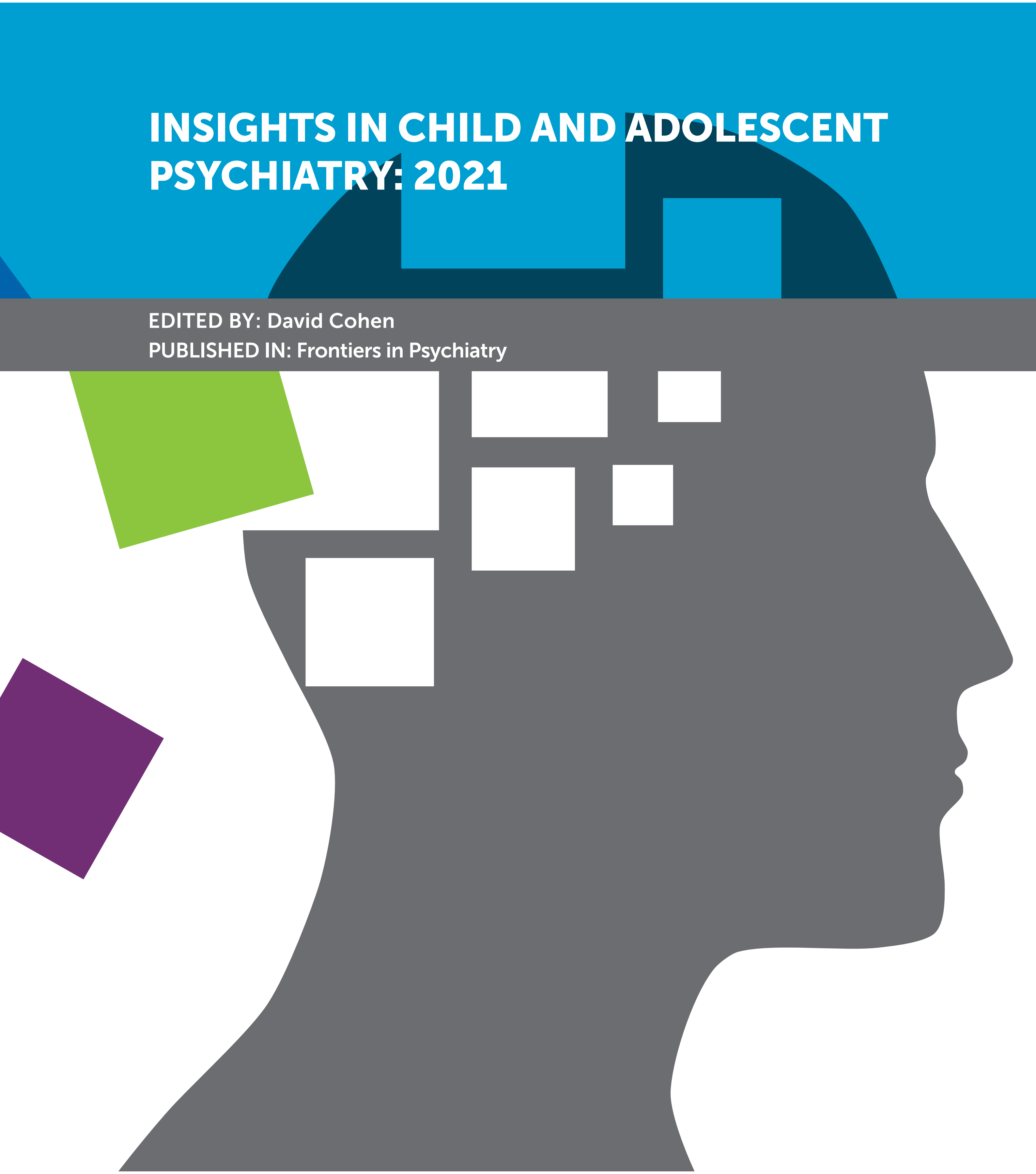
INSIGHTS IN CHILD AND ADOLESCENT PSYCHIATRY: 2021

EDITED BY: David Cohen
PUBLISHED IN: Frontiers in Psychiatry



frontiers Research Topics

ISSN 1664-8714
ISBN 978-2-83250-040-8
DOI 10.3389/978-2-83250-040-8

About Frontiers

Frontiers is more than just an open-access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers Journal Series

The Frontiers Journal Series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the Frontiers Journal Series operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to Quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews.
Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view.
By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the Frontiers Journals Series: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area! Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers Editorial Office: frontiersin.org/about/contact

INSIGHTS IN CHILD AND ADOLESCENT PSYCHIATRY: 2021

Topic Editor:
David Cohen, Sorbonne Universités, France

Citation: Cohen, D., ed. (2022). Insights in Child and Adolescent Psychiatry: 2021. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-83250-040-8

Table of Contents

04 ***Studies on Children With Developmental Coordination Disorder in the Past 20 Years: A Bibliometric Analysis*** **via** ***CiteSpace***
Mei-Qin Wu, De-Qing Wu, Chun-Ping Hu and Lai-Sang Iao

14 ***Individual, Prenatal, Perinatal, and Family Factors for Anxiety Symptoms Among Preschool Children***
Xiuxiu Ding, Jun Wang, Ning Li, Wanying Su, Hao Wang, Qiuxia Song, Xianwei Guo, Mingming Liang, Qirong Qin, Liang Sun, Mingchun Chen and Yehuan Sun

25 ***Change Blindness in Adolescents With Attention-Deficit/Hyperactivity Disorder: Use of Eye-Tracking***
Michal Hochhauser, Adi Aran and Ouriel Grynszpan

35 ***Clinical Implementation and Evaluation of Three Implementation Interventions for a Family-Oriented Care for Children of Mentally Ill Parents (ci-chimps): Study Protocol for a Randomized Controlled Multicenter Trial***
Carolin Laser, Anna Modarressi, Bjørg Eva Skogøy, Andrea Reupert, Anne Daubmann, Alexandra Höller, Antonia Zapf, Silke Pawils, Svenja Taubner, Sibylle Winter, Darryl Maybery and Silke Wiegand-Grefe

44 ***Psychometric Properties of the Interpersonal Needs Questionnaire-15 in Spanish Adolescents***
Sandra Pérez Rodríguez, Joaquín García-Alandete, Blanca Gallego Hernández de Tejada, Verónica Guillén and Jose Heliodoro Marco

53 ***A Multi-Center Study on the Relationship Between Developmental Regression and Disease Severity in Children With Autism Spectrum Disorders***
Chaoqun Hu, Fan Yang, Ting Yang, Jie Chen, Ying Dai, Feiyong Jia, Lijie Wu, Yan Hao, Ling Li, Jie Zhang, Xiaoyan Ke, Mingji Yi, Qi Hong, Jinjin Chen, Shuanfeng Fang, Yichao Wang, Qi Wang, Chunhua Jin, Tingyu Li and Li Chen

60 ***Patterns of Care for Adolescent With Schizophrenia: A Delphi-Based Consensus Study***
Antonio Vita, Stefano Barlati, Antonello Bellomo, Paolo Fusar Poli, Gabriele Masi, Lino Nobili, Gianluca Serafini, Alessandro Zuddas and Stefano Vicari

81 ***School Refusal in Immigrants and Ethnic Minority Groups: A Qualitative Study of Adolescents' and Young Adults' Experiences***
Camille Brault, Isaiah Thomas, Marie Rose Moro and Laelia Benoit

92 ***School-Based Mental Health Initiative: Potentials and Challenges for Child and Adolescent Mental Health***
Kelly Y. C. Lai, Se-Fong Hung, Hannah W. S. Lee and Patrick W. L. Leung

102 ***Attention for Emotion—How Young Adults With Neurodevelopmental Disorders Look at Facial Expressions of Affect***
Jana Bretthauer, Daniela Canu, Ulf Thiemann, Christian Fleischhaker, Heike Brauner, Katharina Müller, Nikolaos Smyrnis, Monica Biscaldi, Stephan Bender and Christoph Klein

frontiers in Psychiatry

REVIEW
published: 06 December 2021
doi: 10.3389/fpsyt.2021.776883

Studies on Children With Developmental Coordination Disorder in the Past 20 Years: A Bibliometric Analysis *via* CiteSpace

Mei-Qin Wu[1]*†, De-Qing Wu[2]†, Chun-Ping Hu[3] and Lai-Sang Iao[4]

[1] Shanghai Key Laboratory of Maternal Fetal Medicine, Department of Women's and Children's Health Care, Shanghai First Maternity and Infant Hospital, School of Medicine, Tongji University, Shanghai, China, [2] Department of Gastroenterology, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai, China, [3] School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [4] Department of Psychology, Nottingham Trent University, Nottingham, United Kingdom

OPEN ACCESS

Edited by:
Kerim Munir,
Boston Children's Hospital,
United States

Reviewed by:
Eloisa Tudella,
Federal University of São Carlos, Brazil
John Cairney,
The University of Queensland, Australia

***Correspondence:**
Mei-Qin Wu
wmqmaomao@163.com

†These authors have contributed equally to this work

Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: *14 September 2021*
Accepted: *02 November 2021*
Published: *06 December 2021*

Citation:
Wu M-Q, Wu D-Q, Hu C-P and Iao L-S (2021) Studies on Children With Developmental Coordination Disorder in the Past 20 Years: A Bibliometric Analysis via CiteSpace. Front. Psychiatry 12:776883. doi: 10.3389/fpsyt.2021.776883

Children with developmental coordination disorder (DCD) have been commonly observed and drawn an increasing amount of attention over the past decades. The aim of the present study is to evaluate the origin, current hotspots, and research trends on children with DCD using a bibliometric tool. After searching with "children" and "developmental coordination disorder" as the "topic" and "title" words, respectively, 635 original articles with 12,559 references were obtained from the electronic databases, Web of Science Core Collection (WoSCC). CiteSpace V.5.7.R2 was used to perform the analysis. The number of publications in this field was increasing over the past two decades. John Cairney from the Department of Family Medicine, McMaster University, Canada, was found to be the most productive researcher. Meanwhile, McMaster University and Canada were the most productive research institution and country, respectively. Reference and journal co-citation analyses revealed the top landmark articles and clusters in this field. *Clumsiness* was the most strength burst keyword. Moreover, *task*, *meta-analysis*, *difficulty*, *adult*, and *impact* will be the active research hotspots in future. These findings provide the trends and frontiers in the field of children with DCD, and valuable information for clinicians and scientists to identify new perspectives with potential collaborators and cooperative countries.

Keywords: developmental coordination disorder, children, web of science, data visualization, burst detection

INTRODUCTION

Children with developmental coordination disorder (DCD) exhibit severe motor clumsiness that interferes with academic achievement and the activities of daily living (1). Symptoms of DCD occur in the early stage of development, but it is often not identified until school age, leaving missed good opportunities for early intervention (2). These children have previously been described with a variety of terms such as developmental dyspraxia, minimal brain dysfunction, perceptual-motor dysfunction, physical awkwardness, or, most commonly, the clumsy child syndrome (3, 4). In 1994, these children were collectively referred to as DCD at an international consensus meeting which held in London, Ontario (5).

In recent years, there has been growing recognition of the consequences, outcomes, and burden for children with DCD. However, after the London consensus meeting, DCD, as a unified terminology, lacks systematic research on global research trends and hotspots in this field. Evaluative bibliometrics is a field of quantitative science that has emerged as a powerful tool to evaluate research performance, which can serve to identify influential articles that have shaped medical practice and fostered new research ideas (6).

CiteSpace, one of the bibliometric analysis tools, which was invented by Dr. Chaomei Chen (School of Information Science and Technology, Drexel University, Philadelphia, PA, USA), has been widely used in other research fields (7–9). Professor Chen Chaomei, as the inventor of CiteSpace, published a visual analysis of the emerging research trends in the field of regenerative medicine, on the Expert Opinion on Biological Therapy in May 2012 (10). This study accurately predicted the winner of the 2012 Nobel Prize in physiology/medicine, the Japanese scholar Shinya Yamanaka (11, 12). This empirical study shows that CiteSpace software plays an important role in literature mining.

However, to the best of our knowledge, CiteSpace analysis has not been reported in the field of children with DCD. In this study, the literatures related to children with DCD were collected and screened to form a specific database. Then, CiteSpace was used to perform statistical calculations and further generate visualization results for different node types. The purpose of this article is to clearly visualize and explain the origin and major milestones of the research in children with DCD, after DCD was used as a unified terminology.

METHODS

Data Source

The retrieval data for measurements and statistical analysis were screened from the Web of Science Core Collection (WoSCC), which provides citation search, giving access to multiple databases that reference cross-disciplinary research and allowing for an in-depth exploration of specialized subfields (13).

Search Strategy

All data were obtained from WoSCC on May 10, 2021; the data retrieval strategy was as follows: (i) Topic = children and Title = developmental coordination disorder; (ii) Document type = article; (iii) Language = English; (iv) Timespan (custom year range) = 2000–2019. Full records and cited references were selected as plain text format and downloaded for further analysis.

Analysis Tool

This study utilized CiteSpace V.5.7.R2 to analyze existing studies related to children with DCD, aiming to provide scientific and intuitive support for clinicians and researchers in this field. CiteSpace, which was created by Dr. Chaomei Chen (School of Information Science and Technology, Drexel University, Philadelphia, PA, USA) and his team in early 2004 (14), was used to perform the bibliometric analysis in this study. CiteSpace is a Java application which combines information visualization methods, bibliometrics, and data mining algorithms in an interactive visualization tool.

Data Analysis

Two separate folders for the DCD project were created. One folder contains data files which were just downloaded. The other folder is the project folder. We did not find duplicate documents that needed to be deleted. The overall selected time span was from January 2000 to December 2019. Then, the time span was sliced into 10 parts corresponding to 10 different colors, each of which was 2 years. The node type was selected according to the type of analysis performed. The size of the circles represents the number of papers published by the country/region, institute or author. The shorter the distance between two circles, the greater the cooperation between the two countries/regions, institutes or authors. Purple rings indicate that these countries/regions, institutes or authors have greater centrality (no <0.1).

RESULTS

General Data

The initial search for children with DCD resulted in 635 original articles published in English between 2000 and 2019, without duplicate record. According to the publication years, although with some fluctuations, the quantity of published articles on children with DCD increased significantly over the studied period, especially from 2005 to 2008, with an average annual growth rate of 65.10% (**Figure 1**).

Quantitative and Cooperation Analysis

Countries/Regions

Figure 2 displays the cooperation network of the productive countries/regions. The size of circles represents the number of publications of countries/regions, and the shorter distance between two circles suggests the more collaboration between individual countries/regions. The purple rings outside the circle refer to centrality. Canada (137) ranks first in the publication quantity, which is followed by England (114) and Australia (104). The top 10 prolific countries/territories in this research field are shown in **Table 1**, which are sorted out from the network summary table.

Institutes

Figure 3 exhibits the major productive co-institutes in the field of children with DCD. The Canadian McMaster University is the most productive and influential institute in this field, with a total number of 54 published articles, and the centrality of 0.74. Brock University, which ranks second in productivity, also locates in Canada. The top 10 prolific institutes in this research field are shown in **Table 2**.

Abbreviations: BOT-2, Bruininks–Oseretsky Test of Motor Proficiency, Second Edition; DCD, developmental coordination disorder; DSM-V, Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition; EACD, European Academy for Childhood Disability; LLR, log-likelihood ratio; MABC-2, Movement Assessment Battery for Children, Second Edition; SOT, sensory organization test; WoSCC, Web of Science Core Collection.

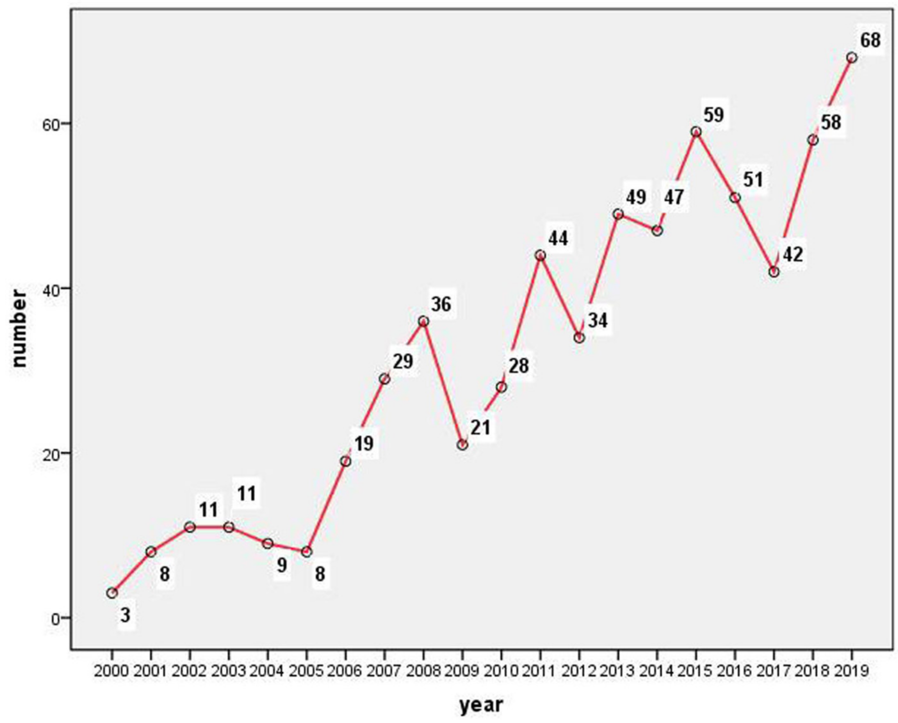


FIGURE 1 | The number of children with DCD publications indexed by WoSCC, 2000–2019.

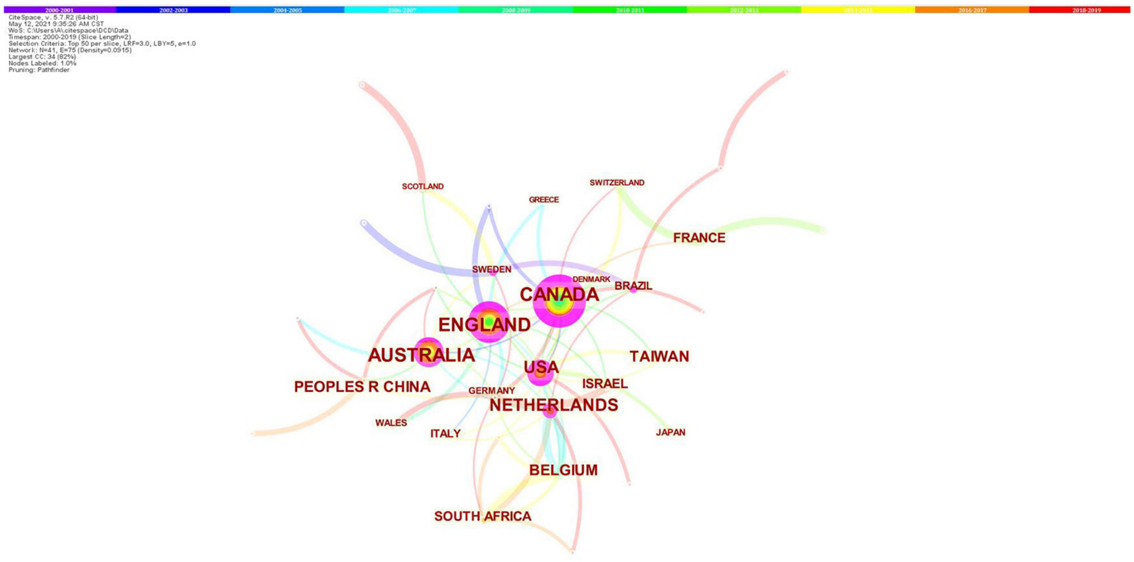


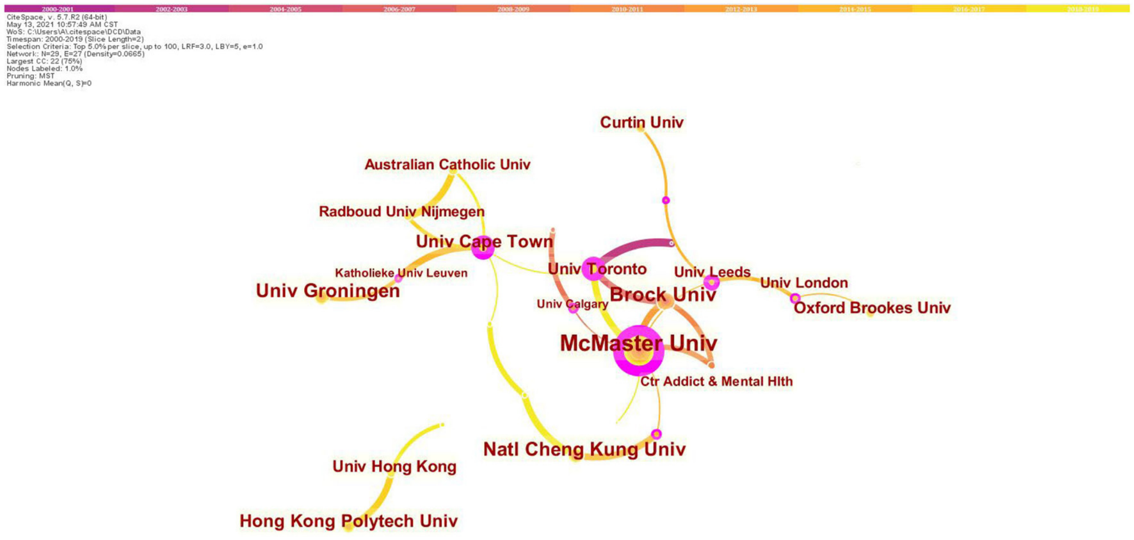
FIGURE 2 | Map of countries/regions cooperative relations in research of children with DCD, 2000–2019. The bigger the circle, the more original articles the country/region published. The shorter and thicker the connection line, the closer the relationship.

Authors

Figure 4 is the co-authorship network map generated by CiteSpace. Regarding the authors who were active, John Cairney from the Department of Family Medicine, McMaster University, Canada, ranks the first (40 publications), followed by Chialiang Tsai from the Institute of Physical Education, Health and Leisure Studies, National Cheng Kung University, Taiwan (22 publications). The top 10 authors are presented in **Table 3**.

TABLE 1 | Top 10 prolific countries/regions in research of children with DCD, 2000–2019.

Ranking	Country/region	Frequency	Centrality	Ranking	Country/region	Frequency	Centrality
1	CANADA	137	0.44	6	TAIWAN	51	0.00
2	ENGLAND	114	0.24	7	BELGIUM	36	0.04
3	AUSTRALIA	104	0.15	8	PEOPLES R CHINA	36	0.10
4	USA	73	0.37	9	SOUTH AFRICA	31	0.02
5	NETHERLANDS	72	0.13	10	FRANCE	26	0.08



```
CiteSpace, v. 5.7.R2 (64-bit)
May 13, 2021 10:57:49 AM CST
WoS: C:\Users\A\.citespace\DCD\Data
Timespan: 2000-2019 (Slice Length=2)
Selection Criteria: Top 5.0% per slice, up to 100, LRF=3.0, LBY=5, e=1.0
Network: N=29, E=27 (Density=0.0665)
Largest CC: 22 (75%)
Nodes Labeled: 1.0%
Pruning: MST
Harmonic Mean(Q, S)=0
```

FIGURE 3 | Map of institutes' cooperative relations in research of children with DCD, 2000–2019. The bigger the circle, the more original articles the institute published. The shorter and thicker the connection line, the closer the relationship.

TABLE 2 | Top 10 prolific institutes in research of children with DCD, 2000–2019.

Ranking	Institute	Frequency	Centrality
1	McMaster University	54	0.74
2	Brock University	27	0.02
3	University of Groningen	24	0.00
4	Natl Cheng Kung University	22	0.07
5	University of Cape Town	20	0.46
6	Hong Kong Polytechnic University	19	0.00
7	University of Toronto	15	0.48
8	Oxford Brookes University	15	0.00
9	University of Hong Kong	14	0.01
10	Curtin University	13	0.00

Research Topic Analysis

Reference Co-citation

After selecting reference as node type for statistical analysis, it shows that 635 original records containing 12,559 references were primary downloaded and entered the database. Colors, moving from purple to yellow, indicate the citation time from 2000 to 2019, respectively. The clusters are named by extracting nominal terms as labels from the titles of the cited articles. The LLR (log-likelihood ratio) algorithm is used as the extraction method. **Figure 5** shows a cluster visualization of the reference co-citation network which is divided into six co-citation clusters including 0# manual dexterity, 1# m shuttle run, 2# sensory organization, 3# suspected DCD, 4# age hypothesis, and 5# physical fitness. The summary of the largest five clusters is shown in **Table 4**.

The top ranked article by citation counts (**Table 5**) is American Psychiatric Association (15) in Cluster #0, with citation counts of 111. The second one is Blank et al. (16) in Cluster #3, with citation counts of 85. The third is Wilson et al. (17) in Cluster #0, with citation counts of 75. The fourth is Zwicker et al. (3) in Cluster #3, with citation counts of 44.

Journal/Instruction Manual Co-citation

A total of 12,559 citation references are from different journals/instruction manuals. **Table 6** lists the top 10 highly cited journals/instruction manuals. The highest cited journal is the Developmental Medicine and Child Neurology, with 548 citations, followed by the Journal of Human Movement Science (547) and Movement Assessment Battery for Children (462).

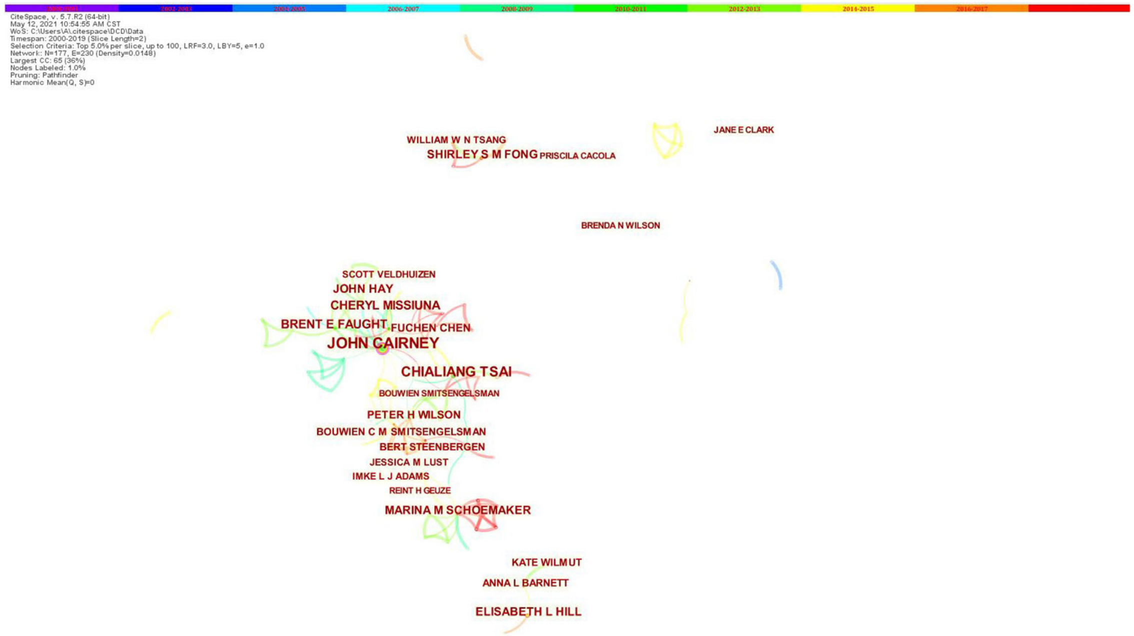


FIGURE 4 | Co-authorship network map in research of children with DCD, 2000–2019. The bigger the circle, the more original articles the author published. The shorter and thicker the connection line, the closer relationship between authors.

TABLE 3 | Top 10 active authors in research of children with DCD, 2000–2019.

Ranking	Author	Publications	Centrality
1	John Cairney	40	0.16
2	Chialiang Tsai	22	0.04
3	Brent E Faught	18	0.03
4	Cheryl Missiuna	17	0.07
5	Elisabeth L. Hill	16	0.00
6	John Hay	14	0.03
7	Shirley S. M. Fong	13	0.00
8	Marina M. Schoemaker	13	0.06
9	Peter H. Wilson	12	0.05
10	Fuchen Chen	11	0.02

Future Research Direction Analysis

The burst detection in CiteSpace is based on Kleinberg's algorithm, which based on modeling the stream using an infinite-state automaton to extract a meaningful structure from document streams that arrive continuously over time (19). These analyses can show the fast-growing topics that last for multiple years as well as a single year. **Figure 6** shows the top 25 keywords with the strongest citation bursts in published articles on children with DCD. The blue line represents the time interval, and the red line refers to the duration of the citation burst. In the keyword's citation burst detection analysis, clumsiness is the strongest burst keyword that appeared in 2000 with the burst strength of 15.15, followed by clumsy children (11.43), motor skill (5.86), and age (5.49). Five frontiers in the field of children with DCD that have impacts on future research are task, meta-analysis, difficulty, adult, and impact.

DISCUSSION

Quantity and Cooperation Analysis

In this study, we utilized information visualization to analyze original articles on children with DCD published from 2000 through 2019. Before the expert meeting 1994, a wide variation in terminology and diagnostic criteria was used to describe children with DCD, hampering the external validity of the scoping review. In 2001, a survey of 234 professionals from the UK, including doctors, occupational therapists, and speech therapists, found that the term "dyspraxia" is much more widely used in the UK rather than DCD (20). So, in 2012, the European Academy for Childhood Disability (EACD) published the recommendations on the definition, diagnosis, and intervention of DCD (16). Unified nomenclature is very critical and the most basic requirement for the diagnosis and treatment of a clinical disease in the later stage. In this study, we identified an increasing number of scientific research publications over the last 20-year period. However, it can be seen from **Figure 1** that the quantity of papers published before 2005 was still very low.

In this article, Canada's contribution to this field is the most outstanding, accounting for 21.57% (137/635) of the articles in this field in the past 20 years. By analyzing the nodes of authors, cooperative relationship with others could be investigated. Dr. Cairney the Director of the Infant and Child Health Research Laboratory at both the University of Toronto and McMaster University (21) (currently Head of the School of Human

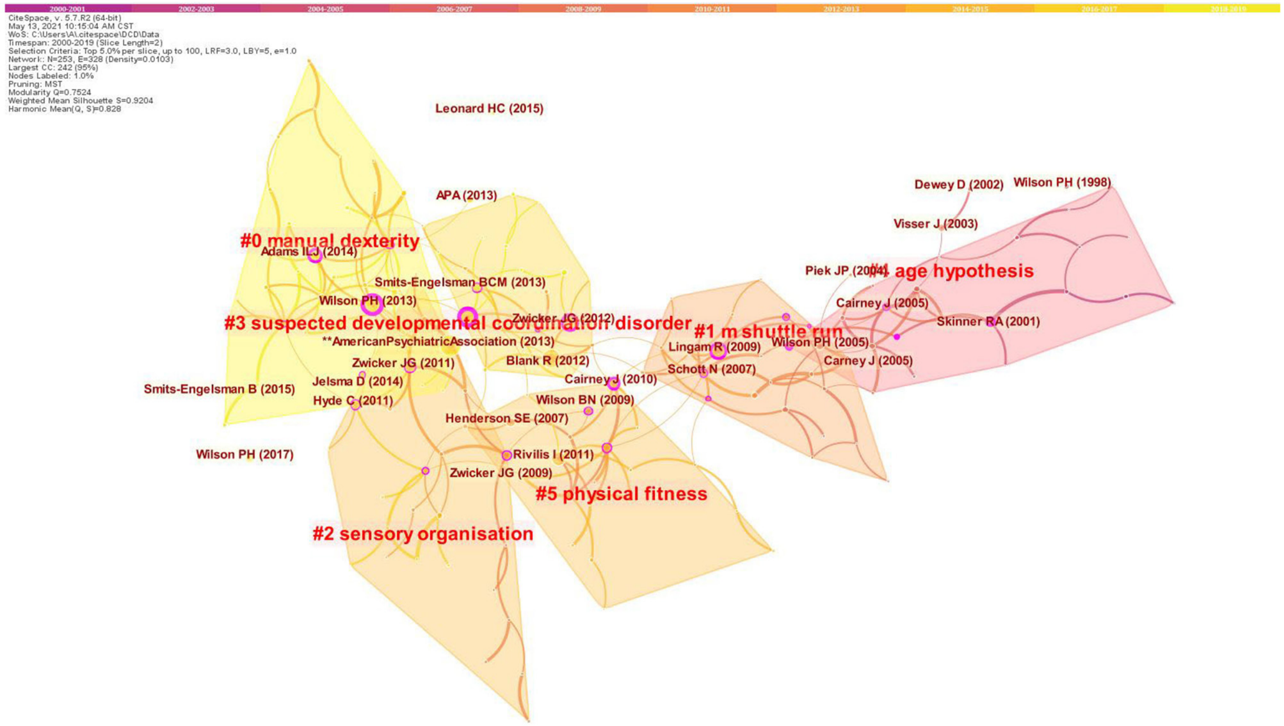


FIGURE 5 | Clustering map of reference co-citation related to research of children with DCD, 2000–2019. The larger the circle, the more frequently it is co-cited. The thicker the purple circle, the stronger the betweenness centrality.

TABLE 4 | Summary of the largest five clusters.

Cluster ID	Size	Silhouette	Label (LLR)	Mean (cite year)	Description
0	32	0.942	Manual dexterity	2013	An important manifestation of developmental coordination disorder
1	24	0.889	M shuttle run	2007	A well-established field measure of maximal oxygen uptake in children
2	24	0.967	Sensory organization	2009	Children with developmental coordination disorder have widespread impairment in their sensory organization
3	21	0.857	Suspected developmental coordination disorder	2011	A group of people exposed to risk factors for developmental coordination disorder
4	21	0.878	Age hypothesis	2002	The activity-deficit between children with and without coordination problems widens with age

Size: the number of references that a cluster contains.
LLR, log-likelihood ratio.

TABLE 5 | Top five co-citation references related to children with DCD, 2000–2019.

Ranking	Frequency	Centrality	Source	Cited reference	References	Cluster
1	111	0.09	DIAGN STAT MAN MENT	American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders. 5th Edition, APA, Washington, DC	(15)	#0
2	85	0.08	DEV MED CHILD NEUROL	European Academy for Childhood Disability (EACD): Recommendations on the definition, diagnosis and intervention of developmental coordination disorder (long version)	(16)	#3
3	75	0.48	DEV MED CHILD NEUROL	Understanding performance deficits in developmental coordination disorder: a meta-analysis of recent research	(17)	#0
4	44	0.31	EUR J PAEDIATR NEURO	Developmental coordination disorder: A review and update	(3)	#3
5	42	0.06	RES DEV DISABIL	Physical activity and fitness in children with developmental coordination disorder: A systematic review	(18)	#5

TABLE 6 | Top 10 highly cited journals in research of children with DCD, 2000–2019.

Ranking	Journal	Frequency	Centrality	Impact factor (2019)
1	Developmental Medicine and Child Neurology	548	0.16	4.406
2	Human Movement Science	547	0.27	2.096
3	Movement Assessment Battery for Children*	462	0.07	—
4	Diagnostic and Statistical Manual of Mental Disorder*	460	0.07	—
5	Research in Developmental Disabilities	353	0.23	1.836
6	Child: Care, Health & Development	320	0.14	1.918
7	Adapted Physical Activity Quarterly	305	0.24	1.462
8	Journal of Child Psychology and Psychiatry	255	0.04	6.129
9	Pediatrics	216	0.05	5.401
10	American Journal of Occupational Therapy	206	0.14	1.952

**These two are manuals.*

Movement and Nutrition Sciences at University of Queensland in Australia), is the most productive researcher in this field. His research examined the relationships among motor skill, physical activity, and physical and mental health in children (22). He is internationally known for his work on DCD and its impact on physical and psychological well-being in children (with the strongest centrality of 0.16). McMaster University also becomes the most productive (frequency: 54) and influential (centrality: 0.74) research institution in this field. Besides, it is obvious that the collaboration in investigating children with DCD is relatively close, mostly linked with institutions with high centrality, such as McMaster University, University of Toronto, and University of Cape Town. The top two institutions both come from Canada, indicating the leading role in this field.

Research Topic

In a co-citation network, references cited by a given article provide valuable information regarding intellectual connections between various scientific concepts (12). The literature represented in the co-citation network is organized into six different clusters. Each node represents a cited article, and the clusters represent a distinct specialty or a thematic concentration. The silhouette value of a cluster measures the quality of a clustering configuration, which ranges between −1 and 1. The higher the silhouette score (recommendation value >0.70), the more consistent of the cluster members are, providing the clusters in comparison have similar sizes (23).

During the past two decades, a significant amount of research has been conducted to study children with DCD. Compromised *manual dexterity* is a hallmark of the DCD symptom profile (24, 25), which has become a focus point of children with DCD research during more recent years. *Manual Dexterity* has also become one of the three components of the Movement Assessment Battery for Children, Second Edition (MABC-2), which is a validated, standardized, and norm-referenced test used to measure motor proficiency in children with DCD (26).

Besides *manual dexterity* problems, children with DCD are also known to have lower levels of physical fitness, including cardiorespiratory fitness, anaerobic capacity, and muscle strength. Sprinting tests are commonly used to assess general anaerobic capacity, but only the *shuttle run* item of the Bruininks–Oseretsky Test of Motor Proficiency, Second Edition (BOT-2), and the 10 × 5 m sprint were investigated, which are currently the best choices (27, 28).

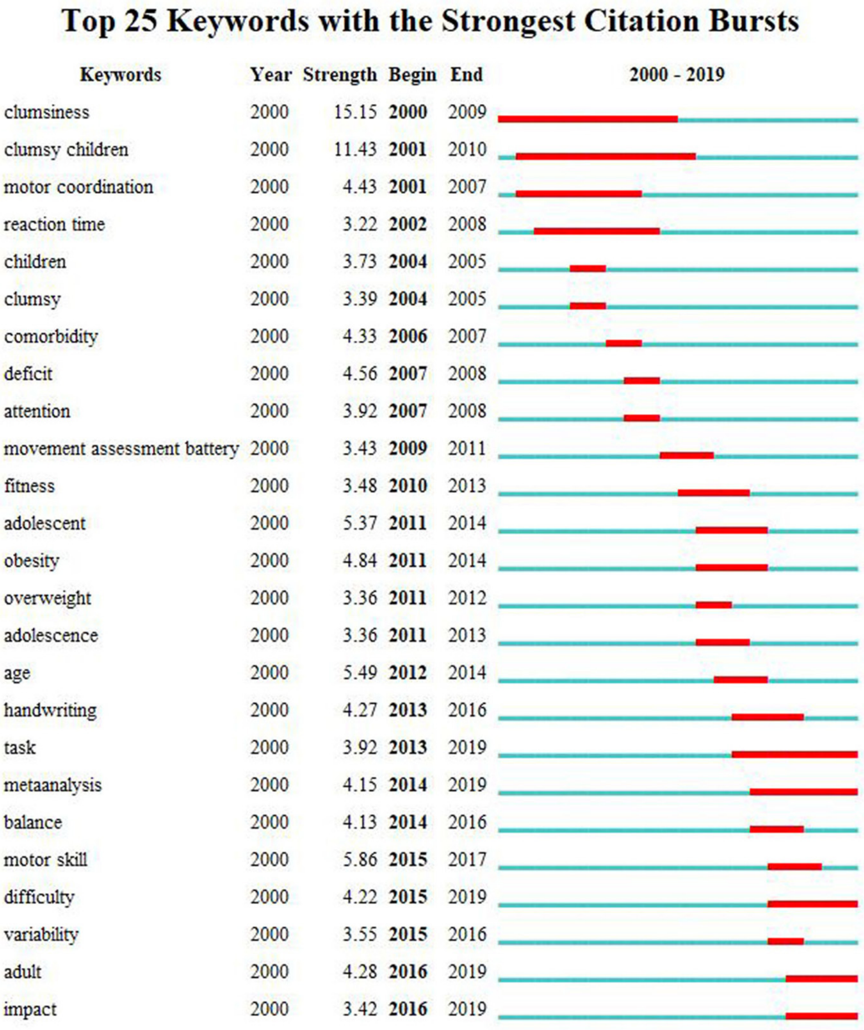
Actually, balance dysfunction is one of the most common sensorimotor impairments observed among children with DCD. However, until now, a comprehensive understanding of the etiology is still lacking. A majority of studies suggested that the impaired postural control can be ascribed to a deficit in central control and *sensory organization* (29). The *sensory organization* test (SOT), which has demonstrated good reliability and validity, was used to evaluate the *sensory organization* of balance control for children with DCD (30, 31).

Age hypothesis was presented that the activity deficit in children with DCD would grow larger as children's play became more complex and rule-bound (32). In other words, problems and secondary consequences in early childhood can persist through childhood and into adolescence and adulthood in children with DCD (33). To prevent these problems, early recognition of *suspected DCD* seems to be paramount in order to give the child the necessary support.

Therefore, many kinds of questionnaires have been designed to detect the play characteristics of young children who are suspected for DCD. The DCDQ-R (Developmental Coordination Disorder Questionnaire, Revised Version) has been shown to be one of the most utilized screening tools for DCD and a useful adjunct in studies using clinical samples (34–36). Further, the DCDQ-R has been revised for use in younger children that are 3 and 4 years of age: the Little DCD Questionnaire or Little DCDQ (18).

Research Fundamental

The top co-cited articles are often considered fundamental and a basis for a certain research field. Based on co-citation networks, top-cited publications are further analyzed to investigate the knowledge base for the field of children with DCD. Therefore, by combining with **Figure 5** (thick purple ring) and **Table 5** (centrality: 0.48 and 0.31), we find that high-quality meta-analysis published in the *DEV MED CHILD NEUROL* by Wilson et al. (17) and literature review published in the *EUR J PAEDIATR NEURO* by Zwicker et al. (3) are the solid foundation of the research in this field. Meta-analysis was also widely used in systematic reviews in many other disciplines and fields. Especially, it plays an important role in the field of evidence-based medicine and public health (37). Among the listed top five co-cited references in **Table 5**, the first two are both guidelines/manuals in this field



Keywords	Year	Strength	Begin	End
clumsiness	2000	15.15	**2000**	2009
clumsy children	2000	11.43	**2001**	2010
motor coordination	2000	4.43	**2001**	2007
reaction time	2000	3.22	**2002**	2008
children	2000	3.73	**2004**	2005
clumsy	2000	3.39	**2004**	2005
comorbidity	2000	4.33	**2006**	2007
deficit	2000	4.56	**2007**	2008
attention	2000	3.92	**2007**	2008
movement assessment battery	2000	3.43	**2009**	2011
fitness	2000	3.48	**2010**	2013
adolescent	2000	5.37	**2011**	2014
obesity	2000	4.84	**2011**	2014
overweight	2000	3.36	**2011**	2012
adolescence	2000	3.36	**2011**	2013
age	2000	5.49	**2012**	2014
handwriting	2000	4.27	**2013**	2016
task	2000	3.92	**2013**	2019
metaanalysis	2000	4.15	**2014**	2019
balance	2000	4.13	**2014**	2016
motor skill	2000	5.86	**2015**	2017
difficulty	2000	4.22	**2015**	2019
variability	2000	3.55	**2015**	2016
adult	2000	4.28	**2016**	2019
impact	2000	3.42	**2016**	2019

FIGURE 6 | Keywords with the strongest citation bursts in published articles on children with DCD, 2000–2019. The timeline is depicted as a blue line, and the time interval that a subject was found to have a burst is shown as a red segment which indicated the beginning year, the ending year, and the duration of the burst.

(15, 16), which play fundamental and instructive roles in the research of children with DCD. These two articles belong to cluster #0 and #3, respectively, which labeled "manual dexterity" and "suspected developmental coordination disorder."

Research Source

The highly cited journals reflect the best source in the research field of children with DCD to a certain extent. *Developmental Medicine* & *Child Neurology* has defined the field of pediatric neurology and childhood-onset neurodisability. It is a multidisciplinary journal, one of the world's leading journals in the whole field of pediatrics. As a kind of specific motor skill developmental disorder, the assessment of DCD is very critical. Therefore, main studies should refer to the assessment tool or manual, such as the MABC-1/2, and the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition (DSM-V).

Future Research Direction

From **Figure 6**, the hot topics switched from *clumsiness*, the burst keyword with the most strength, *clumsy children*, *motor coordination* to *movement assessment battery*, *adolescent*, and finally to *task*, *meta-analysis*, *difficulty*, *adult*, *impact*, and so on. Research foci in children with DCD seems to have shifted from children to adolescent and adult, from research in general symptom to specific assessment. Moreover, research foci mainly focused on clinical research rather than basic science or mechanism. Based on the evolution of keywords bursts and the ending year displayed with red segment, the future research trends in this field could be concluded as follows.

①DCD is a neurodevelopmental abnormality found in healthy children and persisting in "*adulthood*," which may "*impact*" everyday living (38). Therefore, new studies were conducted for "*adolescents/adults*" in the latest recommendations in 2019 to update the recommendations in 2012 (35). In recent years, many case–control and longitudinal studies have been reported (39, 40), and it will become one of the hot spots in this field in the future.

②Since motor control and executive function deficits are expressed as a function of "*task type*" and difficulty, interventions for DCD can be broadly categorized into two types: process or deficit-oriented and "*task-specific*" (3, 35). "*Task-specific*" training was found to be useful in improving the performance of children with DCD based on the type of task trained (41, 42). Some reviews and meta-analysis also found that approaches from a task-specific perspective yielded stronger effects, whereas this preliminary evidence is currently insufficient (43, 44). Therefore, it will be also one of the research trends in this field.

Strengths and Limitations

To our knowledge, this bibliometric study is the first of its kind to identify and characterize research in children with DCD. Moreover, our findings provide a clear visual analysis, from the quantity, quality, citation analysis, and so on, of the publications of children with DCD. It will be a good example of visualization analysis available to explore research hotspots in other fields.

There are also some weaknesses to the study. Although we used the WoSCC for our bibliometric analysis, there are other public and commercially available bibliometric databases, such as Scopus, Medline, and PubMed. However, there are some reasons for this choice of database. For example, PubMed records do not include information on cited references so it is not possible to perform citation analysis using PubMed (45).

CONCLUSION

From the current bibliometric analysis of children with DCD publications over the previous 20 years, it is found that related publications increased at a rapid rate. Canada has the highest publication rate and centrality, and the institution and researcher that are most prolific in this field are also from Canada. The analysis and interpretation of the research literature will be very helpful to the clinicians and scientists in this field.

AUTHOR CONTRIBUTIONS

M-QW, D-QW, C-PH, and L-SI contributed to study design and acquisition of research data. M-QW conducted the data analysis. M-QW and D-QW drafted the manuscript. All authors contributed to improvements of the manuscript for important intellectual content and approved the final version for publication.

FUNDING

This study was supported by Shanghai Pudong Municipal Health Commission (PW2020D-11), the Science and Technology Commission of Shanghai Municipality (19140903100), Shanghai Municipal Health Commission (2020YJZX0213), and Clinical Research Plan of Shanghai Hospital Development Center (SHDC2020CR1047B-003). The funders had no role in the conduct of the study, the analysis or interpretation of data, and the preparation, review, or approval of the manuscript.

ACKNOWLEDGMENTS

We are very grateful to express their appreciation to Prof. C. M. Chen, who invented CiteSpace, which is free to use. The authors are indebted to the database of Web of Science, which provided us unrestricted online access.

REFERENCES

1. van Hoorn JF, Schoemaker MM, Stuive I, Dijkstra PU, Rodrigues Trigo Pereira F, van der Sluis CK, et al. Risk factors in early life for developmental coordination disorder: a scoping review. *Dev Med Child Neurol.* (2021) 63:511–9. doi: 10.1111/dmcn.14781
2. Zwicker JG, Lee EJ. Early intervention for children with/at risk of developmental coordination disorder: a scoping review. *Dev Med Child Neurol.* (2021) 63:659–67. doi: 10.1111/dmcn.14804
3. Zwicker JG, Missiuna C, Harris SR, Boyd LA. Developmental coordination disorder: a review and update. *Eur J Paediatr Neurol.* (2012) 16:573–81. doi: 10.1016/j.ejpn.2012.05.005
4. Mandich A, Polatajko HJ. Developmental coordination disorder: mechanisms, measurement and management. *Hum Mov Sci.* (2003) 22:407–11. doi: 10.1016/j.humov.2003.09.001
5. Polatajko H, Fox M, Missiuna C. An international consensus on children with developmental coordination disorder. *Can J Occup Ther.* (1995) 62:3–6. doi: 10.1177/000841749506200101
6. Brandt JS, Hadaya O, Schuster M, Rosen T, Sauer MV, Ananth CV, et al. bibliometric analysis of top-cited journal articles in obstetrics and gynecology. *JAMA Netw Open.* (2019) 2:e1918007. doi: 10.1001/jamanetworkopen.2019.18007
7. Yang L, He L, Ma Y, Wu L, Zhang Z. A visualized investigation on the intellectual structure and evolution of waste printed circuit board research during 2000-2016. *Environ Sci Pollut Res Int.* (2019) 26:11336–41. doi: 10.1007/s11356-019-04590-8
8. Zhang D, Xu JP, Zhang YZ, Wang J, He SY, Zhou X. Study on sustainable urbanization literature based on web of science, scopus, and china national knowledge infrastructure: a scientometric analysis in citespace. *J Clean Prod.* (2020) 264:121537. doi: 10.1016/j.jclepro.2020.121537
9. Azam A, Ahmed A, Wang H, Wang YE, Zhang ZT. Knowledge structure and research progress in wind power generation (wpg) from 2005 to 2020 using citespace based scientometric analysis. *J Clean Prod.* (2021) 295:126496. doi: 10.1016/j.jclepro.2021.126496
10. Chen C, Hu Z, Liu S, Tseng H. Emerging trends in regenerative medicine: a scientometric analysis in citespace. *Expert Opin Biol Ther.* (2012) 12:593–608. doi: 10.1517/14712598.2012.674507
11. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell.* (2006) 126:663–76. doi: 10.1016/j.cell.2006.07.024
12. Chen C, Dubin R, Kim MC. Emerging trends and new developments in regenerative medicine: a scientometric update (2000-2014). *Expert Opin Biol Ther.* (2014) 14:1295–317. doi: 10.1517/14712598.2014.920813
13. Yi F, Yang P, Sheng H. Tracing the scientific outputs in the field of ebola research based on publications in the web of science. *BMC Res Notes.* (2016) 9:221. doi: 10.1186/s13104-016-2026-2
14. Chen C. Searching for intellectual turning points: progressive knowledge domain visualization. *Proc Natl Acad Sci USA.* (2004) 101:5303–10. doi: 10.1073/pnas.0307513100

15. Association AP. Diagnostic and statistical manual of mental disorders. *5th edition, Washington, DC.* (2013).
16. Blank R, Smits-Engelsman B, Polatajko H, Wilson P. European academy for childhood disability (eacd): recommendations on the definition, diagnosis and intervention of developmental coordination disorder (long version). *Dev Med Child Neurol.* (2012) 54:54–93. doi: 10.1111/j.1469-8749.2011.04171.x
17. Wilson PH, Ruddock S, Smits-Engelsman B, Polatajko H, Blank R. Understanding performance deficits in developmental coordination disorder: a meta-analysis of recent research. *Dev Med Child Neurol.* (2013) 55:217–28. doi: 10.1111/j.1469-8749.2012.04436.x
18. Rihtman T, Wilson BN, Parush S. Development of the little developmental coordination disorder questionnaire for preschoolers and preliminary evidence of its psychometric properties in israel. *Res Dev Disabil.* (2011) 32:1378–87. doi: 10.1016/j.ridd.2010.12.040
19. Kleinberg J. Bursty and hierarchical structure in streams. *Data Min Knowl Discov.* (2003) 7:373–97. doi: 10.1023/A:1024940629314
20. Peters JM, Barnett AL, Henderson SE. Clumsiness, dyspraxia and developmental co-ordination disorder: How do health and educational professionals in the uk define the terms? *Child Care Health Dev*. (2001) 27:399–412. doi: 10.1046/j.1365-2214.2001.00217.x
21. Cairney J, Veldhuizen S, Rodriguez MC, King-Dowling S, Kwan MY, Wade T, et al. Cohort profile: the canadian coordination and activity tracking in children (catch) longitudinal cohort. *BMJ Open.* (2019) 9:e029784. doi: 10.1136/bmjopen-2019-029784
22. Professor john cairney, 2021.
23. Li Y, Fang R, Liu Z, Jiang L, Zhang J, Li H, et al. The association between toxic pesticide environmental exposure and alzheimer's disease: a scientometric and visualization analysis. *Chemosphere.* (2021) 263:128238. doi: 10.1016/j.chemosphere.2020.128238
24. Fuelscher I, Caeyenberghs K, Enticott PG, Williams J, Lum J, Hyde C. Differential activation of brain areas in children with developmental coordination disorder during tasks of manual dexterity: an ale meta-analysis. *Neurosci Biobehav Rev.* (2018) 86:77–84. doi: 10.1016/j.neubiorev.2018.01.002
25. Nobusako S, Sakai A, Tsujimoto T, Shuto T, Nishi Y, Asano D, et al. Deficits in visuo-motor temporal integration impacts manual dexterity in probable developmental coordination disorder. *Front Neurol.* (2018) 9:114. doi: 10.3389/fneur.2018.00114
26. Bonney E, Aertssen W, Smits-Engelsman B. Psychometric properties of field-based anaerobic capacity tests in children with developmental coordination disorder. *Disabil Rehabil.* (2019) 41:1803–14. doi: 10.1080/09638288.2018.1446189
27. Aertssen W, Jelsma D, Smits-Engelsman B. Field-based tests of strength and anaerobic capacity used in children with developmental coordination disorder: a systematic review. *Phys Ther.* (2020) 100:1825–51. doi: 10.1093/ptj/pzaa118
28. Cairney J, Hay J, Veldhuizen S, Faught B. Comparison of vo2 maximum obtained from 20 m shuttle run and cycle ergometer in children with and without developmental coordination disorder. *Res Dev Disabil.* (2010) 31:1332–9. doi: 10.1016/j.ridd.2010.07.008
29. Speedtsberg MB, Christensen SB, Andersen KK, Bencke J, Jensen BR, Curtis DJ. Impaired postural control in children with developmental coordination disorder is related to less efficient central as well as peripheral control. *Gait Posture.* (2017) 51:1–6. doi: 10.1016/j.gaitpost.2016.09.019
30. Fong SS, Lee VY, Pang MY. Sensory organization of balance control in children with developmental coordination disorder. *Res Dev Disabil.* (2011) 32:2376–82. doi: 10.1016/j.ridd.2011.07.025
31. Fong SS, Tsang WW, Ng GY. Taekwondo training improves sensory organization and balance control in children with developmental coordination disorder: a randomized controlled trial. *Res Dev Disabil.* (2012) 33:85–95. doi: 10.1016/j.ridd.2011.08.023
32. John C, Hay J, Faught BE, Corna LM, Flouris AD. Developmental coordination disorder, age and play: a test of the divergence in activity-deficit with age hypothesis. *Adapt Phys Act Q.* (2006) 23:261–76. doi: 10.1123/apaq.23.3.261
33. Cantell M, Houwen S, Schoemaker M. Age-related validity and reliability of the dutch little developmental coordination disorder questionnaire (ldcdq-nl). *Res Dev Disabil.* (2019) 84:28–35. doi: 10.1016/j.ridd.2018.02.010
34. Wilson BN, Crawford SG, Green D, Roberts G, Aylott A, Kaplan BJ. Psychometric properties of the revised developmental coordination disorder questionnaire. *Phys Occup Ther Pediatr.* (2009) 29:182–202. doi: 10.1080/01942630902784761
35. Blank R, Barnett AL, Cairney J, Green D, Kirby A, Polatajko H, et al. International clinical practice recommendations on the definition, diagnosis, assessment, intervention, and psychosocial aspects of developmental coordination disorder. *Dev Med Child Neurol.* (2019) 61:242–85. doi: 10.1111/dmcn.14132
36. Patel P, Gabbard C. Adaptation and preliminary testing of the developmental coordination disorder questionnaire (dcdq) for children in india. *Phys Occup Ther Pediatr.* (2017) 37:170–82. doi: 10.3109/01942638.2016.1150383
37. Zhu C, Jiang T, Cao H, Sun W, Chen Z, Liu J. Longitudinal analysis of meta-analysis literatures in the database of isi web of science. *Int J Clin Exp Med.* (2015) 8:3559–65.
38. Farmer M, Echenne B, Drouin R, Bentourkia M. Insights in developmental coordination disorder. *Curr Pediatr Rev.* (2017) 13:111–9. doi: 10.2174/1573396313666170726113550
39. Landgren V, Fernell E, Gillberg C, Landgren M, Johnson M. Attention-deficit/hyperactivity disorder with developmental coordination disorder: 24-year follow-up of a population-based sample. *BMC Psychiatry.* (2021) 21:161. doi: 10.1186/s12888-021-03154-w
40. Warlop G, Vansteenkiste P, Lenoir M, Deconinck FJA. Young adults with developmental coordination disorder adopt a different visual strategy during a hazard perception test for cyclists. *Front Psychol.* (2021) 12:665189. doi: 10.3389/fpsyg.2021.665189
41. Fong SS, Guo X, Liu KP, Ki WY, Louie LH, Chung RC, et al. Task-specific balance training improves the sensory organisation of balance control in children with developmental coordination disorder: a randomised controlled trial. *Sci Rep.* (2016) 6:20945. doi: 10.1038/srep20945
42. Cavalcante Neto JL, Steenbergen B, Zamunér AR, Tudella E. Wii training versus non-wii task-specific training on motor learning in children with developmental coordination disorder: a randomized controlled trial. *Ann Phys Rehabil Med.* (2021) 64:101390. doi: 10.1016/j.rehab.2020.03.013
43. Smits-Engelsman BC, Blank R, van der Kaay AC, Mosterd-van der Meijs R, Vlugt-van den Brand E, Polatajko HJ, et al. Efficacy of interventions to improve motor performance in children with developmental coordination disorder: A combined systematic review and meta-analysis. *Dev Med Child Neurol.* (2013) 55:229–37. doi: 10.1111/dmcn.12008
44. Miyahara M, Hillier SL, Pridham L, Nakagawa S. Task-oriented interventions for children with developmental co-ordination disorder. *Cochrane Database Syst Rev.* (2017) 7:Cd010914. doi: 10.1002/14651858.CD010914.pub2
45. Wu D, Wang S, Hu C, Yan C, Wu M. Ten years of the cohort biobank: bibliometric outcomes. *Biopreserv Biobank.* (2021) 19:269–79. doi: 10.1089/bio.2020.0096

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 20 December 2021
doi: 10.3389/fpsyt.2021.778291

Individual, Prenatal, Perinatal, and Family Factors for Anxiety Symptoms Among Preschool Children

Xiuxiu Ding[1†], **Jun Wang**[1,2†], **Ning Li**[1], **Wanying Su**[1], **Hao Wang**[1], **Qiuxia Song**[1], **Xianwei Guo**[1], **Mingming Liang**[1], **Qirong Qin**[3], **Liang Sun**[4], **Mingchun Chen**[5] and **Yehuan Sun**[1*]

[1] Department of Epidemiology and Health Statistics, School of Public Health, Anhui Medical University, Hefei, China, [2] Department of Maternal, Child and Adolescent Health, School of Public Health, Anhui Medical University, Hefei, China, [3] Ma'anshan Center for Disease Control and Prevention, Ma'anshan, China, [4] Fuyang Center for Disease Control and Prevention, Fuyang, China, [5] Changfeng Center for Disease Control and Prevention, Changfeng, China

Anxiety is one of the most common psychological disorders among children. Few studies have investigated the prevalence and comprehensive factors for anxiety among preschool children in China. This study aimed to assess the prevalence of anxiety and explore influential factors at multiple levels including individual, prenatal and perinatal, and family factors, associated with anxiety symptoms among preschool children. The multisite cross-sectional study was conducted in Anhui Province and included 3,636 preschool children aged 3–6 years. Anxiety symptoms of children were assessed using the Chinese version of the Spence Preschool Anxiety Scale. Logistic regression analyses were performed to explore associations between factors at multiple levels and significant anxiety symptoms, and the model was validated internally using 10-fold cross-validation. Among the participants, 9.1% of children had significant anxiety symptoms. Girls reported more significant anxiety symptoms. Children's poor dietary habits, sleep disturbances, autistic tendencies, and left-behind experience; maternal poor prenatal emotional symptoms; and more caregivers' anxiety symptoms were significantly associated with anxiety symptoms among children. The result of 10-fold cross-validation indicated that the mean area under the curve, sensitivity, specificity, and accuracy were 0.78, 70.45%, 78.18%, and 71.15%, respectively. These factors were slightly different among different subtypes of anxiety symptoms. The results of this study suggested that anxiety symptoms in preschool children were prevalent, particularly in girls. Understanding early-life risk factors for anxiety is crucial, and efficient prevention and intervention strategies should be implemented in early childhood even pregnancy.

Keywords: anxiety, preschool, child, left-behind, prenatal

OPEN ACCESS

Edited by:
David Cohen,
Sorbonne Universités, France

Reviewed by:
Cedric Galera,
Université de Bordeaux, France
Pierre Jacquet,
École Normale Supérieure, France

***Correspondence:**
Yehuan Sun
yhsun_ahmu_edu@yeah.net

[†] *These authors have contributed equally to this work and share first authorship*

Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: *16 September 2021*
Accepted: *19 November 2021*
Published: *20 December 2021*

Citation:
Ding X, Wang J, Li N, Su W, Wang H, Song Q, Guo X, Liang M, Qin Q, Sun L, Chen M and Sun Y (2021) Individual, Prenatal, Perinatal, and Family Factors for Anxiety Symptoms Among Preschool Children. Front. Psychiatry 12:778291. doi: 10.3389/fpsyt.2021.778291

INTRODUCTION

Anxiety is one of the most common psychological disorders among children and is associated with serious academic and social impairments and even adulthood psychological problems (1–4). Studies have demonstrated that the anxiety age of onset is approximately 6 years old (4–6). Preschool children's anxiety is generally moderately stable and tends to persist into childhood and adolescence (7, 8).

