

STUDY PROTOCOL

Open Access



Protocol for the development and testing of the schiZotypy Autism Questionnaire (ZAQ) in adults: a new screening tool to discriminate autism spectrum disorder from schizotypal disorder

Rizwan Parvaiz^{1*} , Erik Vindbjerg², Bernard Crespi³, Francesca Happe⁴, Rik Schallbroeck⁵, Zainab Al-Sayegh¹, Ida-Marie Danielsen¹, Bruce Tonge⁶, Poul Videbech⁷ and Ahmad Abu-Akel⁸

Abstract

Background Autism spectrum disorder (ASD) and schizotypal disorder (SD) both have a heterogenous presentation, with significant overlaps in symptoms and behaviour. Due to elevated recognition and knowledge of ASD worldwide, there is a growing rate of referrals from primary health professionals to specialised units. At all levels of assessment, the differential diagnostic considerations between ASD and SD exert major challenges for clinicians. Although several validated screening questionnaires exist for ASD and SD, none have differential diagnostic properties. Accordingly, in this study, we aim to develop a new screening questionnaire, the schiZotypy Autism Questionnaire (ZAQ), which provides a combined screening for both conditions, while also indicating the relative likelihood of each.

Methods We aim to test 200 autistic patients and 100 schizotypy patients recruited from specialised psychiatric clinics and 200 controls from the general population (Phase 1). The results from ZAQ will be compared to the clinical diagnoses from interdisciplinary teams at specialised psychiatric clinics. After this initial testing phase, the ZAQ will be validated in an independent sample (Phase 2).

Conclusions The aim of the study is to investigate the discriminative properties (ASD vs. SD), diagnostic accuracy, and validity of the schiZotypy Autism Questionnaire (ZAQ).

Funding Funding was provided by Psychiatric Centre Glostrup, Copenhagen Denmark, Sofiefonden (Grant number: FID4107425), Trygfonden (Grant number:153588), Takeda Pharma.

Trial registration Clinical Trials, NCT05213286, Registered 28 January 2022, clinicaltrials.gov/ct2/show/NCT05213286?cond=RAADS&draw=2&rank=1.

Keywords Autism Spectrum Disorder (we prefer Autism Spectrum Condition), Schizotypal Disorder, Questionnaire, Diagnostics

*Correspondence:

Rizwan Parvaiz

rizwan.parvaiz@regionh.dk

Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Background

The psychiatric burden in people with Autism Spectrum Disorder (ASD) [1] is considerably higher compared to neurotypical individuals, with 70% experiencing at least one co-occurring psychiatric disorder and 40% exhibiting two or more psychiatric disorders [2]. In a clinical setting and at all levels of assessment, one of the most difficult differential diagnostic challenges is schizotypal disorder (SD), which shares considerable features with ASD both at the symptomatic level and in the diagnostic criteria (see Fig. 1). Thus, discriminating ASD from SD in a clinical setting is a time-consuming task and demands a high level of expertise of both disorders. An audit of 319 patient cases at our clinic (specialized unit for the assessment of ASD) from January-June 2019 showed that about 37% of the adults referred to our clinic for the assessment

of ASD, did not meet diagnostic criteria. Of these, almost 40% were diagnosed on the schizophrenia spectrum (predominantly SD). To improve diagnostic accuracy, it is therefore not only pertinent but also necessary to investigate discriminating features between ASD and SD and to develop tools to aid clinicians in the assessment.

Autism spectrum disorder

ASD and SD historically and practically have been grounded in two different scientific traditions, which has had a significant impact on the way clinicians assess patients and how the diagnostic criteria have developed (see Fig. 2).

ASD has its roots in the relatively young field of child and adolescent psychiatry, whereas SD comes out of a more than 100-year-old tradition and is primarily based on clinical presentations in adults. Consequently, professionals involved in assessment of ASD and SD often come from different backgrounds and make use of different diagnostic methods. The prevalence estimates of ASD display a high variability across nations worldwide. In most western countries the prevalence is estimated to be 1–2% [3]. Danish data suggest a prevalence of 1.65% or approximately 95,000 persons in Denmark [4]. The case identification and assessment of ASD is challenged by a high rate of comorbidity with depression (50%), anxiety (40%) and ADHD/ADD (40–60%) [5, 6]. The prevalence of comorbidity with SD has to our knowledge not been established. Nevertheless, some indications of the relation between ASD and SD can be estimated by looking at studies comparing ASD with psychosis or schizophrenia spectrum disorders (SSD). Sub-clinical psychotic symptoms occur frequently in ASD patients [7–9], and the prevalence of SSD in adults with ASD are in the range of 4–12% [5].

