

Research Article

Factors Associated with Anxiety Disorders in Chinese Children with Autism Spectrum Disorder in Hong Kong

Luk JS^{1*}; Tang CP²; Yu YW²

¹Pamela Youde Nethersole Eastern Hospital, Hong Kong

²Kwai Chung Hospital, Hong Kong

*Corresponding author: Luk JS

Department of Psychiatry, Pamela Youde Nethersole Eastern Hospital, Lok Man Road, Chai Wan, Hong Kong.

Received: February 01, 2023

Accepted: March 27, 2023

Published: April 03, 2023

Abstract

Background: Autism Spectrum Disorder (ASD) is a pervasive neurodevelopment disorder characterised by impairment in social communication and presence of restricted, repetitive patterns of behaviour, interests, or activities. A growing body of research has shown that children with ASD experience significantly greater anxiety levels than typically developing children. Anxiety disorders have been found to be one of the most prevalent psychiatric comorbidities in this population of children and are associated with debilitating psychosocial impairment.

Objective: This study aimed to examine factors associated with anxiety disorders among Chinese children diagnosed with ASD in Hong Kong.

Methods: This cross-sectional study was conducted at a child and adolescent psychiatry outpatient clinic from August 2019 to April 2020. The sample consisted of one hundred thirty-two subjects aged 6 to <12 years who had a diagnosis of ASD. Structured interviews and questionnaires including the Diagnostic Interview Schedule for Children, Parenting Stress Index-Short Form, Parenting Styles and Dimensions Questionnaire and a socio-demographic questionnaire were administered for the assessment of anxiety disorders and their associated factors.

Results: Greater qualitative deficits in reciprocal social interaction skills, attention-deficit/hyperactivity disorder and maternal mood disorder were found to be significantly associated with anxiety disorders in children with ASD.

Conclusion: Anxiety disorders are prevalent among children with ASD. Early recognition and identification of comorbid anxiety disorders are necessary in the diagnostic process of ASD. This study enriches our understanding of the factors associated with anxiety disorders in this population of children. For future research directions, furthering our understanding on the aetiological pathways, course of illness, and outcome of anxiety disorders in autistic children is highly warranted.

Keywords: Autism spectrum disorder; Anxiety disorder; Chinese children; Hong kong children

Introduction

Autism Spectrum Disorder (ASD) is a pervasive neurodevelopmental disorder characterised by impairment in social communication and presence of restricted, repetitive patterns of behaviour, interests, or activities [2]. A growing body of research has shown that children with ASD experience significantly greater anxiety levels than typically developing children, as well as children with other developmental disorders [19,29,32,34,41,67]. A meta-analysis revealed that 39.6% of au-

tistic young people were comorbid with at least one anxiety disorder [66]. Anxiety in autistic children has been associated with debilitating impairments such as aggression, irritability, depressive symptoms and self-injurious behaviour [16,31]. To facilitate our clinical understanding and local service development, it is important to explore and recognise the factors associated with anxiety disorder in this population of children.

Social Communication Deficits and Anxiety

Social communication deficits are a central and debilitating element of ASD. Evidence has shown that deficits in social skill are significantly associated with anxiety in autistic children [7,10,15,62]. At different phases of development, social competence plays a critical role in navigating a child through social encounters. Deficit in social functioning, such as difficulty in interpreting and understanding other's emotions, could significantly affect the quality and quantity of social interactions. Failure in social integration could be a stressful and anxiety provoking experience for children.

In the presence of social functioning deficits, the likelihood of negative peer interaction has been found to increase [8,64]. Bullying victimisation rate among autistic children was shown to be twice as high as those found in the general population [8]. Children who experienced high levels of bullying victimisation were found to have higher levels of anxiety than children who experienced low level or no victimisation [8].

Attention-Deficit Hyperactivity Disorder and Anxiety

ADHD is among the most common psychiatric comorbidities in autistic children with prevalence rates ranging from 28% to 83% [13,20,30,35,3,40,45,53,57]. Anxiety disorders are common among children with ADHD. As shown in the Multimodal Treatment study of children with ADHD, 33.5% of the subjects met the DSM-III-R criteria for an anxiety disorder [39], while a local study yielded a comparable rate of anxiety disorders (27.5%) in school-age children with ADHD [55]. Autistic children and comorbid ADHD, as compared to children with a sole diagnosis of ASD, have been found to have higher levels of anxiety and lower quality of life [3,12].

Parenting, Parenting Stress and Children's Anxiety

Theoretical models of anxiety disorders have hypothesised the role of parenting in the development and maintenance of childhood anxiety [11,74]. Parenting plays an important role in shaping a child's early environment and the emotional climate within a parent-child dyad. A high level of parental warmth, responsiveness and autonomy granting are proposed to cultivate children's perception of mastery and internal locus of control, which fosters anxiety reduction [11,44,60,74].

In contrast, excessive parental control is hypothesised to limit children's sense of mastery and development of autonomy, contributing to high trait anxiety [11,74]. A meta-analysis supported that a higher level of warmth and autonomy-granting were associated with lower levels of anxiety in children, whereas a higher level of parental control and aversiveness were associated with higher levels of anxiety in children [44].

Comparing the different parenting styles, authoritarian parenting, characterised by a low level of warmth and a high level of control, is found to be associated with higher levels of anxiety in youth [73].

Parents of autistic children are burdened with specific stresses in raising their children, commonly contributed by social stigma, coordination of their children's care, their children's behavioural and emotional problems, and concerns towards their children's future development [24,28,33,69,77]. Compared to parents of typically developing children and children with other disabilities, parents of autistic children are found to have significantly higher levels of parenting stress [23].

Parenting stress is found to share a significant association with children's anxiety and internalising symptoms [51,61,68] such association is also observed in autistic young people [31].

Parental Psychiatric Disorders and Children's Anxiety

Psychiatric disorders are common among parents of autistic children, with higher prevalence rates than parents of typically developing children [27,77]. The relationship between parental and offspring psychopathologies is well established in literature. Growing evidence has suggested familial predisposition in anxiety disorders; offspring of parents with anxiety or depressive disorders have been shown to have a heightened risk of developing internalising problems and anxiety disorders themselves [6,21,72]. A longitudinal examination has shown that the offspring of depressed parents, compared to those of non-depressed parents, have a threefold increase in risk of developing anxiety disorders [71]. Whereas offspring of mothers with a lifetime history of anxiety disorder compared to offspring of mothers without anxiety disorder, are at doubled risk of developing anxiety disorders [43].

Objective

This study aimed to examine the factors associated with anxiety disorders in Chinese school-age children diagnosed with ASD in a child and adolescent psychiatry out patient clinic in Hong Kong.

Methods

This was a cross-sectional study examining the prevalence of anxiety disorders among Chinese school-age children diagnosed with ASD. This study was conducted at the Yumatei Child and Adolescent Mental Health Service (YMTCAMHS) from August 2019 to April 2020. The YMTCAMHS is a regional specialist outpatient clinic serving children and adolescents under the age of 18 years in the Kowloon West and Kowloon Central Clusters of Hong Kong; these regions have a total population of 2.4 million, which is approximately one third of the total population in Hong Kong [9].

Potential eligible Chinese subjects aged 6 to <12 with a diagnosis of ASD determined by psychiatrists, who fulfilled the exclusion criteria and had attended YMTCAMHS from July 2018 to June 2019, were identified from electronic databases via Clinical Management System and Clinical Data Analysis and Reporting System. Subsequently, subjects were selected via computer-generated simple random sampling to be recruited into the study. Written informed consent and assent were obtained from the subjects' parents and the subjects, respectively. All recruited subjects' parents were interviewed by the principal investigator with the Developmental, Dimensional and Diagnostic Interview (3Di) to confirm the subjects' diagnosis of ASD.