A longitudinal study from Canada has indicated that 14.7% of preschool children maintain constantly elevated anxiety symptoms from 1.5 to 5.0 years of age (9). One recent study exploring the trajectories of anxiety symptoms from preschool to school age has suggested that high stable anxiety beginning at preschool age is associated with lower school engagement, poorer peer relations, and greater functional impairment during the later school age (10). Researchers have proposed that preschool age may be an optimal developmental window for anxiety prevention or early intervention (11).

Currently, considerable research efforts have been made to improve knowledge surrounding the aetiology of anxiety, which is believed to be affected by genetic vulnerability and environmental factors (10, 12–18). Previous classical twin studies point genetic background as the predominant factor for the emergence of anxiety-related behaviours (19), while a 30–40% heritability is reported (20). Individual internal characteristics such as age, gender, and children's emotional and behavioural characteristics are involved in susceptibility to anxiety. Some studies have shown that younger children report higher anxiety symptoms than older children (21, 22). Regarding gender differences, the results show a relatively incongruent picture in previous research (2, 22–24). Children's behavioural problems such as sleep disturbances, depression, high behavioural inhibition, attention-deficit hyperactivity disorder symptoms, and peer victimisation seem to predict follow-up anxiety (3, 10, 25). The influence of external environmental factors throughout foetal and early childhood involving prenatal, perinatal, and parental and family factors cannot be underestimated (12, 26, 27). With the development of the developmental origins of adult disease (DOHaD) theory (28), researchers traced these factors back to the pregnancy period according to the foetal programming mechanisms (29, 30). Evidence from cohort studies has indicated that preterm birth, caesarean section, hypertensive disorders of pregnancy, prenatal and postnatal anxiety, depression, and distress increase the risk of offspring anxiety (14, 27, 31–33). Given that the family exerts important influence on a child's development, researchers have noted the role of family factors in child anxiety. Some adverse family factors such as parental corporal punishment and abuse are positively associated with childhood anxiety (16, 34). Additionally, children who were separated from parents too early have more anxiety symptoms (17). In addition, one study has proposed a novel evidence for environmental transmission, and the anxiety of parents and children may influence each other in different ways (12). Severe early adversities may trigger chronic and neurobiologically distinct internalising symptoms starting from the preschool period (15). Therefore, it is of great importance to understand the impacts of early-life risk factors on children's anxiety. Thus far, numerous studies surrounding these issues are predominantly focused on school-aged children and from Western countries. However, only a few studies with small sample sizes and exploring only limited factors have been conducted among preschool children in China (35–37).

Taken together, the findings from previous research show that it is critical to better understand anxiety symptoms during the preschool period and its potential risk factors to minimise the negative effects on these children. In the current study, we hypothesised that exposure to prenatal and perinatal adversities, individual problematic behaviours, and adverse family environmental factors from pregnancy to early childhood might increase the risks of preschool children's anxiety. This study aims to ascertain whether comprehensive factors including individual, prenatal, perinatal, and family factors are associated with anxiety among preschool children and provide scientific evidence supporting the use of early-life interventions based on multisite cross-sectional survey.

MATERIALS AND METHODS

Participants

This multisite cross-sectional study was conducted in 26 kindergartens of four counties including Funan county in Fuyang City, Changfeng county and Fexi county in Hefei City, and Bowang district (same as county administrative level) in Ma'anshan City, located in the north, middle, and south of Anhui Province from September 2019 to January 2020. A total of 3,802 questionnaires were distributed in the initial investigation. Finally, 3,636 effective questionnaires were collected with a total response rate of 95.6%, after checking for completeness and logic. Participants, including 3,636 preschool children aged 3–6 years and their primary caregivers, voluntarily participated in the investigation. Children and their caregivers with cognitive impairment, deafness, or language communication barriers and children with severe mental or physical illnesses were excluded. Prior to data collection, caregivers' consent was obtained. Then, caregivers were invited to complete a structured questionnaire through a face-to-face interview. The study was approved by the Ethics Committee of Anhui Medical University (20180402), and confidentiality was assured.

Independent Variables

Individual Characteristics

Individual characteristics included children's age, gender, body mass index (BMI), dietary habits, sleep disturbances, and autistic tendencies. Children's age and gender were collected by using a questionnaire based on primary caregivers' self-reports. Children's BMI was calculated by dividing the weight (kg) by height (m) squared (weight and height measured by investigators), and the World Health Organization Child Growth Standards for age- and sex-specific cutoffs were employed (38). Dietary habits of preschool children were assessed by caregivers' reports using the adapted Identification and Management of Feeding Difficulties scale (IMFeD) (39), which consists of 17 items, and higher total scores indicate better dietary habits. Cronbach's alpha coefficient of IMFeD was 0.887 in this study. Children's sleep disturbances were measured with the Children's Sleep Habits Questionnaire (CSHQ) (40), which contains 33 items and scores of every item based on caregivers' recollection of children's sleep behaviours occurring over a recent week. Higher total scores indicate greater sleep disturbances, and Cronbach's alpha value was 0.668 in this study. Autistic tendencies of preschool children were assessed using the Chinese version of the Clancy Autism Behaviour Scale (CABS) (41). The CABS contains 14 items, and higher total scores indicate greater autistic tendencies. Cronbach's alpha coefficient of the CABS was 0.809 in this study.

Prenatal and Perinatal Factors

Data on prenatal and perinatal factors were obtained from the questionnaire including gestational age (weeks), birth weight (g), delivery mode, pregnancy complications (hypertension, diabetes, and anaemia), maternal prenatal and postnatal emotional symptoms, and exclusive breastfeeding. Preterm birth was defined as a gestational age < 37 weeks. Low birth weight was defined as infants with a birth weight below 2,500 g.

Family Factors

Information on region of kindergartens, parental education, parental marital status, parenting attitude, children's sibling, left-behind experience, and monthly household income (RMB) was collected from the questionnaire by the caregivers' response on the questionnaire. Left-behind experience was defined as the experience that children who had been left behind by one or both parent(s) who migrated to other cities for employment for more than 6 consecutive months. Contact physical abuse (hit or slapped the child on the bottom; hit or slapped the child on the hand, arm, or leg; pushed or shook the child, pulled the child's ears or other parts of the body; kicked the child very hard with the foot; hit or slapped the child on the face or head; hit or slapped the child on the bottom with an object; and hit the child very hard with fist) was assessed through the caregivers reporting the experience in the previous year. If one form of physical abuse was mentioned, the contact physical abuse variable was defined as "yes." Caregiver's anxiety symptoms were evaluated using the Self-Rating Anxiety Scale (SAS) (42). The SAS contains 20 items in total, and the sum score of all items is the raw score. In the present study, the standard score which was calculated by multiplying 1.25 by the raw score was used. Higher standard scores of anxiety show a higher level of anxiety symptoms. Cronbach's alpha coefficient of the SAS was 0.82 (42).

Dependent Variables

Anxiety symptoms of preschool children were assessed using the Chinese version of the Spence Preschool Anxiety Scale (SPAS) (22). This scale has displayed good reliability and validity in a sample of Chinese preschool children (22, 36). The scale is a 28-item anxiety symptoms measure for preschool children. The SPAS includes 5 subscales: separation anxiety disorder, physical injury fears, social phobia, obsessive-compulsive disorder, and generalised anxiety disorder. Each subscale item was scored on a 5-point scale ranging from 0 (not at all true) to 4 (very often true). The scores of the total scale and each subscale could be obtained by calculating the sum of all relevant items. The total scale score was $\geq$48 having significant anxiety symptoms (43). Children with scores falling in the upper quartile of the distribution were deemed as having significant subtypes of anxiety symptoms, and the cutoff value was separation anxiety disorder $\geq$6, physical injury fears $\geq$12, social phobia $\geq$7, obsessive-compulsive disorder $\geq$6, and generalised anxiety disorder $\geq$5, respectively. In our study, Cronbach's alpha value for the subscales ranged from 0.613 to 0.728 and that for the total scale was 0.903.

Statistical Analysis

Continuous variables are described as the mean ± standard deviation (SD), and differences between groups were tested by Student's *t* tests or analysis of variance. Categorical variables were expressed as frequencies and percentages, and the chi-squared (χ^2) test was utilised for comparisons. Logistic regression analyses were conducted to explore the associations of children's total anxiety symptoms and anxiety symptoms in five subtypes with individual, prenatal and perinatal, and family factors; and odds ratio (OR) and its 95% confidence interval (*CI*) were reported. To select the optimal regression equation, variables with $p < 0.05$ were entered into multivariate logistic regression models and those with $p < 0.10$ were retained in the final model using the forward stepwise manner. The 10-fold cross-validation method was used to assess the performance (area under the curve (AUC), sensitivity, specificity, and accuracy) of the multivariate regression model to avoid overfitting. The entire dataset was divided into 10 non-overlapping equivalent subsets; nine subsets were used to produce a prediction model, and the model was validated with the last subset. The procedure was repeated 10 times to ensure that each subset was applied once for model verification. Cross-validation was performed using the "caret" and "pROC" package in R software (Version 4.1.0, R Foundation for Statistical Computing, Vienna, Austria). Other analyses were conducted using SPSS software version 23.0 (SPSS Inc., USA). All *p*-values < 0.05 (two-tailed test) were considered to be statistically significant.

RESULTS

Sample Characteristics

A total of 3,802 questionnaires were issued; after checking for completeness and logic, 3,636 effective questionnaires were finally collected. Comparisons of some variables based on preschool children's anxiety symptoms are shown in **Table 1**. Of the 3,636 preschool children, the mean age was 4.5 ± 0.9 years; 45.8% were girls. The prevalence of anxiety symptoms was higher in girls than in boys. Significant differences between subjects displaying significant anxiety and those not displaying significant anxiety were detected in child dietary habits, sleep disturbances, and autistic tendencies; prenatal and postnatal emotional symptoms, pregnancy complications; and region of kindergartens, parental education, parenting attitude, children's sibling, left-behind experience, contact physical abuse, and caregivers' anxiety symptoms.

Prevalence and Scores of Anxiety Symptoms

As presented in **Table 2**, the mean total score of anxiety symptoms was 25.3 (SD = 15.5). A total of 330 (9.1%) children met the criteria for significant anxiety symptoms. When stratified by age, the results indicated that preschool children aged 3 years

TABLE 1 | Individual, prenatal and perinatal, and family factors by preschool children's anxiety symptoms.

Variables		**Sample**	**Significant anxiety symptoms *n* (%) or means ± SD**		***p*-value**
			Yes (n = 330)	**No (n = 3,306)**	
Individual characteristics					
Age	Year	3,636	4.6 ± 0.9	4.5 ± 0.9	0.295
Gender	Boys	1,970	157 (8.0)	1,813 (92.0)	**0.012**
	Girls	1,666	173 (10.4)	1,493 (89.6)	
Body mass index	Normal	3,029	275 (9.1)	2,754 (90.9)	0.989
	Overweight or obesity	607	55 (9.1)	552 (90.9)	
Dietary behaviour	Score	3,636	62.7 ± 13.0	70.2 ± 11.5	**<0.001**
Sleep disturbances	Score	3,636	53.8 ± 6.9	49.0 ± 6.7	**<0.001**
Autistic tendencies	Score	3,636	10.9 ± 4.7	7.3 ± 4.5	**<0.001**
Prenatal and perinatal factors					
Delivery mode	Vaginal delivery	2,092	205 (9.8)	1,887 (89.2)	0.077
	Caesarean section	1,544	125 (8.1)	1,419 (91.9)	
Low birth weight	No	3,489	313 (9.0)	3,176 (91.0)	0.284
	Yes	147	17 (11.6)	130 (88.4)	
Preterm birth	No	3,517	317 (9.0)	3,200 (91.0)	0.475
	Yes	119	13 (10.9)	106 (89.1)	
Prenatal emotional symptoms	Pleasure or fair	3,415	289 (8.5)	3,126 (91.5)	**<0.001**
	Poor	221	41 (18.6)	180 (81.4)	
Postnatal emotional symptoms	Pleasure or fair	3,330	290 (8.7)	3,040 (91.3)	**0.011**
	Poor	306	40 (13.1)	266 (86.9)	
Pregnancy complications	No	3,150	274 (8.7)	2,876 (91.3)	**0.044**
	Yes	486	56 (11.5)	430 (88.5)	
Exclusive breastfeeding	Yes	1,979	179 (9.0)	1,800 (91.0)	0.943
	No	1,657	151 (9.1)	1,506 (90.9)	
Family factors					
Region of kindergartens	Hefei	1,056	76 (7.2)	980 (92.8)	**0.026**
	Fuyang	1,595	164 (10.3)	980 (89.7)	
	Ma'anshan	985	76 (9.1)	980 (90.9)	
Highest household education	Middle school and below	1,754	190 (10.8)	1,564 (89.2)	**<0.001**
	High school and above	1,882	140 (7.4)	1,742 (92.6)	
Sibling	Yes	2,492	242 (9.7)	2,250 (90.3)	**0.049**
	No	1,144	88 (7.7)	1,056 (92.3)	
Left-behind experience	No	2,173	166 (7.6)	2,007 (92.4)	**<0.001**
	Yes	1,463	164 (11.2)	1,299 (88.8)	
Parental marital status	Married	3,515	315 (9.0)	3,200 (91.0)	0.196
	Divorced/widowed	121	15 (12.4)	106 (87.6)	
Monthly household income (RMB)	<5,000	1,611	154 (9.6)	1,457 (90.4)	0.365
	≥5,000	2,025	176 (8.7)	1,849 (91.3)	
Parenting attitude	Generally accordant	1,751	120 (6.9)	1,631 (93.1)	**<0.001**
	Generally discordant	1,885	210 (11.1)	1,675 (88.9)	
Contact physical abuse	No	581	40 (6.9)	541 (93.1)	**0.045**
	Yes	3,055	290 (9.5)	2,765 (90.5)	
Caregivers' anxiety symptoms	Score	3,636	41.5 ± 10.4	35.2 ± 8.5	**<0.001**

Bold values denote p values significant at the 0.05 level.

were found to score significantly higher on the separation anxiety disorder subscale ($p = 0.017$), with no significant difference in different age groups on scores of the total scale and other subscales. Significant gender differences were detected in the total anxiety scale and all subscales ($p < 0.05$).

Differences of Significant Anxiety Symptoms in Individual, Prenatal and Perinatal, and Family Factors

Compared with their peers, children with significant anxiety symptoms were more likely to be girls and to have siblings;

TABLE 2 | Anxiety symptoms scores (mean ± SD) for overall sample and subgroups of preschool children.

		Stratified by age				**Stratified by gender**		
Anxiety symptoms	**Total sample (*N* = 3,636)**	**3 year (*N* = 1,253)**	**4 year (*N* = 1,247)**	**5–6 years (*N* = 1,136)**	***p*-value**	**Boys (*N* = 1,970)**	**Girls (*N* = 1,666)**	***p*-value**
Total score	25.3 ± 15.5	25.4 ± 15.4	24.9 ± 15.4	25.6 ± 15.6	0.539	24.2 ± 15.1	26.5 ± 15.9	**<0.001**
Separation anxiety disorder	4.4 ± 3.3	4.6 ± 3.3	4.4 ± 3.3	4.2 ± 3.3	**0.017**	4.3 ± 3.3	4.5 ± 3.3	**0.034**
Physical injury fears	8.6 ± 5.6	8.5 ± 5.5	8.6 ± 5.7	8.8 ± 5.7	0.567	8.0 ± 5.4	9.3 ± 5.8	**<0.001**
Social anxiety	4.9 ± 3.8	4.9 ± 3.8	4.8 ± 3.9	5.1 ± 3.8	0.088	4.8 ± 3.8	5.1 ± 3.9	**0.007**
Obsessive-compulsive disorder	4.1 ± 3.5	4.2 ± 3.5	4.0 ± 3.4	4.2 ± 3.5	0.543	4.0 ± 3.4	4.3 ± 3.5	**0.017**
Generalised anxiety disorder	3.2 ± 2.9	3.3 ± 2.9	3.1 ± 2.8	3.3 ± 2.8	0.094	3.1 ± 2.8	3.3 ± 3.0	**0.038**

Bold values denote p values significant at the 0.05 level.

left-behind experience; poor dietary habits; more sleep disturbances; more autistic tendencies; mothers who had poor prenatal and postnatal emotional symptoms; mothers who had pregnancy complications; region of kindergartens in Fuyang; parents with middle school or less education or discordant parenting attitudes; experienced contact physical abuse; and caregivers with more anxiety symptoms ($p < 0.05$; **Table 1**).

Associations Between Potential Factors and Anxiety Symptoms

The result of bivariate correlations indicated that children's gender, dietary habits, sleep disturbances, and autistic tendencies; prenatal and postnatal emotional symptoms and pregnancy complications; and parental education, monthly household income, parenting attitude, contact physical abuse, and caregivers' anxiety symptoms were associated with children's anxiety symptoms (**Supplementary Table 1**).

As shown in **Table 3**, the results of multivariate logistic regression analysis indicated that girls (OR = 1.50; $p = 0.001$), left-behind experience (OR = 1.29; $p = 0.043$), more sleep disturbances (OR = 1.05; $p < 0.001$), more autistic tendencies (OR = 1.12; $p < 0.001$), poor prenatal emotional symptoms (OR = 1.54; $p = 0.027$), and caregivers with more anxiety symptoms (OR = 1.03; $p < 0.001$) were associated with increased risks of significant anxiety symptoms. In contrast, better dietary habits (OR = 0.98; $p < 0.001$) were associated with a decreased risk of significant anxiety symptoms.

To further investigate the relevant factors of five subtypes of anxiety symptoms among preschool children, the multivariate logistic regression analyses were separately performed (**Table 4**). The results of the analyses showed that girls, sleep disturbances, and more autistic tendencies were significantly associated with increased risks of all anxiety subtypes. Better dietary habits were associated with a decreased risk of all anxiety subtypes except for obsessive-compulsive disorder. Poor prenatal emotional symptoms increased the risks of generalised anxiety disorder, and poor postnatal emotional symptoms enhanced the odd of separation anxiety disorder. Pregnancy complications increased the risk of obsessive-compulsive disorder. The region of kindergartens in Ma'anshan was associated with increased risks of all anxiety subtypes except for separation anxiety disorder. Left-behind experience was at increased risk of physical injury fears. In addition, caregiver anxiety symptoms were significantly associated with increased odds of all anxiety subtypes.

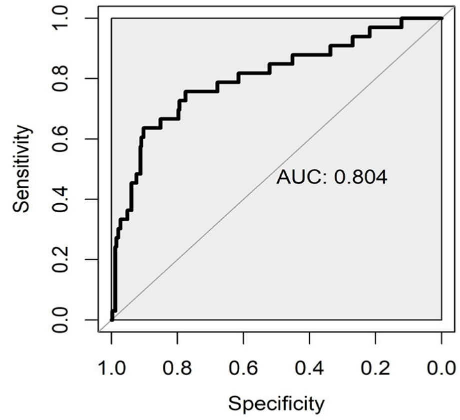


FIGURE 1 | Receiver operating characteristic curves (ROC) for the predictive performance of regression model of anxiety symptoms.

The receiver operator characteristic (ROC) curve based on the highest accuracy of 10-fold cross-validation for the regression model of anxiety symptoms is presented in **Figure 1**. The result of 10-fold cross-validation indicated that the mean AUC, sensitivity, specificity, and accuracy were 0.78 (95% CI: 0.76–0.80), 70.45% (95% CI: 61.60–79.31%), 78.18% (95% CI: 71.50–84.87%), and 71.15% (95% CI: 63.67–78.64%), respectively. The multivariate regression models for most subtypes of anxiety symptoms demonstrated acceptable discriminative accuracy (**Supplementary Table 2**).

DISCUSSION

Due to the scarcity of large sample data regarding preschool children's anxiety symptoms in China, we conducted this cross-sectional study, including 3,636 preschool children, to explore the prevalence of anxiety symptoms and comprehensive factors. The present study found that 9.1% of child participants had significant anxiety symptoms, which was within the reported prevalence range of 7.5–22.2% from European countries and America (2–4, 24, 44), and higher than the rate of 3.3% in one Chinese study (36), but lower than that of other two

TABLE 3 | Logistic regression models of significant anxiety symptoms and associated factors among preschool children.

Variables	**Univariate analysis**		**Multivariate analysis**	
	***OR* (95% CI)**	***p*-value**	***OR* (95% CI)**	***p*-value**
Individual characteristics				
Age (year)	1.07 (0.94–1.21)	0.295	-	-
Girls (vs. boys)	1.34 (1.07–1.68)	**0.012**	1.50 (1.18–1.91)	**0.001**
Overweight or obesity (vs. normal)	1.00 (0.74–1.35)	0.989	-	-
Dietary behaviour	0.96 (0.95–0.96)	**<0.001**	0.98 (0.97–0.99)	**<0.001**
Sleep disturbances	1.09 (1.08–1.11)	**<0.001**	1.05 (1.03–1.07)	**<0.001**
Autistic tendencies	1.18 (1.15–1.21)	**<0.001**	1.12 (1.09–1.15)	**<0.001**
Prenatal and perinatal factors				
Caesarean section (vs. vaginal delivery)	0.81 (0.64–1.02)	0.078	-	-
Low birth weight (vs. no)	1.33 (0.79–2.23)	0.285	-	-
Preterm birth (vs. no)	1.24 (0.69–2.23)	0.476	-	-
Poor prenatal emotional symptoms (vs. pleasure or fair)	2.46 (1.72–3.53)	**<0.001**	1.54 (1.05–2.27)	**0.027**
Poor postnatal emotional symptoms (vs. pleasure or fair)	1.58 (1.11–2.25)	**0.012**	-	-
Pregnancy complications (vs. no)	1.37 (1.01–1.85)	**0.044**	-	-
No exclusive breastfeeding (vs. yes)	1.01 (0.80–1.27)	0.943	-	-
Family factors				
Region of kindergartens in Fuyang (vs. Hefei)	1.48 (1.11–1.96)	**0.007**	-	-
Region of kindergartens in Ma’anshan (vs. Hefei)	1.30 (0.94–1.78)	0.110	-	-
High school and above (vs. middle school and below)	0.66 (0.53–0.83)	**<0.001**	0.79 (0.61–1.01)	0.058
Sibling (vs. no)	1.29 (1.00–1.67)	**0.050**	-	-
Left-behind experience (vs. no)	1.53 (1.22–1.92)	**<0.001**	1.29 (1.01–1.65)	**0.043**
Divorced/widowed (vs. married)	1.44 (0.83–2.50)	0.198	-	-
Monthly household income (RMB) $\geq$5,000 (vs. $<$5,000)	0.90 (0.72–1.13)	0.366	-	-
Discordant parenting attitude (vs. accordant)	1.70 (1.35–2.15)	**<0.001**	-	-
Contact physical abuse (vs. no)	1.42 (1.01–2.00)	**0.046**	-	-
Caregivers’ anxiety symptoms	1.07 (1.06–1.08)	**<0.001**	1.03 (1.02–1.05)	**<0.001**

Bold values denote p values significant at the 0.05 level.

Chinese studies with rates of 14.1 and 15.2% (35, 43). The wide range of prevalence rates for anxiety may be due to the populations’ inherent population differences among countries and various assessment scales being used in different studies. These prevalence rates indicate that the anxiety of preschool children cannot be ignored.

Regarding individual characteristics, one interesting finding was that significant gender differences were detected for the scores of total and subtypes of anxiety symptoms. This finding was supported by one study, which has indicated that girls are affected significantly more often than boys by anxiety disorder, and gender differences might begin at preschool age (24). However, Franz found that girls reported significantly more separation anxiety disorder than boys did (2). On the contrary, no significant gender differences are detected for preschool children’s anxiety in some other studies (22, 23). In contrast to gender differences, age differences only partially appeared. Although previous studies have indicated that younger children display higher scores of anxiety symptoms than older children (21, 22), the present study showed that 3-year-old children had higher scores of separation anxiety disorder, which may be attributed to their transition from the family to kindergarten. In China, most children, particularly the 3-year-old children, have just entered kindergarten. These children may experience a fear of separation as they attempt to adapt to the kindergarten life. The reasons for this separation anxiety are ambiguous, and more studies on the development and the mechanism of gender and age differences are needed for further investigation.

In addition, this study confirmed the associations between emotional and behavioural problems and anxiety among preschool children. The findings demonstrated that poor dietary habits, sleep disturbances, and autistic tendencies were associated with anxiety symptoms in preschool children. Indeed, the notion that problematic behaviours are often comorbid with mental disorders has been raised over the years (10, 45, 46). One study among 2- to 6-year-old children has indicated that anxiety symptoms are associated with a higher score of dietary behavioural problems (45). Sleep disturbances (such as late bedtime and short sleep duration) affect problematic behaviours including anxious behaviour in 5-year-old children (47). A longitudinal study has shown that infant sleep disturbances at 2 and 24 months predict anxiety symptoms at 3 years, and a bidirectional association with anxiety symptoms preceding later sleep problems seems to exist (25). Recent research has reported that anxiety symptoms are present in preschool children with autism spectrum disorder more than in typically developing

TABLE 4 | Multivariate logistic regression models anxiety symptoms in different subtypes and associated factors among preschool children.

Variables	Separation anxiety disorder		Physical injury fears		Social anxiety		Obsessive-compulsive disorder		Generalised anxiety disorder	
	***OR* (95% CI)**	***p*-value**	***OR* (95% CI)**	***p*-value**	***OR* (95% CI)**	***p*-value**	***OR* (95% CI)**	***p*-value**	***OR* (95% CI)**	***p*-value**
Individual characteristics										
Girls (vs. boys)	1.29 (1.09–1.51)	**0.002**	1.75 (1.49–2.06)	**<0.001**	1.36 (1.15–1.60)	**<0.001**	1.27 (1.10–1.47)	**0.001**	1.25 (1.05–1.49)	**0.014**
Dietary behaviour	0.99 (0.98–0.99)	**<0.001**	0.99 (0.98–1.00)	**0.007**	0.99 (0.98–1.00)	**0.008**	–	–	0.99 (0.98-0.99)	**<0.001**
Sleep disturbances	1.05 (1.03–1.06)	**<0.001**	1.04 (1.03–1.05)	**<0.001**	1.02 (1.01–1.04)	**<0.001**	1.01 (1.00–1.02)	**0.032**	1.03 (1.02-1.05)	**<0.001**
Autistic tendencies	1.12 (1.10–1.14)	**<0.001**	1.06 (1.04–1.08)	**<0.001**	1.16 (1.13–1.18)	**<0.001**	1.10 (1.09–1.13)	**<0.001**	1.15 (1.12-1.17)	**<0.001**
Prenatal and perinatal factors										
Poor prenatal emotional symptoms (vs. pleasure or fair)	–	–	–	–	–	–	–	–	1.42 (1.03-1.95)	**0.031**
Poor postnatal emotional symptoms (vs. pleasure or fair)	1.38 (1.05–1.80)	**0.019**	–	–	–	–	–	–	–	-
Pregnancy complications (vs. no)	–	–	–	–	–	–	1.33 (1.09–1.64)	**0.006**		
Family factors										
Region of kindergartens in Fuyang (vs. Hefei)	–	–	1.08 (0.89–1.32)	0.448	0.95 (0.78–1.16)	0.596	1.16 (0.98-1.39)	0.090	1.17 (0.94-1.45)	0.161
Region of kindergartens in Ma'anshan (vs. Hefei)	–	–	1.41 (1.14–1.76)	**0.002**	1.41 (1.14–1.76)	**0.002**	1.45 (1.19–1.76)	**<0.001**	1.45 (1.14-1.85)	**0.002**
Left-behind experience (vs. no)	–	–	1.26 (1.07–1.49)	**0.005**	–	–	–	–	–	**–**
Caregivers' anxiety symptoms	1.03 (1.02–1.04)	**<0.001**	1.02 (1.01–1.03)	**<0.001**	1.04 (1.03–1.05)	**<0.001**	1.01 (1.01–1.03)	**0.003**	1.04 (1.03-1.05)	**<0.001**

Bold values denote p values significant at the 0.05 level.

children (45). In addition, a nationwide twin cohort study from Sweden discovers positive relationships between autistic-like traits and anxiety symptoms (48). This study provides more evidence on the effects of emotional and behavioural problems on preschool children's anxiety.

When referring to prenatal and perinatal factors, the results of univariate analysis revealed that poor prenatal and postnatal emotional symptoms and pregnancy complications were associated with significant anxiety symptoms in preschool children, and poor prenatal emotional symptoms were still statistically significant in multivariate analysis. Early exposure to adversities particularly during pregnancy may affect the development of the child's brain and mental health (30, 49). In line with this study, previous research has shown that children exposed to prenatal and postnatal adverse emotional symptoms are at higher risks of anxiety (27, 50). Evidence has indicated that prenatal stress has programming effects on the foetal hypothalamic–pituitary–adrenal (HPA) axis (51). Alterations in the foetal HPA axis can be long-term; therefore, the offspring may have an elevated risk of psychiatric disorders in childhood (52). Besides, associations between prenatal/perinatal risk factors and children's anxiety disorders could be mediated through parenting and family functioning or alterations in infant brain structure and function (53, 54). In addition, studies have indicated that prenatal and perinatal adversities have negative effects on mother–infant interactions, infant temperament, sleep, mental development, autism, and internalising behavior (55, 56). It should be noted that prenatal/perinatal factors and some individual factors reported above are prone to coexistence and accumulation, which can result in child anxiety.

Family played an important role in child development. A recent meta-analysis has shown that left-behind children (LBC) have an 85% higher risk of anxiety than non-LBC

(57). Consistent with the literature, the results of this study revealed that LBC had a 29% increased risk of anxiety and a 46% increased risk of social anxiety. Parental labour migration and the resulting parent–child separation is common in China and leads to changes in the family environment (58). Although parental labour migration may bring economic benefits for families, it may generate hidden costs for the health of LBC (57, 59). Given that parental labour migration can sometimes not be avoided, multidimensional interventions including proactive policies and protective factors are warranted to prevent LBC from adverse health outcomes. Additionally, the results of this study suggested that caregivers' anxiety symptoms were positively associated with preschool children' anxiety symptoms. This finding is supported by theoretical models of the intergenerational transmission of anxiety, which indicates multiple pathways for the transmission of anxious cognition and behaviours (60, 61). Research has reported that caregivers or parents seem to create an anxiety-rearing environment by modelling anxious behaviours, exerting too much control over their children, and promoting anxious cognitions through the use of verbal threats, which fosters anxiety in the offspring (13, 60–63). Overall, more prospective studies are needed to clarify the association between caregivers' anxiety symptoms and preschool children's anxiety symptoms and relevant mechanistic research may benefit prevention and treatment intervention programs for anxiety.

While the underlying mechanisms of anxiety disorders are not fully understood, studies on animals and humans suggest that they are multifactorial disorders caused by the interaction between genetic and environmental factors. Researchers have proposed the genetic and epigenetic risks in the aetiology of anxiety disorders, especially in the case of familial aggregation (64, 65). Available data suggest that first-degree relatives of patients are more susceptible to developing an anxiety disorder compared with relatives of the healthy control group (20). Meanwhile, several risk genes contributing to the development of anxiety disorders have been identified (66). However, genetic factors do not act in isolation in anxiety disorders but rather interact with environmental factors. The interaction between genetic and environmental factors has been explained by epigenetic mechanisms in recent years (67, 68). The review by Babenko et al. (68, 69) concluded that prenatal stress can trigger epigenetic changes in the placenta and brain and then induce powerful influences on offspring mental health in human studies and animal models. Moreover, one study has demonstrated that effects of prenatal depressive symptoms and socioeconomic status on foetal brain development are partially modulated by genetic risk, which further confirmed gene–environment interdependence (70). Although this study included individual internal and external factors, genetic factors were limited. Future studies should pay more attention to the interaction between genetic and environmental factors.

One strength of this study is the larger sample size of preschool children and the age-appropriate validated measurement tools to assess children's anxiety symptoms. Another strength is that this study comprehensively explored factors at multiple levels of social ecology including individual, prenatal and perinatal, and family factors, which might provide a more holistic understanding of influencing factors for anxiety symptoms among preschool children. Despite these strengths, several limitations of this study should be noted. First, this study was based on the responses of a parental or other primary caregiver on a questionnaire, and prenatal and perinatal factors were retrospectively collected; hence, the possibility of reporting and recall bias cannot be eliminated. Second, preschool children were only selected from Anhui Province and a convenience sample. Thus, the external validity of the results and generalizability to the general population are partially limited. Third, this study employed a cross-sectional design, making it difficult to identify a causal relationship. Besides, in this study, these factors from pregnancy to early childhood occur sequentially or display coexistence and accumulation, and we cannot clarify their relationships. Although we applied relevant optimal models to control confounding factors, we still cannot clarify whether the interactions of the various factors amplify or attenuate the risk of child anxiety. Future longitudinal studies are required to examine causal pathways in these relationships and to determine the potential effects and interactions of prenatal, perinatal, and family factors on anxiety symptoms. Additionally, research on the underlying mechanism is important to implement prevention and intervention programs for anxiety.

In conclusion, anxiety symptoms in preschool children were prevalent, particularly in girls. Many factors from pregnancy to preschool age involving children's poor dietary habits, sleep disturbances, autistic tendencies, left-behind experience, maternal poor pregnancy emotional symptoms, and more caregiver anxiety symptoms were associated with significant anxiety symptoms among preschool children. The findings highlighted the importance of understanding early-life risk factors for anxiety, and efficient prevention and intervention strategies should be implemented in early childhood even to the perinatal period.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article and **Supplementary Material**. Further inquires can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Anhui Medical University. Written informed consent to participate in this study was provided by the participant's legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

XD designed this study and wrote the manuscript. NL, WS, HW, QS, XG, ML, QQ, LS, and MC recruited the participants, administered the assessment, and undertook the data collation and analysis. JW and YS guided and revised the writing. All authors listed have read the final manuscript and approved it for publication.

FUNDING

This work was supported by the National Natural Science Foundation of China (Grant Number: 81872704) and the Natural Science Foundation in Higher Education of Anhui (Grant Number: KJ2020A0208).

ACKNOWLEDGMENTS

We acknowledge the efforts of the research team, the local Centre for Disease Control and Prevention, and all kindergartens as well as all the children and families who participated in this research.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.778291/full#supplementary-material

REFERENCES

1. Ezpeleta L, Keeler G, Erkanli A, Costello EJ, Angold A. Epidemiology of psychiatric disability in childhood and adolescence. *J Child Psychol Psychiatry.* (2001) 42:901–14. doi: 10.1111/1469-7610.00786
2. Franz LMBC, Angold AMRC, Copeland WPD, Costello EJPD, Towe-Goodman NPD, Egger HMD. Preschool anxiety disorders in pediatric primary care: prevalence and comorbidity. *J Am Acad Child Psy.* (2013) 52:1294–303. doi: 10.1016/j.jaac.2013.09.008
3. Wichstrøm L, Belsky J, Berg-Nielsen TS. Preschool predictors of childhood anxiety disorders: a prospective community study. *J Child Psychol Psyc.* (2013) 54:1327–36. doi: 10.1111/jcpp.12116
4. Petresco S, Anselmi L, Santos IS, Barros AJD, Fleitlich-Bilyk B, Barros FC, et al. Prevalence and comorbidity of psychiatric disorders among 6-year-old children: 2004 Pelotas birth cohort. *Soc Psych Psych Epid.* (2014) 49:975–83. doi: 10.1007/s00127-014-0826-z
5. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. *Arch Gen Psychiatry.* (2005) 62:593. doi: 10.1001/archpsyc.62.6.593
6. Merikangas KR, He JP, Burstein M, Swanson SA, Avenevoli S, Cui L. et al. Lifetime prevalence of mental disorders in US adolescents: results from the national comorbidity survey replication-adolescent supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry.* (2010) 49:980–9. doi: 10.1016/j.jaac.2010.05.017
7. Bosquet M, Egeland B. The development and maintenance of anxiety symptoms from infancy through adolescence in a longitudinal sample. *Dev Psychopathol.* (2006) 18:517–50. doi: 10.1017/S0954579406060275
8. Bufferd SJ, Dougherty LR, Carlson GA, Rose S, Klein DN. Psychiatric disorders in preschoolers: continuity from ages 3 to 6. *Am J Psychiatry.* (2012) 169:1157–64. doi: 10.1176/appi.ajp.2012.12020268
9. Côté SM, Boivin M, Liu X, Nagin DS, Zoccolillo M, Tremblay RE. Depression and anxiety symptoms: onset, developmental course and risk factors during early childhood. *J Child Psychol Psyc.* (2009) 50:1201–8. doi: 10.1111/j.1469-7610.2009.02099.x
10. Kertz SJ, Sylvester C, Tillman R, Luby JL. Latent class profiles of anxiety symptom trajectories from preschool through school age. *J Clin Child Adolesc.* (2019) 48:316–31. doi: 10.1080/15374416.2017.1295380
11. Lau EX, Rapee RM. Prevention of anxiety disorders. *Curr Psychiat Rep.* (2011) 13:258–66. doi: 10.1007/s11920-011-0199-x
12. Ahmadzadeh YI, Eley TC, Leve LD, Shaw DS, Natsuaki MN, Reiss D, et al. Anxiety in the family: a genetically informed analysis of transactional associations between mother, father and child anxiety symptoms. *J Child Psychol Psyc.* (2019) 60:1269–77. doi: 10.1111/jcpp.13068
13. Field AP, Lester KJ, Cartwright-Hatton S, Harold GT, Shaw DS, Natsuaki MN, et al. Maternal and paternal influences on childhood anxiety symptoms: a genetically sensitive comparison. *J Appl Dev Psychol.* (2020) 68:101123. doi: 10.1016/j.appdev.2020.101123
14. Guhn M, Emerson SD, Mahdaviani D, Gadermann AM. Associations of birth factors and socio-economic status with indicators of early emotional development and mental health in childhood: a population-based linkage study. *Child Psychiat Hum D.* (2020) 51:80–93. doi: 10.1007/s10578-019-00912-6
15. Klein AM, Schlesier-Michel A, Otto Y, White LO, Andreas A, Sierau S, et al. Latent trajectories of internalizing symptoms from preschool to school age: a multi-informant study in a high-risk sample. *Dev Psychopathol.* (2019) 31:657–81. doi: 10.1017/S0954579418000214
16. Liu L, Wang M. Parental corporal punishment and child anxiety in China: the moderating role of HPA-axis activity. *J Affect Disorders.* (2020) 273:500–7. doi: 10.1016/j.jad.2020.04.055
17. Liu Z, Li X, Ge X. Left too early: the effects of age at separation from parents on Chinese rural children's symptoms of anxiety and depression. *Am J Public Health.* (2009) 99:2049–54. doi: 10.2105/AJPH.2008.150474
18. Silberg JL, Gillespie N, Moore AA, Eaves LJ, Bates J, Aggen S, et al. Shared genetic and environmental influences on early temperament and preschool psychiatric disorders in hispanic twins. *Twin Res Hum Genet.* (2015) 18:171–8. doi: 10.1017/thg.2014.88
19. Trzaskowski M, Zavos HM, Haworth CM, Plomin R, Eley TC. Stable genetic influence on anxiety-related behaviours across middle childhood. *J Abnorm Child Psychol.* (2012) 40:85–94. doi: 10.1007/s10802-011-9545-z
20. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. *Am J Psychiatry.* (2001) 158:1568–78. doi: 10.1176/appi.ajp.158.10.1568
21. Spence SH, Rapee R, McDonald C, Ingram M. The structure of anxiety symptoms among preschoolers. *Behav Res Ther.* (2001) 39:1293–316. doi: 10.1016/S0005-7967(00)00098-X
22. Wang M, Zhao J. Anxiety disorder symptoms in Chinese preschool children. *Child Psychiat Hum D.* (2015) 46:158–66. doi: 10.1007/s10578-014-0461-7
23. Lavigne JV, Lebailly SA, Hopkins J, Gouze KR, Binns HJ. The prevalence of ADHD, ODD, depression, and anxiety in a community sample of 4-year-olds. *J Clin Child Adolesc Psychol.* (2009) 38:315–28. doi: 10.1080/15374410902851382
24. Paulus FW, Backes A, Sander CS, Weber M, von Gontard A. Anxiety disorders and behavioral inhibition in preschool children: a population-based study. *Child Psychiat Hum D.* (2015) 46:150–7. doi: 10.1007/s10578-014-0460-8
25. Jansen PW, Saridjan NS, Hofman A, Jaddoe VW, Verhulst FC, Tiemeier H. Does disturbed sleeping precede symptoms of anxiety or depression in toddlers? the generation R study. *Psychosom Med.* (2011) 73:242–9. doi: 10.1097/PSY.0b013e31820a4abb
26. Towe-Goodman NRP, Franz LM, Copeland WP, Angold AM, Egger HM. Perceived family impact of preschool anxiety disorders. *J Am Acad Child Psy.* (2014) 53:437–46. doi: 10.1016/j.jaac.2013.12.017
27. Bendiksen B, Aase H, Diep LM, Svensson E, Friis S, Zeiner P. The Associations between pre- and postnatal maternal symptoms of distress and preschooler's symptoms of ADHD, oppositional defiant disorder, conduct disorder, and anxiety. *J Atten Disord.* (2020) 24:1057–69. doi: 10.1177/1087054715616185
28. Barker DJ. The origins of the developmental origins theory. *J Intern Med.* (2007) 261:412–7. doi: 10.1111/j.1365-2796.2007.01809.x

29. Lewis AJ, Austin E, Knapp R, Vaiano T, Galbally M. Perinatal maternal mental health, fetal programming and child development. *Healthcare.* (2015) 3:1212–27. doi: 10.3390/healthcare3041212
30. Lautarescu A, Craig MC, Glover V. Prenatal stress: effects on fetal and child brain development. *Int Rev Neurobiol.* (2020) 150:17–40. doi: 10.1016/bs.irn.2019.11.002
31. Dachew BA, Scott JG, Mamun A, Alati R. Hypertensive disorders of pregnancy and the risk of anxiety disorders in adolescence: findings from the Avon longitudinal study of parents and children. *J Psychiatr Res.* (2019) 110:159–65. doi: 10.1016/j.jpsychires.2019.01.001
32. Hentges RF, Graham SA, Fearon P, Tough S, Madigan S. The chronicity and timing of prenatal and antenatal maternal depression and anxiety on child outcomes at age 5. *Depress Anxiety.* (2020) 37:576–86. doi: 10.1002/da.23039
33. Ståhlberg T, Khanal P, Chudal R, Luntamo T, Kronström K, Sourander A. Prenatal and perinatal risk factors for anxiety disorders among children and adolescents: a systematic review. *J Affect Disorders.* (2020) 277:85–93. doi: 10.1016/j.jad.2020.08.004
34. Berber Çelik Ç, Odaci H. Does child abuse have an impact on self-esteem, depression, anxiety and stress conditions of individuals? *Int J Soc Psychiatr.* (2020) 66:171–8. doi: 10.1177/0020764019894618
35. Wu G, Bai L, Shi Q, Ren H, Wang H. Relationship between preschool children's anxiety and behavior problems. *Chin J Woman Child Health Res.* (2016) 27:1173–6. doi: 10.3969/j.issn.1673-5293.2016.10.003
36. Xu Y, Yan Q, Tong L. Study on the associations between parenting stress and anxiety symptoms among urban preschoolers. *Chin J Child Health Care.* (2020) 28:563–7. doi: 10.11852/zgetbjzz2019-1129
37. Zhou F, Zhu M, Jiang H, Feng X. The effect of early intervention in preschool children anxiety. *China Mod Doctor.* (2015) 53:59–61. Available online at: https://kns.cnki.net/kcms/detail/detail.aspx?FileName=ZDYS201511021&DbName=CJFQ2015
38. World Health Organization. *WHO Child Growth Standards: Methods And Development* (2006).
39. Deng C, Zhang W, Jin Y, Feng JH, Liu QJ, Liu YL, et al. Analysis of relationship between eating problems of 1-5 years old children and the feeding behavior. *Chin J Child Health Care.* (2012) 20:686–8. Available online at: https://kns.cnki.net/kcms/detail/detail.aspx?FileName=ERTO201208009&DbName=CJFQ2012
40. Liu Z, Wang G, Tang H, Wen F, Li N. Reliability and validity of the children's sleep habits questionnaire in preschool-aged Chinese children. *Sleep Biol Rhythms.* (2014) 12:187–93. doi: 10.1111/sbr.12061
41. Sun X, Allison C, Auyeung B, Matthews FE, Zhang Z, Baron-Cohen S, et al. Comparison between a mandarin Chinese version of the childhood autism spectrum test and the Clancy autism behaviour scale in mainland China. *Res Dev Disabil.* (2014) 35:1599–608. doi: 10.1016/j.ridd.2014.02.005
42. Tanaka-Matsumi J, Kameoka VA. Reliabilities and concurrent validities of popular self-report measures of depression, anxiety, and social desirability. *J Consult Clin Psychol.* (1986) 54:328–33. doi: 10.1037//0022-006x.54.3.328
43. Fu Z, Hao J, Chen S, Qiao S, Guo L, Ding Y, et al. Investigation of the status of anxiety and related factors for the preschool children in Harbin. *Chin J Child Health Care.* (2013) 1:10–2. Available online at: https://kns.cnki.net/kcms/detail/detail.aspx?FileName=ERTO201301003&DbName=CJFQ2013
44. Bufferd SJ, Dougherty LR, Carlson GA, Klein DN. Parent-reported mental health in preschoolers: findings using a diagnostic interview. *Compr Psychiat.* (2011) 52:359–69. doi: 10.1016/j.comppsych.2010.08.006
45. Johnson CR, DeMand A, Shui A. Relationships between anxiety and sleep and feeding in young children with ASD. *J Dev Phys Disabil.* (2015) 27:359–73. doi: 10.1007/s10882-015-9419-3
46. Chase RM, Pincus DB. Sleep-related problems in children and adolescents with anxiety disorders. *Behav Sleep Med.* (2011) 9:224–36. doi: 10.1080/15402002.2011.606768
47. Suda M, Nagamitsu S, Obara H, Shimomura G, Ishii R, Yuge K, et al. Association between children's sleep patterns and problematic behaviors at age 5. *Pediatr Int.* (2020) 62:1189–96. doi: 10.1111/ped.14267
48. Lundström S, Chang Z, Kerekes N, Gumpert CH, Råstam M, Gillberg C, et al. Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults. *Psychol Med.* (2011) 41:2423–33. doi: 10.1017/S0033291711000377
49. O'Donnell KJ, Glover V, Barker ED, O'Connor TG. The persisting effect of maternal mood in pregnancy on childhood psychopathology. *Dev Psychopathol.* (2014) 26:393–403. doi: 10.1017/S0954579414000029
50. Lawrence PJ, Creswell C, Cooper PJ, Murray L. The role of maternal anxiety disorder subtype, parenting and infant stable temperamental inhibition in child anxiety: a prospective longitudinal study. *J Child Psychol Psyc.* (2020) 61:779–88. doi: 10.1111/jcpp.13187
51. Weinstock M. Alterations induced by gestational stress in brain morphology and behaviour of the offspring. *Prog Neurobiol.* (2001) 65:427–51. doi: 10.1016/S0301-0082(01)00018-1
52. Moisiadis VG, Matthews SG. Glucocorticoids and fetal programming part 1: Outcomes. *Nat Rev Endocrinol.* (2014) 10:391–402. doi: 10.1038/nrendo.2014.73
53. Adamson B, Letourneau N, Lebel C. Prenatal maternal anxiety and children's brain structure and function: a systematic review of neuroimaging studies. *J Affect Disorders.* (2018) 241:117–26. doi: 10.1016/j.jad.2018.08.029
54. Matvienko-Sikar K, Murphy G, Murphy M. The role of prenatal, obstetric, and post-partum factors in the parenting stress of mothers and fathers of 9-month old infants. *J Psychosom Obstet Gynaecol.* (2018) 39:47–55. doi: 10.1080/0167482X.2017.1286641
55. Field T. Postnatal anxiety prevalence, predictors and effects on development: a narrative review. *Infant Behav Dev.* (2018) 51:24–32. doi: 10.1016/j.infbeh.2018.02.005
56. Wang C, Geng H, Liu W, Zhang G. Prenatal, perinatal, and postnatal factors associated with autism: a meta-analysis. *Medicine.* (2017) 96:e6696. doi: 10.1097/MD.0000000000006696
57. Fellmeth G, Rose-Clarke K, Zhao C, Busert LK, Zheng Y, Massazza A, et al. Health impacts of parental migration on left-behind children and adolescents: a systematic review and meta-analysis. *Lancet.* (2018) 392:2567–82. doi: 10.1016/S0140-6736(18)32558-3
58. Wen M, Lin D. Child development in rural China: children left behind by their migrant parents and children of nonmigrant families. *Child Dev.* (2012) 83:120–36. doi: 10.1111/j.1467-8624.2011.01698.x
59. Qin J, Albin B. The mental health of children left behind in rural China by migrating parents: a literature review. *J Public Ment Health.* (2010) 9:4–16. doi: 10.5042/jpmh.2010.0458
60. Fisak B, Grills-Taquechel AE. Parental modeling, reinforcement, and information transfer: risk factors in the development of child anxiety? *Clin Child Fam Psych.* (2007) 10:213–31. doi: 10.1007/s10567-007-0020-x
61. Murray L, Creswell C, Cooper PJ. The development of anxiety disorders in childhood: an integrative review. *Psychol Med.* (2009) 39:1413–23. doi: 10.1017/S0033291709005157
62. Aktar E, MajdandŽić M, de Vente W, Bögels SM. Parental social anxiety disorder prospectively predicts toddlers' fear/avoidance in a social referencing paradigm. *J Child Psychol Psyc.* (2014) 55:77–87. doi: 10.1111/jcpp.12121
63. McLeod BD, Wood JJ, Weisz JR. Examining the association between parenting and childhood anxiety: a meta-analysis. *Clin Psychol Rev.* (2007) 27:155–72. doi: 10.1016/j.cpr.2006.09.002
64. Meier SM, Deckert J. Genetics of anxiety disorders. *Curr Psychiatry Rep.* (2019) 21:16. doi: 10.1007/s11920-019-1002-7
65. Gottschalk MG, Domschke K. Novel developments in genetic and epigenetic mechanisms of anxiety. *Curr Opin Psychiatry.* (2016) 29:32–8. doi: 10.1097/YCO.0000000000000219
66. Schiele MA, Domschke K. Epigenetics at the crossroads between genes, environment and resilience in anxiety disorders. *Genes, Brain and Behavior.* (2018) 17:e12423. doi: 10.1111/gbb.12423
67. Bartlett AA, Singh R, Hunter RG. Anxiety and epigenetics. *Adv Exp Med Biol.* (2017) 978:145–66. doi: 10.1007/978-3-319-53889-1_8
68. Babenko O, Kovalchuk I, Metz GA. Stress-induced perinatal and transgenerational epigenetic programming of brain development and mental health. *Neurosci Biobehav Rev.* (2015) 48:70–91. doi: 10.1016/j.neubiorev.2014.11.013
69. Fatima M, Srivastav S, Mondal AC. Prenatal stress and depression associated neuronal development in neonates. *Int J Dev Neurosci.* (2017) 60:1–7. doi: 10.1016/j.ijdevneu.2017.04.001
70. Qiu A, Shen M, Buss C, Chong YS, Kwek K, Saw SM, et al. Effects of antenatal maternal depressive symptoms and socio-economic status on neonatal brain

development are modulated by genetic risk. *Cereb Cortex.* (2017) 27:3080–92. doi: 10.1093/cercor/bhx065

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 28 February 2022
doi: 10.3389/fpsyt.2022.770921

Change Blindness in Adolescents With Attention-Deficit/Hyperactivity Disorder: Use of Eye-Tracking

Michal Hochhauser[1], Adi Aran[2] and Ouriel Grynszpan[3]*

[1] *Department of Occupational Therapy, Ariel University, Ariel, Israel,* [2] *Neuropedeatric Unit, Shaare Zedek Medical Center, Jerusalem, Israel,* [3] *Laboratoire Interdisciplinaire des Sciences du Numérique, Université Paris-Saclay, Orsay, France*

Objective: This study investigated change detection of central or marginal interest in images using a change-blindness paradigm with eye tracking.

Method: Eighty-four drug-naïve adolescents [44 with attention-deficit/hyperactivity disorder (ADHD)/40 controls with typical development] searched for a change in 36 pairs of original and modified images, with an item of central or marginal interest present or absent, presented in rapid alternation. Collected data were detection rate, response time, and gaze fixation duration, latency, and dispersion data.

Results: Both groups' change-detection times were similar, with no speed–accuracy trade-off. No between-group differences were found in time to first fixation, fixation duration, or scan paths. Both groups performed better for items of central level of interest. The ADHD group demonstrated greater fixation dispersion in scan paths for central- and marginal-interest items.

Conclusion: Results suggest the greater gaze dispersion may lead to greater fatigue in tasks that require longer attention duration.

Keywords: change blindness, attention-deficit hyperactivity disorder, adolescents, eye tracking, fixations, attention, cognitive load

Edited by:
Pradipta Biswas,
Indian Institute of Science (IISc), India

Reviewed by:
Kesong Hu,
Lake Superior State University,
United States
Thomas Andrillon,
INSERM U1127 Institut du Cerveau et
de la Moelle épinière (ICM), France

****Correspondence:***
Michal Hochhauser
michalho@ariel.ac.il

Specialty section:
This article was submitted to
Child and Adolescent Psychiatry,
a section of the journal
Frontiers in Psychiatry

Received: *05 September 2021*
Accepted: *03 February 2022*
Published: *28 February 2022*

Citation:
Hochhauser M, Aran A and
Grynszpan O (2022) Change
Blindness in Adolescents With
Attention-Deficit/Hyperactivity
Disorder: Use of Eye-Tracking.
Front. Psychiatry 13:770921.
doi: 10.3389/fpsyt.2022.770921

INTRODUCTION

Attention-based mechanisms play an essential role in development, redirecting cognitive resources to new or salient stimuli, and facilitating information processing and adaptive response (1). Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition characterized by impaired attention, hyperactivity, and impulsivity (2). Although diagnosed most commonly in childhood, it has been shown to be a lifelong disorder that negatively affects everyday functioning (3). Various studies have shown that in adolescence, the inattentional features are dominant and often manifest as limited attention span, disengagement, or distractibility (4). As children with ADHD progress to adolescence, core symptoms of hyperactivity/impulsivity tend to decrease over time, although inattention tends to persist (5, 6). Studies have shown that deficits in visual processing, vigilance, and inhibition continue into adolescence, at the same time, showing inconsistencies in response times impairments specifically in adolescence (7). Thus, adolescents may differ from children with regard to their neuropsychological profile of cognitive control and attention.

A range of experimental paradigms have been used to study different aspects of change detection. For instance, visual-search tests are perceptual tasks requiring attention and active scanning to detect a feature change in a particular object among other objects [i.e., distractors (8)]. In their review, Mullane and Klein (9) concluded that single-feature search (the target differs from the distracters based on one simple perceptive feature, e.g., shape) is relatively preserved in ADHD participants, but serial search (target and distracters share more than one perceptive feature, e.g., shape and color) produced inconsistent results. Although studies of visual search tasks in ADHD provide useful information on detection rates and accuracy in locating an item in an array, they do not offer an exhaustive understanding of change detection, especially when it comes to detecting transient change. Detection of transient change relies on the extended memory span of focal attention to bind together the elements of complex stimuli.

Change blindness is a perceptual phenomenon that occurs when a transient change in a visual stimulus is introduced and the observer does not notice it right away (10). Many individuals experience difficulties due to this phenomenon (11, 12) and surprisingly fail to perceive large changes occurring in scenes (12–14). For example, observers often fail to notice major differences introduced into an image while it flickers off and on again.

Experimental paradigms used to test change blindness involve visual attention in such a way that both perceptual and semantic characteristics of the visual scene combine to create a priority list that determines which items to attend first. According to Rensink et al. (10) and Auvray et al. (15), under normal viewing conditions, transient changes in the visual field are automatically detected by low-level perceptual mechanisms. Therefore, attention is extrinsically attracted to the location where the change occurred. Change blindness paradigms are based on the use of experimental protocols successfully masking the local transients that would normally cause the automatic perception of change.

Rensink (16, 17) and Rensink et al. (10) created experimental conditions based on a flicker paradigm task. In the flicker paradigm, an original and modified image of any size and type are presented in rapid alternation with a blank screen placed between successive images. When the blank screen lasts for more than 80 ms, it masks the local transients responsible for automatic perception of change. When attention is no longer automatically directed where change occurs, observers must rely on their scene memory and deliberate control of attention to detect what may have changed. Observers must scan an image, encoding the scene piece by piece (10). Given the number of potential features and objects in a typical natural scene, many aspects of a scene may not be preserved in memory across views. Under this condition, if changes occur in areas that attract more attention, they tend to be detected more quickly. Conversely, if changes occur in areas that attract attention less, they tend to be detected more slowly (18, 19).

An item in the visual field can attract attention due to its perceptual saliency or because of its relevance for the viewer. Studies have found that, in the general population, changes to high-salience features were fixated sooner and for shorter durations and were detected faster and with higher accuracy than those made to low-salience features (20). When saliency features are equalized between different pairs of images in a change-blindness flicker task, differences in change detection will be guided mostly by the viewer's interest for the objects displayed on the images. Rensink et al. (10) characterized these differences as related to the semantic properties of the objects in the images and showed higher performances in the detection of items of central interest (attracting more attention) compared to those of marginal interest (attracting less attention).

In such experimental tasks, change detection performances rely on prolonged search periods and shifts of focal attention to the change for it to become conscious. Focal attention to change is not sufficient for conscious detection of change in change blindness flicker tasks: attention can be directed to changes—that is, changes can be stared at "blankly," without the change being perceived. A further consolidation process supported by working memory seems to be required for conscious detection (21, 22). Interestingly, Martinussen et al.'s (23) meta-analysis showed spatial working memory in children with ADHD compared to controls.

Few studies have investigated change blindness in individuals with ADHD and, as far as known to the authors, none with adolescents. Cohen (24) found that children with ADHD were faster than typically developing children in specifically detecting marginal changes. The authors presumed that that the children with ADHD possibly had not utilized the stereotyped, repetitive scan path that typifies central interest changes in typically developing children. Instead, they may have used a less systematic, more disorganized scan path, which paradoxically happened to serve them in identifying marginal interest changes in the flicker task. In contrast, Maccari et al. (25) found that children with ADHD performed more slowly and less accurately than controls in detecting marginal changes. Cohen and Shapiro (26) found no differences in change-detection times between adults with and without ADHD, but those with ADHD had more commission errors compared to controls, indicating a speed–accuracy performance tradeoff. These inconsistencies may have stemmed from inclusion criteria, treatment differences between groups, or methodological differences.

Türkan et al. (27) used eye tracking in a change-blindness study and found that children with ADHD made shorter fixations on the changed area than did typically developing children. The change-detection performances of children with ADHD were also less accurate compared to TD children. These findings aligned with known difficulties in ADHD with sustaining the attention necessary to encode the scene properties and goal-oriented behavior.

However, different experimental paradigms using eye tracking can yield contrasting outcomes. For instance, Karatekin and Asarnow (28) used a task in which children were asked to explore static pictures to answer specific questions. They found no difference between participants with ADHD and typical development in the time spent viewing relevant and irrelevant regions, fixation duration (an estimate of processing rate), or distance between fixations. In contrast, in a different study, students with ADHD had more fixations, which were also significantly shorter than were the controls' fixations (29). Furthermore, an additional study found that although the

ADHD and typical development groups did not differ in fixation duration, visual scanning of children with ADHD was discontinuous, uncoordinated, and chaotic compared with the controls (30).

In summary, few studies have used a change-blindness paradigm to investigate visual attention in people with ADHD. These studies reported contradicting results regarding change-detection performance of people with ADHD. They investigated change blindness in children (24, 25, 27), and one investigated adults (26), whereas the adolescent population has not yet been studied. Only one change blindness study used an eye-tracker device (27).

Thus, the aim of this study was two-fold. The first was to compare the change-detection performance of adolescents with ADHD to that of adolescents with typical development, using a change-blindness paradigm. We compared change detection time and error rates in items of central and marginal interest. An additional goal was to refine the investigation of the attentional process by examining gaze patterns using eye tracking. We compared time to first fixation (TFF) on the changed item (i.e., first-fixation latency), and total fixation duration (TFD) on the changed item (i.e., total time spent fixating on the changed item). We also compared scan paths and gaze dispersion.

We hypothesized that ADHD participants would have longer change-detection times, particularly in detecting marginal interest changes because they require greater attentional control, whereas central interest changes semantically pop out from the picture (10). Alternatively, we expected that ADHD participants would have a higher error rate because a speed–accuracy tradeoff usually occurs.

We also expected that limited attentional resources would cause participants with ADHD to have longer gaze TFD on the marginal interest changed items compared to the group with typical development. We assumed that, because detecting marginal change requires an item-by-item scan of the entire image using comparison strategies and working memory, it gives rise to longer identification times if processing is inefficient or speed is slowed. We hypothesized that first-fixation latency (TFF) would be longer for marginal interest changed items for the same reasons. These in turn, we speculated, might cause the ADHD group to exhibit longer scan paths and greater gaze dispersion because they might need to often backtrack to detect the change.

METHODS

Participants

The sample size was calculated by using G*Power for detecting moderate effects with a statistical power of 95%, with alpha at 0.05 (31). The initial sample included 89 adolescents, with an age range of 12–19 years, without evident motor disturbances or intellectual or neurological impairments. Five participants (three with ADHD, two with typical development) had insufficient data due to technical difficulties. Consequently, the final sample consisted of 84 adolescents.

The ADHD group comprised 44 participants (15 girls, 34.1%; 29 boys, 65.9%); the group with typical development (TD group) comprised 40 participants (18 girls, 45.0%; 22 boys, 55.0%). The groups did not differ with respect to age (**Table 1**). Adolescents who were diagnosed with ADHD were recruited from the Pediatric Neurology Unit of the Shaare Zedek Medical Center. The diagnosis of ADHD was made by an experienced clinician based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (2). It included the Disruptive Behavior Disorders Rating Scale (DBDRS) and a structured diagnostic interview with the parents. Adolescents were included if they scored outside the normal range on the inattention or hyperactivity/impulsivity subscale of the DBDRS, wherein six or more items must be endorsed as "pretty much" or "very much" to meet criteria. Inclusion criteria for both the ADHD and TD groups included absence of chronic medications and attending a regular classroom setting.

TABLE 1 | Participant characteristics in change blindness experiment.