To aid in case identification of ASD, several screening questionnaires have been developed, including the

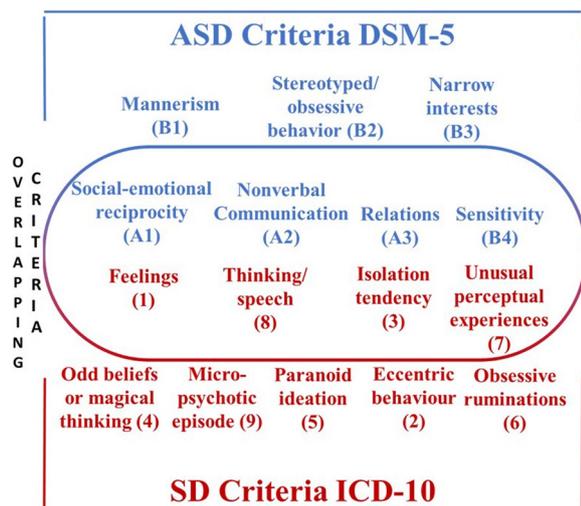


Fig. 1 Diagnostic criteria for Autism Spectrum Disorder (ASD) and Schizotypal Disorder (SD). The encircled criteria mark the highest degree of clinical overlap

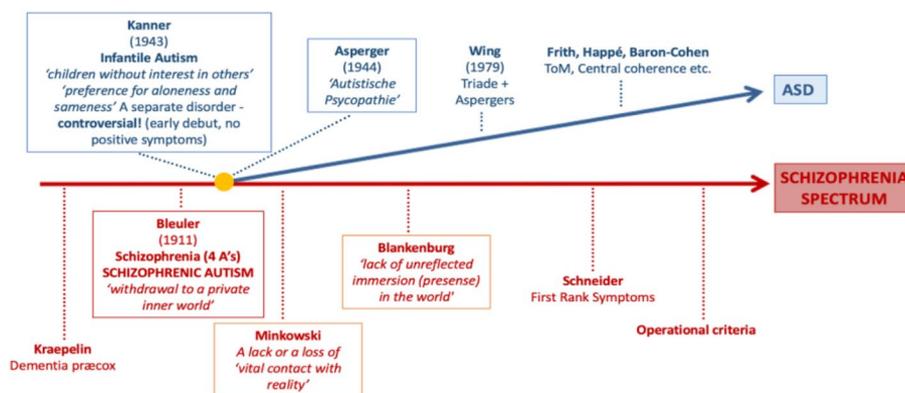


Fig. 2 Development of concepts and criteria (figure provided by Maria Nilsson)

Autism Spectrum Quotient (AQ) [10], the Ritvo Adult Asperger Diagnostic Scale Revised (RAADS-R) [11], and the Social Responsiveness Scale (SRS) [12]. Importantly, however, several studies indicate that such questionnaires do not differentiate well between autistic individuals and individuals with SSD [13, 14].

Schizotypal disorder

SD is also a heterogeneous disorder with an estimated prevalence of 4.6% and a high rate of comorbidity [15, 16]. The diagnosis can be made if at least 4 out of 9 ICD-10 criteria are met (see Fig. 1). Although debated [17], SD is considered a crucial construct in the development of SSD [18]. Thus, early diagnosis is important for prognosis, as 25–48% of SD patients are prodromal and go on to develop SSD [17, 19]. The prevalence of comorbidity between ASD and SD, which is the main focus of this study, has to our knowledge not been described in any detail. However, the prevalence of ASD in individuals with SSD seems to be substantially increased relative to the general population, although estimates vary widely [20].

Several psychometrically robust questionnaires are available to assess features of and screen for SD. In adult populations these notably include the Schizotypal Personality Questionnaire Brief Revised (SPQ-BR) [21], the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) [22], the Multidimensional Schizotypy Scale (MSS) [23], the Cardiff Anomalous Perception Scale (CAPS) [24], and the Community Assessment of Psychic Experience (CAPE) [25]. In children, these notably include the Melbourne Assessment of Schizotypy in Kids (MASK) [26] and the Schizotypy Personality Questionnaire in Children (SPQ-C) [27], (see Table 2). To our knowledge, none of these have significant psychometric power to discriminate SD from ASD.

Given significant difficulties in discriminating between ASD and SD and the serious consequences that case misclassification can have for treatment and prognosis, we have sought to develop the schizotypy Autism Questionnaire (ZAQ) to aid clinicians in the assessment of and discrimination between ASD and SD in adults at the case identification stage. A pilot version of this novel screening questionnaire ZAQ, containing 130 questions, has been developed at the Mental Health Centre, Capital Region of Copenhagen. This will be tested in 300 psychiatric patients and 200 healthy controls from May 2022 – April 2023, which constitutes Phase 1 of this study. Psychometric data analysis from this study will constitute the empirical foundation for the development of the final version of ZAQ. This final version, which pending statistical recommendations is expected to contain

approximately 60 questions, will undergo subsequent validation in an independent sample (Phase 2).

Methods

Description of the creation of ZAQ

To construct the ZAQ, we first performed an exhaustive literature search to identify potential discriminating features between ASD and SD. Complementing the literature search, we interviewed three experienced clinicians who identified discriminating factors based on their clinical knowledge. Altogether, we identified 38 features which appeared to differentiate ASD and SD. These features constituted 11 subscales, subsumed under 6 subdomains (see Table 1). Identification of potentially discriminating features has been the primary focus. Once identified these features were grouped together into well-defined subscales. To present an overview, these subscales are grouped together in subdomains, highlighting the areas showing potential for discrimination [28, 29].

Secondly, the research group identified several psychometrically-validated assessment and screening questionnaires for schizotypy and ASD (see Table 2). From this list of questionnaires, questions were extracted based on their clinical face validity, factor loadings from the validity studies of these questionnaires, and reliability scores (e.g., test–retest reliability). This process yielded approximately 950 questions (version 1 ZAQ).