A further assessment was conducted on the same day using the Chinese version of the National Institute of Mental Health Diagnostic Interview Schedule for Children- Version 5 (NIMH DISC-5), parent version for the assessment of comorbid anxiety disorders and attention-deficit/hyperactivity disorder. Subjects' parents were invited to complete the Parenting Styles and Dimensions Questionnaire (PSDQ), Parenting Stress Index-Short Form (PSI-SF), and a sociodemographic data questionnaire. The principal investigator was blinded to the results of the questionnaires prior to the completion of the 3Di and NIMH DISC-5. Ethics approval was obtained from the Kowloon West Cluster Research Ethics Committee.

Subjects

The inclusion criteria include children who are ethnic Chinese, age 6 to <12 years, and have a diagnosis of ASD determined by a psychiatrist and confirmed by the 3Di. Subjects with known severe mental illnesses (such as psychosis, mania), intellectual disability, severe neurological disorders, chromosomal abnormalities, severe medical disorders that required long-term treatment, active substance abuse, or parents who are unable to comprehend Chinese are excluded from the study.

Developmental, Dimensional and Diagnostic Interview (3Di)

The Developmental, Dimensional and Diagnostic Interview (3Di) is a standardised computer-based parent-report interview, developed and validated [58]. The pervasive developmental disorder module of the 3Di is primarily designed to assess dimensions of autistic traits in children with normal intelligence. It generates dimensional scores on domains of qualitative abnormalities in reciprocal social interaction skills, qualitative impairments in language and communication skills, and repetitive and stereotyped behaviours, as well as categorical diagnosis. The 3Di has excellent test-retest and interrater reliabilities. The sensitivity and specificity were 1.0 and >0.97, respectively [58]. The translated Chinese version of the 3Di pervasive developmental disorder module has a sensitivity of 0.95 and specificity of 0.77 [36]. With the changes in the diagnostic criteria of ASD in the DSM-5 [2], Mandy and colleagues (2012) tested the 3Di subscales using confirmatory factor analysis and concluded that the two-factor model of the DSM-5 was well represented in the 3Di.

National Institute of Mental Health Diagnostic Interview Schedule for Children, Parent Version (NIMH DISC)

The National Institute of Mental Health Diagnostic Interview Schedule for Children (NIMH DISC) is a highly structured respondent-based diagnostic interview designed to assess psychiatric disorders in children and adolescents. There are a total of six modules assessing thirty-four common childhood psychiatric disorders upon a one-year time frame. The interview has parallel parent and youth reported versions, designed for individuals in the age ranges of 6 to 17 years, and 9 to 17 years, respectively.

The parent version was adopted in the present study as it is designed for children within the age range of our sample (6 to <12 years), as well as its better test-retest reliability than that of the youth version [26]. Multiple symptoms are assessed, and the scoring programme combines the symptom responses to determine whether a disorder criterion is fulfilled. Recommendations by the DISC Development Group are followed for the impairment criteria; an impairment score of three is considered to be clinically significant. Literature has supported the reliability and validity of the NIMH DISC, including a translated Chinese version for the use in Hong Kong [26,54], which has been widely adopted in local studies. Over the years, various versions of NIMH DISC have been generated to match the evolving classification systems. The latest version- NIMH DISC-5 was developed based on the DSM-5 classification [2].

Parenting Stress Index- Short Form (PSI-SF)

The Parenting Stress Index- Short Form (PSI-SF) is a self-reported questionnaire designed for caregivers to assess parenting stress [1]. The questionnaire comprised thirty-six items, rated on a five-point Likert scale. It consists of three subscales

(parental distress, parent-child dysfunctional interaction and difficult child) and a total stress score. Parents with a total stress score at or above the 90th percentile are considered to be experiencing clinically significant levels of stress and are recommended for professional assistance. The Chinese version of the PSI-SF has demonstrated satisfactory psychometric properties and good reliability coefficients [75].

Parenting Styles and Dimensions Questionnaire (PSDQ)

The Parenting Styles and Dimensions Questionnaire (PSDQ) is a self-reported questionnaire developed for parents of preschool and school-age children to evaluate parenting styles [50]. The questionnaire comprised sixty-two items, rated on a five-point Likert scale. Three parenting styles and eleven subdimensions are assessed. Each parenting style contains several subdimensions. The mean score of all items within a subdimension is calculated. Each parenting style is measured by taking the mean score of all its subdimensions. The questionnaire shows good reliability and has been used by researchers internationally. Cronbach's alpha values for authoritative, authoritarian, and permissive parenting are 0.91, 0.86 and 0.75, respectively [50]. The Chinese version of the PSDQ demonstrated good reliability and validity [18]. The subscale scores correlate with each factor significantly with a coefficient of correlation between 0.732 and 0.951. Confirmatory factor analysis shows good construct validity.

Sociodemographic Data

Through a structured questionnaire and subject's case record, information regarding the subject's sociodemographic background, medical and psychiatric history, schooling history, and bullying history, as well as the family's sociodemographic background and psychiatric history were obtained.

Sample Size

Referencing overseas literature with study designs resembling the present study, specifically studies that were based on clinical samples and used standardised diagnostic interviews, the prevalence estimates of anxiety disorders among autistic children ranged from 43.5% to 84.1% [13,45-47]. Taking the average value of 66% as the estimated prevalence with a 95% Confidence Interval (CI) and a 9% margin of error, the sample size required for the present study was estimated to be 107 subjects.

Data Analysis

Statistical analysis was performed using the Statistical Program for Social Sciences 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA computer software).

Results

A total of 150 subjects selected via computer-generated simple random sampling were invited to participate in the study. Of these subjects, 9 refused to participate due to time constraints and privacy concerns, and 9 failed to reach the diagnostic cut-offs of all three subscales in the 3Di.

The final sample consisted of 132 subjects. Comparing the enrolled subjects with the subjects who did not participate in the study, no statistically significant differences in age, sex, or school year were found. The sample recruitment process is summarised in (Figure 1).

Subject and Family Characteristics

The sample consisted of 115 boys (87.1%) and 17 girls (12.9%). The mean age of the subjects was 8.9 years ($SD=1.7$). 69 subjects (52.3%) were diagnosed with comorbid ADHD as assessed by the NIMH DISC-5. All subjects were educated in mainstream primary school.

The characteristics of the subjects are summarised in Table 1. The mean ages of fathers and mothers were 45.8 years ($SD=7.6$) and 42.2 years ($SD=5.5$), respectively. A total of 47 subjects (35.6%) had a family history of psychiatric disorder. 32 mothers (24.2%) and 3 fathers (2.3%) reported a history of depression, while 4 mothers (3.0%) and 1 father (0.8%) reported a history of anxiety disorders. Depression and anxiety disorders were grouped as mood disorders for subsequent bivariate and multivariate analyses. The characteristics of family are summarised in Tables 2 and 3.