Characteristic	TD ($N = 40$) *Mean ± SD*	ADHD ($N = 44$) *Mean ± SD*	p
Age	14.6 ± 2.13	14.6 ± 2.06	0.89
Gender	*Male:22; female:18*	*Male:29; female:15*	0.37
	1.45 ± 0.5	1.34 ± 0.48	

TD, group with typical development; ADHD, group with attention-deficit/hyperactivity disorder.

The ADHD group included 15 children who met the criteria for the ADHD/C subtype (exhibit both inattentiveness and hyperactivity/impulsiveness symptoms), 14 who met the criteria for ADHD/A (show predominantly inattentive symptoms), and 15 who met the criteria for ADHD/B (show prevalently hyperactivity/impulsivity symptoms).

Adolescents in the comparison (TD) group were selected from a local school and attended a regular classroom setting but were excluded from the study if they had above-cutoff scores on the DBDRS. The study was approved by the [blinded] University's Ethical Review Board and by the Helsinki Committee of the Hospital. A written informed assent and consent was obtained from the participants and their parents signed an informed consent.

Materials and Apparatus

The experimental stimuli consisted of 36 pairs of real-world scene images, 18 of which were adopted from Rensink et al. (10) and the other 18 from selected from Hochhauser et al. (32). Two additional image pairs from the same sources were used for practice trials. Each picture measured 1,008 × 720 pixels. Each pair of images were identical, apart from a single difference in the presence or absence of a particular object or area.

Following the method indicated by Rensink et al. (10), the pairs of images were divided into two equal groups where changes were either of high-level interest (*central*) or of low-level interest (*marginal*). The images were matched on psychometric properties, location of change, size of change, conspicuity of change, and intensity (33). The images had been validated for use for the change-blindness paradigm in previous studies (10, 32).

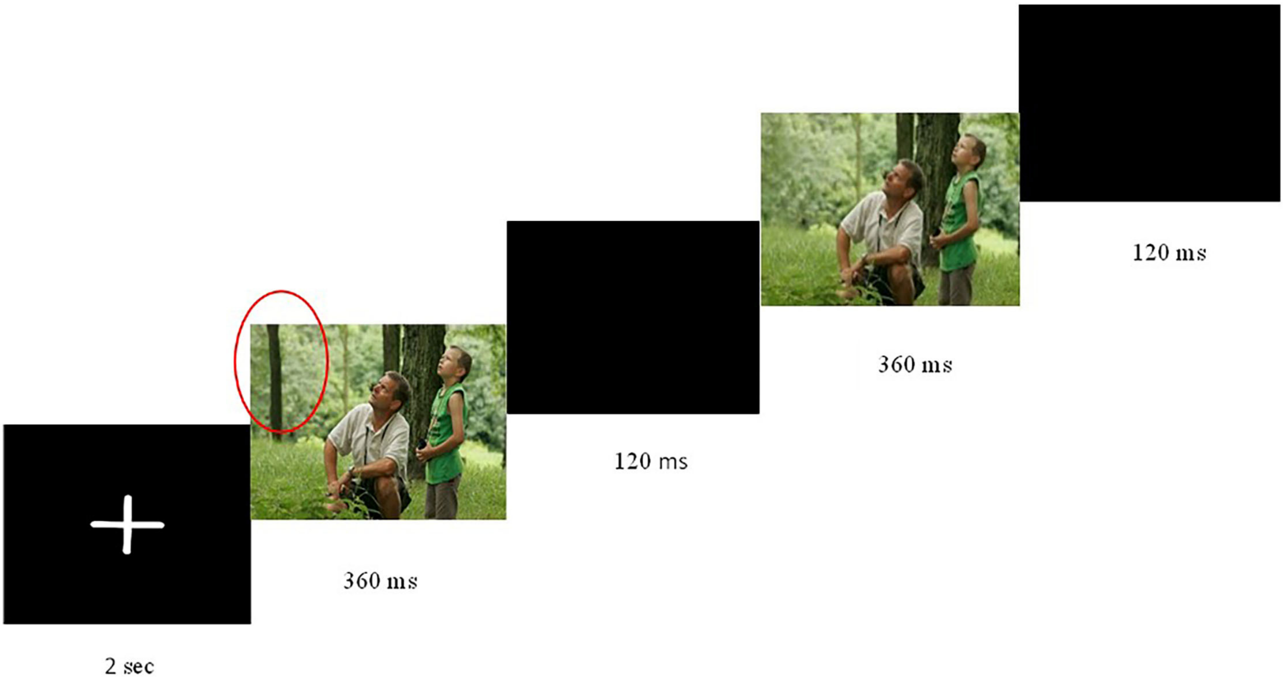


FIGURE 1 | Flicker paradigm used to test change blindness. A pair of images was presented, each for 360 ms, with an intervening blank screen of 120 ms. Cycle repeated until participants responded or 45 s elapsed. Image accessed at Wikimedia Commons, the free media repository.

The images were displayed on a 17-in screen in a "flicker" paradigm from a viewing distance of about 50 cm. Responses were collected *via* the computer mouse. The stimuli were presented using a Tobii X2-60 eye tracker, which is non-invasive and allows for free, unconstrained movement of the head and body (www.tobii.com). For each image, we analyzed gaze data on an AOI that circumscribed the changing item with an 0.5-visual degree margin (5 mm) to account for the eye tracker's accuracy error. We computed TFD and TFF based on fixations that fell in this AOI.

Procedure

The images were presented in counterbalanced trials in two test blocks with a 1–2 min rest period in between. Each trial started with a fixation cross (apparent size in visual angles: 1 × 1°) appearing for 1 s. It was followed by a briefly displayed (360 ms) scene image, followed by a gray blank scene displayed for 120 ms, followed by another image displayed for 360 ms, and a repetition of this sequence (**Figure 1**). The sequence alternated between a scene and its modified version, repeating itself until the participant clicked the mouse or until 45 s had elapsed. This response was based on the task instructions, which specified that the participants had to indicate as quickly as possible, but without guessing, what the change in the scene was. The response time measure, recorded in milliseconds, was the time at which the mouse click occurred. Following the mouse click, the participant had to verbally describe the change to the experimenter. For the trial to be classified as a correct response, the participant had to verbally identify and locate the changing item. Trials in which the participant made a mouse click response but did not correctly identify the item that changed in the scene were scored as an error. Two practice trials were conducted before starting the main experiment. During the actual experiment, no feedback was provided.

Participants were tested individually in a silent room. Before they began, they received a brief overview of the experiment and were instructed to click on the mouse as soon as they detected that one object appeared and disappeared, and then to verbally describe the change. Participants were told that a change would occur on every trial and were encouraged to keep searching for differences and not give up before the end of the trial. A 9-point calibration of the eye tracker was applied before each experiment.

Data Analysis

A group (ADHD, Control) × level of interest (central, marginal) repeated measures analysis of variance (ANOVA) was carried out for change-detection times (i.e., time to first mouse click) and eye-tracking metrics. The ANOVA for percentage of errors included an additional factor for the type of error (omission or commission; that is, missed items or incorrect detections). Change-detection times and eye-tracking metrics in trials in which participants did not detect the change were not included in the analyses. Eye-tracking metrics included the TFF (the amount of time that it took the respondent to first gaze at the changing item), TFD on the changing item, mean scan path (average of the distance between every two sequential points), total scan path

TABLE 2 | Change-blindness task: results of repeated measures ANOVA, response times (s), duration (s), scan path (mm), and gaze dispersion by group.

Change blindness	**TD ($N = 40$) ($M \pm SD$)**		**ADHD ($N = 44$) ($M \pm SD$)**		**Level of interest $df(1, 82)$**		**Group effect $df(1, 82)$**		**Interaction effect $df_{(1,82)}$**	
Level of interest	**Central**	**Marginal**	**Central**	**Marginal**	F	η^2	F	η^2	F	η^2
Time to first mouse click	3.00 ± 0.97	8.03 ± 2.43	3.66 ± 1.35	8.25 ± 2.73	363.9***	0.82	0.02	–	0.73	–
Time to first fixation	1.07 ± 0.58	4.23 ± 1.91	1.18 ± 0.59	4.24 ± 2.12	236.4***	0.75	0.05	–	0.08	–
Total fixation duration	0.88 ± 0.47	1.15 ± 0.66	1.01 ± 0.55	1.30 ± 0.71	31.1***	0.28	0.01	–	0.03	–
Scan path	7.23 ± 3.77	6.91 ± 3.48	8.41 ± 5.51	7.45 ± 3.32	6.21**	0.07	1	–	1.6	–
Total scan path	18.68 ± 11.37	58.93 ± 32.86	22.51 ± 13.32	63 ± 44.68	122***	0.6	0.57	–	0.001	–
Gaze dispersion	0.02 ± 0.01	0.03 ± 0.02	0.03 ± 0.02	0.04 ± 0.02	40.4***	0.32	5.72**	0.1	0.39	–

TD, group with typical development; ADHD, group with attention-deficit/hyperactivity disorder; Mean scan path, average distance between fixations; Total scan path, total distance between successive fixations; Gaze dispersion, the smallest convex area enclosing all the fixation points.

***$p \leq 0.01$; ***$p \leq 0.001$.*

(total distance between successive fixations), and gaze dispersion. Gaze dispersion was computed by identifying the smallest convex area enclosing all the fixation points. A convex hull was computed for each trial of every participant with Matlab®. The areas of the convex hulls were then averaged over the trials of each participant in each condition to provide a metric for dispersion. Data was analyzed by using IBM SPSS Statistics for Windows, Version 23.0. When appropriate, *post-hoc t*-tests were performed using the Bonferroni adjustment.

RESULTS

Percentage of Errors

There were no errors for the central level of interest in either the ADHD or TD group; therefore, data analysis was applied only for the marginal level of interest. There was a main effect for type of error, $F_{(1,82)} = 7.03$, $p \leq 0.01$, $\eta^2 = 0.01$ (ADHD: omission $M \pm \text{SD} = 0.004 \pm 0.02$, commission $M \pm SD = 0.002 \pm 0.01$; TD: omission $M \pm SD = 0.01 \pm 0.02$, commission $M \pm SD = 0.00 \pm 0.005$). However, the percentage of errors did not differ between groups, $F_{(1,82)} = 0.83$, $p = 0.36$, nor was there an interaction effect between type of error (i.e., omissions/missed items or commissions/incorrect detections) and group, $F_{(1,82)} = 2.6$, $p = 0.11$.

Change Detection Times

Table 2 presents the data for change-detection times (time to first mouse click), TFF, TFD, scan paths, and fixation dispersion for central- and marginal-level of interest among the adolescents with ADHD and with TD.

Detection times (time to first mouse click) were longer for marginal items compared with central items, $F_{(1,82)} = 363.9$, $p \leq 0.001$, $\eta^2 = 0.82$. There was no significant difference between the ADHD and TD groups, $F_{(1,82)} = 0.02$, $p = 0.26$, and no interaction effect between groups and levels of interest, $F_{(1,82)} = 0.73$, $p = 0.84$ (**Figure 2**).

Changed Items TFF

The results revealed a main effect for level of interest, $F_{(1,82)} = 236.4$, $p \leq 0.001$, $\eta^2 = 0.75$, showing that both groups were slower to look at the marginal items, but no significant difference between groups, $F_{(1,82)} = 0.05$, $p = 0.83$, and no interaction effects, $F_{(1,82)} = 0.08$, $p = 0.79$, were found (**Figure 3**).

Changed Items TFD

The results revealed a main effect for level of interest, $F_{(1,82)} = 31.1$, $p \leq 0.001$, $\eta^2 = 0.28$, showing that both groups looked longer at the marginal items, but no significant difference between groups, $F_{(1,82)} = 0.01$, $p = 0.72$, and no interaction effects, $F_{(1,82)} = 0.03$, $p = 0.57$ were found (**Figure 4**).

Scan Paths

Mean scan path (average distance between sequential points) findings for the ADHD group (Central: $M = 8.41$, $SD = 5.51$; Marginal: $M = 7.45$, $SD = 3.32$) and controls (Central: $M = 7.23$, $SD = 3.77$; Marginal: $M = 6.91$, $SD = 3.48$) revealed a main effect for levels of interest, $F_{(1,82)} = 6.21$, $p \leq 0.01$, $\eta^2 = 0.07$, but no interaction effect, $F_{(1,82)} = 1.6$, $p = 0.21$, or between-group effect $F_{(1,82)} = 1$, $p = 0.32$.

Total scan path (total distance between successive fixations) findings for the ADHD group (Central: $M = 22.51$, $SD = 13.32$; Marginal: $M = 63$, $SD = 44.68$) and controls (Central: $M = 18.68$, $SD = 11.37$; Marginal; $M = 58.93$, $SD = 32.86$) revealed a main effect for levels of interest, $F_{(1,82)} = 122$, $p \leq 0.001$, $\eta^2 = 0.6$, but no interaction effect, $F_{(1,82)} = 0.001$, $p = 0.97$, or between-group effect, $F_{(1,82)} = 0.57$, $p = 0.45$.

Gaze Dispersion

Gaze dispersion (area of the convex hull of fixation points) analysis revealed a main effect for levels of interest, $F_{(1,42)} = 40.4$, $p \leq 0.001$, $\eta^2 = 0.32$, and a main effect for groups, $F_{(1,42)} = 5.72$, $p \leq 0.01$, $\eta^2 = 0.1$, with no interaction effect for these two factors, $F_{(1,42)} = 0.39$, $p = 0.54$ (**Figure 5**).

DISCUSSION

The purpose of this study was to compare the visual attention of adolescents with and without ADHD. We used a change-blindness task on an age group that has not been studied before, that is, adolescence. Contrary to our hypothesis and

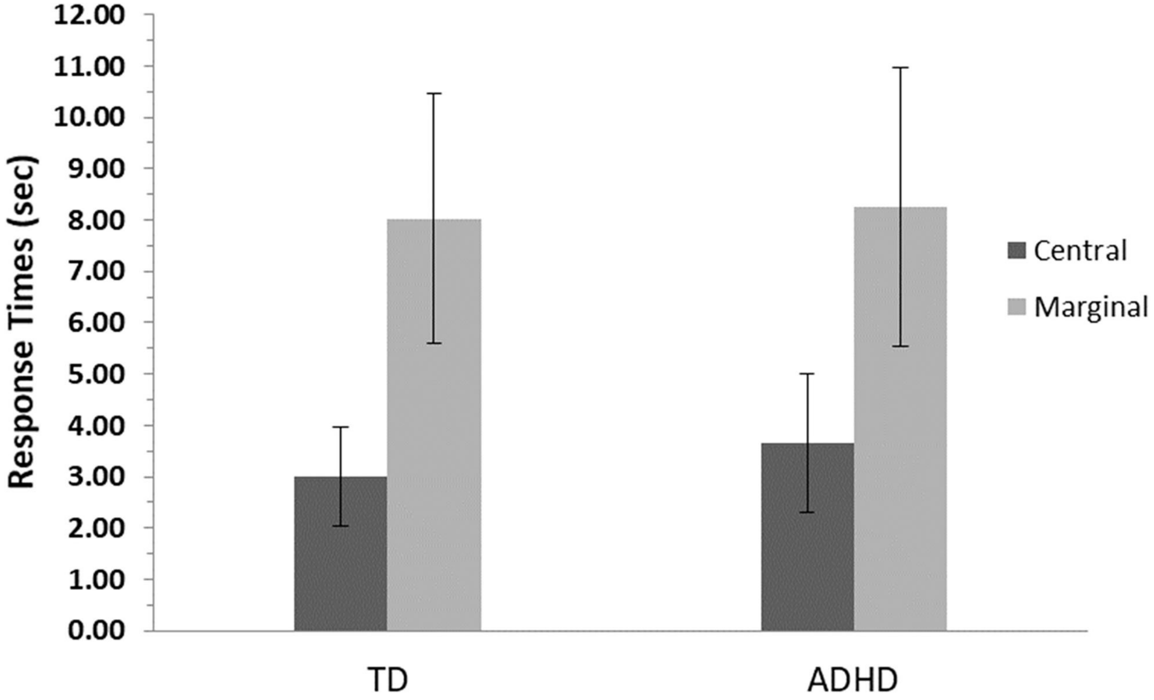


FIGURE 2 | Detection time means and standard errors for central- and marginal-interest changes by group. TD, group with typical development; ADHD, group with attention-deficit/hyperactivity disorder. Detection time measured as time to first mouse click. A significant difference was found between levels of interest (central/marginal) for the two groups ($p \leq 0.001$); however, no differences were found between groups.

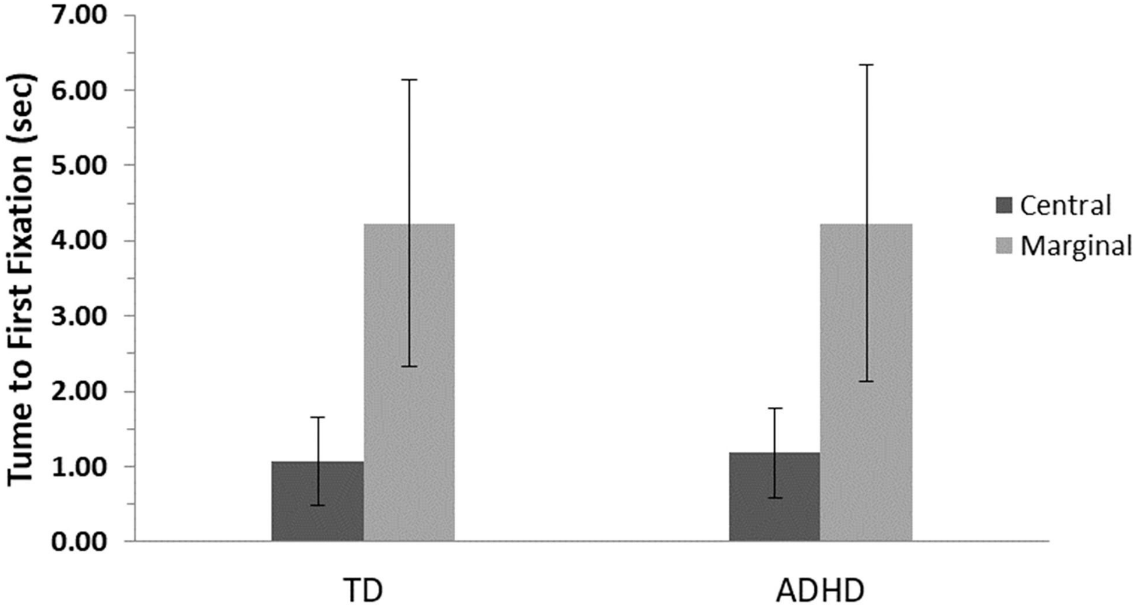


FIGURE 3 | First fixation means and standard errors for central- and marginal-interest changes by group. TD, group with typical development; ADHD, group with attention-deficit/hyperactivity disorder. A significant difference was found between levels of interest (central/marginal) for the two groups ($p \leq 0.001$); however, no differences were found between groups.

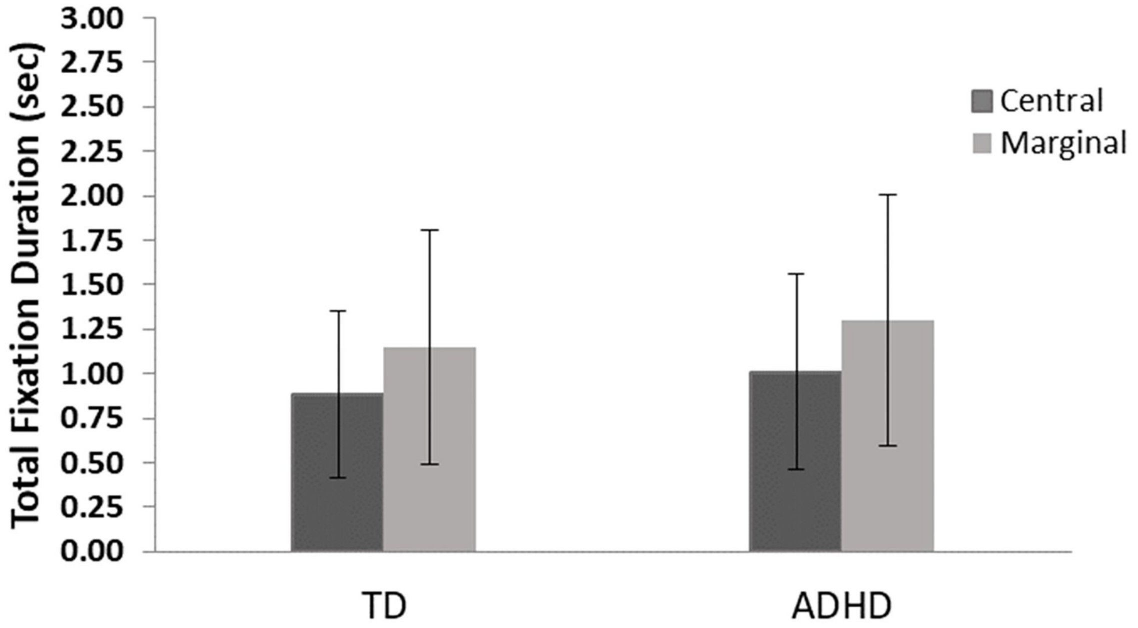


FIGURE 4 | Total fixation duration means and standard errors for central- and marginal-interest changes by group. TD, group with typical development; ADHD, group with attention-deficit/hyperactivity disorder. A significant difference was found between levels of interest (central/marginal) for the two groups ($p \leq 0.001$); however, no differences were found between groups.

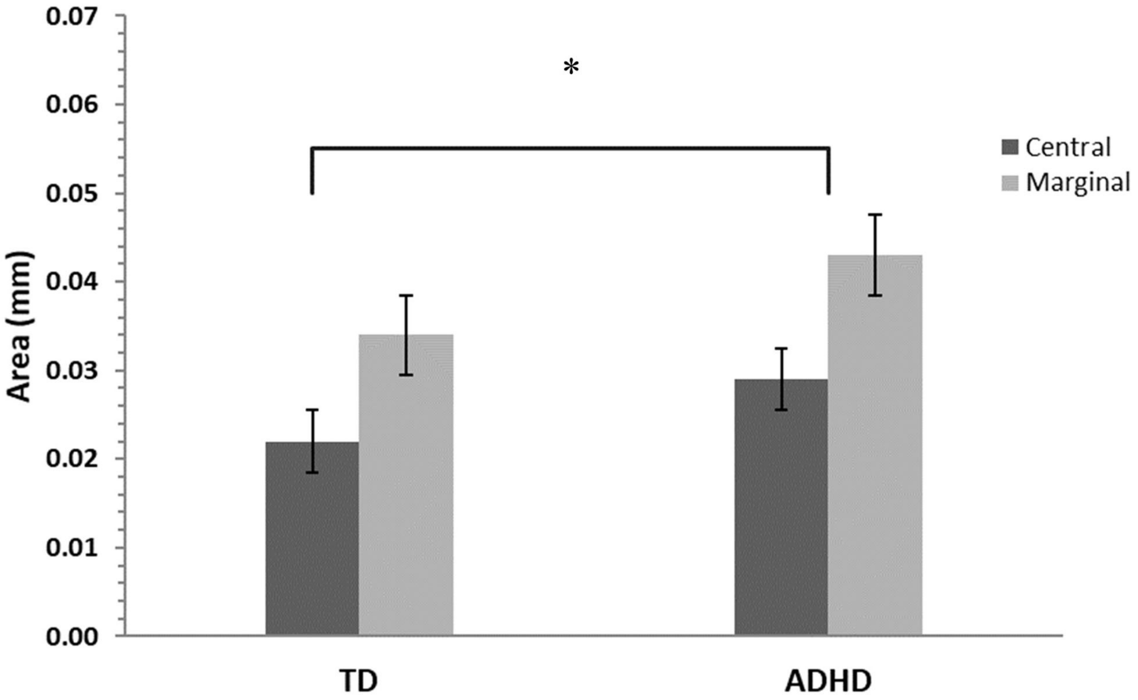


FIGURE 5 | Gaze dispersion means and standard errors for central- and marginal-interest changes by group. TD, group with typical development; ADHD, group with attention- deficit/hyperactivity disorder. A significant difference was found between groups ($p \leq 0.01$) and between levels of interest (central/marginal) for the two groups ($p \leq 0.001$), however there was no interaction effect. The asterisk is to show significance.

a previous study among children (25), the adolescent ADHD group performed similar to the controls in the number of errors, response times, and TFF, as well as TFD on the changing item and measures of scan paths. Moreover, similar to the controls, the ADHD group demonstrated greater response times, greater time to first fixation, longer fixation durations, and longer scan paths when detecting marginal changes compared to central changes. Nonetheless, the results showed a significant difference between the ADHD group and controls in their gaze fixation dispersion. The adolescents with ADHD demonstrated larger spatial coverage than did their typically developing peers.

The lack of difference between the ADHD and TD groups on performance metrics such as the detection rate and detection times can be interpreted in light of the perceptual cognitive load theory (34). According to theory, a major determinant of the ability to focus attention while eluding distraction is whether the task being performed involves a sufficiently high "perceptual load." *Perceptual load* has been operationally defined as either the quantity of stimuli entailing perceptual processing or the complexity of perceptual judgments (35). When the task processing involves high load (e.g., requiring complex perceptual judgments or searching among many items), perception of distractors is reduced or even eliminated. Moreover, although beyond the main scope of this paper, cognitive load has found to influence oculomotor behavior (36, 37).

In the current study, the change-blindness task necessitated complex perceptual judgement. For example, the marginal condition required inhibition of distracting features that were semantically relevant to the scene displayed, although they were irrelevant to the required task of detecting change. The analysis of results did not yield evidence that change-detection times were longer in participants with ADHD compared to those with typical development. The ADHD group did not show different speed–accuracy tradeoffs that could be a sign of them being tired or having difficulties concentrating. Hence, the "perceptual cognitive load" required by the change-blindness task may have helped those with ADHD to focus. This explanation is in line with a study that tested the perceptual cognitive load theory in individuals with ADHD (38) and whose results indicated that conditions of increased perceptual cognitive load facilitated task engagement in people with ADHD with reduced distraction. We therefore suggest that, although it may seem counterintuitive, performing a challenging task with a high cognitive load might have in fact facilitated the performances of adolescents with ADHD in the present study.

Time to first fixation and TFD on the changed items followed the same trend as percentage of errors and detection times—that is, there were no differences between participants with ADHD and the TD controls. These results contrast with the results of Türkan et al. (27), who found shorter fixations in children with ADHD and less accurate detection performances. This could suggest that, as they reach adolescence, individuals with ADHD may be able to perform as well as their typically developing peers in change-blindness tasks.

Nonetheless, one can deliberate that in the wake of the current knowledge of executive functioning difficulties, such as working memory, in people with ADHD (39), the task should have challenged them. As mentioned earlier, working memory plays a central role in change-blindness tasks (21, 22). A study by Yeh et al. (40) revealed that young adults with better working-memory capacities gazed at the targets more frequently and for longer times than did participants with lower working-memory capacities. It was therefore reasonable to expect differences in eye-tracking measures in the present study due to the weaker working-memory performances reported with ADHD (23).

A feasible argument for the ability of the participants in the current study to overcome working-memory difficulties is compensatory attentional processes, such as stimulus-driven attention, as opposed to goal-directed attention. Working-memory deficits might not affect attentional control adversely in individuals with ADHD when the task design or stimuli provide extrinsic reinforcement of the task set and rules. For instance, Burgess et al. (41) administered the Color-Word Stroop task to participants with ADHD and found they had poorer performances only for the congruent condition; that is, when color-words were written in the same ink color as the word. Those authors suggested that the inherent conflict between the ink color and the word provided a subtle reminder of the task sets and rules.

Burgess et al.'s (41) results suggest that intrinsic working-memory difficulties affect attentional control less when task stimuli support task-set maintenance. The flicker used to implement the change-blindness paradigm in the present experiment may have acted as a reminder of the task sets by generating a regular stimulus-driven signal of the change between the two versions of the displayed image. This aligns with Corbetta and Shulman (1), who maintained that two networks of brain areas are involved in controlling attention: The first one relies on cognitive information to direct attention to relevant objects in a visual scene; the second is associated with attention control driven by stimulus properties rather than cognitive processes (e.g., "bottom-up" control of attention, which explains why people are drawn to "oddball" stimuli that are very different from the background). As such, the flicker-based change-blindness paradigm used in the current study differs from more conventional visual-search tasks in that it provides a stimulus-driven reminder of the task sets throughout the duration of the task.

Differences were nevertheless found when analyzing gaze dispersion. Those differences did not appear in mean and total scan paths measures, probably because such metrics were too coarse. They did appear, however, when considering the convex hulls of fixation points. It appears that the participants with ADHD tended to survey a larger portion of the image. The increase in gaze fixation area may reflect a greater proclivity to attend to a new stimulus, even when asked to goal orient on detecting a change, and a relatively attenuated propensity to continue processing the current stimulus, creating fixation scatter.

It is further possible that "fixation scatter" may reflect an imbalance between the bottom-up stimulus-driven and the top-down attentional-control mechanisms that govern visual attention (1). These results showing greater gaze dispersion are consistent with the findings of Jayawardena et al. (42), who revealed that adults with ADHD do not visually scan stimulus items using a path similar to adults without ADHD. Krejtz et al. (43) also indicated that although adults with ADHD had fixations to salient visual cues similar to adults without ADHD, they demonstrated less structured and more chaotic scan patterns. Mohammadhasani et al. (30) found that, compared to children with typical development, children with ADHD did not follow a typical scan path; instead, their visual scanning was discontinuous, uncoordinated, and chaotic. In Munoz et al.'s (44) study investigating the control of visual fixation in a task requiring prolonged fixation, ADHD participants generated more intrusive saccades during periods when they were required to maintain steady fixation. The authors proposed that ADHD participants have reduced ability to suppress unwanted saccades and control their fixation behavior voluntarily, which is consistent with the fronto-striatal pathophysiology linked to difficulty in inhibition.

This is the first study to our knowledge that used change blindness to assess visual attention in adolescents with ADHD. Two previous studies (25, 27) showed that children without attention deficits perform better in change-detection tasks than do those with ADHD, whereas Cohen and Shapiro (26) showed there were no differences in adults. The present study with adolescents showed no differences on performance metrics (percentage of errors and detection times), TFF, and TFD on the changing items but did reveal an increased dispersion of gaze. Of particular relevance is the fact that the stimuli were presented in a flicker paradigm, which perhaps biased the participants (i.e., attracted and maintained attention). However, previous ADHD studies on change blindness relied on the same paradigm. Future studies can address this limitation by implementing change-blindness experiments without a flicker as, for instance, those based on continuity errors in film cuts (45). Additional limitations were that the participants were not formally tested for IQ; thus, the ADHD and control group were not matched on IQ scores. However, participants' academic levels were queried, and the groups were matched to them.

An additional issue for further investigation is that of ecological validity; that is, the extent to which the stimuli and protocol approximate the real-life situation of adolescents with ADHD. This study may shed light on the visual-attention patterns adolescents with ADHD exhibit when required to attend to images portraying various real-life contexts. However, we strongly recommend investigating whether the conclusions hold when associated with everyday tasks that require "functional attention."

CONCLUSIONS

This study attempted to gain insight on the attentional performances of adolescents with ADHD, using a change-blindness paradigm with naturalistic images. The use of eye tracking enabled analyzing gaze patterns, such as TFF and TFD on the changing item, as well as the scan paths and fixation dispersion. Adolescents with ADHD detected changes with similar accuracy and speed compared to controls but with gaze dispersed across larger areas. Our results with regards to accuracy should not be taken as conclusive because there possibly was a ceiling effect related to the difficulty of the tasks, and that more difficult tasks would result in some more subtle between-group differences. The greater gaze dispersion in the ADHD group sheds light on the distinctive attentional mode of people with ADHD, suggesting less structured gaze patterns and a lack of inhibition of intrusive saccades. Future directions should investigate whether this gazing behavior is beneficial over time, or if it causes fatigue or lower efficiency when completing longer tasks. Furthermore, this study substantiates the potential assets of eye tracking as a comprehensive tool for assessing attentional deficits in those who are suspected of having ADHD.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Helsinki Committee Shaare Zedek Medical Center. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

MH conceptualized, designed and performed experiments, analyzed data, and co-wrote the paper. AA provided Helsinki approval management and medical guidance. OG analyzed data and co-wrote the paper. All authors contributed to the article and approved the submitted version.

FUNDING

Open access publication fees received from Ariel University.

REFERENCES

1. Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci.* (2002) 3:201–15. doi: 10.1038/nrn755
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Health Disorders (5th ed.).* Arlington, VA (2019).
3. Barkley RA (editor). *Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment (4th ed.)*. New York, NY: Guilford Press (2015).
4. Wehmeier PM, Schacht A, Barkley RA. Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life. *J Adolesc Health*. (2010) 46:209–17. doi: 10.1016/j.jadohealth.2009.09.009
5. Francx W, Zwiers MP, Mennes M, Oosterlaan J, Heslenfeld D, Hoekstra PJ, et al. White matter microstructure and developmental improvement of hyperactive/impulsive symptoms in attention-deficit/hyperactivity disorder. *J Child Psychol Psychiatry*. (2015) 56:1289–97. doi: 10.1111/jcpp.12379
6. Willcutt EG, Nigg JT, Pennington BF, Solanto MV, Rohde LA, Tannock R, et al. Validity of DSM-IV attention deficit/hyperactivity disorder

symptom dimensions and subtypes. *J Abnorm Psychol*. (2012) 121:991. doi: 10.1037/a0027347

7. Franke B, Michelini G, Asherson P, Banaschewski T, Bilbow A, Buitelaar JK, et al. Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan. *Euro Neuropsychopharmacol*. (2018) 28:1059–88. doi: 10.1016/j.euroneuro.2018.08.001
8. Treisman AM, Gelade G. A feature-integration theory of attention. *Cogn Psychol*. (1980) 12:97–136. doi: 10.1016/0010-0285(80)90005-5
9. Mullane JC, Klein RM. Literature review: visual search by children with and without ADHD. *J Attent Disord*. (2008) 12:44–53. doi: 10.1177/1087054707305116
10. Rensink RA, O'Regan JK, Clark JJ. To see or not to see: the need for attention to perceive changes in scenes. *Psychol Sci*. (1997) 8:368–73. doi: 10.1111/j.1467-9280.1997.tb00427.x
11. Simons DJ, Ambinder MS. Change blindness: theory and consequences. *Curr Dir Psychol Sci*. (2005) 14:44–8. doi: 10.1111/j.0963-7214.2005.00332.x
12. Simons DJ, Rensink RA. Change blindness: past, present, and future. *Trends Cogn Sci*. (2005) 9:16–20. doi: 10.1016/j.tics.2004.11.006
13. Simons DJ. Current approaches to change blindness. *Vis cogn*. (2000) 7:1–15. doi: 10.1080/135062800394658
14. Simons DJ, Levin DT. Change blindness. *Trends Cogn Sci*. (1997) 1:261–7. doi: 10.1016/S1364-6613(97)01080-2
15. Auvray M, Gallace A, Tan HZ, Spence C. Crossmodal change blindness between vision and touch. *Acta Psychol*. (2007) 126, 79–97. doi: 10.1016/j.actpsy.2006.10.005
16. Rensink RA. Seeing, sensing, and scrutinizing. *Vision Res*. (2000) 40:1469–87. doi: 10.1016/S0042-6989(00)00003-1
17. Rensink RA. Internal vs. external information in visual perception. In: *Proceedings of the 2nd International Symposium on Smart Graphics*. Hawthorne, NY (2002). p. 63–70. doi: 10.1145/569005.569015
18. Henderson JM. Human gaze control during real-world scene perception. *Trends Cogn Sci*. (2003) 7:498–504. doi: 10.1016/j.tics.2003.09.006
19. Hollingworth A, Henderson JM. Semantic informativeness mediates the detection of changes in natural scenes. *Visual Cogn*. (2000) 7:213–35. doi: 10.1080/135062800394775
20. LaPointe MRP, Milliken B. Conflicting effects of context in change detection and visual search: a dual process account. *Canad J Exp Psychol*. (2017) 71:40–51. doi: 10.1037/cep0000105
21. Lyyra P, Astikainen P, Hietanen JK. Look at them and they will notice you: distractor-independent attentional capture by direct gaze in change blindness. *Vis cogn*. (2017) 26:25–36. doi: 10.1080/13506285.2017.1370052
22. Yao R, Street W, Simons DJ, Jensen MS, Street WN. Change blindness and inattentional blindness. *WIREs Cognitive Science*. (2011) 2:529–46. doi: 10.1002/wcs.130
23. Martinussen R, Hayden J, Hogg-Johnson S, Tannock R. A meta-analysis of working memory impairments in children with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. (2005) 44:377–84. doi: 10.1097/01.chi.0000153228.72591.73
24. Cohen AL. *Performance on the Flicker Task and Conners' CPT in children with ADHD* (Doctoral dissertation), Auburn University; ProQuest Dissertations and These Global, Auburn, AL (2009).
25. Maccari L, Casagrande M, Martella D, Anolfo M, Rosa C, Fuentes LJ, et al. Change blindness in children with ADHD: A selective impairment in visual search? *J Atten Disord*. (2013) 17:620–7. doi: 10.1177/1087054711433294
26. Cohen AL, Shapiro SK. Exploring the performance differences on the flicker task and the conners' continuous performance test in adults with ADHD. *J Atten Disord*. (2007) 11:49–63. doi: 10.1177/1087054706292162
27. Türkan BN, Amado S, Ercan ES, Perçinel I. Comparison of change detection performance and visual search patterns among children with/without ADHD: evidence from eye movements. *Res Dev Disabil*. (2016) 49:205–15. doi: 10.1016/j.ridd.2015.12.002
28. Karatekin C, Asarnow RF. Exploratory eye movements to pictures in childhood-onset schizophrenia and attention-deficit/ hyperactivity disorder (ADHD). *J Abnorm Child Psychol*. (1999) 27:35–49.
29. Navarro O, Gonzalez AL, Molina AI. Experience of use of eye tracking technology with children who have attention problems. In: *2018 International Symposium on Computers in Education*. Jerez (2018). doi: 10.1109/SIIE.2018.8586721
30. Mohammadhasani N, Nucita A, Iannizzotto G. Atypical visual scan path affects remembering in ADHD. *J Int Neuropsychol Soc*. (2019) 26:557–66. doi: 10.1017/S135561771900136X
31. Faul F, Erdfelder E, Lang AG, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. (2007) 39:175–91. doi: 10.3758/BF03193146
32. Hochhauser M, Aran A, Grynszpan O. How adolescents with autism spectrum disorder (ASD) spontaneously attend to real-world scenes: use of a change blindness paradigm. *J Autism Dev Disord*. (2018) 48:502–10. doi: 10.1007/s10803-017-3343-6
33. O'Regan KJ, Deubel H, Clark JJ, Rensink RA. Picture changes during blinks: looking without seeing and seeing without looking. *Vis Cognit*. (2000) 7:191–211. doi: 10.1080/135062800394766
34. Lavie N, Tsal Y. Perceptual load as a major determinant of the locus of selection in visual attention. *Percept Psychophys*. (1994) 56:183–97. doi: 10.3758/BF03213897
35. Lavie N. Distracted and confused? Selective attention under load. *Trends Cogn Sci*. (2005) 9:75–82. doi: 10.1016/j.tics.2004.12.004
36. Prabhakar G, Mukhopadhyay A, Murthy L, Madan M, Sachin D, Biswas P. Cognitive load estimation using ocular parameters in automotive. *Transp Eng*. (2020) 2:100008. doi: 10.1016/j.treng.2020.100008
37. Walter K, Bex P. Cognitive load influences oculomotor behavior in natural scenes. *Sci Rep*. (2021) 11:1–12. doi: 10.1038/s41598-021-91845-5
38. Forster S, Robertson DJ, Jennings A, Asherson P, Lavie N. Plugging the attention deficit: perceptual load counters Increased distraction in ADHD. *Neuropsychology*. (2014) 28:91–7. doi: 10.1037/neu0000020
39. Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/ hyperactivity disorder: a meta-analytic review. *Biol Psychiatry*. (2005) 57:1336–46. doi: 10.1016/j.biopsych.2005.02.006
40. Yeh YC, Tsai JL, Hsu WC, Lin CF. A model of how working memory capacity influences insight problem solving in situations with multiple visual representations: an eye tracking analysis. *Think Skills Creat*. (2014) 13:153–67. doi: 10.1016/j.tsc.2014.04.003
41. Burgess GC, Depue BE, Ruzic L, Willcutt EG, Du YP, Banich MT. Attentional control activation relates to working memory in attention-deficit/hyperactivity disorder. *Biol Psychiatry*. (2010) 67:632–40. doi: 10.1016/j.biopsych.2009.10.036
42. Jayawardena G, Michalek A, Jayarathna S. Eye gaze metrics and analysis of AOI for indexing working memory towards predicting ADHD. *arXiv [Preprint]* arXiv:1906.07183 (2019).
43. Krejtz K, Duchowski A, Szmidt T, Krejtz I, González Perilli F, Pires A, et al. Gaze transition entropy. *ACM Trans Appl Percept*. (2015) 13:1–20. doi: 10.1145/2834121
44. Munoz DP, Armstrong IT, Hampton KA, Moore KD. Altered control of visual fixation and saccadic eye movements in attention-deficit hyperactivity disorder. *J Neurophysiol*. (2003) 90:503–14. doi: 10.1152/jn.00192.2003
45. Levin DT, Simons DJ. Failure to detect changes to attended objects in motion pictures. *Psychon Bull Rev*. (1997) 4:501–6. doi: 10.3758/BF03214339

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychiatry

STUDY PROTOCOL
published: 28 February 2022
doi: 10.3389/fpsyt.2022.823186

Clinical Implementation and Evaluation of Three Implementation Interventions for a Family-Oriented Care for Children of Mentally Ill Parents (ci-chimps): Study Protocol for a Randomized Controlled Multicenter Trial

Carolin Laser[1]*, *Anna Modarressi*[1], *Bjørg Eva Skogøy*[2], *Andrea Reupert*[3], *Anne Daubmann*[4], *Alexandra Höller*[4], *Antonia Zapf*[4], *Silke Pawils*[5], *Svenja Taubner*[6], *Sibylle Winter*[7], *Darryl Maybery*[8] and *Silke Wiegand-Grefe*[1]*

[1] Department of Child and Adolescent Psychiatry and Psychotherapy, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany, [2] Nordland Hospital Trust, Nordland Research Institute, Bodø, Norway, [3] Krongold Clinic, Faculty of Education, Monash University, Clayton, VIC, Australia, [4] Department of Medical Biometry and Epidemiology, University Medical Centre Hamburg–Eppendorf, Hamburg, Germany, [5] Institute and Outpatients Clinic of Medical Psychology, Centre for Psychosocial Medicine, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany, [6] Center for Psychosocial Medicine, Institute for Psychosocial Prevention, University Hospital Heidelberg, Heidelberg, Germany, [7] Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Charité Berlin, Berlin, Germany, [8] Department of Rural Health, Monash University, Clayton, VIC, Australia

Edited by:
Melvyn Weibin Zhang,
Institute of Mental Health, Singapore

Reviewed by:
Shekhar Seshadri,
National Institute of Mental Health and Neurosciences (NIMHANS), India
Yasodha Rohanachandra,
University of Sri Jayewardenepura, Sri Lanka

***Correspondence:**
Carolin Laser
c.laser@uke.de
Silke Wiegand-Grefe
swiegand-grefe@uke.de

Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: *26 November 2021*
Accepted: *01 February 2022*
Published: *28 February 2022*

Citation:
Laser C, Modarressi A, Skogøy BE, Reupert A, Daubmann A, Höller A, Zapf A, Pawils S, Taubner S, Winter S, Maybery D and Wiegand-Grefe S (2022) Clinical Implementation and Evaluation of Three Implementation Interventions for a Family-Oriented Care for Children of Mentally Ill Parents (ci-chimps): Study Protocol for a Randomized Controlled Multicenter Trial. Front. Psychiatry 13:823186. doi: 10.3389/fpsyt.2022.823186

Background: In Germany, approximately three million children under the age of eighteen have a mentally ill parent. These children are at an increased risk of developing a mental illness themselves (1) as well as a physical illness (2). While research has identified numerous evidence-based family-oriented interventions, little is known about how to implement such interventions effectively and efficiently in clinical practice in Germany. This implementation study (ci-chimps) evaluates three clinical implementation projects with three different implementation interventions for the optimal implementation of the tailored family-oriented preventive and therapeutic interventions in the CHIMPS-NET (children of mentally ill parents—research network) with an implementation model for children of mentally ill parents.

Methods: A two-group randomized controlled multicenter trial will examine changes in family-oriented practice and aspects of implementation at baseline as well as at 12- and 24-months follow-up. The CHIMPS-Network consists of 20 clinical centers. The centers in the intervention group receive the support of all of the three implementation interventions: (1) optimal pathways to care, (2) education and a training program for professionals, and (3) systematic screening for children. The centers in the control group do not receive this specific implementation support.

Discussion: While we know that children of mentally ill parents are an important target group to be addressed by preventive and therapeutic interventions, there is often a lack of structured implementation of family-oriented interventions in clinical practice in Germany. Using a randomized controlled multicenter trial design with a large and wide-ranging sample (clinics for adult psychiatry and clinics for child and adolescent psychiatry, university clinics and clinics at the real health care) will provide a robust understanding of implementing family-oriented changes in German clinical practice.

Trial Registration: The CHIMPS-NET-study was registered with the German Clinical Trials Register on 2019-12-19 (DRKS00020380) and with Clinical Trials on 2020-4-30 (NCT04369625), the ci-chimps-study was registered with the German Clinical Trials Register (DRKS00026217) on 2021-08-27, the Clinical Trials registration is in review process.

Keywords: children of mentally ill parents, implementation research, family implementation interventions, randomized controlled trial, multicenter trial

BACKGROUND

In Germany, approximately three million children under the age of 18 have a mentally ill parent (1). These children are at an increased risk of developing a mental illness themselves (1) as well as a physical illness (2). Not all children will be impacted in the same way, and children's outcomes vary depending on the severity and chronicity of the parents' illness, the support provided to the family, environmental factors (such as poverty and housing) and the timing of the illness in relation to the child's age (references see below) (1). To mitigate mental symptoms and concomitant diseases in these children and adolescents, Wiegand-Grefe et al. developed a low-frequency family-oriented intervention for children of mentally ill parents: CHIMPS (3). The term CHIMPS stands for "Children of mentally ill parents." The acronym CHIMPS might be considered stigmatizing however we have used it positively by employing a chimpanzee as our project mascot. We argue that this makes the acronym fun and playful and thus engaging to children. The CHIMPS intervention has been manualized (3) and evaluated in waiting-list-controlled pilot studies (4–7), which indicates improvements in the mental health of the children (4), the health-related quality of life and social support of children and their families (5), the family functioning (6) and congruent and successful parental coping strategies (7). Furthermore, in the next step, this CHIMPS intervention program has been evaluated in a BMBF funded, multicenter trial (8).

In the current "Children of mentally ill parents-research network" (CHIMPS-NET), funded by the innovation fund at the GB-A, the CHIMPS intervention where updated and more adapted to the heterogeneous needs of each family. In CHIMPS-NET, in a stepped care model, every family with a mentally ill parent and with children from age 3–18 years is screened regarding his/her family functioning and the mental health state of his/her children and adolescents and the parents and allocated to different interventions according to his/her indication and the requirements. For further information about the different family-oriented preventive and therapeutic interventions in CHIMPS-NET, for the design of the evaluation studies, as well for the inclusion and exclusion criteria to each intervention see the study protocol of the central project CHIMPS-NET (9). This publication focused the implementation interventions and the design of the overarching implementation study ci-chimps.

Implementation Research for Interventions for Children of Mentally Ill Parents

Because of the knowledge and the increasing awareness that children of mentally ill parents are an important target group to be addressed by preventive interventions, there are numerous programs and tools (10, 11). But there is often a lack of structured implementation of family-oriented interventions in clinical practice not only in Germany (10–13). Implementation can be defined as a specified set of activities designed to put into practice an activity or program of known dimensions (14). Lauritzen et al. describe three general implementation categories: "paper implementation," "process implementation," and "performance implementation" (13). Paper implementation puts new policies and procedures into place but does not change practice in itself. Process implementation incorporates new procedures into an organization, and performance implementation provides content and tools to practitioners, so that new procedures and processes have functional components for change. Ci-chimps belongs to the performance implementations by giving the clinical centers new tools like the screening (15).

Personal attitudes like self-reported skills and knowledge, beliefs about job role, and perceptions of workplace support seem to have a notable impact in supporting a successful and sustainable implementation (11, 16–20). Furthermore, organizational factors, such as reporting systems, meeting structures, leadership and supervision, are closely associated with satisfaction with the implementation process (11, 17, 19–21).

For family-oriented practice, the following barriers are reported: organizational barriers [policies, leadership and management (22–24)], high workload (22–24), patient-oriented treatment (24), no routines in identifying affected families (21–23), and gaps in mental health professionals' knowledge, and skills about children of mentally ill parents (21–23).

Abbreviations: BMBF, bundesministerium für bildung und forschung (federal ministry of education and research); CHIMPS, children of mentally ill parents; CHIMPS-NET, children of mentally ill parents research network; CHIMPS-P, CHIMPS-prevention (families with noticeable problems but no own diagnosis yet); CHIMPS-T, CHIMPS-therapy; Ci-chimps, the clinical implementation study of CHIMPS with three implementation interventions; FFMHPQ, family focused mental health practice questionnaire; GB-A, gemeinsamer bundesausschuss (joint federal committee); ICQ, implementation components questionnaire; ISS, implementation satisfaction scale; SPSS, statistical package for the social sciences.

Gregg et al. summarized in their review factors influencing family-oriented practice in a detailed overall diagram with two main parts: Practitioner factors and workplace factors. They subclassify practitioner factors in personal attitudes like beliefs about family-oriented practice and professional subfactors like training and education, job role, skills and knowledge. Workplace factors were subclassified in service-related subfactors e.g., available resources and work setting and support-related subfactors like workplace support and time and workload (11).

Maybery and Reupert are providing an overview of the barriers regarding family-oriented practice. They have designed a model based on a hierarchy with the main factors "organizational policies and procedures (including managerial support)," "workers attitude, knowledge and skills," and "barriers families themselves bring in" (22). Lauritzen and Reedtz adapted this model for Norway and added the two factors "organization of mental health care services" and "geographical conditions" (13). These papers present the international state of knowledge of the implementation of interventions especially for this target group of children of mentally ill parents.

The Implementation Model of the CHIMPS-NET Consortium

The implementation science showed that evidence-based interventions will not be effective if not properly implemented (19). In order to achieve a successful implementation, all CHIMPS interventions are based on the Australian model by Maybery and Reupert (22) and the Norwegian model by Lauritzen and Reedtz (13). The CHIMPS-NET consortium specifies the content of prevention and care according to the German healthcare system setting, including adult psychiatry and child and adolescent psychiatry, and develops an own implementation process based on three implementation interventions. **Figure 1** shows the three subprojects (SP) for implementing and realizing the hierarchical components of an evidence-based implementation process including the following subprojects: "optimal pathways to prevention and care" [SP1], "improved institutional anchoring and professionals' attitudes, knowledge and skills" [SP2], "systematic screening, early detection, and family engagement" [SP3]. This systematical implementation process is developed to improve the implementation of prevention [SP4a] and therapy [SP4b]." SP5 realizes the online intervention i-chimps, and [SPs 6–8] realizes the medical, health economic, and qualitative evaluation [SPs 6–8]. In summary, ci-chimps realizes an overarching multicenter study to evaluate the implementation process with three implementation interventions [SP 1–3].

Ci-chimps also includes multiple interfaces with general medicine/primary care, pediatrics, youth healthcare services, and public sector services catering for the educational and residential needs of children. In the CHIMPS-NET model, the implementation of CHIMPS-P and CHIMPS-T in the model regions will be well-prepared through interventions at the interfaces, and in this way placed into an environment where experts from psychiatry and psychotherapy for children, adolescents, and adults as well as youth welfare and the civil sector are sensitized for the special requirements of those families. This implementation comprises all aspects of interdisciplinary and intersectional implementation, specific psychosocial intervention for children of parents with mental illness, quality assurance, cost-effectiveness, sustainability, and transfer.

The Three Implementation Interventions in CHIMPS-NET

The main aim of ci-chimps is the evaluation of the effect of the three implementation interventions in CHIMPS-NET. Referring to this hierarchy, we deduce our three implementation interventions 1) optimal pathways to care, 2) education and training program for the professionals, and 3) systematic screening. To examine the utility of the supported implementation of CHIMPS-NET, a controlled trial design is used. With these three implementation interventions, we want to support the clinical implementation of the family-oriented interventions in CHIMPS-NET.

1) **Optimal pathways to care**

The first implementation measure focuses on optimal ways of caring for mentally ill patients who are also parents with children living in the household. The main goals of this intervention are the specific information of the referring physician, the indicated referral of mentally ill parents, and the consideration of underage children living in the household of the inpatient referral. The two main components are the evaluation of the attitudes of the medical and psychotherapeutic referrers toward the target group, and the intervention as well as the development and implementation of an optimal care pathway. First there is an analysis of the potential and actual referrer network. In the next step information is sent to these referrer network and in the last step there will be an evaluation and an follow-up analysis of the referrer network. The optimization of the allocation is organized by Silke Pawils (University Medical Center Hamburg-Eppendorf).

2) **Education and training program for the professionals**

The second implementation intervention concerns the improvement of the professionals' attitudes, knowledge, and skills. The two main components here being the assessment of the current state in all institutions within the clinical centers as well as the development and implementation of an education and training program. The employees of the randomized clinical centers in the intervention group will get a 3-h training. This intervention is organized by Svenja Taubner (University Hospital Heidelberg, Germany). Due to the Covid-19-pandemic, the training of medical staff is organized as two webinars. The first webinar contains knowledge about risks in mentally ill parents and intervention skills on how to address family-related problems with mentally ill parents or children, respectively. Herewith, a bi-focal perspective is demonstrated i.e., having the needs of parents on the one hand and of children on the other hand in mind when assessing needs and offering support. The second webinar is offered in an interactive format to discuss the content of the first webinar and specific implementation barriers between youth and adult

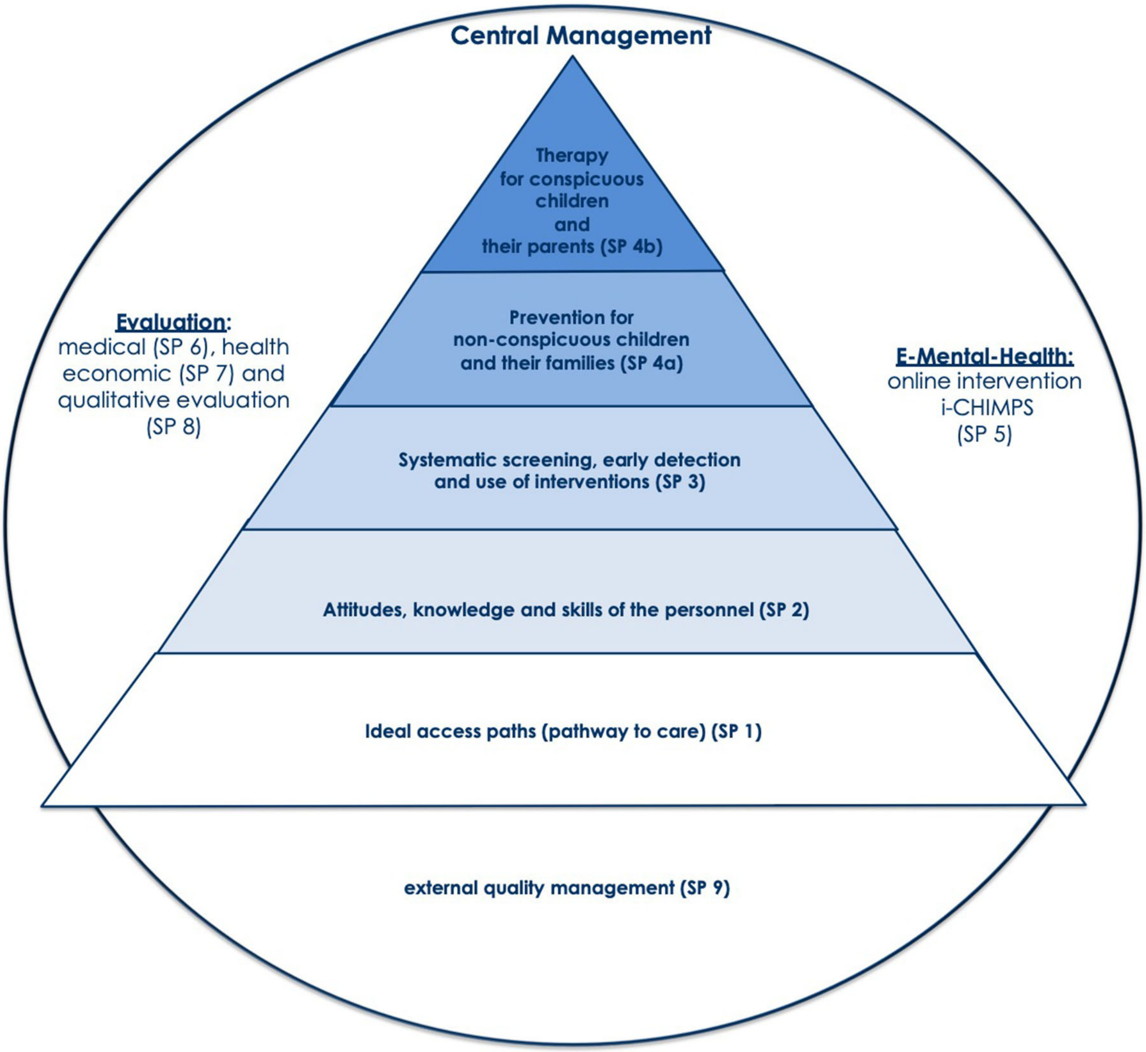


FIGURE 1 | The CHIMPS-NET Implementation Model [based on (22) and first published (25)] for the health care for children and their mentally ill parents.

psychiatric services as well as the practice of skills. Changes in attitudes toward working with mentally ill parents will be assessed over three times using the same online survey with the translated family-focused mental health practice questionnaire (26). The contents of the webinar have been published in more detail (27).

3) **Systematic screening**

The third implementation intervention includes a systematic screening process to improve the detection of mentally ill parents with affected children. Employees of the clinical centers fill out two short questionnaires with the parents. This intervention project is organized by Sibylle M. Winter (Charité, Berlin, Germany).

The first main question is whether psychiatric patients have responsibility for minors. If this question is answered in the affirmative, parents are presented with two short screening questionnaires of one page each. In the context of the study, sensitivity and specificity will be determined in comparison to standardized instruments (CBCL) and information collected during the family intervention.

The first questionnaire called "Children-Screening" (15) was developed specifically for children of mentally ill parents and piloted in the clinic for child and adolescent psychiatry of Charité. It records in short all potential mental health problems of a child. If the score is above the cut-off, further psychiatric assessment should be made. The second questionnaire called "Family-Screening" (15) was designed as a risk screening and records family risk and protective factors as well as incidences of domestic violence and neglect. The goal is to evaluate support needs for families. The result is presented in a traffic light system (RED-YELLOW-GREEN). RED indicates an urgent need for support. This questionnaire was developed in the child abuse clinic of the Charité and is also piloted there. Both questionnaires are not yet standardized, validated tools.

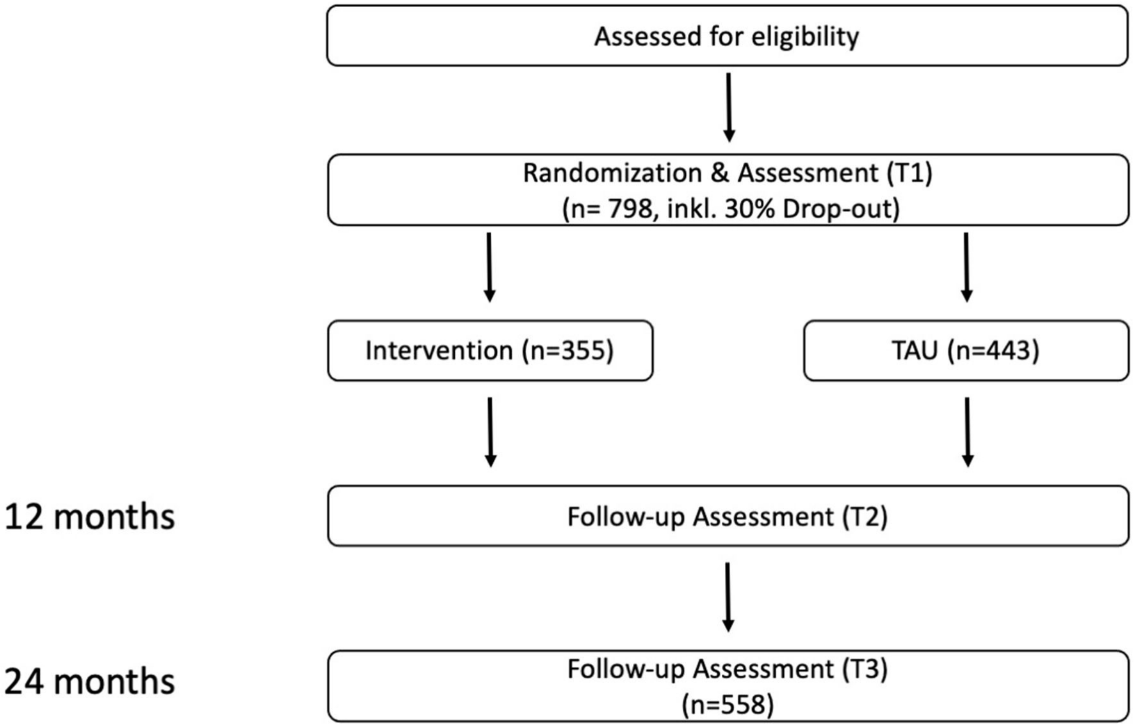


FIGURE 2 | Study design.

