., Schreibman, L., Haas, R.H., Akshoomoff, N.A., Courchesne, R.Y., 2001. Unusual brain growth patterns in early life in patients with autistic disorder: an MRI study. Neurology 57, 245–254.

Critchley, H.D., Daly, E.M., Bullmore, E.T., Williams, S.C., Van Amelsvoort, T., Robertson, D.M., Rowe, A., Phillips, M., McAlonan, G., Howlin, P., Murphy, D.G., 2000. The functional neuroanatomy of social behaviour: changes in cerebral blood flow when people with autistic disorder process facial expressions. Brain 123, 2203–2212.

Dairoku, H., Yamanaka, K., Fujita, K., Maekawa, H., 2009. Short forms of Japanese WAIS-III for estimating FSIQ. Proceedings of the 73rd Annual Convention of the Japanese Psychological Association, p. 433.

Dolan, R.J., Vuilleumier, P., 2003. Amygdala automaticity in emotional processing. Ann. NY Acad. Sci. 985, 348–355.

Eisenberger, N.I., Lieberman, M.D., 2004. Why rejection hurts: a common neural alarm system for physical and social pain. Trends Cogn. Sci. 8, 294–300.

Fitzgerald, D.A., Angstadt, M., Jelsone, L.M., Nathan, P.J., Phan, K.L., 2006. Beyond threat: amygdala reactivity across multiple expressions of facial affect. Neuroimage 30, 1441–1448.

Frith, U., Frith, C., 2003. Development and neurophysiology of mentalizing. Phil. Trans. R. Soc. Lond. B 358, 459–473.

Frith, C., Frith, U., 2006. The neural basis of mentalizing. Neuron 50, 531–534.
Fujita, K., Maekawa, H., Dairoku, K., Yamanaka, K., 2006. A Japanese Version of the WAIS-III. Nihon Bunka Kagakusha, Tokyo (in Japanese).
Gervais, H., Belin, P., Boddaert, N., Leboyer, M., Coez, A., Sfaello, I., Barthélémy, C., Brunelle, F., Samson, Y., Zilbovicius, M., 2004. Abnormal cortical voice processing in autism. Nat. Neurosci. 7, 801–802.
Geschwind, D.H., Levitt, P., 2007. Autism spectrum disorders: developmental disconnection syndromes. Curr. Opin. Neurobiol. 17, 103–111.
Hall, J., Whalley, H.C., McKirdy, J.W., Sprengelmeyer, R., Santos, I.M., Donaldson, D.I., McGonigle, D.J., Young, A.W., McIntosh, A.M., Johnstone, E.C., Lawrie, S.M., 2009. A common neural system mediating two different forms of social judgement. Psychol. Med. 8, 1–10.
Harris, N.S., Courchesne, E., Townsend, J., Carper, R.A., Lord, C., 1999. Neuroanatomic contributions to slowed orienting of attention in children with autism. Cogn. Brain Res. 8, 61–71.
Hazlett, E.A., Buchsbaum, M.S., Hsieh, P., Haznedar, M.M., Platholi, J., LiCalzi, E.M., Cartwright, C., Hollander, E., 2004. Regional glucose metabolism within cortical Brodmann areas in healthy individuals and autistic patients. Neuropsychobiology 49, 115–125.
Haznedar, M.M., Buchsbaum, M.S., Metzger, M., Solimando, A., Spiegel-Cohen, J., Hollander, E., 1997. Anterior cingulate gyrus volume and glucose metabolism in autistic disorder. Am. J. Psychiatry 154, 1047–1050.
Haznedar, M.M., Buchsbaum, M.S., Wei, T.C., Hof, P.R., Cartwright, C., Bienstock, C.A., Hollander, E., 2000. Limbic circuitry in patients with autism spectrum disorders studied with positron emission tomography and magnetic resonance imaging. Am. J. Psychiatry 157, 1994–2001.
Herbert, M.R., Ziegler, D.A., Deutsch, C.K., O'Brien, L.M., Lange, N., Bakardjiev, A., Hodgson, J., Adrien, K.T., Steele, S., Makris, N., Kennedy, D., Harris, G.J., Caviness Jr., V.S., 2003. Dissociations of cerebral cortex, subcortical and cerebral white matter volumes in autistic boys. Brain 126, 1182–1192.
Herbert, M.R., Ziegler, D.A., Deutsh, C.K., Brien, L.M., Kennedy, D.N., Filipek, P.A., 2005. Brain asymmetries in autism and developmental language disorder: a nested whole-brain analysis. Brain 128, 213–226.
Huang, H., Zhang, J., Jiang, H., Wakana, S., Poetscher, L., Miller, M.I., van Zijl, P.C., Hillis, A.E., Wytik, R., Mori, S., 2005. DTI tractography based parcellation of white matter: application to the mid-sagittal morphology of corpus callosum. Neuroimage 26, 195–205.
Inada, N., Kamio, Y., in press. Short forms of the Japanese version WISC-III for assessment of children with autism spectrum disorders. Japanese Journal of Child and Adolescent Psychiatry.
Jackson, P.L., Meltzoff, A.N., Decety, J., 2005. How do we perceive the pain of others? A window into the neural processes involved in empathy. Neuroimage 24, 771–779.
Just, M.A., Cherkassky, V.L., Keller, T.A., Minshew, N.J., 2004. Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain 127, 1811–1821.
Kamio, Y., Yukihiro, R., Adachi, J., Ichikawa, H., Inoue, M., Uchiyama, T., Kurita, H., Sugiyama, T., Tsujii, M., 2006. Reliability and validity of the Pervasive Developmental Disorder (PDD)-Autism Society Japan Rating Scale (PARS): a behavior checklist for adolescent and adults with PDDs. Clin. Psychiatr. (Seishin-Igaku) 48, 495–505 (in Japanese).
Kamio, Y., Tsujii, H., Inada, N., Kuroda, M., Koyama, T., Uno, Y., Okudera, T., Ichikawa, H., Takaki, A., 2009. Validation of the Japanese version of the social responsiveness scale: comparison with PDD-Autism Society Japan rating scales (PARS). Seishin Igaku (Clin. Psychiatr.) 51, 1101–1109 (in Japanese).
Kaufmann, W.E., Cooper, K.L., Mostofsky, S.H., Capone, G.T., Kates, W.R., Newschaffer, C.J., Bukelis, I., Stump, M.H., Jann, A.E., Lanham, D.C., 2003. Specificity of cerebellar vermian abnormalities in autism: a quantitative magnetic resonance imaging study. J. Child Neurol. 18, 463–470.
Ke, X., Tang, T., Hong, S., Hang, Y., Zou, B., Li, H., Zhou, Z., Ruan, Z., Lu, Z., Tao, G., Liu, Y., 2009. White matter impairments in autism, evidence from voxel-based morphometry and diffusion tensor imaging. Brain Res. 1265, 171–177.
Kennedy, D.P., Redcay, E., Courchesne, E., 2006. Failing to deactivate: resting functional abnormalities in autism. Proc. Natl Acad. Sci. USA 103, 8275–8280.
Kleinhans, N.M., Johnson, L.C., Richards, T., Mahurin, R., Greenson, J., Dawson, G., Aylward, E., 2009. Reduced neural habituation in the amygdala and social impairments in autism spectrum disorders. Am. J. Psychiatry 166, 467–475.
Kurita, H., Miyake, Y., Katsuno, K., 1989. Reliability and validity of the Childhood Autism Rating Scale-Tokyo Version (CARS-TV). J. Autism Dev. Disord. 19, 389–396.
Lee, J.E., Bigler, E.D., Alexander, A.L., Lazar, M., DuBray, M.B., Chung, M.K., Johnson, M., Morgan, J., Miller, J.N., McMahon, W.M., Lu, J., Jeong, E.K., Lainhart, J.E., 2007. Diffusion tensor imaging of white matter in the superior temporal gyrus and temporal stem in autism. Neurosci. Lett. 424, 127–132.
Monk, C.S., McClure, E.B., Nelson, E.E., Zarahn, E., Bilder, R.M., Leibenluft, E., Charney, D.S., Ernst, M., Pine, D.S., 2003. Adolescent immaturity in attention related brain engagement to emotional facial expressions. Neuroimage 20, 420–428.
Morris, J.P., Pelphrey, K.A., McCarthy, G., 2005. Regional brain activation when approaching a virtual human on a virtual walk. J. Cogn. Neurosci. 17, 1744–1752.
Müller, R.A., 2007. The study of autism as a distributed disorder. Ment. Retard. Dev. Disabil. Res. Rev. 13, 85–95.
Nimchinsky, E.A., Gilissen, E., Allman, J.M., Perl, D.P., Erwin, J.M., Hof, P.R., 1999. A neuronal morphologic type unique to humans and great apes. Proc. Natl Acad. Sci. USA 96, 5268–5273.
Olson, I.R., Plotzker, A., Ezzyat, Y., 2007. The enigmatic temporal pole: a review of findings on social and emotional processing. Brain 130 (1718–17), 31.
Papadakis, N.G., Xing, D., Houston, G.C., Smith, J.M., Smith, M.I., James, M.F., Parsons, A.A., Huang, C.L., Hall, L.D., Carpenter, T.A., 1999. A study of rotationally invariant and symmetric indices of diffusion anisotropy. Magn. Reson. Imaging 17, 881–892.
Pardini, M., Garaci, F.G., Bonzano, L., Roccatagliata, L., Palimieri, M.G., Pompili, E., Coniglione, F., Krueger, F., Ludovici, A., Floris, R., Benassi, F., Emberti, Gialloreti, L., 2009. White matter reduced streamline coherence in young men autism and mental retardation. Eur. J. Neurol. 16, 1185–1190.
Pelphrey, K.A., Carter, E.J., 2008. Brain mechanisms for social perception: lessons from autism and typical development. Ann. NY Acad. Sci. 1145, 283–299.
Pierce, K., Courchesne, E., 2001. Evidence for a cerebellar role in reduced exploration and stereotyped behavior in autism. Biol. Psychiatry 49, 655–664.
Pierce, K., Haist, F., Sedaghat, F., Courchesne, E., 2004. The brain response to personally familiar faces in autism: findings of fusiform activity and beyond. Brain 127, 2703–2716.
Pierpaoli, C., Jezzard, P., Basser, P.J., Barnett, A., Di Chiro, G., 1996. Diffusion tensor MR imaging of the human brain. Radiology 201, 637–648.
Pugliese, L., Catani, M., Ameis, S., Dell'Acqua, F., Thiebaut, de Schotten, M., Murphy, C., Robertson, D., Deeley, Q., Daly, E., Murphy, D.G., 2009. The anatomy of extended limbic pathways in Asperger syndrome: a preliminary diffusion tensor imaging tractography study. Neuroimage 47, 427–434.

