(South et al., 2007; Smith et al., 2013), and this is supported by the fact that deficits in EF are very often seen in patients with neurodevelopmental disorders, including ASD and ADHD. Several studies have proposed that the symptoms of ADHD mainly arise from a primary deficit in a specific EF domain such as response inhibition (Corbett et al., 2009) or working memory (Willcutt et al., 2005), while the symptoms of ASD arise from a primary deficit in planning and flexibility (Sinzig et al., 2008). Therefore, a specific deficit in EF might lead to a characteristic pattern of behavioral symptoms and cognitive features in individuals with both disorders, although we have to consider any shared neurological basis between ASD and ADHD.

To identify distinct domains of EF that underlie the specific deficits seen in ASD and ADHD, several comparative studies have been conducted using EF tests such as the Wisconsin Card Sort Test (WCST) for flexibility, the Tower of Hanoi (ToH) for planning, and the Stroop color-word test for inhibition. However, these studies have focused on only a few specific EF domains (inhibition, planning, set-shifting, and working memory) and have used diversified subjects (e.g., a wide ranging age group, high functioning autism [HFA] vs. Asperger disorder, ADHD vs. typical development [TD]). Because of these limitations, previous findings have yielded inconsistent results. The EF tests used in previous studies might provide inadequate information to conclude which domains of EF are specifically impaired in each disorder. Therefore, it is necessary to examine cognitive function of subjects using a comprehensive neuropsychological battery that can evaluate each EF domain in detail.

The developed computerized EF battery of the Cambridge Neuropsychological Test Automated Battery (CANTAB®) is another method of assessing EF in pediatric clinical populations. Researchers have used the CANTAB® specifically to evaluate EF (Goldberg et al., 2005; Rhodes et al., 2005; Coghill et al., 2007; Gau and Shang, 2010b). The CANTAB® has a number of advantages over other measures of EF as it provides a standard computerized-administration (controlling for variations across examiners), has more than 20 subtests to evaluate EF, is nonverbal, uses a touch-screen response, and provides empirical evidence for the role of prefrontal and medial temporal brain regions in the implementation of the CANTAB® tasks (Luciana and Nelson, 2002). Therefore, it is a suitable test battery for children with developmental disorders.

Recently, Goldberg et al. (2005) examined inhibition, planning, set-shifting, and working memory functions in a sample of children aged 8–12 years with HFA, ADHD, and TD by using the CANTAB®. In the study, the subjects were carefully assessed to screen for comorbid impulsivity or hyperactivity in autism. The study concluded that response inhibition, planning, and set-shifting were similar across the three groups of ASD, ADHD, and TD subjects, and only impaired spatial working memory (SWM) in the ADHD and HFA groups were reported (Goldberg et al., 2005). On the other hand, because rigorous case control studies by using the CANTAB® are rare, confounding evidence has been suggested (Hughes et al., 1994; Kempton et al., 1999).

Few studies have directly compared behavioral symptoms, cognitive features, and EF across ASD and ADHD groups in addition to the age-, sex-, and IQ-matched controls. To the best of our knowledge, this is the first CANTAB® study implemented using multidimensional assessments with vigilant case control. The aim of this study was to distinguish between ASD and ADHD by identifying characteristic features of children with these disorders, by using multidimensional assessments: various screening behavioral checklists, cognitive assessments, and comprehensive neurological test battery. We carefully assessed potential participants to screen out comorbid ADHD symptoms in ASD and comorbid ASD symptoms in ADHD. Additionally, we selected normally developing children as a control group to avoid the effects of sample bias. To measure children's cognitive abilities, we chose four tasks from the CANTAB® that, according to previous research, showed promise for distinguishing between ASD and ADHD: rapid visual information processing, spatial working memory, delayed matching to sample, and spatial span. The results obtained in this experiment were interpreted in detail based on the framework of cognitive psychology.

## 2. Methods

### 2.1. Participants

Participants in this study included 11 children with high functioning (IQ > 75) ASD, 15children with ADHD, and 19 children with TD. The demographic information for the groups is provided in Table 2. All children with ASD and ADHD were treated as outpatients at the Hiratani Pediatric Clinic (HPC), which is one of the largest clinics for children with developmental disorders in Japan. In the HPC, in addition to medical treatment, individual educational classes and group psychotherapy are provided by speech therapists and clinical psychologists. The participants were required to be free of any medications resulting in active central nervous system except for methylphenidate. All patients were required to be off medication for at least 24 h prior to the administration of the experimental tasks. This period is considered sufficient to ensure full washout. Furthermore all participants were required to have an IQ of 75 or more. Participants with known medical causes of autism, including fragile X syndrome and tuberous sclerosis, and those with other neurological disorders, including epilepsy, were excluded from the study.

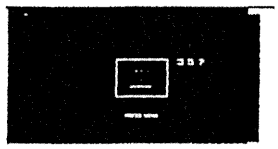
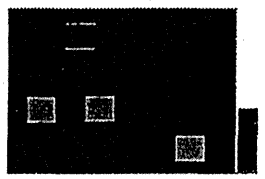
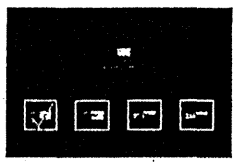
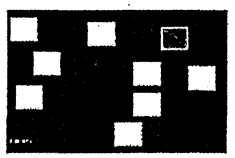
Age and sex matched TD compared children who had received treatment for allergy and common cold as outpatients were also recruited from the HPC. Children were not included if they had any psychiatric diagnosis or family history of social or attention related problems. To exclude any psychiatric diagnosis including suspected ADHD or ASD, all TD subjects underwent an extensive child psychiatric examination, conducted by an experienced child and adolescent psychiatrist according to DSM-IV-TR criteria.

The ASD group comprised 11 boys with a formal diagnosis of either high-functioning Autistic disorder or Asperger's disorder. In each case, the diagnosis had been made by more than two expert child psychiatrists and pediatricians according to established criteria (DSM-IV-TR) (American Psychiatric Association, 2000). Children were excluded if they had been diagnosed with either ADHD or Hyperkinetic Disorder. Furthermore, all subjects in the ASD group met the full DSM-IV-TR criteria of high-functioning autistic disorder or Asperger's disorder, and were excluded if they had even sub-threshold ADHD characteristics. To make a definitive diagnosis, other psychiatrists or pediatricians and clinical psychologists who had handled their therapy confirmed the diagnosis based on clinical observation.

The ADHD group comprised 13 boys and 2 girls with a formal diagnosis of ADHD. The diagnosis was based on (DSM-IV-TR) (American Psychiatric Association, 2000) criteria. Children were excluded if they had additional disorders such as pervasive developmental disorder, Tourette syndrome, obsessive-compulsive disorder, or conduct disorder. Moreover, subjects with any ADHD symptoms were excluded from this group. As previously mentioned, psychiatrists, pediatricians, and technical professionals involved in the care of the subjects made the final diagnosis.

All participants lived near the HPC and did not receive any public assistance. Additionally, none of the children had experienced parental divorce or any form of maltreatment, suggesting that they shared common socio-economic status.

**Table 1**
CANTAB tests used in the assessment and their key output variables.

| Order (core domain) | Sample | Domain and associated CANTAB test | Test description (approximate time for administration) | Key measures |
|---|---|---|---|---|
| 1 (Attention) |  | Rapid visual information processing (RVP) | Rapid visual information processing (RVP) is a test of sustained attention (similar to the continuous performance task) and has proved useful in many studies in which drugs are used to help develop a disease model. It is sensitive to dysfunction in the parietal and frontal lobe areas of the brain and is also a sensitive measure of general performance (7 min). | # Measures cover latency, probabilities and sensitivity<br># Hits, misses, false alarms and rejections |
| 2 (Executive function) |  | Spatial working memory (SWM) | SWM is a test of the participant's ability to retain spatial information and to manipulate remembered items in working memory. It is a self-ordered task, which also assesses heuristic strategy. This test is a sensitive measure of frontal lobe and 'executive' dysfunction. It has been shown in recent studies that impaired performance on SWM emerges as a common factor in prepsychosis (8 min). | # Measures for SWM include errors<br># Measure of strategy, and latency measures |
| 3 (Visual Memory) |  | Delayed matching to sample (DMS) | Delayed matching to sample (DMS) assesses forced choice recognition memory for novel non-verbalisable patterns, and tests both simultaneous and short term visual memory. This test is primarily sensitive to damage in the medial temporal lobe area, with some input from the frontal lobes (10 min). | # Latency (the participant's speed of response), the numbers of correct patterns selected, and statistical analysis measuring the probability of an error after a correct or incorrect response. |
| 4 (Executive function) |  | Spatial span (SSP) | White squares are shown, some of which briefly change color in a variable sequence. The participant must then touch the boxes which changed color in the same order that they were displayed by the computer (for clinical mode) or in the reverse order (for reverse mode). The number of boxes increases from two at the start of the test to nine at the end, and the sequence and color are varied through the test (10 min). | # Covering span length (the longest sequence successfully recalled), errors, number of attempts and latency. |

### 2.2. Instruments and neurocognitive testing

#### 2.2.1. High-functioning autism spectrum screening questionnaire (ASSQ)

The ASSQ is designed to identify school-aged children who may need a more comprehensive evaluation due to suspected ASD. It consists of 27 items scored on a 3-point scale: not true (0), somewhat true (1), and certainly true (2). Possible scores range from 0 to 54, with high scores indicating a high symptom load (Ehlers et al., 1999). The Japanese version of ASSQ was standardized by Ii et al. (2003) and it has confirmed good reliability and validity.

#### 2.2.2. Brief autism quotient (brief AQ)

Baron-Cohen et al. developed a self-reporting questionnaire, the autism-spectrum quotient (AQ) for screening normally intelligent adolescents and adults with high functioning pervasive developmental disorder (Baron-Cohen et al., 2001). Allison et al. established a short version of AQ which has 10 items (for the adult, adolescent, and child versions) (Allison et al., 2012). At a cut-off point of 6 on the brief AQ child, sensitivity was 0.91, and specificity was 0.89 (Allison et al., 2012). In this study, a cut-off point of 6 was applied.

#### 2.2.3. Japanese version of the ADHD-Rating Scale-IV

The ADHD Rating Scale-IV is a reliable and easy-to-administer instrument both for diagnosing ADHD in children and adolescents and for assessing treatment response (DuPaul et al., 1998). The Japanese version of the home form of the ADHD-RS was standardized by Yamasaki et al. (2002), and was developed with good reliability and validity (Tani et al., 2010). ASSQ, Brief AQ, and ADHD-RS-IV were rated by participant's parents.

#### 2.2.4. WISC-IV (Japanese version)

All participants completed the 10 Wechsler Intelligence Scale for Children (WISC-IV) subtests comprising the four indexes (VCI, PRI, WMI, and PSI) (Japanese WISC-IV Publication Committee, 2010). The Japanese version of the WISC-IV was standardized for Japanese children aged 5–16 years, and was shown to have good reliability and validity.

#### 2.2.5. CANTAB®

We employed the CANTAB® to assess the EFs that are impaired or spared in ASD or ADHD. The newly developed computerized EF battery of the CANTAB® was developed to assess specific disabilities in children with developmental disorders such as ASD and ADHD.