METHODS

Aims and Hypotheses of the Study

In ci-chimps, we aim to determine if three implementation interventions are helpful in improving the clinical implementation of the CHIMPS-NET interventions. Additionally, we want to identify factors hindering or promoting implementation processes. In order to monitor the impact of the three implementation interventions, we will use the translated version of the "Family Focused Mental Health Practice Questionnaire (FFMHPQ)" (26) and the translated version of the "Implementation Components Questionnaire (ICQ)" (28). The introduction of these questionnaires in Germany has not yet been reported. So the aims of the study are 1) the cultural and linguistic adaptation of the "Family Focused Mental Health Practice Questionnaire" (26) and the "Implementation Components Questionnaire" (28) from English to German, 2) the first introduction of these questionnaires in Germany, 3) the evaluation of the effect of the three implementation interventions in CHIMPS-NET, and 4) the identification of factors which hinder or promote implementation processes of family-oriented interventions using the example of CHIMPS-NET intervention.

More specifically, the following hypotheses will be tested:

H1: In this randomized controlled multicenter trial, we will compare the family-oriented practice between the clinical centers receiving the support of the three implementation interventions and the clinical centers not receiving the support of the implementation interventions. Our primary hypothesis is that clinical centers receiving at least one of the implementation interventions work more family-oriented than clinical centers without the support. Higher values after 12- and 24-months follow-up compared to the baseline mean a higher family-oriented practice. This is measured with the translated version of the "Family Focused Mental Health Practice Questionnaire."

H2: Furthermore, with our secondary hypothesis, we will compare the personnel's satisfaction regarding the implementation of the CHIMPS-NET project between the clinical centers receiving additionally the support of the three implementation interventions and the clinical centers not receiving the support of the implementation interventions. The personnel's satisfaction regarding the implementation of the CHIMPS-NET project is higher in the clinical centers receiving the implementation interventions than the personnel's satisfaction in the clinical centers without the three implementation interventions. This is measured with the translated version of the "Implementation Components Questionnaire" where higher values mean higher personnel satisfaction.

Study Design

As you can see in **Figure 2** the ci-chimps study is a two-group randomized controlled multicenter trial with assessments at baseline as well as at 12- and 24-months follow-up. It is one part of the superior project CHIMPS-NET, wherefore an own study protocol is in preparation (9). The ci-chimps study will be conducted from January 2020 to September 2023. The ci-chimps project's preparation phase includes the translation of the questionnaires FFMHPQ and the ICQ and the randomization of the clinical centers. The first measurement (baseline) takes place from January 2020 to May 2021. We stopped the baseline assessment after the last implementation intervention and defined this point as the end of the implementation interventions. During this year we implemented the superior project CHIMPS and the three implementation interventions of ci-chimps in the clinical centers. The second assessment will be in May 2022 and the follow-up in May 2023.

Study Setting

At the beginning of the study, 21 clinical centers located in 15 federal states in Germany were part of the CHIMPS-NETwork. Each clinical center has two subordinate clinics: one of the children and adolescent psychiatric department and one of the adult psychiatric department. Only 19 of the 21 clinical centers were randomized such that nine centers will receive additional support of all of the three implementation interventions (intervention group), and the remaining 10 clinical centers will be the control group and will not get specific implementation support. Hamburg (University Medical Centre Hamburg-Eppendorf, Germany), as the headquarter, and Munich (University Medical Center, Department of Psychiatry and Psychotherapy, Munich, Germany) are conducting their own study) are not randomized. Unfortunately, one clinical center of the intervention group left the study after a few weeks, so eight clinical centers remain in the intervention group and 10 in the control group. Because we defined the number of cases per clinical center, the unequal allocation to the intervention and control group leads to the consequence that the number of cases is different for the intervention- and the control group (TAU) as seen in **Figure 1**.

Participants

Sample Size and Power Calculation

This study will be conducted in 18 clinical centers and 31 employees on average per clinical center will be required to detect a difference at 12 and 24 months follow-up regarding family-oriented practice measured with FFMHPQ between the clinical centers receiving the support of the three implementation interventions and the clinical centers not receiving the support of the implementation interventions of 0.4 (Cohen's d) with 80% power, a two-sided alpha of 5% and a cluster effect of 5% (intraclass correlation coefficient of 0.05). This results in a sample size of 558 employees (31 per clinical center). Assuming a proportion of 30% incompletely completed questionnaires, we aim to recruit 798 employees.

Randomization

The random allocation of the clinical centers that receive or do not receive the support in a ratio of 1:1 was conducted according to a central randomization list generated with the statistical software R version 3.6.3 by the Department of Medical Biometry and Epidemiology (University Medical Centre Hamburg-Eppendorf, Germany) outside the recruitment and clinic. Originally, 18 centers participated in the study. After the randomization, another center was recruited. This center was randomized individually. At the end of this procedure, one center withdrew its participation in the study. So, we have an allocation ratio of 8:10.

Criteria for Inclusion

Every employee involved in the treatment of the patients (Medicine, Psychology, Nurses) of every clinical center that is part of the CHIMPS-NET project will be invited to participate in the ci-chimps study.

Criteria for Exclusion

There are no explicit criteria for exclusion.

Outcome Measures

Sociodemographic Questions

Besides age, gender and profession, we record with a specifically designed questionnaire, in which clinical center the employees work, how long they have been employed there and how strongly they are involved in the CHIMPS-NET-project.

Family Focused Mental Health Practice Questionnaire (FFMHPQ)

The "Family Focused Mental Health Practice Questionnaire (FFMHPQ)" (29) has 18 subscales, comprising a total of 53 items and measures numerous aspects relevant for family-oriented practice from the employee's point of view, on a 7-point Likert scale (ranging from strongly disagree to strongly agree plus "not applicable"). In addition to organizational and political aspects (e.g., workplace support, guidelines, local conditions, workload), the questionnaire determines the needs of hospital employees (e.g., knowledge transfer, skills about family issues, their interest in working with children, parents, and families) and families (e.g., psychoeducation). It also takes into account "external" factors such as the general organization of the health system and geographical conditions, as well as socio-demographic data. The Cronbach's alpha coefficients of the FFMHPQ range from 0.70 to 0.90 for most subscales. The FFMHPQ has demonstrated excellent face and content validities (29).

Implementation Components Questionnaire (ICQ-35)

In ci-chimps, we are using the shorter version of the "Implementation Components Questionnaire (ICQ-35)" (30). The 35 items questionnaire has nine subscales with five choices of response: "not applicable, yes, sometimes, no, don't know." The employees are asked to rate their perceived level of integration of the intervention within their clinical center. It determines special components of implementation, like selection or training of the employees. The Cronbach's alphas of the subscales range from 0.67 to 0.83. The original long version of the ICQ has 89 items and was first adapted in Norway (31, 32) from an earlier version of the Measures of Implementation Components of the National Implementation Research Network Frameworks by Ogden et al. (31) and Fixsen et al. (32). It has been shown to have good psychometric validity (32).

Implementation Satisfaction Scale (ISS)

Additionally, we are using the 4 item "Implementation Satisfaction Scale (ISS)" (30) which is part of the ICQ. It measures how satisfied the employees are with the implementation process on a 5-point Likert scale (ranging from strongly disagree to strongly agree). The Cronbach's alpha of the implementation satisfaction scale is 0.88 (30).

Translation Procedure

Up to now, the FFMHPQ has been used in different settings (e.g., family helplines, adult psychiatry) in various occupational groups (e.g., nurses, doctors) in Australia, Portugal, Thailand, Japan, Ireland, and Norway. The introduction of this questionnaire in Germany is still missing. The same applies to the ICQ and ISS. Adapting the FFMHPQ, the ICQ and the ISS to Germany should enable more effective implementation of family-oriented interventions in the regular healthcare system in the future.

According to the cross-cultural translation procedure recommended by Beaton and Guillemin (33), the questionnaires are translated from English to German and back into English. Two translators with German as their first language independently translate the questionnaire from English to German. Both versions (T1 and T2) are compared, differences are discussed and a third combined version T12 (synthesis from both translations) is developed. In the next step, two translators with English as their first language translate the questionnaire version T12 from German back into English (BT1 and BT2). Subsequently, the original questionnaires, the versions T1, T2, T12, BT1, and BT2 as well as the interim reports are discussed and evaluated within the framework of an expert committee. As a final step in the adaptation process, clinic employees are asked how they interpret the items and evaluate the questionnaire (applicability test). All questionnaires were slightly modified or reworded to adapt them to our target group.

Statistical Analysis

Data Coding and Analysis

All statistical analyses will be performed with SPSS (version 26.0 or newer). Means and standard deviations or median and 1st and 3rd quartiles, as appropriate, for the continuous variables as well as absolute and relative frequencies for the categorical variables of the whole sample and the respective treatment groups will be calculated and presented. The primary analysis will be conducted with the intention to treat (ITT) population consisting of all employees. The employees of a clinical center are subject to the same influences and cluster effects. Hence, for the primary endpoint, operationalized as the difference to baseline, a mixed linear model will be performed with treatment group, time, and baseline value as fixed effects, and clinical center as a random effect. The interaction between the treatment group and time will be tested and will be eliminated from the model if it is not statistically significant. The result of the primary analysis is the contrast of the treatment group after 18 months. Only this result will be considered in a confirmatory manner. The two-sided type I error will be set to 5%. It is possible that the fluctuation of employees in the clinical centers is so low that we can extend the model to a longitudinal model. The secondary endpoints will be examined in an exploratory manner with the same model in the case of continuous endpoints and with a similarly mixed Poisson regression in the case of count data. Results will be reported and published according to the CONSORT statement for cluster randomized trials (34).

DISCUSSION

While research has identified good evidence-based family-oriented interventions like CHIMPS that improve the quality of life of families, little is known about how to implement such interventions most effectively and efficiently in clinical practice in Germany. A strength of this ci-chimps -study is the use of a randomized controlled multicenter trial design with a large and wide-ranging sample. We are including both the child and adolescent as well as adult psychiatric departments and all professionals within a clinical center to get a better understanding of the implementation barriers. It could be a limitation that we can't ensure that the same employees fill out all four measurement times. For the first time in Germany, the translated versions of the questionnaires FFMHPQ and ICQ are used in Germany, so there is no German psychometric data yet. However, both original versions have demonstrated good psychometric validities in previous studies. Thus, it can be assumed that the translated German versions will show good psychometric validities as well.

Generally, it should be considered that ci-chimps is a purely questionnaire-based study, relying on the principle of self-disclosure. Therefore, the tendency toward social desirability cannot be ruled out. However, it can be assumed that this potential trend does not significantly affect the results, because the focus is on the comparison between employees from different clinical centers and the probability is high that this tendency can be found for both groups.

With ci-chimps, the implementation of CHIMPS is being supported for the first time. In previous studies of CHIMPS, there were no specific implementation interventions. Therefore, it should be considered that we can only measure an overall intervention effect. It is not possible to compare the three implementation interventions amongst each other. However, we are sure that with ci-chimps we will be able to identify training needs in clinics in order to improve the implementation of family-oriented interventions like CHIMPS-NET in the future.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethik Kommission der Ärztekammer Hamburg. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

CL and AM are responsible for the data and implementation study management. SW-G is the principal researcher of this implementation study ci-chimps, in cooperation with DM, AR, and BS, and of the whole CHIMPS-NET. CL drafted the manuscript with the help of SW-G, DM, and BS. SW-G, DM, and AR were substantially involved in the conception of the study and contributed to its design. AD, AH, and AZ are supported by the paragraphs on statistical methods and the randomization of the clinical centers. SP, ST, and SW realized as the project leaders the three implementation interventions. All authors have participated in the editing of the manuscript and have read and approved the final manuscript.

FUNDING

The study described in this protocol was funded by the German Federal Joint Committee (G-BA).

ACKNOWLEDGMENTS

We would like to thank all cooperation partners and clinical centers in Germany, who participate in the study and support us in the collection of data: Clinic for Psychiatry and Psychotherapy and Clinic for Child and Adolescent Psychiatry of Josefinum Augsburg and Kempten; Clinic for Psychiatry and Psychotherapy and Clinic for Child and Adolescent Psychiatry of the Evangelical Clinic Bethel, Bielefeld; Clinic for Psychiatry and Psychotherapy, Charité, Berlin; University Medical Center, Department of Psychiatry and Psychotherapy, Cologne; Psychiatry, Psychotherapy and Psychosomatics of Helios Clinics, Erfurt; University Medical Center, Department of Psychiatry, Psychosomatics and Psychotherapy, Frankfurt/Main; University Medical Centre for Psychiatry and Psychotherapy at the Immanuel Clinical Center Rüdersdorf, Frankfurt/Oder and the Child and Adolescent Psychiatry Frankfurt/Oder; University Medical Center, Department of Psychiatry and Psychotherapy, Freiburg; Clinic for General Psychiatry and Psychotherapy at the LWL Clinic Gütersloh and the Child and Adolescent Psychiatry at the LWL Clinic Hamm-Bochum; Centre for Psychosocial Medicine, University Medical Centre Hamburg-Eppendorf; University Medical Center Saarland, Department of Psychiatry and Psychotherapy, Homburg; Clinical psychology and psychotherapy of adulthood at the University Hospital, Koblenz – Landau and Clinic for Psychiatry and Psychotherapy Pfalz; University Medical Centre, Department of Psychiatry and Psychotherapy, Leipzig; University Medical Center, Department of Psychiatry and Psychotherapy and Department for Child and Adolescent Psychiatry, Magdeburg; University Medical Center, Department of Psychiatry and Psychotherapy and Department for Child and Adolescent Psychiatry, Marburg; University Medical Center for Psychiatry and Psychotherapy, Munich; Clinic for Psychiatry, Neurology, Psychosomatics and Psychotherapy in Childhood and Adolescence at the University Medical Center, Rostock; Psychiatry and Psychotherapy of Helios Clinics, Schwerin, Germany; General psychiatry and psychotherapy with polyclinic of the University Hospital, Tübingen; University Medical Center, Department of Psychiatry and Psychotherapy II, Ulm-Günzburg, Germany.

REFERENCES

1. Plass-Christl A, Haller AC, Otto C, Barkmann C, Wiegand-Grefe S, Hölling H, et al. Parents with mental health problems and their children in a German population based sample: results of the BELLA study. *PLoS ONE.* (2017) 12:e0180410. doi: 10.1371/journal.pone.0180410
2. Pierce M, Hope HF, Kolade A, Gellatly J, Osam CS, Perchard, et al. Effects of parental mental illness on children's physical health: systematic review and meta-analysis. *Br J Psychiatry.* (2020) 217:354–63. doi: 10.1192/bjp.2019.216
3. Wiegand-Grefe S, Halverscheid S, Plass A. *Kinder und Ihre Psychisch Kranken Eltern: Familienorientierte Prävention-der CHIMPs-Beratungsansatz.* Göttingen: Hogrefe (2011).
4. Wiegand-Grefe S, Cronemeyer B, Plass A, Schulte-Markwort M, Petermann, F. Comparison of mental abnormalities in children of mentally ill parents from different points of view: effects of a manualized family intervention. *Kind Entw.* (2013) 22:31–40. doi: 10.1026/0942-5403/a000096
5. Wiegand-Grefe S, Werkmeister S, Bullinger M, Plass A, Petermann, F. Health-related quality of life and social support of children with mentally ill parents: effects of a manualized family intervention. *Kind Entw.* (2012) 21:64–73. doi: 10.1026/0942-5403/a000071
6. Wiegand-Grefe S, Alberts J, Petermann F, Plass A. Differential perspectives on family functioning and interfamilial relationships: the effect of a manualized intervention program on children of mentally ill parents. *Kind Entw.* (2016) 25:77–88. doi: 10.1026/0942-5403/a000192
7. Wiegand-Grefe S, Cronemeyer B, Halverscheid S, Redlich A, Petermann, F. Coping strategies of psychiatrically ill parents and psychological abnormalities of their children through the focus of a manualised family intervention. *ZPPP.* (2013) 61:51–8. doi: 10.1024/1661-4747/a000140
8. Wiegand-Grefe S, Filter B, Busmann M, Kilian R, Kronmüller K-T, Lambert M, et al. Evaluation of a family-based intervention program for children of mentally ill parents: study protocol for a randomized controlled multicenter trial. *Front Psychiatry.* (2021) 11:561790. doi: 10.3389/fpsyt.2020.561790
9. Wiegand-Grefe S, Taczkowski J, Modaressi A, Adema B, Hot A, Daubmann A, et al. Evaluation of three family-oriented tailored, need-adapted preventive and psychotherapeutic interventions and one webbased intervention for Children and adolescents of mentally ill parents in a stepped care model – the children of mentally ill - research network (CHIMPS-NET): Study protocol for a randomized controlled multicenter trial.
10. Falkov A, Goodyear M, Hosman CMH, Biebel K, Skogøy BE, Kowalenko N, et al. A systems approach to enhance global efforts to implement family-focused mental health interventions. *Child Youth Serv.* (2016) 37:175–93. doi: 10.1080/0145935X.2016.1104104
11. Gregg L, Adderley H, Calam R, Wittkowski A. The implementation of family-focused practice in adult mental health services: a systematic review exploring the influence of practitioner and workplace factors. *Int J Ment Health Nurs.* (2021) 30:885–906. doi: 10.1111/inm.12837
12. Siegenthaler E, Munder T, Egger, M. Effect of preventive interventions in mentally ill parents on the mental health of the offspring: systematic review and meta-analysis. *J Am Acad Child Adolesc Psychiatry.* (2012) 51:8–17.e8. doi: 10.1016/j.jaac.2011.10.018
13. Lauritzen C, Reedtz, C. Knowledge transfer in the field of parental mental illness: objectives, effective strategies, indicators of success, and sustainability. *Int J Ment Health Syst.* (2015) 9:6. doi: 10.1186/1752-4458-9-6
14. Fixsen DL, Naoom SF, Blasé KA, Friedman RM, Wallace F, Burns, et al. Implementation research: a synthesis of the literature. Dean L. Fixsen: The National Implementation Research Network (2005).
15. Holl-Etten AK, Bentz L, Calvano C, Winter SM. Screening zur frühen Identifizierung des psychosozialen Unterstützungsbedarfs bei Kindern psychisch erkrankter Eltern. *Psychotherapeut.* (2021) 30:312–17. doi: 10.1007/s00278-021-00561-y
16. Wlodarczyk O, Metzner F, Pawils, S. Bundesweite Befragung zur Versorgungssituation und -hindernissen von Kindern psychisch kranker Eltern aus Sicht der Erwachsenenpsychiatrie. *Psychiat Prax.* (2017) 44:393–9. doi: 10.1055/s-0042-115824

17. Allchin B, Weimand BM, O'Hanlon B, Goodyear, M. Continued capacity: factors of importance for organizations to support continued Let's Talk practice - a mixed-methods study. *Int J Ment Health Nurs.* (2020) 29:1131–43. doi: 10.1111/inm.12754
18. Biebel K, Nicholson J, Woolsey, K. Implementing an intervention for parents with mental illness: building workforce capacity. *Psychiatr Rehabil J.* (2014) 37:209–15. doi: 10.1037/prj0000046
19. Mulligan C, Furlong M, McGilloway S. Promoting and implementing family-focused interventions for families with parental mental illness: scoping and installation. *Adv Ment Health*. (2019) 18:202–16. doi: 10.1080/18387357.2019.1614466
20. Shah-Anwar S, Gumley A, Hunter S. Mental health professionals' perspectives of family-focused practice across child and adult mental health settings: a qualitative synthesis. *Child Youth Serv.* (2019) 40:383–404. doi: 10.1080/0145935X.2019.1591947
21. Skogøy BE, Ogden, T, Weimand B, Ruud T, Sørgaard K, Maybery D. Predictors of family focused practice: organisation, profession, or the role as child responsible personnel? *BMC Health Serv Res.* (2019) 19:793. doi: 10.1186/s12913-019-4553-8
22. Maybery D, Reupert, A. Parental mental illness: a review of barriers and issues for working with families and children. *J Psychiatr Ment Health Nurs.* (2009) 16:784–791. doi: 10.1111/j.1365-2850.2009.01456.x
23. Maybery D, Foster K, Goodyear M, Grant A, Tungpunkom P, Skogoy BE, et al. How can we make the psychiatric workforce more family focused? In: Reupert A, Maybery D, Nicholson J, Gopfert M, Seeman MV, editors. *Parental Psychiatric Disorder: Distressed Parents and Their Families.* 3 ed. Cambridge: Cambridge University Press (2015). pp. 301–11.
24. Goodyear M, Hill TL, Allchin B, McCormick F, Hine R, Cuff R, et al. Standards of practice for the adult mental health workforce: meeting the needs of families where a parent has a mental illness. *Int J Ment Health Nurs.* (2015) 24:169–80. doi: 10.1111/inm.12120
25. Wiegand-Grefe S. *Unterstützung für Kinder und Jugendliche mit psychisch erkrankten Eltern im "Children of mentally ill parents network". Bundesweites Forschungs-, Versorgungs- und Implementierungsmodell.* Schwerpunkt: Kinder und psychisch kranke Eltern – Übersichten (2022). doi: 10.1007/s00278-021-00565-8
26. Laser C, Reupert A, Wiegand-Grefe S, Maybery, D. Fragebogen zur familienorientierten Arbeit im psychosozialen Gesundheitswesen – deutsche Übersetzung des "Family Focused Mental Health Practice" von Maybery, Goodyear & Reupert. (2019).
27. Taubner S, Kasper L, Hauschild S, Wiegand-Grefe S, Georg, A. Bifokale Perspektive in der Arbeit mit Familien mit psychisch erkrankten Eltern. *Psychotherapeut*. (2021) 67:1–8. doi: 10.1007/s00278-021-00557-8
28. Laser C, Skogøy BE, Maybery D, Wiegand-Grefe S. Implementierungs-Komponenten-Fragebogen (2019).
29. Maybery D, Goodyear M, Reupert, A. The family-focused mental health practice questionnaire. *Arch Psychiatr Nurs.* (2012) 26:135–44. doi: 10.1016/j.apnu.2011.09.001
30. Skogøy BE, Sørgaard K, Maybery D, Ruud T, Stavnes K, Kufås E, et al. Hospitals implementing changes in law to protect children of ill parents: a cross-sectional study. *BMC Health Serv Res.* (2018) 18:609. doi: 10.1186/s12913-018-3393-2
31. Ogden T, Bjørnebekk G, Kjøbli J, Patras J, Christiansen T, Taraldsen, et al. Measurement of implementation components ten years after a nationwide introduction of empirically supported programs – a pilot study. *Implement Sci.* (2012) 7:49. doi: 10.1186/1748-5908-7-49
32. Fixsen DL, Ward C, Blase K, Naoom S, Metz A, Louison L. *Assessing Drivers Best Practices.* Chapel Hill, NC: Active Implementation Research Network (2018).
33. Beaton DE, Bombardier C, Guillemin F, Ferraz, M.B. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine.* (2000) 25:3186–91. doi: 10.1097/00007632-200012150-00014
34. Campbell MK, Elbourne DR, Altman DG, CONSORT Group. CONSORT statement: extension to cluster randomised trials. *BMJ.* (2004) 328:702–8. doi: 10.1136/bmj.328.7441.702

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 08 March 2022
doi: 10.3389/fpsyt.2022.833400

Psychometric Properties of the Interpersonal Needs Questionnaire-15 in Spanish Adolescents

Sandra Pérez Rodríguez [1]*, Joaquín García-Alandete [1], Blanca Gallego Hernández de Tejada [2], Verónica Guillén [1,3] and Jose Heliodoro Marco [1,3]

[1] Department of Personality, Evaluation and Psychological Treatment, Faculty of Psychology, University of Valencia, Valencia, Spain, [2] Department of Personality, Assessment and Therapeutic Intervention, Catholic University of Valencia, Valencia, Spain, [3] Ciber Fisiopatología Obesidad y Nutrición (CIBEROBN), Madrid, Spain

Background: Thwarted Belongingness (TB) and Perceived Burdensomeness (PB) are considered risk factors of suicide behavior in the Interpersonal Theory of Suicide and constitute the main factors of the Interpersonal Needs Questionnaire—INQ.

Aims: The present study analyzes the internal consistency, construct validity, and invariance across sex and age of the INQ-15, which comprises two subscales, in a sample of Spanish community adolescents.

Methods: Participants were 1,536 adolescents from 12 to 19 years old. The INQ-15, the total number of non-suicidal self-injuries (NSSI), the Hopelessness Scale, and the Purpose in Life Test-Adolescents (PIL-A) were used.

Results: The INQ-15 showed good internal consistency for TB ($\overline{\omega} = 0.88$) and PB ($\overline{\omega} = 0.78$) subscales and construct and concurrent/discriminant validity in the whole sample. Both the PB and TB subscales showed a good fit {$SB\chi^2_{(9)} = 6.448$, $p = 0.694$, CFI = 1.000, RMSEA = 0.000 [90% CI (0.000, 0.022)] and $SB\chi^2_{(27)} = 248.973$, $p = 0.000$, CFI = 0.922, RMSEA = 0.073 [90% CI (0.065, 0.082)]}, respectively. Regarding the invariance analyses, we found (1) non-invariance in the PB subscale across sex groups and metric, scalar, and stric invariance across age groups, and (2) that it was not possible to perform the invariance analysis for the TB subscale across both sex and age because the fit was not adequate for both boys and 12–15 years old groups. Positive and significant relationships were found between the INQ-15 subscales and hopelessness and NSSI frequency, and negative and significant correlations with meaning in life.

Conclusions: The INQ-15 is a valid instrument for assessing TB and PB in Spanish adolescents. Future studies should analyze the invariance of this instrument in adolescents across sex and age.

Keywords: adolescents, psychometric properties, Interpersonal Needs Questionnaire-15 (INQ-15), Spanish, multi-group confirmatory factor analysis

OPEN ACCESS

Edited by:
Amanda Venta,
University of Houston, United States

Reviewed by:
S. M. Yasir Arafat,
Enam Medical College, Bangladesh
Mario Ángel González,
University of Guadalajara, Mexico

***Correspondence:**
Sandra Pérez Rodríguez
sandra.perez@uv.es

Specialty section:
This article was submitted to
Child and Adolescent Psychiatry,
a section of the journal
Frontiers in Psychiatry

Received: *11 December 2021*
Accepted: *31 January 2022*
Published: *08 March 2022*

Citation:
Pérez Rodríguez S, García-Alandete J, Gallego Hernández de Tejada B, Guillén V and Marco JH (2022) Psychometric Properties of the Interpersonal Needs Questionnaire-15 in Spanish Adolescents. Front. Psychiatry 13:833400. doi: 10.3389/fpsyt.2022.833400

INTRODUCTION

Suicide, Perceived Burdensomeness, and Thwarted Belongingness

Suicide is a serious global public health issue (1). In the year 2018 in Spain (2), 3,679 people ended their lives, making suicide the leading non-natural cause of death and the second cause of death in adolescents and young adults. Literature on suicide has shown that about one-third of people with suicide ideation attempt suicide (3, 4), and the same trend has been found in adolescents (5). For this reason, some authors (6, 7) have highlighted that it is crucial to identify the factors that lead to developing suicide ideation and those that drive people to make a suicide attempt.

From the ideation to action framework, the Interpersonal Theory of Suicide (IPTS) (8, 9) posits that both Perceived Burdensomeness (PB: the perception of being a burden to others) and Thwarted Belongingness (TB: loneliness and the perception of not receiving any kind of reciprocal care) are necessary and independent factors in developing passive suicide ideation (desire for death). Some empirical evidence supports the links between PB, TB, and suicide ideation [e.g., (6, 10, 11)]. To develop active suicide ideation, the person needs to think that these two states will not change in the future, thus leading to hopelessness (9). Finally, to reach suicidal behavior, according to the IPTS, the patient must acquire the capacity for suicide through fearlessness toward death and increased pain tolerance, which, in turn, develop through repeated experiences of painful events, such as exposure to violence. A broad subset of research has supported the theory in adults [e.g., (12)] and adolescents [e.g., (13–15)].

A Scale for Assessing Perceived Burdensomeness and Thwarted Belongingness: The Interpersonal Needs Questionnaire

To test the aforementioned constructs of PB and TB, the Interpersonal Needs Questionnaire (INQ-25) was developed for use by researchers in the investigation of the etiology of suicidal behavior, as well as by clinicians as part of a risk assessment framework (6). This scale includes 25 items rated on a 7-point Likert type scale (0 = Not at all true for me; 7 = Very true for me), with 10 items assessing PB and 15 assessing TB. In order to reduce the administration time and improve multicollinearity (16), different INQ versions have been proposed.

A 12-item version (7 items for PB, 5 for TB) (16) was developed, for which the authors found adequate internal consistency indexes: TB, $\alpha = 0.85$, PB, $\alpha = 0.89$. Freedenthal et al. (17) carried out a confirmatory factor analysis of the INQ-12 in a sample of adult American undergraduate students, confirming both factors. Internal consistency was above 0.90 for both subscales, and both had adequate convergent validity.

An alternative 18-item version was published (6), and Marty et al. (18) explored its psychometric properties in a sample of American community older adults. A principal axis factor analysis showed two factors consistent with the PB and TB constructs and both PB and TB provided evidence for convergent validity. However, in this work, the authors did not carry out a confirmatory factor analysis of the instrument.

Van Orden et al. (19) explored the psychometric properties of the INQ-25 in five different samples of American undergraduate students, adult outpatients, and healthy older adults; after analyzing its factorial structure, they proposed a version with 15 items; 6 items assessing PB (items 1–6) and 9 assessing TB (items 7–15). Items 7, 8, 10, 13, 14, and 15 are reverse-worded and scored. Similar results were found using this version in a sample of American military personnel (20). Results from the multiple group CFA confirmed a two-factor structure and its invariance across the different groups. Convergent and divergent validity were found for PB, but divergent validity was not found for TB.

A multicentric study carried out with Hispanic participants used a Spanish translation of the INQ-15 (21) in three samples of American young adults, Mexican patients and young adults, and Spanish college students. The authors found that the 15-item version did not adequately fit the data from the three samples, and that a 9-item 2-factor solution provided the best fit. Both subscale scores demonstrated good internal consistency, 1-week test-retest reliability, and convergent validity. In addition, the instrument also showed measurement invariance across nationalities and clinical severity in the three samples. However, low divergent validity was found. Teo et al. (22) confirmed the two-factor structure of the INQ-15 in young adults in Singapore with good internal consistency, concurrent, convergent, predictive, and discriminant validity.

Moreover, it has been found that cut-off scores of the INQ-15 of 17 for PB and 37 for TB correctly classificated high-risk and low-risk women with chronic illnesses, thus supporting the clinical relevance of the instrument (23). Mitchell et al. (24) also found INQ-15 as a useful instrument to predict suicide ideation-related outcomes in psychiatric inpatients.

A study explored the structure of the INQ-15 in a German adult community and a clinical sample (25). The results revealed that the PB scale showed good fit in the clinical sample, but not in the general population. In addition, a TB 5-item version fit the clinical sample, but not the general population. In addition, Wang et al. (26) found adequate psychometric properties of the INQ-15 in Chinese migrant industrial workers, finding that predicted adequately suicide ideation in this population.

The IPTS has obtained growing evidence for its validity in adolescent samples (27). These authors highlighted the need to validate the IPTS constructs in adolescence, given that some items validated in adults "might need to be changed or supplemented to capture the relevant constructs in the context of adolescence" [(27), p. 8] because adolescence is a developmental stage that involves great emotional instability and can affect psychological adjustment (28). In addition, adolescence has been found to be a period when the risk of engaging in self-injurious behaviors increases [i.e., (29)]. However, few studies have explored the psychometric properties and factorial structure of the INQ (19) in community adolescents. Among them, Hill et al. (30) compared the psychometric properties of the different

INQ versions, including the INQ-15 (10, 12, 15, 18, and 25 items) (6, 17, 18, 31), in three sample of American college students and adolescents from an inpatient unit. The authors reported acceptable psychometric properties for all the INQ versions but highlighted the best fit for the 15- and 10-item versions, thus recommending them for future research. In all the samples, good internal consistency was found for both subscales, as well as adequate concurrent predictive validity of suicidal ideation.

Podlogar et al. (32) translated and validated the INQ-15 in a sample of 307 Slovenian 12 to 17-year-old adolescents, confirming a 12-item version and two-factor solution (TB and PB) with six items in each factor. In addition, the authors found adequate concurrent and divergent validity and stability across a period of 7 months.

In a recent study, El Behadli et al. (33) explored the structure of the INQ-25 in American adolescents, reducing the scale to 10 items, five per scale. Large correlations were found between the original scale and the new scale, along with good reliability and validity indexes. And finally, a recent study (34) compared five versions of the INQ in Chinese adolescent samples, finding that the INQ-15, the INQ-12 and the INQ-10 were the most suitable versions for teenagers (12–18 years).

In sum, an increasing number of studies are analyzing the psychometric properties, factorial structure, and clinical utility of the different versions of the INQ. Nevertheless, there is high heterogeneity in the analyzed versions across studies, and some of them have identified limitations mainly related to high intercorrelations between subscale scores or low divergent validity for the TB subscale (19, 21). As Podlogar et al. (32) pointed out, the INQ-15 is the first empirically derived and psychometrically validated version of the original version of the INQ. To our knowledge, to date only two studies have explored the psychometric properties of the INQ-15 in adolescents: Hill et al. (30) in American clinical adolescents and Podlogar et al. (32) in Slovenian community adolescents. In addition, although Silva et al. (21) recently proposed a Spanish translation for different Hispanic samples, no studies have translated the INQ-15 and explored its factorial structure in Spanish adolescents, and there is still a need for instruments to screen risk factors for suicide in Spain.

The Present Study

The main objective of the present study was to translate the INQ-15 into Spanish and confirm its internal consistency and two-factor structure in a Spanish sample of community adolescents between 12 and 19 years old. Moreover, we aimed to analyze the invariance of the INQ-15 across sex and age (12–15 and 16–19 years) and explore the validity of the scale. We expected to find statistically significant positive correlations between the PB and TB subscales and non-suicidal self-injury (NSSI) frequency and hopelessness, and negative correlations with meaning in life.

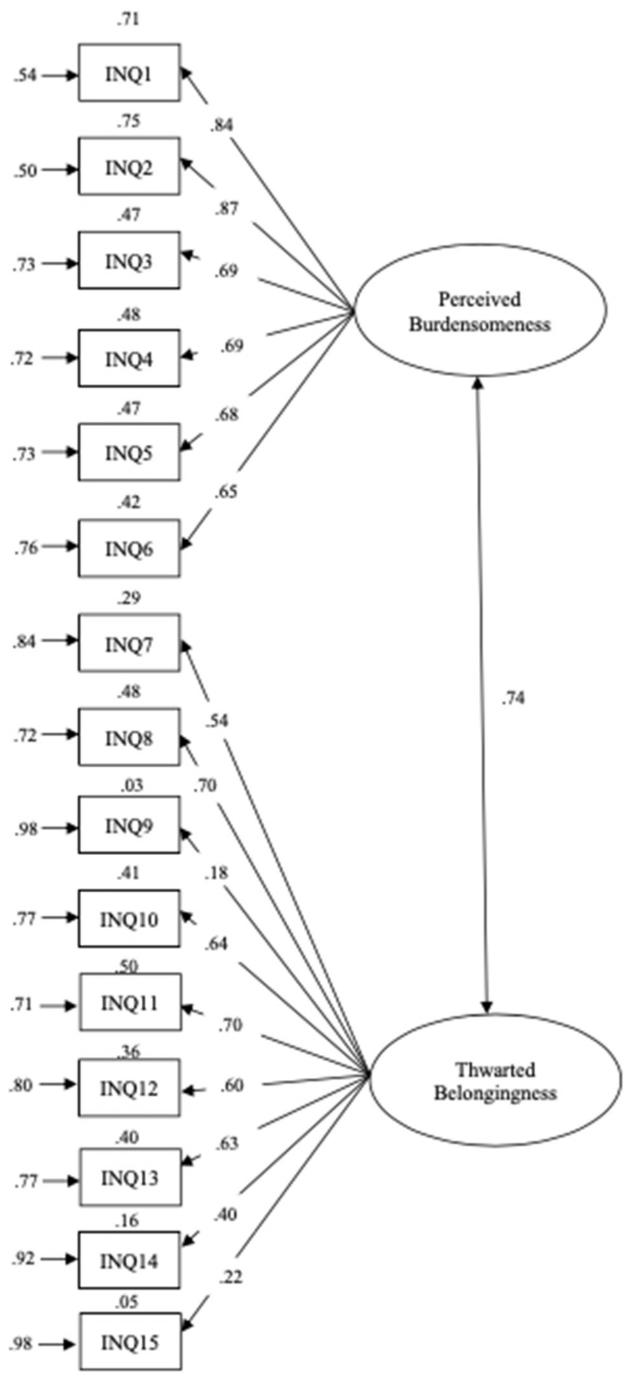


FIGURE 1 | Model for the INQ-15 obtained in the present study. Values at the top of each rectangle are R^2; values at the left of each rectangle are errors.

METHODS

Procedure and Participants

The study procedure was approved by the ethical committees of the university. A university professor of Scientific English and a member of the research team translated the ISAS to Spanish. A synthesis of both versions was carried out solving the discrepancies, and then two experts English-Spanish translators carried out a back-translation. Three members of the research team independently reviewed the final version of the instrument,

TABLE 1 | Sociodemographic variables.

$N = 1,536$	n (%)	Range
Age M (SD)	14.87 (1.58)	12–19
Men	739 (48.11)	
Women	797 (51.89)	
12–15 years old	985 (64.13)	
16–19 years old	551 (35.87)	

following directions proposed by Arafat et al. (35). We carried out a pilot study with 50 students to improve the questionnaire's administration and the wording of the instrument.

Researchers on the team contacted the principals of 22 schools and high schools in different areas all over Spain. Nine agreed to participate in the study. Students were recruited through classroom announcements, and consent letters were sent home by the administrators of the schools. Participation was voluntary and anonymous, and participants did not receive any compensation for participating in this study. We followed the World Health Organization (36) definition of adolescents as people from 10 to 19 years old. The inclusion criteria were: males or females between 12 and 19 years old (lower secondary and—high school in Spain) and provide their informed consent and/or that of their parents. The exclusion criteria were the refusal of the students and/or their parents to participate in the study and being under 12.

The study sample, composed of students from different Spanish provinces, was recruited between September 2016 and June 2018. A total of 1,733 adolescents were initially approached, of whom 193 (11.16%) were not included: 22 (1.27%) refused to participate in the study or did not obtain their parents' consent, and 171 (9.89%) did not completely fulfill the assessment protocol.

Therefore, a total of 1,536 participants between 12 and 19 years old, $M = 14.87$, $SD = 1.58$, were included in the study and assessed on their socio-demographic characteristics and a subset of psychological variables that were analyzed in a broader NSSI risk-factor study. The boys' group included 739 (48.11%) participants, and the girls' group included 797 (51.89%) participants. A total of 985 (64.13%) adolescents were 12–15 years old, and 551 (35.87%) were 16–19 years old. For the data collection, students filled in online questionnaires, always with the help of one or two members of the research team (**Table 1**).

Instruments

Interpersonal Needs Questionnaire-15 Items

The INQ-15 (19) is a self-report measure composed of 15 items that evaluate the main constructs of interpersonal suicide theory (8): PB (items 1–6), and TB (items 7–15). The items are answered on a 1–7 Likert scale. In this study, both the PB and TB dimensions showed high and acceptable internal consistency, $\overline{\omega} = 88$ and $\overline{\omega} = 78$, respectively.

Purpose in Life-Adolescents

The Purpose in Life-Adolescents (37) is a 9-item adaptation of the Spanish version of (38) PIL (39) for assessing meaning in life in adolescents. The PIL-A is answered on a Likert scale (1–7). In this study, the PIL-A showed a good fit, $SB\chi^2_{(26)} = 47.157$, $p = 0.007$, CFI = 0.997, RMSEA = 0.023 [90% CI (0.012, 0.033)] and high internal consistency, $\overline{\omega} = 0.89$.

Inventory of Statements About Self-Injury [ISAS Part I]

The presence of NSSI was evaluated using the ISAS (40) part I of the ISAS. The ISAS-I asks about the lifetime frequency of 12 different NSSI behaviors performed intentionally and without suicidal intent (e.g., banging/hitting self, biting, burning, carving, and cutting). Adolescents were asked how many times they had injured themselves.

Beck Hopelessness Scale

The Beck Hopelessness Scale (41) is a 20-item scale designed to assess negative expectations about the future. It has high internal consistency, $\alpha = 0.93$, and it has also been validated in a Spanish sample (42). In our sample, the BHS showed a good fit, $SB\chi^2_{(167)} = 196.059$, $p = 0.062$, CFI = 0.996, RMSEA = 0.011 [90% CI (0.000, 0.016)] and good internal consistency, $\overline{\omega} = 0.84$.

Statistical Analyses

First, the means (and standard deviations), skewness and kurtosis (and standard errors), Kolmogorov-Smirnoff normality test, and corrected item-total correlations of the INQ-15 items and subscales were calculated. A Confirmatory Factor Analysis (CFA) was carried out to evaluate the structural invariance of the INQ-15. Because data distribution was not normal, the Robust Maximum Likelihood estimation (43) was used. Likewise, given that the INQ-15 is an ordinal scale, the Diagonally Weighted Least Squares (DWLS) method was used. Fit indices included the Comparative Fit Index (CFI; a value ≥ 0.90 indicates acceptable fit and a value ≥ 0.95 indicate good model fit) and the Root Mean Square Error of Approximation (RMSEA; a value < 0.080 indicates acceptable model fit and a value < 0.050 indicates good model fit) [e.g., (44)]. The correlation between the PB and TB subscales was assumed when performing the INQ-15 CFA in the whole sample, the boys' and girls' groups, and the 12–15 and 16–19-year-old groups.

Increasingly restrictive models were iteratively examined to determine the degree of model invariance across sex (boys/girls) and age (12–15 years/16–19 years) (45). To evaluate the fit difference between nested models, the differences between the CFI fit index (ΔCFI) and the RMSEA index (ΔRMSEA) were used: Values ≤ 0.01 on ΔCFI (46) and an increase < 0.015 on the ΔRMSEA (47) indicate invariance.

The convergent validity of the INQ-15 was reported using the correlation with the number of NSSI and the HS scale, and the discriminant validity was obtained using the correlation with the PIL-A, a measure of meaning in life that has been related to PB and TB (18). These correlations were computed using Spearman's *rho* (ρ), the differences between boys' and girls' correlations were calculated (48), and effect-sizes (49) were reported.

The free software JASP for Windows (50) was used to carry out these statistical analyses.

RESULTS

Descriptive Statistics of the Scales Used in the Present Study

Table 2 shows the descriptive statistics of the INQ-15 items and both the PB and TB dimensions of the INQ-15, as well as the corrected item-total correlations. Data distribution was not normal: the skewness value for items 1–5, 7, and 13, as well as for the PB subscale, was > 2, and the kurtosis value for items 4 and 5 was > 7 (51). The Kolmogorov-Smirnov normality test was significant for all the INQ-15 items and subscales. The correlation between the PB and TB subscales, $\rho = 0.51$, was assumed when performing the CFA of the INQ-15.

Multi-Group Confirmatory Factor Analysis of the INQ-15

In the whole sample, the PB subscale showed a good fit, $SB\chi^2_{(9)} = 6.448$, $p = 0.694$, CFI = 1.000, RMSEA = 0.000 [90% CI (0.000, 0.022)], and the TB showed an acceptable fit, $SB\chi^2_{(27)} = 248.973$, $p = 0.000$, CFI = 0.922, RMSEA = 0.073 [90% CI (0.065, 0.082)]. All parameters were statistically significant at the 0.05 level (**Figure 1**).

Table 3 shows the baseline models for the boys' and girls' groups, as well as the analysis of invariance of the INQ-15 subscales across sex and age (if needed).

PB Invariance

The PB subscale showed a good fit in the boys' group, CFI $>$ 0.95, and an acceptable fit in the girls' group, CFI $>$ 0.90. The RMSEA index was $<$0.050 for both sex groups. The configural model showed a good fit, CFI $>$ 0.95 and RMSEA $<$ 0.050. For the metric invariance, although the ΔCFI was below 0.01, the ΔRMSEA above 0.015 suggested non-invariance. Regarding the age groups, the baseline and configural model was adequate for both the 12–15 and 16–19 year-old, and metric, scalar, and strict invariance were obtained, with ΔCFI and ΔRMSEA values below the recommended 0.01 and 0.015, respectively.

TB Invariance

In both boys and girls groups, the RMSEA was acceptable, with a value higher than 0.050, but lower than 0.080. The CFI $>$ 0.95 was adequate for the girls' group, both the CFI $<$ 0.90 was inadequate for the boys' group (therefore, the invariance analysis was not performed). Regarding the age groups, the model was adequate for the 16–19 year-old group, CFI $>$ 0.95 and RMSEA $<$ 0.050, but inadequate for the 12–15 year-old group, CFI $<$ 0.90 and RMSEA $>$ 0.80 (therefore, the invariance analysis was not performed).

Convergent and Discriminant Validity of the INQ-15

Table 4 shows the correlations between the INQ-15 subscales and the ISAS intrapersonal and interpersonal functions, NSSI frequency to determine convergent validity, and the PIL-A to determine discriminant validity. Regarding the convergent validity, PB and TB showed positive but low significant correlations with NSSI frequency and HS. In the case of discriminant validity, negative and significant moderate-high correlations were found between the PIL-A and both the PB and TB subscales from the INQ-15.

The differences between boys' and girls' correlations and the effect-sizes of these differences were calculated. The correlations between both PB and TB and HS, NSSI frequency, and the PIL-A were higher for girls, and the differences between girls and boys were significant for the correlations between the PB subscale and HS, NSSI frequency, and the PIL-A, as well as for the correlation between TB and the PIL-A. Of these differences, the PB-HS, PB-PIL-A, and TB-PIL-A showed a small effect-size, and the PB-NSSI showed no effect, according to Cohen (49).

DISCUSSION

The main aims of the present study were: (1) to translate and confirm the internal consistency and two-factor structure of the INQ-15 in a Spanish sample of community adolescents between 12 and 19 years old; (2) to analyze the invariance of the INQ-15 across sex and age (12–15 and 16–19 year-olds); and (3) to analyze the validity of the scale.

We obtained good internal consistency for both the PB and TB subscales, $\overline{\omega} = 0.88$ and $\overline{\omega} = 0.78$, respectively, which are similar to those obtained in previous studies with college students [e.g., (30)] and lower than those obtained in other studies with adult psychiatric outpatients [e.g., (52)] and adolescents between 12 and 17 years old (32). Moreover, the results obtained in the present study support the factorial validity of the two-factor INQ-15, as proposed and confirmed by Van Orden et al. (19) and Nademin et al. (20): six items make up PB (1–6), and nine items form TB (7–15). Van Orden et al. (19) confirmed the factorial structure of the INQ-15 in undergraduate students, adult outpatients, and older adults. Nademin et al. (20) confirmed it in military personnel, and Hill et al. (30) in college students. However, the two studies that analyzed the factorial structure of the INQ-15 in adolescents did not confirm this 15-item structure (30, 32). Podlogar et al. (32) referred to the wording valence rather than construct overlap to explain their results. In our study, we did not find wording problems, and all the items properly represented the two constructs. Thus, this study supports the 15-item version in Spanish adolescents, thus adding to the instruments available to screen risk factors for suicide in Spain.

As for the structure validity of the INQ-15 subscales according to sex and age, the model for the PB subscale was adequate for boys and girls, as well as for both age groups. The model for the TB subscale was adequate only for the girls and the 16–19 year-old group. Because the model for the TB subscale was inadequate in the boys' group, the invariance analysis was carried out only for the PB subscale. The configural model showed good values. Regarding the metric invariance, although the ΔCFI was notably lower than the recommended 0.01, the ΔRMSEA was higher than 0.015 (47). Together [Cfr. (53)], these results

TABLE 2 | Descriptive statistics of the items and subscales of the INQ-15.

INQ-15	*M (SD)*	Skewness (*SE*)	Kurtosis (*SE*)	Kolmogorov-Smirnov normality test[a]	Corrected item total correlation
Item 1	1.668 (1.364)	**2.011 (0.062)**	3.420 (0.125)	0.462**	0.841**
Item 2	1.613 (1.330)	**2.190 (0.062)**	4.263 (0.125)	0.471**	0.858**
Item 3	1.577 (1.333)	**2.429 (0.062)**	5.475 (0.125)	0.475**	0.768**
Item 4	1.269 (0.966)	**4.037 (0.062)**	**17.145 (0.125)**	0.522**	0.739**
Item 5	1.370 (1.074)	**3.156 (0.062)**	**10.151 (0.125)**	0.507**	0.734**
Item 6	2.249 (1.737)	1.144 (0.062)	0.367 (0.125)	0.365**	0.768**
Item 7	1.502 (1.202)	**2.493 (0.062)**	5.924 (0.125)	0.485**	0.555**
Item 8	2.610 (1.846)	0.775 (0.062)	−0.375 (0.125)	0.306**	0.698**
Item 9	2.463 (2.206)	1.177 (0.062)	−0.161 (0.125)	0.381**	0.397**
Item 10	1.850 (1.588)	1.805 (0.062)	2.385 (0.125)	0.439**	0.659**
Item 11	2.257 (1.763)	1.148 (0.062)	0.323 (0.125)	0.368**	0.719**
Item 12	2.206 (1.756)	1.232 (0.062)	0.539 (0.125)	0.379**	0.635**
Item 13	1.674 (1.446)	**2.167 (0.062)**	3.962 (0.125)	0.465**	0.641**
Item 14	4.982 (1.333)	−1.512 (0.062)	2.200 (0.125)	0.352**	0.569**
Item 15	4.787 (1.475)	−1.524 (0.062)	1.861 (0.125)	0.406**	0.407**
PB ($\overline{\omega} = 88$)	9.746 (6.148)	**2.344 (0.062)**	6.189 (0.125)	0.271**	
TB ($\overline{\omega} = 78$)	24.33 (18.547)	1.120 (0.062)	1.417 (0.125)	0.132**	

PB, Perceived Burdensomeness; TB, Thwarted Belongingness. Items 1–6 were correlated with the PB subscale; items 7–15 were correlated with the TB subscale. In bold, the skewness values higher than 2 and the kurtosis (proper) higher than 7 (51).

[a] *Lilliefors significance correlation.*

***$p < 0.01$.*

TABLE 3 | Test of invariance across sex and age for the INQ-15 subscales.

	Subscale	Invariance	$SB\chi^2$ (*df*)	*p*	CFI	RMSEA (90% CI)	$\Delta SB\chi^2$ (Δdf)	ΔCFI	ΔRMSEA
Sex	PB	Baseline boys	3.004 (9)	0.964	1.000	0.000 (0.000, 0.000)			
		Baseline girls	3.965 (9)	0.914	1.000	0.000 (0.000, 0.015)			
		Configural	6.969 (18)	0.990	1.000	0.000 (0.000, 0.000)			
		Metric	34.583 (24)	0.075	0.993	0.024 (0.000, 0.041)	27.614 (6)	0.007	**0.024**
	TB	Baseline boys	133.346 (27)	0.000	**0.890**	0.073 (0.061, 0.086)			
		Baseline girls	123.866 (27)	0.000	0.951	0.067 (0.055, 0.079)			
Age	PB	Baseline 12-15	2.614 (9)	0.978	1.000	0.000 (0.000, 0.000)			
		Baseline 16-19	4.647 (9)	0.864	1.000	0.000 (0.000, 0.025)			
		Configural	7.261 (18)	0.988	1.000	0.000 (0.000, 0.000)			
		Metric	14.204 (24)	0.942	1.000	0.000 (0.000, 0.006)	6.943 (6)	0.000	0.000
		Scalar	19.168 (29)	0.917	1.000	0.000 (0.000, 0.010)	4.964 (5)	0.000	0.000
		Strict	20.838 (35)	0.972	1.000	0.000 (0.000, 0.000)	1.670 (6)	0.000	0.000
	TB	Baseline 12-15	245.214 (27)	0.000	**0.881**	**0.091** (0.080, 0.101)			
		Baseline 16-19	42.493 (27)	0.029	0.985	0.032 (0.010, 0.050)			

PB, Perceived Burdensomeness; TB, Thwarted Belongingness.
In bold, CFI < 0.90 and RMSEA > 0.080.

indicate that the INQ-15 subscales did not show invariance across sex. Therefore, we could not analyze the differences in the PB and TB scales according to sex [e.g., (54, 55)]. Future studies should analyze the invariance in the INQ-15 across sex, to carry out further analyses of sex-related differences in the PB and TB subscales.

Because the model for the TB subscale was inadequate in the group of 12–15-year-old, the invariance analysis was carried out only for the PB subscale and all the estimated standardized factor loadings were significant.

Regarding convergent validity, PB and TB showed positive, significant correlations with frequency of NSSI and hopelessness. These associations show that the two factors of the IPTS, the perception of being a burden and loneliness and the perception of not receiving any kind of reciprocal care, are related to other factors included in the theory (hopelessness), but also to other

TABLE 4 | Convergent and divergent validity of the INQ-15 subscales.

INQ-15 subscales	Whole sample (n = 1,536)			Boys (n = 739)			Girls (n = 797)			Comparison of boys' and girls' correlations (Z)			Effect size for the difference between the boys' and girls' correlations[a]		
	HS	NSSI	PIL-A	HS	NSSI	PIL-A	HS	NSSI	PIL-A	HS	NSSI	PIL-A	HS	NSSI	PIL-A
PB	0.26***	0.26***	−0.49***	0.43***	0.22***	−0.43***	0.51***	0.30***	−0.55***	−2.01*	−1.68*	3.10***	0.103 (S)	0.086 (N)	0.158 (S)
TB	0.24***	0.24***	−0.51***	0.42***	0.21***	−0.45***	0.47***	0.27***	−0.56***	−1.22	−1.25	2.90**			0.148 (S)

PB, Perceived Burdensomeness; TB, Thwarted Belongingness; HS, Hopelessness; NSSI, Non-Suicidal Self-Injuries; PIL-A, Purpose in Life-Adolescents; (S), Small effect; (N), Non effect.

[a] *Cohen (49).*

$^{*}p < 0.05$.

$^{**}p < 0.01$.

$^{***}p < 0.001$.

variables classically linked to suicide, such as NSSI [i.e., (56, 57)] supporting the validity of the INQ-15 for assessing suicide-like constructs. Likewise, PB and TB showed negative associations with the protective factor meaning in life. That is, the more the adolescent perceives that her/his life makes sense, is meaningful and trustful, and is worth living, the less he/she feels like a burden to others and thinks his/her belongingness is altered or lacking.

Finally, we found positive associations between PB, hopelessness, and the frequency of NSSI, as well as negative associations between PB and TB and between TB and meaning in life, but they were stronger in girls than in boys. Although the simple correlations do not allow us to draw conclusions about the nature of these differences, these results could point to sex-related differences in the PB and TB subscales (54, 55) and in the relationships between these subscales and other variables. Future studies on this issue are needed.

Strengths and Clinical Implications

Although several studies have explored the factorial structure and psychometric properties of the INQ-15 [i.e., (19, 21)], this is the first study to confirm the factorial structure of the INQ-15 in a Spanish sample of community adolescents. The results support the validity of the instrument for assessing suicide-like constructs in Spain, where this is an important problem in young populations that requires valid and reliable measures. In addition, we used a broad sample that allowed us to test the factorial structure of the instrument.

Limitations and Future Research

The current study has some limitations. First, data distribution was not normal for several items and the PB subscale of the INQ-15. Second, due to the lack of a re-test measurement, we cannot corroborate the temporal stability of the Spanish version of the INQ-15. In addition, because this study is part of a broader study of NSSI in Spanish adolescents, we did not examine the convergent validity of the INQ-15 with other validated measures of suicide-like behaviors, such as suicide ideation or attempts, which is an important flaw in this study. Thus, future longitudinal studies are needed to examine the predictive power of PB and TB in the occurrence of suicide plans and attempts in Spanish adolescents.

CONCLUSION

Our results suggest that it is appropriate to use the INQ-15 to assess PB and TB in Spanish adolescents from 12 to 19 years old. However, future research should specifically revise the model fit of the INQ-15 in boys and adolescents between 12 and 15 years old, as well as its invariance across sex and age.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the Catholic University of Valencia, Research Code UCV2015-2016/0025-V2. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

SP: design, verify evolution of research, data curation, data analyses, writing original draft, writing review and editing the manuscript, and project administration. JG-A: data curation, data analyses, writing original draft, and writing review and editing the manuscript. BG: sample assessment, data analyses, and writing review and editing the manuscript. VG: data analyses and review and editing the manuscript. JM: design, verify evolution of research, data curation, data analyses, writing review and editing the manuscript, and project administration. All authors contributed to the article and approved the submitted version.

FUNDING

Funding for the study was provided by R + D + I Projects of the State Programs Oriented to the Challenges of Society, within the framework of the State Research Plan Scientific and Technical and Innovation, with Code: PID2019-111036RB-I00, from Ministry of Science and Innovation of Spain.

