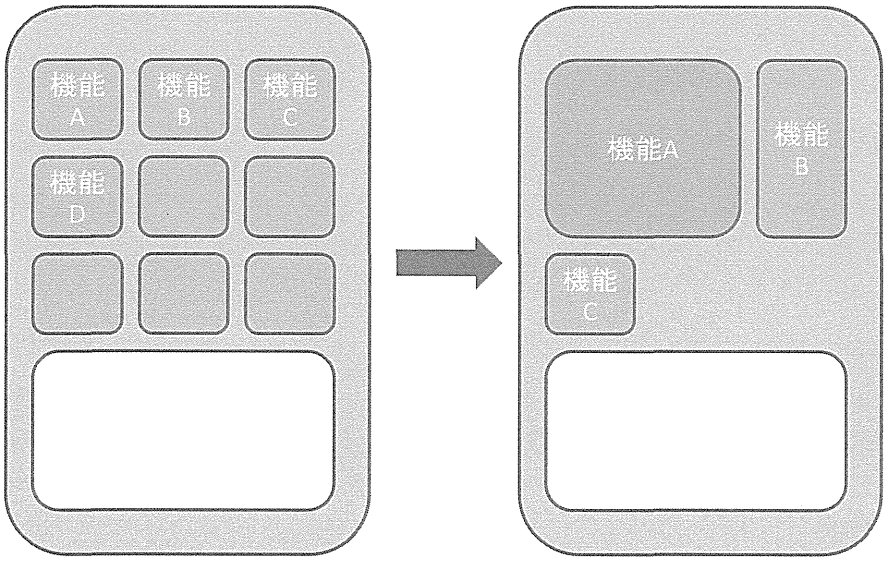

図 1　EMA 実施の際の負担軽減の例

EMA を実施するアプリのトップ画面において、不要なボタンは削除し、必要なボタンを大きくする、わかりやすい色で表示するなど、本研究の対象と目的に合致した負担の少ないユーザーインターフェースを開発した。

平成 26 年度　厚生労働科学研究委託費　障害者対策総合研究事業
障害者対策総合開発事業（精神障害分野）

委託業務成果報告（業務項目）

「発達障害者の就労定着を支援する多次元スマートセンシングシステムの開発」

業務項目
連続データ解析の実施とアルゴリズムの開発

担当責任者
山本　義春　東京大学大学院教育学研究科　教授

研究協力者
中村　亨　　東京大学大学院教育学研究科　特任准教授
金　鎭赫　　東京大学大学院教育学研究科　特任研究員

研究要旨

本業務項目では、携帯情報端末（スマートフォン）を用いて被験者から環境・生理状態（音圧・照度・脈波等）に関するデータを得るためのセンシングシステムを開発した。このセンシングシステムを用いて、屋内外環境の両方において、自然な動作で違和感なく簡便に音圧・照度・加速度・指尖容積脈波を測定することができ、さらに脈波信号の時間周波数解析等により、ecological momentary assessment (EMA)時の分時脈拍数・分時呼吸数も推定できた。したがって、日常生活下においても携帯情報端末により被験者から得られた環境・生理状態に関するデータを用いて、環境刺激に対する過敏性を定量的に評価できる可能性が示唆された。今後、発達障害のある青年・成人に1週間の連続装用を実施してデータ収集を行うことで、本センシングシステムの有用性の実証的検討を行う予定である。

A．研究目的

本業務項目では、携帯情報端末により被験者から環境・生理状態（音圧・照度・脈波等）に関するデータを得るためのセンシングシステムを開発し、これらの連続データを統合して解析するアルゴリズムの開発を行う。脈波信号の時間周波数解析等により、ecological momentary assessment (EMA)時の分時脈拍数、分時呼吸数を推定するアルゴリズムを開発することで、環境刺激に対する過敏性を定量的に評価する解析手法を開発する。

B．研究方法

これまで担当責任者らが開発・使用してきた携帯情報端末（スマートフォン）のアプリケー

ションに、自己申告だけでなくそれを行った際の環境要因や生理状態を客観的指標として定量測定するための改良を加えた。具体的には、業務項目「発達障害者の主観評価法の開発」で開発された EMA に同期してスマートフォン内蔵の光・音等のセンサー信号を記録、カメラを利用して１～２分の短時間で指尖脈波信号を連続記録する機能を付加した。脈波信号の時間周波数解析等により、EMA 時の分時脈拍数、分時呼吸数を推定するアルゴリズムを開発した。定型発達および発達障害を有する青年・成人を対象にモニタリング試用を行ってデータを収集し解析を行った。また使用後の感想をもとに、必要な改変を検討した。

（倫理面への配慮）

本研究の予備的研究は、国立精神・神経医療研究センター（NCNP）および東京大学の倫理委員会の承認を受けており、臨床研究の倫理指針に基づく手続きを遵守した。現時点までは変更の修正を必要としていない。

実施に際しては、臨床研究に関する倫理指針に基づく手続きを遵守する。本研究の成人の対象者は本人から書面によるインフォームド・コンセントを得る。同意能力に制限のある成人または未成年の対象者の研究参加については、書面によるインフォームド・コンセントを保護者から得る。医療機関や学校など関係諸機関の既存データのうち、個人データを含まない臨床情報が必要な場合には、情報提供について本人あるいは保護者からインフォームド・コンセントを得たうえで諸機関に依頼する。研究のプロセスで得られた個人情報は個人情報保護法に基づき漏洩のないよう厳重に取り扱う。収集された電子化データはプライバシー保護に十分に配慮して NCNP および東京大学において業務主任者および業務項目の担当責任者の管理のもとで厳重に保管する。学会発表など結果を公表する際には、原則として多数例を統計処理した結果のみを発表し、単一症例の場合にも数学的処理を経たデータのみを発表し、プライバシー保護に十分配慮する。