**Table 2**
Demographic data for children among typically developing (TD), autism spectrum disorders (ASDs), and attention deficit hyperactivity disorder (ADHD) subjects.

| | TD ($N$=19) | ASD ($N$=11) | ADHD ($N$=15) |
|---|---|---|---|
| Age $M$ (SD) | 11.4 (1.6) | 12.0 (2.2) | 10.8 (1.8) n.s. |
| FSIQ $M$ (SD) | 111.8 (13.4) | 105.6 (14.3) | 103.8 (14.9) n.s. |
| Gender (M/F) | 12/7 | 11/0 | 13/2 |
| Medicated (%) | 0 | 2 (18.2%)[a] | 13 (86.7%)[b] |
| Pubic financial assistance | 0 | 0 | 0 |
| Parental separation | 0 | 0 | 0 |

One-way analysis of variance, all differences in scores are significant. $^{*}p<.05$, $^{**}p<.01$.
[a] One was received risperidone, the other was received osmotically controlled-release oral delivery system – methylphenidate.
[b] All were received osmotically controlled-release oral delivery system – methylphenidate.

As shown in Table 1, we selected four tasks from the CANTAB®: Rapid Visual Information Processing (RVP) in which the core domain is attention; spatial working memory (SWM) in which the core domain is EF; delayed matching to sample (DMS) in which the core domain is visual memory; and spatial span (SSP) in which the core domain is EF. Thirteen children with ADHD and two children with ASD were medicated. Before administering the CANTAB® test and WISC-IV, stimulant medication was withheld for 24 h, which is considered as a sufficient washout period (Greenhill, 1998).

### 2.3. Statistical analysis

All quantitative data was tested for homoscedasticity. Next, to assess the differences among the three groups, we conducted a one-way analysis of variance (one-way ANOVA), and Tukey's honestly significant difference (HSD) test was used for post hoc analysis when the $F$ value was significant. All analysis was completed using IBM SPSS version 20.

### 2.4. Ethic

The protocol used for this study was approved by the ethics committee of the Tokyo University of Social Welfare and the University of Fukui. After a complete explanation of the study, written informed consent was obtained from each subject and their parent.

## 3. Results

### 3.1. Demographic data for children and their family in the three groups

No significant differences were observed in the mean age or the mean score on full scale IQ among the three groups. All participants with ADHD received methylphenidate via osmotically controlled release oral delivery system (OROS). None of the families of any participants received any kind of welfare, and none of the children had experienced parental separation such as divorce or bereavement.

### 3.2. Group comparison of psychological assessment scores

The psychological assessment scores for children in the TD, ASD, and ADHD groups are shown in Table 3. The mean scores of the ASSQ were as follows: 2.3 (SD = 3.4) for TD, 28.1 (SD = 8.8) for ASD, and 14.1 (SD = 7.5) for ADHD. There was a significant main effect of group ($F(2, 44) = 55.2$, $p < .01$). Post hoc analysis using Dunnett's T3 test revealed that the ASD group had a significantly higher score than either the ADHD or the TD groups, and the ADHD group had a significantly higher score than the TD group. This result indicates that the ASD group had marked autistic symptoms compared to the other groups, and the ADHD group showed significant autistic tendencies compared to the TD group. Similarly, results from the brief AQ score followed the pattern of the ASSQ, i.e., a significant main effect of group ($F(2, 44) = 40.1$, $p < .01$). Further, Dunnett's T3 test revealed that the ASD group had a significantly higher score than that for either the ADHD or TD groups, and the ADHD group had a significantly higher score than that for the TD group. We confirmed that parents of children with ADHD had evaluated that he/she also experienced some kinds of autistic symptoms. In the meantime, the mean total scores of ADHD-RS-IV were as shown: 2.0 (SD = 2.7) for TD, 12.0 (SD = 5.9) for ASD, and 20.2 (SD = 12.7) for ADHD. There was a significant main effect of group ($F(2, 44) = 21.5$, $p < .01$), and the post hoc analysis with Dunnett's T3 test showed that the ADHD group had significantly higher scores than that for either the ASD or TD groups, and the ASD group had significantly higher scores than that of the TD group. This result suggested that children with ASD had some ADHD symptoms. In addition, the mean ADHD-RS-IV inattention scores were as follows: 1.3 (SD = 1.5) for TD, 8.4 (SD = 4.7) for ASD, and 17.8 (SD = 21.2) for ADHD. There was a significant main effect of group

**Table 3**
Psychological assessment scores for children among typically developing (TD), autism spectrum disorders (ASDs), and attention deficit hyperactivity disorder (ADHD) subjects.

| | | TD ($N$=19) | ASD ($N$=11) | ADHD ($N$=15) | $F$ value[a] | Post hoc analyses[b] |
|---|---|---|---|---|---|---|
| ASSQ Score $M$ (SD) | | **2.3 (3.4)** | **28.1 (8.8)** | **14.1 (7.5)** | **55.2**** | ASD > ADHD > TD |
| $N$ (percentage of more than cut-off) | | 0 (0%) | 9 (81.8%) | 3 (20%) | | |
| Brief-AQ Score $M$ (SD) | | **2.5 (1.8)** | **7.6 (2.0)** | **5.0 (2.6)** | **20.1**** | ASD > ADHD > TD |
| $N$ (percentage of more than cut-off) | | 0 (0%) | 9 (81.8%) | 6 (40%) | | |
| ADHD-RS-IV Total Score $M$ (SD) | | **2.0 (2.7)** | **12.0 (5.9)** | **20.2 (12.7)** | **21.5**** | ADHD > ASD > TD |
| | 80% tile | 0 (0%) | 2 (18.2%) | 8 (53.3%) | | |
| | 85% tile | 0 (0%) | 1 (9.1%) | 7 (46.7%) | | |
| | 93% tile | 0 (0%) | 0 (0%) | 6 (40%) | | |
| ADHD-RS-IV Inattention Score $M$ (SD) | | **1.3 (1.5)** | **8.4 (4.7)** | **17.8 (21.2)** | **7.3**** | ADHD > TD, ASD > TD |
| | 80% tile | 0 (0%) | 3 (27.3%) | 9 (60%) | | |
| | 85% tile | 0 (0%) | 1 (9.1%) | 6 (40%) | | |
| | 93% tile | 0 (0%) | 1 (9.1%) | 6 (40%) | | |
| ADHD-RS-IV Hyperactivity and Impulsivtity score $M$ (SD) | | **0.7 (1.5)** | **3.6 (3.5)** | **12.7 (22.9)** | **3.5*** | ADHD > TD |
| | 80% tile | 0 (0%) | 2 (18.2%) | 6 (40%) | | |
| | 85% tile | 0 (0%) | 1 (9.1%) | 3 (20%) | | |
| | 93% tile | 0 (0%) | 0 | 2 (13.3%) | | |

[a] One-way analysis of variance, all differences in scores are significant. $^{*}p<.05$, $^{**}p<.01$.
[b] Method of Dunnett's T3 is adopted because all variables do not have homoscedasticity.

**Table 4**
Cognitive assessment (WISC-IV) scores for children among typically developing (TD), autism spectrum disorders (ASDs), and attention deficit hyperactivity disorder (ADHD) subjects.

| | TD ($N$=19) | | ASD ($N$=11) | | ADHD ($N$=15) | | $F$ value[a] | Post hoc analyses[b] |
|---|---|---|---|---|---|---|---|---|
| | $M$ | SD | $M$ | SD | $M$ | SD | | |
| FSIQ | 111.8 | 13.4 | 105.4 | 14.3 | 103.8 | 14.9 | 1.5 | |
| Composite scores | | | | | | | | |
| Verbal comprehension | 107.5 | 11.9 | 103.1 | 17.3 | 103.1 | 12.4 | 0.6 | |
| Perceptual reasoning | 111.9 | 11.6 | 103.9 | 12.2 | 104.9 | 13.1 | 2.0 | |
| Working memory | 109.1 | 17.2 | 111.6 | 16.6 | 101.2 | 21.7 | 1.2 | |
| Processing speed | 105.0 | 10.9 | 97.4 | 10.2 | 99.3 | 11.3 | 2.1 | |
| Subtests | | | | | | | | |
| Vocabulary | 11.5 | 2.5 | 10.4 | 2.8 | 10.7 | 2.6 | 0.8 | |
| Similarities | 11.0 | 2.4 | 11.7 | 3.4 | 11.5 | 2.3 | 0.4 | |
| Comprehension | 11.7 | 2.9 | 9.8 | 3.2 | 9.7 | 3.2 | 2.3 | |
| Block design | 11.7 | 2.6 | 12.2 | 3.1 | 11.1 | 4.1 | 0.4 | |
| **Picture concepts** | **11.2** | **2.6** | **8.7** | **2.5** | **10.1** | **2.1** | **3.6*** | TD > ASD |
| Matrix reasoning | 12.4 | 2.2 | 10.9 | 2.7 | 11.1 | 2.2 | 2.0 | |
| Digit span | 11.2 | 3.4 | 11.9 | 2.7 | 10.3 | 4.4 | 0.7 | |
| Letter-number sequencing | 12 | 3.5 | 12.2 | 3.3 | 10.3 | 3.6 | 1.4 | |
| Coding | 11.0 | 2.0 | 9.2 | 2.6 | 9.2 | 2.6 | 3.2 | |
| Symbol search | 11.2 | 3 | 10.2 | 2.2 | 10.9 | 2.1 | 0.5 | |

[a] One-way analysis of variance. *$p < .05$.
[b] Tukey's honestly significant difference test is adopted because all variables are normally-distributed and have homoscedasticity.

($F(2, 44) = 7.3, p < .01$), and the post hoc Dunnett's T3 test revealed that both the ADHD and ASD groups had significantly higher scores than that of for the TD group. For the mean of ADHD-RS-IV hyperactive and impulsivity score, a significant main effect of group ($F(2, 44) = 3.5, p < .05$) was observed, and we confirmed that the ADHD group had a significantly higher score than that of the TD group by post hoc analyses. This suggested that children with ASD showed more inattentive tendencies rather than hyperactive and impulsive symptoms compared to the tendencies shown by children with TD.

### 3.3. Group comparison of cognitive assessment (WISC-IV)

The mean scores of WISC-IV for TD, ASD, and ADHD group are shown in Table 4. There were no significant differences in full scale IQ and all composite scores. The ASD group scored significantly lower on the subtest of "Picture concept" compared to the TD group ($F(2, 36) = 2.72, p < .05$).

### 3.4. Group comparison of neuropsychological battery (CANTAB®) scores

Table 5 shows the results of neuropsychological battery scores for children in the three groups. On the SWM test, a significant difference between groups was seen ($F(2, 45) = 3.64, p < .05$). Tukey's HSD post hoc tests showed that the ADHD group had a significantly lower score than the TD group. In contrast, there were no significant differences among the three groups on the scores of RVP, DSM, or SSP.

## 4. Discussion

The purpose of the present study was to identify particular unique and common features in children with ASD and ADHD, using a variety of screening behavioral checklists, cognitive assessments, and a comprehensive neuropsychological test battery. It is well-known that ASD and ADHD are often comorbid in childhood and early adolescence, often leading to misdiagnosis and less than optimal treatment strategies. We conducted multiple assessments for children with ASD and ADHD, as well as TD children, based on our hypnotized that it is possible to discriminate between the two groups by identifying psychological, behavioral, cognitive, and EF features.