REFERENCES

1. World Health Organization. *Suicide Worldwide in 2019: Global Health Estimates*. Geneva (2021).
2. Instituto Nacional de Estadística. *Defunciones por suicidios*. (2022). Available online at: https://www.ine.es/jaxiT3/Datos.htm?tpx=49948
3. Kessler RC, Borges G, Walters EE. Prevalence of and risk factors for life- time suicide attempts in the National Comorbidity Survey. *Arch Gen Psychiatry*. (1999) 56:617–26. doi: 10.1001/archpsyc.56.7.617
4. Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Williams D. Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. *Br J Psychiatry*. (2008) 192:98–105. doi: 10.1192/bjp.bp.107.040113
5. Nock MK, Green JG, Hwang I, Mclaughlin KA, Sampson NA, Zaslavsky AM, et al. Prevalence, correlates, and treatment of lifetime suicidal behaviour among adolescents: results from the national comorbidity survey replication adolescent supplement. *JAMA Psychiatry*. (2013) 70:300–10. doi: 10.1001/2013.jamapsychiatry.55
6. Joiner TE Jr, Van Orden KA, Witte TK, Selby EA, Ribeiro JD, Lewis R, et al. Main predictions of the interpersonal-psychological theory of suicidal behavior: empirical tests in two samples of young adults. *J Abnorm Psychol*. (2009) 118:634–46. doi: 10.1037/a0016500
7. May AM, Klonsky ED. What distinguishes suicide attempters from suicide ideators? A meta-analysis of potential factors. *Clin Psychol Sci Pract*. (2016) 23:5–20. doi: 10.1037/h0101735
8. Joiner TE Jr. *Why People Die by Suicide*. Cambridge, MA: Harvard University Press (2005).
9. Van Orden KA, Witte TK, Cukrowicz KC, Braithwaite SR, Selby EA, Joiner TE Jr. The interpersonal theory of suicide. *Psychol Rev*. (2010) 117:575. doi: 10.1037/a0018697
10. Hill RM, Pettit JW. Perceived burdensomeness and suicide-related behaviors in clinical samples: current evidence and future directions. *J Clin Psychol*. (2014) 70:631–43. doi: 10.1002/jclp.22071
11. Wilson KG, Kowal J, Henderson PR, Mcwilliams LA, Péloquin K. Chronic pain and the interpersonal theory of suicide. *Rehabil Psychol*. (2013) 58:111–5. doi: 10.1037/a0031390
12. Joiner TE Jr, Silva C. Why people die by suicide: further development and tests of the interpersonal-psychological theory of suicidal behavior. In: Shaver PR, Mikulincer M, editors. *Meaning, Mortality, and Choice: The Social Psychology of Existential Concerns*. Washington, DC: American Psychological Association (2012). p. 325–36.
13. Eaddy M, Zllo L, Horton SE, Hughes JL, Kennard B, Diederich A, et al. A theory driven investigation of the association between emotion dysregulation and suicide risk in a clinical adolescent sample. *Suic Life Threat Behav*. (2019) 49:928–40. doi: 10.1111/sltb.12472
14. Horton SE, Hughes JL, King JD, Kennard BD, Westers NJ, Mayes TL, et al. Preliminary examination of the interpersonal psychological theory of suicide in an adolescent clinical sample. *J Abnorm Child Psychol*. (2016) 44:1133–44. doi: 10.1007/s10802-015-0109-5
15. King JD, Horton SE, Hughes JL, Eaddy M, Kennard BD, Emslie GJ, et al. The interpersonal-psychological theory of suicide in adolescents: a preliminary report of changes following treatment. *Suicide Life Threat Behav*. (2018) 48:294–304. doi: 10.1111/sltb.12352
16. Van Orden KA, Witte TK, Gordon KH, Bender TW, Joiner TE Jr. Suicidal desire and the capability for suicide: tests of the interpersonal-psychological theory of suicidal behavior among adults. *J Consult Clin Psychol*. (2008) 76:72–83. doi: 10.1037/0022-006X.76.1.72
17. Freedenthal S, Lamis DA, Osman A, Kahlo D, Gutierrez PM. Evaluation of the psychometric properties of the Interpersonal Needs Questionnaire-12 in samples of men and women. *J Clin Psychol*. (2011) 67:609–23. doi: 10.1002/jclp.20782
18. Marty MA, Segal DL, Coolidge FL, Klebe KJ. Analysis of the psychometric properties of the interpersonal needs questionnaire (INQ) among community-dwelling older adults. *J Clin Psychol*. (2012) 68:1008–18. doi: 10.1002/jclp.21877
19. Van Orden KA, Cukrowicz KC, Witte TK, Joiner TE, Jr. Thwarted belongingness and perceived burdensomeness: construct validity and psychometric properties of the interpersonal needs questionnaire. *Psychol Assess*. (2012) 24:197–215. doi: 10.1037/a0025358
20. Nademin E, Jobes DA, Pflanz SE, Jacoby AM, Ghahramanlou-holloway M, Campise R, et al. An investigation of interpersonal-psychological variables in Air Force suicides: a controlled-comparison study. *Arch Suicide Res*. (2008) 12:309–26. doi: 10.1080/13811110802324847
21. Silva C, Hurtado G, Hartley C, Rangel JN, Hovey JD, Pettit JW, et al. Spanish translation and validation of the Interpersonal Needs Questionnaire. *Psychol Assess*. (2018) 30:e21–37. doi: 10.1037/pas0000643
22. Teo D, Suárez L, Oei T. Validation of the interpersonal needs questionnaire of young male adults in Singapore. *PLoS ONE*. (2018) 13:e0198839. doi: 10.1371/journal.pone.0198839
23. Brookings JB, Pederson CL. INQ-15 cut-off scores for suicidal ideation screening of women with chronic, invisible illnesses. *Clin Psychol Psychother*. (2019) 26:273–5. doi: 10.1002/cpp.2343
24. Mitchell SM, Brown SL, Roush JF, Bolaños AD, Littlefield AK, Marshall AJ, et al. The clinical application of suicide risk assessment: a theory-driven approach. *Clin Psychol Psychother*. (2017) 24:1406–20. doi: 10.1002/cpp.2086
25. Upegui-arango LD, Forkmann T, Nielsen T, Hallensleben N, Glaesmer H, Spangenberg L, et al. Psychometric evaluation of the interpersonal needs questionnaire (INQ) using item analysis according to the Rasch model. *PLoS ONE*. (2020) 15:e0232030. doi: 10.1371/journal.pone.0232030
26. Wang R, Chen Y, Hu F, Wang Z, Cao B, Xu C, et al. Psychometric properties of interpersonal needs questionnaire-15 for predicting suicidal ideation among migrant industrial workers in China. *Int J Environ Res Public Health*. (2021) 18:7583. doi: 10.3390/ijerph18147583
27. Stewart SM, Eaddy M, Horton SE, Hughes J, Kennard B. The validity of the interpersonal theory of suicide in adolescence: a review. *J Clin Child Adoles Psychol*. (2017) 46:437–49. doi: 10.1080/15374416.2015.1020542
28. Najman JM, Heron MA, Hayatbakhsh MR, Dingle K, Jamrozik K, Bor W, et al. Screening in early childhood for risk of later mental health problems: a longitudinal study. *J Psychiatr Res*. (2008) 42:694–700. doi: 10.1016/j.jpsychires.2007.08.002
29. Plener PL, Schumacher TS, Munz LM, Groschwitz RC. The longitudinal course of non-suicidal self-injury and deliberate self-harm: a systematic review of the literature. *Borderline Pers Disord Emot Dysregul*. (2015) 2:2. doi: 10.1186/s40479-014-0024-3
30. Hill RM, Rey Y, Marin CE, Sharp C, Green KL, Pettit JW. Evaluating the interpersonal needs questionnaire: comparison of the reliability, factor structure, and predictive validity across five versions. *Suicide Life Threat Behav*. (2014) 45:302–14. doi: 10.1111/sltb.12129
31. Bryan CJ. The clinical utility of a brief measure of perceived burdensomeness and thwarted belongingness for the detection of suicidal military personnel. *J Clin Psychol*. (2010) 67:981–92. doi: 10.1002/jclp.20726
32. Podlogar T, Žiberna J, Poštuvan V, Kerr DCR. Belongingness and burdensomeness in adolescents: slovene translation and validation of the Interpersonal Needs Questionnaire. *Suicide Life Threat Behav*. (2016) 47:336–52. doi: 10.1111/sltb.12276
33. El-Behadli AF, Beitra D, Zullo L, Mbroh H, and Stewart SM. Measuring thwarted belongingness and perceived burdensomeness in clinically depressed and suicidal youth: Refinement and reduction of the interpersonal needs questionnaire. *Sui Life-Threat Behav*. (2019) 49:1463–72. doi: 10.1111/sltb.12527

34. Quan J, Yu X, Cai Y, Tu D. Comparison of psychometric characteristics for five versions of the interpersonal needs questionnaire in teenagers sample. *Front Psychol*. (2021) 12:1888. doi: 10.3389/fpsyg.2021.676361
35. Arafat SY, Chowdhury HR, Qusar MMAS, Hafez MA. Cross cultural adaptation and psychometric validation of research instruments: a methodological review. *J Behav Health.* (2016) 5:129–36. doi: 10.5455/jbh.20160615121755
36. World Health Organization. *Adolescent Friendly Health Services: An Agenda for Change*. Geneva (2003).
37. García-Alandete J, Gallego B, Pérez S, Marco-Salvador JH. Meaning in life among adolescents: factorial invariance of the purpose in life test and buffering effect on the relationship between emotional dysregulation and hopelessness. *Clin Psychol Psychother*. (2019) 26:24–34. doi: 10.1002/cpp.2327
38. Crumbaugh JC, and Maholick LT. *Manual of Instructions for the Purpose in Life Test.* Saratoga, CA: Viktor Frankl Institute of Logotherapy (1969).
39. García-Alandete J, Rosa E, Sellés P. Estructura factorial y consistencia interna de una versión española del Purpose-In-Life Test [Factorial structure and internal consistency of a Spanish version of the Purpose-In-Life Test]. *Univ Psychol.* (2013) 12:517–30. doi: 10.11144/Javeriana.UPSY12-2.efci
40. Klonsky ED, Glenn CR. Assessing the functions of non-suicidal self-injury: psychometric properties of the inventory of statements about self-injury (ISAS). *J Psychopathol Behav Assess.* (2009) 31:215–9. doi: 10.1007/s10862-008-9107-z
41. Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol.* (1974) 42:861–5. doi: 10.1037/h0037562
42. Viñas F, Villar E, Caparrós B, Juan J, Cornellá M, Pérez I. Feelings of hopelessness in a Spanish university population: descrip- tive analysis and its relationship to adapting university, depressive symptomatology and suicidal ideation. *Soc Psychiatry Psychiatr Epidemiol.* (2004) 39:326–34. doi: 10.1007/s00127-004-0756-2
43. Satorra A, Bentler PM. A scaled difference chi-square test statistic for moment structure analysis. *Psychometrika*. (2001) 66:507–14. doi: 10.1007/BF02296192
44. Hair JF, Anderson RE, Tatham RL, Black WC. *Multivariate Data Analysis* (6th ed.). Upper Saddle River, NJ: Pearson Prentice Hall (2006).
45. Vandenberg RJ, Lance CE. A review and synthesis of the measurement invariance literature: suggestions, practices, and recommendations for organizational research. *Organ Res Methods.* (2000) 3:4–70. doi: 10.1177/109442810031002
46. Cheung GW, Rensvold RB. Evaluating goodness of fit indexes for testing measurement invariance. *Struct Equ Model.* (2002) 9:235–55. doi: 10.1207/S15328007SEM0902_5
47. Chen FF. Sensitivity of goodness of fit indexes to lack of measurement invariance. *Struct Equ Model.* (2007) 14:464–504. doi: 10.1080/10705510701301834
48. Eid M, Gollwitzer M, Schmitt M. *Statistik und Forschungsmethoden Lehrbuch [Handbook of Statistics and Research Methods]*. Weinheim: Beltz. (2011).
49. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale, NJ: Erlbaum (1988).
50. JASP Team. *JASP (Version 0.11.1) [Computer Software]*. (2019). Available online at: https://jasp-stats.org/ (accessed January 2022).
51. Kim HY. Statistical notes for clinical researchers: assessing normal distribution (2) using skewness and kurtosis. *Restor Dentistry Endodontics.* (2013) 38:52–4. doi: 10.5395/rde.2013.38.1.52
52. Mitchell SM, Brown SL, Roush JF, Tucker RP, Cukrowicz KC, Joiner TE Jr. The interpersonal needs questionnaire: statistical considerations for improved clinical application. *Assessment.* (2020) 27:621–37. doi: 10.1177/1073191118824660
53. Lai K, Green SB. The problem with having two watches: assessment of fit when RMSEA and CFI Disagree. *Multivar Behav Res*. (2016) 51:220–39. doi: 10.1080/00273171.2015.1134306
54. Hill RM, Hatkevich C, Pettit JW, Sharp C. Gender and the interpersonal-psychological theory of suicide: a three-way interaction between perceived burdensomeness, thwarted belongingness, and gender. *J Soc Clin Psychol.* (2017) 36:799–813. doi: 10.1521/jscp.2017.36.10.799
55. Hill RM, Hunt QA, Oosterhoff B, Yeguez CE, Pettit JW. Perceived burdensomeness among adolescents: a mixed-methods analysis of the contexts in which perceptions of burdensomeness occur. *J Soc Clin Psychol.* (2019) 38:585–604. doi: 10.1521/jscp.2019.38.7.585
56. Pérez S, Ros MC, Folgado JEL, Marco JH. Non-suicidal self-injury differentiates suicide ideators and attempters and predicts future suicide attempts in patients with eating disorders. *Suicide Life Threat Behav*. (2019) 49:1220–31. doi: 10.1111/sltb.12521
57. Victor SE, Klonsky ED. Correlates of suicide attempts among self-injurers: A meta-analysis. *Clin Psychol Rev.* (2014) 34:282–97. doi: 10.1016/j.cpr.2014.03.005

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers
in Psychiatry

ORIGINAL RESEARCH
published: 09 March 2022
doi: 10.3389/fpsyt.2022.796554

A Multi-Center Study on the Relationship Between Developmental Regression and Disease Severity in Children With Autism Spectrum Disorders

Chaoqun Hu[1†], Fan Yang[1†], Ting Yang[1], Jie Chen[1], Ying Dai[1], Feiyong Jia[2], Lijie Wu[3], Yan Hao[4], Ling Li[5], Jie Zhang[6], Xiaoyan Ke[7], Mingji Yi[8], Qi Hong[9], Jinjin Chen[10], Shuanfeng Fang[11], Yichao Wang[12], Qi Wang[13], Chunhua Jin[14], Tingyu Li[1] and Li Chen[1]*

[1] Growth, Development and Mental Health Center of Children and Adolescents, Chongqing Key Laboratory of Childhood Nutrition and Health, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, China, [2] Department of Developmental and Behavioral Pediatric, The First Hospital of Jilin University, Changchun, China, [3] Department of Children's and Adolescent Health, Public Health College of Harbin Medical University, Harbin, China, [4] Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [5] Department of Children Rehabilitation, Hainan Women and Children's Medical Center, Haikou, China, [6] Xi'an Children's Hospital, Xi'an, China, [7] Child Mental Health Research Center of Nanjing Brain Hospital, Nanjing, China, [8] Department of Child Health Care, The Affiliated Hospital of Qingdao University, Qingdao, China, [9] Maternal and Child Health Hospital of Baoan, Shenzhen, China, [10] Department of Child Healthcare, Shanghai Children's Hospital, Shanghai Jiao Tong University, Shanghai, China, [11] Children's Hospital Affiliated to Zhengzhou University, Zhengzhou, China, [12] NHC Key Laboratory of Birth Defect for Research and Prevention, Hunan Provincial Maternal and Child Health Care Hospital, Changsha, China, [13] Deyang Maternity & Child Healthcare Hospital, Deyang, China, [14] Department of Children Health Care, Capital Institute of Pediatrics, Beijing, China

OPEN ACCESS

Edited by:
*Idan Menashe,
Ben-Gurion University of the Negev,
Israel*

Reviewed by:
*Mor Absa Loum,
University of Thies, Senegal
Milica Pejovic-Milovancevic,
Institute of Mental Health (Belgrade),
Serbia*

***Correspondence:**
*Li Chen
chenli@cqmu.edu.cn*

† These authors have contributed equally to this work

Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: 21 October 2021
Accepted: 04 February 2022
Published: 09 March 2022

Citation:
Hu C, Yang F, Yang T, Chen J, Dai Y, Jia F, Wu L, Hao Y, Li L, Zhang J, Ke X, Yi M, Hong Q, Chen J, Fang S, Wang Y, Wang Q, Jin C, Li T and Chen L (2022) A Multi-Center Study on the Relationship Between Developmental Regression and Disease Severity in Children With Autism Spectrum Disorders. Front. Psychiatry 13:796554. doi: 10.3389/fpsyt.2022.796554

Introduction: This study aimed to investigate the prevalence of developmental regression in children with Autism Spectrum Disorder (ASD) and to explore its relationship with disease severity.

Methods: We finally included 1,027 ASD children aged 2–5 years from 13 cities in China: 138 with regressive ASD and 889 with non-regressive ASD. The Social Responsiveness Scale (SRS), Autism Behavior Checklist (ABC), Child Autism Rating Scale (CARS), and Children Neuropsychological and Behavioral Scale-Revision 2016 (CNBS-R2016) were used to evaluate the core symptoms and developmental status of children in the two groups.

Results: Among the 1,027 ASD children eventually included, 138 (13.44%) cases showed regressive behavior and the average regression occurring age was 24.00 (18.00–27.00) months. Among the regressive children, 105 cases (76.09%) had language regression, 79 cases (57.25%) had social regression, and 4 cases (2.90%) had motor regression. The total scores of ABC and the sub-score of sensory and stereotypic behavior ($\beta = 5.122$, 95% CI: 0.818, 9.426, $P < 0.05$; $\beta = 1.104$, 95% CI: 0.120, 2.089, $P < 0.05$; $\beta = 1.388$, 95% CI: 0.038, 2.737, $P < 0.05$), the SRS total scores and the sub-score of autistic mannerisms ($\beta = 4.991$, 95% CI: 0.494, 9.487, $P < 0.05$; $\beta = 1.297$, 95% CI: 0.140, 2.453, $P < 0.05$) of children in the regressive group were all higher than the non-regressive group. The total developmental quotient (DQ) of CNBS-R2016 and the DQ of gross motor, fine motor, adaptive behavior, language ($\beta = -5.827$, 95% CI: −11.529, −0.125, $P < 0.05$) and personal society in the regressive group were lower than the non-regressive group and the proportion of children with intelligent developmental impairment was higher the non-regressive group.

Conclusion: Regressive autism is mainly manifested as language and social regression. Children with regressive ASD have more severe core symptoms, lower neurodevelopmental level DQ, and more serious disease degree than children with non-regressive ASD, which requires further etiological examinations and more clinical attention.

Keywords: autism spectrum disorder, regression, disease severity, relationship, multi-center study

INTRODUCTION

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by persistent impairments in social interaction and communication, and the presence of restrictive and repetitive patterns of behavior, interests and activities, and sensory anomalies (1). The latest report in the United States shows that the prevalence has risen from 1.7% in 2018 (2) to 2.27% in 2021 (3). In China, the prevalence was 0.7% in 2020 (4). The onset of behavioral signs of ASD is usually conceptualized as occurring in one of three ways: an early onset pattern, in which children demonstrate delays and deviances in social and communication development early in life; a regressive pattern, in which children develop largely as expected for some period and then experience a substantial decline in or loss of previously developed skills; and a developmental stagnation pattern, which is characterized by intact early skills that fail to progress or transform into more advanced developmental achievements (5). Developmental regression in ASD is typically defined as a child's developmental milestones (language, social, motor, and other skills) at the corresponding age stage that have stabilized for more than 3 months, and then a single or multiple behavioral regression occurs. One commonly utilized criterion for language regression, complete loss of expressive language skills after acquiring at least five words and using them for at least 3 months (6). Previous findings indicate that most children with ASD showed an early onset pattern, but recent studies have shown that the frequency of regressive patterns is higher than before (7, 8). At present, there is still a lack of large-scale surveys on the relationship between the developmental regression of ASD children and the disease severity in China. Therefore, this study investigated the developmental regression of children with ASD in 13 cities across the country, and explored the relationship between the type of ASD and the severity of the disease, in order to provide a basis for clinical diagnosis and treatment.

MATERIALS AND METHODS

Patients

All research participants aged 2–5 were recruited from the China Multi-center Preschool Autism Project (CMPAP). From May 2018 to December 2019, the project recruited ASD children from 13 cities where the project sub-centers are located-northern, eastern, western, southern, and central China. According to the completion of the questionnaire, it was confirmed that the effective sample size of 1,027 cases was included. The area where the sub-centers are located is defined as: the north (Heilongjiang, Qingdao, and Changchun); the east (Shanghai and Nanjing); the west (Chongqing, Deyang, and Xi'an); the south (Shenzhen, Hainan, and Hunan); the middle (Wuhan and Zhengzhou).

Selection Criteria

Autism Spectrum Disorder children were recruited from outpatient clinics and special education institutions. The diagnosis of ASD was performed by psychiatrist, psychologists, or developmental behavioral pediatrician with extensive experience and using the Diagnosis and Statistical Manual of Mental Disorders-fifth edition (DSM-5) (9). ASD children with the following conditions were excluded: (1) children with brain injury; (2) children with severe physical and sensory impairment (blindness, deafness); (3) independent neurodevelopmental disorders and neurological diseases; and (4) other acute and chronic diseases. The inclusion and exclusion criteria of the regression group in this study were: (1) A detailed description of regressive behavior was the basis for inclusion. Parents needed to explain the detailed time point at which the behavioral skills previously mastered by ASD children began to regress, such as social, language, and motor. (2) "Regression" was defined as the loss of these abilities after appearing and remaining for more than 3 months, rather than being lost within a short period of time after the abilities appear. (3) Language regression was defined as loss of more than five spoken words used communicatively in children more than 18 months of age. For social and motor regression, when there was a clear indication of loss of social interest or motor skills, it was determined as regression regardless of age.

Scales and Questionnaires

Autism Spectrum Disorder Child Health Questionnaire includes detailed content such as basic child information, family environment information, health status after birth, and description of developmental regression. Among them, the developmental regression includes: whether there is regression, the regression occurring age, and the detailed description of the regression behavior.

The Autism Behavior Checklist

Autism Behavior Checklist (ABC) consists of 57 items in five dimensions, including sensory, relating, stereotypic behavior, language, and social self-help. Which is completed by parents to describe the behavioral characteristics of children with ASD. A score of 53 was used as thresh-old value for the diagnosis of autism, while scores for children with autism should be ≥ 67 (10).

The Social Responsiveness Scale

A scale filled out by parents to assess the social ability of autism. A total of 65 items consists of 5 subscales including social awareness, social cognition, social communication, social motivation and autistic mannerisms. Normal children's assessment score should be <65. The higher the total score, the more severe the social disorder (11).

Child Autism Rating Scale

This scale is used by professionals to assess the symptoms and severity of autism, and is suitable for children over 2 years old. A total of 15 items are scored using four levels of 1, 2, 3, and 4. The total score is 30–36 points, and the items below three points are less than five items indicates mild-moderate autism; the total score is ≥ 36 points and at least 5 items with a score higher than three points indicates severe autism (12).

The Revised Children Neuropsychological and Behavior Scale

It is assessed by professionals and used to assess the neurodevelopmental level of children aged 0–6 in the six domains of gross motor, fine motor, adaptive behavior, language, personal society, and autism warning behavior. $DQ < 70$ in each domain indicates developmental disorders. The warning behavior score <7 indicates normal, and >30 indicates highly suspected ASD, which can be used for risk identification and prediction of ASD (13).

Statistical Analysis

SPSS statistical software 26.0 was used for statistical analysis. The Kolmogorov–Smirnov goodness-of-fit test was used to test the distribution of each dataset for normality before analysis. Continuous variables were described as mean ± standard deviation (M ± SD) and medians (inter-quartile ranges) [M (IQR)]. Categorical variables were described as n (%). Differences in demographic data betweeen groups were assessed by using the Chi-Square test or Mann–Whitney test. Multivariate (adjusted for age and gender) linear regression models were used to compare the scores of the Autism symptom scale and developmental level scale between the regressive and non-regressive groups. A $P < 0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics

According to the inclusion and exclusion criteria, a total of 1,027 ASD children aged 2–5years were enrolled in this study (**Figure 1**), with an average age of 3.55(2.95–4.18) years, including 844 males and 183 females (male: female = 4.61:1). There were 138 (13.44%) children had regressive autism (Regressive group, R) with a median (IQR) age of 3.64(2.90–4.24) years and 889 (86.56%) children had non-regressive autism (Non-regressive group, NR) with a median (IQR) age of 3.54(2.95–4.18) years. There was no significant difference in the age of children between the two groups ($z = -0.329$, $P = 0.742$) (**Table 1**). There was also no significant difference in region and residence ($x^2 = 4.211$, 0.198, $P = 0.378$, 0.906).

General Description of Developmental Regression

The average age of the onset of regression was 24.00(18.00–27.00) months. Among them, the regression rate of male children was 13.40% (113/843), and that of female children was 13.66% (25/183). The difference was not statistically significant ($x^2 = 0.010$, $P = 0.922$). Among the regressive children, 105 cases (76.09%) had language regression, 79 cases (57.25%) had social regression, and 4 cases (2.90%) had motor regression (**Table 2**).

Comparison of Autism Behavior Checklist, Social Responsiveness Scale, Child Autism Rating Scale, and Communication Warning Behavior Scores Between Regressive Group and Non-regressive Group

The results of multivariate (adjusting for age and gender) linear regression models are shown in **Table 3**. The regressive ASD children had higher scores than non-regressive ASD children in the ABC total score and the scores of sub-items, and the

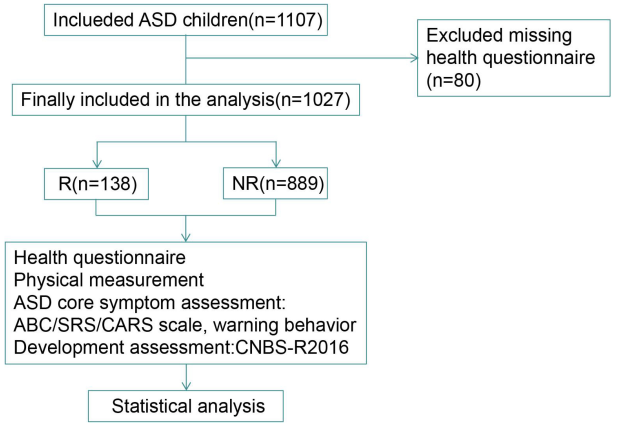


FIGURE 1 | Flowchart of the study participants. R, regressive group; NR, non-regressive group.

TABLE 1 | Demographic characteristics of the participants in R and NR groups.

Variable	R (*n* = 138)	NR (*n* = 889)	Z/x^2	*P*
Average age (years), median (IQR)	3.64(2.90–4.24)	3.54(2.95–4.18)	$z = -0.329$	0.742
Gender, *n* (%)			$x^2 = 0.010$	0.922
Male	113(81.88)	731(82.22)		
Female	25(18.12)	158(17.77)		
Region, *n* (%)			$x^2 = 4.211$	0.378
North	37(26.81)	235(26.43)		
East	12(8.70)	112(12.60)		
West	44(31.88)	221(24.86)		
South	27(19.57)	194(21.82)		
Middle	18(13.04)	127(14.29)		
Residence, *n* (%)			$x^2 = 0.198$	0.906
Urban	102(73.91)	671(75.48)		
Rural	34(24.64)	204(22.95)		
Miss	2(1.45)	14(1.57)		

Data was shown as Median (IQR) or number (percentage). Chi-square test and Mann–Whitney test were used in the analysis. R, regressive group; NR, non-regressive group; IQR, interquartile range.

TABLE 2 | Detail description of the regressive skills.

Variable	Frequency (*n* = 138)	Percentage
Language regression	58	42.03
Social regression	33	23.91
Language and social regression	43	31.16
Language and motor regression	1	0.72
All three of the above	3	2.17

differences in sensory (β = 1.104, 95% CI: 0.120, 2.089, $P < 0.05$), stereotypic behavior (β = 1.388, 95% CI: 0.038, 2.737, $P < 0.05$) and ABC total score (β = 5.122, 95% CI: 0.818, 9.426, $P < 0.05$) were statistically significant.

The regressive ASD children also had higher scores in the Social Responsiveness Scale (SRS) total score and the scores of sub-items compared with the non-regressive ASD children, while there were only two statistically significant differences in autistic mannerisms score (β = 1.297, 95% CI: 0.140, 2.453, $P < 0.05$) and SRS total score (β = 4.991, 95% CI: 0.494, 9.487, $P < 0.05$) between the two groups.

The Child Autism Rating Scale (CARS) total score in the regression group was slightly lower than that in the non-regression group, however, the difference is not statistically significant. The regressive ASD children also had a higher score in the communication warning behavior totle score (β = 4.553, 95% CI: −0.007, 9.112, $P = 0.05$).

Comparison of the Developmental Levels Between Regressive Group and Non-regressive Group

It can be seen from **Table 4** that the Revised Children Neuropsychological and Behavior Scale (CNBS-R2016) general quotient (GQ) and DQ of gross motor, fine motor, adaptive behavior, language, and personal-social in the regression group are all lower than the non-regression group. The difference in language was statistically significant between the two groups (β = −5.827, 95% CI: −11.529, −0.125, $P < 0.05$).

DISCUSSION

Although previous studies have gradually paid attention to the regressive ASD, there is still a lack of large sample investigations on its rates and onset of regression, regression subtypes, and disease severity in China. Therefore, this study conducted the first nationwide multi-center study to further describe the onset pattern of regressive ASD and its relationship with the severity of the disease. Our research results showed that although the prevalence rates for regressive ASD was not very high, it was more serious than non-regressive ASD.

Findings from the meta-analysis indicated that regression prevalence varies with different regression classification methods and sampling methods (14). Recent reviews in retrospective studies reported the rate of regression ranging from 10 to 50% (15–17), and overall prevalence rate for regression was 30% (8). However, in some prospective studies, the detection rate of retrogression was as high as 80% (18, 19). Ozonoff et al. analyzed the reason why the results of the two research methods are so different may be that prospective studies can observe earlier and more subtle regressive behaviors (5). Moreover, there were also some prospective studies conducted in high-risk siblings with a family history of ASD, so the incidence of regression was higher (14, 20).

Our research results suggested that the incidence of regression was 13.44%, which was lower than the domestic retrospective research result (32.97%) of Wu et al. (21). The reason may be that our study only included children whose parents had detailed descriptions of specific regression behaviors, and quantified and standardized the language skills of the children before regression; all ASD children who reported language regression before the age of 18 months were excluded, which is more stringent than some studies that use 15 months as the occurring time

TABLE 3 | Differences in autism symptoms in ASD children with and without regression.

Item	R (*n* = 138)	NR (*n* = 889)	β (95%CI)	*P*
ABC (*n*1 = 134, *n*2 = 847)				
Sensory	9.00(4.00–12.00)	7.00(3.00–11.00)	1.104(0.120, 2.089)	**0.028**
Relating	16.50(9.00–20.00)	13.00(7.00–18.00)	1.381(−0.114, 2.875)	0.070
Stereotypic behavior	9.50(4.00–14.00)	6.50(2.00–12.00)	1.388(0.038, 2.737)	**0.044**
Language	12.50(5.75–19.00)	11.00(5.75–16.00)	0.916(−0.381, 2.214)	0.166
Social self-help	12.00(9.00–16.00)	11.00(7.00–15.00)	0.807(−0.175, 1.790)	0.107
ABC total score	60.00(39.755–71.25)	48.00(36.00–63.25)	5.122(0.818, 9.426)	**0.020**
SRS (*n*1 = 117, *n*2 = 759)				
Social awareness	12.50(9.75–14.25)	12.00(9.00–13.00)	0.289(−0.357, 0.934)	0.381
Social cognition	19.00(16.00–22.00)	18.00(15.00–21.00)	0.784(−0.103, 1.670)	0.083
Social communication	32.50(28.75–42.25)	32.00(26.00–38.00)	1.712(−0.053, 3.477)	0.057
Social motivation	16.50(11.75–20.00)	15.00(12.00–18.00)	0.922(−0.057, 1.902)	0.065
Autistic mannerisms	16.00(10.00–19.25)	12.00(9.00–17.00)	1.297(0.140, 2.453)	**0.028**
SRS total score	97.76 ± 24.81	88.86 ± 22.16	4.991(0.494, 9.487)	**0.030**
CARS (*n*1 = 120, *n*2 = 739)				
CARS total score	32.50(30.00–38.00)	33.00(28.00–38.00)	−0.001(−1.317, 1.314)	0.998
Communication warning behavior total score (*n*1 = 94, *n*2 = 624)	44.00(30.00–62.50)	40.50(25.00–58.00)	4.553(−0.007, 9.112)	0.050

Multivariate linear regression was used for adjusted model (adjusting for age and gender); β (95%CI), regression coefficient (95% confidence interval); n1, the sample of regressive group; n2, the sample of non-regressive group. ABC, Autism Behavior Checklist; SRS, The Social Responsiveness Scale; CARS, Child Autism Rating Scale.

TABLE 4 | Differences in developmental quotient in ASD children with and without regression.

Item	R (*n* = 138)	NR (*n* = 889)	B (95%CI)	*P*
CNBS-R2016 (*n*1 = 95, *n*2 = 630)				
Gross motor	73.50(63.75–85.25)	78.00(65.00–89.00)	−2.574(−7.086, 1.938)	0.263
Fine motor	57.00(48.00–66.00)	58.00(47.00–70.00)	−3.708(−7.888, 0.472)	0.082
Adaptive behavior	59.50(45.75–70.25)	62.00(49.00–75.00)	−3.450(−8.141, 1.241)	0.149
Language	44.50(29.75–62.00)	46.00(33.00–67.00)	−5.827(−11.529, −0.125)	**0.045**
Personal society	51.00(40.50–61.00)	52.00(43.00–64.00)	−4.232(−8.728, 0.264)	0.065
GQ	59.50(47.00–66.00)	59.00(50.90–70.25)	−3.965(−8.051, 0.084)	0.055

Multivariate linear regression was used for adjusted model (adjusting for age and gender); β (95%CI), regression coefficient (95% confidence interval); n1, the sample of regressive group; n2, the sample of non-regressive group. CNBS-R2016,Children Neuropsychological and Behavioral Scale-Revision 2016.

for language regression (22). According to the definition of language development milestones, generally speaking, "language descriptions" appear in babies at the age of 6–12 months, which is unconscious pronunciation, and there is no clear direction. While the general age of children who have acquired at least 5 different words is 1.5–2 years old. Because parents can easily confuse the above criteria, language regression does not include children whose regression occurring before 1.5 years in this study. In addition, like some other studies (22, 23), our research only focused on the regressions in three aspects: language, social, and motor, and did not include more aspects such as imagination, gestures, fine motor, and adaptability, thus causing a lower regression prevalence.

Regarding the age of onset of regression, Tan et al. reviewed other studies and concluded that the average occurring age was 1.65 years or 19.80 months (8). In this study, parents reported that the average age of retrogression onset was 24.00 months. A large number of retrospective studies are in the form of parents' reports. Due to recall bias, the age of regression onset reported by parents of older children may be later than the actual age (5, 19). Therefore, more large-scale prospective studies are needed to investigate the regression.

Many studies have focused on the severity of symptoms in children with regressive ASD, but the conclusions are not consistent. Most studies suggested that the core symptoms of ASD in regression children were more severe than the non-regression children (24–26). However, some studies suggested that there was no significant difference in clinical symptoms and disease severity between children with and without regressive ASD (23, 27). The inconsistency of research results may be due to the small sample size and the small age of the included children. The potentially destructive effects of regressive ASD may not be obvious in younger children, and this effect becomes more significant when the children are older and the test scores become more stable.

In our study, the scores of ABC and SRS of the regression group were significantly higher than the non-regression group, indicating that the regression group's disease was more severe. In addition, we also found that the CNBS DQ scores in the regression group were lower than the non-regression group and the proportion of intellectual developmental impairment is also higher in the regression group, suggesting the regression group ASD children have lower neurodevelopmental levels. Which is consistent with the results of Bradley et al. (28).

Recently, a small-sample prospective study conducted by Martin et al. also found that the regression group and the non-regression group showed different clinical manifestations and prognosis in terms of the severity of autism symptoms and neurodevelopment (29). The regression group in the initial investigation showed more severe ASD symptoms and lower overall developmental levels. After 24 months of follow-up, the differences in overall developmental levels between the two groups persisted. Therefore, it is recommended to use developmental regression as a danger warning signal. Once discovering developmental regression, there is no need to wait for a clear diagnosis, and early intervention should be started immediately. In the future, we should also conduct further research on the pathophysiology and genetic mechanism of the causes of more severe disease and more serious clinical manifestations of regressive autism.

The results of this multi-center study are representative of the developmental regression of children with ASD in our country, and may provide a reference for clinicians and parents. But at the same time, this study also has certain limitations: (1) Because this research is a retrospective study, there is a certain recall bias, and there may be some deviations in the occur age of regression and whether the regression behavior occurred. (2) This study adopted the form of questionnaire survey, which has certain requirements for the comprehension and cognition level of the person who completes the questionnaire, so there may be a certain amount of information bias.

CONCLUSION

This multi-center study found that the prevalence of regressive ASD was low, and regressive skills were mainly manifested in language and social. However, due to its more severe clinical symptoms and worse prognosis, both medical staff and parents should actively monitor the development levels of children, so as to identify regression in time, and conduct early intervention training. Next, we will carry out a large-sample prospective cohort study to further explore the more subtle development trajectory of children with ASD, and provide data support for in-depth understanding of the disease pattern of ASD.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Children's Hospital of Chongqing Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

CH and FY completed the statistical analyses, drafted the initial manuscript, and reviewed and revised the manuscript. TY, JieC, YD, FJ, LW, YH, LL, JZ, XK, MY, QH, JinC, SF, YW, QW, and CJ contributed to the conceptualization and design of the study and supervised the data collection. TL and LC conceptualized and designed the study and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

FUNDING

The present study was supported by the National Natural Science Foundation of China (Nos. 81771223 and 81770526) from TL and JieC, the Guangzhou Key Project in Early diagnosis and treatment of autism spectrum disorders (202007030002), the Guangdong Key Project in Development of new tools for diagnosis and treatment of Autism (2018B030335001) from TL, and the Youth Innovation Team of Future Medical Support Plan of Chongqing Medical University (No. W0037) from LC.

REFERENCES

1. Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J. Autism spectrum disorder. *Lancet.* (2018) 392:508–20. doi: 10.1016/S0140-6736(18)31129-2
2. Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z, et al. Prevalence of autism spectrum disorder among children aged 8 years–autism and developmental disabilities monitoring network, 11 sites, United States, 2014. *MMWR Surveill Summ.* (2018) 67:1–23. doi: 10.15585/mmwr.ss6706a1
3. Maenner MJ, Shaw KA, Bakian AV, Bilder DA, Durkin MS, Esler A, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years–autism and developmental disabilities monitoring network, 11 sites, United States, 2018. *MMWR Surveill Summ.* (2021) 70:1–16. doi: 10.15585/mmwr.ss7011a1
4. Zhou H, Xu X, Yan W, Zou X, Wu L, Luo X, et al. Prevalence of autism spectrum disorder in China: a nationwide multi-center population-based study among children aged 6 to 12 years. *Neurosci Bull.* (2020) 36:961–71. doi: 10.1007/s12264-020-00530-6
5. Ozonoff S, Iosif AM. Changing conceptualizations of regression: what prospective studies reveal about the onset of autism spectrum disorder. *Neurosci Biobehav Rev.* (2019) 100:296–304. doi: 10.1016/j.neubiorev.2019.03.012
6. Zwaigenbaum L. Perspectives on regressive onset in autism: looking forward on looking back. *Neurosci Biobehav Rev.* (2019) 103:399–400. doi: 10.1016/j.neubiorev.2019.06.025
7. Gadow KD, Perlman G, Weber RJ. Parent-reported developmental regression in autism: epilepsy, IQ, schizophrenia spectrum symptoms, and special education. *J Autism Dev Disord.* (2017) 47:918–26. doi: 10.1007/s10803-016-3004-1

8. Tan C, Frewer V, Cox G, Williams K, Ure A. Prevalence and age of onset of regression in children with autism spectrum disorder: a systematic review and meta-analytical update. *Autism Res.* (2021) 14:582–98. doi: 10.1002/aur.2463
9. First MB. Diagnostic and statistical manual of mental disorders, 5th edition, and clinical utility. *J Nerv Ment Dis.* (2013) 201:727–9. doi: 10.1097/NMD.0b013e3182a2168a
10. Rellini E, Tortolani D, Trillo S, Carbone S, Montecchi F. Childhood autism rating scale (CARS) and autism behavior checklist (ABC) correspondence and conflicts with DSM-IV criteria in diagnosis of autism. *J Autism Dev Disord.* (2004) 34:703–8. doi: 10.1007/s10803-004-5290-2
11. Cen CQ, Liang YY, Chen QR, Chen KY, Deng HZ, Chen BY, et al. Investigating the validation of the Chinese Mandarin version of the social responsiveness scale in a Mainland China child population. *BMC Psychiatry.* (2017) 17:51. doi: 10.1186/s12888-016-1185-y
12. Schopler E, Reichler RJ, DeVellis RF, Daly K. Toward objective classification of childhood autism: childhood autism rating scale (CARS). *J Autism Dev Disord.* (1980) 10:91–103. doi: 10.1007/BF02408436
13. Li HH, Feng JY, Wang B, Zhang Y, Wang CX, Jia FY. Comparison of the children neuropsychological and behavior scale and the griffiths mental development scales when assessing the development of children with autism. *Psychol. Res. Behav. Manag.* (2019) 12:973–81. doi: 10.2147/PRBM.S225904
14. Ozonoff S, Gangi D, Hanzel EP, Hill A, Hill MM, Miller M, et al. Onset patterns in autism: variation across informants, methods, and timing. *Autism Res.* (2018) 11:788–97. doi: 10.1002/aur.1943
15. Stefanatos GA. Regression in autistic spectrum disorders. *Neuropsychol Rev.* (2008) 18:305–19. doi: 10.1007/s11065-008-9073-y
16. Barger BD, Campbell JM, McDonough JD. Prevalence and onset of regression within autism spectrum disorders: a meta-analytic review. *J Autism Dev Disord.* (2013) 43:817–28. doi: 10.1007/s10803-012-1621-x
17. Thurm A, Manwaring SS, Luckenbaugh DA, Lord C, Swedo SE. Patterns of skill attainment and loss in young children with autism. *Dev Psychopathol.* (2014) 26:203–14. doi: 10.1017/S0954579413000874
18. Brignell A, Williams K, Prior M, Donath S, Reilly S, Bavin EL, et al. Parent-reported patterns of loss and gain in communication in 1- to 2-year-old children are not unique to autism spectrum disorder. *Autism.* (2017) 21:344–56. doi: 10.1177/1362361316644729
19. Ozonoff S, Iosif AM, Baguio F, Cook IC, Hill MM, Hutman T, et al. A prospective study of the emergence of early behavioral signs of autism. *J Am Acad Child Adolesc Psychiatry.* (2010) 49:256–66.e1-2.
20. Jones EJ, Gliga T, Bedford R, Charman T, Johnson MH. Developmental pathways to autism: a review of prospective studies of infants at risk. *Neurosci Biobehav Rev.* (2014) 39:1–33. doi: 10.1016/j.neubiorev.2013.12.001
21. Wu QR, Fang H, Li Y, Feng M, Xiao T, Xiao X, et al. Clinical characteristics analysis of autistic disorder children with regression. *J Clin Psychiatry.* (2017) 27:78–80.
22. Thompson L, Gillberg C, Landberg S, Kantzer AK, Miniscalco C, Barnevik Olsson M, et al. Autism with and without regression: a two-year prospective longitudinal study in two population-derived Swedish cohorts. *J Autism Dev Disord.* (2019) 49:2281–90. doi: 10.1007/s10803-018-03871-4
23. Jones LA, Campbell JM. Clinical characteristics associated with language regression for children with autism spectrum disorders. *J Autism Dev Disord.* (2010) 40:54–62. doi: 10.1007/s10803-009-0823-3
24. Zachor DA, Ben-Itzchak E. Specific medical conditions are associated with unique behavioral profiles in autism spectrum disorders. *Front Neurosci.* (2016) 10:410. doi: 10.3389/fnins.2016.00410
25. Kalb LG, Law JK, Landa R, Law PA. Onset patterns prior to 36 months in autism spectrum disorders. *J Autism Dev Disord.* (2010) 40:1389–402. doi: 10.1007/s10803-010-0998-7
26. Wiggins LD, Rice CE, Baio J. Developmental regression in children with an autism spectrum disorder identified by a population-based surveillance system. *Autism.* (2009) 13:357–74. doi: 10.1177/1362361309105662
27. Shumway S, Thurm A, Swedo SE, Deprey L, Barnett LA, Amaral DG, et al. Brief report: symptom onset patterns and functional outcomes in young children with autism spectrum disorders. *J Autism Dev Disord.* (2011) 41:1727–32. doi: 10.1007/s10803-011-1203-3
28. Bradley CC, Boan AD, Cohen AP, Charles JM, Carpenter LA. Reported history of developmental regression and restricted, repetitive behaviors in children with autism spectrum disorders. *J. Dev. Behav. Pediatr.* (2016) 37:451–6. doi: 10.1097/DBP.0000000000000316
29. Martin-Borreguero P, Gómez-Fernández AR, De La Torre-Aguilar MJ, Gil-Campos M, Flores-Rojas K, Perez-Navero JL. Children with autism spectrum disorder and neurodevelopmental regression present a severe pattern after a follow-up at 24 months. *Front Psychiatry.* (2021) 12:644324. doi: 10.3389/fpsyt.2021.644324

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Psychiatry

ORIGINAL RESEARCH
published: 30 March 2022
doi: 10.3389/fpsyt.2022.844098

Patterns of Care for Adolescent With Schizophrenia: A Delphi-Based Consensus Study

Antonio Vita[1], Stefano Barlati[1], Antonello Bellomo[2], Paolo Fusar Poli[3], Gabriele Masi[4], Lino Nobili[5], Gianluca Serafini[6], Alessandro Zuddas[7] and Stefano Vicari[8,9]*

[1] Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, [2] Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [3] Department of Nervous System and Behavior Sciences, University of Pavia, Pavia, Italy, [4] Stella Maris, Scientific Institute of Child Neurology and Psychiatry, Pisa, Italy, [5] Child Neuropsychiatry, Genoa and Department of Neuroscience (DINOGMI), IRCCS G. Gaslini Institute, University of Genoa, Genoa, Italy, [6] Department of Neuroscience, University of Genoa, Genoa, Italy, [7] Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy, [8] Department of Life Sciences and Publich Health, Catholic University and Bambino Gesù, Rome, Italy, [9] Children's Hospital, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Rome, Italy

Background: The current conceptualization of schizophrenia as neurodevelopmental disorder should lead to innovative public health policies in terms of a reorganization of the mental health care systems, particularly in the transition from adolescence to adulthood, to reduce personal, familiar, and social costs and burdens. The purpose of the project was to perform a survey among a panel of Italian schizophrenia experts, to share evidence-based information on adolescent schizophrenia and explore the degree of consensus among professionals in the following four macro-areas: early diagnosis; pharmacological treatment; health care system organization and transition process from adolescent to adulthood; and psychosocial interventions.

Methods: The consensus process consisted of a two-step web-based Delphi method, which took place between June and November 2021. The survey was developed by a panel of four psychiatrists and four child neuropsychiatrists, identified as key opinion leaders (KOLs). The KOLs identified 21 statements involving a total of 70 items with a major need of clarification on early-onset schizophrenia (EOS). The survey was distributed to 86 specialists in psychiatry and child neuropsychiatry.

Results: The results revealed a large agreement among the expert group on all the investigated areas of adolescent schizophrenia patterns of care and management. Consensus was ultimately reached for 67 items of the Delphi survey (95.7%), while negative consensus was reached for 2 items and no consensus was reached for 1 item.

Conclusions: Overall, results showed a significant gap between the acquired scientific knowledge and clinical practice. In this scenario, it should be necessary to plan specific initiatives at a multiple level, to edit recommendations on clinical decision-making, as well as to prompt changes at the political and organizational levels, also involving scientific societies, patients, and family associations, to overcome the barriers that delay the implementation process.

Keywords: adolescent schizophrenia, Delphi method, early diagnosis, expert consensus, pattern of care, treatment gaps

OPEN ACCESS

Edited by:
Veit Roessner,
University Hospital Carl Gustav Carus,
Dresden, Germany

Reviewed by:
Paola Rocca,
University of Turin, Italy
Filip Rybakowski,
Poznan University of Medical
Sciences, Poland

****Correspondence:***
Stefano Barlati
stefano.barlati@unibs.it

Specialty section:
This article was submitted to
Child and Adolescent Psychiatry,
a section of the journal
Frontiers in Psychiatry

***Received:** 27 December 2021*
***Accepted:** 08 March 2022*
***Published:** 30 March 2022*

Citation:
Vita A, Barlati S, Bellomo A, Poli PF, Masi G, Nobili L, Serafini G, Zuddas A and Vicari S (2022) Patterns of Care for Adolescent With Schizophrenia: A Delphi-Based Consensus Study. Front. Psychiatry 13:844098. doi: 10.3389/fpsyt.2022.844098

INTRODUCTION

Schizophrenia is a highly prevalent, severe mental illness, representing one of the main causes of years lost due to disability (YLD) in adults in Europe (1). Schizophrenia onset usually occurs in late adolescence or early adulthood, but it is frequently anticipated by a prodromal phase, in which cognitive impairment, negative symptoms and poor social functioning occur several years before the first episode of psychosis (2). Within the broader psychosis spectrum, childhood and adolescence schizophrenia are peculiar disorders (3). Particularly, in adolescent it is more often a severe and debilitating psychotic disorder with considerable impairments in psychosocial, educational, and occupational functioning with a heavy burden on health care services. Despite the relatively high (up to 5%) prevalence of psychotic symptoms in otherwise healthy children, childhood-onset schizophrenia (COS) is rare, so epidemiologic incidence data with diagnoses based on standardized clinical assessments are lacking. Since clinical, cognitive, genetic, and neuroimaging characteristics of early-onset schizophrenia (EOS) patients are, in part, outlined, current findings point toward continuity between the early and adult-onset schizophrenia, with the former possibly being a more severe variant of the latter (4), suggesting the needs to implement mental health systems to improve possible interventions, especially in the transition from youth to adult facilities. The purpose of the present paper is to provide an exhaustive evaluation of adolescent schizophrenia, covering epidemiologic, neurobiological, and clinical features, in order to identify feasible treatments plans, both pharmacological and psychosocial, reducing personal, familiar, and society burdens, and improving prognosis, psychosocial functioning, and quality of life (QoL). Moreover, the paper covers initial programs aimed to rethink mental health system in the transition from adolescence to adulthood. Specifically, a Delphi approach was used to share evidence-based information on adolescent schizophrenia and assess the degree of consensus among professionals in the following investigation areas: (i) early diagnosis; (ii) pharmacological treatment; (iii) health care system organization and transition process from adolescent to adulthood; and (iv) psychosocial interventions.

In the following section, we report a summary of the evidence provided by the scientific board, that lead to some brief and explicit statements on adolescent schizophrenia.

A General Overview: Adolescence as a Major Risk Phase for Psychopathology

Schizophrenia is currently described as a neurodevelopmental disorder due to the interaction of different genetic and environmental factors that act long before the beginning of pathophysiological processes (5). Although psychotic onset is generally in early adulthood, less common in adolescence and quite rare in childhood, about 11–18% of patients present with their first episode of psychosis before the age of 18 (6, 7). Hence if schizophrenia peak onset is generally between 15 and 25 years of age (8), incidence rates increase around 14 years of age (9), with ∼39% of male and 23% of female patients developing schizophrenia before 19 years of age (10). Schizophrenia before the age of 18 years is usually divided into two categories. Early onset schizophrenia (EOS) presents between the ages of 13 and 17 years, whereas very-early-onset schizophrenia (VEOS) presents at or before the age of 12 years. An early identification after the onset of psychotic symptoms is aimed at reducing possible adverse factors that determine poor psychosocial functioning and QoL in young patients (11–15). Among these factors, the duration of untreated psychosis (DUP), that is the time from the onset of psychotic symptoms to the commencement of adequate treatment, is one of the main issues (16). In this context, the early detection and treatment of help-seeking individuals and of those already in the earliest phases of a psychotic disorder is currently considered as the most promising strategy to improve treatment outcomes and long-term prognosis, and thus to reduce worst consequences of a full-blown psychotic disorder in youth populations (17).

Adolescent Schizophrenia: Nosographic Background and Clinical Dimensions

If among children, schizophrenia is definitively a rare neuropsychiatric disorder with incidence rates at around 0.04% based on the observations from the National Institutes of Mental Health (NIMH) cohort (18, 19), adolescent schizophrenia is a devastating disorder, probably underdiagnosed and undertreated, characterized by greater clinical severity and worse outcomes compared to the adult-onset disorder (20, 21). In this scenario, although several definitions are currently applied to describe children and adolescent patients with early onset schizophrenia with no apparent consensus (22), some definitions should be highlighted. Based on age at onset, VEOS emerges before 12 years, while EOS starts before 17 years (23). VEOS was found to have a prevalence rate of 1/10,000, while EOS at around 1–2/100 (18). Since these operational definitions might be overlapping, two more strictly classifications are provided: COS is defined with an age of onset at 12 years or younger, while adolescent-onset schizophrenia is defined as beginning between 13 and 17 years (24). According to the scientific literature and for better understanding of the text, we will consider the terms EOS as adolescent schizophrenia and VEOS as COS (3). Despite these attempts in identifying the different forms of early-onset psychosis, at a nosological level patients with adolescent schizophrenia (EOS) or with COS (VEOS) are diagnosed using the same criteria as for adult-onset schizophrenia (AOS), following the Diagnostic and Statistical Manual [DSM-5; (25)] or the International Classification of Diseases, 10th Revision (26). This categorical approach could lead to not recognizing the juvenile variants of schizophrenia, with serious consequences for young subjects. From this point of view, a dimensional approach, rather than a categorical one, could favor early recognition and intervention of adolescent schizophrenia and COS (20, 27). At a developmental level, adolescent schizophrenia has been associated with poor premorbid functioning and developmental delays in reaching crucial milestones (28). At a clinical level, adolescent schizophrenia, compared to adult-onset schizophrenia is more commonly characterized by an insidious onset (21, 24), with prevalent negative symptoms (20, 29). Summing up these data, a systematic review, involving 1.506 patients with child or adolescent psychosis, showed peculiar clinical features in these samples: auditory hallucinations (81.9%), delusions (77.5%; mainly persecutory), thought disorders (65.5%), bizarre or disorganized behavior (52.8%), and negative symptoms (flat or blunted affect) (52.3%). Moreover, high comorbid rates such as posttraumatic stress disorder (PTSD) (34.3%), attention-deficit/hyperactivity disorder (ADHD), disruptive behavior disorders (33.5%), and substance abuse/dependence (32.0%) were also reported (30). In addition, cognitive impairment is a common feature of adolescent schizophrenia (31, 32), which occurs at the time of illness onset and once established, appears to be stable over time, without continued deterioration (33, 34). Regarding illness progression and outcomes, adolescent schizophrenia shows worse prognosis, with a severe and chronic course, so that only a minority of patients is able to get symptomatic remission and functional recovery (21, 35, 36). Taking these observations together, a recent systematic review confirmed that predictors of worse clinical, cognitive, and functional outcomes in adolescent schizophrenia are represented by premorbid difficulties, symptom severity at baseline (especially of negative symptoms) and longer DUP (37). Among these factors, current literature highlighted the association between greater clinical severity, worse outcomes, and longer DUP (38), that for adolescent schizophrenia is 3 to 5 times longer than the DUP in AOS (30).

Adolescent Schizophrenia: Early Diagnosis

With these notions in mind, worldwide mental health policies are claimed to give priority to early intervention services for children and adolescents. Adolescent schizophrenia is grossly diagnosed with the same criteria of International Classification of Diseases (26) and Diagnostic and Statistical Manual [DSM-5; (25)], as used for adult patients. Thus, a good quality assessment should include a detailed history from all possible sources as well as a physical and mental state examination. In particular, psychotic symptoms dimensions, comorbid psychiatric and medical conditions such as developmental disorders (including speech and language difficulties), comorbid substance abuse, risk of harms/suicidality as well as psychosocial functioning, and socio-cultural milieu of the patient and family should be evaluated (17, 27, 39). Moreover, medical work-up is always needed with basic pediatric assessment (e.g., routine laboratory testing), neurological and cognitive examination, neuroimaging, and tests for specific medical syndromes (e.g., genetic, infectious, autoimmune, rheumatologic, metabolic, and toxicology screens) (39). However, clinicians should keep in mind that a definitive diagnosis of early-onset/adolescent schizophrenia requires time and repeated assessments since clinical presentations tend to change especially during the first few years of the psychotic disorder. Therefore, adolescent schizophrenia diagnosis should be made with caution and sensitivity as it is associated with significant negative psychosocial consequences, both for the patients and their caregivers (27, 39).

Adolescent Schizophrenia: Treatment Options and Patterns of Care

As in AOS, treatment decisions in the adolescent schizophrenia population should be drawn by consulting all figures involved in the care of these patients, particularly, their caregivers, taking into account familiar perspectives and dynamics (17, 21). Clinicians should provide an integrated approach, including pharmacological, psychological, psychosocial, rehabilitative, and family-oriented interventions to address all the needs of the patients and their families (24, 27, 39). Admission at acute inpatient facility is recommended when the adolescent exhibits suicidal projects or attempts, self-injurious behaviors, aggression, severe agitation, poor general psychical conditions or when the familiar milieu is unsupportive or even hostile (39).

Pharmacological Interventions

At pharmacological level, antipsychotic agents are considered as the first line of treatment in the youth population. The main goals of pharmacotherapy interventions are to menage acute psychotic states and prevent relapse, always minimizing possible adverse events (24). Particularly, second-generation agents (SGAs) are typically offered as the first choice in early-onset/adolescent schizophrenia (27, 40, 41). Drugs like risperidone, aripiprazole, quetiapine, paliperidone, and olanzapine have actually received Food and Drug Administration (FDA) approval for treating schizophrenia in adolescents 13 years and older (42) since reductions of psychotic symptoms severity were observed compared to placebo (40). To date, in Europe only three SGAs - oral aripiprazole, oral paliperidone and lurasidone - have received approval from the European Medicine Agency (EMA) for treating adolescents with schizophrenia. Specifically, oral aripiprazole and oral paliperidone are recommended for adolescents aged 15 year and older. Since its positive efficacy and safety in adolescents - aged 13–17 years - with acute schizophrenia, lurasidone has been recently approved by EMA for adolescent schizophrenia starting from 13 years of age. Lurasidone favorable efficacy and safety profile in adolescent schizophrenia patients aged 13–17 years has also been demonstrated in the long-term period, through a 2-year extension study of the former (43). A recent network meta-analysis, including 28 randomized controlled trials (RCTs) with 3.003 participants, confirmed these findings, showing that olanzapine, risperidone, lurasidone, aripiprazole, quetiapine, paliperidone, and asenapine were significantly better than placebo, while haloperidol, trifluperazine, loxapine, and ziprasidone were not (44). Moreover, clozapine was found to be significantly more effective than all other included antipsychotics (44). However, clozapine should be proposed as a second-line agent in child and adolescent samples especially in treating refractory conditions: this is due to potential adverse events of clozapine, including risk of agranulocytosis, seizures, and metabolic disturbances (19, 45). Clinicians should keep in mind a higher risk of extrapyramidal symptoms (EPS), akathisia, prolactin elevation, sedation, cardiovascular effects (QTc prolongation, orthostatic hypotension, tachycardia, and pericarditis) and metabolic effects such as weight gain, dyslipidemia, glucose intolerance were reported in adolescent

TABLE 1 | Characteristics of responders in the Delphi survey.

Characteristics of responders (*N* = 70)	Values*
Gender (female)	48.6%
Mean age (years)	51 ± 10.8
Role	
Hospital	67%
Territorial service	33%
Specialist with also academic role	21%
Italian region	
Northern Italy	51.4%
Central Italy	22.9%
Southern Italy	25.7%
Years of experience	
5–10	17%
11–20	33%
21–30	26%
>31	24%

**Values in table are presented as a percentage or as the mean ± standard deviation.*

population rather than in adults, with polypharmacotherapy contributing to an increased risk (41, 46, 47). Although existing data indicate similar efficacy between first generation antipsychotics (FGAs) and SGAs (48), SGAs were also found to improve QoL and social functioning in adolescent schizophrenia samples (44). In particular, quetiapine and lurasidone were significantly more efficacious than placebo at improving QoL (43), while no significant effects were observed for asenapine and aripiprazole (44). On the other hand, risperidone, aripiprazole and lurasidone showed significantly better improvements in social functioning compared to placebo (44). However, despite the established efficacy, antipsychotic discontinuation is a common phenomenon also in adolescent schizophrenia patients. A national survey found that approximately 75% of the sample discontinued SGAs within 18 months of initiating treatment (49) and the Treatment of Early Onset Schizophrenia Spectrum Disorders Study (TEOSS) found that only 12% of subjects completed the 12-months period of taking their medications (50). Several reasons should explain this issue, mostly including presenting adverse events due to prescribed drugs (47). Thus, to limit this problem, clinician should keep in mind that FGAs are not recommended over SGAs in adolescent patients with schizophrenia due to increased risks of EPS and akathisia (27). On the other hand, a recent open-label study highlighted that, in the long-term, lurasidone in adolescents (13–17 years) with schizophrenia was associated with minimal effects on body weight, lipids, glycemic, and prolactin indices (43), while metanalytic evidence confirmed a reduced discontinuation rates for lurasidone over other antipsychotic agents (51). Guidelines recommend to carefully consider tolerability profile in the selection of an antipsychotic with a specific patient (51), taking into account several factors including tolerability drugs profile, patient and family preference, drug cost and availability (41, 47, 52).

Psychosocial Interventions

Since pharmacological treatments showed limited efficacy on negative and cognitive symptoms, and functional recovery in these populations (21), there is a growing interest in non-pharmacological approaches such as psychosocial interventions, although few data is available to date in adolescent schizophrenia patients. Adjunctive psychosocial interventions should be provided in combination with medications to reduce morbidity burden and promote treatment adherence and alliance (21). Preliminary evidence is provided for cognitive remediation (CR) efficacy in the first episode or in early schizophrenia, despite more research is needed to confirm the efficacy and the effectiveness of CR in the early course of schizophrenia (53). Concerning psychotherapy, although cognitive behavioral therapy (CBT) is an established treatment in AOS sample, only one report is currently available targeting early-onset patients (54). Only preliminary evidence was obtained with psychoeducation interventions (24), showing lower rates of rehospitalization in a small sample of adolescents with early onset psychosis (55). More recently, a RCT assessed the efficacy of a comprehensive psychoeducation problem solving intervention group in 55 adolescents with early onset schizophrenia and their parents (56). In this perspective, family-oriented interventions are particularly relevant during the early phases of the disorder (57), and current meta-analytic evidence confirmed the efficacy of family support interventions to reduce relapse and rehospitalization rates in this population (58). In this way, family support interventions resulted in improved caregivers' psychological health and general wellbeing and in reduced burdens of care (58).

Health Care System Organization and Transition Process From Adolescent to Adulthood

In order to reduce personal, familiar, social costs and burdens, innovative public health policies are needed in terms of a practicable reorganization of the mental health care systems. A structural problem is that in most European countries, mental health care for children and adolescents with psychiatric problems is independent and operationally separated from that for adults (59). This type of organization, also reflecting differences in specific training programs for resident doctors, could lead to difficulties in the transition from adolescence to adulthood between mental health services, bringing the patients to receive less support in adult facilities and troubled changes in diagnosis and treatments (29). Thus, two alternative models of transition between child/adolescent and adult' services may be considered. The first model is based on the identification of a transitional team operating independently from youth and adult services: this model has been implemented in prevention and early intervention in psychosis programs, although the main weakness of this model is the introduction of additional splits within the system (29). Otherwise, the interlocking model requires the use of multidisciplinary care protocols interlocking child/adolescent and adults' services in which transition from these facilities is guaranteed by sharing all information and recommendations about several aspects of psychiatric pathways performed up to now (29). In Italy, the interlocking model was advised by the National Action Plan for Mental Health manifesto (60) providing recommendations in order to develop experimental projects aimed at prevention and early intervention. In particular, it was mostly recommended the creation of integrated and multidisciplinary teams, including both youth and adult mental health services, also involving families, educational facilities and environmental context. On the other hand, the ITAlian Partnership for Psychosis Prevention (ITAPP) project included five Clinical High Risk for Psychosis (CHR-P) academic centers across Italy, representing a promising template for transitional mental health services, aimed at early detection and intervention. In fact, serving both adolescents and young adults with multidisciplinary and integrated interventions, ITAPP project is aimed at developing specialized facilities that bridge the gap in the transitioning phase from youth to adulthood, thus ameliorating presenting symptoms, delaying, and preventing psychosis onset while reducing DUP (61).

Objective

The purpose of this study was to perform a Delphi survey among a panel of Italian schizophrenia experts, in order to obtain a qualified consensus in managing patients with adolescent schizophrenia. In particular, the aims were to identify the characteristics of adolescent patients with schizophrenia, to define the best pathways for the management of schizophrenia in adolescent patients, especially in the transition phase, to understand the available psychopharmacological and psychosocial treatments and their impact on the patients' QoL, to identify patients' and caregivers' needs, and to find actions to address stigma.

The Delphi approach was used to share evidence-based information on adolescent schizophrenia and assess the degree of consensus among professionals in the following four macro-areas: (i) early diagnosis; (ii) pharmacological treatment; (iii) health care system organization and transition process from adolescent to adulthood; and (iv) psychosocial interventions.

MATERIALS AND METHODS

The Delphi method is a structured technique aimed at obtaining by repeated rounds of questionnaires a consensus opinion from a panel of experts in areas wherein evidence is scarce and opinion is important (62, 63). In the present manuscript, the consensus process consisted of a two-step web-based Delphi method, which took place between June and November 2021. The survey was developed by a panel of eight physicians (four psychiatrists, four child neuropsychiatrists) identified as key opinion leaders (KOLs) in their respective fields in Italy. The KOLs met to fully analyse the published literature and discuss the unmet needs about early-onset and adolescent schizophrenia. The first step of question sourcing served to collect an initial pool of feedback on areas that the KOLs considered most critical based on their clinical practice. Comments were then analyzed and coded into themes, grouping subsets of related items of enquiry. The organization of themes and items into a coherent and meaningful set of statements for the Delphi questionnaire was further informed by a literature review on the management of EOS. The first draft of the Delphi questionnaire was submitted to the KOLs for critical appraisal and improvement of the draft to ensure that items were relevant to the research question, were clearly worded and did not overlap with previous items. The KOLs identified 21 statements involving a total of 66 items with a major need of clarification, focused on the following topics: (i) early diagnosis; (ii) pharmacological treatment; (iii) health care system organization and transition process from adolescent to adulthood; and (iv) psychosocial interventions. Once developed, the survey was distributed to 86 specialists in psychiatry and child neuropsychiatry via an online survey platform with anonymized results. Panelists were psychiatrists and child neuropsychiatrists selected by the scientific board, working in academic and non-academic settings with solid experience in the field of schizophrenia (at least 5 years of clinical experience). The size of the expert panel was determined by involving specialists from 15 Italian regions, in order to have a representative sample of the national territory and a homogeneous distribution. Panelists were invited to rate their level of agreement or disagreement on each statement using a 5-point Likert scale, scored from 1 to 5 (1, extremely disagree; 2, disagree; 3, agree; 4, mostly agree; and 5, extremely agree). Results were expressed as a percentage of respondents who scored each item as 1 or 2 (disagreement) or as 3, 4, or 5 (agreement). A cutoff of 66% of agreement/disagreement was chosen a priori to represent positive or negative consensus, respectively. No consensus was reached when $< 66\%$ of the answers fell in the same category (62, 63). In the first round of the Delphi survey, there were 70 respondents among the 86 invited panelists. For the statements and items on which consensus had not been achieved, panelists were asked to rate again in a second round their agreement/disagreement. The second round was completed by all the 70 panelists who responded to the first round. **Table 1**, in results section, shows demographic characteristics of responders. Descriptive statistics were performed to summarize the results.