In a first round of evaluation of their face-validity, these 950 questions were presented to six experienced clinicians—each with extensive (+ 5 years) clinical knowledge in either ASD or SD and who were not associated with the research group. These clinicians assessed how their patients would answer these 950 questions. Importantly, questionnaires measuring schizotypy were assessed by clinicians with ASD experience and vice versa. This evaluation retained 195 questions (version 2 ZAQ). All items of the version 2 ZAQ then underwent a second round of evaluation by 5 autistic patients and 2 schizotypy patients. Of these 195 questions, judged on the basis of their unambiguity and clarity, the final 130 questions entering Phase 1 of the study were selected. The resulting subscales ranged from 5–19 items.

Recruitment and testing

We have designed a multicenter, prospective, non-randomized experimental study, where adult patients will be recruited from May 2022 – April 2023. A group of 300 patients will be recruited from 2 outpatient clinics located at Mental Health Centre Copenhagen: 200 patients (see power calculation) will be recruited from the pool referred to the specialised clinic for diagnostic assessment of ASD at Mental Health Centre Copenhagen, and 100 patients will be recruited from

Table 1 Summary of the domains, subdomain and subscales serving as the theoretical framework for ZAQ^a

Main ZAQ-domains	Subdomain	Subset of items on which responses between individuals with ASD or SD might differ	Subscales	Number of questions
Diagnostic criteria	Autism	Stereotyped behavior, narrow interests, hyper-hyposensitivity to sensory stimuli	1. Stereotyped behavior	14 questions
			2. Hypersensitivity + Narrow interest	11 questions
	Schizotypy	Self-disorders, hyper-reflexivity, magical ideation, positive schizotypy	3. Self-disorders	17 questions
			4. Magical ideation + positive schizotypy	13 questions
			5. Disorganised schizotypy	5 questions
			6. Negative schizotypy	10 questions
Clinical features	Clinical trajectories	Time of onset of symptoms, childhood symptoms	7. Clinical trajectories and symptoms	19 questions
Psychological theory	Theory of Mind (ToM)	Inference of intentions of others, ToM performance, self-referential hypermentalisation, facial emotion perception	8. Theory of Mind	13 questions
	Local vs. global processing	Local vs. global processing, imagination and creativity, reading abilities, word interpretation, savant feature, apophenia	9. Local vs. global processing	8 questions
Cognitive features	Attention, memory	Selectivity of attention, selective memory/false memory, working memory performance	10. Cognition	12 questions
			11. Higher Cognitive Functions	9 questions

^a Note: For a comprehensive account, see also references [28, 29]

the specialised psychosis clinic at Mental Health Centre with an SD diagnosis. Additionally, a group of 200 adults from the general population without a psychiatric diagnosis will be recruited as a control group. Inclusion and exclusion criteria are detailed in Table 3. The data will be collected on-line and managed through a secure server with full compliance with Personal Data Handling laws of Denmark.

In all three outpatient clinics, the diagnostic assessment will be carried out as usual and will follow gold standard guidelines in their respective fields. The diagnostic assessment of ASD will be performed by clinicians who are not involved in the study. Using DSM 5, the assessment will be based on clinical interviews (minimum 4 h, including childhood history and differential diagnostic assessment) and supplemented by a semi-structured interview (Adult Asperger Assessment, AAA). Video recordings from AAA assessment and the clinical assessment will be presented at a multidisciplinary meeting, with at least 2 experienced clinicians, who will finalize the diagnostic conclusion. A schematic showing the flow of patients is depicted in Fig. 3. The result from this initial phase of the study will undergo psychometric analysis and items displaying

adequate validity and discriminating power will be selected for the final ZAQ questionnaire (Phase 2).

Considerations related to the statistical analysis

Statistical models and analyses

Factorial evaluation First, the dimensionality of the ZAQ will be evaluated with confirmatory factor analysis (CFA). If modification indices suggest a better fit from altered subscales, e.g., by relocating individual items to other subscales, these hypotheses will be included in the subsequent unidimensional tests.

Unidimensional construct evaluation Responses to the proposed subscales of the ZAQ will each be analysed with a unidimensional item response theory (IRT) model. The 1-parameter logistic Rasch model represents the gold standard of construct validation and offers stronger inferences than less restricted models. If applicable, violations of the assumption of local dependence and no differential item functioning (DIF) may be accommodated by the extended graphical log-linear Rasch model [49]. If the assumption of *tau* equivalence is violated and this cannot be solved — e.g., by excluding a minimal number of

Table 2 Scales and questionnaires used in the development of the schizotypy Autism Questionnaire (ZAQ)