### 4.1. Demographic data and psychological and behavioral characteristics

As shown in Table 2, all subjects in the study were aged between 10 and 15 years, providing a relatively narrow age bracket. Additionally, there were no significant differences in the mean scores of FSIQ between the three groups, suggesting a high degree of homogeneity in their overall cognitive abilities. Some previous studies have used a computerized battery of tests to show that children with ADHD and ASD have deficits in EF such as

**Table 5**
Neuropsychological battery (CANTAB) scores for children among Typically Developing (TD), autism spectrum disorders (ASD), and attention deficit hyperactivity disorder (ADHD) subjects.

| | TD ($N$=19) | | ASD ($N$=11) | | ADHD ($N$=15) | | $F$ value[a] | Post hoc analyses[b] |
|---|---|---|---|---|---|---|---|---|
| | $M$ | SD | $M$ | SD | $M$ | SD | | |
| MOT | 90.7 | 32.3 | 90.6 | 22.7 | 104.2 | 35.6 | 0.9 | |
| RVP | 238.9 | 79.8 | 241.8 | 27.7 | 254.7 | 61.2 | 0.3 | |
| SWM (Between errors standard score) | 0.58 | 0.63 | -0.027 | 1.09 | -0.024 | 0.76 | 3.3* | TD < ADHD |
| SWM (strategy standard score) | 0.46 | 1.14 | -0.29 | 1.13 | -0.16 | 0.87 | 1.3 | |
| DMS (percent correct alldelays standard score) | 0.27 | 1.43 | 0.19 | 1.36 | 0.7 | 0.95 | 0.7 | |
| DMS (percent correct simultaneous standard score) | 0.26 | 1.03 | 0.14 | 1.13 | 0.48 | 0.73 | 0.4 | |
| DMS (prob error given error standard score) | -0.32 | 1.90 | 0.24 | 1.34 | 0.76 | 0.56 | 1.8 | |
| SSP (standard score) | 0.86 | 1.04 | 0.47 | 0.85 | 0.33 | 1.04 | 1.3 | |

[a] One-way analysis of variance. *$p < .05$.
[b] Tukey's honestly significant difference test is adopted because all variables are normally-distributed and have homoscedasticity.

inhibition, planning, set-shifting, and SWM (Goldberg et al., 2005; Corbett et al., 2009). While those findings provide strong evidence for the existence of differences in EF between children with ADHD and ASD, large differences in age and IQ between the groups would have a significant effect on the results. In a study by Corbett et al. (2009), children with ASD scored approximately about 18 points lower than that by children with TD. In addition, Goldberg et al. (2005) found that the mean FSIQ of children with high functioning autism was significantly lower than that for the other two groups. Therefore, we aimed to minimize group differences in age and IQ to allow adequate examination of the specific characteristics of each group. Additionally, none of the families who participated in our study received any public financial assistance, and all the children had two biological parents, suggesting that there was little difference in socio-economic status.

### 4.2. Group comparison of psychological assessment scores

According to DSM-IV TR and ICD-10, a diagnosis of autism or Asperger's syndrome precludes a diagnosis of ADHD. However, despite the different conceptualization, population-based twin studies have reported symptom overlap, and a recent epidemiologically based study reported a high rate of ADHD in both autism and ASD (Taurines et al., 2012).

As shown in Table 3, according to the results of the ASSQ and brief AQ, which are considered to evaluate the degree of autistic behavioral symptoms, children with ASD had markedly high scores compared to both the other groups. More than 80% of the subjects in the ASD group scored above the cut-off point scores, while only 20% of the subjects in the ADHD group scored above the cut-off point scores (>19 for ASSQ; >6 for brief AQ). Our findings suggest that the ASD and ADHD groups might share common characteristics; on the other hand, subtle behavioral differences between the two groups were also noted.

ADHD-RS version IV has been widely used as an evaluation tool for children and adolescents with ADHD. Our statistical analyses showed that, regarding the total score, the ADHD group had markedly higher scores than that for either the ASD or TD groups. Additionally, the ADHD and ASD groups had higher scores than that for the TD group on the in inattention subscale. In contrast, there were no significant differences between the hyperactivity and impulsivity scores for the ASD and TD groups. Therefore, our findings suggest that a tendency toward inattention might be frequently found in both the groups, while hyperactivity and impulsivity were evident only in the ADHD group; these findings are in accordance with those shown in previous studies. Therefore, by concurrently using brief AQ, ASSQ, and ADHD-RS, it should be possible to discriminate between the two groups based on their symptomatology.

### 4.3. Group comparison between cognitive assessment scores

Our results show that the ASD group had a lower score than the TD group in Picture concept, which is a subscale of perceptual reasoning. There were no significant differences among the three groups in FSIQ and four index scores. Some studies of children with ASD and ADHD by using WISC have indicated that performance pattern differences between the two groups exist on verbal intelligence (Zayat et al., 2011) or verbal comprehension and vocabulary (Koyama et al., 2006). Oliveras-Rentas et al. (2012) revealed that impaired processing speed is associated with increased autism communication symptoms. Similarly, Mayes and Calhoun (2008) showed that children with HFA had higher scores in "Picture concept" compared to other subtests. Our findings, however, did not support this. There are relatively few studies on relationships between precise WISC profile and these disorders. Our results implied that IQ score differences might be very small when age, sex, and socio-economic status are controlled.

### 4.4. Group comparison of CANTAB® scores

Our results show that the ADHD group had a significantly lower score than that of the TD group when considering the between errors standard score of SWM; no group differences were found in performance in the RVP, DMS, and SSP tasks. Because of the lack of group differences in three tasks, it appears that children with ASD and ADHD have no difficulties in perceptual processing or with visual and spatial short-term memory. On the other hand, performance of the ADHD group in the SWM task was significantly lower than that of the TD and ASD groups. The SSP and SWM tasks require temporary retention of spatial information. Since there was no significant difference between the performance of the ASD and ADHD groups in the SSP task, it seems that these children have no difficulty in retaining spatial information. If this is the case, why was performance of the ADHD group in the SWM task lower than that of the ASD group? Unlike the SSP task, the SWM task requires not only temporary retention but also active processing. While the SSP and DMS tasks require children to temporarily retain visuospatial information, the SWM tasks also requires them to look for a target hidden in the box. As mentioned above, children with ADHD have no difficulty in retaining spatial information. Therefore, it is possible that children with ADHD have a deficit in active processing. However, there is another possibility to explain the low performance of children with ADHD in the SWM task. Even though the RVP task requires active processing (i.e., looking for a target), performance of the ASD and ADHD groups was the same, indicating that children with ADHD *do not* have difficulty in looking for a target in this task. Thus, we need to look at a different aspect of the SWM task. In the SWM task, children are required to conduct both temporary retention and active processing simultaneously. It is possible that compared to children with ASD, children with ADHD have difficulty in *simultaneously using two cognitive functions*, since there were no group differences regarding performance in the RVP, DMS, and SSP tasks. Impaired EFs in ADHD become more apparent with increasing task demands (Gau and Shang, 2010a,b). However, this theoretical argument remains a matter of speculation and would be an interesting subject of future research.

In other previous studies, Goldberg et al. (2005) showed that both children with HFA and ADHD performed worse than controls in remembering the locations where tokens were previously found. Similarly, Corbett et al. (2009) showed significant differences in both the between errors standard score and the strategy standard score of the SWM (ASD < TD; ASD < ADHD). Our results are in agreement with those shown in previous studies, which suggested a wide range of significant differences among other measures such as SSP (Spatial Span subtest; ASD < TD, ADHD < TD) (Corbett et al., 2009).

According to Luciana's (2003) review, by the age of 12 years, children have not yet reached adult levels of task performance in the SWM test in terms of either error scores or strategy scores. Additionally, she pointed out that the ability to associate specific disorders with distinctive performance profiles has so far been limited by small clinical samples and varying subtask batteries across studies. Interestingly, our findings are partly consistent with the results of the analyses by Luciana (2003). However, we believe that not only the CANTAB® battery but also a combination of assessments could reveal complex EF features among different developmental disorders.

To summarize, several studies evaluated the EF in children with ASD and with ADHD by using CANTAB®. However, these studies

yielded inconsistent results in the subtests of CANTAB®. This lack of robustness in the findings may be due to the relatively small sample sizes. However, our sample was relatively homogeneous compared with those of previous studies in term of age, sex, IQ, and socio-economic status. We carefully controlled these variables, which allowed us to observe clear differences between children with ASD and those with ADHD in the SWM task. To our knowledge, this is the first study to use the CANTAB® to investigate EF in children aged between 10 and 15 years with ASD or ADHD in Japan. Although the CANTAB® is not a perfect method, it does have many advantages in evaluating the EF for children with neurodevelopmental disorders. Our research findings will contribute to resolving inconsistencies in this field of study.

## 5. Limitations

The current study has a number of limitations that need to be considered. Firstly, the number of participants in the study was not large, and the ratio of males to females was imbalanced. Secondly, the number of subtests in the neuropsychological battery was limited. If we conducted many more subtests of the CANTAB®, additional findings might be uncovered. Thirdly, the participants who were on medication had their medication withheld for 24 h prior to taking the CANTAB® test and WISC assessment, which might have affected on our results.

## 6. Conclusions

We identified specific cognitive features in children with ASD and ADHD by using multidimensional screening behavioral checklists, cognitive assessments, and a comprehensive neuropsychological battery. We could distinguish between ASD and ADHD by using a combination of various assessments, because two groups showed unique characteristics in their cognitive ability and EF. In conclusion, although ASD and ADHD have many overlapping features, we can reach a comprehensive distinction by focusing on behavioral, cognitive, and EF features. The scores on the ASSQ, brief AQ, and "Picture concept" subscale of the WISC-IV are useful in making a differential diagnosis of ASD. Additionally, the scores of the ADHD-RS-IV and SWM of the CANTAB® battery were helpful in making a differential diagnosis of ADHD. The results of the CANTAB® suggest that children with ADHD have difficulty in *simultaneously using two cognitive functions.*

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## Contributors

N.M. and M.I. wrote the manuscripts. S.A., K.K., M.H., and M.A conducted experiments. N.M., T.N, and K.I. analyzed data. H.K. and Y.W conducted critical revision of the article for important intellectual content.

## Conflict of interest

The authors declare no conflict of interest associated with this manuscript.

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RESEARCH ARTICLE Open Access

# Verification of the utility of the social responsiveness scale for adults in non-clinical and clinical adult populations in Japan

Reiko Takei[1], Junko Matsuo[2], Hidetoshi Takahashi[1], Tokio Uchiyama[3], Hiroshi Kunugi[2] and Yoko Kamio[1*]

**Abstract**

**Background:** Recently great attention has been paid to the still unmet clinical needs of most adults with autism spectrum disorder (ASD) who live in the community, an increasing number of whom visit psychiatric clinics to seek accurate diagnosis and treatment of concurrent psychiatric symptoms. However, different from the case of children diagnosed with ASD in childhood, it is difficult in adults to identify the ASD symptoms underlying psychopathology and to differentiate ASD from other psychiatric disorders in general psychiatric practice. This study aimed to verify the utility of the Social Responsiveness Scale-Adult version (SRS-A), a quantitative measure for identifying ASD symptoms, in non-clinical and clinical adult populations in Japan.