C．研究結果

本業務項目で開発したセンシングシステムのモニタリング試用を行ったところ、屋内外環境の両方において、スマートフォンを用いた自然な動作で違和感なく簡便に、音圧・照度・加速度・指尖容積脈波を測定することができた。さらに、指尖容積脈波信号の時間周波数解析により、分時脈拍数・分時呼吸数を推定できた。

D＆E．考察および結論

本業務項目では、これまで担当責任者らが開発・使用してきたスマートフォンのアプリケーションに、EMA に同期してスマートフォン内蔵の光・音等のセンサー信号を記録、カメラを利用して短時間で指尖脈波信号を連続記録する機能を付加し、被験者から環境・生理状態（音圧・照度・脈波等）に関するデータを得るためのセンシングシステムを開発した。定型発達および発達障害を有する青年・成人を対象にモニター試用を行ってデータを収集し解析を行った。屋内外環境の両方において、スマートフォンを用いた自然な動作で違和感なく簡便に、音圧・照度・加速度・指尖容積脈波を測定することができ、さらに、分時脈拍数・分時呼吸数も推定できた。したがって、日常生活下においても携帯情報端末により被験者から得られた環境・生理状態に関するデータを用いて、環境刺激に対する過敏性を定量的に評価できる可能性が示唆された。

平成 26 年 11 月からの短い期間ではあったが、センシングシステムは、ほぼ完成したと考えられる。今後は、本委託業務の他の業務項目で開発した、発達障害に特化した EMA、感覚過敏に関するチェックリスト作成を用いて、定型発達および発達障害のある青年・成人を対象に 1 週

間の日常生活下での連続装用を実施してデータ収集を行うことで、本センシングシステムの有用性の実証的検討を行い、発達障害に特化した行動・心理・生理・環境状態センシングシステムの開発の完成を計画している。

G. 研究発表

1. 論文発表

なし

2. 学会発表

① Fatigue and mood assessed with the DRM and EMA. Yamamoto Y. Conference on developments in the day reconstruction method, University of Southern California, Los Angeles, California, USA. Jan 2015.

H. 知的財産権の出願・登録状況

1. 特許取得　　現在のところ、予定なし。
2. 実用新案登録　現在のところ、予定なし。
3. その他　　現在のところ、予定なし。

Ⅲ. 学会等発表実績

様式第１９

学　会　等　発　表　実　績

委託業務題目　「発達障害者の就労定着を支援する多次元スマートセンシングシステムの開発」
機関名　独立行政法人　国立精神・神経医療研究センター

１．学会等における口頭・ポスター発表

発表した成果（発表題目、口頭・ポスター発表	発表者氏名	発表した場所（学会等名）	発表した時期	国内・外の別
Fatigue and mood assessed with the DRM and EMA.　（口頭）	山本義春.	Conference on developments in the day reconstruction method, University of Southern California, Los Angeles, California.	Jan 8-9, 2015	国外
学校メンタルヘルス管理用フォーマットの開発とその実際の使用.　（口	長尾圭造，高橋秀俊，駒田幹彦.	第45回全国学校保健・学校医大会，ホテル日航金沢，石川県金沢市	2014.11.8.	国内
自閉症スペクトラム障害の聴覚誘発脳磁界反応について.　（口頭）	高橋秀俊，軍司敦子，廣永成人，　萩原綱一，　飛松省三，　神尾陽子.	日本臨床脳磁図コンソーシアム　サテライトシンポジウム，福岡国際会議場，福岡県福	2014.11.19.	国内
Do early autistic symptoms predict later mental health problems?　（ポスター）	Kamio Y, Ogino K, Iida Y, Endo A, Komatsu S, Takahashi H, Ishitobi M, Miyake	9TH International Conference on Early Psychosis-To the new horizon, the Keio Plaza Hotel, Tokyo.	Nov 17-19, 2014	国内
日本における思春期・青年期の自殺予防活動.　（口頭）	長尾圭造，高橋秀俊.	モーズレー病院/ロンドン大学児童青年期精神医学専門研修～九州大学病院セミナー2014，九州大学病院同窓会館，福岡市	2014.11.22-23.	国内
自閉症スペクトラムの聴覚誘発定常ガンマ律動に関する検討（続報）.　（ポスター）	高橋秀俊，軍司敦子，金子裕，廣永成人，萩原綱一，稲垣真澄，飛松省三，花川隆，神尾陽子.	第4回IBICシンポジウム，国立精神・神経医療研究センター，東京都小平市.	2015.2.5	国内
自閉症スペクトラム障害における語用論理解の脳磁図研究:予備的検討.　（ポスター）	秋元頼孝，高橋秀俊，軍司敦子，金子裕，花川隆，馬塚れい子，神尾陽子.	第4回IBICシンポジウム，国立精神・神経医療研究センター，東京都小平市.	2015.2.5	国内