Prevalence Rate and Associated Factors

The one-year prevalence rate of any anxiety disorder was 28.8%. Bivariate analysis was performed to compare the variables between subjects with and without comorbid anxiety disorders. Comparing the two groups of subjects, subjects with anxiety disorders were found to have significantly higher percentages of comorbid ADHD ($\chi^2=5.578$, $p=.018$), antipsychotic use ($p=.007$), ADHD medication use ($\chi^2=5.321$, $p=.021$), social skills training ($\chi^2=5.851$, $p=.016$) and social exclusion ($\chi^2=13.032$, $p<.001$). Significantly higher levels of qualitative deficits in reciprocal social interaction skills ($U=171.5$, $p<.001$) and repetitive and stereotyped behaviours ($U=1340.0$, $p=.025$) were noted in subjects with comorbid anxiety disorders. Among the investigated family variables, subjects with comorbid anxiety disorders were found to have significantly higher percentages of having a family history of psychiatric disorder ($\chi^2=11.562$, $p=.001$) and maternal mood disorder ($\chi^2=17.301$, $p<.001$). Parents of subjects with comorbid anxiety disorders were shown to have significantly greater levels of maternal parenting stress ($t(130)=4.243$, $p<.001$), paternal verbal hostility ($t(130)=2.281$, $p=.024$), and paternal corporal punishment ($t(130)=2.120$, $p=.036$). Bivariate analysis results are summarised in (Tables 4 to 12). Logistic regression was conducted to examine the relationship between anxiety disorders and variables that were found to have a p -value of $<.1$ in bivariate analysis. Candidate variables including ADHD ($p=.018$), qualitative deficits in reciprocal social interaction skills ($p<.001$), repetitive and stereotyped behaviours ($p=.025$), physical bullying ($p=.062$), verbal bullying ($p=.077$), social exclusion ($p<.001$), antipsychotic use ($p=.007$), social skills training ($p=.016$), maternal mood disorder ($p<.001$), maternal PSI-SF total stress score ($p<.001$), paternal verbal hostility ($p=.024$), paternal corporal punishment ($p=.036$), maternal reasoning/induction ($p=.076$) and maternal verbal hostility ($p=.073$) were entered into the regression model. The variable ADHD medication use was not entered into the logistic regression as it highly correlated with the variable ADHD, given that 95.7% of the subjects with comorbid ADHD were treated with ADHD medication. The maternal PSI-SF total stress score was entered into the regression model instead of the PSI-SF subscale scores, in view of the high correlation between the variables. In the final regression model, the p -value of the Hosmer and Lemeshow goodness-of-fit test was .585, indicating a good fit for the model. The multivariate analysis revealed that higher level of qualitative deficits in reciprocal social interaction skills (adjusted odds ratio (OR)=2.68, 95% CI [1.82, 3.95], $p<.001$), presence of maternal mood disorder (adjusted

$OR=17.80$, 95% CI [2.86, 110.66], $p=.002$) and comorbid ADHD (adjusted $OR=16.00$, 95% CI [2.41, 106.28], $p=.004$) were significantly associated with anxiety disorders in autistic children, after controlling for age and sex. The results of the multivariate analysis are summarised in Table 13.

Table 1: Characteristics of the subjects.

	Mean \pm SD	
	N	%
Age	8.9 \pm 1.7	
Sex		
Male	115	87.1
Female	17	12.9
Place of Birth		
Hong Kong	126	95.5
Mainland China	6	4.5
Living Arrangement		
Both parents	120	90.9
One parent	12	9.1
Primary Caretaker		
Father	17	12.9
Mother	111	84.1
Grandparent	4	3.0
School Grade		
Primary 1	12	9.1
Primary 2	25	18.9
Primary 3	20	15.2
Primary 4	24	18.2
Primary 5	27	20.5
Primary 6	24	18.2
History of Grade Retention	19	14.4
History of School Transfer	15	11.4
Victim of Bullying in the Past Year		
Physical bullying	25	18.9
Verbal bullying	44	33.3
Social exclusion	34	25.8
Long-term Physical Illness		
Asthma	3	2.3
Attention-Deficit/Hyperactivity Disorder	69	52.3
Psychiatric Pharmacological Intervention		
Antidepressant	1	0.8
Antipsychotic	8	6.1
ADHD medication	66	50.0
Psychiatric Nonpharmacological Intervention		
Psychological intervention	24	18.2
Social skills training	95	72.0
Speech therapy	68	51.5
Play therapy	36	27.3

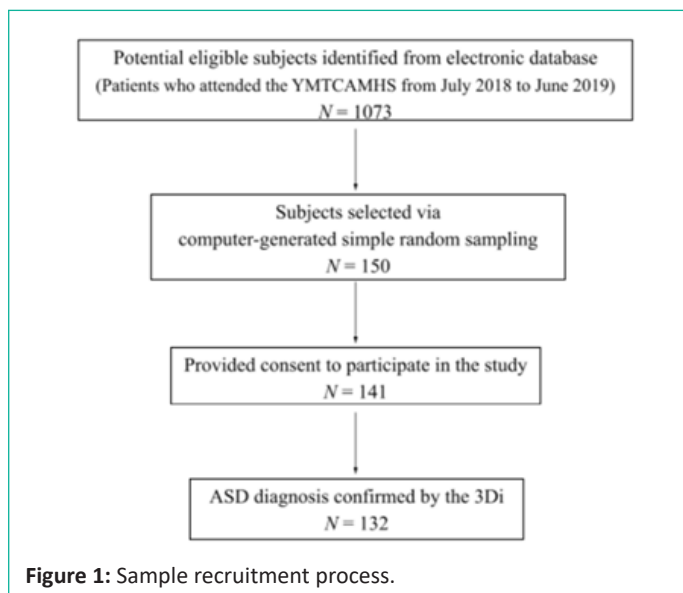


Figure 1: Sample recruitment process.

Table 2: Characteristics of the family.

	Mean ± SD	
Father's Current Age	45.8 ± 7.6	
Mother's Current Age	42.2 ± 5.5	
	N	%
Parents' Marital Status		
Not married	1	0.8
Married	119	90.2
Divorced/separated	12	9.1
Father's Occupation		
Manager & administrator	11	8.3
Professional	5	3.8
Associate professional	23	17.4
Clerical support worker	11	8.3
Service & sales worker	42	31.8
Craft and related worker	10	7.6
Plant & machine operator	12	9.1
Elementary occupation	7	5.3
Unemployed/homemaker	11	8.3
Mother's Occupation		
Manager & administrator	7	5.3
Professional	1	0.8
Associate professional	10	7.6
Clerical support worker	26	19.7
Service & sales worker	19	14.4
Craft and related worker	0	0
Plant & machine operator	0	0
Elementary occupation	0	0
Unemployed/homemaker	69	52.3
Monthly Household Income (HK\$)		
<\$9999	7	5.3
\$10000-20000	31	23.5
\$20001-30000	38	28.8
\$30001-40000	13	9.8
\$40001-50000	18	13.6
>\$50001	25	18.9
Number of Siblings		
0	67	50.8
1	56	42.4
2	7	5.3
3	2	1.5

Table 3: Characteristics of the family's psychiatric background.

	N	%
Family History of Psychiatric Disorder	47	35.6
Paternal Psychiatric Disorder		
None	126	95.5
Depression	3	2.3
Anxiety disorder	1	0.8
Psychotic disorder	2	1.5
Maternal Psychiatric Disorder		
None	96	72.7
Depression	32	24.2
Anxiety disorder	4	3.0
Sibling Psychiatric Disorder		
None	116	87.9
ASD	13	9.8
ADHD	12	9.1
Anxiety disorder	2	1.5
Family History of Substance Misuse	2	1.5

Table 4: Comparison of characteristics between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		Test Value	p-value
	Mean±SD		Mean±SD		Mean±SD		t=-	
Age	8.9±1.7		9.0±1.7		8.7±1.6		0.823	.412
	N	(%)	n	(%)	n	(%)		
Sex								.393 ^f
Male	115	(87.1)	80	(85.1)	35	(92.1)		
Female	17	(12.9)	14	(14.9)	3	(7.9)		
Place of Birth								.801 ^f
Hong Kong	126	(95.5)	90	(95.7)	36	(94.7)		
Mainland China	6	(4.5)	4	(4.3)	2	(5.3)		
Living Arrangement								.325 ^f
Both parents	120	(90.9)	87	(92.6)	33	(86.8)		
One parent	12	(9.1)	7	(7.4)	5	(13.2)		
Primary Caretaker								.265 ^f
Father	17	(12.9)	10	(10.6)	7	(18.4)		
Mother	111	(84.1)	80	(85.1)	31	(81.6)		
Grandparent	4	(3.0)	4	(4.3)	0	(0)		
School Grade							$\chi^2 = 1.011$.337 ^c
Primary 1 to 3	57	(43.2)	38	(40.4)	19	(50.0)		
Primary 4 to 6	75	(56.8)	56	(59.6)	19	(50.0)		
Grade Retention	19	(14.4)	12	(12.8)	7	(18.4)	$\chi^2 = 0.702$.402 ^c
School Transfer	15	(11.4)	11	(11.7)	4	(10.5)		> .999 ^f
Victim of Bullying in the Past Year								
Physical bullying	25	(18.9)	14	(14.9)	11	(28.9)	$\chi^2 = 3.481$.062 ^c
Verbal bullying	44	(33.3)	27	(28.7)	17	(44.7)	$\chi^2 = 3.123$.077 ^c
Social exclusion	34	(25.8)	16	(17.0)	18	(47.4)	$\chi^2 = 13.032$	* < .001 ^c

Note: Continuous data were analysed by independent-samples t-test. Categorical data were analysed by ^c Pearson's chi-square test or ^f Fisher's exact test. *p<.05.