**Methods:** The total sample aged 19 to 59 years consisted of a non-clinical population ($n$ =592) and clinical population with and without ASD ($n$ =142). We examined score distributions of the Japanese version of the scale, and the effects of gender, age, and rater on the distribution. We analyzed factor structure and internal consistency in the non-clinical normative sample, and analyzed convergent, divergent, and discriminative validities in the clinical sample. We applied receiver operator characteristic (ROC) analysis to determine optimal cutoff scores discriminating the ASD clinical population from the non-ASD clinical population.

**Results:** The score distributed continuously, which replicated findings in children. For non-clinical adults, except in men aged 19 to 24 years, we found no or few gender, age, or rater effects. Both single- and two-factor models were supported for adults. Total SRS-A scores demonstrated high internal consistency and capably discriminated adults with ASD from those with non-ASD psychiatric disorders such as major depressive disorder, schizophrenia, and bipolar disorder with an overlap across diagnoses. Moderate to high correlations of the SRS-A with other-rated ASD measures indicated sufficient convergent validity. Based on the ROC analysis, we recommend cutoff points by gender for use in clinical settings.

**Conclusion:** This study provides additional supportive evidence that the Japanese version SRS-A can reliably and validly measure ASD symptoms in non-clinical and clinical adult populations, and thus can serve as a useful tool for ASD research as well as for secondary screening in Japanese adults.

**Keywords:** Autism spectrum disorder, Adult, Screening, Questionnaire, Psychiatric population

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## Background

According to a recent epidemiological study [1], autistic spectrum disorder (ASD) is currently estimated to be 1% of the adult population, a figure that approximates that in the child population [2]. Recently, ASD in adulthood has attracted considerable interest in the field of general psychiatry. It has been identified that most adults with ASD living in the community still had unmet clinical needs and are socially disadvantaged [1,3]. In line with this worldwide trend, in Japan, an increasing number of adults with ASD visit psychiatric clinics with a diverse range of chief complaints, seeking either accurate diagnosis and a medical certificate needed to receive transition support for employment or treatment of concurrent psychiatric symptoms such as depression or anxiety [4]. However, unlike in children diagnosed with ASD, clinical manifestations in adult patients first diagnosed with ASD in adulthood are often complex: deficits in social reciprocity tend to be less apparent in adults with high-functioning ASD, especially outside situations that demand responses to complex social cues, or when adults with ASD mask their deficits using compensation strategies. For these reasons, it is difficult to identify ASD symptoms underlying adulthood-onset psychopathology and differentiate ASD from other psychiatric disorders in general psychiatric practice, which can lead to misdiagnosing ASD symptoms as psychosis [5].

In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [6], a category of pervasive developmental disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) [7] has been converted to a new category of ASD in which ASD severity is quantitatively rated according to current difficulties. Further, because of a nonexistent natural boundary between affected and unaffected individuals [8,9], the DSM-5 has a new category of social (pragmatic) communication disorder for individuals with marked deficits in social communication but who do not otherwise meet ASD criteria (i.e., those with subthreshold ASD) [6]. The availability of quick, easy-to-use, and validated screening tools for identifying autistic traits and symptoms for psychiatric patients would help make appropriate diagnoses, reduce misdiagnoses, and plan appropriate treatment or support according to individual patient needs.

To date, the few self-report questionnaires available for identifying ASD in adulthood include the autism-spectrum quotient (AQ) [10-12], the Ritvo Autism Asperger's Diagnostic Scale [13], or the Ritvo Autism Asperger Diagnostic Scale-Revised [14]. By contrast, a few questionnaires such as the Social Responsiveness Scale-Adult version (SRS-A) [15], or the Autism Spectrum Disorder in Adults Screening Questionnaire [16] must be completed by another adult (e.g., family member, close friend, or professional). The SRS-A was modified from the SRS [17], a quantitative measure of autistic traits in children. The original SRS has been extensively validated in clinical and subclinical child populations as well as in general child populations not only in the U.S. [8,15,17-19] but also in Europe [20], South America [21], and Asia [9,22]. The SRS can distinguish children with ASD from children with any other or no psychiatric disorder and is generally unrelated to IQ in the normal range [9]. The SRS, a quantitative measure of autism, is also sensitive to autistic traits and symptoms even in subthreshold ASD conditions [9]. It is extremely useful for research purposes such as genetic epidemiological research [19,23] or in research assessing brain-behavior relationships [24]. Its utility for detecting autism-related genetic loci [25] or cross-species research [26] has been suggested.

However, at this time, only a few validation studies of the SRS-A exist [15,27,28]. Therefore, the main purpose of this study was to determine the score distribution of the Japanese version SRS-A in a non-clinical Japanese adult population, and to assess its factor structure, reliability, and validity. Based on our findings in clinical populations with and without ASD, optimal cutoff scores are recommended.

## Methods

### Participants

The normative sample included 592 participants (257 university students and 335 private company or hospital workers; men, 41.6%) aged 19 to 59 years. Another adult who knew each participant well, such as a parent, spouse, sibling, or close friend, answered an SRS-A questionnaire with complete anonymity. After excluding survey responses with missing data, we used complete data sets from 458 participants (men, 45.2%) (Tables 1 and 2). Excluded responses ($n$ =134) were 22.6% of the obtained responses and most often were from participants in adolescence (56.7% of incomplete responses), followed by those in middle age (26.1%) and early adulthood (17.2%). Among them ($n$ =134), 97 (72.4%) did not specify who the rater was, and the rest were excluded due to missing SRS-A answers. In this study, we included only complete SRS-A questionnaires with responses having specified gender, age, and rater data for further analyses.

The validation sample consisted of 65 patients diagnosed with ASD (ASD group; men, 67.7%) and 78 patients diagnosed with non-ASD psychiatric disorders (non-ASD group; men, 50%) (Table 3). Both the ASD and non-ASD clinical groups included research volunteers registered at the National Center of Neurology and Psychiatry (NCNP) and patients from several specialized developmental clinics. Our research team that included specialized child psychiatrists diagnosed participants in the ASD group according to DSM-IV-TR (20: autistic disorder;

**Table 1 Mean total scores of the Social Responsiveness Scale for Adults (SRS-A) in the normative sample by sex and age**

| Age group (years) | SRS-A total score | | | | |
|---|---|---|---|---|---|
| | | Male | | Female | |
| | Total *N* | *N* | Mean (*SD*) | *N* | Mean (*SD*) |
| Adolescence (19–24) | 183 | 87 | 53.4 (27.8)*** | 96 | 36.5 (21.2)*** |
| Early adulthood (25–39) | 122 | 53 | 36.2 (25.1) | 69 | 36.3 (22.6) |
| Middle age (40–59) | 153 | 67 | 35.9 (26.1) | 86 | 30.1 (20.0) |
| Total | 458 | 207 | 43.3 (27.8) | 251 | 34.3 (21.3) |

***Men scored significantly higher than women in the 19–24 age band ($p < .001$).

28: Asperger's disorder; 17: pervasive developmental disorder-not otherwise specified [PDD-NOS]). In addition to clinical diagnosis, we evaluated 51 of the 65 participants using either the Autism Diagnostic Observation Schedule (ADOS) or a semi-structured interview scale developed, validated, and widely used in Japan [23]. Participants in the non-ASD group were diagnosed with any DSM-IV-TR Axis I mental disorder (30: major depressive disorder; 26: schizophrenia including schizoaffective disorder; 17: bipolar I and II disorders; 4: anxiety disorders; 1 personality disorder) based on either a brief standardized interview (the Mini-International Neuropsychiatric Interview) or clinical assessment by a psychiatrist. All participants were clinically judged to have intellectual functioning within the normal range. The intelligence quotients (IQs) of 29 participants in the ASD group and 15 participants in the non-ASD group were confirmed by formal cognitive testing (mean IQ, 104.4 ± 13.8, 91.6 ± 12.2, respectively). All participants in the ASD group were rated by their mothers, while those in the non-ASD group were rated by their mothers or spouses.

## Measures

### *The social responsiveness scale for adults*

The Social Responsiveness Scale for Adults (SRS-A) is a 65-item questionnaire of autistic traits used with adults, with modified wording of the original SRS [17]. Similar to the SRS for children, each SRS-A item is scored on a 4-point scale with total scores ranging from 0 to 195, with higher scores indicating higher degrees of social impairment. For the Japanese adaptation, the original SRS-A was translated into Japanese by members of our research team (Y.K., H.T.) with permission from Western Psychological Services (WPS). In translating the SRS-A into Japanese, translations were adopted from the Japanese version of the SRS [8] whenever possible to ensure consistency across the child and adult versions. This translation was back-translated into English by independent translators and the last author (Y.K.), and one of the developers (J.C.) confirmed item equivalence in the two languages. The original developers and WPS then approved the final Japanese version, which we used in this study.

### *The autism diagnostic observational schedule*

The Autism Diagnostic Observational Schedule (ADOS) is a semi-structured behavioral assessment of social interaction, communication, and stereotyped behaviors. The original diagnostic algorithm generates scores for each of three domains of autism. Diagnostic classification is made by exceeding two cutoffs: autism and autism spectrum. To meet the ADOS criteria for autism or autism spectrum, the cutoff must be reached in both the social and communication domains and the sum of social and communication scores. In this study, we used the sum scores of the Japanese version ADOS (Module 4) [29] to assess participants in the ASD group.

### *The pervasive developmental disorders-autism society Japan rating scale*

The Pervasive Developmental Disorders-Autism Society Japan Rating Scale (PARS) is a semi-structured interview useful for children and adults, and its scores are correlated with the scores of the Autism Diagnostic Interview-Revised, demonstrating criterion-related validity of the

**Table 2 Mean total scores of the SRS-A in the normative sample by rater and number of participants by rater, gender, and age band**

| Rater type | Mean (*SD*) | *N* (M;F) | Adolescence *N* (M;F) | Early adulthood *N* (M;F) | Middle age *N* (M;F) |
|---|---|---|---|---|---|
| Mother | 39.8 (25.2) | 148 (49;99) | 126 (44;82) | 21 (4;17) | 1 (1;0) |
| Father | 57.9 (26.1) | 49 (40;9) | 47 (39;8) | 2 (1;1) | 0 (0;0) |
| Spouse | 33.1 (21.7) | 205 (98;107) | 1 (0;1) | 79 (40;39) | 125 (58;67) |
| Siblings, friends, or others | 34.5 (20.0) | 56 (20;36) | 9 (4;5) | 20 (8;12) | 27 (8;19) |
| Total | 38.2 (24.7) | 458 (207;251) | 183 (87;96) | 122 (53;69) | 153 (67;86) |

**Table 3 Mean total scores of the SRS-A of the ASD and Non-ASD Groups**

| | ASD group mean (*SD*), range | Non-ASD group mean (*SD*), range |
|---|---|---|
| *N* (Male: Female) | 65 (44:21) | 78 (38:40) |
| Age Mean (SD), Range | 27.3 (7.7),19-51*** | 34.8 (10.6) , 20–59 |
| SRS-A scores | 87.6 (29.1), 32-153*** | 54.7 (24.4), 12-106 |
| Rater Mother | 65 (44:21) | 46 (24:22) |
| Spouse | 0 | 32 |
| *Mother ratings* | | |
| Age | 26.3 (6.4), 19-51† | 28.4 (6.5), 20-43 |
| SRS-A scores Male | 89.4 (29.1), 33-167*** | 64.3 (34.8), 12-106 |
| Female | 79.8 (26.9), 42-119** | 57.2 (25.7), 13-106 |
| Total | 86.9 (28.7), 33–167*** | 60.9 (30.6) , 12–106 |

**$p < .01$; ***$p < .001$; †$p > .05$.

PARS [30]. In this study, to assess participants in the ASD group, we used the PARS version for adolescents and adults, whose reliability and validity were demonstrated [31] and whose scores were strongly correlated with the SRS scores for adolescents ($r = 0.77$, $p < .001$) [32].