２．学会誌・雑誌等における論文掲載

掲載した論文（発表題目）	発表者氏名	発表した場所（学会誌・雑誌等名）	発表した時期	国内・外の別
Verification of the utility of the Social Responsiveness Scale for Adults in non-clinical and clinical adult populations in	Takei R, Matsuo J, Takahashi H, Uchiyama T, Kunugi H, Kamio Y	BMC Psychiatry 14:302. doi: 10.1186/s12888-014-0302-z.	2014 Nov	国外
Association between delayed bedtime and sleep-related problems among community-dwelling 2-year-old	Kitamura S, Enomoto M, Kamei Y, Inada I, Moriwaki A, Kamio Y, Mishima K.	Journal of Physiological Anthropology	2015 (in press)	国外
Autistic-like traits in adult patients with mood disorders and schizophrenia.	Matsuo J, Kamio Y, Takahashi H, Ota M, Teraishi T, Hori H, Nagashima A, Kinoshita Y, Ishida I, Hiraishi M, Takei R, Higuchi T, Motohashi N, Kunugi	PLOS ONE	2015 (in press)	国外
自閉スペクトラム症と精神科的併存症.	石飛信、荻野和雄、高橋秀俊、原口英之、神尾陽子	臨床精神医学, 第44巻1号	2015 Jan	国内

（注１）発表者氏名は、連名による発表の場合には、筆頭者を先頭にして全員を記載すること。
（注２）本様式はexcel形式にて作成し、甲が求める場合は別途電子データを納入すること。

Ⅳ. 研究成果の刊行物・別刷

Takei et al. BMC Psychiatry 2014, 14:302
http://www.biomedcentral.com/1471-244X/14/302

BMC Psychiatry

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

* Correspondence: kamio@ncnp.go.jp
[1]Department of Child and Adolescent Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8553, Japan
Full list of author information is available at the end of the article

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

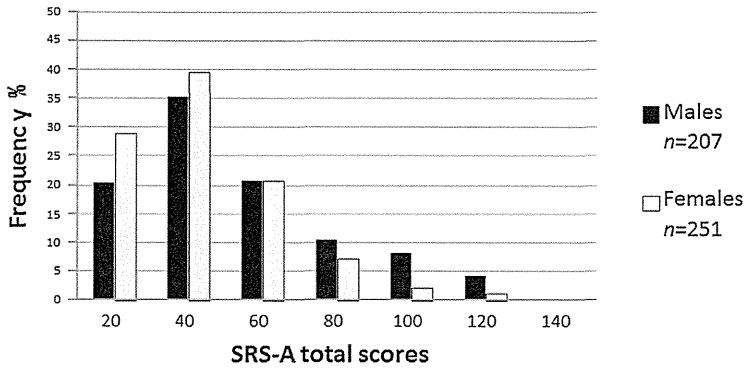

Figure 1 Distribution of Social Responsiveness Scale for Adults (SRS-A) total scores in the normative sample (n = 458).

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, η^2 = 0.03) and gender (p = .001, η^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.

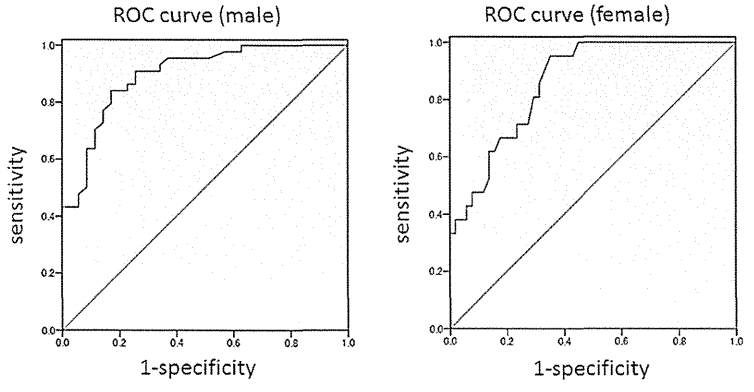

Figure 2 Receiver operating characteristics (ROC) curve of the SRS-A conducted for the validation sample (n = 143) (Left: male, Right: female).

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.

Acknowledgements

This study was supported by research grants from the Ministry of Health, Labour and Welfare of Japan (H22-SEISHIN-IPPAN-016 to Dr. Uchiyama and H20-KOKORO-004 to Dr. Kamio). We would like to thank Drs. Satoshi Hashimoto, Kaoruko Izumi, Yoshihiro Nabeshima, Mari Umeda, Hirohisa Hida, Itsuka Seido, Masatsugu Tsujii, Yoshiyuki Shimoda, Ikuko Nakano, Yuki Kawakubo, Hidenori Yamasue, Miho Kuroda, Naoji Kondo, Reiko Fukatsu, and Takeshi Nishiyama for data collection. Special thanks goes to Dr. Ryoji Yukihiro for statistical advice. The authors have no conflicts of interest to declare with respect to this article.

Author details

[1]Department of Child and Adolescent Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8553, Japan. [2]Department of Mental Disorder Research, National Center of Neurology and Psychiatry, Tokyo, Japan. [3]Department of Faculty of Human Development, Fukushima University Graduate School, Fukushima, Japan.