Table 5: Comparison of the medical and psychiatric background between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		Test Value	p-value
	N	(%)	n	(%)	n	(%)		
Long-term Physical Illness	3	(2.3)	3	(3.2)	0	(0)		.557 ^f
ADHD	69	(52.3)	43	(45.7)	26	(68.4)	$\chi^2=5.578$	*.018 ^c
Psychiatric Pharmacological Intervention								
Antidepressant	1	(0.8)	0	(0)	1	(2.6)		.288 ^f
Antipsychotic	8	(6.1)	2	(2.1)	6	(15.8)		*.007 ^f
ADHD medication	66	(50.0)	41	(43.6)	25	(65.8)	$\chi^2=5.321$	*.021 ^c
Psychiatric Nonpharmacological Intervention								
Psychological intervention	24	(18.2)	14	(14.9)	10	(26.3)	$\chi^2=2.373$.123 ^c
Social skills training	95	(72.0)	62	(66.0)	33	(86.8)	$\chi^2=5.851$	*.016 ^c
Speech therapy	68	(51.5)	47	(50.0)	21	(55.3)	$\chi^2=0.300$.584 ^c
Play therapy	36	(27.3)	25	(26.6)	11	(28.9)	$\chi^2=0.075$.784 ^c

Note: Categorical data were analysed by ‘Pearson’s chi-square test or ‘Fisher’s exact test. ADHD: Attention-Deficit/Hyperactivity Disorder.

Table 6: Comparison of the father’s characteristics between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		Test Value	p-value
	Mean±SD	Mean ± SD	Mean±SD	Mean ± SD	Mean±SD	Mean ± SD		
Father’s Current Age	45.8±7.6	46.0±7.6	45.1±7.5	45.1±7.5	45.1±7.5	45.1±7.5	t=-0.661	.510
Father’s Age at Childbirth	36.3±7.4	36.5±7.3	35.8±7.6	35.8±7.6	35.8±7.6	35.8±7.6	t=-0.471	.638
	N	(%)	n	(%)	n	(%)		
Father’s Educational Level								>.999 ^f
Primary or less	1	(0.8)	1	(1.1)	0	(0)		
Secondary	77	(58.3)	55	(58.5)	22	(57.9)		
Diploma	24	(18.2)	17	(18.1)	7	(18.4)		
University or above	30	(22.7)	21	(22.3)	9	(23.7)		
Father’s Occupation								.779 ^f
Managers & administrator	11	(8.3)	8	(8.5)	3	(7.9)		
Professional	5	(3.8)	3	(3.2)	2	(5.3)		
Associate professional	23	(17.4)	19	(20.2)	4	(10.5)		
Clerical support worker	11	(8.3)	6	(6.4)	5	(13.2)		
Service & sales worker	42	(31.8)	31	(33.0)	11	(28.9)		
Craft and related worker	10	(7.6)	7	(7.4)	3	(7.9)		
Plant & machine operator	12	(9.1)	9	(9.6)	3	(7.9)		
Elementary occupation	7	(5.3)	4	(4.3)	3	(7.9)		
Unemployed/homemaker	11	(8.3)	7	(7.4)	4	(10.5)		
Father’s Marital Status								.119 ^f
Not married	1	(0.8)	0	(0)	1	(2.6)		
Married	119	(90.2)	87	(92.6)	32	(84.2)		
Divorced/separated	12	(9.1)	7	(7.4)	5	(13.2)		
Father’s Years of Hong Kong Residency								.410 ^f
≥7 years	125	(94.7)	90	(95.7)	35	(92.1)		
<7 years	7	(5.3)	4	(4.3)	3	(7.9)		

Note: Continuous data were analysed by independent-samples t-test. Categorical data were analysed by ^f Fisher’s exact test.

Table 7: Comparison of the mother’s characteristics between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		Test Value	p-value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD		
Mother’s Current Age	42.2±5.5	42.4±5.6	41.8±5.0	41.8±5.0	41.8±5.0	41.8±5.0	t=-0.530	.597
Mother’s Age at Childbirth	32.7±5.1	32.8±5.2	32.5±4.8	32.5±4.8	32.5±4.8	32.5±4.8	t=-0.266	.790
	N	(%)	n	(%)	n	(%)		
Mother’s Educational Level							$\chi^2=1.337$.512 ^c
Secondary	89	(67.4)	66	(70.2)	23	(60.5)		
Diploma	19	(14.4)	13	(13.8)	6	(15.8)		
University or above	24	(18.2)	15	(16.0)	9	(23.7)		
Mother’s Occupation								.263 ^f
Managers & administrator	7	(5.3)	3	(3.2)	4	(10.5)		
Professional	1	(0.8)	1	(1.1)	0	(0)		
Associate professional	10	(7.6)	7	(7.4)	3	(7.9)		
Clerical support worker	26	(19.7)	16	(17.0)	10	(26.3)		
Service & sales worker	19	(14.4)	13	(13.8)	6	(15.8)		
Unemployed/homemaker	69	(52.3)	54	(57.4)	15	(39.5)		
Mother’s Marital Status								.119 ^f
Not married	1	(0.8)	0	(0)	1	(2.6)		
Married	119	(90.2)	87	(92.6)	32	(84.2)		
Divorced/separated	12	(9.1)	7	(7.4)	5	(13.2)		
Mother’s Years of Hong Kong Residency								.366 ^f
≥7 years	117	(88.6)	85	(90.4)	32	(84.2)		
<7 years	15	(11.4)	9	(9.6)	6	(15.8)		

Note: Continuous data were analysed by independent-samples t-test. Categorical data were analysed by ^c Pearson’s chi-square test or ^f Fisher’s exact test.

Table 8: Comparison of the household characteristics between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		p-value
	N	(%)	n	(%)	n	(%)	
Monthly Household Income (HK\$)							.491 ^f
<\$9999	7	(5.3)	5	(5.3)	2	(5.3)	
\$10000-20000	31	(23.5)	25	(26.6)	6	(15.8)	
\$20001-30000	38	(28.8)	27	(28.7)	11	(28.9)	
\$30001-40000	13	(9.8)	8	(8.5)	5	(13.2)	
\$40001-50000	18	(13.6)	10	(10.6)	8	(21.1)	
>\$50001	25	(18.9)	19	(20.2)	6	(15.8)	
Number of Siblings							.579 ^f
0	67	(50.8)	48	(51.1)	19	(50.0)	
1	56	(42.4)	41	(43.6)	15	(39.5)	
2	7	(5.3)	4	(4.3)	3	(7.9)	
3	2	(1.5)	1	(1.1)	1	(2.6)	

Note: Categorical data were analysed by ^f Fisher’s exact test.