### *The autism-spectrum quotient-Japanese version*

The AQ is a 50-item self-report scale for identifying high-functioning autism in individuals with normal intelligence [10,12]. Each item is scored on a 4-point scale with total scores ranging from 0 to 50; higher scores indicate more severe autism. In this study, we used the Japanese version of the AQ (AQ-J) [11] to assess autistic traits of participants of both ASD and non-ASD groups.

### Analysis

In our normative data collection, the gender ratio in each age band was not significantly different ($\chi^2 = 0.68$, *ns*) (see Table 1). However, there was a natural selection bias for rater type depending on the participant's gender ($\chi^2 = 37.6$, $p < .001$) or age ($\chi^2 = 346.7$, $p < .001$) (see Table 2). Therefore, instead of performing an analysis of variance (ANOVA) using gender, age band, and rater type as between-subjects factors for this sample, a two-way ANOVA was performed to reveal the effects of gender and age (two factors, gender × age band; adolescence, 19–24 years; early adulthood, 25–39 years; and middle age, 40–59 years) with total SRS-A scores of the normative sample as a dependent variable. Second, in order to examine rater-dependent effects in the normative sample, we conducted a two-way ANOVA for adolescent participants with total SRS-A scores as a dependent variable, and rater type (mother, father) and gender (male, female) as between-subjects independent variables, because a substantial number of adolescents were rated by either mothers or fathers. Third, we performed confirmatory factor analysis (CFA) to examine the most parsimonious model suggested by extensive prior research on the SRS [9,18,20,33]. To do so, we used MPlus 7.11 with a robust weighted least squares estimator on the normative sample and treated the SRS-A data as ordered categorical variables. Fourth, we calculated internal consistency (Cronbach's α) for 65 total items in the normative sample. Fifth, to examine convergent and divergent validities, we computed Pearson's coefficients between the SRS-A, ADOS, PARS, AQ-J, and IQ scores for the validation sample. To consider how well the SRS-A distinguishes between ASD and non-ASD psychiatric disorders, we performed *t*-tests, one-way ANOVA, and receiver operating characteristic (ROC) analyses for the validation sample. We compared mean SRS-A total scores between the ASD and non-ASD groups using a *t*-test, and between diagnostic subcategories within each group using one-way ANOVA. Based on ROC, we determined optimal cutoff points for ASD screening. All analysis except for CFA was performed using SPSS 17.0 J for Windows. We used an alpha level of .05 for all statistical tests.

### Ethical considerations

The study protocol was approved by the Ethics Committee of the NCNP, Japan. For the validation sample, we obtained written informed consent to participate in this study from adult participants and the caregivers of each child.

## Results

### SRS-A total scores of the normative sample and effects of gender, age, and rater

In the normative sample, the distribution of SRS-A total scores for each gender showed that men generated higher scores than women (Figure 1), as in the SRS for children. Table 1 shows mean (*SD*) SRS-A scores by gender and age. The main effects, gender ($p = .003$, $\eta^2 = 0.02$) and age ($p < .001$, $\eta^2 = 0.05$), and the interaction between gender and age ($p < .005$, $\eta^2 = 0.02$) were all significant, but with a small effect size. As for simple main effects, scores were not significantly affected by different age groups in women, whereas adolescent men scored significantly higher than men in early adulthood and middle age, with a moderate effect size (*ps* < .001, each with $d = 0.64$, 0.64). We observed a significant gender difference only between adolescent men and women ($p < .001$, $d = 0.68$).

Regarding the rater, our sample had a natural selection bias for rater type depending on the participant's gender or age (see Table 2). Although only two participants in early adulthood were rated by fathers and only one in middle age were rated by parents, 95% of adolescents were rated by either a mother or father. Mothers of adolescents rated their daughters (82/126) twice as often as

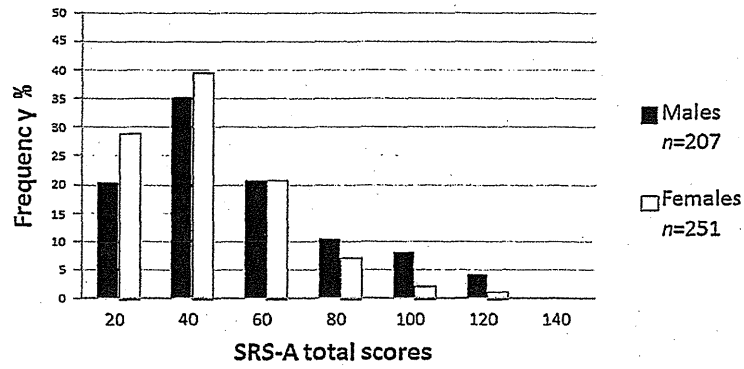


**Figure 1** Distribution of Social Responsiveness Scale for Adults (SRS-A) total scores in the normative sample ($n$ = 458).

they did their sons (44/126) in this sample. In contrast, fathers of adolescents rated their sons (39/47) five times as often as their daughters (8/47). The majority of participants in early adulthood (65%) and middle age (82%) were rated by their spouses. The ANOVA results for adolescent participants revealed no significant interaction between gender and rater type, but did show a significant main effect of rater type ($p$ = .01, $\eta^2$ = 0.03) and gender ($p$ = .001, $\eta^2$ = 0.06). That is, father ratings (64.0 ± 28.5, 41.2 ± 18.3, for men and women, respectively) were significantly higher than mother ratings (46.1 ± 24.8, 35.6 ± 22.8, for men and women, respectively) for each gender in this age band. However, because this study was not designed to systematically examine the rater effect, we are unable to draw a conclusion about rater-dependent effects on scores according to the participant's age or gender from this sample.

### Factor structure

The single factor model was subjected to CFA using all 65 items from the normative sample. The estimate for root mean square error of approximation (RMSEA) was 0.048 and the 90% confidence interval (CI) was 0.045–0.050. An acceptable model should have an RMSEA less than 0.05, and the probability that the RMSEA of the single factor model is less than 0.05 is 97.2%, indicating a good model fit. In addition, the comparative fit index (CFI) and Tucker Lewis Index (TLI) were 0.894 and 0.890, respectively, where these values close to 0.90 indicate a reasonable fit. These findings provide further support for a single factor model underlying the multiple aspects of autistic traits and symptoms. Given that Frazier et al. [33] validated the two-factor model of ASD proposed by DSM-5 [6] based on data from a large sample of children and adults, we tested whether the two-factor model (one factor comprising 53 social-communication [SC] items and another comprising 12 autism mannerisms [AM] items) has a good fit. We found that the two-single factor model adequately fits, to almost the same degree as the single factor model (RMSEA, 0.047; 90% CI, 0.045–0.049; probability of RMSEA <0.05, 98.9%; CFI, 0.896; and TLI, 0.893). Very high correlations were observed between SC and AM ($r$ =0.91, 95% CI: 0.890–0.935). The high correlation between these two ASD domains suggests that total scores will be adequately represented by a single factor structure.

### Reliability

Cronbach's α for the normative sample was 0.96, indicating strong internal consistency.

### Validity

#### *Convergent validity*

The correlation between the SRS-A and PARS scores was relatively strong ($n$ =14, 12 ASD, 2 non-ASD, $r$ =0.62, $p$ = .019). The correlation between the SRS-A and the ADOS module 4 scores was moderate (37 ASD, $r$ =0.34, $p$ = .037). The correlation between the SRS-A and AQ-J scores ($n$ =76, men 52.6%; 33 ASD, 43 non-ASD; mean age ± SD [range], 35.5 ± 11.4 [20–59] years) was significant but weak ($r$ =0.25, $p$ = .030).

#### *Divergent validity*

For the available IQ data ($n$ =44), the SRS-A score did not significantly correlate with IQ ($r$ = −0.09, *ns*).

#### *Discriminative validity*

The ASD group scored significantly higher than the non-ASD group ($p$ < .001, $d$ =1.07) (Table 3). When SRS-A scores were compared between the groups according to gender, both men ($p$ < .001, $d$ =1.14) and women ($p$ = .005, $d$ =0.84) scored significantly higher in the ASD group than in the non-ASD group. Further, gender differences in SRS-A scores were not significant in either the ASD or non-ASD group. Because the findings from our normative sample scores suggested rater bias, only mother ratings were compared between groups (Table 3). Again, participants with ASD scored significantly higher than those without ASD ($p$ < .001, $d$ =0.88). Age of this subgroup did

not significantly differ between groups. Within groups, SRS-A scores revealed no significant gender differences. SRS-A scores in the ASD group did not significantly differ by subcategory (autistic disorder, 99.2 ± 28.3; Asperger's disorder, 83.7 ± 31.2; and PDD-NOS, 80.4 ± 23.4). Within the non-ASD group, SRS-A scores did not significantly differ by co-occurring disorder (major depressive disorder, 48.9 ± 26.9; schizophrenia, 59.8 ± 25.9; bipolar disorder, 53.7 ± 23.0; other disorders, 64.8 ± 36.7).

Due to the gender-biased score distributions found in the normative sample (Figure 1), we generated a ROC curve for each gender in the validation sample (Figure 2). Area under the curve was 0.896 (95% CI: 0.83–0.97, $p < .001$) for men and 0.859 (95% CI: 0.78–0.94, $p < .001$) for women, with both moderately able to discriminate ASD and non-ASD psychiatric disorders in a clinical population. Youden index values (sensitivity + specificity-1) were maximized at a score of 65 for men and 52 for women, at which sensitivity was 0.84 and specificity was 0.81 for men, and sensitivity was 0.95 and specificity was 0.61 for women. These cutoff values are highly sensitive to ASD among various psychiatric disorders and might be suitable for identifying possible ASD in clinical settings. To make a definite diagnosis, the next step is a detailed interview with appropriate examination and history taking.

## Discussion

This study provides some evidence supporting the continuous distribution of autistic traits in a non-clinical adult population using the Japanese version of the SRS-A, and the satisfactory reliability and validity of the Japanese version SRS-A for adults aged 19 to 59 years. The Japanese version SRS-A was shown to be capable of detecting ASD and autistic traits/symptoms among a psychiatric population and also screening for ASD. The finding of continuous distribution of autistic traits in a non-clinical adult population as measured by the SRS-A and its single factor structure is closely similar to what has been observed in children [9,18,20]. The SRS-A provides additional evidence about the nature of the autistic spectrum [6]. Mean SRS-A scores corresponded to mean parent-rated SRS scores in Japanese children [9]. The effects of gender or age on SRS-A scores among a non-clinical adult population in this study were overall minimal, being similar to previously reported parent-rated scores in a child population aged 7 to 15 years [9]. Only in adolescents did we observe a significant gender difference with a moderate effect size. However, this male-dominant difference found in adolescent participants could be explained by age-dependent rater bias. Regarding rater effects, we could examine these for adolescent participants only due to practical restraints of the collected data. Our results demonstrated that, father ratings were significantly higher than mother ratings for adolescents. In an examination of a twin sample, Constantino and Todd (2005) reported strong parent-offspring correlations of subthreshold autistic traits as measured by the SRS [27], indicating that autistic traits are strongly heritable for the pairing. According to that study, the father-offspring correlation was higher than that of the mother-offspring pairing, and that of the father-son pairing was the strongest at 0.58. It is unclear whether such father-son similarity in social responsiveness might have affected the extremely high father ratings of their adolescent sons in this study. Given that the special status of fathers as the rater has not been observed in the U.S. standardization sample [15], pp. 44, alternatively our finding might better be explained by Japanese fathers' high expectations of their sons approaching adulthood (i.e., they are no longer children but also not yet independent adults). The interrelationship between rater type, gender, and age remains to be replicated by larger-scale studies in Japan and in other cultures. Taken together, when interpreting the information SRS-A provides, we must keep in mind various factors, especially rater type in terms of social expectations within sociocultural contexts.