Scales and Questionnaires					
Scales/Questionnaires	References for validation	Scales/questionnaires	References for validation	Scales/questionnaires	References for validation
Schizotypy					
SPQ Schizotypal Personality Questionnaire	Raine 1991 [30]	Theory of Mind TH.O.M.A.S Theory of Mind Assessment Scale	Bosco et al. 2009 [31]	Autism Spectrum Disorder (ASD) RAADS-R Ritvo Autism Asperger Diagnostic Scale- Revised	Ritvo et al. 2011 [11]
O-LIFE Oxford-Liverpool Inventory of Feelings and Experiences	Mason et al. 2005 [22]	Self-Referential Hinting Task	Wastler & Lenzenweger 2019 [33]	SRS Social Responsiveness Scale	Constantino et al. 2003 [12]
MSS Multidimensional Schizotypy Scale	Kwapil et al. 2018 [23]	Strange Stories	Happé 1994 [35]	AQ Autism Spectrum Quotient	Baron-Cohen et al. 2001 [10]
CAPE Community Assessment of Psychic Experience	Konings et al. 2006 [25]	TAS-20 Toronto Alexithymia Scale	Bagby et al. 1994 [37]	EQ Empathy Quotient	Baron-Cohen & Wheelwright 2004 [38]
PAGE-R	Fach et al. 2013 [40]	ADI-r Autism Diagnostic Interview-Revised	Lord et al. 1994 [41]	RBS Repetitive Behaviour Scale	Lam et al. Aman 2007 [42]
MASK Melbourne Assessment of Schizotypy in Kids	Jones et al. 2015 [26]	Self-disorders		SPQ Sensory perception quotient	Tavassoli et al. 2014 [44]
CAPS Cardiff Anomalous Perception Scale	Bell et al. 2006 [24]	EASE (Semi Structured) Examination of Anomalous Self-Experience	Parnas et al. 2005 [46]		
		SQUEASE6 Short Questionnaire 6 of EASE	Møller 2018 [47]		
		IPASE Inventory of Psychotic-Like Anomalous Self-Experiences	Cicero et al. 2019 [48]		
				WMS Working Memory Scale	Vallat-Azouvi 2012 [32]
				DFlex Detail and Flexibility	Roberts et al. 2011 [34]
				DOSPERT Domain Specific Risk Taking	Blais and Weber 2006 [36]
				CRT Cognitive reflection task	Frederick 2005 [39]
				CAQ Creative assessment questionnaire	Carson et al. 2005 [43]
				ARHQ Adult Reading History Questionnaire	Lefly and Pennington 2000 [45]

Table 3 Inclusion and exclusion criteria

Inclusion Criteria: Patients 18–65 years (ASD and non-ASD psychiatric)	Exclusion Criteria: Patients (ASD and non-ASD psychiatric)
WAIS-IV or Raven IQ > 85, no-clinical suspicion of intellectual disability and minimum 11 years of education	Insufficient Danish language skills
Completion of: <ul style="list-style-type: none"> - Clinical Assessment - Adult Asperger Assessment (AAA) - Psychopathology evaluation using DSM-5 - A conclusion based on multidisciplinary consensus 	Acute psychiatric illness prompting departure/dismissal from the diagnostic assessment
Controls: Are matched with age, gender, marital status, number of children, and educational level	Controls: Concurrent or prior psychiatric diagnosis (self-report)

under-discrimination items — a more flexible 2-parameter logistic model may be adapted.

Deriving a general factor The results of the unidimensional results will be used to select an appropriate multidimensional model in which all subscales reflect a general ZAQ trait. If no indications of DIF were found, a higher-order CFA model will be used, specified in line with the validated unidimensional model (e.g., item interaction terms and/or loading restrictions if applicable). Otherwise, a multidimensional IRT model will be used, ensuring an unbiased trait estimation across subgroups.

Concurrent validity and screening accuracy The latent ZAQ estimate will be evaluated against the diagnostic outcome using logistic regression and a receiver operating characteristic (ROC) curve. The predictive power is evaluated by the area under the curve (AUC) and the sensitivity and specificity at their equilibrium, reflecting equal importance of correct identification in both groups. To promote the generalisability of the results, K-fold cross-validation will be used to dynamically divide the sample into training and testing subsamples.

Post-hoc analysis A post-hoc analysis driven by the diagnostic data can increase model performance, while also posing a risk of overfitting the model to the data and thereby reducing the generalizability of the results. To counteract the latter, only modifications considered clinically meaningful by the clinical experts of the research group will be incorporated, and results will either serve purely as hypotheses or will be stabilised with bootstrap aggregation.

In Phase 1, the diagnostic discrimination of each item is evaluated with logistic regression on the diagnostic outcome. Where clinically meaningful, the model will be modified to promote the influence of highly predictive items while also retaining parsimony. The resulting model will serve as a hypothesis in Phase 2.

For the Phase 2 post-hoc analysis, the suitable procedure will depend on the consistency of the ZAQ across Phase 1 and 2. If the ZAQ was mainly shortened, with limited modifications to the items carried over to Phase 2, it will allow for a supervised machine learning based-model on a combined Phase 1 and Phase 2 sample. This analysis will use a random forest algorithm and overfitting will be controlled by bootstrap aggregation and by splitting the sample into training and validation sets. Otherwise, the post-hoc analysis procedure of Phase 1 will be repeated, to inform hypotheses for future studies.

Power calculation

Acceptable diagnostic prediction by the ZAQ would manifest as an $AUC \geq 0.7$ in the ROC analysis [50]. Establishing this with confidence relies on the variance of the ZAQ trait estimate, which can only be estimated at Phase 1 completion. For the factor analysis, no formal consensus exists for the minimum sample size [51]. While a minimum of $n = 200$ is a popular rule of thumb, Kline [52] suggests an ideal sample-to-item ratio of 20:1 in CFA. This corresponds to $n \leq 360$ for the separate subscales (≤ 18 items) and 2600 at the aggregate level (130 items). Assuming the ZAQ is abbreviated to 60 items for Phase 2 and taking into account the stabilising effect of pilot testing, we may reasonably consider a combined clinical and non-clinical sample of 500 to provide a ratio of 8:1. This ensures reasonable factorial stability at the aggregate level while offering excellent statistical power at the subscale level.