Received: 25 August 2013 Accepted: 16 October 2014
Published online: 18 November 2014

References

1. Brugha TS, McManus S, Bankart J, Scott F, Purdon S, Smith J, Bebbington P, Jenkins R, Meltzer H: **Epidemiology of autism spectrum disorders in adults in the community in England.** *Arch Gen Psychiatry* 2011, **68**:459–465.
2. Fombonne E: **Epidemiology of pervasive developmental disorders.** *Pediatr Res* 2009, **65**:591–598.
3. Kamio Y, Inada N, Koyama T: **A nationwide survey on quality of life and associated factors of adults with high-functioning autism spectrum disorders.** *Autism* 2013, **17**:16–27.
4. Kamio Y, Inokuchi E: **Hattasushogaisya to Seishinkairyo no Yakuwari: Saikin no Keiko to Kongo no Kadai [Psychiatric practice's role for individual with developmental disorders: current trend and future issues].** *J Jpn Assoc Psychiatr Hosp* 2009, **28**:14–20 (in Japanese).
5. Cochran DM, Dvir Y, Frazier JA: **"Autism-plus" spectrum disorders: intersection with psychosis and the schizophrenia spectrum.** *Child Adolesc Psychiatr Clin N Am* 2013, **22**:609–627.
6. American Psychiatric Association: *Diagnostic and statistical manual of mental disorders.* 5th edition. Washington, DC: American Psychiatric Association; 2013.
7. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. Text Revision.* Washington, DC: American Psychiatric Association; 2000.
8. Constantino JN, Todd RD: **Autistic traits in the general population: a twin study.** *Arch Gen Psychiatry* 2003, **60**:524–530.
9. Kamio Y, Inada N, Moriwaki A, Kuroda M, Koyama T, Tsujii H, Kawakubo Y, Kuwabara H, Tsuchiya KJ, Uno Y, Constantino JN: **Quantitative autistic traits ascertained in a national survey of 22,529 Japanese schoolchildren.** *Acta Psychiatr Scand* 2013, **128**:45–53.
10. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E: **The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians.** *J Autism Dev Disord* 2001, **31**:5–17.
11. Kurita H, Koyama T, Osada H: **Autism-spectrum quotient-Japanese version and its short forms for screening normally intelligent persons with pervasive developmental disorders.** *Psychiatry Clin Neurosci* 2005, **59**:490–496.
12. Wakabayashi A, Baron-Cohen S, Wheelwright S, Tojo Y: **The autism-spectrum quotient (AQ) in Japan: a cross-cultural comparison.** *J Autism Dev Disord* 2006, **36**:263–270.
13. Ritvo RA, Ritvo ER, Guthrie D, Yuwiler A, Ritvo MJ, Weisbender L: **A scale to assess the diagnosis of autism and Asperger's disorder in adults (RAADS): a pilot study.** *J Autism Dev Disord* 2008, **38**:213–223.
14. Ritvo RA, Ritvo ER, Guthrie D, Ritvo MJ, Hufnagel DH, McMahon W, Tonge B, Mataix-Cols D, Jassi A, Attwood T, Eloff J: **The Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R): a scale to assist the diagnosis of Autism spectrum disorder in adults: an international validation study.** *J Autism Dev Disord* 2011, **41**:1076–1089.
15. Constantino JN, Gruber CP: *Social Responsiveness Scale, Second Edition (SRS-2).* Los Angeles: Western Psychological Services; 2012.
16. Nylander L, Gillberg C: **Screening for autism spectrum disorders in adult psychiatric out-patients: a preliminary report.** *Acta Psychiatr Scand* 2001, **103**:428–434.
17. Constantino JN, Gruber CP: *Social Responsiveness Scale (SRS).* Los Angeles: Western Psychological Services; 2005.
18. Constantino JN, Gruber CP, Davis S, Hayes S, Passanante N, Przybeck T: **The factor structure of autistic traits.** *J Child Psychol Psychiatry* 2004, **45**:719–726.
19. Constantino JN, Hudziak JJ, Todd RD: **Deficits in reciprocal social behavior in male twins: evidence for a genetically independent domain of psychopathology.** *J Am Acad Child Adolesc Psychiatry* 2003, **42**:458–467.
20. Bölte S, Poustka F, Constantino JN: **Assessing autistic traits: cross-cultural validation of the social responsiveness scale (SRS).** *Autism Res* 2008, **1**:354–363.
21. Fombonne E, Marcin C, Bruno R, Tinoco CM, Marquez CD: **Screening for autism in Mexico.** *Autism Res* 2012, **5**:180–189.
22. Wang J, Lee LC, Chen YS, Hsu JW: **Assessing autistic traits in a Taiwan preschool population: cross-cultural validation of the Social Responsiveness Scale (SRS).** *J Autism Dev Disord* 2012, **42**:2450–2459.
23. Reiersen AM, Constantino JN, Volk HE, Todd RD: **Autistic traits in a population-based ADHD twin sample.** *J Child Psychol Psychiatry* 2007, **48**:464–472.
24. Noriuchi M, Kikuchi Y, Yoshiura T, Kira R, Shigeto H, Hara T, Tobimatsu S, Kamio Y: **Altered whilte matter fractional anisotropy and social impairment in children with autism spectrum disorder.** *Brain Res* 2010, **1342**:141–149.
25. Duvall JA, Lu A, Cantor RM, Todd RD, Constantino JN, Geschwind DH: **A quantitative trait locus analysis of social responsiveness in multiple autism families.** *Am J Psychiatry* 2007, **164**:656–662.
26. Marrus N, Faughn C, Shuman J, Petersen S, Constantino J, Povinelli D, Pruett JR: **Initial description of a quantitative, cross-species (chimpanzee-human) social responsiveness measure.** *J Am Acad Child Adolesc Psychiatry* 2011, **50**:508–518.
27. Constantino JN, Todd RD: **Intergenerational transmission of subthreshold autistic traits in the general population.** *Biol Psychiatry* 2005, **57**:655–160.
28. Bölte S: **Brief report: the social responsiveness scale for adults (SRS-A): initial results in a German cohort.** *J Autism Dev Disord* 2012, **42**:1998–1999.
29. Kuroda M, Inada N, Yukihiro R, Uchiyama T, Hirose K, Uno U, Kamio Y: **Autism Diagnosis Observation Schedule (ADOS-G): Nihongoban zen module no shinraisei to datousei ni kansuru kenkyu. [Reliability and validity of the Japanese version of ADOS-G, module 1–4].** In *Annual Report of Research Supported by Health and Labour Sciences Research Grants.* Edited by Uchiyama T. Fukushima: Fukushima University; 2013:31–38 [in Japanese].
30. Ito H, Tani I, Yukihiro R, Adachi J, Hara K, Ogasawara M, Inoue M, Kamio Y, Nakamura K, Uchiyama T, Ichikawa H, Sugiyama T, Hagiwara T, Tsujii M: **Validation of an interview-based rating scale developed in Japan for pervasive developmental disorders.** *Res Autism Spect Dis* 2012, **6**:1265–1272.
31. Kamio Y, Yukihiro R, Adachi J, Ichikawa H, Inoue M, Uchiyama T, Kurita H, Sugiyama T, Tsujii M: **Reliability and validity of the pervasive developmental disorder (PDD)–autism society Japan rating scale (PARS): a behavior checklist for adolescent and adults with PDDs.** *Clin Psychiatr (Seishin-Igaku)* 2006, **48**:495–505 (in Japanese).