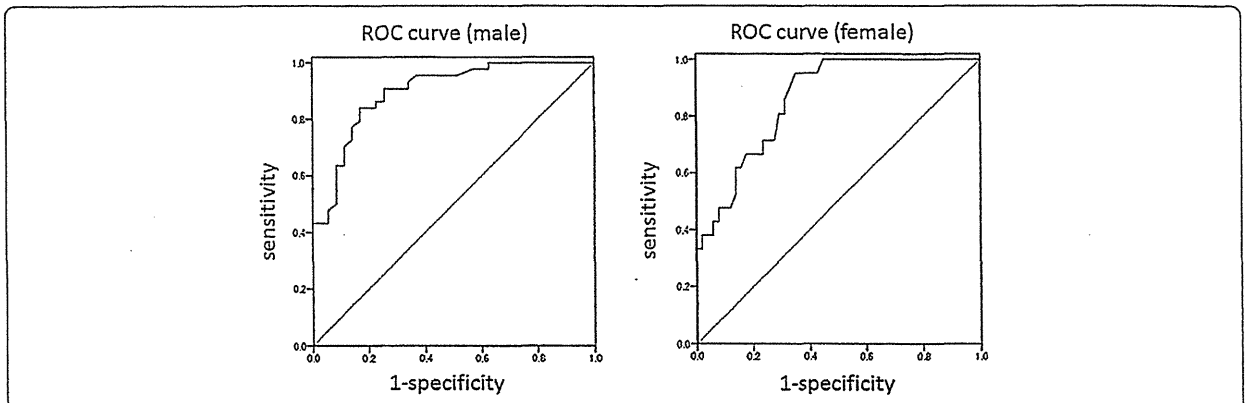


**Figure 2** Receiver operating characteristics (ROC) curve of the SRS-A conducted for the validation sample ($n = 143$) (Left: male, Right: female).

From the viewpoint of cross-cultural comparison, the score distribution in this study is comparable to that of U.S. data [15,27]. The mean scores in our non-clinical sample rated by various raters (19–59 years; 43.3 for men, 34.3 for women) are comparable to those rated by mixed raters (18–89 years; 42.2 for men, 38.8 for women) reported in the SRS-2 Manual [15], pp. 44. As for spouse ratings of participants in early adulthood or middle age, the mean scores in our non-clinical subsamples (33.1, male 48.8%) were very similar to those of U.S. data rated by spouses (30–55 years; 31.7 for men, 30.0 for women) [27]. However, the scores in our sample were lower compared to those of German adults with typical development (19–79 years, 55.5 for mixed sex) as reported by Bölte [28]. The reason for this discrepancy between Bölte's and our scores is not clear because rater-type details were not mentioned in Bölte [28]. As emphasized in the SRS-2 Manual [15] as well as in Bölte [28], the effect of rater type, which varies depending on an adult's age, gender, or living situation, might be crucial and should be systematically studied in future research.

Regarding convergent validity, correlations between the SRS-A and ADOS or PARS ranged from moderate to relatively strong (the latter two of which were assessed based on direct or indirect clinician observation), and these correlations provide support that the Japanese version SRS-A measures the same clinical aspects of the autism spectrum as do validated measurements. By contrast, the weak correlation between the SRS-A and AQ-J might be because the AQ-J is self-rated, and suggests that these two questionnaires might measure different aspects of the autistic spectrum.

Although the Japanese version SRS-A capably discriminated adults with ASD from those without ASD but having any other psychiatric diagnosis such as major depressive disorder, schizophrenia, or bipolar disorder, we observed no gap but rather an overlap in the score distribution between the two clinical groups (with and without ASD) in our study. This finding is consistent with that observed for school-age children [9], although the non-ASD child clinical population in that previous study [9] included adjustment disorder, attention-deficit/hyperactivity disorder (ADHD), and anxiety and other disorders, making it more diverse than the non-ASD adult clinical population in the present study. Recent genetic, molecular, and cytologic research highlights shared contributory mechanisms between ASD and major adult-onset psychiatric disorders (i.e., major depressive disorder, bipolar disorder, schizophrenia [34], and behavioral-cognitive commonalities [5,35]). Further, concurrent depression and anxiety symptoms, which are likely accompanied by transient psychotic symptoms, are found not only in individuals with ASD but also in those with subthreshold autistic symptoms [36,37]. Given this transdiagnostic commonality, the overlap in the SRS-A score distribution in the present study suggests that a proportion of the non-ASD clinical population might have autistic traits/symptoms despite having subthreshold ASD, which can lead to clinical difficulties in differential diagnosis. Because such clinical uncertainty from concurrent psychiatric symptoms is likely to result in misdiagnosis that overlooks ASD, our result that the SRS-A has discriminative ability for ASD with high sensitivity would prove the clinical usefulness of the instrument as a secondary screening tool in psychiatric practice. From a therapeutic viewpoint, it is important to detect autistic symptoms of not only threshold ASD but also subthreshold autistic conditions among various psychiatric populations so that appropriate treatment based on a comprehensive clinical evaluation can be given [36,37]. To this end, we recommend cut-off scores of 65 for men and 52 for women, which are similar to those for Japanese children [9], even though there are some adults who do not meet the diagnostic criteria of ASD above the cut-off.

This study has several limitations. First, our sample size was small, from which we examined a subsample using validated instruments measuring autistic traits and severity or IQ. The non-ASD clinical group mainly included participants diagnosed with schizophrenia and depressive or bipolar disorders, although other various psychiatric comorbidities are also common in adults with ASD, notably anxiety disorder and ADHD [38]. Replication in a larger psychiatric population including anxiety disorder and ADHD is needed. Second, our normative sample did not include individuals aged 60 or more for whom the SRS-2 manual gives higher scores [15], pp. 44. Third, we did not examine inter-rater agreement, which can explain differences due to rater type found in this study as well as test-retest reliability. Fourth, we did not examine the self-report SRS-A. A comparison between other-report and self-report questionnaires would add evidence about rater type in measuring this kind of behavior [39,40].

## Conclusion

This study replicated the original SRS-A study in a Japanese population and extended previous studies on the child version of the SRS to an adult population. That is, the SRS-A distributed continuously in the non-clinical population, and the other-report SRS-A rated by parents, spouses, siblings, and close friends was found to be reliable across gender and age, except in the youngest men aged 19 to 24 years. Furthermore, the SRS-A is useful for detecting ASD and autistic traits/symptoms among psychiatric patients and also for capably discriminating ASD from non-ASD psychiatric disorders such as major

depression and schizophrenia. We have recommended optimal cutoff scores feasible for use in clinical settings.

### Abbreviations

ADOS: Autism Diagnostic Observation Schedule; ANOVA: Analysis of variance; AQ: Autism-spectrum quotient; AQ-J: Japanese version of the autism-spectrum quotient; ASD: Autism spectrum disorder; DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; IQ: Intelligence quotient; PARS: Pervasive Developmental Disorders-Autism Society Japan Rating Scale; PDD-NOS: Pervasive developmental disorder-not otherwise specified; SRS-A: Social Responsiveness Scale-Adult version.

### Competing interests

The authors declare that they have no competing interests.

### Authors' contributions

RT, JM, TU, HT, and TK collected the data. RT and YK performed the statistical analysis and wrote the manuscript. All authors read and approved the final manuscript.

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# Attenuation of the contingency detection effect in the extrastriate body area in autism spectrum disorder

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ABSTRACT

Detection of the contingency between one's own behavior and consequent social events is important for normal social development, and impaired contingency detection may be a cause of autism spectrum disorder (ASD). To depict the neural underpinnings of this contingency effect, 19 adults with ASD and 22 control participants underwent functional MRI while imitating another's actions and their actions being imitated by the other. As the extrastriate body area (EBA) receives efference copies of one's own movements, we predicted that the EBA would show an atypical response during contingency detection in ASD. We manipulated two factors: the congruency of the executed and observed actions, and the order of action execution and observation. Both groups showed the congruency effect in the bilateral EBA during imitation. When action preceded observation, the left EBA of the control group showed the congruency effect, representing the response to being imitated, indicating contingency detection. The ASD group showed a reduced contingency effect in the left EBA. These results indicate that the function of the EBA in the contingency detection is altered in ASD.



## 1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by difficulties in social communication and social interaction, and restricted, repetitive patterns of behavior,

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interests or activities (DSM-5; American Psychiatric Association, 2013). The impairments in social communication and social interaction include both verbal and nonverbal behaviors. One of the impaired nonverbal behaviors is body gesture. Individuals with ASD have a fundamental impairment in gestural interaction in terms of social cause–effect representation ("I smile, therefore another person smiles"; i.e., social contingency detection, Gergely, 2001; Nadel, 2002), which is a basic element of the development of social communication skills (Mundy and Sigman, 1989). When being imitated, typically-developing children frequently changed their actions and looked at the person they were interacting with. However, most children with ASD did not display these behaviors (Nadel, 2002).

In order to account theoretically for the deficit in social contingency detection in ASD, Gergely and Watson (1999) postulated the presence of a "contingency detection module (CDM)", which functions to establish the primary representation of the bodily self as well as the later orientation toward reactive social objects. This module is innately set to preferentially explore perfect response-contingent stimulation. Around 3 months of age, the CDM is "switched" toward a preference for less-than-perfect contingent actions of others, such as reciprocal imitation (Bahrick and Watson, 1985; Gergely and Watson, 1999). In contrast, children with ASD fail to switch their preference from perfect to less-than-perfect contingency. As a result, children with ASD become less sensitive to less-than-perfect contingency situations, such as being imitated, and spend more time in repetitive motor activity in order to seek out self-related perfect contingency (Gergely, 2001). Although this hypothesis might explain the pathological origin of ASD, the neural underpinnings of the CDM are not yet understood.

Previous neuroimaging studies suggest that the occipito-temporal region is related to the detection of the congruency between one's own and another person's actions when imitating and being imitated (Decety et al., 2002; Chaminade et al., 2005). Within the occipito-temporal region, one candidate region is the extrastriate body area (EBA), which is selectively activated when viewing the human body (Downing et al., 2001) and the movements of one's own body (Astafiev et al., 2004; Orlov et al., 2010). Previous neuroimaging studies have reported that the bilateral lateral occipito-temporal region around the EBA shows a "congruency effect": it is strongly activated when one's own and another's actions were congruent (i.e., imitating and being imitated) compared to when they were different (Decety et al., 2002; Chaminade et al., 2005). These findings suggest that the EBA may be the "comparator" of the efference copy/proprioceptive information of one's own actions and the visual information received about another's actions.