Ethical considerations

The study will be conducted in accordance with the Helsinki Declaration 1964, including subsequent revisions. Participants will only be included after signing an informed consent based on oral and written information. The participants may, at any time, choose to withdraw from the study without being required to explain and without affecting the person's future treatment. The study is approved by the Ethical Committee of the Capital

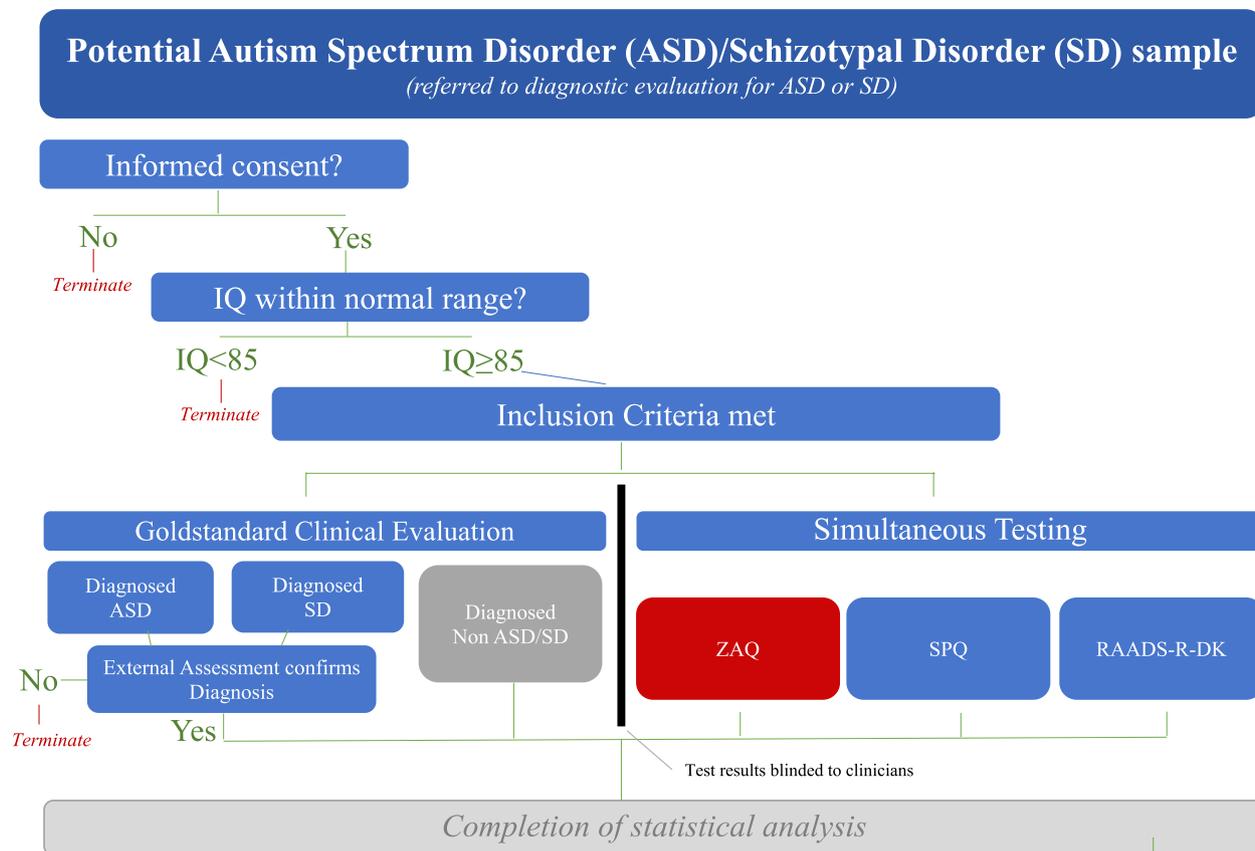


Fig. 3 Flow diagram Phase 1 of the ZAQ-study. Patients will undergo clinical evaluation and be divided into 3 groups: Patients with an ASD (Autism Spectrum Disorder) diagnosis, SD (schizotypal Disorder) diagnosis, neither ASD nor SD diagnosis. In parallel and independent from the clinical evaluation, participants will be assessed with the ZAQ schiZotypy Autism Questionnaire), RAADS-R-DK (Ritvo Adult Aspergers diagnostic Schedule – Revised – Danish translation) and SPQ (Schizotypy Personality Questionnaire)

Region of Denmark (approval number H-21039423), and the project is reported to the Danish Data Protection Agency. The study investigators are under the impression that the questionnaires and investigations will not lead to any discomfort for the subjects. There are no known expected short- or long-term risks associated with the present study.

Outcome

We hypothesize that the ZAQ will provide acceptable discrimination between ASD and SD, as indicated by an $AUC \geq 0.7$. The ZAQ will retain a clinically meaningful factor structure, instructing further research on distinct sub-constructs. Lastly, the positive predictive value of the cut-off score will have strong clinical power regarding the selection of which patients need further diagnostic examination in either a specialised clinic for the assessment of psychotic disorders or a clinic for the assessment of ASD.

Discussion

The main incentive to conduct this study has arisen from a clinical need to improve case identification of patients before referring to either ASD or SD assessment. Wrong initial case identification can lead to unacceptable clinical trajectories for the patients. An overlooked prodromal SSD in an autism clinic can delay onset of necessary treatment. A misdiagnosis of a patient in a unit for assessment of SSD can lead to treatment with antipsychotics when not warranted. Thus, incorrect referral can have severe negative consequences for the patient and is cost inefficient. ZAQ is designed to help avoid these unsatisfying trajectories and is primarily developed to alleviate difficulties in the initial case identifying phase of clinical assessment.