Table 9: Comparison of the family’s psychiatric background between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)		No Anxiety Disorder (n=94)		Presence of Anxiety Disorder (n=38)		Test Value	p-value
	N	(%)	n	(%)	n	(%)		
Family History of Psychiatric Disorder	47	(35.6)	25	(26.6)	22	(57.9)	$\chi^2=11.562$	*.001^c
Paternal Psychiatric Disorder								
Mood disorder	4	(3.0)	2	(2.1)	2	(5.3)		.578 ^f
Psychotic disorder	2	(1.5)	2	(2.1)	0	(0)		>.999 ^f
Maternal Psychiatric Disorder								
Mood disorder	36	(27.3)	16	(17.0)	20	(52.6)	$\chi^2=17.301$	*<.001^c
Sibling Psychiatric Disorder								
ASD	13	(9.8)	7	(7.4)	6	(15.8)		.145 ^f
ADHD	12	(9.1)	6	(6.4)	6	(15.8)		.089 ^f
Anxiety disorder	2	(1.5)	1	(1.1)	1	(2.6)		.504 ^f
Family History of Substance Misuse	2	(1.5)	1	(1.1)	1	(2.6)		.494 ^f

Note: Categorical data were analysed by ^c Pearson’s chi-square test or ^f Fisher’s exact test. ASD: Autism Spectrum Disorder; ADHD: Attention-Deficit/Hyperactivity Disorder.

*p<.05.

Table 10: Comparison of the Developmental, Dimensional and Diagnostic Interview (3Di) scores between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)	No Anxiety Disorder (n=94)	Presence of Anxiety Disorder (n=38)	U	p-value
	Median (IQR)	Median (IQR)	Median (IQR)		
Reciprocal Social Interaction Skills Qualitative Deficits [10]^a	14.1 (13.0-19.0)	13.4 (13.0-14.4)	20.1 (18.9-21.6)	171.5	*<.001
Language and Communication Skills Qualitative Impairments [8]^a	15.0 (12.1-18.0)	15.0 (12.4-17.9)	15.0 (11.6-19.0)	1756.5	.882
Repetitive and Stereotyped Behaviours [3]^a	6.1 (5.0-8.0)	6.0 (5.0-7.4)	6.7 (5.4-8.6)	1340.0	*.025

Note: Continuous data were analysed by the Mann-Whitney U test. ^a Cut-off scores for the three subscales of the 3Di according to Skuse et al. [58].

*p<.05.

Table 11: Comparison of the PSI-SF scores between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)	No Anxiety Disorder (n=94)	Presence of Anxiety Disorder (n=38)	t	p-value
	Mean±SD	Mean±SD	Mean±SD		
Father					
Total Stress	68.8±11.1	68.1±10.9	70.4±11.4	1.081	.282
PD	29.3±4.6	28.9±4.4	30.1±5.0	1.281	.202
P-CDI	27.5±3.6	27.2±3.4	28.4±4.1	1.638	.107
DC	31.1±3.3	30.9±3.3	31.6±3.4	1.102	.272
Mother					
Total Stress	84.9±18.6	79.8±17.1	94.0±18.4 ^a	4.243	*<.001
PD	33.4±9.4	31.2±8.6	39.1±9.0	4.746	*<.001
P-CDI	31.7±7.8	30.2±7.6	35.3±7.3	3.526	*.001
DC	39.3±8.9	37.5±8.1	43.8±9.3	3.851	*<.001

Note: Continuous data were analysed by independent-samples t-test. PD: Parental Distress; P-CDI: Parent-Child Dysfunctional Interaction; DC: Difficult Child. ^a>90th percentile, indicating clinically significant levels of stress.

*p<.05.

Table 12: Comparison of the PSDQ scores between subjects with and without comorbid anxiety disorder.

	Total Sample (N=132)	No Anxiety Disorder (n=94)	Presence of Anxiety Disorder (n=38)		
	Mean±SD	Mean±SD	Mean±SD	t	p-value
Father					
Authoritative	3.1±0.7	3.1±0.7	3.1±0.6	-0.440	.661
Warmth/support	3.1±0.7	3.2±0.8	3.0±0.7	-1.490	.139
Reasoning/induction	3.2±0.8	3.1±0.8	3.1±0.8	-0.062	.951
Democratic participation/ autonomy granting	2.9±0.7	2.9±0.7	3.0±0.9	0.973	.332
Responsiveness	3.1±0.6	3.1±0.6	3.2±0.7	0.327	.744
Authoritarian	2.3±0.5	2.2±0.5	2.4±0.5	1.652	.101
Verbal hostility	2.6±0.7	2.6±0.6	2.9±0.7	2.281	*.024
Corporal punishment	1.9±0.6	1.9±0.6	2.1±0.7	2.120	*.036
Non-reasoning/punitive strategies	1.9±0.5	1.9±0.5	2.0±0.6	0.672	.503
Directiveness	2.8±0.7	2.8±0.7	2.9±0.7	0.614	.540
Permissive	2.6±0.6	2.6±0.6	2.6±0.4	-0.076	.939
Lacks follow through	2.9±0.6	2.9±0.6	2.8±0.6	-0.440	.661
Ignoring misbehaviour	2.1±0.5	2.1±0.5	2.2±0.6	1.287	.204
Lacks self-confidence	2.8±1.3	2.8±1.5	2.7 ± 0.5	-0.317	.752
Mother					
Authoritative	3.7±0.6	3.7±0.5	3.8±0.7	0.957	.340
Warmth/support	3.9±0.6	3.9±0.6	3.9±0.7	0.008	.994
Reasoning/induction	3.7±0.7	3.7±0.7	3.9±0.9	1.788	.076
Democratic participation/autonomy granting	3.4±0.8	3.3±0.8	3.5±0.8	1.029	.305
Responsiveness	3.4±0.7	3.4±0.6	3.5±0.8	0.830	.408
Authoritarian	2.4±0.5	2.4±0.4	2.5±0.5	1.276	.204
Verbal hostility	2.8±0.6	2.7±0.5	2.9±0.7	1.810	.073
Corporal punishment	2.0±0.5	2.0±0.5	2.1±0.5	0.376	.708
Non-reasoning/punitive strategies	2.0±0.5	1.9±0.6	2.0±0.5	0.943	.347
Directiveness	3.1±0.6	3.1±0.6	3.2±0.7	1.104	.272
Permissive	2.6±0.4	2.6±0.4	2.7±0.5	1.169	.245
Lacks follow through	3.0±0.6	3.0±0.5	3.1±0.7	1.214	.227
Ignoring misbehaviour	2.1±0.5	2.1±0.5	2.1±0.5	-0.437	.663
Lacks self-confidence	2.6±0.5	2.6±0.5	2.8±0.6	1.467	.145

Note: Continuous data were analysed by independent-samples t-test. *p<.05.

Table 13: Multivariate analysis of factors associated with comorbid anxiety disorder.

	Unadjusted OR [95% CI of OR]	p-value	*Adjusted OR [95% CI of OR]	p-value
Reciprocal Social Interaction Skills Qualitative Deficits	2.66 [1.83, 3.87]	<.001	2.68 [1.82, 3.95]	<.001
Maternal Mood Disorder	16.03 [2.96, 86.81]	.001	17.80 [2.86, 110.66]	.002
Attention-Deficit/Hyperactivity Disorder	15.78 [2.50, 99.71]	.003	16.00 [2.41, 106.28]	.004

Note: Hosmer and Lemeshow goodness-of-fit test, Chi-square statistics: 6.558, p=.585. *Odds ratio is adjusted by age and sex.

Discussion

The present study is the first local study examining the factors associated with anxiety disorders among school-age autistic children based on the DSM-5 classification [2]. In accordance with past literature, higher level of qualitative deficits in reciprocal social interaction skills was found to be significantly associated with anxiety disorders in the present study [7,10,15,62]. Several processes have been proposed to underlie the link between anxiety and social functioning. First, children with deficits in social skills are likely to have greater difficulties in forming and maintaining peer relationships, which could induce stress and loneliness. Evidence has shown that autistic children who harbour a greater sense of social loneliness experience a higher level of anxiety [72]. Second, the likelihood of negative peer interaction is increased in the presence of deficits in social functioning [8,64]. As shown in the present study, social exclusion was significantly more common among children with anxiety disorders than among those without anxiety disorder ($p < .001$). Adverse social experiences as such could in turn precipitate a vicious cycle of social avoidance and anxiety. Third, anxiety could conversely undermine social functioning [14]. Through reinforcing social avoidance and withdrawal, anxiety reduces one's opportunities to exercise and refine learned social skills, and thereby perpetuates deficits in social functioning. Social functioning and anxiety are closely related and should be addressed concomitantly in therapy. To better understand the causal nature and dynamic interaction of this relationship over time, longitudinal examination is warranted.