Saarela, M.V., Hari, R., 2008. Listening to human walking together activates the social brain circuitry. Soc. Neurosci. 3, 401–409.
Sadakata, T., Kakegawa, W., Mizoguchi, A., Washida, M., Kato-Senba, R., Shoutoh, F., Okamoto, T., Nakashima, H., Kimura, K., Tanaka, M., Sekine, Y., Itohara, S., Yuzaki, M., Nagao, S., Furuichi, T., 2007a. Impaired cerebellar development and function in mice lacking CAPS2, a protein involved in neurotrophin release. J. Neurosci. 27, 2472–2482.
Sadakata, T., Washida, M., Iwayama, Y., Shoji, S., Sato, Y., Ohkura, T., Katoh-Semba, R., Nakajima, M., Sekine, Y., Tanaka, M., Nakamura, K., Iwata, Y., Tsuchiya, K.J., Mori, N., Detera-Wadleigh, S.D., Ichikawa, H., Itohara, S., Yoshikawa, T., Furuichi, T., 2007b. Autistic-like phenotypes in *Cadps2*-knockout mice and aberrant *CADPS2* splicing in autistic patients. J. Clin. Invest. 117, 931–943.
Sahyoun, C.P., Belliveau, J.W., Soulieres, I., Schwartz, S., Mody, M., 2010. Neuroimaging of the functional and structural networks underlying visuospatial vs. linguistic reasoning in high-functioning autism. Neuropsychogia 48, 86–95.
Schopler, E., Reichler, R.J., Renner, B.R., 1988. Childhood Autism Rating Scale. Western Psychological Services, Los Angeles, CA.
Siegal, M., Varley, R., 2002. Neural systems involved in "theory of mind". Nat. Rev. Neurosci. 3, 463–471.
Simms, M.L., Kemper, T.L., Timbie, C.M., Bauman, M.L., Blatt, G.J., 2009. The anterior cingulated cortex in autism: heterogeneity of qualitative and quantitative cytoarchitectonic features suggests possible subgroup. Acta Neuropathol. 118, 673–684.
Sparks, B., Friedman, S., Shaw, D., Alyward, E., Echelard, D., Artru, A., Maravilla, K.R., Giedd, J.N., Munson, J., Dawson, G., Dager, S.R., 2002. Brain structural abnormalities in young children with autism spectrum disorder. Neurology 59, 184–192.
Sundaram, S.K., Kumar, A., Makki, M.I., Behen, M.E., Chugani, H.T., Chugani, D.C., 2008. Diffusion tensor imaging of frontal lobe in autism spectrum disorder. Cereb. Cortex 18, 2659–2665.
Tachimori, H., Osada, H., Kurita, H., 2003. Childhood autism rating scale-Tokyo version for screening pervasive developmental disorders. Psychiatry Clin. Neurosci. 57, 113–118.
Taylor, J., Fragopanagos, N., 2005. The interaction of attention and emotion. Neural Netw. 18, 353–369.
Thakkar, K.N., Polli, F.E., Joseph, R.M., Tuch, D.S., Hadjikhani, N., Barton, J.J., Manoach, D.S., 2008. Response monitoring, repetitive behavior and anterior cingulated abnormalities in autism spectrum disorder (ASD). Brain 131, 2464–2478.
Townsend, J., Courchesne, E., Singer-Harris, N., Covington, J., Westerfield, M., Lyden, P., Lowry, T.P., Press, G.A., 1999. Spatial attention deficits in patients with acquired or developmental cerebellar abnormality. J. Neurosci. 19, 5632–5643.
Wang, A.T., Dapretto, M., Hariri, A.R., Sigman, M., Bookheimer, S.Y., 2004. Neural correlates of facial affect processing in children and adolescents with autism spectrum disorder. J. Am. Acad. Child Adolesc. Psychiatry 43, 481–490.
Wechsler, D., 1991. Wechsler Intelligence Scale for Children, 3rd ed. The Psychological Corporation, San Antonio, TX.
Wechsler, D., 1997. Wechsler Adult Intelligence Scale, 3rd ed. Psychological Corporation, San Antonio, TX.
Weissman, D.H., Perkins, A.S., Woldorff, M.G., 2008. Cognitive control in social situations: a role for the dorsolateral prefrontal cortex. Neuroimage 40, 955–962.
Wicker, B., Fonlupt, P., Hubert, B., Tardif, C., Gepner, B., Deruelle, C., 2008. Abnormal cerebral effective connectivity during explicit emotional processing in adults with autism spectrum disorder. SCAN 3, 135–143.
Williams, J.H.G., Waiter, G.D., Gilchrist, A., Perrett, D.I., Murray, A.D., Whiten, A., 2006. Neural mechanisms of imitation and "mirror neuron" functioning in autistic spectrum disorder. Neuropsychologia 44, 610–621.
Witelson, S.F., 1989. Hand and sex differences in the isthmus and genu of the human corpus callosum. A postmortem morphological study. Brain 112, 799–835.
Yurgelun-Todd, D.A., Killgore, W.D., 2006. Fear-related activity in the prefrontal cortex increases with age during adolescence: a preliminary fMRI study. Neurosci. Lett. 406, 194–199.