Abbreviations

- ZAQ SchiZotypy Autism Questionnaire
- ASD Autism Spectrum Disorder
- SD Schizotypal Disorder
- ADHD Attention Deficit Hyperactivity Disorder

ADD	Attention Deficit Disorder
SSD	Schizophrenia Spectrum Disorder
RAADS-R	Ritvo Adult Asperger Diagnostic Scale Revised
SRS	Social Responsiveness Scale
SPQ-BR	Schizotypal Personality Questionnaire Brief Revised
O-LIFE	Oxford-Liverpool Inventory of Feelings and Experiences
MMS	Multidimensional Schizotypy Scale
CAPS	Cardiff Anomalous Perception Scale
CAPE	Community Assessment of Psychic Experience
MASK	Melbourne Assessment of Schizotypy in Kids (MASK)
SPQ-C	Schizotypy Personality Questionnaire in Children
Tom	Theory of Mind
CFA	Confirmatory Factor Analysis
IRT	Item Response Theory
DIF	Differential Item Functioning
RUC	Receiver Operating Characteristics
AUC	Area under the Curve

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12888-023-04690-3>.

Additional file 1: Supplementary file 1. ZAQ English Version. schiZotropy Autism Questionnaire (ZAQ) in English version.

Acknowledgements

We would like to extend our sincere gratitude to Lise Nyholm, Casper Buchardt, Benjamin Sneider, Ane-Kristine Klemmensen, Peter Winning Iepsen, Lenart Bertil Jansson, Anja Sønderkov Sesler, Daniel Martin Godthjælp Nielsen, Maja Zandersen, Kim Berg Engersgaard Johannessen and Simon Mølgaard for their hard work, time and assessments of the questions proposed for the first versions of ZAQ.

Further we would like to acknowledge and appreciate the leadership at Psychiatric Center Glostrup, especially Head of Psychiatric Center Mette Bertelsen Fredsgaard, Chief physician Darius Mardosas, Development manager Kirsten Tofterup, Chief consultant Bolette Søndergaard and Team leader Nina Ginnerup for encouraging our work and providing funding for the project.

Heartfelt thanks to all the members of Team ADHD and Autism at Psychiatric Center Glostrup for supporting and embracing the extra clinical workload created by this research project and finally a huge gratitude to Research assistant Stine Algart for her dedicated and invaluable contribution in all aspects of the project.

Authors' contributions

RP initiated the study, procured the funding conceptualized and constructed the original manuscript, to which all authors contributed significant intellectual input. AAA contributed significantly to paper conceptualization and the final editing of the paper. ZAS edited the paper and procured funding. IMD edited the paper. EV contributed to paper conceptualization and writing the statistical analysis. FH contributed to paper conceptualization and editing the paper. RS contributed to paper conceptualization and editing the paper. BC contributed to paper conceptualization and editing the paper. BT contributed to paper conceptualization and editing the paper. PV contributed to paper conceptualization and editing the paper. All authors read and approved the final manuscript.

Funding

Funding was provided by Psychiatric Centre Glostrup, Copenhagen Denmark, Sofiefonden (Grant number: FID4107425) and Trygfonden (Grant number: 153588). Apart from the financial support the sponsors had no further involvement in the study or publication. The protocol has not been peer reviewed during the funding process.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study is approved by the Ethical Committee of the Capital Region of Denmark (approval number H-21039423), and the project is reported to the Danish Data Protection Agency. The study will be conducted in accordance with the Helsinki Declaration 1964, including subsequent revisions. Participants will only be included after signing an informed consent based on oral and written information. The participants may, at any time, choose to withdraw from the study without being required to explain and without affecting the person's future treatment. The study investigators are under the impression that the questionnaires and investigations will not lead to any discomfort for the subjects. There are no known expected short- or long-term risks associated with the present study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Signed ICMJE forms have been obtained and can be provided upon request.

Author details

¹ Department of ADHD and Autism, Mental Health Services, Capital Region of Denmark, Copenhagen, Denmark. ² Competence Centre for Transcultural Psychiatry, Mental Health Centre Ballerup, Copenhagen, Denmark. ³ Department of Biological Sciences, Simon Fraser University, Burnaby, BC V5A 1S6, Canada. ⁴ Social, Genetic & Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. ⁵ Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, Netherlands. ⁶ Centre for Developmental Psychiatry and Psychology, Monash University, Melbourne, Australia. ⁷ Center for Neuropsykiatrisk Depressionsforskning Psykiatrisk Center Glostrup, Nordstjernevej 41, Glostrup, Copenhagen 2600, Denmark. ⁸ School of Psychological Sciences, University of Haifa, 3498838 Haifa, Israel.