The present study revealed a high comorbidity rate between ASD and ADHD (52.3%), concurring with both local and overseas evidence [35,38,57]. Comorbid ADHD was shown to be significantly associated with anxiety disorders in autistic children. Autistic children with comorbid ADHD are speculated to face more complex difficulties throughout their growth and development. Compared to children with a sole ASD diagnosis, those with comorbid ADHD have been found to associate with lower adaptive functioning, greater conduct problems and higher ASD symptom severity, specifically in the domain of social functioning [3,35,49,59,76]. Impairment has been shown to affect various aspects of an individual including home life, classroom learning and leisure activity [35]. These factors could all potentially contribute to their greater distress, lower quality of life and higher susceptibility to anxiety development [35,56]. Our findings carry strong implications for clinicians to specifically assess anxiety symptoms during the diagnostic process of ASD, notably in those with comorbid ADHD.

The present study also found significant association between maternal mood disorder and anxiety disorders in autistic children, which echoes findings from researches conducted on typically developing children [6,21,43,71,72,]. The mechanism underlying the association is believed to be interplay between genetic and environmental influences. Research has indicated genetic determinants as a substantial source of familial aggregation in anxiety disorders, as supported by family, twin, and high-risk studies. Heritability across anxiety disorders is estimated to range between 30% to 40% [25], supporting a genetic contribution. Environmental factors are likely to contribute to the remaining variance. Several processes have been proposed. It is hypothesised that children learn anxiety through parental modelling. As proposed in Bandura's social learning theory, children learn behaviour expressed by their parents through vicarious learning [4]. Mothers who are depressed or anxious tend

to demonstrate catastrophic and negative interpretations of situations, producing anxiety-related learning experiences for their children. With prolonged contact, children may gradually internalise and mimic fearful behaviour expressed by their depressed or anxious mothers, contributing to their own development of anxiety [17]. Conversely, children could influence the psychological well-being of their parents. Children with anxiety disorders could present with various emotional and behavioural problems, which could in turn induce stress and anxiety in their parents [24]. Maternal depression has been shown to be associated with infant attachment insecurity [5], while attachment insecurity is considered closely related to anxiety disorders in children [70]. Considering that autistic children generally have lower attachment security than typically developing children [52,65], the presence of maternal mood disorder could further impede the formation of attachment security, thereby increasing children's vulnerability in developing anxiety disorders [70]. The relationship between childhood anxiety disorders and maternal mood disorder is complex and is speculated to be reciprocal over time.

Bivariate analysis showed significantly higher levels of parenting stress among mothers of children with anxiety disorders than mothers of those without anxiety disorders, $t(130)=4.243$, $p < .001$, while the parenting stress levels between fathers of children with and without anxiety disorders showed no statistically significant difference, $t(130)=1.081$, $p = .282$. Subsequent multivariate analysis revealed no significant association between anxiety disorders and the parenting stress in both mothers and fathers. A previous study that demonstrated an association between parenting stress and children's anxiety had based their assessment of anxiety on a dimensional approach in symptom measurement [51]. In contrast, the present study adopted a categorical approach in generating diagnosis of anxiety disorders. With the use of a categorical approach, the association between parenting stress and anxiety symptoms that had not reached a diagnostic cut-off of an anxiety disorder would have been masked. Furthermore, the association between parenting stress and children's anxiety disorders could be mediated by other factors, such as parents' stress coping behaviour and their level of social support. Looking at the overall sample, mothers were found to have significantly higher parenting stress ($M=84.9$, $SD=18.6$) than fathers ($M=68.8$, $SD=11.1$), $t(214)=-8.045$, $p < .001$. Mothers of children with anxiety disorders were revealed to have a mean PSI-SF total stress score ($M=94.0$, $SD=18.4$) exceeding the 90th percentile, indicating clinically significant level of parenting stress that required professional assistance. Our results echo the findings of a local study that revealed significant parenting stress among mothers of autistic children [77]. Despite the absence of significant association shown in the present study, parenting stress should not be overlooked in the assessment of autistic children and should be managed accordingly. Further research is required to tease out the potential mediating variables between maternal parenting stress and anxiety disorders in autistic children.

The present study has several strengths. First, computer-generated simple random sampling was adopted to minimise sampling bias. Second, the adoption of a sample with a narrow age range allowed focused examination of the clinical profile of anxiety disorders in school-age autistic children. Third, the study had a high response rate of 94%, and a relatively large sample size in comparison to previous studies. Fourth, highly structured diagnostic interviews were used to establish the diagnoses of ASD and anxiety disorders, providing results with

high diagnostic validity and reliability. Finally, this was the first local study examining the associated factors of anxiety disorders in autistic children based on the DSM-5 diagnostic criteria [2]. Nevertheless, the findings should be interpreted in the context of the following methodological limitations. First, this study had a cross-sectional design, causality between anxiety disorders and the associated factors could therefore not be established. To better understand causality and the longitudinal course of illness, prospective follow-up studies are warranted. Second, the sample was recruited from a child and adolescent psychiatry outpatient clinic. Selection bias was potentially introduced, and the sample may not be a true representation of all autistic children. Third, the assessments relied solely on parents as informants, introducing potential informant bias. Without information from other informants, the results may be an incomplete reflection of a child's condition. Finally, this study lacked a control group. It would be highly beneficial for future studies to include controls to allow direct comparison between autistic children and typically developing children

Conclusion

Anxiety disorders are prevalent among Chinese school-age autistic children in Hong Kong. This study enriches our understanding of the associated factors of anxiety disorders in this population of children. Early recognition and identification of comorbid anxiety disorders are necessary in the diagnostic process of ASD. Extra attention should be given to children with a comorbid diagnosis of ADHD, given its significant association with anxiety disorders. Considering the significant association between maternal mood disorder and anxiety disorders in autistic children, evaluation of parents' psychiatric profiles is highly indicated, in order to identify at-risk individuals and to tailor the support for both the children and their families. In light of the significant association between anxiety disorders and reciprocal social interaction skills, it is implied that anxiety-related and ASD-related deficits should not be viewed as separate entities in therapy. ASD therapy components such as social skills training should be incorporated as part of the treatment for anxiety disorders in autistic children. As shown in the present study and previous literature, autistic children are highly comorbid with ADHD, while ADHD is significantly associated with anxiety disorders. Adequate intervention should be implemented to optimise the control of ADHD symptoms in minimising the level of impairment experienced. The findings of the present study provide an important next step in the development of local services for autistic children with comorbid anxiety disorders. For future research directions, furthering our understanding of the aetiological pathways, course of illness, and outcome of anxiety disorders in autistic children is highly warranted.