Research in Autism Spectrum Disorders 5 (2011) 330–336

Contents lists available at ScienceDirect

Research in Autism Spectrum Disorders

Journal homepage: http://ees.elsevier.com/RASD/default.asp

Reliability and validity of the Japanese version of the Modified Checklist for autism in toddlers (M-CHAT)

Naoko Inada [a], Tomonori Koyama [a], Eiko Inokuchi [a], Miho Kuroda [a,b], Yoko Kamio [a,*]

[a] 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

[b] Department of Psychology, Faculty of Human Relations, Tokai Gakuin University, 5-68 Nakakirino, Kakamigahara, Gifu 504-8511, Japan

ARTICLE INFO

Article history:
Received 31 March 2010
Received in revised form 16 April 2010
Accepted 23 April 2010

Keywords:
Autism spectrum disorders (ASD)
Early detection
Modified Checklist for autism in toddlers (M-CHAT)
Reliability
Short version
Validity

ABSTRACT

Early detection and intervention is essential for children with autism spectrum disorders (ASD). Therefore, we examined the reliability and validity of the Japanese version of the Modified Checklist for autism in toddlers (M-CHAT), a 23-item, yes–no questionnaire regarding early autistic symptoms completed by parents of children at 18–24 months of age. Herein, the reliability of the M-CHAT was investigated for children 4–20 months of age. The M-CHAT score (the number of failed items) was found to be significantly correlated among 24 mother–father pairs (Pearson's $r = .933$), representing good inter-rater reliability. The test–retest reliability was satisfactory, with 22 mothers providing almost equal M-CHAT scores on two different occasions ($r = .990$). Significant correlations were observed between the M-CHAT score and the Childhood Autism Rating Scale-Tokyo version score in 25 two-year-old children ($r = .581$), indicating good concurrent validity. The M-CHAT score was significantly higher in 20 children later diagnosed with ASD compared with reference children ($n = 1167$), revealing sufficient discriminant validity. A short version of the M-CHAT using 9 items was proposed and effectively differentiated children with ASD from reference children. The efficacy of the Japanese version of the M-CHAT was demonstrated for first-level screening in the general population.

1. Introduction

Autism spectrum disorders (ASD) reportedly affect 1–2% of children (Baird et al., 2006; Baron-Cohen et al., 2009; Kawamura, Takahashi, & Ishii, 2008). Early detection is considered essential for children with ASD based on findings of clinical studies that have shown that early intervention subsequent to early detection can enhance their potential (Dawson et al., 2010) and lead to "optimal outcome" (Sutera et al., 2007). To date, some ASD screening tools, such as the Checklist for autism in toddlers (CHAT) (Baron-Cohen, Allen, & Gillberg, 1992), the Modified Checklist for autism in toddlers (M-CHAT) (Robins, Fein, Barton, & Green, 2001), the Early Screening of Autistic Traits Questionnaire (ESAT) (Swinkels et al., 2006), and the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT) (Matson et al., 2009) have been developed for the early detection of ASD.

Japan has established a national health check-up system that provides all children, from infants to 3-year-olds, with regular free routine check-ups. This check-up system is well organized and health check-ups at 18 and 36 months effectively determine the children's language/intellectual development. Because socio-communication abnormalities in ASD begin to manifest at 1 year of age (Kamio, Tobimatsu, & Fukui, in press), the check-up at 18 months of age appears to provide a good opportunity to detect early symptoms of ASD. The M-CHAT, a 23-item, parent-report questionnaire (Robins et al., 2001), may

* Corresponding author. Tel.: +81 42 341 2711; fax: +81 42 346 1944.
E-mail address: kamio@ncnp.go.jp (Y. Kamio).

1750-9467/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rasd.2010.04.016

enhance the current system, since the checklist was developed for children 18–24 months of age and is easy to administer without increasing the burden on both the families and check-up staff.

For the aforementioned reasons, we developed the Japanese version of the M-CHAT. After a preliminary study (Kamio & Inada, 2006), with the permission of the authors, we added some illustrations (items 7, 9, 17, and 23: see M-CHAT Information, Robins, n.d.) in order to encourage caregivers to notice negative symptoms (attenuated typical development). The primary aim of this study is to establish the reliability and validity of the Japanese M-CHAT.

To the best of our knowledge, the inter-rater reliability and test–retest reliability of the M-CHAT have not been examined. This may be because most children in the targeted age range (18–24 months) are expected to pass almost all the M-CHAT items, thus, yes–no answers are skewed toward positive responses. To avoid such a "ceiling effect" in responses, inter-rater and test–retest reliabilities should be examined for children at different developmental stages. In the current study, the reliability of the Japanese version of the M-CHAT was examined for young children in the first and second years of life who are expected to fail some M-CHAT items (Inada, Kamio, & Koyama, in press).

Although satisfactory internal consistency of the M-CHAT has been reported (Kleinman et al., 2008; Robins et al., 2001), the checklist contains some dummy/buffer items (Baron-Cohen et al., 1992; Robins et al., 2001) that obscure the aim of screening from caregivers. Those items are not directly related to the behaviors of children with ASD; in other words, some items of the M-CHAT may not have face validity. As 6 items were selected from the original M-CHAT as "critical items" (Kleinman et al., 2008; Robins et al., 2001), a more simple but effective short version might be useful. Thus, a second aim of this study is to explore the critical items on the Japanese M-CHAT in order to create a short version.

2. Methods

2.1. Participants and procedures

2.1.1. Reliability sample

Reliability data were collected from voluntary parents recruited from local nursery schools or several communities. Inter-rater reliability data were collected from the mothers and fathers of 24 children (13 males; mean age = 10.0 months, SD = 4.3 months, range = 4–17 months) and test–retest reliability data were collected from the mothers of 22 children (12 males; mean age = 12.8 months, SD = 5.8 months, range = 4–20 months) with a mean interval of 8.3 days (range = 4–14 days). The caregivers were not particularly familiar with ASD or the general development of children and were not told the aim of the study before giving their answers.

2.1.2. Validity sample

The concurrent validity was examined using data from 25 children (17 males; mean age = 24.0 months, SD = .7 months, range = 23–26 months), who lived in Nishi-Tokyo city, Japan, and were consecutively referred to the authors due to developmental concerns between December 2008 and December 2009. The mothers of the children answered the M-CHAT prior to the diagnostic evaluations. Two child psychiatrists and two certificated clinical psychologists who did not know the results of the M-CHAT assessed the children in a team using the Childhood Autism Rating Scale-Tokyo version (CARS-TV), which is the Japanese version of the CARS (Schopler, Reichler, DeVellis, & Daly, 1980) and has been demonstrated to be reliable and valid for evaluating autistic symptoms in children (Kurita, Miyake, & Katsuno, 1989; Tachimori, Osada, & Kurita, 2003). The CARS has been reported to be useful for toddlers 2 years of age (Chlebowski, Green, Barton, & Fein, in press).