Received: 12 August 2022 Accepted: 14 March 2023

Published online: 28 March 2023

References

- Lai MC, Baron-Cohen S. Identifying the lost generation of adults with autism spectrum conditions. *Lancet Psychiatry*. 2015;2(11):1013–27.
- DeFilippis M. Depression in children and adolescents with autism spectrum disorder. *Children*. 2018;5(9):112.
- Chiarotti F, Venerosi A. Epidemiology of autism spectrum disorders: a review of worldwide prevalence estimates since 2014. *Brain Sci*. 2020;10(5):274.
- Schendel DE, Thorsteinsson E. Cumulative incidence of autism into adulthood for birth cohorts in Denmark, 1980–2012. *JAMA*. 2018;320(17):1811.
- Hossain MM, Khan N, Sultana A, Ma P, McKyer ELJ, Ahmed HU, et al. Prevalence of comorbid psychiatric disorders among people with autism spectrum disorder: an umbrella review of systematic reviews and meta-analyses. *Psychiatry Res*. 2020;287:112922.
- Mannion A, Leader G. Comorbidity in autism spectrum disorder: a literature review. *Res Autism Spectr Disord*. 2013;7(12):1595–616.
- Sullivan S, Rai D, Golding J, Zammit S, Steer C. The association between autism spectrum disorder and psychotic experiences in the Avon Longitudinal Study of Parents and Children (ALSPAC) Birth Cohort. *J Am Acad Child Adolesc Psychiatry*. 2013;52(8):806–814.e2.
- Goto A, Miyawaki D, Kusaka H, Okada Y, Asada N, Iwakura Y, et al. High prevalence of non-psychotic delusions in children with high-functioning pervasive developmental disorder. *Osaka City Med J*. 2015;61(2):73–80.
- Eussen MLJM, de Bruin EI, Van Gool AR, Louwerse A, van der Ende J, Verheij F, et al. Formal thought disorder in autism spectrum disorder predicts