32. Kamio Y, Tsujii H, Inada N, Inokuchi E, Kuroda M, Koyama T, Uno Y, Okudera T, Ichikawa H, Takaki A: **Validation of the Japanese verion of the social responsiveness scale: comparison with PDD–autism society Japan rating scales (PARS).** *Clin Psychiatr (Seishin-Igaku)* 2009, **51**:1101–1104 (in Japanese).
33. Frazier TW, Ratliff KR, Gruber C, Zhang Y, Law PA, Constantino JN: **Confirmatory factor analytic structure and measurement invariance of quantitative autistic traits measured by the social responsiveness scale-2.** *Autism* 2014, **18**:31–44.
34. De Lacy N, King BH: **Revisiting the relationship between autism and schizophrenia: toward an integrated neurobiology.** *Annu Rev Clin Psychol* 2013, **9**:555–587.
35. Chung YS, Barch D, Strube M: **A meta-analysis of mentalizing impairment in adults with schizophrenia and autism spectrum disorder.** *Schizophr Bull* 2014, **40**:602–616.
36. Lundström S, Chang Z, Kerekes N, Gumpert CH, Råstam M, Gillberg C, Lichtenstein P, Anckarsäter H: **Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults.** *Psychol Med* 2011, **41**:2423–2433.
37. Moriwaki A, Kamio Y: **Associations between autistic traits and psychiatric issues in Japanese school children and adolescents.** *Jap J Autistic Spectrum* 2013, **10**:11–17 (in Japanese).
38. Hofvander B, Delorme R, Chaste P, Nydén A, Wentz E, Ståhlberg O, Herbrecht E, Stopin A, Anckarsäter H, Gillberg C, Råstam M, Leboyer M: **Psychiatric and psychosocial problem in adults with normal intelligence autism spectrum disorders.** *BMC Psychiatry* 2009, **9**:35. doi:10.1186/1471-244X-9-35.
39. Kanne SM, Abbacchi AM, Constantino JN: **Multi-informant ratings of psychiatric symptom severity in children with autism spectrum disorders: the importance of environmental context.** *J Autism Dev Disord* 2009, **396**:856–864.
40. Ingersoll B, Hopwood CJ, Wainer A, Brent Donnellan M: **A comparison of three self-report measures of the broader autism phenotype in a non-clinical sample.** *J Autism Dev Disord* 2011, **41**:1646–1657.

doi:10.1186/s12888-014-0302-z
Cite this article as: Takei *et al.*: Verification of the utility of the social responsiveness scale for adults in non-clinical and clinical adult populations in Japan. *BMC Psychiatry* 2014 **14**:302.

臨床精神医学 44 (1)：37－43，2015

特集

今日の自閉スペクトラム症，子どもから大人まで

Autism spectrum disorder today, from chilhood to adulthood

自閉スペクトラム症と精神科的併存症

石飛　信* 荻野　和雄* 高橋　秀俊*
原口　英之* 神尾　陽子*

Key Words：自閉スペクトラム症(autism spectrum disorder：ASD)，精神科的併存症(psychiatric comorbidity)

抄録：自閉症スペクトラム障害(Autism Spectrum Disorder，以下ASD)では，多彩な精神科的併存症が認められ，主要徴候とも密接に関与しながら多彩な臨床像を形成する。したがって，ASDを有する児・成人の支援を考えるうえで，あらゆる発達段階において併存症を含めた包括的視点からの状態像把握が重要となる。本稿では，ASDにみられるさまざまな精神科的併存症について概説し，その評価・治療上の問題点についても考察を加える。

はじめに

自閉スペクトラム症/自閉症スペクトラム障害(Autism Spectrum Disorder，以下ASD)は，DSM-5では，A)複数の状況下における社会的コミュニケーションおよび対人的相互反応の持続的な欠陥，B)行動・興味・活動の限局された反復的・常同的な様式の2つの主要徴候が幼少期早期に出現する発達障害と定義され[2]，従来の自閉症，アスペルガー障害，特定不能の広汎性発達障害などの下位診断群を包含する概念である。ASDを有する児童および成人では，約70％の症例で1つ以上の精神科的または身体的併存症(comorbidity)が認められる[13]。これらの併存症の特性や重症度は，成長発達や本人を取り巻く状況(発達障害特性を考慮した支援体制の有無など)によって変化し，各ASD個人のQOLを大きく左右する因子となる。また，これらの併存症は，個人差はあるものの主要徴候と複合的に関与しながら多彩な臨床像を形成するため，各年代において主要徴候のみならず併存症も的確に把握し，包括的視点から状態像の把握を行うことが，ASDを有する児・成人の支援を考えるうえで重要である。