The discriminant validity was investigated using M-CHAT data from 1187 children (612 males), which had been collected at free health check-ups for 18-month-olds in Munakata city, Fukuoka prefecture, Japan, between April 2005 and March 2007. Of these children, 20 (16 males) were identified as having ASD at age 3. Based on detailed clinical assessments and comprehensive parental interviews on their developmental history independent of the M-CHAT results, the diagnoses were confirmed by expert consensus among our research team (two experienced psychiatrists and a certificated clinical psychologist) according to the DSM-IV-TR criteria for pervasive developmental disorders (PDD) (American Psychiatric Association, 2000). Of the 20 children with ASD, 7 children (6 males) were diagnosed with autistic disorder (autism) and the remaining 13 children (10 males) were diagnosed with PDD not otherwise specified (PDD-NOS). The remaining 1,167 children (596 males) who completed a 3-year health check-up conducted by health professionals including pediatric neurologists were grouped as a reference group in this study.

2.1.3. Ethical issues

The protocol of this study was approved by the ethics committee of the National Center of Neurology and Psychiatry, Japan. Written informed consent to participate in our study was obtained from the caregivers of each of the children.

2.2. Data analysis

2.2.1. Reliability

For inter-rater reliability, Pearson's correlation coefficient (r) was calculated between the M-CHAT score (the number of failed items) of mothers and that of fathers. In addition, we calculated kappa coefficients (κ) for each of the 23 items. Similarly, the test–retest reliability was examined using the first (test) and second (retest) answers.

2.2.2. Validity

The concurrent validity was examined by calculating Pearson's correlation coefficient (r) between the M-CHAT score and the CARS-TV total score. To examine the discriminant validity, we compared the M-CHAT scores among the autism, PDD-NOS, and reference groups by analysis of variance (ANOVA), and post hoc comparisons were conducted with Bonferroni's correction. The pass rate for each of the 23 items was compared between the ASD (both the autism and PDD-NOS) and the reference groups using Fisher's exact test with Bonferroni's correction.

2.2.3. Short version

Based on the above item analysis, we proposed a short version of the Japanese M-CHAT and compared the internal consistency (Cronbach's α) between the full and short versions. Similar to the full version (see above), a correlation with the CARS-TV total score and comparison among the autism, PDD-NOS, and reference groups were examined.

2.2.4. Screening utility

Using a validation sample from Munakata city ($n = 1187$), we preliminarily reported the sensitivity, specificity, and positive/negative predictive values for predicting later diagnosis of ASD in children at 18 months of age.

All statistical analyses were performed using SPSS 18.0J for Windows and the level of statistical significance was set at .05 (two-tailed).

3. Results

3.1. Reliability

3.1.1. Inter-rater reliability

A significant positive correlation was observed between the M-CHAT scores (the number of failed items) of mothers and fathers ($r = .933$, $p < .001$). As shown in Table 1, kappa coefficients (κ) for inter-rater reliability were significant for 14 (κ ranges .417–1.000, mean = .712) out of 18 items. For 5 items on which the coefficient could not be calculated, the raw agreement rates were very high, exceeding .917. However, κ were not significant for the following four items: item 8 (Functional play), 14 (Responds to name), 18 (Unusual finger movement) and 22 (Stares at nothing).

3.1.2. Test–retest reliability

The first and second M-CHAT scores were significantly positively correlated ($r = .990$, $p < .001$). As shown in Table 1, 16 of the 18 items showed moderate to high test–retest reliability (κ ranges .645–1.000, mean = .912). For the 5 items for which kappa values could not be calculated, the raw agreement rates were satisfactorily high. However, the κ were not significant for items 11 (Oversensitive to noise) and 14 (Responds to name).

Table 1
Kappa coefficients (κ) of the Japanese version of the Modified Checklist for autism in toddlers (M-CHAT).

Item no.	M-CHAT item	Inter-rater ($n = 24$)	Test–retest ($n = 22$)
1.	Enjoys being swung	.958[a]	1.000[a]
2.	Interest in other children	.700**	1.000**
3.	Climbs up stairs	.915**	1.000**
4.	Enjoys peek-a-boo	.917[a]	1.000**
5.	Pretend play	.600**	1.000**
6.	Imperative pointing	.727**	.909**
7.	Declarative pointing	.909**	.908**
8.	Functional play	.111	.909**
9.	Brings objects to show	.808**	.817**
10.	Eye contact	.958[a]	.955[a]
11.	Oversensitive to noise	.514**	−.065
12.	Responds to smile	1.000[a]	1.000[a]
13.	Imitation of action	.667**	.879**
14.	Responds to name	−.167	.327
15.	Point following	.664**	.792**
16.	Walking	1.000**	1.000**
17.	Gaze-following	.750**	.817**
18.	Unusual finger movement	.111	.645**
19.	Gaining parent's attention	.565**	1.000**
20.	Wondering hearing	.958[a]	1.000[a]
21.	Understands what is said	.727**	1.000**
22.	Stares at nothing	.263	.955[a]
23.	Social reference	.417*	.909**

* $p < .05$.
** $p < .01$.
[a] Figure is the raw agreement rate as kappa could not be calculated.

Table 2
The M-CHAT scores (the number of failed items) at 18 months of age.

	Mean	SD	$F_{(2,1184)}$
Full version			73.8**
Autism ($n = 7$)	4.71	4.54	
Pervasive developmental disorders not otherwise specified (PDD-NOS) ($n = 13$)	2.46	1.56	
Reference ($n = 1167$)	.58	.99	

Note: Any post hoc comparisons with Bonferroni's correction were significant ($p < .001$).
** Analysis of variance (ANOVA), $p < .01$.

3.2. Validity

3.2.1. Concurrent validity

The M-CHAT score was significantly correlated with the CARS-TV total score in 25 children 23–26 months of age ($r = .581$, $p = .002$).

3.2.2. Discriminant validity

As shown in Table 2, the mean M-CHAT score at 18 months of age differed significantly among the diagnostic groups. The M-CHAT score was the highest in the autism group, followed by the PDD-NOS and the reference groups, respectively.

Table 3 shows that the pass rate at 18 months of age in children later diagnosed with ASD was significantly lower than that of the reference children for the following 11 items: item 5 (Pretend play), 6 (Imperative pointing), 7 (Declarative pointing), 8 (Functional play), 9 (Brings objects to show), 13 (Imitation of action), 14 (Responds to name), 15 (Point following), 17 (Gaze-following), 21 (Understands what is said), and 23 (Social reference).

3.3. Short version

Based on the above analyses for each of the 23 items, we developed a short version of the Japanese M-CHAT consisting of 9 items (items 5, 6, 7, 9, 13, 15, 17, 21, and 23). Cronbach's α for the short version (.752) improved compared to that of the full version (.556), suggesting that the short version has superior internal consistency compared to the full version.

The number of failed items in the short version (M-CHAT-SV score) was significantly correlated with the CARS-TV total score in 25 children 23–26 months of age ($r = .615$, $p = .001$). The mean M-CHAT-SV score at 18 months of age differed significantly among the diagnostic groups ($F = 81.5$, d.f. = 2, 1184, $p < .001$), and all post hoc comparisons with Bonferroni's correction demonstrated a significant difference in the mean M-CHAT-SV score among the autism (mean = 3.43, SD = 3.41), PDD-NOS (mean = 1.62, SD = 1.71), and reference (mean = .20, SD = .72) groups.

Table 3
Pass rate of each item at 18 months of age.