References

- Abidin RR. Parenting Stress Index, Third Edition: Professional Manual. Odessa, FL: Psychological Assessment Resources, Inc. 1995.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Washington, DC: Author. 2013.
- Avni E, Ben-Itzhak E, Zachor DA. The presence of comorbid ADHD and anxiety symptoms in autism spectrum disorder: Clinical presentation and predictors. *Frontiers in Psychiatry*. 2018; 9: 717.
- Bandura A. Social learning theory. General Learning Corporation. 1973.
- Barnes J, Theule J. Maternal depression and infant attachment security: A meta-analysis. *Infant Mental Health Journal*. 2019; 40: 817-834.
- Beidel DC, Turner SM. At Risk for Anxiety: I. Psychopathology in the Offspring of Anxious Parents. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1997; 36: 918-924.
- Bellini S. The Development of Social Anxiety in Adolescents With Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities*. 2006; 21: 138-145.
- Cappadocia MC, Weiss JA, Pepler D. Bullying Experiences Among Children and Youth with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*. 2012; 42: 266-277.
- Census and Statistics Department. Population Census. 2011.
- Chang Y, Quan J, Wood JJ. Effects of Anxiety Disorder Severity on Social Functioning in Children with Autism Spectrum Disorders. *Journal of Developmental and Physical Disabilities*. 2012; 24: 235-245.
- Chorpita BF, Barlow DH. The development of anxiety: The role of control in the early environment. *Psychological Bulletin*. 1998; 124: 3-21.
- Craig F, Lamanna AL, Margari F, Matera E, Simone M, et al. Overlap between autism spectrum disorders and attention deficit hyperactivity disorder: Searching for distinctive/Common clinical features. *Autism Research*. 2015; 8: 328-337.
- De Bruin EI, Ferdinand RF, Meester S, De Nijs PF, Verheij F. High Rates of Psychiatric Co-Morbidity in PDD-NOS. *Journal of Autism and Developmental Disorders*. 2007; 37: 877-886.
- Duvekot J, Ende J, Verhulst FC, Greaves-Lord K. Examining bidirectional effects between the autism spectrum disorder (ASD) core symptom domains and anxiety in children with ASD. *Journal of Child Psychology and Psychiatry*. 2017; 59: 277-284.
- Factor RS, Ryan SM, Farley JP, Ollendick TH, Scarpa A. Does the Presence of Anxiety and ADHD Symptoms Add to Social Impairment in Children with Autism Spectrum Disorder? *Journal of Autism and Developmental Disorders*. 2017; 47: 1122-1134.
- Farrugia S, Hudson J. Anxiety in adolescents with Asperger syndrome: Negative thoughts, behavioral problems, and life interference. *Focus on Autism and Other Developmental Disabilities*. 2006; 21: 25-35.
- Fisak B, Grills-Taquechel AE. Parental modeling, reinforcement, and information transfer: Risk factors in the development of child anxiety? *Clinical Child and Family Psychology Review*. 2007; 10: 213-231.
- Fu Y, Hou X, Qin Q, Meng H, Xie P, et al. Can Parenting Styles and Dimensions Questionnaire (PSDQ) Be Used in China? *Psychology*. 2013; 04: 535-540.
- Gillott A, Furniss F, Walter A. Anxiety in High-Functioning Children with Autism. *Autism*. 2001; 5: 277-286.
- Gjevik E, Eldevik S, Fjæran-Granum T, Sponheim E. Kiddie-SADS Reveals High Rates of DSM-IV Disorders in Children and Adolescents with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*. 2011; 41: 761-769.
- Goodman SH, Rouse MH, Connell AM, Broth MR, Hall CM, et al. Maternal depression and child psychopathology: A meta-analytic review. *Clinical Child and Family Psychology Review*. 2011; 14: 1-27.
- Green J, Gilchrist A, Burton D, Cox A. Social and Psychiatric Functioning in Adolescents with Asperger Syndrome Compared with Conduct Disorder. *Journal of Autism and Developmental Disorders*.

- ders. 2000; 30: 279-293.
23. Hayes SA, Watson SL. The Impact of Parenting Stress: A Meta-analysis of Studies Comparing the Experience of Parenting Stress in Parents of Children With and Without Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. 2012; 43: 629-642.
 24. Herring S, Gray K, Taffe J, Tonge B, Sweeney D, et al. Behaviour and emotional problems in toddlers with pervasive developmental disorders and developmental delay: associations with parental mental health and family functioning. *Journal of Intellectual Disability Research*. 2006; 50: 874-882.
 25. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *American Journal of Psychiatry*. 2001; 158: 1568-1578.
 26. Ho T, Leung PW, Lee C, Tang C, Hung S, et al. Test-retest reliability of the Chinese version of the Diagnostic Interview Schedule for Children-Version 4 (DISC-IV). *Journal of Child Psychology and Psychiatry*. 2005; 46: 1135-1138.
 27. Hodge D, Hoffman CD, Sweeney DP. Increased Psychopathology in Parents of Children with Autism: Genetic Liability or Burden of Caregiving? *Journal of Developmental and Physical Disabilities*. 2011; 23: 227-239.
 28. Ilias K, Cornish K, Kummar AS, Park MS, Golden KJ. Parenting Stress and Resilience in Parents of Children With Autism Spectrum Disorder (ASD) in Southeast Asia: A Systematic Review. *Frontiers in Psychology*. 2018; 9: 280.
 29. Ishimoto Y, Yamane T, Matsumoto Y. Anxiety levels of children with developmental disorders in Japan: Based on reports provided by parents. *Journal of Autism and Developmental Disorders*. 2019; 49: 3898-3905.
 30. Joshi G, Petty C, Wozniak J, Henin A, Fried R, et al. The Heavy Burden of Psychiatric Comorbidity in Youth with Autism Spectrum Disorders: A Large Comparative Study of a Psychiatrically Referred Population. *Journal of Autism and Developmental Disorders*. 2010; 40: 1361-1370.
 31. Kerns CM, Kendall PC, Zickgraf H, Franklin ME, Miller J, et al. Not to Be Overshadowed or Overlooked: Functional Impairments Associated With Comorbid Anxiety Disorders in Youth With ASD. *Behavior Therapy*. 2015; 46: 29-39.
 32. Kim JA, Szatmari P, Bryson SE, Streiner DL, Wilson FJ. The Prevalence of Anxiety and Mood Problems among Children with Autism and Asperger Syndrome. *Autism*. 2000; 4: 117-132.
 33. Koegel RL, Schreibman L, Loos LM, Dirlich-Wilhelm H, Dunlap G, et al. Consistent Stress Profiles in Mothers of Children with Autism. *Journal of Autism and Developmental Disorders*. 1992; 22: 205-216.
 34. Kuusikko S, Pollock-Wurman R, Jussila K, Carter AS, Mattila M, et al. Social Anxiety in High-functioning Children and Adolescents with Autism and Asperger Syndrome. *Journal of Autism and Developmental Disorders*. 2008; 38: 1697-1709.
 35. Kwok CY, Lai YC, Luk SL, Hung SF, Leung WL. Prevalence of Comorbid Attention Deficit Hyperactivity Disorder (ADHD) in Chinese Hong Kong Children with Autism Spectrum Disorder (ASD). *Austin Journal of Autism & Related Disabilities*. 2017; 3: 1044.
 36. Lai KY, Leung PW, Mo FY, Lee MM, Shea CK, et al. Validation of the Developmental, Dimensional and Diagnostic Interview (3Di) Among Chinese Children in a Child Psychiatry Clinic in Hong Kong. *Journal of Autism and Developmental Disorders*. 2014; 45: 1230-1237.
 37. Leung PW, Hung S, Ho T, Lee C, Liu W, et al. Prevalence of DSM-IV disorders in Chinese adolescents and the effects of an impairment criterion. *European Child & Adolescent Psychiatry*. 2008; 17: 452-461.
 38. Leyfer OT, Folstein SE, Bacalman S, Davis NO, Dinh E, et al. Comorbid Psychiatric Disorders in Children with Autism: Interview Development and Rates of Disorders. *J Autism Dev Disord*. 2006; 36: 849-861.
 39. March JS, Swanson JM, Arnold LE, Hoza B, Conners CK, et al. Anxiety as a Predictor and Outcome Variable in the Multimodal Treatment Study of Children with ADHD (MTA). *Journal of Abnormal Child Psychology*. 2000; 28: 527-541.
 40. Mattila M, Hurtig T, Haapsamo H, Jussila K, Kuusikko-Gauffin S, et al. Comorbid Psychiatric Disorders Associated with Asperger Syndrome/High-functioning Autism: A Community- and Clinic-based Study. *Journal of Autism and Developmental Disorders*. 2010; 40: 1080-1093.
 41. Mayes SD, Calhoun SL, Murray MJ, Zahid J. Variables associated with anxiety and depression in children with autism. *Journal of Developmental and Physical Disabilities*. 2011; 23: 325-337.
 42. Mayes SD, Calhoun SL, Murray MJ, Ahuja M, Smith LA. Anxiety, depression, and irritability in children with autism relative to other neuropsychiatric disorders and typical development. *Research in Autism Spectrum Disorders*. 2011; 5: 474-485.
 43. McClure EB, Brennan PA, Hammen C, Le Brocque RM. Parental Anxiety Disorders, Child Anxiety Disorders, and the Perceived Parent-Child Relationship in an Australian High-Risk Sample. *Journal of Abnormal Child Psychology*. 2001; 29: 1-10.
 44. McLeod BD, Wood JJ, Weisz JR. Examining the association between parenting and childhood anxiety: A meta-analysis. *Clinical Psychology Review*. 2007; 27: 155-172.
 45. Mukaddes NM, Fateh R. High rates of psychiatric co-morbidity in individuals with Asperger's disorder. *World Journal of Biological Psychiatry*. 2010; 1-7.
 46. Mukaddes NM, Hergüner S, Tanidir C. Psychiatric disorders in individuals with high-functioning autism and Asperger's disorder: Similarities and differences. *The World Journal of Biological Psychiatry*. 2010; 11: 964-971.
 47. Muris P, Steerneman P, Merckelbach H, Holdrinet I, Meesters C. Comorbid Anxiety Symptoms in Children with Pervasive Developmental Disorders. *Journal of Anxiety Disorders*. 1998; 12: 387-393.
 48. Powell B, Cooper G, Hoffman K, Marvin B. *The Circle of Security: Enhancing Attachment in Early Parent-Child Relationships*. NY: Guilford Press. 2014.
 49. Rao PA, Landa RJ. Association between severity of behavioral phenotype and comorbid attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders. *Autism*. 2013; 18: 272-280.
 50. Robinson CC, Mandleco B, Olsen SF, Hart CH. Authoritative, Authoritarian, and Permissive Parenting Practices: Development of a New Measure. *Psychological Reports*. 1995; 77: 819-830.
 51. Rodriguez CM. Association Between Independent Reports of Maternal Parenting Stress and Children's Internalizing Symptomatology. *Journal of Child and Family Studies*. 2011; 20: 631-639.
 52. Rutgers AH, Bakermans-Kranenburg MJ, Ijzendoorn MH, Berckelaer-Onnes IA. Autism and attachment: A meta-analytic review. *Journal of Child Psychology and Psychiatry*. 2004; 45: 1123-1134.
 53. Salazar F, Baird G, Chandler S, Tseng E, O'sullivan T, et al. Co-