本稿では，ASDにみられるさまざまな精神科的併存症について概説し，その評価・治療上の問題点についても考察を加える。

ASDにみられる精神科的併存症

ASDにみられる精神科的併存症は，注意欠如多動性障害・強迫性障害・睡眠障害・チック・気分障害(うつ病，双極性障害)・パニック・癇

Psychiatric comorbidity associated with ASD

* *ISHITOBI Makoto, OGINO Kazuo, TAKAHASHI Hidetoshi, HARAGUCHI Hideyuki and KAMIO Yoko*　独立行政法人国立精神・神経医療研究センター精神保健研究所児童・思春期精神保健研究部〔〒187-8553 東京都小平市小川東町4-1-1〕

癇・自傷行為・被害関係妄想・フラッシュバック体験(タイムスリップ現象)・カタトニア・不安障害(限局性恐怖症，全般性不安障害，社会不安障害)など非常に多岐にわたる[13]。これらの精神科的併存症には，ASDでの高い合併率が報告されている精神疾患のほか，主要徴候を背景に，発達障害特性を意識した支援が行き届かないことで二次的に出現するものまでさまざまである。以下，代表的な併存症について解説する。

1. 注意欠如多動性障害

注意欠如多動性障害(Attention-Deficit/Hyperactivity Disorder：以下AD/HD)は，従来のDSM-Ⅳ-TR[3]によると，7歳以前に始まる「不注意」と「多動・衝動性」を特徴とする発達障害と定義されていた。DSM-Ⅳ-TRでは，ASDとAD/HDは，基本的に異なる疾患概念とされ，診断の併記も認められていなかったが，実臨床場面においては，ASDにAD/HD症状を伴う頻度は決して低いとはいえず，Leyferら[14]のASDにおける精神科的併存症を調査した研究によると，クリニック通院中の109名のASD児(5～17歳：平均9.2±2.7歳)において，その72％がなんらかの併存症を有し，併存症の内訳としてAD/HDが30.6％であった。また，遂行機能の観点から両障害を比較した研究[24]により，ASD，AD/HDに共通して認められた注意の維持やWorking Memoryの障害の存在から，共通した病態が指摘されている。このような実状をふまえ，DSM-5では「ASDとAD/HDの診断併記」が認められるようになり，ASDとAD/HDの併存が疑われる症例の的確なアセスメントが，今後いっそう重要になる。野村[20]は，両障害が類似した症状を呈しうることや相互的に関与し合う可能性を意識したうえで，幼少期から現在に至るまでの生活歴や行動特性の詳細な評価を行い，AD/HD症状出現のetiologyを可能な限り明確にすることがテーラーメイドな治療方針の決定に不可欠であるとしている。たとえば，AD/HDが疑われて来院した症例において，そのASD特性がこれまで周囲から十分に理解されずに，本人への接し方や生活設定が不適切であることが，AD/HD症状出現の主要因となっている場合，まずは対応の構造化を図るなどのASD特性に応じた対応法を試みる必要がある。また，詳細は他稿に譲るが，両障害の併存が疑われる症例に対するAD/HD治療薬を用いた薬物治療も重要な治療選択肢の1つであり，併存例に対する薬物治療ストラテジーの確立が今後の重要課題である。

2. 精神病症状

ASDでは，被害関係妄想や幻覚体験などの精神病症状の併存が時にみられることが知られている。Hofvanderら[10]は，知的障害を有さないASD成人122名(16～60歳；中央値29歳)における精神科的併存症の調査研究を行い，12％に精神病性障害を認めたと報告している。ASDにおける精神病症状併存の要因として，いじめや環境への不適応を契機として状況依存的に被害的な認知に傾いてしまうことや，ASD特有の固執性の言動や反響言語が統合失調症に特徴的な徴候(対話性幻聴，独語)と誤って判断されることなどが考えられている。一方で，近年，ASDと統合失調症の間には共通した遺伝的背景の存在も示唆されており[6]，両者は相互排他的ではなく，実際に合併例もみられる。上記のように，ASDにみられる精神病症状のetiologyは多様であるため，その介入法に関するエビデンスは乏しい。ASDにおいて精神病症状を認めた場合，発達歴・臨床経過・精神病症状の色彩を総合的に判断し，ASD特性を考慮しながら十分な横断的・縦断的評価を行いながら，環境調整や薬物治療の効果を注意深く観察していくことが重要である[21]。