Item no.	M-CHAT item	Autism spectrum disorders (ASD) ($n = 20$)	Reference ($n = 1167$)	Corrected p
1.	Enjoys being swung	95.0%	99.9%	.769
2.	Interest in other children	100.0%	99.7%	1.000
3.	Climbs up stairs	100.0%	99.6%	1.000
4.	Enjoys peek-a-boo	100.0%	99.7%	1.000
5.	Pretend play	75.0%	97.9%	.002**
6.	Imperative pointing	80.0%	98.6%	.006**
7.	Declarative pointing	70.0%	97.9%	.000**
8.	Functional play	70.0%	93.7%	.030*
9.	Brings object to show	75.0%	98.2%	.001**
10.	Eye contact	90.0%	99.1%	.433
11.	Oversensitive to noise	95.0%	83.2%	1.000
12.	Responds to smile	100.0%	99.9%	1.000
13.	Imitation of action	80.0%	99.1%	.001**
14.	Responds to name	85.0%	99.8%	.001**
15.	Point following	85.0%	99.1%	.024*
16.	Walking	100.0%	99.7%	1.000
17.	Gaze-following	65.0%	95.4%	.001**
18.	Unusual finger movement	95.0%	97.9%	1.000
19.	Gaining parent's attention	85.0%	97.7%	.286
20.	Wondering hearing	95.0%	100.0%	.388
21.	Understands what is said	85.0%	99.1%	.030*
22.	Stares at nothing	90.0%	91.7%	1.000
23.	Social reference	60.0%	94.7%	.000**

* Fisher's exact test with Bonferroni's correction, $p < .05$.
** Fisher's exact test with Bonferroni's correction, $p < .01$.

Table 4
Cut-off value and related measures for predicting later diagnosis of autism spectrum disorders (ASD) in children at 18 months of age.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Full version (M-CHAT score)				
≥1	.800	.609	.034	.994
≥2	.750	.893	.107	.995
≥3	.550	.961	.193	.992
≥4	.350	.978	.212	.989
Short version (M-CHAT-SV score)				
≥1	.650	.885	.088	.993
≥2	.550	.958	.183	.992
≥3	.400	.981	.267	.990
≥4	.200	.990	.250	.986

Note: Children with ASD, $n = 20$; reference, $n = 1167$. Short version of the Japanese M-CHAT consists of 9 items (items 5, 6, 7, 9, 13, 15, 17, 21, and 23).

3.4. Screening utility (preliminary report)

Table 4 shows the cut-off value and related measures for predicting later diagnosis of ASD in children at 18 months of age. In order to maintain a balance between sensitivity and specificity, failing 2/23 items and 1/9 items was thought to provide the best cut-off; however, low positive predictive values indicated that there were many false positives.

4. Discussion

In this study, we demonstrated the reliability and validity of the Japanese version of the M-CHAT, identified its critical items in order to produce a short version, and reported preliminary information regarding the utility of the full/short version as a screening tool for early detection of ASD.

To the best of our knowledge, this is the first study to confirm that the M-CHAT has good inter-rater and test–retest reliabilities for infants and toddlers in the first 2 years of life. The present results suggest that caregivers can provide reliable answers to most of the items on the Japanese version of the M-CHAT. As to the test–retest reliability, a relatively short interval between tests was used in this study because children at this age develop very rapidly, which might have caused memory effect and *false* consistency. Future studies should be conducted to confirm the reliability of the M-CHAT for toddlers with an ASD diagnoses.

The Japanese version of the M-CHAT showed concurrent validity with the CARS, which has been reported to be useful for evaluating autistic symptoms in toddlers 2 years of age (Chlebowski et al., in press). In addition, the M-CHAT score was high in children later diagnosed with ASD, particularly in children with autism. These results reflect the high validity of the Japanese M-CHAT and support its use as a ASD screening tool for toddlers. Further replication studies are necessary using other standardized measurements such as the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000) and/or Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994).

Although the children who were evaluated in the present study were slightly younger than those administered the original M-CHAT (Kleinman et al., 2008; Robins et al., 2001), children 18 months of age who are later diagnosed with ASD showed lower pass rates on 5 out of the 6 "critical items" of the original M-CHAT (items 2, 7, 9, 13, 14, and 15) except item 2 (Interest in other children). Item 2 was originally included in the CHAT (Baron-Cohen et al., 1992) and was also found to be sensitive to diagnosis of ASD when asked retrospectively to Japanese caregivers in clinical settings (Koyama et al., in press). Its high pass rate (100%) in children with ASD in this study indicates that caregivers were not aware of the child's disinterest toward other children. At the age of 18 months, Japanese caregivers may still interpret a lack of interest in other children as modesty or shyness rather than a symptom.

Item 14 (Responds to name) is one of the "critical items" on the original M-CHAT (Kleinman et al., 2008; Robins et al., 2001) and similarly showed significant discriminative power for the 18-month-old children in the present study. However, as neither inter-rater nor test–retest reliability were confirmed, we conservatively excluded this item from the short version. Four children were rated as "pass" by their mother but were rated "fail" by their father, while 3 children were rated conversely. Two children who had first failed this item were rated as "pass" the second time by their mother, whereas one child was rated conversely. These inconsistencies were found in older children as well as younger children. Although this item (Does your child respond to his/her name when you call?) was intended to ask about children's ability to respond to caregivers' social approach by calling, it may be ambiguous for parents of children in the age range of this study. Since the item had good validity for the early detection of ASD in our study, it appears that rephrasing for clarity is necessary.

We created a 9-item short version of the Japanese M-CHAT with higher internal consistency and similar validity compared to the full version. This simpler screening tool may have a practical advantage. As there are no reverse items (items 11, 18, 20, and 22) in the short version, the practical load on the check-up staff may be reduced. Although a single screening using parent-report questionnaires can never predict an ASD diagnosis precisely (Bryson, Rogers, & Fombonne, 2003), it can

be the first step in the multistage screening process as health check-ups provide valuable opportunities for screening young children aged 18–24 months.

The low positive predictive value observed in our epidemiological community sample was consistent with the findings of the original M-CHAT for the low-risk sample (Kleinman et al., 2008), indicating many false positives were involved in the early screening process using the M-CHAT. Kleinman et al. (2008) reported that the positive predictive value was improved from .11 to .65 by adding a follow-up telephone interview. Considering that multistage screenings are necessary for effective early detection of ASD (Bryson et al., 2003), the Japanese version of the M-CHAT, which has acceptable sensitivity, may be appropriate for a first-level screening targeting the general population.

Although only a preliminary finding, in terms of the sensitivity and specificity, the best cut-off value for the Japanese version of the M-CHAT was failure on 2/23 items, which is lower than failure on 3/23 items using in the original M-CHAT (Robins et al., 2001). This was due to the higher pass rate in Japanese 18-month-old children who are later diagnosed with ASD compared with their American counterparts (Robins et al., 2001). The 6-month difference in age between the Japanese and American children may in part explain this inconsistency. Alternatively, it may be explained by the tendency of Japanese people to avoid making definite answers, even if they have some concerns. Thus, the yes–no questions of the M-CHAT may not have accurately reflected the Japanese caregivers' observations. Modifying the response style to a Likert scale, as used in the Chinese version (Wong et al., 2004), might produce different results.

Due to the small sample size, we should avoid over generalizing the findings of this study, especially the cut-off score. As for use, some modifications may be necessary according to the age of children and cultural attitudes and values. Furthermore, long-term follow-up is necessary because the current scores could change if new ASD cases are detected in the future. Nonetheless, based on the present results, the Japanese version of the M-CHAT, as well as its short version, are considered reliable and valid for use as a first-level screening tool for early detection of ASD in the general population.

Acknowledgements

This study was supported by a Research Grant from the Research Institute of Science and Technology for Society of the Japan Science and Technology Agency and by Research Grants (H19-SHOGAI-008, H19-KOKORO-006 and H20-KOKORO-004) from the Ministry of Health, Labour and Welfare of Japan. We would like to thank Ms. Shizuka Omori for her help with data collection.

References

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th text revised ed.). Washington, DC: Author.