If the EBA is the neural substrate of the CDM, we can predict that activity in the EBA during contingency detection between one's own actions and the resulting actions of others should be reduced in ASD. However, to our knowledge, no previous neuroimaging study has examined the effect of ASD on the neural network underlying contingency detection. In the present study, we examined brain activation of adults with ASD when they imitated hand actions and when their hand actions were imitated. Based on a previous study on being imitated (Decety et al., 2002), we manipulated the two factors: (1) the congruency between observed and executed actions (congruent/incongruent) and (2) the order of executed and observed actions (the participants executed the action BEFORE/AFTER observing the action of another person). In this task design, we were particularly interested in whether adults with ASD have abnormal congruency effect in being imitated (BEFORE conditions). If EBA corresponds to CDM, the EBA in adults with ASD should show reduced activity in BEFORE conditions.

## 2. Materials and methods

### 2.1. Participants

Nineteen adults with ASD and twenty-two typically-developing adults participated in the present study. The protocol was approved by the ethics committee of the University of Fukui (Japan), and the study was conducted in accordance with the Declaration of Helsinki. Participants were excluded if they had a history of major medical or neurological illness including epilepsy, significant head trauma, or a lifetime history of alcohol or drug dependence. Written informed consent was obtained from each participant after a complete explanation of the study. Handedness was assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). All participants' intelligence quotient (IQ) scores were obtained using the Wechsler Adult Intelligence Scale-III (WAIS-III) (Wechsler, 1997). We also measured the autism-spectrum quotient (AQ) total score (Baron-Cohen et al., 2001), which has been validated in a clinical sample (Woodbury-Smith et al., 2005).

#### 2.1.1. High-functioning ASD group

Eighteen males and one female (mean ± standard deviation [SD] age = 24.8 ± 4.4 years) were recruited at the Department of Neuropsychiatry of the University of Fukui Hospital (Japan) and the Department of Psychiatry and Neurobiology of Kanazawa University Hospital (Japan) (Table 1). Two psychiatrists (6th and 16th authors) diagnosed the participants as ASD based on the DSM-5 classifications (American Psychiatric Association, 2013) and standardized criteria using the Diagnostic Interview for Social and Communication Disorders (DISCO) (Wing et al., 2002). These two authors were trained in the diagnosis of ASD under T. Uchiyama and are qualified to use the DISCO Japanese edition (2007). The DISCO has good psychometric properties (Nygren et al., 2009), and it contains items on early development and activities of daily life, giving the interviewer some idea of the level of functioning in several different areas, not only social functioning and communication (Wing et al., 2002). Eight of 19 patients took medications including antipsychotics (four patients), antidepressants (four patients), anxiolytics (four patients) and hypnotics (three patients) at MRI examination day. Four of 19 patients with ASD have comorbidity with obsessive compulsive disorder (two patients), anxiety disorder (one patient) and atopic dermatitis (one patient).

#### 2.1.2. Control group

Twenty-two age-matched typically-developing volunteers (20 males and 2 females) were recruited from the local community for the CTL group (mean ± SD age = 24.2 ± 3.7 years; Table 1). They were screened to exclude individuals who had a first-degree relative with an axis I disorder based on DSM-5 criteria. The full-scale IQ (FSIQ) scores of all participants were greater than 75, and the mean FSIQ scores of each group were over 100. Although there was a significant difference in FSIQ scores between the ASD and CTL groups ($t(39) = 2.6$, $p < .05$, two-sample $t$-test), there was no significant difference in verbal IQ scores between the two groups ($t(39) = 1.6$, $p > .1$, two-sample $t$-test). In contrast, the AQ total scores and sub-scores were significantly higher in the ASD group than in the CTL group (both $p < .01$, two-sample $t$-test; Table 1).

### 2.2. MRI parameters

All functional volumes were acquired using T2*-weighted gradient-echo echo-planar imaging (EPI) sequences with a 3 Tesla MR imager (Sigma Horizon; GE Medical Systems, Milwaukee, Wisconsin). A volume consisted of 37 oblique slices, each 3.0 mm in thickness, with a 15% gap, in order to cover the entire cerebral and cerebellar cortices. The axial slices were acquired sequentially in

**Table 1**
Demographic data and rating scale scores.

| Subjects | CTL subjects | ASD subjects | *T* value | *P* |
|---|---|---|---|---|
| Number | 22 | 19 | | |
| Males | 20 | 18 | | |
| Females | 2 | 1 | | |
| Handedness (right/left) | 21/1 | 18/1 | | |
| Age | 24.2 ± 3.7 | 24.8 ± 4.4 | .48 | .630 |
| WAIS-III | | | | |
| Full scale IQ | 114.5 ± 8.1 | 104.3 ± 15.5 | 2.60 | .015* |
| Verbal IQ | 114.8 ± 9.6 | 108.2 ± 15.8 | 1.59 | .122 |
| Performance IQ | 110.5 ± 10.4 | 98.3 ± 17.0 | 2.80 | .008** |
| AQ | | | | |
| Total scores | 13.3 ± 3.5 | 33.5 ± 7.2 | 11.10 | <.001*** |
| Social skill scores | 1.9 ± 1.9 | 7.2 ± 2.5 | 7.59 | <.001*** |
| Attention switching scores | 3.4 ± 1.7 | 7.6 ± 1.7 | 7.90 | <.001*** |
| Attention to detail scores | 3.6 ± 1.7 | 5.8 ± 2.9 | 2.98 | .006** |
| Communication scores | 1.7 ± 1.3 | 7.0 ± 3.0 | 7.23 | <.001*** |
| Imagination scores | 2.7 ± 1.5 | 5.8 ± 2.1 | 5.43 | <.001*** |

ASD, autism spectrum disorder; CTL, control; WAIS-III, Wechsler Adult Intelligence Scale Third Edition; AQ, Autism Spectrum Quotient. Handedness was assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). Age, WAIS-III IQ scores, and AQ scores are shown as mean ± SD. *$p < .05$, **$p < .01$, ***$p < .001$ with independent-samples *t*-tests comparing ASD and CTL participants.

ascending order. The time interval between two successive acquisitions of the same slice (repetition time [TR]) was 2500 ms, the flip angle (FA) was 80°, the echo time (TE) was 30 ms, the field of view (FOV) was 192 mm × 192 mm, the digital in-plane resolution was 64 × 64 pixels, and each pixel was 3 mm × 3 mm. For each participant, a high-resolution anatomical T1-weighted image was also acquired using three-dimensional inversion recovery-prepared fast spoiled-gradient recalled acquisition in the steady state (SPGR) sequencing (TR = 11.3 ms; TE = 5.3 ms; FA = 10°; 320 × 192 matrix; voxel dimensions = .75 mm × 1.25 mm × 1.60 mm). Head motion was minimized by placing comfortable but tight-fitting foam padding around each participant's head.

### 2.3. Experimental setup

Presentation 0.90 software (Neurobehavioral Systems, CA, USA) implemented on a Windows-based desktop computer (Dimension 9200, Dell Computer Co., Round Rock, TX, USA) was used for audio-visual stimuli presentation and response collection. A liquid-crystal display (LCD) projector (TH-AE900; Matsushita Electric Industrial Co. Ltd., Osaka, Japan) projected the visual stimuli, which the participants viewed via a mirror attached to the head coil of the MRI scanner. The auditory stimuli were presented via MRI-compatible headphones (Visual Stim Controller; Resonance Technology Inc., CA, USA). For each participant, the volume of the sound was adjusted to an appropriate level for task execution in the context of the MR scanner noise. A high-definition (HD) digital video camera (HDR-XR520V, Sony, Tokyo, Japan) was used to record participants' gestures during the fMRI experiment. Each participant performed one run of the finger-gesture task as pre-scan training prior to entering the fMRI scanning room. We confirmed that all of the participants could comfortably make the finger gestures before the experiment started.

### 2.4. Task procedures

#### 2.4.1. EBA localizer task

We employed a conventional block design to localize the EBA (Downing et al., 2001). Each participant was asked to observe photographs of body parts, faces, outdoor scenes, and cars (viewing angle = 10.8° × 14.4°). Each run consisted of 21 blocks, each of which lasted for 15 s. The first, sixth, eleventh, sixteenth, and twenty-first blocks were fixation-only baseline conditions. Twenty photographs from one of the four object categories were presented successively in each block. Adobe Photoshop software (Adobe Systems Inc., CA, USA) was used to transform all color photographs to grayscale images, and the luminance was adjusted so that it was matched between the different categories of objects. The matrix size of the photographs was 400 × 300 pixels. Each photograph was presented for 300 ms, and the inter-stimulus interval was 450 ms. Each object category block was repeated four times. A 10-s fixation-only baseline condition was added before the first baseline block (10 s + 15 s × 21 blocks = 325 s, 130 volumes in total). In order to maintain the participants' attention on the screen, we asked them to complete a color-detection task in which a fixation cross changed color from white to red twice during the inter-stimulus intervals in each block. Participants were asked to press a button with their right hand as soon as the fixation cross changed color. Each participant completed two runs of the localizer task.

#### 2.4.2. Finger-gesture task

During the task, participants were required to make finger gestures to indicate the numbers from 1 to 5 (Fig. 1A) in response to an instruction cue, while observing another individual's hand gesture. Participants could not see their own hands. We employed a 2 × 2 factorial design, including the congruency of executed and observed hand gestures (congruent [C]/incongruent [I]), and the order of the participant's and the other's actions (AFTER [A]/BEFORE [B]). In "C" conditions, the executed and observed gestures were the same; in "I" conditions, the executed and observed gestures were different. In "A" conditions, the participants actively selected and executed the action after the observation of another's action; and in "B" conditions, the participants executed the action before they observed the other's action (Fig. 1B).