RESULTS

The first round of the Delphi survey had a response rate of 81.4%, whereas 100% of panelists who responded to round 1 completed also round 2. The average age of the respondents was 51 years, 34 (48.6%) were females, 34 (48.6%) were specialists in psychiatry and 36 (51.4%) in child neuropsychiatry. **Table 1** summarizes the characteristics of responders in the Delphi survey, also including their role, years of clinical experience, and geographical distribution.

In round 1, consensus was reached for 64 of the 66 statements and items (96.7%), while no consensus was reached for two statements. The second round was performed on the two statements for which consensus had not been reached, after revising and clarifying the items. Specifically, one statement was split into two items, while the second one was edited into four clearer items, getting a final number of statements and items of 70. Overall, consensus was ultimately reached for 67

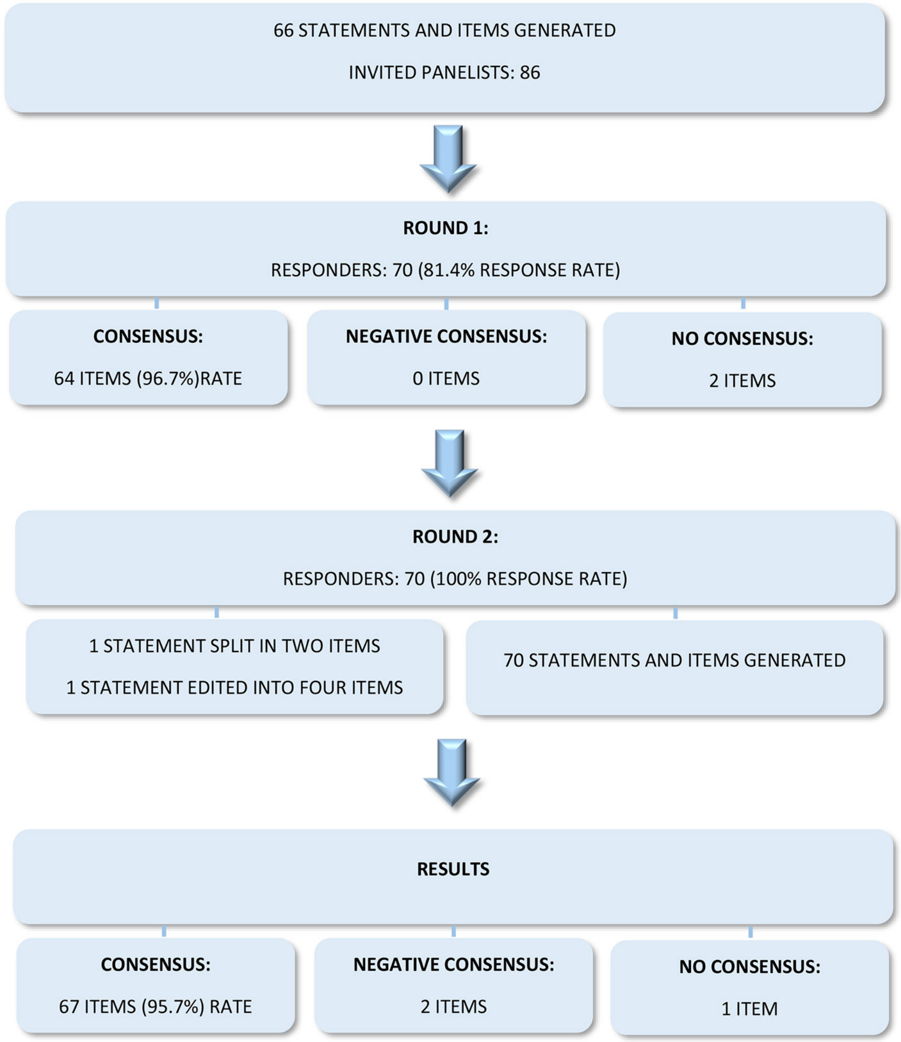


FIGURE 1 | Delphi survey flowchart.

items of the Delphi survey (95.7%), while negative consensus was reached for 2 items and no consensus was reached for 1 item (**Figure 1**).

Tables 2.1, **2.2** summarize all the statements and items of the consensus, indicating the percentages of agreement and disagreement, mean, median, mode and standard deviation for each of them.

Major statements, grouped in the four macro-areas, are reported below.

Early Diagnosis

This area includes eight statements and 19 items, concerning: the DUP, the importance of an early diagnosis and an early intervention, the diagnostic process, the use of assessment tools, and the challenges and the barriers for an early recognition. In the second round of the survey, one statement of this investigating area (statement - 7) was split in two items. More in detail, a high consensus was reached in the following items: reducing DUP, recognizing adolescents at risk of developing psychosis and in prodromal phase, investigating the presence of other neurodevelopment disorders and other comorbidity using standardized and validated assessment tools, and hospitalization (if necessary) only in structures specifically dedicated for this development stage. Furthermore, a broad consensus was obtained regarding the barriers and obstacles in recognition and in early identification of subjects with adolescent schizophrenia, such as the lack of human resources and trained operators, the scarcity of investments and specific dedicated programs and the adverse role of stigma. On the other hand, a negative consensus was expressed regarding the need of hospitalization in any patients with first-episode psychosis.

TABLE 2.1 | List of consensus statements and Delphi survey results.

Area of investigation	Statement/Item	Disagreement (score 1–2)	Agreement (Score 3–5)
EARLY DIAGNOSIS – The importance of an early diagnosis of schizophrenia in youth: instruments, procedures, challenges (stigma), role of psychiatrists and patients/caregivers	1 – One of the most important objectives is the reduction of DUP, that is the period between the onset of psychotic symptoms and the moment in which the patient is adequately taken charge of with suitable treatment.	1%	99%
	2 – Significant evidence exists of a relationship between a prolonged DUP and the worst outcome of schizophrenia.	1%	99%
	3 – The prolonged and untreated state of active psychosis can have a neurotoxic action in the SNC.	1%	99%
	4 – The principal barriers of an early identification of a patient with SCZ in youth are:		
	4.1 - Lack/deficiency of dedicated human resources	7%	93%
	4.2 – Lack/deficiency of dedicated investments	4%	96%
	4.3 – Absence/lack of specific programs	16%	84%
	4.4 – Lack of trained operators	13%	87%
	4.5 – Stigma	16%	84%
	5 - Early intervention in subjects at high risk of schizophrenia or with prodromal symptoms is able to prevent or delay progression toward an overt psychotic disorder and to improve prognosis of the disorder as a whole.	3%	97%
	6 – In the diagnostic procedure course of SCZ in youth, it is necessary to investigate the presence of:		
	6.1 – Genetic vulnerability (first degree relatives affected)	1%	99%
	6.2 – Autism spectrum disorder	0%	100%
	6.3 – Communication (language) disorders	13%	87%
	6.4 **-** Intellectual disability	7%	93%
	6.5 – Attention deficit disorders/hyperactivity (ADHD)	14%	86%
	6.6 – Mood disorders	7%	93%
	6.7 – Social anxiety disorder	6%	94%
	6.8 – Symptoms of social withdrawal	0%	100%
	7 - A psychotic onset always requires hospitalization in a child/adolescent psychiatric hospital	41% (lack of consensus)	59% (lack of consensus)
	Second round – revision: 7a **-** A psychotic onset always requires hospitalization	70% (no consensus)	30% (no consensus)
	Second round – revision: 7b **-** Hospitalization for a psychotic onset in adolescence (or under 18 years of age) should always be carried out in a specific hospital dedicated to this age range	4%	96%
	8 – In order to reach an effective early diagnosis of schizophrenia in youth a diagnostic assessment with reliable and validated measures is needed	6%	94%
PHARMACOLOGICAL TREATMENT – Pharmacological treatment of schizophrenia in adolescents: criteria for the choice of antipsychotic therapy (symptom control, tolerability, psychosocial functioning, quality of life)	9 – The choice of treatment with antipsychotic drugs in adolescence should take into consideration:		
	9.1 - the clinical characteristics of the patient	0%	100%
	9.2 – the phase of the disease	4%	96%
	9.3 – eventual use simultaneously with substances of abuse	0%	100%
	9.4 – the presence of medical comorbidities (e.g., metabolic disorders)	1%	99%
	9.5 – the side effects of the drugs	0%	100%
	10 - The off-label pharmacological treatment of schizophrenia in adolescents should be based on the scientific evidence published in international journals.	4%	96%

(Continued)

TABLE 2.1 | Continued

Area of investigation	Statement/Item	Disagreement (score 1–2)	Agreement (Score 3–5)
	11 - Second generation antipsychotic drugs should be the first choice of treatment in patients with SCZ with onset in adolescence or in young adults.	0%	100%
	12 - The management of youth with SCZ should always include:		
	12.1 – Pharmacological treatment	4%	96%
	12.2 – Cognitive behavioral therapy	6%	94%
	12.3 – Psychosocial interventions for the patient	0%	100%
	12.4 – Psychoeducational interventions for family/caregivers	0%	100%
	12.5 – The possibility of treatment options having a low threshold or proximity treatment	6%	94%
	12.6 – Therapeutic options shared with families	0%	100%
	12.7 – Close collaboration between hospital and community psychiatrists	1%	99%
	13 – In the management of an antipsychotic treatment for adolescents with schizophrenia, it is always important to consider that:		
	13.1 – clozapine has demonstrated greater efficacy in treatment resistant	0%	100%
	13.2 – the choice of antipsychotic treatment should be based on its efficacy on positive symptoms	14%	86%
	13.3 - the choice of antipsychotic treatment should be based on the profile of the side effects	4%	96%
	13.4 - the choice of antipsychotic treatment should be based on its efficacy in improving cognitive symptoms and/or the psychosocial functioning	0%	100%
	13.5 – the perception of the subjective wellbeing of the adolescent with schizophrenia is, for the most part, influenced by tolerability of the antipsychotics rather than by their specific activity on psychotic symptoms	13%	87%
	14 - Patients with an initial psychotic episode have a good response even to low doses of antipsychotic drugs and tend to develop more side effects to pharmacological therapy	29%	71%
	15 – In the long term, pharmacological management of adolescent patients with SCZ should include:		
	15.1 – Individual periodic evaluation of the risks and benefits of the pharmacological therapy	1%	99%
	15.2 – Continuous use of the antipsychotic drug in order to prevent relapse, hospitalization and deterioration of the cognitive or psychosocial functioning	14%	86%
	15.3 – Use of the antipsychotics associated with a long-term good tolerability decreases the risk of side effects (sedation, cardiac toxicity, metabolic effects, endocrines, tardive dyskinesia, etc.), with negative effect on the compliance	0%	100%
	15.4 – Decrease the antipsychotic dosage only if conditions of sufficient clinical stability are guaranteed	3%	97%
	15.5 – Discontinuation of the antipsychotic therapy only if conditions of sufficient clinical stability are guaranteed	41% (lack of consensus)	59% (lack of consensus)
	Second round – revision (15.5): 15 – Over the long term, pharmacological management of adolescent patients with SCZ should include:		
	15.5.1 - Discontinuation of the antipsychotic treatment if the conditions of clinical remission are guaranteed for at least one year	76% (no consensus)	24% (no consensus)
	15.5.2 - Discontinuation of the antipsychotic treatment if the conditions of functional remission are guaranteed for at least 1 year	64% (lack of consensus)	36% (lack of consensus)

(Continued)

TABLE 2.1 | Continued

Area of investigation	Statement/Item	Disagreement (score 1–2)	Agreement (Score 3–5)
	15.5.3 - Discontinuation of the antipsychotic treatment if the conditions of clinical remission are guaranteed for at least 2 years	29%	71%
	15.5.4 - Discontinuation of the antipsychotic treatment if the conditions of functional remission are guaranteed for at least 2 years	21%	79%
	15.6 – Continuous use of psychosocial treatment independently of the use of that drug	0%	100%
	15.7 – In the case of discontinuation of the pharmacological treatment therapy, continuous clinical monitoring should, however, be guaranteed	1%	99%
	15.8 – Discontinuation of pharmacological treatment after a period of between 1 and 2 years after symptomatic remission presents a greater risk of relapse and hospitalization, and this risk should be discussed with the patient and the family.	7%	93%
	16 – Switching to another antipsychotic in the treatment of adolescent patients affected by schizophrenia:		
	16.1 – it should be considered only in the case of scarce tolerability and/or reduced efficacy	10%	90%
	16.2 – The use of antipsychotics with a more favorable profile should always be taken into account	1%	99%
	16.3 – it should always be taken into account in patients with medical comorbidities	3%	97%
	16.4 – it should always be carefully evaluated in the case of increased self-injurious/suicidal risk	1%	99%
ORGANIZATION OF SERVICES/TRANSITION PROCESS – The organization of services for an optimal management of the patient in all phases of the disorder, with focus on the transition process in the adolescent schizophrenic patient: optimal procedures and areas of improvement in the collaboration between the services of child/adolescent and adult psychiatry	17 – A service dedicated to identifying and treating subjects at risk or those affected by an initial psychotic episode must:		
	17.1 – present characteristics of personalisation and specificity of the interventions	0%	100%
	17.2 – be able to offer suitable informative activities to the general practitioners to the regional health service operators and to the population	1%	99%
	18 – Taking in charge of "complex cases", in particular those medical comorbidities, must also include in the treatment team:		
	18.1 – Neuropsychiatry	4%	96%
	18.2 – Adult psychiatrist	9%	91%
	18.3 – Psychiatrist expert in substance abuse	13%	87%
	18.4 – Case manager recognized as the contact person in the course of cure and trade union during the transition process	0%	100%
	19 – In order to favor access to the mental health services of adolescent and young adult patients with schizophrenia, it would be necessary to:		
	19.1 – Promote the realization of specific protocols of collaboration in the field (between services of Child/Adolescent Psychiatry, mental health for adults and of Substance Abuse)	1%	99%
	19.2 – Promote the realization of specific protocols of collaboration between the services of mental health for adolescents, pediatricians and general practitioners	3%	97%
	19.3 – Promote a close relationship between the mental health services for adolescents and areas of youth aggregation (school, social services, associations, sports)	1%	99%

(Continued)

TABLE 2.1 | Continued

Area of investigation	Statement/Item	Disagreement (score 1–2)	Agreement (Score 3–5)
	19.4 – Ensure the continuity of the cure in the transition between the services of the Child/Adolescent psychiatry and the services of mental health for adults by means of multidisciplinary specialist teams	0%	100%
	19.5 – Favor the knowledge of mental health problems by means of "new" means of communication, such as Internet and social networks.	1%	99%
	19.6 – Guarantee the presence of services of the child/adolescent psychiatry in every region	0%	100%
	19.7 – Make material on SCZ available to the patient and their family/caregivers	4%	96%
PSYCHOSOCIAL INTERVENTIONS – Role of psychosocial interventions in support to pharmacological therapy in youth with schizophrenia	20 - For adolescents with schizophrenia, psychoeducation should always be directed to both the patients and their caregivers, and to their peers	0%	100%
	21 - Psychotherapeutic interventions, social skills training, cognitive rehabilitation and family interventions should be provided to all patients, but should not be considered alternatives to pharmacotherapy	0%	100%

DUP, Duration of Untreated Psychosis; SCZ, schizophrenia.

Pharmacological Treatment

This area includes eight statements and 32 items, concerning: the choice of antipsychotic treatment, FGAs and SGAs, the use of off-label drugs, the efficacy on positive, negative and cognitive symptoms, side effects, safety, the duration of treatment, the presence of comorbidities, a concomitant substance abuse, when considering a switch, clinical and functional outcome, patient wellbeing, and family involvement. In the second round of the survey, one statement of this investigating area (statement – 15; item 15.5) was edited into four items. In particular, a broad consensus was achieved in the following items: the importance of the choice of antipsychotic treatments on the basis of the clinical characteristics, such as the stage of the illness, the presence of medical comorbidities and eventual concomitant substance abuse, also taking into account side effects, safety, and the characteristics of the drug, such as the preference for SGAs, and the efficacy on positive, negative, and cognitive symptoms. Furthermore, a large consensus was also obtained regarding the need of a continuous pharmacological treatment, shared with the patient and the family, better if integrated with psychosocial interventions, considering not only the symptomatic, but also the functional remission and the subjective wellbeing. A broad agreement was additionally expressed concerning the off-label drugs utilization, the utility of clozapine in resistant patients, and when considering a switch to other antipsychotics. Concerning this last point, a high consensus was achieved regarding the need of a switch in cases of reduced clinical efficacy and poor tolerability, including metabolic side effects, the presence of medical comorbidities and a high suicidal risk. Instead, the experts displayed a lack of or a negative consensus about the opportunity to stop an antipsychotic therapy. More specifically, they seem to advise against a suspension of antipsychotics after 1 year of treatment, even if there is a clinical and/or functional remission, while they show some agreement on the possibility to stop antipsychotics after at least 2 years of treatment, only if there is a clinical and/or functional remission.

Health Care System Organization and Transition Process From Adolescent to Adulthood

This area includes three statements and 13 items, concerning: the characteristics of a mental health service for adolescents, the multidisciplinary team-working, the role of the case manager, how to facilitate access to mental health services, how to promote transition between child neuropsychiatry and adult psychiatry, and how to ensure continuity of care in the early phases of schizophrenia. The experts considered the need to implement a service dedicated to the early identification and early intervention, which would operate in close collaboration with the local services, including general practitioners and population. Furthermore, the management of complex patients should include a joint and integrated work between the services of child neuropsychiatry and adult psychiatry, also including the services for addiction and identifying a case manager. Finally, a broad consensus was also reached with respect to the characteristics required to facilitate the access to the mental health services for adolescents and young adults. More specifically, it would be necessary to implement some collaboration protocols between child neuropsychiatry services, adult mental health services, addiction services, pediatricians, and general practitioners, in order to ensure a continuity of care in the early phases of schizophrenia and to promote the process of transition between child neuropsychiatry and adult psychiatry. This process could be facilitated implementing specialized multidisciplinary

TABLE 2.2 | Mean, median, mode and standard deviation of the consensus statement.

	Strongly disagree	Disagree	Agree	More than agree	Strongly agree		Weighted mean	Standard deviation	Median	Mode	Weighted mean	Standard deviation	Median	Mode
	1	**2**	**3**	**4**	**5**									
Statement 1	0	1	1	10	58	70	0.7	0.7	0.5	#N/D	27.8	30.6	10.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 2	0	1	5	17	47	70	0.7	0.7	0.5	#N/D	26.5	21.6	17.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 3	0	1	8	30	31	70	0.7	0.7	0.5	#N/D	24.9	13.0	30.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 4.1	1	4	7	33	25	70	3.0	2.1	2.5	#N/D	23.2	13.3	25.0	#N/D
Tot disagree/agree	7.1%			92.9%		100.0%								
Statement 4.2	0	3	13	28	26	70	2.0	2.1	1.5	#N/D	23.4	8.1	26.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 4.3	0	11	10	30	19	70	7.3	7.8	5.5	#N/D	20.4	10.0	19.0	#N/D
Tot disagree/agree	15.7%			84.3%		100.0%								
Statement 4.4	0	9	15	26	20	70	6.0	6.4	4.5	#N/D	20.8	5.5	20.0	#N/D
Tot disagree/agree	12.9%			87.1%		100.0%								
Statement 4.5	2	9	20	22	17	70	6.7	4.9	5.5	#N/D	19.4	2.5	20.0	#N/D
Tot disagree/agree	15.7%			84.3%		100.0%								
Statement 5	0	2	5	27	36	70	1.3	1.4	1.0	#N/D	25.3	15.9	27.0	#N/D
Tot disagree/agree	2.9%			97.1%		100.0%								
Statement 6.1	0	1	9	17	43	70	0.7	0.7	0.5	#N/D	25.8	17.8	17.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 6.2	0	0	13	22	35	70	0.0	0.0	0.0	0.0	25.2	11.1	22.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 6.3	2	7	25	17	19	70	5.3	3.5	4.5	#N/D	19.8	4.2	19.0	#N/D
Tot disagree/agree	12.9%			87.1%		100.0%								
Statement 6.4	1	4	25	17	23	70	3.0	2.1	2.5	#N/D	21.5	4.2	23.0	#N/D
Tot disagree/agree	7.1%			92.9%		100.0%								
Statement 6.5	0	10	25	20	15	70	6.7	7.1	5.0	#N/D	19.2	5.0	20.0	#N/D
Tot disagree/agree	14.3%			85.7%		100.0%								
Statement 6.6	0	5	15	25	25	70	3.3	3.5	2.5	#N/D	22.5	5.8	25.0	25.0
Tot disagree/agree	7.1%			92.9%		100.0%								
Statement 6.7	0	4	15	25	26	70	2.7	2.8	2.0	#N/D	22.9	6.1	25.0	#N/D
Tot disagree/agree	5.7%			94.3%		100.0%								
Statement 6.8	0	0	7	22	41	70	0.0	0.0	0.0	0.0	26.2	17.0	22.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 7	5	24	23	6	12	70	17.7	13.4	14.5	#N/D	12.8	8.6	12.0	#N/D

(Continued)

TABLE 2.2 | Continued

	Strongly disagree 1	Disagree 2	Agree 3	More than agree 4	Strongly agree 5		Weighted mean	Standard deviation	Median	Mode	Weighted mean	Standard deviation	Median	Mode
Tot disagree/agree	41.4%			58.6%		100.0%								
Second round-revision Statement 7a	10	39	13	3	5	70	29.3	20.5	24.5	#N/D	6.3	5.3	5.0	#N/D
Tot disagree/agree	70.0%			30.0%		100.0%								
Second round-revision Statement 7b	0	3	8	19	40	70	2.0	2.1	1.5	#N/D	25.0	16.3	19.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 8	1	3	20	17	29	70	2.3	1.4	2.0	#N/D	22.8	6.2	20.0	#N/D
Tot disagree/agree	5.7%			94.3%		100.0%								
Statement 9.1	0	0	5	14	51	70	0.0	0.0	0.0	0.0	27.2	24.4	14.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 9.2	1	2	11	19	37	70	1.7	0.7	1.5	#N/D	24.5	13.3	19.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 9.3	0	0	11	19	40	70	0.0	0.0	0.0	0.0	25.8	15.0	19.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 9.4	0	1	6	15	48	70	0.7	0.7	0.5	#N/D	26.5	22.1	15.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 9.5	0	0	7	17	46	70	0.0	0.0	0.0	0.0	26.6	20.3	17.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 10	0	3	7	22	38	70	2.0	2.1	1.5	#N/D	24.9	15.5	22.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 11	0	0	10	18	42	70	0.0	0.0	0.0	0.0	26.0	16.7	18.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 8	1	3	20	17	29	70	2.3	1.4	2.0	#N/D	22.8	6.2	20.0	#N/D
Tot disagree/agree	5.7%			94.3%		100.0%								
Statement 9.1	0	0	5	14	51	70	0.0	0.0	0.0	0.0	27.2	24.4	14.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 9.2	1	2	11	19	37	70	1.7	0.7	1.5	#N/D	24.5	13.3	19.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 9.3	0	0	11	19	40	70	0.0	0.0	0.0	0.0	25.8	15.0	19.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 9.4	0	1	6	15	48	70	0.7	0.7	0.5	#N/D	26.5	22.1	15.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 9.5	0	0	7	17	46	70	0.0	0.0	0.0	0.0	26.6	20.3	17.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								

(Continued)

TABLE 2.2 | Continued

	Strongly disagree	Disagree	Agree	More than agree	Strongly agree		Weighted mean	Standard deviation	Median	Mode	Weighted mean	Standard deviation	Median	Mode
	1	2	3	4	5									
Statement 10	0	3	7	22	38	70	2.0	2.1	1.5	#N/D	24.9	15.5	22.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 11	0	0	10	18	42	70	0.0	0.0	0.0	0.0	26.0	16.7	18.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 12.1	0	3	11	19	37	70	2.0	2.1	1.5	#N/D	24.5	13.3	19.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 12.2	0	4	21	24	21	70	2.7	2.8	2.0	#N/D	22.0	1.7	21.0	21.0
Tot disagree/agree	5.7%			94.3%		100.0%								
Statement 12.3	0	0	5	13	52	70	0.0	0.0	0.0	0.0	27.3	25.1	13.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 12.4	0	0	1	18	51	70	0.0	0.0	0.0	0.0	27.5	25.4	18.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 12.5	0	4	19	23	24	70	2.7	2.8	2.0	#N/D	22.4	2.6	23.0	#N/D
Tot disagree/agree	5.7%			94.3%		100.0%								
Statement 12.6	0	0	7	20	43	70	0.0	0.0	0.0	0.0	26.3	18.2	20.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 12.7	0	1	2	16	51	70	0.7	0.7	0.5	#N/D	27.1	25.2	16.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 13.1	0	0	14	16	40	70	0.0	0.0	0.0	0.0	25.5	14.5	16.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 13.2	0	10	25	23	12	70	6.7	7.1	5.0	#N/D	18.9	7.0	23.0	#N/D
Tot disagree/agree	14.3%			85.7%		100.0%								
Statement 13.3	0	3	23	16	28	70	2.0	2.1	1.5	#N/D	22.8	6.0	23.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 13.4	0	0	7	32	31	70	0.0	0.0	0.0	0.0	25.3	14.2	31.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 13.5	1	8	21	21	19	70	5.7	4.9	4.5	#N/D	20.2	1.2	21.0	21.0
Tot disagree/agree	12.9%			87.1%		100.0%								
Statement 14	0	20	24	18	8	70	13.3	14.1	10.0	#N/D	15.3	8.1	18.0	#N/D
Tot disagree/agree	28.6%			71.4%		100.0%								
Statement 15.1	0	1	1	19	49	70	0.7	0.7	0.5	#N/D	27.0	24.2	19.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 15.2	0	10	19	24	17	70	6.7	7.1	5.0	#N/D	19.8	3.6	19.0	#N/D
Tot disagree/agree	14.3%			85.7%		100.0%								
Statement 15.3	0	0	3	20	47	70	0.0	0.0	0.0	0.0	27.0	22.2	20.0	#N/D

(Continued)

TABLE 2.2 | Continued

	Strongly disagree 1	Disagree 2	Agree 3	More than agree 4	Strongly agree 5		Weighted mean	Standard deviation	Median	Mode	Weighted mean	Standard deviation	Median	Mode
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 15.4	0	2	20	25	23	70	1.3	1.4	1.0	#N/D	22.9	2.5	23.0	#N/D
Tot disagree/agree	2.9%			97.1%		100.0%								
Statement 15.5	6	23	20	10	11	70	17.3	12.0	14.5	#N/D	12.9	5.5	11.0	#N/D
Tot disagree/agree	41.4%			58.6%		100.0%								
Second round - revision (15.5) Statement 15.5.1	6	47	11	6	0	70	33.3	29.0	26.5	#N/D	4.8	5.5	6.0	#N/D
Tot disagree/agree	75.7%			24.3%		100.0%								
Statement 15.5.2	6	39	15	8	2	70	28.0	23.3	22.5	#N/D	7.3	6.5	8.0	#N/D
Tot disagree/agree	64.3%	35.7%	100.0%											
Statement 15.5.3	2	18	28	14	8	70	12.7	11.3	10.0	#N/D	15.0	10.3	14.0	#N/D
Tot disagree/agree	28.6%	71.4%	100.0%											
Statement 15.5.4	3	12	30	9	16	70	9.0	6.4	7.5	#N/D	17.2	10.7	16.0	#N/D
Tot disagree/agree	21.4%	78.6%	100.0%											
Statement 15.6	0	0	8	25	37	70	0.0	0.0	0.0	0.0	25.8	14.6	25.0	#N/D
Tot disagree/agree	0.0%	100.0%	100.0%											
Statement 15.7	0	1	1	13	55	70	0.7	0.7	0.5	#N/D	27.5	28.4	13.0	#N/D
Tot disagree/agree	1.4%	98.6%	100.0%											
Statement 15.8	1	4	20	17	28	70	3.0	2.1	2.5	#N/D	22.3	5.7	20.0	#N/D
Tot disagree/agree	7.1%	92.9%	100.0%											
Statement 16.1	0	7	11	25	27	70	4.7	4.9	3.5	#N/D	22.3	8.7	25.0	#N/D
Tot disagree/agree	10.0%	90.0%	100.0%											
Statement 16.2	0	1	11	25	33	70	0.7	0.7	0.5	#N/D	24.8	11.1	25.0	#N/D
Tot disagree/agree	1.4%	98.6%	100.0%											
Statement 16.3	0	2	16	22	30	70	1.3	1.4	1.0	#N/D	23.8	7.0	22.0	#N/D
Tot disagree/agree	2.9%	97.1%	100.0%											
Statement 16.4	0	1	14	21	34	70	0.7	0.7	0.5	#N/D	24.7	10.1	21.0	#N/D
Tot disagree/agree	1.4%	98.6%	100.0%											
Statement 17.1	0	0	0	20	50	70	0.0	0.0	0.0	0.0	27.5	25.2	20.0	#N/D
Tot disagree/agree	0.0%	100.0%	100.0%											
Statement 17.2	0	1	4	21	44	70	0.7	0.7	0.5	#N/D	26.3	20.1	21.0	#N/D
Tot disagree/agree	1.4%	98.6%	100.0%											

(Continued)

TABLE 2.2 | Continued

	Strongly disagree	Disagree	Agree	More than agree	Strongly agree		Weighted mean	Standard deviation	Median	Mode	Weighted mean	Standard deviation	Median	Mode
	1	2	3	4	5									
Statement 18.1	0	3	5	13	49	70	2.0	2.1	1.5	#N/D	26.0	23.4	13.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 18.2	0	6	15	18	31	70	4.0	4.2	3.0	#N/D	22.7	8.5	18.0	#N/D
Tot disagree/agree	8.6%			91.4%		100.0%								
Statement 18.3	0	9	19	22	20	70	6.0	6.4	4.5	#N/D	20.4	1.5	20.0	#N/D
Tot disagree/agree	12.9%			87.1%		100.0%								
Statement 18.4	0	0	6	13	51	70	0.0	0.0	0.0	0.0	27.1	24.2	13.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 19.1	0	1	1	23	45	70	0.7	0.7	0.5	#N/D	26.7	22.0	23.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 19.2	0	2	4	22	42	70	1.3	1.4	1.0	#N/D	25.8	19.0	22.0	#N/D
Tot disagree/agree	2.9%			97.1%		100.0%								
Statement 19.3	0	1	9	25	35	70	0.7	0.7	0.5	#N/D	25.2	13.1	25.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 19.4	0	0	2	15	53	70	0.0	0.0	0.0	0.0	27.6	26.5	15.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 19.5	0	1	19	30	20	70	0.7	0.7	0.5	#N/D	23.1	6.1	20.0	#N/D
Tot disagree/agree	1.4%			98.6%		100.0%								
Statement 19.6	0	0	3	15	52	70	0.0	0.0	0.0	0.0	27.4	25.5	15.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 19.7	0	3	11	26	30	70	2.0	2.1	1.5	#N/D	23.9	10.0	26.0	#N/D
Tot disagree/agree	4.3%			95.7%		100.0%								
Statement 20	0	0	5	24	41	70	0.0	0.0	0.0	0.0	26.3	18.0	24.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								
Statement 21	0	0	8	18	44	70	0.0	0.0	0.0	0.0	26.3	18.6	18.0	#N/D
Tot disagree/agree	0.0%			100.0%		100.0%								

#N/D, dataset does not contain duplicate values.

cross teams to the different services. Full consensus was also demonstrated regards the need to ensure the presence of child neuropsychiatry services in every territory at a national level. Lastly, it emerged how important it is to give a particular attention to the correct dissemination of information to patients and family members, also through the new social media, as well as promoting a close relationship with the areas of youth aggregation.

Psychosocial Interventions

This area includes two statements, concerning: psychoeducational interventions for the patient and for the family, evidence-based rehabilitation interventions, and integrated treatments. This area of investigation also obtained a full consensus. In particular among rehabilitation interventions, those evidence-based, such as psychoeducation, social skills training, and cognitive rehabilitation, should be taken into account.

DISCUSSION

A two-step Delphi approach was used to share evidence-based information on early-onset/adolescent schizophrenia management, assessing the degree of consensus among specialists in psychiatry and child neuropsychiatry on the following key issues: (i) early diagnosis; (ii) pharmacological treatment; (iii) health care system organization as well as transition process from adolescent to adulthood; and (iv) psychosocial interventions. The results of the survey revealed a large consensus among the experts on all the investigated areas of adolescent schizophrenia patterns of care and management.

A high consensus was reached in the first area of investigation about early diagnosis and intervention and, particularly, the importance of the following variables: reducing DUP, recognizing adolescents at risk of developing psychosis and in prodromal phase, investigating the presence of other neurodevelopment disorders and other comorbidity using standardized and validated assessment tools, and hospitalization (if necessary) only in structures specifically dedicated for this development stage. Furthermore, a broad consensus was obtained regarding the barriers and obstacles in recognition and in early identification of subjects with adolescent schizophrenia, such as the lack of human resources and trained operators, the scarcity of investments and specific dedicated programs and the adverse role of stigma. These results show how psychiatrists and child neuropsychiatrists, in accordance with the scientific literature, and ministerial and regional recommendations, are completely aware of the importance of early recognition and intervention, even in subjects at risk of psychosis and in the prodromal phases (16, 17, 60). However, this approach is not always applied and is not feasible throughout the national territory, due to some barriers identified by the survey.

On the other hand, a negative consensus was expressed regarding the need of hospitalization in any patients with first-episode psychosis. This interesting result, in agreement with national and international literature (64, 65), could mean the necessity and the awareness of the experts to implement a community intervention, not based only on hospitalization.

The survey demonstrated a broad consensus in the second area of investigation that is the pharmacological treatment. In particular, it was outlined the importance of the choice of antipsychotic treatments on the basis of the clinical characteristics of the patient, such as the stage of the illness, the presence of medical comorbidities and eventual concomitant substance abuse. Side effects and the characteristics of the drug, such as the preference for SGAs, the efficacy on positive, negative and cognitive symptoms and the safety must be also considered. Furthermore, a large consensus was also obtained regarding the need of a continuous pharmacological treatment, shared with the patient and the family, better if integrated with psychosocial interventions, considering not only the symptomatic, but also the functional remission and the subjective wellbeing. A broad agreement was additionally expressed concerning the off-label drugs utilization (an option which could be considered, for example, for adolescent patients with demonstrated non-adherence to approved antipsychotics or in those with reduced clinical response or occurrence of adverse effects associated with approved antipsychotics), the utility of clozapine in resistant patients, and when considering a switch to other antipsychotics. In particular, for this last point, a high consensus was achieved regarding the need of a switch in cases of reduced clinical efficacy and poor tolerability, including metabolic side effects, the presence of medical comorbidities and a high suicidal risk. Regarding this area of investigation, results show that the choice of an antipsychotic therapy requires a careful and comprehensive patient assessment, giving attention not only to the symptomatic remission, but also to the functional remission and subjective wellbeing (35). In this regard, it is relevant to remind that the aim of schizophrenia treatment is not the remission of specific psychotic symptoms, but the improvement of functional outcomes and quality of life, always keeping in mind patient goals (66). Moreover, the risk/benefit ratio between effectiveness and side effects should be weighted for each patient (i.e., the long-term risk of metabolic side effects) (67). It should be emphasized how these results are in line with the international literature (15, 68–70). Instead, the experts displayed a lack of or a negative consensus about the opportunity to stop an antipsychotic therapy. More specifically, they seem to advise against a suspension of antipsychotics after 1 year of treatment, even if there is a clinical and/or functional remission, while they show some agreement on the possibility to stop antipsychotics after at least 2 years of treatment, only if there is a clinical and/or functional remission. It is interesting to note that this result is in any case consistent with the non-definitive and controversial international scientific literature on this still debated topic (71–74). The duration of maintenance treatment following a first-episode of schizophrenia is one of the most debated issue in the treatment of youth with schizophrenia, that has been addressed in a well-conducted systematic review performed by Keating et al. (72). In this regard, although good quality guidelines to assist in pharmacological treatment optimization exist, authors pointed out the inconsistencies between guidelines after the first-episode, underlining that the evidence base required to answer key health questions relevant to the pharmacological treatment of first-episode schizophrenia is still limited.

The third investigated area on the health care system organization and transition process from adolescent to adulthood reached high rates of consensus. In particular, the experts considered the need to implement a service, with specific characteristics, dedicated to the early identification and early intervention, which would operate in close collaboration with the local services, including general practitioners and population. Furthermore, the management of complex patients should include a joint and integrated work between the services of child neuropsychiatry and adult psychiatry, also including the services for addiction and identifying a case manager. Finally, a broad consensus was also reached with respect to the characteristics required to facilitate the access to the mental health services for adolescents and young adults. More specifically, it would be necessary to implement some collaboration protocols between child neuropsychiatry services, adult mental health services, addiction services, pediatricians, and general practitioners, in order to ensure a continuity of care in the early phases of schizophrenia and to promote the process of transition between child neuropsychiatry and adult psychiatry. This process could be facilitated implementing specialized multidisciplinary cross teams to the different services. Full consensus was also demonstrated regards the need to ensure the presence of child neuropsychiatry services in every territory at a national level. Lastly, it emerged how important it is to give a particular attention to the correct dissemination of information to patients and family members, also through the new social media, as well as promoting a close relationship with the areas of youth aggregation. Overall, in line with the existing scientific literature (75), this area of investigation about the organization of mental health services and on the transition process from adolescent to adulthood obtained a broad consensus among experts. Despite this agreement, the mental health services reality is not always the same expressed in the survey results and the dedicated services for early recognition and intervention, especially in the acute phases, are not uniformly spread throughout the national territory. Furthermore, these services, when existing, are not always well-integrated with each other, and do not work in multidisciplinary teams, therefore without promoting a stable patient health care path and a suitable transition between neuropsychiatry and adult psychiatry.

The fourth area of investigation obtained a full consensus on the use of integrated psychotherapeutic and psychosocial interventions. Among rehabilitation interventions, those evidence-based should be taken into account, in particular psychoeducation aimed at both patients and family members, social skills training, and cognitive rehabilitation. Again, the experts' panel was absolutely in agreement with the scientific literature (76–78). As in previous research fields taken into account in the present survey, such as the implementation of early recognition and identification services, evidence-based rehabilitation interventions and integrated treatments showed a significant gap between the acquired scientific knowledge and clinical practice. This means that, despite the growing scientific literature on these topics, a major concern is that evidence-based rehabilitation interventions and integrated treatments are not largely available in the real-world setting of mental health services (79).

Lastly, cost-effectiveness is an issue common to all the four investigated areas. In fact, both for early diagnosis, pharmacological and psychosocial treatments, as well as health care system organization, it is relevant to consider resources. In the real-world setting of adolescents and adults Mental Health Services, adequate resources for implementing the best clinical-therapeutic practices are not always available. In this scenario, even if psychotherapeutic and psychoeducational approaches may be helpful, but with very low evidence in youth (80), pharmacotherapy should always be the first option, even when other interventions are unavailable. However, it should also be highlighted that many psychosocial interventions, such as psychoeducation (81) and other integrated interventions (82), may be both clinically beneficial and cost-effectiveness in the early stages of the schizophrenia spectrum disorders.

Limitations

In this project some limitations are to be addressed. First, adherence to drug therapy and in particular the use of long-acting injectable (LAI) antipsychotics was not directly investigated. Second, the results may not be representative of the entire national territory and may not be generalizable to other Countries. Third, the survey involved only specialists in child neuropsychiatry and in adult psychiatry, but not pediatricians, general practitioners, other mental health workers, and patients and family association members, so it does not cover the views of all the stakeholders involved in this complex field.

CONCLUSION

To our knowledge, this is the first Delphi-based consensus survey on patterns of care in adolescent schizophrenia, involving experts and specialists in child neuropsychiatry and in adult psychiatry. The results of this consensus Delphi approach revealed a large agreement among the expert group of Italian specialists in child neuropsychiatry and in adult psychiatry on all the investigated areas of adolescent schizophrenia patterns of care and management. In particular, the level of agreement was maximum in the following crucial issues: early diagnosis; pharmacological treatment; health care system organization as well as transition process from adolescent to adulthood; and psychosocial interventions. Overall, results showed a significant gap between the acquired scientific knowledge and clinical practice. This means that, despite the growing scientific literature on early-onset/adolescent schizophrenia management, a major concern is that knowledge is not largely available in the real-world setting of mental health services. Of particular interest is that this science-to-service gap seems to be well-recognized by Italian specialists, who identify the lack of human resources and trained operators and the paucity of investments and specific dedicated programs as the main barriers that do not allow to fill the gap.

In this scenario, it should be necessary to program specific training events on adolescent/early onset schizophrenia and on the transition process, to draft and spread agreement protocols between child neuropsychiatry and adult psychiatry and to set up multidisciplinary teams transversal to services. Moreover, appear crucial to edit recommendations on clinical decision-making as well as to prompt changes at the political and organizational levels, also involving scientific societies, patients and family associations and all the stakeholders involved, in order to overcome the barriers that delay the implementation process.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The study was based on a survey that does not involve the participation of human subjects nor patient data management. Consequently, this study did not require ethical approval. All experts involved in the Delphi survey were informed of the study's objectives and the possibility of publishing the results in a peer-reviewed article. The participation was voluntary.

AUTHOR CONTRIBUTIONS

All authors contributed to the writing and editing of the manuscript. All authors approved the final version of the manuscript.

FUNDING

GM was supported by funds of the Italian Ministry of Health: Ricerca Corrente (Project 2.10, PI Gabriele Masi). The authors declare that this study received funding from Angelina Pharma. The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication.

ACKNOWLEDGMENTS

The authors would like to thank Ethos srl for logistic support in conducting the Delphi study.

External Validators

Paolo Cacciani, Brescia
Pietro De Rossi, Roma
Giacomo Deste, Brescia
Giovanni Valeri, Roma

Delphi Expert Panel Group:

Veronica Aiello, Genova
Mario Altamura, Bari
Anna Rita Atti, Bologna
Gianfranca Auricchio, Napoli
Roberto Averna, Roma
Elena Barletta, Genova
Luigi Basso, Bolzano
Stefano Berloffa, Pisa
Paola Bona, Savona
Albacenzina Borelli, Foggia
Stefania Borghetti, Milano
Carmela Bravaccio, Napoli
Pietro Calcagno, Genova
Angela Carofiglio, Bari
Alessandro Carozzi, Milano
Manuela Carpaneto, Alessandria
Alessandra Carta, Sassari
Sara Carucci, Cagliari
Chiara Caucci, Teramo
Nicolò Cipriani, Genova
Giulio Corrivetti, Salerno
Giulia D'Acunto, Pisa
Andrea De Giacomo, Bari
Elisa De Grandis, Genova
Gianluigi Di Cesare, Roma
Diana Di Pietro, Roma
Andrea Escelsior, Genova
Mauro Ferrara, Roma
Giuliana Gai, Genova
Roberto Gaggero, Genova
Gabriele Giacomini, Genova
Giuseppe Imperadore, Verona
Dario Lamonaca, Verona
Silvestro La Pia, Napoli
Riccardo Loparrino, Firenze
Liliana Lorettu, Sassari
Luciano Luccherino, Arezzo
Francesco Margari, Foggia
Chiara Margarita, Roma
Stefania Millepiedi, Viareggio
Maria Giulia Nanni, Ferrara
Silvia Paba, Cagliari
Sara Pacella, Genova
Giulia Piccinini, Genova
Sara Pignatelli, Genova
Maurizio Pincherle, Macerata
Tiziana Pisano, Firenze
Anna Polito, Foggia
Nicola Poloni, Varese
Matteo Porcellana, Milano
Andrea Presta, Genova
Pier Paolo Rizzo, Genova
Matteo Rocchetti, Pavia
Vincenzo Santospirito, Matera
Valeria Scandurra, Siena
Renato Scifo, Catania
Irene Serio, Savona
Michele Severini, Ancona
Laura Siri, Genova
Bruno Spinetoli, Roma

Luca Tarantola, Vercelli
Sarah Tosato, Verona
Marco Toscano, Milano
Sabrina Trudu, Cagliari
Fabiana Vercellino, Alessandria
Caterina Viganò, Milano
Benedetto Vitiello, Torino
Carmelo Zaffora, Messina
Elisabetta Zanotto, Genova
Spyridon Zotos, Ferrara

REFERENCES

1. Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jönsson B, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol.* (2011) 21:655–79. doi: 10.1016/j.euroneuro.2011.07.018
2. Lieberman JA, Perkins D, Belger A, Chakos M, Jarskog F, Boteva K, Gilmore J. The early stages of schizophrenia: speculations on pathogenesis, pathophysiology, therapeutic approaches. *Biol Psychiatry.* (2001) 50:884–97. doi: 10.1016/S0006-3223(01)01303-8
3. Clemmensen L, Vernal DL, Steinhausen HC. A systematic review of the long-term outcome of early onset schizophrenia. *BMC Psychiatry.* (2012) 12:150. doi: 10.1186/1471-244X-12-150
4. Kyriakopoulos M, Frangou S. Pathophysiology of early onset schizophrenia. *Int Rev. Psychiatry.* (2007) 19:315–24. doi: 10.1080/09540260701486258
5. Seidman LJ, Mirsky AF. Evolving notions of schizophrenia as a developmental neurocognitive disorder. *J Int Neuropsychol Soc.* (2017) 23:881–92. doi: 10.1017/S1355617717001114
6. Schimmelmann BG, Conus P, Cotton S, McGorry PD, Lambert M. Pre-treatment, baseline, and outcome differences between early-onset and adult-onset psychosis in an epidemiological cohort of 636 first-episode patients. *Schizophr Res.* (2007) 95:1–8. doi: 10.1016/j.schres.2007.06.004
7. Amminger GP, Henry LP, Harrigan SM, Harris MG, Alvarez-Jimenez M, Herrman H, et al. Outcome in early-onset schizophrenia revisited: findings from the early psychosis prevention and intervention centre long-term follow-up study. *Schizophr Res.* (2011) 131:112–9. doi: 10.1016/j.schres.2011.06.009
8. Sham PC, MacLean CJ, Kendler KS. A typological model of schizophrenia based on age at onset, sex and familial morbidity. *Acta Psychiatr Scand.* (1994) 89:135–41. doi: 10.1111/j.1600-0447.1994.tb01501.x
9. Dalsgaard S, Thorsteinsson E, Trabjerg BB, Schullehner J, Plana-Ripoll O, Brikell I, et al. Incidence rates and cumulative incidences of the full spectrum of diagnosed mental disorders in childhood and adolescence. *JAMA Psychiatry.* (2020) 77:155–64. doi: 10.1001/jamapsychiatry.2019.3523
10. Loranger AW. Sex difference in age at onset of schizophrenia. *Arch Gen Psychiatry.* (1984) 41:157–61. doi: 10.1001/archpsyc.1984.01790130053007
11. Cannon TD, Cadenhead K, Cornblatt B, Woods SW, Addington J, Walker E, et al. Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. *Arch Gen Psychiatry.* (2008) 65:28–37. doi: 10.1001/archgenpsychiatry.2007.3
12. Fusar-Poli P, Bonoldi I, Yung AR, Borgwardt S, Kempton MJ, Valmaggia L, et al. Predicting psychosis: meta-analysis of transition outcomes in individuals at high clinical risk. *Arch Gen Psychiatry.* (2012) 69:220–9. doi: 10.1001/archgenpsychiatry.2011.1472
13. Pontillo M, Tata MC, Averna R, Gargiullo P, Guerrera S, Vicari S. Clinical profile, conversion rate, and suicidal thinking and behaviour in children and adolescents at ultra-high risk for psychosis: a theoretical perspective. *Res Psychother.* (2020) 23:455. doi: 10.4081/ripppo.2020.455
14. Pontillo M, Averna R, Tata MC, Chieppa F, Pucciarini ML, Vicari S. Neurodevelopmental trajectories and clinical profiles in a sample of children and adolescents with early- and very-early-onset schizophrenia. *Front Psychiatry.* (2021) 12:662093. doi: 10.3389/fpsyt.2021.662093
15. Maj M, van Os J, De Hert M, Gaebel W, Galderisi S, Green MF, et al. The clinical characterization of the patient with primary psychosis aimed at personalization of management. *World Psychiatry.* (2021) 20:4–33. doi: 10.1002/wps.20809
16. Penttil,ä M, Jääskeläinen E, Hirvonen N, Isohanni M, Miettunen J. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry.* (2014) 205:88–94. doi: 10.1192/bjp.bp.113.127753
17. National Institute for Health and Clinical Excellence (NICE): Guidance. *Psychosis and Schizophrenia in Children and Young People: Recognition and Management. National Collaborating Centre for Mental Health (UK).* Leicester: British Psychological Society (2013). Available online at: https://www.nice.org.uk/guidance/cg155 (accessed March 8, 2022).
18. Driver DI, Gogtay N, Rapoport JL. Childhood onset schizophrenia and early onset schizophrenia spectrum disorders. *Child Adolesc Psychiatr Clin N Am.* (2013) 22:539–55. doi: 10.1016/j.chc.2013.04.001
19. Driver DI, Thomas S, Gogtay N, Rapoport JL. Childhood-onset schizophrenia and early-onset schizophrenia spectrum disorders: an update. *Child Adolesc Psychiatr Clin N Am.* (2020) 29:71–90. doi: 10.1016/j.chc.2019.08.017
20. Hollis C. Adolescent schizophrenia. *Adv Psychiatr Treat.* (2000) 6:83–92. doi: 10.1192/apt.6.2.83
21. Hollis C, Birchwood M, Garralda E, James A, McDougall T, Morrison A. *Psychosis and Schizophrenia in Children and Young People: Evidence Update March 2015: A Summary of Selected New Evidence Relevant to NICE Clinical Guideline 155 'Psychosis and Schizophrenia in Children and Young People: Recognition and Management'.* London: National Institute for Health and Care Excellence. Available online at: https://www.ncbi.nlm.nih.gov/books/NBK552055/ (accessed March 8, 2022).
22. Newton R, Rouleau A, Nylander AG, Loze JY, Resemann HK, Steeves S, et al. Diverse definitions of the early course of schizophrenia-a targeted literature review. *NPJ Schizophr.* (2018) 4:21. doi: 10.1038/s41537-018-0063-7
23. Werry JS. Child and adolescent (early onset) schizophrenia: a review in light of DSM-III-R. *J Autism Dev Disord.* (1992) 22:601–24. doi: 10.1007/BF01046330
24. Remschmidt H, Theisen F. Early-onset schizophrenia1. *Neuropsychobiology.* (2012) 66:63–9. doi: 10.1159/000338548
25. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5h edition. DSM-5. Washington, DC: American Psychiatric Association (2013).
26. WHO. *The ICD-10 Classification of Mental and Behavioural Disorders.* Genève: World Health Organization (1993).
27. McClellan J, Stock S. Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. *J Am Acad Child Adolesc Psychiatry.* (2013) 52:976–90. doi: 10.1016/j.jaac.2013.02.008
28. Hollis C. Child and adolescent (juvenile onset) schizophrenia. A case control study of premorbid developmental impairments. *Br J Psychiatry.* (1995) 166:489–95. doi: 10.1192/bjp.166.4.489
29. De Berardis D, De Filippis S, Masi G, Vicari S, Zuddas A. A neurodevelopment approach for a transitional model of early onset schizophrenia. *Brain Sci.* (2021) 11:275. doi: 10.3390/brainsci11020275
30. Stentebjerg-Olesen M, Pagsberg AK, Fink-Jensen A, Correll CU, Jeppesen P. Clinical characteristics and predictors of outcome of schizophrenia-spectrum psychosis in children and adolescents: a systematic review. *J Child Adolesc Psychopharmacol.* (2016) 26:410–27. doi: 10.1089/cap.2015.0097
31. Frangou S. Cognitive function in early onset schizophrenia: a selective review. *Front Hum Neurosci.* (2010) 3:79. doi: 10.3389/neuro.09.079.2009
32. Harvey PD, Isner EC. Cognition, social cognition, and functional capacity in early-onset schizophrenia. *Child Adolesc Psychiatr Clin N Am.* (2020) 29:171–82. doi: 10.1016/j.chc.2019.08.008
33. Kravariti E, Morris RG, Rabe-Hesketh S, Murray RM, Frangou S. The Maudsley early-onset schizophrenia study: cognitive function in adolescent-onset schizophrenia. *Schizophr Res.* (2003) 65:95–103. doi: 10.1016/S0920-9964(03)00067-7
34. Vita A, Barlati S, De Peri L, Deste G, Sacchetti E. Schizophrenia. *Lancet.* (2016) 388:1280. doi: 10.1016/S0140-6736(16)31674-9
35. Vita A, Barlati S. Recovery from schizophrenia: is it possible? *Curr Opin Psychiatry.* (2018) 31:246–55. doi: 10.1097/YCO.0000000000000407

36. Vyas NS, Patel NH, Puri BK. Neurobiology and phenotypic expression in early onset schizophrenia. *Early Interv Psychiatry.* (2011) 5:3–14. doi: 10.1111/j.1751-7893.2010.00253.x
37. Díaz-Caneja CM, Pina-Camacho L, Rodríguez-Quiroga A, Fraguas D, Parellada M, Arango C. Predictors of outcome in early-onset psychosis: a systematic review. *NPJ Schizophr.* (2015) 1:14005. doi: 10.1038/npjschz.2014.5
38. Coulon N, Godin O, Bulzacka E, Dubertret C, Mallet J, Fond G, et al. Early and very early-onset schizophrenia compared with adult-onset schizophrenia: French FACE-SZ database. *Brain Behav.* (2020) 10:e01495. doi: 10.1002/brb3.1495
39. Grover S, Avasthi A. Clinical practice guidelines for the management of schizophrenia in children and adolescents. *Indian Psychiatry J.* (2019) 61:277–93. doi: 10.4103/psychiatry.IndianJPsychiatry_556_18
40. Kumra S, Oberstar JV, Sikich L, Findling RL, McClellan JM, Vinogradov S, et al. Efficacy and tolerability of second-generation antipsychotics in children and adolescents with schizophrenia. *Schizophr Bull.* (2008) 34:60–71. doi: 10.1093/schbul/sbm109
41. Lee ES, Kronsberg H, Findling RL. Psychopharmacologic treatment of schizophrenia in adolescents and children. *Child Adolesc Psychiatr Clin N Am.* (2020) 29:183–210. doi: 10.1016/j.chc.2019.08.009
42. Christian R, Saavedra L, Gaynes BN, Sheitman B, Wines RCM, Jonas DE, et al. *Future Research Needs for First- and Second-Generation Antipsychotics for Children and Young Adults* Rockville, MD: Agency for Healthcare Research and Quality (US) (Future Research Needs Papers, No. 13) (2012). Available online at: https://www.ncbi.nlm.nih.gov/books/NBK84660/ (accessed March 8, 2022).
43. Correll CU, Findling RL, Tocco M, Pikalov A, Deng L, Goldman R. Safety and effectiveness of lurasidone in adolescents with schizophrenia: results of a 2-year, open-label extension study. *CNS Spectr.* (2022) 1:118–28. doi: 10.1017/S1092852920001893
44. Krause M, Zhu Y, Huhn M, Schneider-Thoma J, Bighelli I, Chaimani A, et al. Efficacy, acceptability, and tolerability of antipsychotics in children and adolescents with schizophrenia: a network meta-analysis. *Eur Neuropsychopharmacol J Eur Coll Neuropsychopharmacol.* (2018) 28:659–74. doi: 10.1016/j.euroneuro.2018.03.008
45. Gogtay N, Rapoport J. Clozapine use in children and adolescents. *Expert Opin Pharmacother.* (2008) 9:459–65. doi: 10.1517/14656566.9.3.459
46. Correll CU, Penzner JB, Parikh UH, Mughal T, Javed T, Carbon M, et al. Recognizing and monitoring adverse events of second-generation antipsychotics in children and adolescents. *Child Adolesc Psychiatr Clin N Am.* (2006) 15:177–206. doi: 10.1016/j.chc.2005.08.007
47. Solmi M, Fornaro M, Ostinelli EG, Zangani C, Croatto G, Monaco F, et al. Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: a large scale systematic meta-review of 78 adverse effects. *World Psychiatry.* (2020) 19:214–32. doi: 10.1002/wps.20765
48. Pagsberg AK, Tarp S, Glintborg D, Stenstrøm AD, Fink-Jensen A, Correll CU, et al. Acute antipsychotic treatment of children and adolescents with schizophrenia-spectrum disorders: a systematic review and network meta-analysis. *J Am Acad Child Adolesc Psychiatry.* (2017) 56:191–202. doi: 10.1016/j.jaac.2016.12.013
49. Olfson M, Gerhard T, Huang C, Lieberman JA, Bobo WV, Crystal S. Comparative effectiveness of second-generation antipsychotic medications in early-onset schizophrenia. *Schizophr Bull.* (2012) 38:845–53. doi: 10.1093/schbul/sbq172
50. Sikich L, Frazier JA, McClellan J, Findling RL, Vitiello B, Ritz L, et al. Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study. *Am J Psychiatry.* (2008) 165:1420–31. doi: 10.1176/appi.ajp.2008.08050756
51. Arango C, Ng-Mak D, Finn E, Byrne A, Loebel A. Lurasidone compared to other atypical antipsychotic monotherapies for adolescent schizophrenia: a systematic literature review and network meta-analysis. *Eur Child Adolesc Psychiatry.* (2020) 29:1195–205. doi: 10.1007/s00787-019-01425-2
52. Kendall T, Hollis C, Stafford M, Taylor C. Guideline Development Group. Recognition and management of psychosis and schizophrenia in children and young people: summary of NICE guidance. *BMJ.* (2013) 23:346:f150. doi: 10.1136/bmj.f150
53. Barlati S, De Peri L, Deste G, Fusar-Poli P, Vita A. Cognitive remediation in the early course of schizophrenia: a critical review. *Curr Pharm Des.* (2012) 18:534–41. doi: 10.2174/138161212799316091
54. Müller H, Kommescher M, Güttgemanns J, Wessels H, Walger P, Lehmkuhl G, et al. Cognitive behavioral therapy in adolescents with early-onset psychosis: a randomized controlled pilot study. *Eur Child Adolesc Psychiatry.* (2020) 29:1011–22. doi: 10.1007/s00787-019-01415-4
55. Rund BR, Moe L, Sollien T, Fjell A, Borchgrevink T, Hallert M, et al. The psychosis project: outcome and cost-effectiveness of a psychoeducational treatment programme for schizophrenic adolescents. *Acta Psychiatr Scand.* (1994) 89:211–8. doi: 10.1111/j.1600-0447.1994.tb08094.x
56. Calvo A, Moreno M, Ruiz-Sancho A, Rapado-Castro M, Moreno C, Sánchez-Gutiérrez T, et al. Intervention for adolescents with early-onset psychosis and their families: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry.* (2014) 53:688–96. doi: 10.1016/j.jaac.2014.04.004
57. Addington J, Coldham EL, Jones B, Ko T, Addington D. The first episode of psychosis: the experience of relatives. *Acta Psychiatr Scand.* (2003) 108:285–9. doi: 10.1034/j.1600-0447.2003.00153.x
58. Claxton M, Onwumere J, Fornells-Ambrojo M. Do family interventions improve outcomes in early psychosis? A systematic review and meta-analysis. *Front Psychol.* (2017) 8:371. doi: 10.3389/fpsyg.2017.00371
59. Signorini G, Singh SP, Marsanic VB, Dieleman G, Dodig-Curkovi,ć K, et al. The interface between child/adolescent and adult mental health services: results from a European 28-country survey. *Eur Child A dolesc Psychiatry.* (2018) 27:501–11. doi: 10.1007/s00787-018-1112-5
60. *National Action Plan for Mental Health Manifesto.* (2013). Available online at: https://www.salute.gov.it (accessed March 8, 2022).
61. Fusar-Poli P, Minichino A, Brambilla P, Raballo A, Bertolino A, Borgatti R, et al. ITAlian partnership for psychosis prevention (ITAPP): improving the mental health of young people. *Eur Psychiatry.* (2021) 64:e62. doi: 10.1192/j.eurpsy.2021.2232
62. Giannarou L, Zervas E. Using Delphi technique to build consensus in practice. *Int J Bus Sci Appl Manage.* (2014) 9:65–82.
63. Jorm AF. Using the Delphi expert consensus method in mental health research. *Aust N Z J Psychiatry.* (2015) 49:887–97. doi: 10.1177/0004867415600891
64. Kane JM, Robinson DG, Schooler NR, Mueser KT, Penn DL, Rosenheck RA, et al. Comprehensive versus usual community care for first-episode psychosis: 2-year outcomes from the NIMH RAISE early treatment program. *Am J Psychiatry.* (2016) 173:362–72. doi: 10.1176/appi.ajp.2015.15050632
65. Parabiaghi A, Confalonieri L, Magnani N, Lora A, Butteri E, Prato K, et al. Integrated programs for early recognition of severe mental disorders: recommendations from an italian multicenter project. *Front Psychiatry.* (2019) 10:844. doi: 10.3389/fpsyt.2019.00844
66. Mohr P, Galderisi S, Boyer P, Wasserman D, Arteel P, Ieven A, et al. Value of schizophrenia treatment I: the patient journey. *Eur Psychiatry.* (2018) 53:107–15. doi: 10.1016/j.eurpsy.2018.06.007
67. Tandon R, Lenderking WR, Weiss C, Shalhoub H, Barbosa CD, Chen J, et al. The impact on functioning of second-generation antipsychotic medication side effects for patients with schizophrenia: a worldwide, cross-sectional, web-based survey. *Ann Gen Psychiatry.* (2020) 19:42. doi: 10.1186/s12991-020-00292-5
68. Bernardo M, Vieta E, Saiz Ruiz J, Rico-Villademoros F, Alamo C, Bobes J, et al. Recommendations for switching antipsychotics. A position statement of the Spanish Society of Psychiatry and the Spanish Society of Biological Psychiatry. *Rev Psiquiatr Salud Ment.* (2011) 4:150–168. doi: 10.1016/j.rpsm.2011.07.003
69. Thomas SP, Nandhra HS, Singh SP. Pharmacologic treatment of first-episode schizophrenia: a review of the literature. *Prim Care Comp CNS Disord.* (2012) 14:PCC.11r01198. doi: 10.4088/PCC.11r01198
70. National Institute for Health and Clinical Excellence (NICE). *Psychosis and Schizophrenia in Children and Young People: Recognition and Management.* London: National Institute for Health and Care Excellence (2016).
71. Crespo-Facorro B, Pelayo-Teran JM, Mayoral-van Son J. Current data on and clinical insights into the treatment of first episode nonaffective psychosis: a comprehensive review. *Neurol Ther.* (2016) 5:105–30. doi: 10.1007/s40120-016-0050-8

72. Keating D, McWilliams S, Schneider I, Hynes C, Cousins G, Strawbridge J, et al. Pharmacological guidelines for schizophrenia: a systematic review and comparison of recommendations for the first episode. *BMJ Open.* (2017) 7:e013881. doi: 10.1136/bmjopen-2016-013881
73. Kishi T, Ikuta T, Matsui Y, Inada K, Matsuda Y, Mishima K, et al. Effect of discontinuation v. maintenance of antipsychotic medication on relapse rates in patients with remitted/stable first-episode psychosis: a meta-analysis. *Psychol Med.* (2019) 49:772–779. doi: 10.1017/S0033291718001393
74. Murray RM, Quattrone D, Natesan S, van Os J, Nordentoft M, Howes O, et al. Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics? *Br J Psychiatry.* (2016) 209:361–5. doi: 10.1192/bjp.bp.116.182683
75. Correll CU, Galling B, Pawar A, Krivko A, Bonetto C, Ruggeri M, et al. Comparison of early intervention services vs treatment as usual for early-phase psychosis: a systematic review, meta-analysis, and meta-regression. *JAMA Psychiatry.* (2018) 75:555–65. doi: 10.1001/jamapsychiatry.2018.0623
76. Bighelli I, Rodolico A, García-Mieres H, Pitschel-Walz G, Hansen WP, Schneider-Thoma J, et al. Psychosocial and psychological interventions for relapse prevention in schizophrenia: a systematic review and network meta-analysis. *Lancet Psychiatry.* (2021) 8:969–80. doi: 10.1016/S2215-0366(21)00243-1
77. Nibbio G, Barlati S, Cacciani P, Corsini P, Mosca A, Ceraso A, et al. Evidence-based integrated intervention in patients with schizophrenia: a pilot study of feasibility and effectiveness in a real-world rehabilitation setting. *Int J Environ Res Public Health.* (2020) 17:3352. doi: 10.3390/ijerph17103352
78. Vita A, Barlati S, Ceraso A, Nibbio G, Ariu C, Deste G, et al. Effectiveness, core elements, and moderators of response of cognitive remediation for schizophrenia: a systematic review and meta-analysis of randomized clinical trials. *JAMA Psychiatry.* (2021) 78:848–58. doi: 10.1001/jamapsychiatry.2021.0620
79. Vita A, Barlati S. The implementation of evidence-based psychiatric rehabilitation: challenges and opportunities for mental health services. *Front Psychiatry.* (2019) 10:147. doi: 10.3389/fpsyt.2019.00147
80. Daruvala R, Kumar A, Datta SS. Do psychological interventions work for psychosis in adolescents? *Schizophr Bull.* (2021) 47:692–94. doi: 10.1093/schbul/sbaa132
81. Breitborde NJ, Woods SW, Srihari VH. Multifamily psychoeducation for first-episode psychosis: a cost-effectiveness analysis. *Psychiatr Serv.* (2009) 60:1477–83. doi: 10.1176/ps.2009.60.11.1477
82. Rosenheck R, Leslie D, Sint K, Lin H, Robinson DG, Schooler NR, et al. Cost-effectiveness of comprehensive, integrated care for first episode psychosis in the NIMH RAISE early treatment program. *Schizophr Bull.* (2016) 42:896–906. doi: 10.1093/schbul/sbv224

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers | Frontiers in Psychiatry

ORIGINAL RESEARCH
published: 11 April 2022
doi: 10.3389/fpsyt.2022.803517

School Refusal in Immigrants and Ethnic Minority Groups: A Qualitative Study of Adolescents' and Young Adults' Experiences

Camille Brault[1], *Isaiah Thomas*[2], *Marie Rose Moro*[3,4,5] *and Laelia Benoit*[2,3,5]*

[1] Etablissement Public de Santé Ville-Evrard, Neuilly sur Marne, Paris, France, [2] Yale Child Study Center, Yale School of Medicine, New Haven, CT, United States, [3] Maison des Adolescents—Maison de Solenn, Hôpital Cochin, AP-HP, Paris, France, [4] University of Paris, Faculty of Psychology, Boulogne-Billancourt, Paris, France, [5] Inserm U1018, Team DevPsy, CESP, Paris Saclay University, Paris, France

OPEN ACCESS

Edited by:
David Cohen,
Sorbonne Universités, France

Reviewed by:
Carolyn Gentle-Genitty,
Indiana University Bloomington,
United States
Ilan Katz,
University of New South
Wales, Australia
Kerry John Kennedy,
The Education University of
Hong Kong, Hong Kong SAR, China

Correspondence:
Laelia Benoit
laelia.benoit@yale.edu

Specialty section:
This article was submitted to
Child and Adolescent Psychiatry,
a section of the journal
Frontiers in Psychiatry

Received: *28 October 2021*
Accepted: *14 March 2022*
Published: *11 April 2022*

Citation:
Brault C, Thomas I, Moro MR and
Benoit L (2022) School Refusal in
Immigrants and Ethnic Minority
Groups: A Qualitative Study of
Adolescents' and Young Adults'
Experiences.
Front. Psychiatry 13:803517.
doi: 10.3389/fpsyt.2022.803517

Background: School refusal is one cause of school absenteeism along with truancy, and the two can be difficult to distinguish. School absenteeism behaviors among students in transcultural situations (immigrants or children of immigrants) and from ethnic minority groups are subject to misdiagnosis and decreased access to care. To improve the care provided, this exploratory study addresses the experience of adolescents and young adults engaging in school refusal, from immigrant and ethnic minority groups.