Baird, G., Simonoff, E., Pickles, A., Chandler, S., Loucas, T., Meldrum, D., et al. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: The Special Needs and Autism Project (SNAP). *Lancet, 368*, 210–215.

Baron-Cohen, S., Allen, J., & Gillberg, C. (1992). Can autism be detected at 18 months?: The needle, the haystack, and the CHAT. *British Journal of Psychiatry, 161*, 839–843.

Baron-Cohen, S., Scott, F. J., Allison, C., Williams, J., Bolton, P., Matthews, F. E., et al. (2009). Prevalence of autism-spectrum conditions: UK school-based population study. *British Journal of Psychiatry, 194*, 500–509.

Bryson, S. E., Rogers, S. J., & Fombonne, E. (2003). Autism spectrum disorders: Early detection, intervention, education, and psychopharmacological management. *Canadian Journal of Psychiatry, 48*, 506–516.

Chlebowski, C., Green, J. A., Barton, M. L., & Fein, D. (in press). Using the childhood autism rating scale to diagnose autism spectrum disorders. *Journal of Autism and Developmental Disorders* [Epub ahead of print].

Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., et al. (2010). Randomized, controlled trial of an intervention for toddlers with autism: The Early Start Denver Model. *Pediatrics, 125*, e17–e23.

Inada, N., Kamio, Y., & Koyama, T. (in press). Developmental chronology of preverbal social behaviors in infancy using the M-CHAT: Baseline for early detection of atypical social development. *Research in Autism Spectrum Disorders*.

Kamio, Y., & Inada, N. (2006). 1-sai 6-kagetsu kenshin ni okeru kouhansei hattatsu shougai no souki hakken ni tsuite no yobiteki kenkyu [A preliminary study on the early detection of pervasive developmental disorders at 18-month check-up]. *Seishin Igaku, 48*, 981–990 (in Japanese).

Kamio, Y., Tobimatsu, S., & Fukui, H. (in press). Developmental disorders. In J. Decety, & J. Cacioppo (Eds.), *The handbook of social neuroscience*. Oxford: Oxford University Press.

Kawamura, Y., Takahashi, O., & Ishii, T. (2008). Reevaluating the incidence of pervasive developmental disorders: Impact of elevated rates of detection through implementation of an integrated system of screening in Toyota, Japan. *Psychiatry and Clinical Neurosciences, 62*, 152–159.

Kleinman, J. M., Robins, D. L., Ventola, P. E., Pandey, J., Boorstein, H. C., Esser, E. L., et al. (2008). The modified checklist for autism in toddlers: A follow-up study investigating the early detection of autism spectrum disorders. *Journal of Autism and Developmental Disorders, 38*, 827–839.

Koyama, T., Inokuchi, E., Inada, N., Kuroda, M., Moriwaki, A., Katagiri, M., et al. (in press). Utility of the Japanese version of the Checklist for Autism in Toddlers (CHAT-J) for predicting pervasive developmental disorders at age 2. *Psychiatry and Clinical Neurosciences*.

Kurita, H., Miyake, Y., & Katsuno, K. (1989). Reliability and validity of the Childhood autism rating scale-Tokyo version (CARS-TV). *Journal of Autism and Developmental Disorders, 19*, 389–396.

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Jr., Leventhal, B. L., DiLavore, P. C., et al. (2000). The autism diagnostic observation schedule-generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30*, 205–223.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*, 659–685.

Matson, J. L., Wilkins, J., Sevin, J. A., Knight, C., Boisjoli, J. A., & Sharp, B. (2009). Reliability and item content of the Baby and Infant Screen for Children with aUtIsm Traits (BISCUIT): Parts 1–3. *Research in Autism Spectrum Disorders, 3*, 336–344.

Robins, D. L., Fein, D., Barton, M. L., & Green, J. A. (2001). The modified checklist for autism in toddlers: An initial study investigating the early detection of autism and pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 31*, 131–144.

Robins, D. L. (n.d.). M-CHAT Information. Retrieved April 1, 2010, from http://www2.gsu.edu/~psydlr.

Schopler, E., Reichler, R. J., DeVellis, R. F., & Daly, K. (1980). Toward objective classification of childhood autism: Childhood Autism Rating Scale (CARS). *Journal of Autism and Developmental Disorders, 10*, 91–103.

Sutera, S., Pandey, J., Esser, E. L., Rosenthal, M. A., Wilson, L. B., Barton, M., et al. (2007). Predictors of optimal outcome in toddlers diagnosed with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 37*, 98–107.

Swinkels, S. H., Dietz, C., van Daalen, E., Kerkhof, I. H., van Engeland, H., & Buitelaar, J. K. (2006). Screening for autistic spectrum in children aged 14 to 15 months. I. The development of the Early Screening of Autistic Traits Questionnaire (ESAT). *Journal of Autism and Developmental Disorders, 36*, 723–732.

Tachimori, H., Osada, H., & Kurita, H. (2003). Childhood autism rating scale-Tokyo version for screening pervasive developmental disorders. *Psychiatry and Clinical Neurosciences, 57*, 113–118.

Wong, V., Hui, L. H., Lee, W. C., Leung, L. S., Ho, P. K., Lau, W. L., et al. (2004). A modified screening tool for autism (Checklist for Autism in Toddlers [CHAT-23]) for Chinese children. *Pediatrics, 114*, e166–e176.

自閉症スペクトラム障害の早期発見をめぐって

神尾陽子

はじめに

「発達障害」のある子どもへの対応について、ようやく社会全体が危機感を持って真剣に取り組もうと動き始めています。

厚生労働省は発達障害者支援事業を、文部科学省は特別支援教育を、そして環境省は発達障害を含む子どもの健康に影響を及ぼす遺伝と環境の相互作用を調べる全国調査（エコチル調査）に向けて、それぞれ動き出しました。幼児期の早期発見と早期介入は自閉症対策の要であり[1]、わが国を含む世界各国で自閉症スペクトラム障害（重度の自閉症から軽度のアスペルガー症候群や非定型自閉症、特定不能の広汎性発達障害などの下位群までを包括する広い臨床単位）の早期発見と早期介入の取り組みが始まっています[2]。

自閉症的特徴の強い子どもは、対人以外の発達面でも多様な困難を持ちやすい傾向がみられる一方で[3][4]、大人にはない素晴らしい回復力も秘めています。本稿では、自閉症スペクトラム障害のある子どもたちへの対応に、今求められる理解と課題について、乳幼児期を中心に述べます。

かみお・ようこ
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部長。医学博士。専門は児童精神医学。京都大学医学部卒業。京都大学医学部精神神経科、九州大学大学院人間環境学研究院を経て、二〇〇六年より現職。著書に『自閉症』（分担執筆、星和書店、二〇〇九年）、『発達障害の臨床心理学』（共著、東京大学出版会、二〇一〇年）、『発達と脳』（共著、医学書院、二〇一〇年）など。

早期診断の時期とは？

ここで「早期」としている時期は、同じ自閉症スペクトラム障害という診断でも、全般的発達や言語の遅れの有無によって幅があります。技術上は、早くて一歳、遅くても三歳で診断可能と考えられますが、実際には就学後に初めて周囲に気づかれる場合や、なかには社会に出てから自ら気づき診断を求めるケースも多いのが実情です。

最も早く診断可能なのは、知的障害を伴う自閉症で、言語の遅れや呼びかけても反応がない、人への関心が乏しく感覚遊びに没頭する、多動など、顕著な行動特徴を示すので、たいてい一歳代で気づかれます。とはいっても必ずしもすべての典型的自閉症の子どもが一歳六カ月健診で発見されているわけではなく、多動を伴わないおとなしいタイプの子どもは見逃されやすい傾向にあります。一方、知能に遅れがない高機能自閉症やことばをよく話すアスペルガー症候群に代表される高機能タイプでは、一歳六カ月で診断可能なケースもありますが、三歳になるまでは判断に迷うことも少なくありません。