3. 不安障害

児童・青年期のASDでは，その11～84％において不安症状が合併すると報告されており，全般性不安障害・社交不安障害・限局性恐怖症などさまざまなタイプの不安障害の合併が報告されている[26]。前述したHofvanderら[10]は，ASD成人患者122名の中で，不安障害の有病率は50％と，気分障害(53％)に次いで高いと報告した。その内訳は全般性不安障害18例(15％)，社交恐怖16例(13％)，パニック障害13例(11％)，限局性恐怖症7例(6％)，その他の不安障害が3例であった。不安障害の併存は，臨床サンプルにおいて高率に認められるだけでなく，地域ベースの疫学調査においても高率であるとの報告がなされている。Simonoffら[22]は，地域の一般集団56,946人から抽出した112名のASD児(10～14歳；平均12歳)に対し，併存症の有無を包括的に評価し，約70％のケースで1つ以上の精神科的併存症を有し，内訳として，社交不安障害(29.2％)が最多であったとしている。以上のように，ASDを有する児・成人双方において不安障害は高率に合併し，その出現形態は，年齢・認知機能・ASDの主要徴候の程度による影響を受ける可能性が示唆されている[26]。ASDにおける不安症状は，日常生活スキルの低下や他者との関係性構築に支障をきたし，抑うつやひきこもりの要因となりうるため[7]，ASDを有する児・成人の状態像を把握するにあたり，不安症状の評価を意識的に行う必要がある。一方，ASDの不安症状は他覚的に把握しにくく，質問紙でもスクリーニングしにくいとする報告もあり[9]，早期発見に関する課題が残る。治療については，近年Vasaら[25]によって行われた「ASDを有する若年者の不安に対する治療」に関するsystematic reviewによると，薬物療法としてはcitalopramとbuspironeの有効性が示されているものの，いずれもopen label trialでありエビデンスレベルは十分とはいえない。非薬物治療として，これまで認知行動療法を用いた9つの臨床研究が報告されており(うち8つがRCT)，高機能ASDの71.4％で有効であったとされている。2013年8月にNational Institute for Health and Care Excellence (NICE)より出版された最新のNICE clinical guideline ('Autism : the management and support of children and young people on the autism spectrum')[12]においても，不安症状に対して認知行動療法が推奨されている。

4. 気分障害

ASDに併存する気分障害の有病率に関しては，主に気分症状の言明が可能な高機能群を対象にした研究がいくつか報告されている。Ghaziuddinら[8]は，8～51歳(平均15歳)のアスペルガー障害の児童および成人35人に半構造化面接を行い，うち13名(37％)がうつ病を併存し，年齢が高いほどその合併率が高いことを報告している。また，並木ら[19]の行った高機能ASD 386名(平均年齢11.1±7.6歳)を対象にした気分障害の併存に関する横断調査によると，41名に気分障害(気分変調障害17名，大うつ病性障害24名)の併存が認められ，年齢が上がるほどその有病率が高かった。年齢が上がるにつれてうつ病性障害の有病率が高くなる要因の1つとして，山下[29]は，高機能ASDにおけるうつ病発症に関する心理社会的側面について言及し，ASDの認知行動特性を背景にした否定的体験の蓄積から社会生活上での困難さの気づきが増し，自己評価の低下や混乱を引き起こすことがうつ病発症の準備状況となりうると考察している。Munesueら[18]は，精神科外来受診中の青年期の高機能ASD 44名において，12名に双極性障害，4名に大うつ病性障害の併存を報告し，青年期ASDの状態像評価において，双極性障害を念頭に置くことの重要性を指摘している。次に，ASDにおける気分障害の臨床像と診断上の問題点について触れる。ASDを有する人では，たとえ高い言語的知能を有していても，自身の感情を認識し，悲哀感などのうつ病の中核症状を自発的に言語化することが困難なことは多い。また言語以外の表情や態度を介した感情表出も乏しいことが多いため，周囲からその変化が見逃される可能性もある。さらに，抑うつ症状が，常同行為の増加といった"(ASDの)主要徴候の増悪"に見える症状として出現する場合や，イライラ・自傷行為・攻撃性の増悪・catatonia(詳細は後述)というかたちで表出す

る場合もある。つまり，ASDを有する人では，気分障害の症状がASD症状にマスクされて他覚的に認識されにくいうえに，その症状の現れ方が，非定型的で，個々人によって独特なため，過小診断となる可能性がある。上記を念頭に，ASDの気分障害を評価する際は，「普段の行動特性との相違」をより意識することが重要となる[29]。すなわち，睡眠や食欲(食事量や体重)，排泄状況などの生理的側面の変化に加え，活動性の低下や動作の緩慢化の有無，こだわり行動や身辺自立行動の変化といった客観的事実に基づき状態像の把握に努める。これは，気分障害に限らずASDを有する人の状態像を把握するために重要な視点であり，特に知的障害を伴うASDにおける気分障害の存在を推測するために重要となる[1]。ASDの気分障害への介入については，まず心理社会的介入として，ASDの認知行動特性とその特性ゆえに生じやすいライフイベントや社会状況での困難さを，医療者を含めた周囲の人間が理解することが治療導入に不可欠である。そのうえで，他の併存症(不安障害など)の有無を含めた状態像を総合的に判断し，薬物治療の適応などを検討することになる。薬物治療に関しては，ASDに併存した気分障害に特化したガイドラインは存在しないため，通常のガイドラインに従い標的症状に対する薬剤選択を行うこととなる。基本的に少量より投与を開始し，ASDにおける双極性障害の高い合併率も念頭に置きながら，易怒性や衝動性の増悪の有無や他の併存症の変化も含めた慎重なモニタリングを心がけ，効果判定を行う必要がある。

5. 強迫性障害

強迫性障害における強迫症状と，ASDにおけるこだわりや常同行動との異同に関しては以前より議論されてきた。ASDの強迫関連行動は，"自我親和的"であるとみなされてきたが，近年，高機能ASDを有する人の中に，自我異和的な強迫症状を呈し自ら医療機関を受診するものが存在することも明らかになりつつある。Bejerotは，難治例の強迫性障害を呈する者の一部にASD特性を有する一群が存在することを受け，強迫性障害の下位分類として"autistic dimension"を提案し，発達障害の観点から強迫性障害の症例の状態像を検討することの重要性を提唱している[4]。ASDをベースに持つ強迫性障害の臨床上の特徴について，山下[30]は，"hoarding(溜め込み)"の存在を指摘している。介入に関しては，認知行動療法と抗うつ薬や非定型抗精神病薬を用いた薬物療法に関する報告が多数あり，これらの介入法の有効性が示唆されている一方で，介入の効果は限局的であるとする報告もある。ASDの強迫関連行動は，個々人の認知行動特性により多種多様であり，治療法の選択は個々の症例ごとに全体像を把握したうえでの検討が必要である。