Methods: Sixteen participants between the ages of 16 and 20 years old presenting with school refusal were interviewed for this qualitative study. All participants were either immigrants, children of immigrants, or from an ethnic minority group. We conducted a qualitative analysis based on Interpretative Phenomenological Analysis.

Results: Participants experienced school refusal as a loss of identity and as a failure to achieve what was perceived as parental expectations of success, which triggered feelings of worthlessness, shame, and guilt. The loss of a peer group, namely their classmates, as a result of school absenteeism was experienced as a marginalization from the larger society. Although participants denied having personally experienced racism, some of them recalled their parents experiencing racism at school.

Conclusion: School refusal complicates identity construction, autonomy, and integration into society. For adolescents and young adults from immigrant and ethnic minority backgrounds, it also triggers guilt, transgenerational traumatic memories, and the fear of marginalization. In addition to validated therapies for school refusal, sociological, intersectional, and cross-cultural tools would be a valuable addition to treatment.

Keywords: school refusal, immigrant, youth, school absenteeism, ethnic minority, adolescence, racism, qualitative study

INTRODUCTION

For several years, the classification of school absenteeism behaviors has been refined to improve access to appropriate support. Heyne et al. (1) define four categories of "school attendance problems": school refusal, truancy, academic withdrawal, and academic exclusion. In 2020, 6.8% of students in French public high schools displayed school absenteeism, defined by the French Ministry of Education as at least 2 days of unjustified absences per month (2). Dropping out of school before graduation can have a significant impact on future career prospects, especially in France where college diplomas are greatly valued (3). Accordingly, young people who dropped out of high school without receiving a diploma or who did not enter college after completing high school have a higher unemployment rate in France than in other European countries; in 2017, the unemployment rate of these young people was three times higher than that of students who completed 2 years of college (4).

School absenteeism occurs at higher rates among immigrant students than among non-immigrant students in European countries (5). In 2018, 6.4 million immigrants were living in France, and 7.5 million of those born in France had at least one immigrant parent, together representing 11.2% of the population (6). Students who are immigrants or whose parents are immigrants are more likely to be admitted to vocational programs after secondary school and to complete their education without a diploma (7). In 2012, Chau compared the academic pathways of immigrant students in France of European and non-European origin (8). The latter group had higher rates of class repetition, low academic performance, and cognitive dropout (i.e., the student attends class but is no longer actively involved in learning). Similarly, the academic success of students who are immigrants or whose parents are immigrants varies according to the parents' country of origin (7). These differences are partially, but not entirely, explained by cultural, socio-demographic, and family characteristics. Most likely, they reflect the impact of racism, be it individual or systemic, and subsequent beliefs about ethnic minorities' reduced chances of academic success.

School refusal is one of the four patterns of school absenteeism and accounts for 5% of child and adolescent psychiatry referrals in France (9). School refusal is defined by Heyne et al. (1) as follows: "(1) a young person is reluctant or refuses to attend school, in conjunction with emotional distress that is temporal and indicative of aversion to attendance (e.g., excessive fearfulness, temper tantrums, unhappiness, unexplained physical symptoms) or emotional distress that is chronic and hindering attendance (e.g., depressed mood, sleep disturbance), usually but not necessarily manifesting in absence (e.g., late arrivals; missing whole school days; missing consecutive weeks, months, or years); (2) the young person does not try to hide the associated absence from their parents (e.g., they are at home and the parents are aware of this), and if they previously hid absence, they stopped doing so once the absence was discovered; (3) the young person does not display severe antisocial behavior, beyond resistance to parental attempts to get them to school; and (4) the parents have made reasonable efforts, currently or at an earlier stage in the history of the problem, to ensure attendance at school, and/or the parents express their desire for their child to attend school full-time". School refusal is frequently associated with other anxious manifestations: phobias regarding transportation; separation anxiety; somatic symptoms (10); behavioral problems, especially in the family setting (11); and depressive symptoms (50%), such as major depression (13.9%) and social withdrawal (12, 13).

A different pattern of school absenteeism is truancy, defined by Heyne et al. (1) as follows: "(1) a young person is absent from school for a whole day or part of the day, or they are at school but absent from the proper location (e.g., in the schoolyard rather than in class); (2) the absence occurs without the permission of school authorities; and (3) the young person typically tries to conceal the absence from their parents". Teasing apart the differences between school refusal and truancy is challenging. According to Heyne et al., "reasonable parental effort" to get the child to go to class is a specific criterion for school refusal. However, in 2008, Kearney (14) elucidated the lack of consensus regarding metrics of parental involvement. In particular, a student who is an immigrant or the child of immigrants is experiencing a cross-cultural situation: the cultural codes at home differ from those expected in the society's institutions, such as school. Cross-cultural aspects must be considered to better understand the behavior of the student and his or her parents. Kearney argues for stronger parent-teacher collaboration in cross-cultural settings to improve the referrals to care for students who experience school refusal (15).

The obstacles to academic achievement that children from marginalized groups face in France are clearly established. However, research on this population of school refusers remains limited. In one 2015 case study, Benoit et al. (16) described an adolescent immigrant for whom school refusal represented an expression of larger struggles with identity. Since then, Rosenthal et al. (17) showed in a qualitative study with 11 immigrant parents of adolescents that these parents feel overwhelmed by school refusal and that they understand it as a failure to fulfill the immigrant narrative's mandate of success. While immigrant parents initially idealized the school system of their new home country, their experiences of rejection and racism led to disappointment and mistrust. Rosenthal argues that parents' customs and culture, immigration history, and experiences of adversity should be part of assessing school refusal to facilitate access to appropriate care. In a qualitative study of 50 French school professionals, Martin et al. showed that school refusal among immigrant students and students whose parents are immigrants can be misinterpreted as truancy, partly because parental efforts to ensure their child's attendance are not perceived by teachers as such (18). Prejudices about parents' attitudes and behaviors lead teachers to conclude that absenteeism does not reflect anxiety, but rather a lack of interest in school on the part of both the student and the family. Thus, both cultural misunderstandings and racism may delay or prevent referral to care for students experiencing school refusal in a cross-cultural situation or students who are part of marginalized ethnic groups, resulting in them dropping out of school. Such inequalities in health care may result in a self-fulfilling prophecy about the prejudice that immigrant students or children of immigrants are less likely to achieve academic success.

Adding to Benoit's case study (16), this study is the first to explore the views and feelings of several adolescents and young adults in a cross-cultural situation (immigrant students, children of immigrants) and/or from ethnic minority groups, regarding their experience of school refusal.

METHODS

Study Design

Given that this study is exploratory, the choice of a qualitative method is particularly relevant. This qualitative study has been carried out according to the COREQ criteria (19). Participants were recruited in four child psychiatry departments in Paris and its suburbs (Seine Saint-Denis and Val-d'Oise) (20). Inclusion criteria were: age $\geq$ 12 years; diagnosis of school refusal; follow-up of at least 6 months; and being born abroad or having at least one parent born abroad (or in the French Caribbean Islands). The definition of school refusal was a combination of Heyne's criteria (1) and the DSM-5 criteria (21): a refusal to attend school resulting in school absenteeism for a period of at least 1 month; the presence of an anxiety disorder as defined by the DSM-5 (excluding obsessive-compulsive disorder or post-traumatic stress disorder) associated with a negative emotional experience; the absence of conduct disorder; and parental awareness of the whereabouts of the child when not in class. As the collection of ethnic data is forbidden by law in France, we did not ask the participants to disclose their self-identified race and ethnicity. However, we deliberately ensured a diverse recruitment dash–including immigrants and children of immigrants–through purposive sampling, in order to explore both cross-cultural experiences and experiences of racism.

All psychiatrists in the four child psychiatry departments were informed of the study and were asked to screen their patients for inclusion. All school refusers are typically expected to be referred to child psychiatry departments. However, school refusers from underrepresented minorities (such as immigrants and ethnic minorities), may not be identified as such and therefore experience barriers in access to child and adolescent psychiatry departments. Consequently, our population of interest was expected to represent a small percentage of the patients experiencing school refusal in these four departments. Participants' psychiatrists offered them the opportunity to participate in the study on a voluntary basis without compensation. Oral and written information was provided, and oral consent was obtained at the beginning of the interview. The location of the interview was decided with the participants according to their convenience (i.e., child psychiatry department, public place, home). No relationship existed between the participants and the interviewer. The interview included sensitizing questions about: the pathway to school refusal (beginning and course); the participants' understanding of school refusal; their experiences at school (relationships with others, academic performance, experiences of stigmatization or racism), their expectations about their own future; their understanding of parental expectations; their experience of mental health care; their family's history of immigration and the languages spoken at home.

Sample

In 2019, 16 semi-structured interviews lasting 45 to 90 min were conducted by two researchers (CB and LB) with adolescents and young adults ages 16 to 21 (see **Table 1**). Because the population of interest is an underrepresented minority among the patients experiencing school refusal in child and adolescent psychiatry departments, the process of identifying and recruiting participants lasted one full year. All patients who were approached about the study agreed to participate. The participants, including immigrants, children of immigrants, and French citizens whose parents were born in the French Caribbean Islands, were representative of minority ethnic groups in France. Their origins reflected the colonial past of France (Algeria, Mali, Morocco, Mauritania) and Great Britain (Ghana, Egypt), the French slave trade in the Caribbean (Guadeloupe, Martinique), intra-European migration (Portugal, Italy, Kosovo), and immigration from the Global South (Turkey, Chile, Colombia, Sri Lanka, Pakistan).

Data Analysis

The interviews were recorded, transcribed, and anonymized. Two researchers (CB and LB) independently analyzed all the interviews using Interpretative Phenomenological Analysis (22), whose phenomenological nature invites the researcher to describe in detail the individual experience based on the participant's own formulation of it and the meaning he/she attributes to his/her experience (23). Thus, phenomenological analysis allows a better understanding of individual experience by placing the subject in the position of expert (22). For each interview, we developed detailed codes-full sentences conveying nuances-about the participant's phenomenological experience (perceptions, feelings, meaning making), and wrote a memo summarizing the participant's unique experience. The codes and memos were discussed with the research group (LB, CB, IT, MRM). As in other inductive methods, we did not need to define an exact number of respondents before the research began. The data were coded to generate categories, which in turn were validated through constant comparisons as new interviews were done. Thus, data analysis, further sampling, and theoretical development continued simultaneously until reaching theoretical sufficiency (24). This study is part of the larger project "From school refusal to psychiatric follow-up", which received a favorable opinion from the Inserm Ethical Evaluation Committee (IRB00003888).

RESULTS

All participants were ashamed of themselves or of their parents, and all of them experienced feelings of loss (of a group of peers, or of a social status). As their phenomenological experiences were similar, we built a common framework reflecting the feelings of shame, and the perceptions of loss shared by all participants. We divided our findings into three broad domains: (1) in search of a lost identity; (2) suspending autonomy and empowerment;

TABLE 1 | Characteristics of the population.

Participants (Pseudonyms)	Gender	Age	Place of birth (PB)	Mother PB	Father PB	School attendance*
Merlin	M	20	France	France	Kosovo (parents born in Albania)	No
Leila	F	18	France	Algeria	Algeria	No
Dalla	F	17	France	Mali born in Senegal	Mali	No
Léa	F	18	France	France	Italy	No
Joseph	M	21	France	Colombia	Colombia	Yes
Ana	F	16	France	France/Spain	Portugal	No
Michel	M	18	France	France	Martinique (French Caribbean islands)	No
Akash	M	18	France	Sri Lanka	Sri Lanka	No
Amina	F	18	Egypt	Egypt	Egypt	No
Najib	M	19	Algeria	Algeria	Algeria	No
Said	M	16	France	Algeria	Moroccan born in Algeria	No
Joss	M	18	France	France	Chile	Yes
Damia	F	16	Turkey	Turkey	Turkey	No
Mariam	F	18	France	France	Pakistan	Yes
Emma	F	16	France	Guadeloupe (French Caribbean islands)	Ghana	No
Jimmy	M	16	France	Martinique (French Caribbean islands)	Mauritania	Yes

**Participant has resumed partial or complete school attendance at the time of the interview.*

and (3) challenges integrating into the host society. These three main domains comprised six main themes and several subthemes that logically fit together with one another. In **Table 2** we summarize these six main themes. In this section, we use quotes conveying nuances that may not be reflected in the broader themes, and thus enrich our understanding of the participants' individual experiences.

In Search of a Lost Identity

All our participants had been surprised by the onset of their school refusal. Only two of them mentioned a traumatic event leading them to avoid school (i.e., the death of a relative). All the other participants did not recall any specific cause and experienced their behavior as unsettling their sense of identity.

Straying From the Path

Previously Identifying as a Successful and Ambitious Student

Most of the participants described themselves as dedicated and successful students, loving school and learning: "I was very fulfilled, I loved learning new things" (Michel). The participants' academic ambitions were reflected in their strategic choices: asking teachers for additional help and guidance, attending study groups, choosing selective high school classes—"the hardest thing" (Akash)—or applying to boarding school in hopes of securing better studying conditions than at home. "[My brothers] are noisy and the boarding school, was going to help me to work better" (Dalla). A pervasive belief was that acceptance into a selective class—such as ones offering a scientific curriculum ("S") as preparation for admission to selective colleges—was the only way to achieve academic success: "I can't do less than the S, there is nothing less than the S, I want to do the S and I will do the S" (Mariam).

TABLE 2 | Domains, themes and sample quotes.

Domain and themes	Sample quotes
I. In search of a lost identity Straying from the path	"I can't explain it anyway, I went from all to nothing and I never thought I would get to this point" (Leila).
Becoming a stranger to oneself	"I don't even know who I am anymore, I've changed too much, I don't know how I would react to certain situations, I feel like I'm lying to myself" (Akash).
II. Suspending autonomy and empowerment Experiences of parental pressure	"In the Middle East, to be successful, there are two jobs. Ideally either an engineer or a doctor. [Leaving medicine] was an atomic bomb. I was the hope of generations" (Amina).
Distancing oneself from familial roots	"[My father] has a strong accent. It bothers me. When he speaks in Arabic in front of my friends, I don't know, it's embarrassing. I'm ashamed of him" (Said).
III. Challenges integrating into the host society Wanting to keep the peace	"Everyone needs a group of peers, not necessarily friends, but a group they can relate to. A group reassures you, a group makes you feel that you exist in society. When you are not part of society you feel a bit rejected" (Najib).
Envisioning hope: a cross-cultural integration into society	"What I would like to study is something where my Spanish language is an advantage" (Joseph).

Being Stunned by One's Own Actions

The participants, who described themselves as model students, perceived their own refusal to go to school as incomprehensible, a source of amazement: "I don't know what happened. [...] I still don't know" (Amina). The participants related their experiences in the passive mode. Like spectators, they could not make sense of the succession of events they described. First came a malaise, which was not limited to academics for most participants. Then a mental block, an inability to go to class, overwhelming their will and their attempts to exercise control: "There is something that prevents me from going there..." (Dalla).

Being in Great Pain

For the participants, school refusal could happen to anyone without warning or a reason. Even though the period of suffering at school could last several weeks or months, the decision to stop going to school seemed to happen suddenly: "I can't explain it anyway, I went from all to nothing and I never thought I would get to this point" (Leila). Once they stopped going to school, participants spent their days at home doing little. They might have, at first, read or played video games, but this eventually stopped and time became suspended. The feeling of being useless, of being a burden to others, arose, revealing depressive symptoms: "I'm useless in the world" (Ana). Some participants reported having dark thoughts or suicidal ideation. Some acted on them; two had engaged in self-injury behavior and one had attempted suicide: "It was a week before my midterms, I attempted suicide" (Michel).

Becoming a Stranger to Oneself

No Longer Recognizing Yourself

Participants found that they no longer recognized themselves and felt disconnected from themselves. "Just the thought of going to class made me anxious. It was really like, this is not me! I don't know, it was like another person coming into my body" (Leila). For some, this disintegration of a coherent identity continued several months after they began refusing to go to school. "I don't even know who I am anymore, I've changed too much, I don't know how I would react to certain situations, I feel like I'm lying to myself" (Akash).

Feeling Ashamed of Oneself

Incomplete homework assignments and academic struggles triggered feelings of shame: "I didn't turn it in on time, I didn't come to class because I was too ashamed of not having finished" (Michel). Finally, participants felt ashamed because they had, according to them, "fallen ill". This shame was so great that they could not talk about it, not even with health care professionals: "I was ashamed to have stopped, I was ashamed to have gotten sick" (Amina). Others thought they were a disgrace to their immediate family, their relatives, and their community because of their "failures": "When I stopped going to school, it was an absolute shame for my father. He is the Italian immigrant who absolutely wants his children to succeed" (Léa). Many participants were afraid of the future because, according to them, the only way to obtain a status is to succeed in school: "If I don't study, I won't have a career, what will I do later?" (Jimmy).

Suspending Autonomy and Empowerment

Experiences of Parental Pressure

A Duty to Succeed

Many of the study participants represented, in their view, their parents' "hope" for academic and professional success. They had one duty—succeed in school: "In the Middle East, to be successful, there are two jobs. Ideally either an engineer or a doctor. [Leaving medicine] was an atomic bomb. I was the hope of generations" (Amina). The difficulties entailed in immigration and relocation were a source of academic pressure that demanded academic success: "They have sacrificed for me, doing jobs they don't like, for their son's future, so I have to give back, doing the best I can, at school" (Joseph). When participants felt that they were no longer able to fulfill their parents' dreams of academic success, a sense of guilt arose. The participants felt obligated to repay their parents by working or costing them as little as possible so that they would no longer be a financial burden: "Even when I went to school, I didn't ask for anything, but now that's one more reason. It's a waste of money" (Akash).

Not Being Understood by Your Loved Ones

Participants found that their families, friends, and school administrations did not understand their school refusal, increasing their sense of isolation: "My parents, they don't understand [...] Nobody understands, nobody can understand" (Said). Parental misunderstanding was sometimes expressed through strong reactions, such as shouting or threats to force the child to attend class, and in other cases, participants' parents did not force them to go: "[My mother] didn't force me to go to school" (Mariam).

Distancing Oneself From Familial Roots

Not Knowing Their Family's Story

Many participants did not have a detailed knowledge of their parents' lives, including their immigration story: "[My father] was probably an adult. Under what conditions, I couldn't tell you" (Mariam). Most participants could name the reasons for immigration or relocation: fleeing a political regime, wanting a better education for their children. Some participants did not mention or were not interested in their parents' immigration: "I don't really care about all that. Since I never asked them too much, and they probably said it but I must have forgotten" (Akash).

The Lack of a Shared Language

Despite the multiplicity of languages encountered in their homes, not all participants could find a common language with their families. Indeed, many participants did not fully master their parents' native tongue, and many had parents who were unable to speak French or had difficulty doing so. This created barriers to communication and understanding: "When the psychologist talked to my parents, there was a translator. I don't speak Tamil as well as them. And at the Tamil psychic, there were words I didn't understand" (Akash). Participants seemed to keep their parents' culture separate from life outside the family environment. Almost all participants used or were surrounded by a language other than French, which they did not use in academic settings.

Being Ashamed of Your Family

The notion of "shame" was very present during the interviews. Some participants were ashamed of their parents' academic career: "I saw her report cards and I said, 'But Mom, aren't you ashamed of yourself?"' (Ana, laughing). Others were ashamed of their parents' language or behavior: "[My father] has a strong accent. It bothers me. When he speaks in Arabic in front of my friends, I don't know, it's embarrassing. I'm ashamed of him" (Said). The children of migrant parents were the only participants ashamed of their parents' accents. This subjective experience was part of a broader feeling of shame of one's parents shared by both migrant children and children whose parents were French. Strikingly, the participants overall had attained a lower level of education than their parents. Indeed, the college degrees of parents who arrived in France as adults were often not recognized, and their current jobs were less prestigious than the positions they would have had in their country of origin. Nevertheless, through school refusal, some participants reconnected with their parents or siblings academic or professional struggles. "I am sure that in my family we are not designed to go to school!" (Ana). They found themselves sharing the burden of finding their way without the security of studies.

The Loss of Parental Authority

Along with the challenges of self-identification or situating themselves in relation to their parents, some participants described growing up without parental guidance: "It was music that educated me. Not my parents" (Joss). Others identified with and attributed their upbringing to an uncle, a brother, a sister, who were seen as role models and were often idealized: "I wish I had a father like my uncle" (Said). Most participants felt that they have had to manage on their own while also refusing help from their parents. This was particularly true in the case of academics; participants described their parents being unable to help with coursework or provide sound advice regarding their academic careers: "I have no one to help me at home" (Amina). At times, participants observed a role reversal, with parents asking for help from their children: "When [my parents] have a letter to write, they are going to ask my sister. They are not going to do it themselves" (Said).

Challenges Integrating Into the Host Society

Wanting to Keep the Peace

Continuing School at All Costs

A painful period, of varying length, separated the onset of the disorder and the complete cessation of going to school. During this period, participants forced themselves to go to school and implemented strategies to cope: going to the school nurse's office, being near a window in class. In spite of headaches, vomiting, crying, sleep disturbances, anxiety attacks, and feelings of dying, they would go back: "I insisted, I continued to go [...], but I still had the lump in my stomach, always, always, all the time" (Dalla). When participants would leave school before the end of the school day, they did not always return home and did not necessarily inform their parents: "I would wait for my parents to leave the apartment, and then I would go home" (Joseph).

Denying Racism at School

During the interviews, the topic of racism at times came up. None of the participants said that they had experienced it at school, and none thought of it as a possible cause for their school refusal. In contrast, two of them reported that their parents may have been victims of racism: "She went to a school, but they didn't like her, my mother, because she was Spanish. There was racism in that school" (Ana). However, some participants point out that their foreign origins can be the butt of "jokes": "At school I was told, 'But Ana, why be smart? You're Portuguese, you'll end up as a house cleaner"' (Ana).

The Fear of Marginalization

According to some participants, the integration in the host country was so important, that their success may have generated the envy of neighbors and acquaintances from their parents' homeland. Leila wondered if she contracted the evil eye in Algeria when neighbors were invited to celebrate her school achievements: "Many people came to my house in Algeria, like 500 people. And I don't know, maybe there were people with bad intentions" (Leila). Many participants mentioned the loss of a group, of a social milieu, concurrent with the start of school refusal. Participants reported that school absenteeism prevented them from feeling "normal" and belonging to the society: "Everyone needs a group of peers, not necessarily friends, but a group they can relate to. A group reassures you, a group makes you feel that you exist in society. When you are not part of society you feel a bit rejected" (Najib).

Envisioning Hope: A Cross-Cultural Integration Into Society

At the time of the interview, only four participants had overcome their school refusal, and returned partially or completely to school. They did not differ from the others regarding age, sex, or origin (see **Table 1**).

Finding Support in Their Parents' Culture

Some participants found within their family, their community, or their culture some relief and answers. Cross-cultural discussions enabled them to find different ways to give meaning to their distress, to navigate it and treat it. It also enabled young people to see how their parents allowed themselves to value or reject certain traditions of their country of birth. "I feel better, since I came back from Algeria. Before leaving, I saw imams, they made me drink six liters of water and vomit afterwards. But my cousin [. . .] told me "you shouldn't see an imam, but a person who deals with [evil eye]. You have to heal evil with evil"... Like witchcraft, stuff like that. But my parents are totally against that." (Leila). Participants were able to seek the help of experts themselves or accept it when their parents offered it. "My parents are so worried that they took me to see a Sri Lankan psychic. He told me that if we could get through this, I would find something I liked, for my studies. And that when I was twenty-three, I was going to get married (laughs).

And that it's the girl I'm going to meet that's going to make me change (laughs). But I don't want to believe that, I don't know what to think. It's absurd, but he also described me well. That I'm the kind of person who does things for others. [. . .] If he was a quack, how would he know all this? [...] Talking to a psychic is. . . weird. But he was saying a lot of true things" (Akash).

Envisioning One's Place in Society

Among the services offered, participants benefited from inpatient hospitalizations or intensive outpatient programs. These arrangements allowed participants to leave home, meet other teenagers, and find support among peers even if their challenges were different. "The intensive outpatient program allowed me to get away from home a bit" (Said). Several participants went back to school, often in fields not previously considered or at different institutions such as the Innovative High School (Pôle Innovant Lycéen, PIL), a pilot program to support absent students as they resume high school: "I was doing what they call a PIL. It was great!" (Joseph). Participants seemed to rediscover their cultural resources when they were getting better and on the path to returning to school: "What I would like to study is something where my Spanish language is an advantage" (Joseph). Several participants got involved in their communities and participated in activities where they received recognition and praise for their cross-cultural skills: "I have joined the choir and I teach them Coptic" (Amina).

DISCUSSION

According to Kearney and Benoit, challenges experienced by students with school attendance problems are exacerbated by disparities in socioeconomic status, childhood adversities, family structure, and neighborhood-level factors (25). Kearney and Benoit argue that advocacy with respect to underrepresented youth with school attendance problems should involve culturally competent care, such as considering family views of the education system, reducing the research-to-practice gap, integrating care across systems (i.e., primary care, education, justice), and developing clinical strategies targeted to specific, high-risk, intersected groups (25). Indeed, cultural and language misunderstandings and racist biases can lead to youth assigned pejorative labels of truancy (18) and caregivers inaccurately viewed as inaccessible, pathological, and unskilled (17). Moreover, young people experiencing high levels of emotional distress can attend school but be absent from the classroom (i.e., remaining in the hallways or playground) (26), leading to punitive rather than restorative care. Our participants experience the intersection of challenges related to school refusal, migration, racism, socioeconomic status, and cultural difference. The distinctive impact of each of these factors on their mental health could not be assessed in this exploratory qualitative study. Nevertheless, their individual experiences may help design culturally competent care for students and families from immigrant and ethnic minority groups.

Previous research on migration have shown that the child, in a cross-cultural context, can experience social and cultural challenges, both those of his parents (i.e., immigration, language barriers) and sometimes his own. Moro (27) describes three periods of vulnerability for the immigrant child: early parent-child interactions (between 0 and 1 year of age), entry into schooling (around 6 to 8 years of age), and early adolescence (between 14 and 16 years of age). Immigration and relocation involve the individual's descendants, and the experience of immigration trauma can be transmitted to the children, whether in the form of a sometimes idealized account or of painful unspoken words (28). Whether it is forced or desired, immigration and relocation can be traumatic, but this trauma will not necessarily have pathological effects; rather, it can also lead parents to model resilience and strength in face of adversity (29). The school environment is not a world linked to the family's culture of origin, and for these children in a cross-cultural situation, entering this space can sometimes be brutal, experienced as exclusion or even violence (30). Although our participants did not report being the target of racist behavior at school, the racism their parents experienced at school remained a painful memory for them. This finding suggests that school might be a place associated with perceptions of suffering, prejudice, and misunderstanding (18), either based on a lived experience or on a transgenerational memory.

In this study, participants described their school refusal as an experience of identity loss. They identified themselves as model students who loved school, which has since become a place associated with painful emotions. Previously, their desire for academic success seemed to be a personal aspiration. But it now appears as a mandate of success imposed by external factors. Faced with their failure, our participants try to make up for their parents' investment; the notion of debt appears, as does that of shame. In this study, shame is present in the family environment (the world inside), but also at school (the world outside). Participants also experience a loss of group membership. They are no longer part of their former group of friends, and this uprooting echoes the literature immigration: leaving the group to which we belong to find ourselves alone in a place where no one is waiting for us (31). Participants describe themselves as strangers to themselves, their families, and their peers. This finding suggests that school refusal may be exacerbated by the intersection of the psychic reorganizations of adolescence and cross-cultural integration. The desire for autonomy and insertion into social life may be challenging when the norms of society appear different–if not opposed–to the ones of the family.

Suspending Cross-Cultural Integration: The Inside/Outside Divide

Psychological research on adolescence suggests that a first step in becoming autonomous from one's parents is the psychic separation from them, that is, the fact of thinking for oneself (32). This developmental stage appeared particularly hindered for our participants, unable both to attend school and to make sense of their refusal. School refusal is usually associated with underlying mental illness such as generalized anxiety disorder, depression, or social phobia. Nevertheless, Catheline argued that it can also at times reflect an avoidance of autonomous thinking (33). Moro et al. argue that the process of individuation is more complex in cross-cultural situations. It is around the time of the entry into kindergarten that the young child must first separate himself or herself from the family environment (the world of the inside) to find a place in the school environment (the world of the outside and the foreign). In a cross-cultural situation, the child experiences a cleavage, where filiation (parental transmission) and affiliation (belonging to a group) are dissociated (27). In adolescence, a period of identity reconstruction, the subject must integrate his filiation and affiliations. When filiation and affiliations are sources of conflict, the adolescent in a cross-cultural situation may experience difficulties navigating the desire to become autonomous from his or her parents and turn to other objects of investment. It is not an easy task to break certain links with one's culture without wanting to abandon it.

Thus, the ties that adolescent immigrants have to their families and their countries of origin are sometimes ambivalent, sometimes conflicting (34, 35). Moreover, in a cross-cultural situation, the adolescent does not always find figures with whom to identify in the host country, either in his or her peer group or in society. By refusing school and remaining at home, the participants in our study may temporarily avoid the challenge of cross-cultural integration (16), and remain in a single cultural envelope, that of the family. The participants are burdened by the expectations of the different worlds in which they grew up, and their school refusal may reveal their difficulties in processing *"the different influences that cross them and in assuming a multiple-identity construction"* (16).

In this study, participants who expressed a positive projection of the future had begun psychotherapy and thus began a period of self-reflection. Acknowledging their cross-cultural skills and the transgenerational impact of their parents' traumatic experiences (immigration, racism, school dropout), may have helped them overcome their difficulties. In the context of school refusal in immigrant and ethnic minority groups, such a psychotherapy may allow students to weave or reweave healthy connections with the school and maintain comforting connections with the parental culture while accepting the emotional weight of transgenerational suffering. Previous work suggests that, to engage in this process, the adolescent should feel authorized to compare the cultures and behaviors of the people around him or her, and that criticism and fears verbalized should be welcomed and validated (16). Thus, we believe that psychotherapy addressing the specific experience of adolescents with school refusal from underrepresented and intersected groups, should be designed and evaluated. Such inclusive and cross-cultural care already exists for migrant populations. It is provided by a trained therapist or, preferably, by a trained team composed of professionals from various ethnic and cultural backgrounds, or even in a specific setting such as a transcultural group consultation (30). A transcultural group setting enables the patient to think about his or her blending by comparing his or her individual experience with the knowledge of the team members.

Suspending the Desire for Autonomy: Shame

In this study, few participants knew the immigration history of their parents. For some of them, there was no common language mastered by all members of the family, which may have resulted in obstacles to communication between parents and adolescents. These findings can be discussed considering the literature on migration. Indeed, identity is rooted in part in a family history and family narrative. Having a foundational story allows one to develop a narrative for oneself. However, the transmission of history mostly occurs through the language of the parents, and sometimes parents are discouraged from speaking to their children in their native language. Also, according to Mansouri (36) the terms used to designate young immigrants and members of ethnic minority groups in France predestine them to be cut off from their filiation: "children of immigration" or "from immigration" as if their genealogy began with immigration (37). Immigrant parents bring a cultural heritage with them when they immigrate and act as representatives of that culture. In the host country, they take on the status of "immigrants in the process of integration" in hopes that their child will become a full-fledged member of the host society (30). However, once well-integrated into the host society, the child may appear as a foreigner in the eyes of his or her parents, as they may also want their child to conform to values and norms from the culture of origin. The adolescent is faced with a dilemma: fitting into the host society while remaining a good representative of his culture of origin.

In this study, academic failure was perceived by some participants as family traits. The attempt of our participants to legitimize their parents' lack of academic success was visible through contradicting attitudes: they were ashamed of their parents' poor academic records, while requesting their help to resume school. Thus, refusing school may have enabled them to reintegrate into the family, whereas academic success separated them from their parents. This finding can be discussed considering the literature on migration and social mobility. The desire for a better life for their children, drive parents to relocate and face years if not decades of precarity (31). Consequently, the "duty to succeed" may be a burden on the shoulders of adolescents, as immigrant parents see their child as the reason for their sacrifice (17). The debt to their parents is "paid" by their successful integration into the host society, in particular by their academic success. But academic success may also be perilous for a good student, as it may involve a change in social class. Gaulejac argues that "every individual who changes social class experiences a more or less intense conflict between his inherited identity, the original identity conferred on him by his family environment, and his acquired identity, the one he constructs in the course of his trajectory" (38). One becomes a stranger in one's own home by changing class because this change requires an act of mourning, of unbinding. Bourdieu uses the term *habitus* to describe the norms specific to each social class, the product of the whole biographical experience of an individual (39); the *habitus* is an integral part of the individual. When the change of class takes place between two social groups marked by the historical domination of one over the other, one will be confronted with an invalidation, a devaluation of the behaviors, *habitus*, and values of the "inferior" classes. Social mobility requires a disincorporation of the original *habitus* and a reincorporation of new *habitus* (38).

Most participants in this study perceived themselves as industrious, self-motivated, and high achieving students. They experienced school refusal as a failure and a shame to themselves, to their parents, to their community, and to society. These findings can be discussed considering the literature on academic success. According to MacInnis et al., academic success may trigger an inferiority complex, *impostor syndrome*, defined as "feeling like a fraud who does not belong" (40). One defense mechanism against it is industriousness. Impostor syndrome is increasingly studied in students from minority groups (ethnic, socio-economic, sexual orientation, gender) and is conceptualized as a trauma resulting from micro-aggressions and repeated rejections (41–45). Intersected groups such as immigrants, and ethnic minorities, may develop impostor syndrome because of racism, rejection, and socio-economic difficulties. When experiencing school refusal, these participants may have felt that their imposture was revealed: the "good student" had disappeared and been replaced by the "child of immigrants".

Several participants had parents born in former French colonies. These participants repeated the word "shame" when referring to their parents' language, culture, and habits. This finding can be discussed considering post-colonial studies. In France, some immigrants face another intersected challenge: the asymmetrical relations between the host country and countries of origin (46). Powerful historical ties, such as colonization or war, also shape cultural representations of "superior" and "inferior" civilizations. Our participants' shame suggests that they may have internalized the prejudice against the social or cultural "inferiority" of their parents.

Taken together, these findings suggest that academic success may create a paradox for these young people: if they succeed, they will become strangers to their families as they change social class and – for some of them – become representants of a country that has oppressed the one of their parents; if they fail, they will dash their parents' hopes and dreams. Thus, considering that "reasonable parental effort" is a specific criterion for school refusal (1) may oversimplify the situation of families with little confidence in their ability to navigate the school system and faced with contradictory attitudes of their child (ambition, blame, shame, impostor syndrome) (17).

Suspending Integration Into Society: Loneliness

Most of our participants appeared afraid of the judgment of others and had experienced stigma and rejection, but they nevertheless lamented the loss of a group and imagined their peers moving forward without them. This finding suggests that school refusal may confront these adolescents with a blow to their identity formation. Interactionist approaches in social sciences have shown that our identity is a multi-layered, changing, and relational experience, as a result of the outside world's perceptions of us, which are then reflected back onto us: we learn to see ourselves through the eyes of others (47). This mirroring process starts during childhood, within the family and continues at school. In adolescence, the group allows identification with others and with different social roles. As Kestemberg points out "the adolescent only exists through the eyes of others" (48). The literature on migration and racism may also be an interesting framework to discuss our participants' experiences, as they belong to an intersected group. Camilleri proposes three identity-based strategies for immigrants when they are faced with a devaluation, an attack on their self-image (49). The first is to avoid conflict by not seeing oneself as the target of a deprecation. This may be the strategy of our participants, when they report the "humor" of their peers, minimizing their derogatory remarks and refusing to interpret them as racist behaviors. The second strategy consists of confronting the devaluation, and the third allows the construction of a critical identity, where the individual accepts some negative judgments and rejects others. This third strategy allows for integration, in fact; by accepting certain negative judgments, we make our own cultural expectations that were previously unknown to us. Thus, one adopts certain criteria from the host culture and retains others from the culture of the homeland. Of these three strategies, only the first one seemed present in the experiences of our participants.

In this study, our participants experienced feelings of social isolation and worthlessness. Not belonging to a peer group was compared by participants to a rejection from society, an experience that their parents may well have faced when arriving in the host society. This finding suggests that the loss of the group may be particularly significant for adolescents in cross-cultural settings, and this hypothesis could be explored in further studies. On a theoretical perspective, Sayad (31) proposes the feeling of "lasting provisional" in the immigrant that characterizes his or her condition. Indeed, while the immigrant has committed to the host country and the idea of staying there, he or she lives there as if the relocation was temporary. The immigrant finds himself torn between two countries: "on the one hand, the exclusion from the host society which, to varying degrees, affects all immigrants and, on the other hand, the break that is not only spatial from the native land" (31). Adolescents of immigrant parents may be told that they are not French, and in their country of origin they may be told the opposite. Thus, our participants may wonder about where they belong, and where they are desired.

Some of the young people in this study have benefited from therapeutic workshops or groups for adolescents of the same age. One of the functions of these groups may be that the adolescents find crucial moments of doing "nothing" before or after the group, in interstitial places, or outside the host institution. Having in mind only the pleasure of being able to meet themselves and others and knowing that they are accepted are a first step toward an integration into social life. Thus, the effectiveness of group therapies where the adolescents rediscover the value of relationships and can share their experiences, might be worth assessing in underrepresented minority groups.

Limits and Perspectives

We acknowledge several limitations. This exploratory research is based on a small sample from a single country, and therefore we cannot generalize the experience of our participants, limiting the strength of recommendations for future practice. Several points could not be addressed in this work, notably reflections on how to help teachers in these situations, and how to improve collaboration between the care providers and the school (18), as well as the work that can be done with the adolescent's family.

The participants in this study experienced the intersection of generic issues faced by migrant young people and of issues faced by students presenting with school attendance problems. However, it is not possible in qualitative research to assess the relative impact of each factor (migration, school absenteeism) neither on their school trajectories, nor on their subjective experiences (i.e., shame). Assessing distinctive causalities would be possible in further studies using a longitudinal cohort design. Meanwhile, criteria to differentiate the types of school absenteeism should be used with caution in cross-cultural situations, and their validity should be further explored in immigrant and ethnic minority groups.

Among other treatments, the psychotherapies recommended for school refusal are individual cognitive-behavioral, family, and multifamily therapies (50–52). Future randomized controlled trials could assess the efficiency of a transcultural, trauma-informed and inclusive psychotherapy program for school refusal. Similarly, therapeutic workshops and peer groups for school refusal could be evaluated, to address the fear of marginalization with activities supporting self-esteem and a sense of belonging in all members of the group. To model diversity and inclusivity, such interventions should be designed and delivered by a team of care providers from various cultural and ethnic background.

CONCLUSION

In this qualitative study, participants from immigrant and ethnic minority groups experiencing school refusal report the perception of the loss of a group, the shame they feel toward their families and themselves, and the fear of social marginalization. This clinical presentation may challenge the diagnostic criteria for school refusal and contribute to misdiagnosis and reduced access to care for students from underrepresented minorities and intersected groups. Along with assessing parents' customs, culture, immigration history, and experiences of adversity to improve screening and referral to care (17), and in addition to other recommended treatments, transcultural therapies for school refusal should be considered and evaluated to help these students make sense of their experience and increase their sense of belonging, while altogether reducing their academic anxieties.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors upon request, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Inserm Ethical Evaluation Committee (IRB00003888). Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

LB designed the study. CB and LB interviewed the 16 adolescents and young adults and independently analyzed the data. CB, IT, MM, and LB discussed the analysis and results. CB, IT, and LB wrote the manuscript. All authors reviewed the manuscript.

FUNDING

This work is supported by the French National Institute of Health and Medical Research (Inserm), and by the Thellie Foundation project improving access to care for school refusal and QUA*Lab*, the Qualitative and Mixed Methods Lab, a collaboration between the the Yale Child Study Center (New Haven, CT), and Inserm, the Institut National de la Santé et de la Recherche Médicale (Paris, France).

REFERENCES

1. Heyne D, Gren-Landell M, Melvin G, Gentle-Genitty C. Differentiation between school attendance problems: why and how? *Cogn Behav Pract.* (2019) 26:8–34. doi: 10.1016/j.cbpra.2018.03.006
2. Available online at: https://www.education.gouv.fr/en-janvier-2020-l-absenteisme-touche-en-moyenne-68-des-eleves-du-second-degre-public-322778.
3. Dubet F, Duru-Bellat M, Vérétout A. *Les sociétés et leur école*. Emprise du diplôme et cohésion sociale Paris: Seuil (2010).
4. Observatoire des inégalités. Le taux de chômage selon le diplôme et l'âge (2019). Available online at: https://www.inegalites.fr/Le-taux-de-chomage-selon-le-diplome-et-l-age
5. Yang K-E, Ham S-H. Truancy as systemic discrimination: anti-discrimination legislation and its effect on school attendance among immigrant children. *Soc Sci J.* (2017) 54:216–26. doi: 10.1016/j.soscij.2017.02.001
6. Beauchemin C, Hamel C, Simon P, Héran F, editors. Trajectoires et origines: enquête sur la diversité des populations en France. *Grandes Enquêtes*. Paris: Ined editions (2015). p. 622.
7. Brinbaum Y, Moguérou L, Primon J-L. Immigrés et descendants d'immigrés en France. *INSEE Références*. INSEE (2012).
8. Chau K, Baumann M, Kabuth B, Chau N. School difficulties in immigrant adolescent students and roles of socioeconomic factors, unhealthy behaviours, and physical and mental health. *BMC Public Health.* (2012) 12:453. doi: 10.1186/1471-2458-12-453
9. Heyne D. School refusal. In: *Practitioner's Guide to Evidence-Based Psychotherapy*. New York, NY, US: Springer Science + Business Media (2006). p. 600–19. doi: 10.1007/978-0-387-28370-8_60
10. Li A, Guessoum SB, Ibrahim N, Lefèvre H, Moro MR, Benoit L, et al. Systematic review of somatic symptoms in school refusal. *Psychosom Med.* (2021) 83:715–23. doi: 10.1097/PSY.0000000000000956
11. Boussand E, Phan O, Benoit L. School refusal and internet gaming disorder in adolescents: narrative review of literature. *Neuropsychiatrie de l'Enfance et de l'Adolescence.* (2021) 69:241–52. doi: 10.1016/j.neurenf.2021.04.013
12. Egger HL, Costello JE, Angold A. School refusal and psychiatric disorders: a community study. *J Am Acad Child Adolesc Psychiatry.* (2003) 42:797–807. doi: 10.1097/01.CHI.0000046865.56865.79
13. Heyne D, King NJ, Tonge BJ, Cooper H. School refusal: epidemiology and management. *Paediatr Drugs.* (2001) 3:719–32. doi: 10.2165/00128072-200103100-00002

14. Kearney CA. School absenteeism and school refusal behavior in youth: a contemporary review. *Clin Psychol Rev.* (2008) 28:451–71. doi: 10.1016/j.cpr.2007.07.012
15. Broussard C. Facilitating home-school partnerships for multiethnic families: school social workers collaborating for success. *Child Sch.* (2003) 25:211–22. doi: 10.1093/cs/25.4.211
16. Benoit L, Barreteau S, Moro MR. ≪ Phobie scolaire chez l'adolescent migrant ≫, la construction identitaire dans une approche transculturelle. *Neuropsychiatrie de l'Enfance et de l'Adolescence.* (2015) 63:84–90. doi: 10.1016/j.neurenf.2014.05.001
17. Rosenthal L, Moro MR, Benoit L. Migrant parents of adolescents with school refusal: a qualitative study of parental distress and cultural barriers in access to care. *Front Psychiatry*. (2020) 10:942. doi: 10.3389/fpsyt.2019.00942
18. Martin R, Moro MR, Benoit L. School refusal or truancy? School personnel misconceptions about school refusers from immigrant families: a qualitative study. *Front Psychiatry.* (2019). doi: 10.3389/fpsyt.2020.00202. [Epub ahead of print].
19. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care.* (2007) 19:349–57. doi: 10.1093/intqhc/mzm042
20. Benoit L, Cottin P, Moro MR. What is a "Maison des adolescents"? a history of integrated youth health care services in France. *Early Interv Psychiatry*. (2018) 12:1000–5. doi: 10.1111/eip.12680
21. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. 5th ed. Washington, DC: American Psychiatric Publishing (2013).
22. Smith JA, editor. *Qualitative Psychology: A Practical Guide to Research Methods*. 2nd ed. Los Angeles, Calif: SAGE Publications (2008) p. 276.
23. Antoine P, Smith JA. Saisir l'expérience : présentation de l'analyse phénoménologique interprétative comme méthodologie qualitative en psychologie. *Psychologie Française.* (2017) 62:373–85. doi: 10.1016/j.psfr.2016.04.001
24. Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant.* (2018) 52:1893–907. doi: 10.1007/s11135-017-0574-8
25. Kearney C, Benoit L. Child and adolescent psychiatry and underrepresented youth with school attendance problems: Integration with systems of care, advocacy, and future directions. *J Am Acad Child Adolesc Psychiatry.* (2022).
26. Jones AM, Suveg C. Flying under the radar: school reluctance in anxious youth. *School Ment Health.* (2015) 7:212–23. doi: 10.1007/s12310-015-9148-x
27. Moro MR, Peiron J, Peiron D. *Enfants de l'immigration, une chance pour l'école: entretiens avec Joanna et Denis Peiron*. Paris: Bayard (2012).
28. Cheng AS. Narratives of second-generation Asian American experience: Legacies of immigration, trauma, and loss [Ph.D.]. Massachusetts, United States: University of Massachusetts Amherst (2005).
29. Moro MR. Parents and infants in changing cultural context: Immigration, trauma, and risk. *Infant Ment Health J.* (2003) 24:240–64. doi: 10.1002/imhj.10054
30. Moro MR, Baubet T. *Psychopathologie Transculturelle*. De l'enfance à l'âge adulte Paris: Masson (2009). doi: 10.1016/B978-2-294-70434-5.00017-4
31. Sayad A. La Double Absence. Des illusions de l'émigré aux souffrances de l'immigré. Le Seuil (2016). p. 303
32. Peter B. The second individuation process of adolescence. *Psychoanal Study Child*. (1967) 22:162–86. doi: 10.1080/00797308.1967.11822595
33. Catheline N, Marcelli D. Psychopathologie de la scolarité: de la maternelle à l'université (3rd edition). Issy-les-Moulineaux: Elsevier Masson (2012).
34. Benoit L, Harf A, Sarmiento L, Skandrani S, Moro MR. Shifting views and building bonds: Narratives of internationally adopted children about their dual culture. *Transcult Psychiatry.* (2018) 55:405–27. doi: 10.1177/1363461518764250
35. Benoit L, Harf A, Skandrani S, Moro MR. Adoption internationale : le point de vue des adoptés sur leurs appartenances culturelles. *Neuropsychiatrie de l'Enfance et de l'Adolescence.* (2015) 63:413–21. doi: 10.1016/j.neurenf.2015.04.008
36. Mansouri M. *Révoltes postcoloniales au cœur de l'Hexagone: Voix d'adolescents*. Paris: Presses Universitaires de France (2013) p. 299. doi: 10.3917/puf.mans.2013.01
37. Moro MR. Nos enfants demain: Pour une société multiculturelle. Paris: Odile Jacob (2010). p. 184.
38. Gaulejac V de. *La névrose de classe: Trajectoire sociale et conflits d'identité suivi d'une lettre d'Annie Ernaux*. Paris: Payot (2016). p. 368.
39. Bourdieu P. *Questions de Sociologie*. Paris: Les Editions de Minuit (1980). p. 268.
40. MacInnis CC, Nguyen P, Buliga E, Boyce MA. Cross-socioeconomic class friendships can exacerbate imposturous feelings among lower-SES students. *J Coll Stud Dev.* (2019) 60:595–611. doi: 10.1353/csd.2019.0056
41. Jaremka LM, Ackerman JM, Gawronski B, Rule NO, Sweeny K, Tropp LR, et al. Common academic experiences no one talks about: repeated rejection, impostor syndrome, and burnout. *Perspect Psychol Sci.* (2020) 15:519–43. doi: 10.1177/1745691619898848
42. Romanelli F. Reflections of a First-Generation College Student, American, and Academician. *Am J Pharm Educ*. (2020) 84:ajpe8007. doi: 10.5688/ajpe8007
43. Simon M. STEMming Within a Double Minority: How the Impostor Syndrome Affects Black Women Ph.D. Students. *Int J Mult Res Approaches.* (2020) 12:185–201. doi: 10.29034/ijmra.v12n2a2
44. Bravata DM, Watts SA, Keefer AL, Madhusudhan DK, Taylor KT, Clark DM, et al. Prevalence, predictors, and treatment of impostor syndrome: a systematic review. *J Gen Intern Med.* (2020) 35:1252–75. doi: 10.1007/s11606-019-05364-1
45. Sonnak C, Towell T. The impostor phenomenon in British university students: relationships between self-esteem, mental health, parental rearing style and socioeconomic status. *Pers Individ Dif.* (2001) 31:863–74. doi: 10.1016/S0191-8869(00)00184-7
46. Hermans HJM, Kempen HJG. Moving cultures: The perilous problems of cultural dichotomies in a globalizing society. *American Psychologist.* (1998) 53:1111–20. doi: 10.1037/0003-066X.53.10.1111
47. Strauss AL. *Mirrors and Masks : the Search For Identity*. The Free Press Glencoe, IL (1959).
48. Kestemberg E. L'identité et l'identification chez les adolescents. *La psychiatrie de l'enfant.* (1962) 5:441.
49. Camilleri C. Les stratégies identitaires des immigrés. In: *L'identité, L'individu, Le groupe, La société*. Sciences Humaines Editions, Auxerre.
50. Roué A, Harf A, Benoit L, Sibeoni J, Moro MR. Multifamily therapy for adolescents with school refusal: perspectives of the adolescents and their parents. *Front Psychiatry*. (2021) 12:624841. doi: 10.3389/fpsyt.2021.624841
51. Maynard BR, Heyne D, Brendel KE, Bulanda JJ, Thompson AM, Pigott TD. Treatment for school refusal among children and adolescents: a systematic review and meta-analysis. *Res Soc Work Pract.* (2018) 28:56–67. doi: 10.1177/1049731515598619
52. Elliott JG, Place M. Practitioner review: school refusal: developments in conceptualisation and treatment since 2000. *J Child Psychol Psychiatry*. (2019) 60:4–15. doi: 10.1111/jcpp.12848

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers | Frontiers in Psychiatry

REVIEW
published: 09 June 2022
doi: 10.3389/fpsyt.2022.866323

School-Based Mental Health Initiative: Potentials and Challenges for Child and Adolescent Mental Health

Kelly Y. C. Lai[1]*†, Se-Fong Hung[1], Hannah W. S. Lee[2] and Patrick W. L. Leung[2]*†

[1] Department of Psychiatry, The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR, China, [2] Department of Psychology, The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR, China

OPEN ACCESS

Edited by:
David Cohen,
Sorbonne Universités, France

Reviewed by:
Say How Ong,
Institute of Mental Health, Singapore
Lilly Augustine,
Jönköping University, Sweden

***Correspondence:**
Kelly Y. C. Lai
kellylai@cuhk.edu.hk
Patrick W. L. Leung
pleung@cuhk.edu.hk

† These authors have contributed equally to this work

Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

***Received:** 31 January 2022*
***Accepted:** 17 May 2022*
***Published:** 09 June 2022*

Citation:
Lai KYC, Hung S-F, Lee HWS and Leung PWL (2022) School-Based Mental Health Initiative: Potentials and Challenges for Child and Adolescent Mental Health.
Front. Psychiatry 13:866323.
doi: 10.3389/fpsyt.2022.866323

School-based mental health support services allow children and adolescents easy access to services without requirement of traveling to clinics and hospitals. We describe a School Mental Health Support Scheme (SMHSS) piloted in Hong Kong and discuss the challenges and learnings from the experience. This conceptual paper argues that accessibility is not the only advantage of such services. Teachers are significant others in child development, alongside with families. They play a central role in impacting the children's/adolescents' needs for competence and adult attachment, while schools provide an expanded social network of peers for one's social relationship. The fulfillment of these needs has powerful implications in the mental health of the children/adolescents. Teachers can help students to develop a sense of competence with self-worth and self-identity *via* providing guidance and feedback, whether they be on one's strengths or weaknesses, with acceptance, tolerance and unconditional positive regard. Particularly, the latter define a form of teacher-student relationship or adult attachment that offers the children/adolescents emotional security and nourishment, protecting them from failings and adversities. Teachers can also supervise and guide their students' social development with peers at schools. A recent meta-analysis has found preliminary evidence that those school-based mental health services integrated into the teachers' routine teaching activities are more effective. Teachers, who are overworked and stressed by the schools' overemphasis on academics and grades, have yet to fully grasp their unique roles in supporting students with mental health needs. This paper ends by advocating a paradigm shift in which both the healthcare professionals and educators should forge a mutually beneficial collaboration in jointly enhancing the mental health of children/adolescents at schools.

Keywords: mental health, school-based services, schools, teachers, healthcare professionals

INTRODUCTION

In our highly competitive world, children and adolescents are living in an increasingly stressful environment, with the need to succeed permeating down from the adult world to the world of adolescents and even very young children. Educational achievement is pushed to the forefront of children's lives, creating stress which hugely impacts their mental health, physical health, family relationship, and social relationship (1, 2). By adolescence, one in seven youths was diagnosed with at least one type of mental disorders (3, 4). Kessler et al. (5, 6) reported that most adult mental health disorders began during childhood and adolescence, with half of the adult cases having an onset at the age of 14 or before. A more recent review showed an even earlier onset (7). To make matters worse, only around 20% of these cases received treatment (8). Without effective treatment, adverse effects were found to persist into adulthood, (7) impeding growth, life opportunities, and wellbeing (5). As a result, effective preventative measures and prompt intervention during childhood and adolescence should be the top priorities in the delivery of mental health care.

Besides families, schools represent the second social environment where children and adolescents spend a lot of their time, and on which a large part of their learning and development depends. Given the above, schools become the venue where early signs of mental health problems can be detected and where access to intervention can be provided promptly (9). This recognition has led to the rise of school-based mental health services, with the aims of promoting mental health awareness, as well as prevention and amelioration of students' mental health problems (10). A recent meta-analysis reported preliminary supportive findings of small-to-medium effect sizes of school-based mental health services in reducing student mental health problems, but strategies that were specifically integrated into teachers' routine teaching activities recorded a larger effect size (11). Yet, teachers were often uncertain about their roles in supporting their students with mental health problems (12). Some even felt that it was beyond their roles since they were not trained in mental health (13).

This present conceptual paper will discuss critically the roles of schools and teachers in the development of children and adolescents. We will review one pilot School Mental Health Support Scheme (SMHSS) in Hong Kong as an example to highlight the challenges and learnings, and look to the ways forward. We will advance the thesis that ready access to mental health services for children/adolescents at schools is not the only advantage of school-based mental health services. Teachers at schools have powerful and unique roles in impacting child development, including mental health, which cannot be substituted by mental health professionals at hospitals/clinics. Above all, a paradigm shift is suggested, in which healthcare professionals and school administrators/teachers should take on an expanded vision of their roles and functions and make a coordinated and mutually beneficial effort to support and optimize the development of students with mental health problems at schools.

BACKGROUND OF THE STUDENT MENTAL HEALTH SUPPORT SCHEME (SMHSS) PILOTED IN HONG KONG

The Student Mental Health Support Scheme (SMHSS) is a pilot school-based program conducted in Hong Kong mainstream schools to examine its feasibility, reactions from different stakeholders, and potential challenges and obstacles. In the following, we will first discuss academic performance as one key stressor for children and adolescents, particularly in Hong Kong, to be followed by a succinct description of the pilot SMHSS, and finally its main challenges and learnings.

Education in Danger of Becoming a Single-Minded Pursuit on Academic Excellence

Currently, there is a growing trend worldwide for schools to put greater sole emphasis on academic performance. The rise of such a trend is urged on by the vigorous competition among students since good academic achievement means entry to better universities, improved job prospects, and improved financial stability (14). These concerns lead to a similarly rising trend of competitions among schools regionally and nationally since academic scores are often taken to measure the success of schools (15). These high-stake assessments and competitions place a massive amount of stress on schools, which in turn push students hard to perform well academically (16, 17).