*2.4.2.1. Stimulus preparation.* We recorded an actress making the five finger gestures shown in Fig. 1A with her left hand using a video camera (Handycam, HDR-SR1; Sony, Tokyo, Japan) with a matrix size of 352 × 240 pixels, a digitization rate of 30.0 frames/s (1 frame = 33.3 ms), and a viewing angle of 16.8° × 9.4°. Each movie clip started when the actress closed her fist, and ended after she made one of the five finger gestures and then closed her fist again. The duration of each movie clip was 700 ms. In order to ensure that all stimuli were 2200 ms in duration, we used Adobe-Premiere software (Adobe Systems Inc., CA, USA) to insert a static picture before and after the movie clip. Two types of stimulus were produced: video clip A, which consisted of the presentation of a static image of a fist for 1200 ms, followed by a motion picture showing a finger gesture for 700 ms, and a static image of a fist for 300 ms; and video clip B, which consisted of the presentation of a static image of a fist

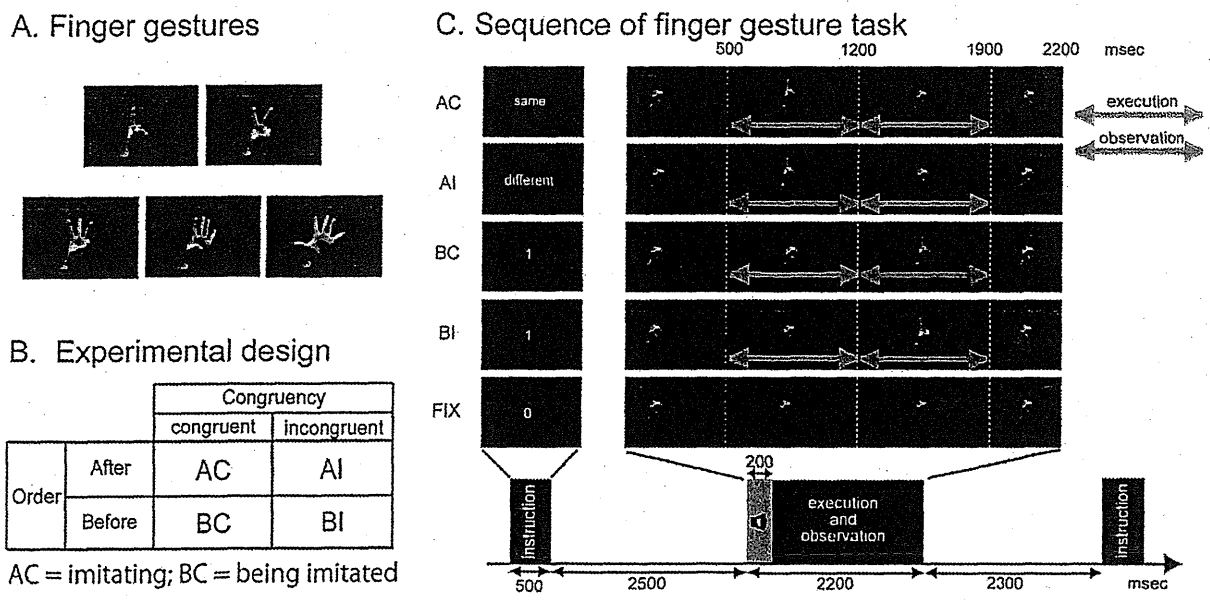


**Fig. 1.** Finger gesture task. (A) Finger gestures: Five finger gestures expressing five numbers were used for the task. (B) Experimental design: 2 × 2 factorial design which manipulated congruency and order. (C) Sequence of finger gesture task: Sequence of each condition (AC, AI, BC, BI and FIX). Participants executed the finger gestures around the time indicated by green arrows. Note that participants could not see their own hands.

for 500 ms, followed by a motion picture showing a finger gesture for 700 ms, and a static image of a fist for 1000 ms. The two video clips were used as stimuli for different conditions, as explained in the following sections.

*2.4.2.2. Conditions.* In the AFTER-congruent (AC) condition, the participants observed the actress's finger gesture and then performed the same gesture, imitating the actress's movement (Fig. 1C, first row). The instruction for the condition ("same") was visually presented for 500 ms. A 200-ms auditory cue was presented 2500 ms after the offset of the visual instruction. At the same time as the auditory cue, video clip B was presented for 2200 ms. Participants were asked to execute the same finger gesture as soon as they observed it. Although the participants were required to match the final hand gesture in the imitating condition, they did not have to conduct the observed actions with the same kinematics (i.e., trajectory, acceleration, and velocity). Before the experiment, we confirmed that each participant could execute the finger gestures within 2200 ms (the time-span of the video clip). We included a 2300-ms interval before the next trial. In total, it took 7500 ms to complete each trial.

The AFTER-incongruent (AI) condition was identical to the AC condition, except that the participant was required to make a finger gesture that differed from that presented on the screen (Fig. 1C, second row). Thus, the participant had to select and execute one of four finger gestures. We instructed the participants to choose each of the four finger gestures equally often.

In the BEFORE-congruent (BC) condition, the participants initially executed a finger gesture and then observed the same gesture, as though they were being imitated (Fig. 1C, third row). In each trial, a number from 1 to 5 was visually presented for 500 ms as the instruction cue. A 200-ms auditory cue was presented 2500 ms after the offset of the visual instructions. The participants were asked to make a finger gesture that expressed the same number as that in the instructions as soon as the auditory cue was presented. At the same time as the auditory cue, video clip A was presented for 2200 ms. There was a 2300-ms interval before the next trial.

The BEFORE-incongruent (BI) condition was identical to the BC condition, except that the observed finger gesture differed from the gesture that was executed by the participants (Fig. 1C, fourth row).

In addition to the four conditions mentioned above, we included a control condition (FIX) in our task design. This served as a control for the instruction cue, the auditory cue, and the visual input of the images of the human hand. The instruction "0" was visually presented for 500 ms (Fig. 1C, fifth row). The auditory cue was presented for the same duration and at the same time as in the other four conditions. Instead of the video clip, the participant observed a static image of a fist for 2200 ms. The participants were instructed to observe the static image of the closed fist and not to execute any movements during the FIX condition.

Each run consisted of 10 trials of each condition, with each trial lasting 7500 ms (10 trials × 5 conditions × 3 volumes = 150 volumes). The order of the trials was pseudo-randomized to optimize the efficiency of the design (Dale, 1999; Friston et al., 1999). The first trial was preceded by 10 s (4 volumes) of the baseline condition, and the last trial was followed by 12.5 s (5 volumes) of the baseline condition (159 volumes in total). Each participant completed four runs.

### 2.5. Data analysis

#### 2.5.1. Behavioral data

We calculated participants' behavioral performance based on the recorded video data. We classified trials as "correct" if the participants accurately performed the instructed action. We also calculated the response time (RT) of the executed actions. For the AFTER conditions, during which the participants imitated the action, the RT was defined as the length of time between the onset of the observed action and the participant's movement. For the BEFORE conditions, during which the participants performed the action first, the RT was defined as the length of time between the onset of the auditory cue (instructing the participants to execute a finger gesture) and the onset of the participant's action.

**Table 2**
Predefined contrasts for the finger-gesture tasks.

| Regressors | AFTER | | BEFORE | | Baseline task |
|---|---|---|---|---|---|
| | Congruent AC (Imitating) | Incongruent AI | Congruent BC (Being imitated) | Incongruent BI | FIX |
| Activity greater than baseline | | | | | |
| c01. AC vs. FIX | 1 | 0 | 0 | 0 | −1 |
| c02. BC vs. FIX | 0 | 0 | 1 | 0 | −1 |
| Congruency effect | | | | | |
| c03. AC vs. AI | 1 | −1 | 0 | 0 | 0 |
| c04. BC vs. BI | 0 | 0 | 1 | −1 | 0 |

Note that the design matrix included other regressors of no interest: a single regressor for missed responses and incorrect trials (if any), and 6 regressors for head motion.

*2.5.2. fMRI analysis*

*2.5.2.1. Pre-processing.* The first four volumes of each run were discarded because of unsteady magnetization. The remaining 155 volumes per run for the finger-gesture task (620 volumes per participant) and 126 volumes per run for the EBA localizer task (252 volumes per participant) were used for the following analyses. The data were analyzed with Statistical Parametric Mapping software (SPM8; Wellcome Department of Imaging Neuroscience, London, UK) implemented in MATLAB (MathWorks, Natick, MA, USA). After realignment of all functional images, slice timing correction was conducted. Then, the high-resolution anatomical image was coregistered to the functional images. The coregistered anatomical image was normalized to a template T1 image that was already fitted to Montreal Neurological Institute [MNI] space (Evans et al., 1994). The parameters from this normalization process were then applied to all functional images, which were resampled to a final resolution of 2 mm × 2 mm × 2 mm. The normalized fMRI images were filtered using a Gaussian kernel of 8 mm (full-width at half-maximum) in the *x*, *y*, and *z* axes.

*2.5.2.2. Statistical analysis.*

*2.5.2.2.1. EBA localizer task.* In the individual analyses, we fitted a general linear model to the fMRI data from each participant (Friston et al., 1994; Worsley and Friston, 1995). Neural activity was modeled with delta functions convolved with the canonical hemodynamic response function (HRF). Each run of the localizer task included 11 regressors. Four regressors (faces, body, scenes, and cars) were modeled at the onsets of each block, and the duration was 15 s. A fifth regressor was modeled for the participant's response to the color-detection task. Motion-related artifacts were modeled as regressors of no interest using the six parameters (three displacements and three rotations) obtained by the rigid-body realignment procedure. The time series for each voxel was high-pass filtered at 1/128 Hz. Assuming a first-order autoregressive model, the serial autocorrelation was estimated from the pooled active voxels with the restricted maximum likelihood (ReML) procedure, and was used to whiten the data (Friston et al., 2002). Global signal changes were utilized to remove global confounding factors such as scanner gain. The parameter estimates for each condition in each individual were compared using linear contrasts.

Contrast images from the individual analyses were then used for the group analysis, with between-participants variance modeled as a random factor. The contrast images obtained from the individual analyses represent the normalized task-related increment of the MR signal of each participant. To define the EBA at the group level, a two-sample *t*-test was conducted on the contrast images of non-face body parts versus the mean of the other three categories in the ASD and CTL groups. The resulting set of voxel values for each contrast constituted the SPM{*t*}, which was transformed to normal distribution units [SPM{*z*}]. The statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons at the cluster level over the whole brain (family-wise error [FWE]), with a height threshold of $Z > 3.09$ (Friston et al., 1996). Brain regions were anatomically defined and labeled according to a probabilistic atlas (Shattuck et al., 2008).

*2.5.2.2.2. Finger-gesture task.* In the individual analyses, one regressor was modeled for the instructions for all conditions, which lasted for 500 ms (Fig. 1C). The trials for each condition (AC, AI, BC, BI, and FIX) were then modeled. Each regressor was modeled from the onset of the video clip for 2200 ms (Fig. 1C). The visual and motor components were similar between the regressors of the four conditions (AC, AI, BC, and BI), with the exception of the timing of the execution and observation of finger gestures between the AFTER and BEFORE conditions, which differed by 1400 ms (Fig. 1C). The five regressors were modeled only for trials in which the participant gave correct answers. If there was a missed response or an incorrect trial in a run, we added another regressor to the design matrix in order to model these trials as effects of no interest. Six regressors modeled motion artifacts in the same way as for the EBA localizer task. Therefore, each run contained 12 or 13 regressors.

In order to implement the group analysis in a random-effects model, we obtained contrast images for each predefined contrast (AC – FIX, BC – FIX, AC – AI and BC – BI; Table 2). For each predefined contrast, we performed a two-sample *t*-test to compare the two groups. In other words, the design matrix for the two-sample *t*-tests included the two regressors, each of which contained the contrast images of a predefined contrast in each group. The statistical thresholds were the same as those used for the EBA localizer task: the statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons at the cluster level over the whole brain (FWE), with a height threshold of $Z > 3.09$ (Friston et al., 1996).

We evaluated the effect of congruency (congruent vs. incongruent) in each group (Table 2). The brain regions which showed greater activation in AC than AI were assessed by the overlap of activation between the AC – AI and AC – FIX contrasts. It was necessary to include AC – FIX, because the negative response of the AC condition below the baseline task can make the interpretation of data difficult. As we conducted a two-sample *t*-test on the AC – AI contrast between the two groups, we evaluated the conjunction between AC – AI and AC – FIX using the inclusive-masking procedure. This approach is identical to the standard conjunction analysis (with the conjunction null, Friston et al., 2005; Nichols et al., 2005), because the whole brain was used as the search volume for the overlap of activation. Thus, this analysis should not bias the statistical inference ("double dipping", Kriegeskorte et al., 2009). Similarly, we evaluated the overlap of activation revealed by the contrasts of BC – BI and BC – FIX. Then, we compared the congruency effect between the ASD group and the CTL group.