6. 睡眠障害

睡眠障害は，ASDにおいて40～80％とほかの発達障害に比しても高率にみられ，主として入眠困難や睡眠維持の困難が報告されている[11]。睡眠障害は，常同行為の増加や社会的スキルの低下，イライラ・衝動性の増悪をもたらし，一見したところASD症状やAD/HD症状の増悪と捉えられる状態を引き起こすことがある[11]。このようなケースでは，衝動性の軽減などを目的に，非定型抗精神病薬やAD/HD治療薬が投薬されている例があるが，こうした対応は症状の改善がみられないばかりか，日中の眠気をもたらすなど睡眠の質のさらなる低下を招き，さらに状態像が悪化することがあるので注意を要する。したがって，ASDの状態像評価にあたり，日頃の睡眠状況を養育者から積極的に聴取し，睡眠障害が日中の行動になんらかの悪影響を及ぼしている可能性について注意深く検討する必要がある[12]。さらに，ASDを有する人に睡眠障害を認めた場合，これまでに述べたような精神科的併存症との関連性がないかについても検討を加える必要がある[12]。ASDを有する人およびその家族の包括的支援を目的に米国で設立されたAutism Treatment Network（ATN）では，睡眠状況の評価法やsleep kitを用いた睡眠衛生への介入法などの情報を公開し，ASDの睡眠障害に関する指針を示しているので参照されたい[15]。また，薬物治療に関しては，ASDの睡眠障害の病態としてメラトニンに関連した異常が数多く報告されていることを受け，欧米を中心にメラトニンの有効性を示すRCTが多数報告されている[11]。

7. 自傷行為・癇癪・パニック

特に知的障害を有するASDを有する人において，時に著しい興奮やパニック，自傷行為がみられることがある。その要因は，同一性保持や感覚過敏を背景に，急な予定や状況の変化，本人の苦手とする感覚刺激などが誘因となる場合や合併する精神疾患の症状の一部として出現する場合などさまざまである[16]。誘因となる状況がはっきりしている場合は，それらの誘因を極力除くことが望ましいが，実際には周囲の人間にその誘因が十分に理解できない場合もあり，環境調整や行動介入だけでは対処困難な例も多い。そのため，非定型抗精神病薬を中心とした薬物治療もあわせて行われることも多い(薬物治療の詳細については他稿参照)。気分障害の項でも述べたように，標的症状以外からも多角的な評価を心掛け，興奮・パニック・自傷行為の背景にあるetiologyを極力明確にする姿勢が重要である。

8. カタトニア(Catatonia, catatonia-like deterioration)

ASDを有する人の主に思春期青年期において，動作が緩慢になり時に止まってしまう・繰り返し行動が増えて動作が先に進まない・他者からの促しなしには次の行動に移れないなどの現象が時にみられる。Wingら[28]は，これらの症状がカタトニア(catatonia)とみなせるとし，ASDとcatatoniaの間の行動特性上の類似点から両者に共通する病態の存在を指摘した。さらに，ASDのcatatoniaの基本症状として，ⅰ)運動と言葉の緩慢化，ⅱ)活動を開始したり，完遂することの困難さ，ⅲ)他者による身体的あるいは言語的な促しに依存することの増加，ⅳ)受動性の増加と自発性低下の4項目を提唱した。また，catatoniaにしばしば伴う症状として，昼夜逆転，反復的儀式行動の増加，パーキンソン様症状，興奮，不安焦燥があるとしている[28]。ASDにみられるcatatoniaの特性として，高岡ら[23]は，典型的な昏迷へ至ることが少ないこと，身体的ないし言語的促しにより軽減すること，興奮が伴うことはあるが基本症状ではない点などをあげている。近年，Wingら[27]も，ASDにみられるcatatoniaが典型的症状を備えていない場合もあるとの理由から，catatonia-like deteriorationという表現を提唱している。Wingらによる有病率と発症年齢に関する報告によると，ASD診断を受けた初診患者506名のうち，30名(6％)がcatatoniaの診断基準を満たし，内訳として1～14歳(0/332：0％)，15～19歳(12/65：17％)，20～24歳(8/48：17％)，25～29歳(3/19：16　％)，30～34歳(5/20：25％)，35歳以上(2/23：9％)であり，思春期青年期に多いことが示されている[28]。発症時期については，9歳以下での発症はなく，10～19歳での発症が23名(76％)であり，10代で初発するケースが多い。また，catatoniaの診断基準を満たした30名の知的レベルはさまざまであり，過去の症例報告からもcatatoniaは知的レベルに関係なく生じることが示唆されている[5]。Catatonia出現の背景因子は，なんらかの外的要因(ストレス，急激な生活状況の変化など)による限局的反復行動の増悪や気分障害をはじめとする併存精神疾患の合併によるなどさまざまである[28]。Wingは，catatoniaの状態にある本人のつらさに共感を示し，家族の理解を促すとともに，活動しやすい環境作りや適切な言動面での促しを行うなどの心理社会的介入の重要性をあげている。また，症例数は少ないものの，高用量のロラゼパムや電気けいれん療法の有効性に関するエビデンスが蓄積しつつあり，特に重症例への治療手段として注目されつつある[5]。