このように、自閉症スペクトラム障害の診断時期に関して、個人差があるとはいえ、三歳になるまでが「早期」と言えるでしょう。したがって、早期支援の「早期」とは、早くて二歳前後、遅くとも就学前をさすものとします。理想的には、アスペルガー症候群のような軽度群であっても自閉症スペクトラムの特性を持つなら、遅くとも三歳健診では子どもの特性を把握し、まず家族に特性を理解してもらい、それから幼稚園や保育園での集団生活でその子どもの生活しにくさについて、なんらかのニーズに応じた支援を開始してほしいものです。

ただし、早いほうが望ましいという理由は以下で述べますが、就学前に支援がなされなかったからといって、必ずしも悲観する必要はありません。気づかれた時点でできるだけ速やかに発達段階に応じたニーズを把握し、的確な対応（それは遅くなればなるほど難しくなるのは事実ですが）がなされるように支援できれば、その子どもにとって良い方向に再び成長していくことも可能です。これも個人差があり、回復力の高いケースもあれば、支援のない状況が長く続いてなかなか回復

への糸口が見つからないケースがあるのは事実です。

早期診断・早期支援はなぜ重要なのか

診断は手段であって、目的ではありません。最終的な目的は、子どもが安定した気持ちで一人ひとり持っている能力を最大限に発揮しすこやかに成長できる生活をサポートしていくこと、にあります。子どものアセスメントで得られる特性把握は、育児への助言、療育サービスの紹介、幼稚園や保育所での支援などに必要な重要な情報です。一人ひとりの子どもの特性を的確に評価したうえでの家族への説明は、家族にとってもより納得のゆく、本当の意味で家族のニーズに沿ったものになります。また、日々のなかでは気づかなかった、子どもの優れた特徴の発見も同時にできれば、意欲を引き出す豊かな環境を整える際の助けにもなります。

自閉症スペクトラム障害に対する生物学的治療法がない現在、早期療育は子どもの社会的発達を促進する重要な手段です。米国からは、自閉症に専門的な内容の療育プログラムでは短期的な効果も報告されています。日本の公的地域サービスはまだ質的にも量的にも不十分と言わざるをえませんが、それでも育児支援も兼ねて早期から母子へ支援することで、子どもの行動の一部ではありますが、こだわりを軽減し、母親の育児への動機づけを高めることが示唆されています。

短期効果だけでなく、成人後の生きがいやＱＯＬ（クオリティ・オブ・ライフ。生活の質）を高める長期的な影響があることも全国調査[4][5]の結果、わかってきました。このことは高機能の自閉症スペクトラム障害の成人において顕著でした。つまり、早い時期から子どもの特性を理解して支援を受けていると、子どもの情緒は安定し、必要以上に自信を失うことなく成長し、さまざまな困難を乗り越えていく力が育っていく可能性を示唆しているのではないでしょうか。つまり、自閉症状が重ければ重いほどＱＯＬが低いといった単純な関係にはない、ということです。

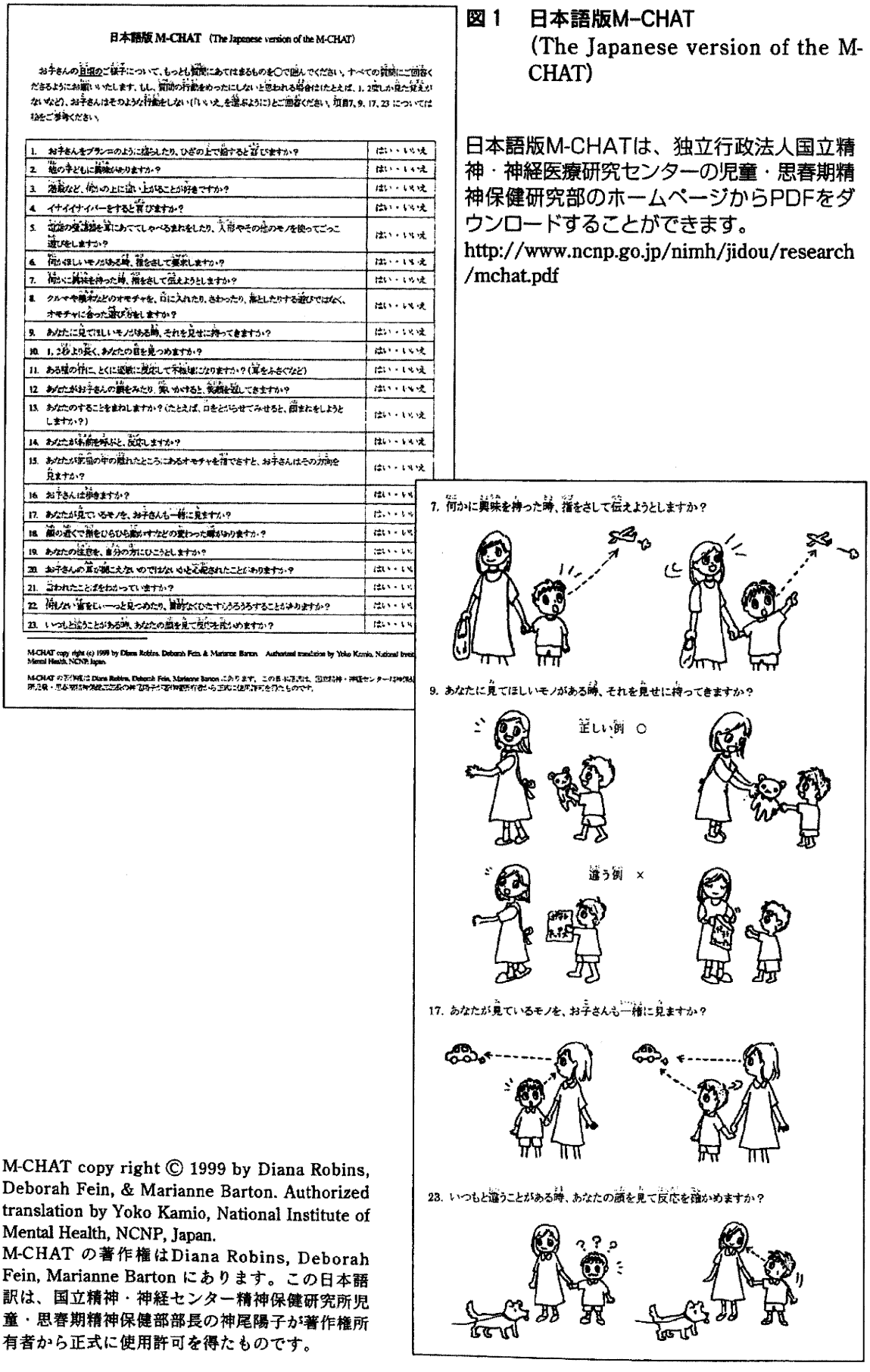
アスペルガー症候群のように自閉症状それ自体が軽度の場合には、むしろ合併するうつや不安などのメンタルな問題の頻度が高く、そのためにＱＯＬが低下するリスクが大きいのです。最近の研究[3]からは、地域で暮らす自閉症スペクトラムの子どもの大半は、医療機

関にかかっているかどうかにかかわらず、なんらかのメンタルな問題も合併していることがわかっています。私たちはこうした調査をするなかで、メンタルな問題も合併したアスペルガー症候群のケースでも、学校での支援が迅速かつ適切に行われ、医療との連携がスムーズになされた場合には、子どもの回復は早いということを知りました。そして一番大事なことは、子ども自身が、大きな困難でも周りの人々に助けてもらって乗り越えられたという自信を得て、さらに大きく成長していったということです。