- future symptom severity, but not psychosis prodrome. *Eur Child Adolesc Psychiatry*. 2015;24(2):163–72.
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(1):5–17.
 11. Ritvo RA, Ritvo ER, Guthrie D, Ritvo MJ, Hufnagel DH, McMahon W, et al. 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(8):1076–89.
 12. Constantino JN, Davis SA, Todd RD, Schindler MK, Gross MM, Brophy SL, et al. Validation of a brief quantitative measure of autistic traits: comparison of the social responsiveness scale with the autism diagnostic interview-revised. *J Autism Dev Disord*. 2003;33(4):427–33.
 13. Spek AA, Wouters SGM. Autism and schizophrenia in high functioning adults: behavioral differences and overlap. *Res Autism Spectr Disord*. 2010;4(4):709–17.
 14. Lugnegård T, Hallerbäck MU, Gillberg C. Asperger syndrome and schizophrenia: Overlap of self-reported autistic traits using the Autism-spectrum Quotient (AQ). *Nord J Psychiatry*. 2015;69(4):268–74.
 15. Kirchner SK, Roeh A, Nolden J, Hasan A. Diagnosis and treatment of schizotypal personality disorder: evidence from a systematic review. *NPJ Schizophr*. 2018;4(1):20.
 16. Pulay AJ, Stinson FS, Dawson DA, Goldstein RB, Chou SP, Huang B, et al. Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Schizotypal Personality Disorder: Results From the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. *Prim Care Companion J Clin Psychiatry*. 2009;11(2):53–67.
 17. Debbane M, Eliez S, Badoud D, Conus P, Fluckiger R, Schultze-Lutter F. Developing psychosis and its risk states through the lens of schizotypy. *Schizophr Bull*. 2015;41(suppl 2):S396–407.
 18. Debbane M, Barrantes-Vidal N. Schizotypy from a developmental perspective. *Schizophr Bull*. 2015;41(suppl 2):S386–95.
 19. Nordentoft M, Thorup A, Petersen L, Øhlenschläger J, Melau M, Christensen TØ, et al. Transition rates from schizotypal disorder to psychotic disorder for first-contact patients included in the OPUS trial. A randomized clinical trial of integrated treatment and standard treatment. *Schizophr Res*. 2006;83(1):29–40.
 20. Chisholm K, Lin A, Abu-Akel A, Wood SJ. The association between autism and schizophrenia spectrum disorders: a review of eight alternate models of co-occurrence. *Neurosci Biobehav Rev*. 2015;55:173–83.
 21. Cohen AS, Matthews RA, Najolia GM, Brown LA. Toward a more psychometrically sound brief measure of schizotypal traits: introducing the SPQ-Brief Revised. *J Pers Disord*. 2010;24(4):516–37.
 22. Mason O, Linney Y, Claridge G. Short scales for measuring schizotypy. *Schizophr Res*. 2005;78(2–3):293–6.
 23. Kwapił TR, Gross GM, Burgin CJ, Raulin ML, Silvia PJ, Barrantes-Vidal N. Validity of the multidimensional schizotypy scale: associations with schizotypal traits and normal personality. *Personal Disord Theory Res Treat*. 2018;9(5):458–66.
 24. Bell V, Halligan PW, Ellis HD. The Cardiff Anomalous Perceptions Scale (CAPS): a new validated measure of anomalous perceptual experience. *Schizophr Bull*. 2006;32(2):366–77.
 25. Konings M, Bak M, Hanssen M, van Os J, Krabbendam L. Validity and reliability of the CAPE: a self-report instrument for the measurement of psychotic experiences in the general population. *Acta Psychiatr Scand*. 2006;114(1):55–61.
 26. Jones HP, Testa RR, Ross N, Seal ML, Pantelis C, Tonge B. The Melbourne assessment of Schizotypy in kids: a useful measure of childhood schizotypal personality disorder. *Biomed Res Int*. 2015;2015:1–10.
 27. Liu J, Wong KKY, Dong F, Raine A, Tuvblad C. The Schizotypal Personality Questionnaire – Child (SPQ-C): psychometric properties and relations to behavioral problems with multi-informant ratings. *Psychiatry Res*. 2019;275:204–11.
 28. Crespi B, Badcock C. Psychosis and autism as diametrical disorders of the social brain. *Behav Brain Sci*. 2008;31(3):241–61.
 29. Crespi BJ, Go MC. Diametrical diseases reflect evolutionary-genetic trade-offs: evidence from psychiatry, neurology, rheumatology, oncology and immunology. *EMPH*. 2015;2015(1):216–53.
 30. Raine A. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R Criteria. *Schizophr Bull*. 1991;17(4):555–64.
 31. Bosco FM, Gabbatore I, Tirassa M, Testa S. Psychometric properties of the theory of mind assessment scale in a sample of adolescents and adults. *Front Psychol*. 2016;7. Available from: <http://journal.frontiersin.org/Article/10.3389/fpsyg.2016.00566/abstract>. [Cited 2022 Apr 22].
 32. Vallat-Azouvi C, Pradat-Diehl P, Azouvi P. The Working Memory Questionnaire: a scale to assess everyday life problems related to deficits of working memory in brain injured patients. *Neuropsychol Rehabil*. 2012;22(4):634–49.
 33. Wastler HM, Lenzenweger MF. Self-referential hypermentalization in schizotypy. *Personal Disord Theory Res Treat*. 2019;10(6):536–44.
 34. Roberts ME, Barthel FMS, Lopez C, Tchanturia K, Treasure JL. Development and validation of the Detail and Flexibility Questionnaire (DFlex) in eating disorders. *Eat Behav*. 2011;12(3):168–74.
 35. Happé FGE. An advanced test of theory of mind: Understanding of story characters' thoughts and feelings by able autistic, mentally handicapped, and normal children and adults. *J Autism Dev Disord*. 1994;24(2):129–54.
 36. Blais AR, Weber EU. Domain-Specific Risk-Taking Scale. American Psychological Association; 2012. Available from: <http://doi.apa.org/getdoi.cfm?doi=10.1037/t13084-000>. [Cited 2022 Apr 22].
 37. Bagby RM, Parker JDA, Taylor GJ. The twenty-item Toronto Alexithymia scale—I. Item selection and cross-validation of the factor structure. *J Psychosom Res*. 1994;38(1):23–32.
 38. Baron-Cohen S, Wheelwright S. The empathy quotient: an investigation of adults with asperger syndrome or high functioning autism, and normal sex differences. *J Autism Dev Disord*. 2004;34(2):163–75.
 39. Frederick S. Cognitive reflection and decision making. *J Econ Perspect*. 2005;19(4):25–42.
 40. Fach W, Atmanspacher H, Landolt K, Wyss T, Rössler W. A comparative study of exceptional experiences of clients seeking advice and of subjects in an ordinary population. *Front Psychol*. 2013;4. Available from: <http://journal.frontiersin.org/article/10.3389/fpsyg.2013.00065/abstract>. [Cited 2022 Apr 22].
 41. Lord C, Rutter M, Le Couteur A. Autism diagnostic interview-revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord*. 1994;24(5):659–85.
 42. Lam KSL, Aman MG. The repetitive behavior scale-revised: independent validation in individuals with autism spectrum disorders. *J Autism Dev Disord*. 2007;37(5):855–66.
 43. Carson SH, Peterson JB, Higgins DM. Reliability, validity, and factor structure of the creative achievement questionnaire. *Creat Res J*. 2005;17(1):37–50.
 44. Tavassoli T, Hoekstra RA, Baron-Cohen S. The Sensory Perception Quotient (SPQ): development and validation of a new sensory questionnaire for adults with and without autism. *Mol Autism*. 2014;5(1):29.
 45. Lefly DL, Pennington BF. Reliability and validity of the adult reading history questionnaire. *J Learn Disabil*. 2000;33(3):286–96.
 46. Parnas J, Møller P, Kircher T, Thalbitzer J, Jansson L, Handest P, et al. EASE: Examination of Anomalous Self-Experience. *Psychopathology*. 2005;38(5):236–58.
 47. Møller P. Schizofreni en forstyrrelse av selvet: forståelsens betydning for klinisk virksomhet. Oslo: Universitetsforl; 2018.
 48. Cicero DC, Neis AM, Klaunig MJ, Trask CL. The Inventory of Psychotic-Like Anomalous Self-Experiences (IPASE): development and validation. *Psychol Assess*. 2017;29(1):13–25.
 49. Kreiner S, Christensen KB. Graphical Rasch Models. In: Mesbah M, Cole BF, Lee MLT, editors. *Statistical Methods for Quality of Life Studies*. Boston, MA: Springer US; 2002. p. 187–203. Available from: http://link.springer.com/10.1007/978-1-4757-3625-0_15. [Cited 2022 Apr 22].
 50. Hosmer DW, Lemeshow S. *Applied logistic regression*. 2nd ed. New York: Wiley; 2000. p. 373 (Wiley series in probability and statistics).
 51. DeVellis RF. *Scale development: theory and applications*. 4th ed. Los Angeles: SAGE; 2017. p. 262.
 52. Kline RB. *Principles and practice of structural equation modeling*. New York: Guilford Press; 2004. p. 366 (Methodology in the social sciences).

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.