- occurring Psychiatric Disorders in Preschool and Elementary School-Aged Children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. 2015; 45: 2283-2294.
54. Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, Differences From Previous Versions, and Reliability of Some Common Diagnoses. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2000; 39: 28-38.
 55. Shea CK, Lee MM, Lai KY, Luk ES, Leung PW. Prevalence of anxiety disorders in Hong Kong Chinese children with ADHD. *Journal of Attention Disorders*. 2014; 22: 403-413.
 56. Sikora DM, Vora P, Coury DL, Rosenberg D. Attention-deficit/Hyperactivity disorder symptoms, adaptive functioning, and quality of life in children with autism spectrum disorder. *Pediatrics*. 2012; 130: S91-S97.
 57. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, et al. Psychiatric Disorders in Children With Autism Spectrum Disorders: Prevalence, Comorbidity, and Associated Factors in a Population-Derived Sample. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2008; 47: 921-929.
 58. Skuse D, Warrington R, Bishop D, Chowdhury U, Lau J, et al. The Developmental, Dimensional and Diagnostic Interview (3di): A Novel Computerized Assessment for Autism Spectrum Disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2004; 43: 548-558.
 59. Sprenger L, Bühler E, Poustka L, Bach C, Heinzl-Gutenbrunner M, et al. Impact of ADHD symptoms on autism spectrum disorder symptom severity. *Research in Developmental Disabilities*. 2013; 34: 3545-3552.
 60. Steinberg L, Elmen JD, Mounts NS. Authoritative Parenting, Psychosocial Maturity, and Academic Success among Adolescents. *Child Development*. 1989; 60: 1424-36.
 61. Stone LL, Mares SH, Otten R, Engels RC, Janssens JM. The Co-Development of Parenting Stress and Childhood Internalizing and Externalizing Problems. *Journal of Psychopathology and Behavioral Assessment*. 2016; 38: 76-86.
 62. Sukhodolsky DG, Scahill L, Gadow KD, Arnold LE, Aman MG, et al. Parent-Rated Anxiety Symptoms in Children with Pervasive Developmental Disorders: Frequency and Association with Core Autism Symptoms and Cognitive Functioning. *Journal of Abnormal Child Psychology*. 2008; 36: 117-128.
 63. Tam K, Chan Y, Wong CM. Validation of the parenting stress index among Chinese mothers in Hong Kong. *Journal of Community Psychology*. 1994; 22: 211-223.
 64. Tantam D. Psychological disorder in adolescents and adults with Asperger syndrome. *Autism*. 2000; 4: 47-62.
 65. Teague SJ, Gray KM, Tonge BJ, Newman LK. Attachment in children with autism spectrum disorder: A systematic review. *Research in Autism Spectrum Disorders*. 2017; 35: 35-50.
 66. Van Steensel FJ, Bögels SM, Perrin S. Anxiety Disorders in Children and Adolescents with Autistic Spectrum Disorders: A Meta-Analysis. *Clinical Child and Family Psychology Review*. 2011; 14: 302-317.
 67. Van Steensel FJ, Heeman EJ. Anxiety Levels in Children with Autism Spectrum Disorder: A Meta-Analysis. *Journal of Child and Family Studies*. 2017; 26: 1753-1767.
 68. Vaughan EL, Feinn R, Bernard S, Brereton M, Kaufman JS. Relationships Between Child Emotional and Behavioral Symptoms and Caregiver Strain and Parenting Stress. *Journal of Family Issues*. 2012; 34: 534-556.
 69. Wang J, Hu YJ, Wang Y, Qin XQ, Xia W, et al. Parenting stress in Chinese mothers of children with autism spectrum disorders. *Social Psychiatry and Psychiatric Epidemiology*. 2013; 48: 575-582.
 70. Warren SL, Huston L, Egeland B, Sroufe LA. Child and Adolescent Anxiety Disorders and Early Attachment. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1997; 36: 637-644.
 71. Weissman MM, Wickramaratne P, Nomura Y, Warner V, Pilowsky D, et al. Offspring of depressed parents: 20 years later. *American Journal of Psychiatry*. 2006; 163: 1001-1008.
 72. White SW, Roberson-Nay R. Anxiety, Social Deficits, and Loneliness in Youth with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*. 2009; 39: 1006-1013.
 73. Wolfradt U, Hempel S, Miles JN. Perceived parenting styles, de-personalisation, anxiety and coping behaviour in adolescents. *Personality and Individual Differences*. 2003; 34: 521-532.
 74. Wood JJ, McLeod BD, Sigman M, Hwang W, Chu BC. Parenting and childhood anxiety: theory, empirical findings, and future directions. *Journal of Child Psychology and Psychiatry*. 2003; 44: 134-151.
 75. Yeh C, Chen M, Li W, Chuang H. The Chinese version of the Parenting Stress Index: a psychometric study. *Acta Paediatrica*. 2001; 90: 1470-1477.
 76. Yerys BE, Bertollo JR, Pandey J, Guy L, Schultz RT. Attention-deficit/Hyperactivity disorder symptoms are associated with lower adaptive behavior skills in children with autism. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2019; 58: 525-533.e3.
 77. Yu YW, Chung KH, Lee YK, Lam WC, Yiu GC. Prevalence of Maternal Affective disorders in Chinese Mothers of Preschool Children with Autism Spectrum Disorders. *East Asian Arch Psychiatry*. 2016; 26: 121-8.