地域での早期発見の実際

わが国には乳幼児健診という世界に誇るべき制度が存在し、一歳六カ月、三歳時にも健診の機会が設けられています。これを活用した自閉症スペクトラム障害の早期発見システムがまだごく一部の地域でしか取り入れられていないのは残念なことです。その背景には、健診に携わる保健師や小児科医が必ずしも発達障害の子どもの発達について十分な知識や経験を持っていないこと、児童精神科医の数が決定的に不足していること、があると思われます。さらに発達を多面的に評価する言語療法士、臨床心理士、作業療法士などの多職種の専門家が全国的には乏しいことも関係しています。このため現状では、早期兆候が見逃されていたり、懸念を持たれた場合でも診断に至らずいたずらに時間が過ぎてしまったり、あるいは療育サービスの待機が長すぎて、サービスを受けることができない、などといった多くの問題があります。多動やかんしゃくが強いと外出もままならず、室内で遊ばせていても一人遊びに没頭し母親を無視する自閉症状は、診断や助言を受けていない母親の不安を高め、ストレスを募らせることになります。

既存の全般的な発達スクリーニングだけでは、知能の遅れのない自閉症スペクトラム障害の子どもを発見することは難しいという現実からも、米国小児科学会が推奨するように、自閉症の発見に有効なスクリーニングを加えるべきと考えます。自閉症の早期兆候のスクリーニングは、慣れれば難しいものではなく、自閉症児以外の社会的発達に困難を持つ子どもに対しても、有用と思われます。こうした目的で多数のスクリーニング尺度が開発されていますが、本稿では世界



日本語版 M-CHAT (The Japanese version of the M-CHAT)

お子さんの日頃のご様子について、もっとも質問にあてはまるものを○で囲んでください。すべての質問にご回答くださるようにお願いいたします。もし、質問の行動をめったにしないと思われる場合はたとえば、1, 2度しか見たことがないなど、お子さんはそのような行動をしない(「いいえ」を選ぶように)とご回答ください。項目7, 9, 17, 23 については右をご参考ください。

1. お子さんをブランコのように揺らしたり、ひざの上で跳ねさせると喜びますか？	はい・いいえ
2. 他の子どもに興味がありますか？	はい・いいえ
3. 階段など、物の上に登り上がることが好きですか？	はい・いいえ
4. イナイイナイバーをすると喜びますか？	はい・いいえ
5. 電話の受話器を耳にあててしゃべるまねをしたり、人形やその他のモノを使ってごっこ遊びをしますか？	はい・いいえ
6. 何か欲しいモノがある時、指をさして要求しますか？	はい・いいえ
7. 何かに興味を持った時、指をさして伝えようとしますか？	はい・いいえ
8. クルマや積木などのオモチャを、口に入れたり、さわったり、振ったりする遊びではなく、オモチャに合った遊び方をしますか？	はい・いいえ
9. あなたに見てほしいモノがある時、それを見せに持ってきますか？	はい・いいえ
10. 1, 2秒より長く、あなたの目を見つめますか？	はい・いいえ
11. ある種の音に、とくに過敏に反応して不快になりますか？(耳をふさぐなど)	はい・いいえ
12. あなたがお子さんの顔をみたり、笑いかけると、笑顔を返してきますか？	はい・いいえ
13. あなたのすることをまねしますか？(たとえば、口をとがらせてみせると、顔まねをしようとしますか？)	はい・いいえ
14. あなたがお子さんを呼ぶと、反応しますか？	はい・いいえ
15. あなたが家屋の中の離れたところにあるオモチャを指でさすと、お子さんはその方向を見ますか？	はい・いいえ
16. お子さんは歩きますか？	はい・いいえ
17. あなたが見ているモノを、お子さんも一緒に見ますか？	はい・いいえ
18. 顔の近くで指をひらひら動かすなどの変わった動きがありますか？	はい・いいえ
19. あなたの注意を、自分の方にひこうとしますか？	はい・いいえ
20. お子さんの耳が聞こえないのではないかと心配されたことがありますか？	はい・いいえ
21. 言われたことばをわかっていますか？	はい・いいえ
22. 特別な目をじーっと見つめたり、目的なくひたすらうろうろすることがありますか？	はい・いいえ
23. いつもと違うことがある時、あなたの顔を見て反応を確かめますか？	はい・いいえ

M-CHAT copy right (c) 1999 by Diana Robins, Deborah Fein & Marianne Barton. Authorized translation by Yoko Kamio, National Institute of Mental Health, NCNP, Japan.

M-CHAT の著作権は Diana Robins, Deborah Fein, Marianne Barton にあります。この日本語訳は、国立精神・神経センター精神保健研究所児童・思春期精神保健部部長の神尾陽子が著作権所有者から正式に使用許可を得たものです。

7. 何かに興味を持った時、指をさして伝えようとしますか？

9. あなたに見てほしいモノがある時、それを見せに持ってきますか？

正しい例 ○

違う例 ×

17. あなたが見ているモノを、お子さんも一緒に見ますか？

23. いつもと違うことがある時、あなたの顔を見て反応を確かめますか？

図1　日本語版M-CHAT
(The Japanese version of the M-CHAT)

日本語版M-CHATは、独立行政法人国立精神・神経医療研究センターの児童・思春期精神保健研究部のホームページからPDFをダウンロードすることができます。
http://www.ncnp.go.jp/nimh/jidou/research/mchat.pdf

各国で広く用いられているM-CHAT（Modified Checklist for Autism in Toddlers）の日本語版をご紹介したいと思います。

日本語版M-CHATは、二十三項目から成る親記入式の質問紙で、共同注意（大人と注意を共有して環境に注意を向ける行動のこと。図1の右下図を参照）、模倣、対人的関心など、一歳前後の重要な社会的行動のマイルストーン（指標）を中心に構成されています[2]（http://www.ncnp.go.jp/nimh/jidou/research/mchat.pdf）。

表1に示したように、共同注意行動を主とする初期の社会的行動は、平均的な子どもではゼロ歳から芽生え、一歳過ぎには過半数が通過し、一歳六カ月ではほとんどの子どもが通過します。こうした社会的発達の土台の上に、新たに獲得される言語がコミュニケーションとしての力を発揮するのです。こうした土台がないまま覚える言語は、高機能自閉症児の膨大な語彙からおわかりのように知識に過ぎず、人とのコミュニケーションにはあまり使われません。言い換えれば、M-CHATは、一歳六カ月までに芽生える社会的発達をチェックするツールでもあるのです。だからこそ一歳六カ月から二歳までという月齢で用いることに意味があり、その時点でこれらに通過できていないということが発達上の問題として把握されるのです。

M-CHATは、このように日本でも有用性が確認されており、最近では全部あるいは一部を健診に活用する自治体も少しずつですが、増えてきています。

これまで私たちは、地域によってスクリーニングのタイミングや方法は、一歳六カ月の集団健診で用いる場合、二歳時の相談で行う場合など、いくつかのバリエーションを経験しています。また、さらに精度を上げるためには、親回答に加えて、短時間で観察可能な項目については健診場面で保健師あるいは心理士が確認を行うなど、工夫の余地もいろいろあると思います。基本的には、一回だけで判断をせず、継続的に電話フォローを行うなど経過をモニターしながら、陽性ケースについては親のニーズを発見し寄りそう方向で進めていきます。面接や親子グループに誘って、支援ニーズの質と量をより詳細に判断するのがよいと思われます。

どの方法が優れているかは一概に比較できませんが、長期の追跡による検証が待たれます。一歳六カ月健診でM-CHATで陽性となるケースを数年追跡した結