When education becomes a single-minded pursuit of academic excellence, it can "make or break" a child. Students who are less academically able may feel side-lined, demoralized, and inferior (18). They may face frequent criticisms from adults (19) or bullying and discrimination from their peers (19–22). In the drive to pursue academic excellence, students' non-academic potentials may be overlooked and alternative opportunities to foster their development neglected. Growing up under such relentless pressures to achieve, some students inevitably develop mental health problems, which, in turn, can lead to academic under-performance, thus running a downward spiral (23, 24).

In Hong Kong, the pursuit of academic excellence is particularly prominent with wide ranging ramifications, given that such value on academics is rooted deeply in traditional Chinese culture. It is also seen as evidence of well-functioning children and successful parents (25, 26). Children rendering poor academic performance are often frowned upon, blamed for their lack of efforts, and labeled as a "failure," leading to a sense of guilt in themselves and a loss of "face" for their families. These views lead to a strong goal orientation and intense competition among Hong Kong students, whose purpose of learning is to out-perform others instead of enjoying intrinsically the learning processes (27).

As a result, immense pressure is piled onto Hong Kong children from a young age. At schools, children face regular tests and examinations. With endless amounts of homework, drilling, and extra tuition, Hong Kong students have little time for relaxation and leisure activities (28). Academic goals become their sources of high anxiety (29, 30). A 6-year longitudinal study particularly indicated that Hong Kong adolescents suffered from increasing hopelessness and reduced life satisfaction (31).

Yet, over-emphasis in academic excellence and grades is not a phenomenon specific to Hong Kong. It is also prevalent in eastern and southern Asian countries, like Singapore, (32) South Korea, (28) or even in Western countries like the USA (33). This overemphasis not only creates stress for students, but also equal stress on teachers, who thus devote a large amount of classroom time to deliver academics and prepare students for tests and examination (34). This in turn results in depriving students of other social experiences and interactions (35). Most teachers do care for the holistic development of children, but they also feel that they already have too many responsibilities, are overworked, and highly stressed (36).

Mental Health Demands and Services for Children and Adolescents in Hong Kong

In Hong Kong, mental health services rely heavily on specialist Child and Adolescent Mental Health Services (CAMHS), which are publicly-funded and hospital-based. While there are community services providing mental health care, these tend to be piecemeal, lacking proper organization and support to them. There is also a lack of collaboration among hospital-based specialists and community practitioners, as well as across different professional disciplines involved in the care of children and adolescents, such as healthcare, education, and welfare. This lack of coordination means that the efforts and effectiveness of mental health care for children and adolescents are severely hampered. Yet, schools represent a social environment where significant challenges and opportunities on child development pervade and therefore presents an appropriate setting for coordinated intervention to take place. Furthermore, it is becoming increasingly evident that the single-minded focus on academic pursuit has serious mental health consequences for Hong Kong students. Against this background, a pilot school-based mental health support service, SMHSS, is developed to strengthen the support to students with mental health problems and to maximize the schools' potentials to positively influence the development of their students. Mental health problems, within the remit of the SMHSS, are broadly defined and include psychiatric symptoms of varying severity, ranging from subclinical to full-blown clinical levels. The full range of psychiatric disorders such as attention-deficit/hyperactivity disorder, autism spectrum disorder, oppositional defiant disorder, conduct disorder, anxiety disorders, depression and psychosis are included.

Aims and Operation of the SMHSS

With an emphasis on multi-disciplinary collaboration within the school setting, the SMHSS aims at (1) strengthening the support to students with mental health problems through early identification and prompt access to interventions, (2) equipping teachers and school social workers with the knowledge and skills to provide support to these students, and (3) encouraging and empowering schools to provide a more nurturing and less stressful environment for all students. In each participating school, a pledge of full support must be committed by the school senior management (Principal/Vice-Principal). A multi-disciplinary team is set up to coordinate services at schools, with an Advanced Practice Nurse (APN) from the public-hospital CAMHS, a designated teacher [i.e., special educational needs coordinator (SENCO)], and a school social worker as core members. SENCOs in Hong Kong are teachers who are given additional training and protected time to cater for the special educational needs (SEN) of students. These students are those with physical and mental disabilities, including mental disorders such as anxiety, depression, attention-deficit/hyperactivity disorder, autism spectrum disorder, etc. Besides the SENCO, other involved school personnel, e.g., other teachers or the school social worker, do not have protected time. The schools also do not have extra funding. The multi-disciplinary team is responsible for assessing and managing the mental health, educational and psychosocial needs of students with mental health problems, and provides the indicated treatment and school-based support. This team also coordinates required services to be provided by other school teachers and educational psychologists, as well as specialists of hospital-based CAMHS, including psychiatrists and clinical psychologists. These hospital-based specialists are encouraged to communicate directly with the school personnel for updates and discussions to forge a close working relationship with the school personnel. The students' progress is monitored through regular multi-disciplinary case conferences held 3–4 times during the school year, as well as working meetings as and when required.

The role of different professionals is delineated as much as possible to reduce duplication and maximize expertise. The SENCOs, with the advice and support of educational psychologists, work with other teachers to implement educational-based management plans, and monitor students' progress. Students' educational needs may be supported by, for example, special remedial measures, as well as strategies to boost confidence and self-esteem, reduce study stress, and improve motivation. School social workers provide socio-emotional support to the students and their parents. They also help link up community resources to match the students' and their families' needs. When necessary, family intervention is referred to relevant outside social service agencies.

Training is provided to participating schools to enhance their knowledge on student mental health and relevant management skills through a 30-h formal series of lectures, workshops and hospital-based clinical attachments. Informal channels of training are effected through working meetings, multi-disciplinary conferences, *ad hoc* discussions and experience sharing, which help to put knowledge into practice, and fine-tune assessment and intervention skills at schools.

The SMHSS is spearheaded and coordinated at the highest level by the government ministry on health care in Hong Kong, namely, the Food and Health Bureau. It establishes a coordinating task force involving relevant disciplines from various government ministries (e.g., the Education Bureau and the Social Welfare Department), statutory bodies (e.g., Hospital Authority), and non-governmental organizations (e.g. NGO), etc.

School and Student Recruitment

Invitation was extended to all schools in Hong Kong by the Education Bureau to solicit their interest in participating in the pilot phase of the SMHSS. Interested schools were then selected by the task force, taking into account a range of factors such as each school's estimated number of students requiring the services of the SMHSS, and the workload that could be managed by the SMHSS teams. A balance was also sought to select schools from across the whole of Hong Kong so as to reduce the bias toward particular socio-economic strata.

Students supported by the SMHSS are identified through two routes. One is through nomination by teachers and school social workers. Another route is through a multi-tiered screening program using Spence Children's Anxiety Scale (SCAS) (37) to identify students with anxiety symptoms. The SMHSS protocol recommends screening of students in the fourth year of primary school (aged 9–10) and the first year of the secondary school (age 12–13), but schools can opt to screen another student year if they wish.

CHALLENGES AND LEARNINGS FROM THE PILOT RUN OF THE SMHSS

Most published studies on school-based mental health services are from Western countries. Their application in non-Western societies is still relatively understudied, with the exception of one recent Singapore study (38). Cultural differences, such as expectations of children's behavior, the emphasis on academic achievement, and the stigma of mental illnesses in different societies, can influence how mental health services are perceived and received at schools. In the following sections, we will discuss the challenges experienced and learnings accumulated from the delivery of the SMHSS in Hong Kong, and suggest ways forward.

Feedback From Stakeholders

Teachers and school social workers appreciate the support provided by healthcare professionals in advising and managing the needs of the students with mental health problems. They find access to clinical information easier and have developed a better understanding of the students' needs. Students and parents in return feel a more supportive school environment. Some students, however, express reservations about skipping lessons to attend the intervention sessions conducted at schools.

Healthcare professionals find working within schools challenging because of the need to understand the culture of the collaborating schools, the interpersonal dynamics, and the personalities involved in order to build up trust that renders the collaboration effective. This requires repeated dialogues, exchanges and sharing. With time, they feel that schools are able to develop a more holistic understanding of the impacts of mental health symptoms on students' functioning and be more accommodating and supportive. Working within the schools also helps them contextualize the students' difficulties and find ways of support that are feasible and relevant, fitting in with what the schools and the families can provide or accept (10). Understanding both the individual and environmental contexts makes dialogue between healthcare professionals and school personnel more relevant and meaningful. In contrast, working solely within hospital-based services, such as the specialist CAMHS, the healthcare professionals may not really know about the real life of the children and adolescents as students outside the hospital setting and thus hamper the applicability of their intervention.

Yet, healthcare professionals are struck by some schools' view that it is the remit of healthcare professionals to provide intervention. Furthermore, arranging a time to meet with the students can also be difficult, dependent on the students' schedules, willingness to skip lessons, and teachers' willingness to release them from lessons. These logistic difficulties mean that healthcare professionals cannot readily meet the students as expected, despite that they are physically present at schools. All these reflect the tussle of priorities between mental health and academics. It is a mindset that needs to be addressed since academic achievement and mental wellbeing are not mutually exclusive choices to be made, but are themselves highly interlinked.

Case Nomination, Screening, and Workload

Nomination by teachers and school social workers is one of the two routes students with mental health problems are referred to the SMHSS. The clinical profiles of the nominated students confirm that they have significant psychopathology, with the majority suffering from neurodevelopmental, anxiety and depressive disorders. Schools are mostly concerned about their emotional and behavioral problems, school attendance problems, study stress, and self-harm behavior. Our experience echoes that of existing literature that teachers and school social workers are well-placed to identify students with mental health needs.

Most of the students identified through screening turn out to have clinically significant anxiety symptoms, but they had not consulted mental health professionals in the past, and were not suspected to have mental health problems by their schools. Further assessment finds most of them to be in need of intervention. However, the percentages agreeing to receive intervention were low, below 60%. Various barriers to services, e.g., stigma, probably exist. The issue of stigma will be discussed in a later section.

Screening brings up many workload and logistics issues. From the schools' perspective, issues such as scheduling the screening exercises into the busy school calendar, allocating time and staff to supervise the questionnaire completion, and the subsequent follow-up of these students are perceived to be burdensome. Crucially, screening uncovers many students previously not suspected to have mental health problems and schools do not feel they have the resources to cope with the extra caseloads. These problems have dampened the enthusiasm for screening. However, screening allows early identification and early intervention. It is essential that school administrators are aware of its benefits, so that adequate manpower and resources can be found to ensure that schools have the capacity to provide more dedicated support to the students who have hitherto undiagnosed mental health problems. However, this is easier said than done. In the sections below, we will return to these school resource and capacity issues in greater depth.

The Challenge of a Paradigm Shift for Healthcare Professionals and School Administrators/Teachers

The Roles of Mental Health Professionals in the SMHSS

Our experience of this pilot trial finds that it is still the healthcare professionals who are primarily involved in delivering intervention and support, while the direct involvement of school personnel is still less than expected. The aim of the SMHSS to empower and build up schools' capacity to support their students is not gaining a great deal of mileage. It may be that old habits die hard and do not get changed easily. There is a tendency for the healthcare professionals to become too "enthusiastic" and take up too much work at schools. This unwittingly goes against one main aim of the SMHSS to build schools' capacity *via* ample participation of the school personnel in the Scheme. Working toward a paradigm shift, a more precise collaborative framework with further well defined roles should be drawn up. Mental health professionals need to remember that the needs of children and adolescents with mental health problems are complex, and are often linked to different contexts and systems. Keeping a focus on empowerment and effective collaboration, healthcare professionals need to have multiple perspectives of their role. First, in fitting with their professional training, they assess and diagnose the mental state and the areas of concern of the referred students. Second, they contextualize the students' needs and difficulties within the students' family and school systems, therefore introducing an ecological perspective and bringing into focus the interactive nature of those risk factors in impacting the students' functioning. This emphasis on the influences of different systems helps put the need for multi-disciplinary collaboration into context. Third, by increasing the schools' knowledge and understanding of mental health problems and how they impact on students' functioning, and through the active involvement of school personnel in supporting their students, they encourage schools to pay attention to their student's mental health and to be cognizant of the benefits of a supportive and accepting school environment on students' functioning. All these perspectives need to be borne in mind so as to put in focus the need for collaboration and the complementary roles of healthcare, educational, and social care professionals in impacting and optimizing students' development, including mental health. The results of a recent meta-analysis of the effectiveness of school-based mental health services echo similar implications (11). Direct involvement of healthcare professionals in running the services at schools does not necessarily produce the best results. Instead, mental health services integrated into teachers' regular teaching activities produce a larger effect size.

The Roles of Teachers/Schools on Child Development

Teachers, on the other hand, need to truly recognize the important roles they play in their students' development. Schools are charged with the responsibility of providing an environment for children to learn, where they develop their potentials, recognize their strengths and weaknesses, build self-confidence and a sense of mastery, and cultivate a life orientation. It is a place where they build up resilience by developing skills to manage life's many challenges. These are the developmental tasks that are crucial during childhood and adolescence. Erik Erikson (39, 40) proposed two psychosocial challenges during these periods: industry vs. inferiority in childhood, and identity vs. role confusion in adolescence. Successful coping to these two challenges results in a sense of industry in which children are confident of their abilities and are willing to challenge themselves, as well as a sense of identity that includes an awareness and acceptance of one's strengths and weaknesses. Ryan and Deci (41, 42), in their self-determination theory, supplemented Erikson's theory by highlighting three basic psychological needs, namely, the need for autonomy, competence, and relatedness. Schooling necessarily puts students in a situation, where their performance is evaluated and compared with peers by teachers. In consequence, the students' sense of competence is determined not only by their own actual task accomplishment, but also by teachers' or schools' expectations and feedback (43). Thus, teachers' or schools' verdicts of academic success result in a sense of industry and confidence about their abilities. Contrarily, when the verdicts are negative, students feel inferior, thus undermining the development of their self-esteem and sense of competence. This is where teachers or schools, as inevitable performance evaluators, have their unique and powerful roles in impacting students toward or away from meeting their developmental challenges. The pursuit of academic grades may be a worldwide reality, yet in providing feedback, whether it be on one's strengths or weaknesses, teachers can show their acceptance and unconditional positive regard toward their students (44, 45). It is to accept the students as who they are, regardless of their ability, achievements, background, and character (46). When teachers do so, it separates the students' behavior and performance from their innate, original self, allowing them to feel inherently valued and respected regardless of their mistakes, flaws, or performance. Furthermore, teachers' acceptance allows students to feel secure, which in turn encourages them to explore their limits and discover their abilities without fear of judgement or rejection (47). They can be bolder to pursue their full potentials and become resilient toward future challenges (47). By acting as nurturing and significant adults, teachers encourage students to develop a trusting relationship with them. Such secure attachment and meaningful relatedness will foster students' positive development, including mental health.

Teachers as attachment figures are especially important for at-risk students, when their parents or families are unable to provide the secure attachment, or who have experienced adversities in growing up (48). Under these circumstances, teachers can act as alternative, substitute attachment figures to provide the security and trust, which can buffer against the damages resulting from behavioral, psychosocial, and demographic risks, such as poverty, childhood abuse, maternal depression, as well as restore behavioral, psychological and social functioning (49–51). At-risk children and adolescents can learn that despite their adverse family environment, yet in another social environment, i.e., schools, they can be cared for and nurtured by their teachers, laying a foundation for healthier development.

Rutter et al. (52) published a landmark study, way ahead of its time, on the significant impacts of schools on the behavior and attainment of their students. Unfortunately, there has not been a huge literature ensuing. Yet, from those available studies, they are generally supportive of the importance of schools/teachers in facilitating or impeding students' development. For example, teachers demonstrating high levels of acceptance, warmth, and unconditional positive regard had students who showed positive educational outcomes, self-competence, motivation, and achievement, (53) as well as psychological adjustment, (54) even among those from disadvantaged background (52). Rucinski et al. (55) reported lower rates of depressive symptoms and externalizing behaviors such as aggression when the quality of teacher-student relationship was positive. The latter also helped to free students from discrimination and stigmas, and increased their help-seeking behavior (56).

Indeed, teachers may be well aware of the impacts mental health problems have on their students' functioning, and the support these students need. Unfortunately, our local teachers are often overworked with large classes (up to 40 students per class), and are both physically and mentally stressed out by fierce competition in securing high grades for their students, the attainment of which defines their success and career as teachers. This narrows the teachers' focus of themselves as mere imparters of book knowledge. Being highly stressed, they are unlikely to exhibit an "enthusiasm" to broaden their roles to be educators of the whole person, or to manage their students' difficulties arising from their mental health problems. These stress, predicament, and ambivalence of our teachers are not likely to be unique to Hong Kong. To address these issues, educators, including school administrators and teachers, may need to revisit and re-kindle their broader vision as educators. This is very much in line with recent calls in other developed countries like the UK and Australia for an educational reform or a policy change in which both academic achievement and students' wellbeing should be focused (28, 57).

With a broad vision in education, a multi-tiered system of mental health care within schools can be established to span prevention to targeted intervention (58). At the universal preventive level, school administrators/teachers, school social workers, as well as students can be mobilized to help develop school-wide strategies to build a nurturing, accepting and tolerant school climate so that students can feel safe, connected, supported, and involved (59, 60). This would be in keeping with Ryan and Deci's theory of the need for relatedness for optimal psychosocial development of each individual (41, 42). At a program level, teachers are well-placed to help design and deliver mental health awareness and promotion programs, as well as to incorporate into their regular curriculum activities to build students' resilience by teaching emotion regulation, problem-solving and social skills, (17) as well as providing the opportunities for students to develop their talents in non-academic areas. Government education officials and school administrators must be fully cognizant and supportive of such needs in the school curriculum. Within the classrooms, teacher-administered behavioral management and psychosocial intervention have been shown to be effective in improving students' externalizing and internalizing behaviors (61). Involving teachers in the delivery of these programs can empower them to have a more prominent role in supporting students, and promote a school and classroom environment that is accepting, nurturing, and conducive to positive learning experiences and good mental health. Furthermore, evidence-based treatment for specific disorders such as anxiety and depression can be delivered in group or individual format by trained school social workers or trained teachers. Training can be provided by mental health professionals, whose roles can be more consultative, assisting in case conceptualization, providing advice, training, and supervision on intervention, and hence building schools' capacity. When clinical needs arise, they will still be on hand to provide direct intervention and hospital-based services. Adopting this multi-tiered approach will enable each discipline, including mental health, education and social work, to better delineate their roles and to contribute meaningfully and effectively within their areas of professional expertise and spheres of influences in a coordinated manner (62).

The Challenge of Stigma and Priorities

Stigma is one of the critical barriers to help-seeking (63). The dissonance between one's preferred self/social identity and the stereotypes of mental illnesses (e.g., mental illnesses representing personality weakness, being "not normal," or not trying hard enough) leads individuals to anticipate negative consequences such as shame, rejection, and discrimination. Worries about disclosure and confidentiality also contribute to the reluctance to seek help (63).

Furthermore, the Chinese culture is regarded as a "face" culture, in which "face" represents one's public image and reputation, so that one's worth is bestowed by others. Compared to western cultures, Chinese culture endorses a higher level of stigma toward mental illnesses, and this difference is accounted for by the concern about "face" (64). Chinese parents of children with mental illnesses are prone to self-stigma as they perceive a lowering of their social standing (65). They are also quick to internalize stigma with a sense of self-blame and responsibility (66). Children brought up in this "face" culture can develop self-stigma from a young age, (67) which is generated from the public stigma that they experience in the community.

The concern about stigma and its influence on help-seeking are evident among students supported by the SMHSS. Some indicate a reluctance to meet healthcare professionals during the school days, as they are worried that other students may notice and start gossiping. Some of the students screened positive will outright decline intervention because of such concern. These findings echo those identified in the western literature (68, 69). Therefore, although providing services in schools allows easier access, the proximity of peers and teachers, and the worries about confidentiality and negative labeling actually work against the willingness to receive services.

In Hong Kong, given the high priority given to academic excellence, another reason often provided for declining intervention is the need to keep up with academic demands. Some students express that they do not want to skip lessons to meet healthcare professionals, while some teachers do not want to release students during lessons. This tussle of priorities between academics and mental health, as if they are mutually exclusive and there has to be a choice one over the other, have to be addressed head on. The SMHSS should make enhanced efforts to educate about mental illnesses and reduce stigma. School administrators/teachers, parents, and students should be guided to understand the reciprocal negative influences of mental illnesses and academic functioning over each other.

Such knowledge may prompt them to accord more urgency to improving mental health and be more willing to accept or render help, while setting realistic and achievable academic goals.

The environment in which help is provided is also important. Adolescents are more likely to seek help if they feel able to trust those from whom they seek help, and this trust includes ensuring confidentiality, feeling listened to and taken seriously, while the care-providers are caring and non-judgmental (69). If the teachers can provide such trusting and accepting environment at schools for those students in need of mental health services, the concerns for stigma and the artificial competing priorities between academics and mental health can be much allayed. The students can feel less hesitant about help seeking and reap the benefits of a more accessible SMHSS.

The Challenge of Manpower and Sustainability

The model of the SMHSS is manpower intensive. It creates extra workload for both teachers and school social workers, when they are expected to become more involved in providing support for students who are already known to have mental health problems. The screening at schools also uncovers more students who are previously not known to have mental health problems. The SMHSS also generates extra workload for hospital-based CAMHS because of the requirement to provide clinical training/supervision at schools. Given the unavoidable limited manpower available, its long-term sustainability needs to be considered. First of all, the number of students directly supported by the SMHSS has to be kept at a manageable level without compromising the quality and intensity of the intervention delivered. To achieve this, it is all the more important that the multi-disciplinary professionals involved must take on a paradigm shift to expand the vision of their roles. Healthcare professionals, for example, must see that there are significant others, e.g., teachers, whose involvement within their areas of expertise needs to be mobilized and empowered to support the varied and complex needs of children and adolescents with mental health problems. They have to reach out to them and take lead to forge a coordinated effort to support them. Teachers have the advantage of having a lot of contact time with their students and are therefore in a position to develop nurturing and accepting relationships with them, while at the same time, coaching them to gain a sense of mastery and self-confidence from the schooling experience, regardless of the presence or absence of mental health problems. These opportunities are unique to teachers at schools and cannot be replaced by healthcare professionals at hospitals. Therefore, the advantage of the SMHSS is not solely related to easy accessibility, and it is not a replacement for specialist CAMHS. More importantly, the SMHSS is intended to capitalize on the powerful influences of teachers/schools in optimizing students' development. The educators, school administrators and teachers alike, should thus take on a paradigm shift in expanding their roles, or in fact, resuming their broader vision, to acknowledge their potentials in being the significant others to impact their students' development. Furthermore, the sustainability of the model requires a political will from the senior government officials in health care and education at the highest level to acknowledge not only the important roles schools can play, but also to mobilize extra manpower and resources, e.g., protected time and extra funding, for the schools/teachers to proactively involve in the support of students' mental health needs. Despite the intensity of the manpower and resources required, healthcare professionals and educators delivering mental health services collaboratively at schools can generate a synergistic effect that benefits their students' development in multiple interrelated pathways: in education, competence, self-identity, mental health, and social relationship, etc, just to name a few. The outcomes will prove to be worthy of the added investment of resources to healthcare services and schools. Indeed, preliminary studies have already confirmed that teachers have a significant role in influencing their students' functioning and mental health (11). In future, health economics research needs to be conducted to indicate that the added resources for early assessment and intervention of students with mental health problems will bring considerable saving for the community in reducing the chronicity of their mental health problems and thus health cost, welfare cost, and loss of productivity, etc (38).

So far, the lessons from the pilot SMHSS in Hong Kong teach us that a paradigm shift from both our healthcare professionals and school personnel is vital for its success and long-term sustainability, as echoed in many other countries (12, 13). This shift is not entirely easy for a range of reasons, including old habits, unclear role delineation, heavy workload or priority tussle. It is going to take some time. More theoretical development, more supportive research, and more actual field trials may be required in order to get everyone on board with a paradigm shift toward a co-sharing/co-ownership, multi-disciplinary collaboration among educators and hospital-based healthcare professionals at schools.

CONCLUSION

Mental health problems in children and adolescents have been posing a serious concern because of their high prevalence, complexities, and increasing service demand. In Hong Kong, a School Mental Health Support Scheme (SMHSS) was piloted with hospital-based healthcare professionals joining hands with school personnel to conduct mental health services at schools. Theories in child development have long suggested that besides family members, teachers are also significant others who can shape the developmental trajectory of children and adolescents. A school environment that provides accepting and nurturing relationships can foster their students' sense of competence, self-esteem and self-worth. Yet, many teachers/schools do not seem to leverage to the full their potential for positive impacts. As such, school-based mental health programmes should not only make services more readily accessible to children/adolescents. They should aim at drawing on teachers'/schools' powerful and unique roles in providing a school environment to meet the developmental needs of children and adolescents in competence, self-identity, attachment and peer relationship. The success in dealing with these developmental challenges is crucial for their mental health. These are roles and opportunities which cannot be taken over by healthcare professionals at hospitals. This conceptual paper draws on the lessons learned from running the SMHSS to call for a paradigm shift amongst hospital-based healthcare professionals and educators to broaden their vision and expand their roles to join force together at schools, capitalizing on their enormous potential in dealing with the sources where children's developmental needs may be unattended or frustrated with mental health problems emerging and perpetuating.

AUTHOR CONTRIBUTIONS

KL, S-FH, and PL conceptualized the themes and messages of this manuscript. KL and HL conducted the literature search and review as well as drafted the initial few versions. KL, S-FH, and PL finalized the manuscript, all involved in final editing and approval of the manuscript. All authors contributed to the article and approved the submitted version.

ACKNOWLEDGMENTS

We greatly appreciate the hard work of the many healthcare professionals, school administrators, teachers, social workers, and educational psychologists involved in this pilot school-based mental health service in Hong Kong, SMHSS.

REFERENCES

1. American Psychological Association. *Stress in America*^{TM} *2020: A National Mental Health Crisis.* (2020). Available online at: https://www.apa.org/news/press/releases/stress/2020/report-october (accessed January 27, 2022).
2. Pascoe MC, Hetrick SE, Parker AG. The impact of stress on students in secondary school and higher education. *Int J Adolesc Youth*. (2020) 25:104–12. doi: 10.1080/02673843.2019.1596823
3. Leung PW, Hung SF, Ho TP, Lee CC, Liu WS, Tang CP, et al. Prevalence of DSM-IV disorders in Chinese adolescents and the effects of an impairment criterion. *Eur Child Adolesc Psychiatry*. (2008) 17:452–61. doi: 10.1007/s00787-008-0687-7
4. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: a meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *J Child Psychol Psychiatry*. (2015) 56:345–65. doi: 10.1111/jcpp.12381
5. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National comorbidity survey replication. *Arch Gen Psychiatry*. (2005) 62:593–602. doi: 10.1001/archpsyc.62.6.593
6. Kessler RC, Amminger GP, AguilarGaxiola S, Alonso J, Lee S, Ustun TB. Age of onset of mental disorders: a review of recent literature. *Curr Opin Psychiatry*. (2007) 20:359. doi: 10.1097/YCO.0b013e32816ebc8c
7. Mulraney M, Coghill D, Bishop C, Mehmed Y, Sciberras E, Sawyer M, et al. A systematic review of the persistence of childhood mental health problems into adulthood. *Neurosci Biobehav Rev*. (2021) 129:182–205. doi: 10.1016/j.neubiorev.2021.07.030
8. Weir K. *Safeguarding Student Mental Health: COVID-19 and its Repercussions are Shining a Light on the Critical Need for School-Based Mental Health Services.* (2020). Available online at: https://www.apa.org/monitor/2020/09/safeguarding-mental-health (accessed January 27, 2020).
9. McLaughlin CL. International approaches to school-based mental health: intent of the special issue. *Sch Psychol Int*. (2017) 38:339–42. doi: 10.1177/0143034317714839
10. Fazel M, Hoagwood K, Stephan S, Ford T. Mental health interventions in schools in high-income countries. *Lancet Psychiatry*. (2014) 1:377–87. doi: 10.1016/S2215-0366(14)70312-8
11. Sanchez AL, Cornacchio D, Poznanski B, Golik AM, Chou T, Comer JS. The effectiveness of school-based mental health services for elementary-aged children: a meta-analysis. *J Am Acad Child Adolesc Psychiatry*. (2018) 57:153–65. doi: 10.1016/j.jaac.2017.11.022
12. Honsinger C, Brown MH. Preparing trauma-sensitive teachers: strategies for teacher educators. *Teach Educ J*. (2019) 12:129–52. Available online at: https://www.ateva.org/journal-1/
13. Graham A, Phelps R, Maddison C, Fitzgerald R. Supporting children's mental health in schools: teacher views. *Teach Teach Theory Pract*. (2011) 17:479–96. doi: 10.1080/13540602.2011.580525
14. Rutter M. Pathways from childhood to adult life. *J Child Psychol Psychiatry*. (1989) 30:23–51. doi: 10.1111/j.1469-7610.1989.tb00768.x
15. Monarrez T, Chingos M. *Can we Measure School Quality Using Publicly Available Data? Center on Education Data and Policy.* (2020). Available online at: https://www.urban.org/sites/default/files/publication/102539/can-we-measure-school-quality-using-publicly-available-data_0.pdf (accessed January 28, 2022).
16. Kouzma NM, Kennedy GA. Self-reported sources of stress in senior high school students. *Psychol Rep*. (2004) 94:314–6. doi: 10.2466/pr0.94.1.314-316
17. O'Reilly M, Svirydzenka N, Adams S, Dogra N. Review of mental health promotion interventions in schools. *Soc Psychiatry Psychiatr Epidemiol*. (2018) 53:647–62. doi: 10.1007/s00127-018-1530-1
18. Robson KL. *Sociology of Education in Canada*. Toronto, ON: eCampusOntario (2019). Available online at: https://ecampusontario.pressbooks.pub/robsonsoced/chapter/__unknown__-6
19. Deb S, Strodl E, Sun H. Academic stress, parental pressure, anxiety and mental health among Indian high school students. *Int J Psychol Behav Sci*. (2015) 5:26–34. doi: 10.5923/j.ijpbs.20150501.04
20. Hawker DS, Boulton MJ. Twenty years' research on peer victimization and psychosocial maladjustment: a meta-analytic review of cross-sectional studies. *J Child Psychol Psychiatry*. (2000) 41:441–55. doi: 10.1111/1469-7610.00629
21. Klomek AB, Sourander A, Gould M. The association of suicide and bullying in childhood to young adulthood: a review of cross-sectional and longitudinal research findings. *Can J Psychiatry*. (2010) 55:282–8. doi: 10.1177/070674371005500503
22. Nakamoto J, Schwartz D. Is peer victimization associated with academic achievement? A meta-analytic review. *Soc Dev*. (2010) 19:221–42. doi: 10.1111/j.1467-9507.2009.00539.x
23. Vilaplana-Pérez A, Pérez-Vigil A, Sidorchuk A, Brander G, Isomura K, Hesselmark E, et al. Much more than just shyness: the impact of social anxiety disorder on educational performance across the lifespan. *Psychol Med*. (2021) 51:861–9. doi: 10.1017/S0033291719003908
24. Tempelaar WM, de Vos N, Plevier CM, van Gastel WA, Termorshuizen F, MacCabe JH, et al. Educational level, underachievement, and general mental health problems in 10,866 adolescents. *Acad Pediatr*. (2017) 17:642–8. doi: 10.1016/j.acap.2017.04.016
25. Watkins DA, Biggs JB. *The Chinese Learner: Cultural, Psychological, and Contextual Influences*. Hong Kong: Comparative Education Research Centre (CERC) (1996).
26. Wu DY. Parental control-psychocultural interpretations of Chinese patterns of socialization. *Int J Psychol*. (1992) 27:230–1.
27. Law YK, Lam SF, Law W, Tam ZW. Enhancing peer acceptance of children with learning difficulties: classroom goal orientation and effects of a storytelling programme with drama techniques. *Educ Psychol*. (2017) 37:537–49. doi: 10.1080/01443410.2016.1214685
28. Cho EY-N, Chan T. Children's wellbeing in a high-stakes testing environment: the case of Hong Kong. *Child Youth Serv Rev*. (2020) 109:104694. doi: 10.1016/j.childyouth.2019.104694
29. Essau CA, Leung PW, Conradt J, Cheng H, Wong T. Anxiety symptoms in Chinese and German adolescents: their relationship with early learning experiences, perfectionism, and learning motivation. *Depress Anxiety*. (2008) 25:801–10. doi: 10.1002/da.20334
30. Hong Kong Paediatric Foundation, Hong Kong Paediatric Society. *20 years Review: Government's Policies are Unable to Meet the Needs Significant Rise in Childhood and Adolescent Mental Health Problems; Youth Suicides Remained*

Serious 70% of Parents Experienced Emotional Disturbances When Caring for Their Children Development of a Comprehensive Child Health Policy With a Timeline and Roadmap Is Crucial. (2017). Available online at: http://www.hkpf.org.hk/download/20%20years%20child%20health%20policy%20review%20press%20release_Eng_20170621_HKPF.pdf (accessed January 27, 2022).

31. Shek DT, Liang LY. Psychosocial factors influencing individual wellbeing in Chinese adolescents in Hong Kong: a 6-year longitudinal study. *Appl Res Qual Life*. (2018) 13:561–84. doi: 10.1007/s11482-017-9545-4
32. McMorran C, Ragupathi K. The promise and pitfalls of gradeless learning: responses to an alternative approach to grading. *J Furth High Educ*. (2020) 44:925–38. doi: 10.1080/0309877X.2019.1619073
33. Anderson LW. A critique of grading: policies, practices, and technical matters. *Educ Policy Anal Arch*. (2018) 26:49. doi: 10.14507/epaa.26.3814
34. Abrams LM, Pedulla JJ, Madaus GF. Views from the classroom: teachers' opinions of statewide testing programs. *Theory Pract*. (2003) 42:18–29. doi: 10.1207/s15430421tip4201_4
35. Winstead L. The impact of NCLB and accountability on social studies: teacher experiences and perceptions about teaching social studies. *Social Studies*. (2011) 102:221–7. doi: 10.1080/00377996.2011.571567
36. Gonzalez A, Peters ML, Orange A, Grigsby B. The influence of high-stakes testing on teacher self-efficacy and job-related stress. *Camb J Educ*. (2017) 47:513–31. doi: 10.1080/0305764X.2016.1214237
37. Li JCH, Lau WY, Au TKF. Psychometric properties of the spence children's anxiety scale in a Hong Kong Chinese community sample. *J Anxiety Disord*. (2011) 25:584–91. doi: 10.1016/j.janxdis.2011.01.007
38. Lim CG, Loh H, Renjan V, Tan J, Fung D. Child community mental health services in Asia Pacific and Singapore's REACH model. *Brain Sci*. (2017) 7:126. doi: 10.3390/brainsci7100126
39. Erikson, EH. Growth and crises of the "healthy personality." In: Senn MJE, editor. *Symposium on the Healthy Personality, Supplement II to the Transactions of the Fourth Conference on Problems of Infancy and Childhood*. New York, NY: Josiah Macy, Jr. Foundation (1950). p. 91–146.
40. Erikson EH. The nature of clinical evidence. *Daedalus*. (1958) 87:65–87.
41. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and wellbeing. *Am Psychol*. (2000) 55:68. doi: 10.1037/0003-066X.55.1.68
42. Ryan RM, Deci EL. *Self-Determination Theory: Basic Psychological Needs in Motivation, Development, and Wellness*. New York, NY: Guilford Publications (2017). doi: 10.1521/978.14625/28806
43. Konold KE, Miller SP, Konold KB. Using teacher feedback to enhance student learning. *Teach Except Child*. (2004) 36:64–9. doi: 10.1177/004005990403600608
44. Makri-Botsari E. Adolescents' unconditional acceptance by parents and teachers and educational outcomes: a structural model of gender differences. *J Adolesc*. (2015) 43:50–62. doi: 10.1016/j.adolescence.2015.05.006
45. Farmer TW, Hamm JV, Dawes M, Barko-Alva K, Cross JR. Promoting inclusive communities in diverse classrooms: teacher attunement and social dynamics management. *Educ Psychol*. (2019) 54:286–305. doi: 10.1080/00461520.2019.1635020
46. Rogers CR. The necessary and sufficient conditions of therapeutic personality change. *J Consult Psychol*. (1957) 21:95. doi: 10.1037/h0045357
47. Swarra A, Mokosińska M, Sawicki A, Sęktas M. The meaning of teacher's unconditional positive regard towards students in educational contexts. In: Nyćkowiak J, Leśny J, editors. *Badania i Rozwój Młodych Naukowców w Polsce - Rodzina, dzieci i młodzież*. Poznań: Młodzi Naukowcy (2017). p. 112–7.
48. Buyse E, Verschueren K, Doumen S. Preschoolers' attachment to mother and risk for adjustment problems in kindergarten: can teachers make a difference? *Soc Dev*. (2011) 20:33–50. doi: 10.1111/j.1467-9507.2009.00555.x
49. Wang MT, Eccles JS. Adolescent behavioral, emotional, and cognitive engagement trajectories in school and their differential relations to educational success. *J Res Adolesc*. (2012) 22:31–9. doi: 10.1111/j.1532-7795.2011.00753.x
50. Kennedy JH, Kennedy CE. Attachment theory: implications for school psychology. *Psychol Schs*. (2004) 41:247–59. doi: 10.1002/pits.10153
51. Sulkowski ML, Simmons J. The protective role of teacher–student relationships against peer victimization and psychosocial distress. *Psychol Sch*. (2018) 55:137–50. doi: 10.1002/pits.22086
52. Rutter M. *Fifteen Thousand Hours: Secondary Schools and their effects on children*. London: Harvard University Press (1979).
53. Cheon SH, Reeve J. A classroom-based intervention to help teachers decrease students' amotivation. *Contemp Educ Psychol*. (2015) 40:99–111. doi: 10.1016/j.cedpsych.2014.06.004
54. Ali S. Perceived teacher and parental acceptance-rejection, and the academic achievement, adjustment, and behavior of children: literature review. *Int J Peace and Dev Stud*. (2011) 2:138–47. doi: 10.5897/IJPDS.9000027
55. Rucinski CL. Teacher–child relationships, classroom climate, and children's social-emotional and academic development. *J Educ Psychol*. (2018) 110:992–1004. doi: 10.1037/edu0000240
56. Ruddy A. *Secondary School Students' Perceptions and Experiences of School Mental Health Climate*. Vancouver, BC: University of British Columbia (2019).
57. Hattie J. *Visible Learning: A Synthesis of Over 800 Meta-Analyses Relating to Achievement*. New York, NY: Routledge (2009).
58. DiGirolamo AM, Desai D, Farmer D, McLaren S, Whitmore A, McKay D, et al. Results from a statewide school-based mental health program: effects on school climate. *School Psych Rev*. (2020) 50:81–98. doi: 10.1080/2372966X.2020.1837607
59. Gase LN, Gomez LM, Kuo T, Glenn BA, Inkelas M, Ponce NA. Relationships among student, staff, and administrative measures of school climate and student health and academic outcomes. *J Sch Health*. (2017) 87:319–28. doi: 10.1111/josh.12501
60. Pate CM, Maras MA, Whitney SD, Bradshaw CP. Exploring psychosocial mechanisms and interactions: links between adolescent emotional distress, school connectedness, and educational achievement. *School Ment Health*. (2017) 9:28–43. doi: 10.1007/s12310-016-9202-3
61. Franklin C, Kim JS, Beretvas TS, Zhang A, Guz S, Park S, et al. The effectiveness of psychosocial interventions delivered by teachers in schools: a systematic review and meta-analysis. *Clin Child Fam Psychol Rev*. (2017) 20:333–50. doi: 10.1007/s10567-017-0235-4
62. Franklin CG, Kim JS, Ryan TN, Kelly MS, Montgomery KL. Teacher involvement in school mental health interventions: a systematic review. *Child Youth Serv Rev*. (2012) 34:973–82. doi: 10.1016/j.childyouth.2012.01.027
63. Clement S, Schauman O, Graham T, Maggioni F, Evans-Lacko S, Bezborodovs N, et al. What is the impact of mental health-related stigma on help-seeking? A systematic review of quantitative and qualitative studies. *Psychol Med*. (2015) 45:11–27. doi: 10.1017/S0033291714000129
64. Chen SX, Mak WW, Lam BC. Is it cultural context or cultural value? Unpackaging cultural influences on stigma toward mental illness and barrier to help-seeking. *Soc Psychol Personal Sci*. (2020) 11:1022–31. doi: 10.1177/1948550619897482
65. Fung KM, Tsang HW, Corrigan PW, Lam CS. Cheng W-M. Measuring self-stigma of mental illness in China and its implications for recovery. *Int J Soc Psychiatry*. (2007) 53:408–18. doi: 10.1177/0020764007078342
66. Mak WW, Kwok YT. Internalization of stigma for parents of children with autism spectrum disorder in Hong Kong. *Soc Sci Med*. (2010) 70:2045–51. doi: 10.1016/j.socscimed.2010.02.023
67. Chan Y, Chan YY, Cheng SL, Chow MY, Tsang YW, Lee C, et al. Investigating quality of life and self-stigma in Hong Kong children with specific learning disabilities. *Res Dev Disabil*. (2017) 68:131–9. doi: 10.1016/j.ridd.2017.07.014
68. Gronholm PC, Nye E, Michelson D. Stigma related to targeted school-based mental health interventions: a systematic review of qualitative evidence. *J Affect Disord*. (2018) 240:17–26. doi: 10.1016/j.jad.2018.07.023

69. Gulliver A, Griffiths KM, Christensen H. Perceived barriers and facilitators to mental health help-seeking in young people: a systematic review. *BMC Psychiatry*. (2010) 10:113. doi: 10.1186/1471-244X-10-113

frontiers | Frontiers in Psychiatry

ORIGINAL RESEARCH
published: 15 June 2022
doi: 10.3389/fpsyt.2022.842896

Attention for Emotion—How Young Adults With Neurodevelopmental Disorders Look at Facial Expressions of Affect

Jana Bretthauer*[1], *Daniela Canu*[2], *Ulf Thiemann*[3], *Christian Fleischhaker*[2], *Heike Brauner*[4], *Katharina Müller*[4], *Nikolaos Smyrnis*[5], *Monica Biscaldi*[2], *Stephan Bender*[1] and *Christoph Klein*[1,2,5]

[1] Department of Child and Adolescent Psychiatry, Medical Faculty, University of Cologne, Cologne, Germany, [2] Clinic for Child and Adolescent Psychiatry, Psychotherapy and Psychosomatics, Faculty of Medicine, Medical Center, University of Freiburg, Freiburg im Breisgau, Germany, [3] Clinic for Psychiatry, Psychosomatics und Psychotherapy in Children and Adolescents, LVR Hospital, Bonn, Germany, [4] Kinder- und Jugendwohnheim Leppermühle, Buseck, Germany, [5] Second Department of Psychiatry, National and Kapodistrian University of Athens, Medical School, University General Hospital "Attikon", Athens, Greece

OPEN ACCESS

Edited by:
Philipp Kanske,
Technical University
Dresden, Germany

Reviewed by:
Jens Richardt Moellegaard Jepsen,
Region Hovedstad Psychiatry,
Denmark
Rutger Jan Van Der Gaag,
Radboud University Nijmegen Medical
Centre, Netherlands
David Quentin Beversdorf,
University of Missouri, United States
Haitham Jahrami,
Arabian Gulf University, Bahrain

***Correspondence:**
Christoph Klein
christoph.klein.kjp@
uniklinik-freiburg.de
orcid.org/0000-0002-9451-4699

Specialty section:
This article was submitted to
Child and Adolescent Psychiatry,
a section of the journal
Frontiers in Psychiatry

Received: *24 December 2021*
Accepted: *20 May 2022*
Published: *15 June 2022*

Citation:
Bretthauer J, Canu D, Thiemann U, Fleischhaker C, Brauner H, Müller K, Smyrnis N, Biscaldi M, Bender S and Klein C (2022) Attention for Emotion—How Young Adults With Neurodevelopmental Disorders Look at Facial Expressions of Affect. Front. Psychiatry 13:842896. doi: 10.3389/fpsyt.2022.842896

While Autism Spectrum Disorder (ASD), Attention-Deficit/Hyperactivity Disorder (ADHD) and Schizophrenia (SCZ) differ in many clinically relevant features such as symptomatology and course, they may also share genetic underpinnings, affective problems, deviancies in social interactions, and are all characterized by some kind of cognitive impairment. This situation calls for a joint investigation of the specifics of cognitive (dys-)functions of the three disorders. Such endeavor should focus, among other domains, on the inter-section of processing cognitive, affective and social information that is crucial in effective real-life interactions and can be accomplished when attentional preferences for human facial expressions of emotions is studied. To that end, attention to facial expressions of basic emotions was examined in young adults with ASD, ADHD, or SCZ in the present study. The three clinical groups were compared with an age-matched group of typically-developing participants (TD) during the free contemplation of five different facial emotions presented simultaneously, by varying identities, through the registration of eye movements. We showed, that dwell times and fixation counts differed for the different emotions in TD and in a highly similar way in ADHD. Patients with ASD differed from TD by showing a stronger differentiation between emotions and partially different attentional preferences. In contrast, the SCZ group showed an overall more restricted scanning behavior and a lack of differentiation between emotions. The ADHD group, showed an emotion-specific gazing pattern that was highly similar to that of controls. Thus, by analyzing eye movements, we were able to differentiate three different viewing patterns that allowed us to distinguish between the three clinical groups. This outcome suggests that attention for emotion may *not* tap into common pathophysiological processes and argues for a multi-dimensional approach to the grouping of disorders with neurodevelopmental etiology.

Keywords: Autism Spectrum Disorder, ADHD, schizophrenia, emotional faces, eye movements (EM)

INTRODUCTION

According to DSM-5 (1), Autism Spectrum Disorder (ASD), and Attention-Deficit/Hyperactivity Disorder (ADHD) both belong to the group of "Neurodevelopmental Disorders" (NDD). This group includes a variety of impairments thought to involve a disorder of brain development (2). Main characteristics include genetic influences, multi-factorial etiologies, onset in childhood, prior to puberty, and a steady clinical course despite developmental changes. Developmental impairments also play a role in Schizophrenia (SCZ) and consequently this disorder is thought to have an etiology of neurodevelopmental abnormalities (3). By contrast to ASD and ADHD, SCZ has been categorized by the DSM-5 in the separate group of "Schizophrenia Spectrum and Other Psychotic Disorders" (SSD) (1).

ASD, ADHD, and SCZ differ in important aspects such as symptomatology and especially their developmental course: ASD onsets in infancy and does not improve much during development, whereas ADHD onsets around the age of 7 years and may show substantial improvements during adolescents (in particular, regarding hyperactivity). SCZ by contrast onsets in late adolescence or young adulthood and shows a variety of courses. While there are multiple differences, these disorders show commonalities in other important domains like deficits in cognitive abilities and social interaction (4, 5). Furthermore, due to genetic overlap between ASD, ADHD, and SCZ and other commonalities including developmental delays, motor deviations, higher incidence in males, frequent comorbidity, and common environmental risk factors, Owen and O'Donovan (6) have proposed to group these disorders (and intellectual disability and bipolar disorder) under the neurodevelopmental continuum model, a further development of earlier neurodevelopmental models of SCZ [e.g., (3)].

Such models call for the joint investigation of these disorders to identify potential common or distinct pathophysiological mechanisms, which would, in turn, speak to nosology and clinical practice. A so called transdiagnostic approach finds support from neuroimaging results. In a recent review, Hoogman et al. (7) conclude that subcortical structures are affected in a similar way in ASD and ADHD, especially in volume. Cortical analyses showed specific differences but also overlaps especially in cortical thickness for ASD and ADHD. Consequently, a joint consideration of disorders with common neurobiological aspects seems reasonable.

Such joint investigation of ASD, ADHD and SCZ has received little attention in previous research [e.g., (8–10)], and the present study is one of the first to consider the cognitive alterations of ASD, ADHD, and SCZ in simultaneous comparison, focusing on attention for facial emotional expressions as a requirement of succeeding social interactions.

Processing the facial expressions of emotions is a special skill in non-verbal communication and indispensable for effective social interactions (11, 12). Most studies that address emotional facial expressions work with the concept of basic emotions, which are defined as facial expressions that can be observed across cultures (13) and include happiness, surprise, fear, anger, disgust, and sadness. These emotions are considered as universally expressed and innately decoded and recognized by typically-developed subjects, already early in childhood (14, 15).

Previous studies have shown differences in the accuracy of *emotion recognition* (ER) between these emotions, with happiness being easier recognized than fear, surprise or anger (16–18), whereas fearful and surprised facial expressions can be confused more easily (19–21).

Studies examining emotion recognition in children and adolescents with ASD, ADHD, or SCZ showed overall inconclusive results. Some studies showed that the recognition of basic emotions in those psychiatric disorders seems to be similar to that of neuro-typical controls [ASD: (22–26); ADHD: (27, 28); SCZ: (29–31)], while other have revealed recognition difficulties [ASD: (23, 32, 33); ADHD: (34–36); SCZ: (37–39)]. The inconsistency of results can be attributed to various methodological aspects (e.g., complexity of the task, time pressure, different stimuli and dependent variables) as well as sample heterogeneity [ASD: (40); ADHD: (41); SCZ: (42)]. For example some subgroups like high functioning and older patients with autism appear to employ compensatory mechanism in basic ER (22, 30, 40, 43, 44). Furthermore, attentional distractibility has been shown by Berggren et al. (45) to influence ER performance in ASD and ADHD. In that study ER problems did not show universally for ASD, and ADHD performance was little different from that of TD. This argues for abnormalities in central executive functions rather than in specific emotion recognition in participants with ADHD (45). Despite the mixed results, it may be assumed that patients with ASD, ADHD and SCZ can recognize at least basic emotional expressions at the simplest level from photos of faces to a comparable extent as healthy control subjects.

Regarding the method of investigation, eye tracking can provide important information about exploration behavior and the accompanying cognitive processes involved in emotion processing (46, 47). Eye movements and fixations can be recorded, by which the active process of seeing is characterized (48). Thus, by recording directed visual attention it is possible to map how subjects explore and reconstruct their visual environment.

To give examples, Green et al. (47) showed increased numbers of fixations for the facial expressions of anger and fear in healthy controls, which they explained by an increased vigilance related to socially threatening stimuli, allowing for a faster and adaptive behavior of the observer. In contrast, Mühlenbeck et al. (49), who looked at fixation times in healthy subjects for different emotional faces (fear, anger, happy, neutral), showed longer fixation times for fearful and shorter ones for angry faces, which argues against a general bias toward negative emotions. Accordingly, varying viewing paths and times of facial expressions can be observed (50). Herbold (12) also found longer viewing times and fixation counts for fearful faces compared to happy, angry, sad, and neutral ones as well as for surprised faces compared to joyful and neutral ones. Such studies therefore suggest that different emotions may cause differences in how faces are viewed, thus pointing to a different orientation of *attention for emotion*, or *attentional preferences*.

Findings from studies investigating eye movements during emotional face processing show abnormalities in face viewing in several psychiatric disorders, including ASD, ADHD, and SCZ, which could contribute to difficulties in complex emotion recognition and thus in social interactions.

In *autism*, abnormalities are shown in different viewing patterns for different emotions with mostly the same accuracy in emotion recognition as in control subjects is seen (51–54). Król and Król (52) examined eye movements in subjects with autism and typically developed subjects during an emotion recognition task in which photographs of faces were to be assigned emotions. Here, the subjects with autism achieved an accuracy of 85%, which was only slightly lower and comparable to that of controls (92%). There were no differences in total fixation number or fixation duration between ASD and TD in any of the tasks used (e.g., emotion recognition task, free viewing task). The authors, however, did not examine further differences between different emotions expressed. Likewise, typical recognition of facial expressions of the six basic emotions was reported by Tang et al. (53). Furthermore, the subjects with autism of that study showed longer fixation times for non-social areas when viewing social scenes. There were, however, no differences in viewing different facial and body areas between groups. These results demonstrate atypical visual processing and prioritizing of social stimuli by individuals with autism with comparable behavioral performance.

However, while it seems that individuals with autism potentially employ altered but functionally preserved processing strategies in emotion recognition (40, 54), some studies examining emotional preferences as revealed by eye fixations have reported an attentional bias away from distressing stimuli such as angry or fearful stimuli in children with ASD (51, 55). For example, García-Blanco et al. (51) found an attentional bias away from angry faces in individuals with autism compared to a control group, but no differences for happy or sad faces. This attentional bias was correlated with higher scores on social communication deficit. Matsuda et al. (56) asked children with ASD to look at photos of individual emotional faces (angry, happy, neutral, sad, surprised) and found no differences in gaze behavior between ASD and TD. However, there was a slight inverse relationship between autistic symptomatology and looking duration for angry faces. In addition to these studies, there are also studies that showed a bias toward looking at distressing stimuli in ASD (51, 57). A recent study by Bochet et al. (58) examined emotional face processing *via* eye-tracking in children with autism and an age-matched TD group. They showed pairs of faces, a neutral face paired with an emotional face, of the same identity. They observed different exploration behavior between ASD and TD. ASD made fewer fixations regarding the emotional faces, from which the authors concluded that emotional faces were less interesting to ASD. A meta-analysis summarizing the results regarding an attentional bias in ASD showed a small but significant and specific effect for a bias toward threatening faces under certain conditions such as line-drawings of emotional faces or in comparison to happy faces (59). Other moderators such as stimulus presentation, response format, reference face, stimulus type, and age had an influence on the strength of this bias. Overall, however, it appears that atypical emotional preferences in ASD have so far not been replicated consistently across studies, necessitating further investigation.

Processing of emotional faces has been studied considerably less in participants with *ADHD* especially in combination with eye movement measurements but suggests typical performance in this group. Schwenck et al. (27), for instance, showed patients with ADHD and control subjects film clips in which a neutral face develops into one of different basic emotions (happy, sad, disgust, fear, anger). They found no differences in reaction times or recognition performance between the groups. Similar results were obtained by Serrano et al. (60), who reported overall typical viewing patterns in participants with ADHD when looking at photos of faces showing the six basic emotions and neutral control faces. While emotion processing *per se* seems to be intact in ADHD, the attentional problems in this group may render important emotional cues unattended (34, 60). In a study by Ahmadi and Judi (61), who looked at viewing preferences during the presentation of emotional face pairs (negative-neutral), there were no differences between children with ADHD and TD subjects regarding the number of first fixations on the emotional expressions. Pishyareh et al. (62) are also one of the few to use eye tracking to study visual exploration of emotional stimuli in children with ADHD. They were able to show that patients with ADHD spend less time looking at pleasant pictures than control subjects when presented with unpleasant or neutral pictures simultaneously. These results provide some evidence that attention for emotion may differ between children with and without ADHD. Again, more data are needed here to draw firmer conclusions.

A large number of studies have shown impaired attentional distribution in participants with *schizophrenia* compared to healthy control subjects, especially when viewing faces compared to other complex stimuli (63–66). Specifically, SCZ participants often show restricted, centrally focused exploration behavior (67, 68) that can be described by reduced scan path length, fewer fixations (69) and shorter fixation durations for faces (70). Despite such constrained exploration patterns, emotion recognition as such seems to be preserved in those with SCZ (71). Importantly, this deviant exploration behavior is also found independently of the expressed emotions of the faces being viewed, suggesting a face-specific and perceptual processing deficit rather than emotion-specific processing deviations or difficulties (72, 73). In line with this reasoning, Asgharpour et al. (69) examined visual attention in SCZ by measuring eye movements during the viewing of pairs of faces consisting of an emotional and a neutral face. They found that SCZ patients showed fewer fixations on faces, regardless of the presence or absence of a displayed emotion.

Importantly, in previous eye movement studies on facial emotion processing, fixation parameters (duration, counts) were typically determined for tasks in which emotions were presented either individually or in pairs (12, 22, 51, 54). Such reduced "choice" of different emotions available for contemplation constrains participants' ability to express attentional preferences in their viewing patterns. This raises the question which emotions are preferred and focused in situations when *several* emotional faces are presented simultaneously. García-Blanco et al. (74), for instance, presented four emotional images (happy, neutral, sad, threatening) simultaneously to participants with bipolar disorder (BD) and recorded eye movements to examine the distribution of attention. They found that patients with bipolar disorder showed increased attention to threatening images compared to healthy individuals, which they interpreted as a vulnerability marker in BD.

To the best of our knowledge, attention for emotional faces has not yet been investigated by presenting several faces simultaneously in psychiatric disorders with profound deficits in social interaction using eye movement recordings. Therefore, this study will examine this most basic level of emotion processing in a direct comparison. Based on these approaches and results, the aim of this study is to look at the exploration behavior of different emotional faces simultaneously in ASD, ADHD, and SCZ and to investigate differences and similarities compared to a healthy control group. (1) We hypothesized that emotion-specific differences in dwell time and fixation count exist for the presented emotions of fear, surprise, happiness, anger and neutral faces. (2) Furthermore emotion-specific group differences in dwell time and fixations are expected to exist between the autism group and the control group, due to the described deviant visual emotion processing in ASD. (3) Since the ADHD group predominantly showed similar visual exploration as healthy control subjects, no group differences are expected. (4) Regarding the clinical groups, compared to a healthy control group, patients with SCZ are expected to show a constrained visual exploration behavior, expressed in a shorter dwell time and fewer fixations for the presented faces, without differentiation of the emotions shown.

METHODS

Participants

The final sample consisted of four groups of participants: $N = 38$ individuals were patients with Attention Deficit/Hyperactivity Disorder (ADHD), $N = 28$ with Autism Spectrum Disorder (ASD), $N = 21$ with Schizophrenia (SCZ) and $N = 41$ individuals were typically-developing participants (TD). All participants had normal or corrected-to-normal vision and no one had a diagnosis of epilepsy or another neurological disease. The groups did not differ significantly in age (see **Table 1**).

Patients with a diagnosis of ADHD or ASD were recruited from the out-patient population of the Clinic for Child and Adolescent Psychiatry, Psychotherapy, and Psychosomatics of the Medical Center, University of Freiburg. Participants with SCZ were recruited from the rehabilitation center "Kinder- und Jugendwohnheim Leppermühle" (Buseck, D) and had received a diagnosis of schizophrenia, schizophreniform or schizoaffective disorder. The typically-developing participants of the healthy control group were recruited through the project database of the department and by posting announcements.

All TD participants were asked for their medical history during a phone screening at the time of enrollment. Any present or past personal or family history of psychiatric disorder (and/or any neurologic condition) was an exclusion criterion. All participants in the clinical groups had received a prior clinical diagnosis. Given the high degree of co-morbidity of ASD and ADHD and the very high degree of all kinds of co-morbidity in all neurodevelopmental disorders, we excluded patients with both ASD and ADHD and also those with a co-morbid substance use disorder. Furthermore, we excluded one patient with SCZ who also had an ADHD diagnosis. Diagnoses of ADHD were confirmed by the German version of the Conners' parent and teacher rating scale (75), interviews with parents and children, and behavioral observations. Diagnoses of ASD were confirmed using the Autism Diagnostic Observation Schedule [ADOS; German version, (76)] and the Autism Diagnostic Interview-Revised [ADI-R; German version, (77)]. To assess the specificity and severity of ADHD and ASD symptoms, plus their absence in the TD group the Social Responsiveness Scale [SRS; German version, (78)] and the Conners' Self and Parent Rating Scale were used. Participants who were taking methylphenidate medication were therefore asked to pause medication 24 h before and during participation. Regarding the SCZ group, all participants of our study had previously taken part in a follow-up study (catamnestic) during which various established research diagnostic measures had been administered, including IRAOS ("Interview for the Retrospective Assessment of the Onset and Course of Schizophrenia and other Psychoses"), CGI/GAF ("Clinical Global Impressions," "Global Assessment of Functioning Scale"), GAS ("Global Assessment Scale"), SAPS/ SANS ("Scale for the Assessment of Positive/Negative Symptoms"), BPRS ("Brief Psychiatric Rating Scale"). Clinical patient records for all participants with SCZ were scrutinized to obtain information about current medication and current previous co-morbid diagnoses. They were treated with (antipsychotic) medication as follows: $N = 11$ Clozapine 150–400 mg, $N = 5$ Aripiprazol 2.5–20 mg; $N = 3$ Olanzapine 5–10 mg; $N = 3$ Quetiapin 300–400 mg; $N = 6$ Dipimperon 20–60 mg; $N = 3$ Risperdal 0.5–4.5 mg; $N = 4$ Venlafaxine 150–225 mg; $N = 3$ Fluoxetin 20 mg; $N = 3$ Escitalopram 20 mg.

IQ was tested using the CFT 20-R (79) for participants in the ADHD, ASD, and TD group and the Wechsler Intelligence Test [WISC-IV for children, WAIS-IV for adults; German version, (80)] for participants in the schizophrenia group. In addition, a 9-item short version of the Raven Standard Progressive Matrices [RSPM, (81)], correlating with the 60-item version by $r = 0.98$ (82), was conducted during the ocular-motor session. Groups differed significantly in IQ (see **Table 1**).

Ethical approval to the study was given by the Ethics Committee of the Albert Ludwigs-University Freiburg (EK124/17). All adult participants signed a consent form, for minors both from parents and minors informed written consent was obtained.

Stimuli

Stimuli for the eye tracking task consisted of photographs of eight female and seven male identities, with each identity showing five different emotional expressions: Happy, fearful, angry, surprised, or neutral expression, resulting in overall 75 facial expressions. The five emotional expressions of one identity were presented simultaneously on five different positions (center, top right,

TABLE 1 | Group characteristics.

Variable	SCZ	ADHD	ASD	TD	$F_{3,124}$	p
N	21	38	28	41		
Mean age (in years) ± SD	19.8 ± 1.7	19.0 ± 2.2	19.4 ± 2.2	18.9 ± 2.1	1.068	0.365
Gender (% female)	29	42	4	63	-	-
SPM (% correct)	47.2 ± 27.2	59.1 ± 23.7	70.2 ± 20.5	68.0 ± 15.8	5.878	0.001

SD, standard deviation; SCZ, schizophrenia; SPM, standard progressive matrices.

bottom right, bottom left, top left; see **Figure 1**). Therefore, one stimulus consisted of five pictures of one identity, each showing one of the five emotions. There were 15 different identities and accordingly 15 stimuli were presented. The positions of the different emotional expressions were pseudo-randomized between trials, such that each emotion was shown unpredictably three times at each of the five positions within the fifteen trials. The images were chosen from the Radboud Faces Database (83) and were presented on a gray background for 15 s each. The free viewing task was developed using EyeLink Experiment Builder (SR Research Ltd., version 2.1.140).

Apparatus

The eye tracker used was an EyeLink 1000 Plus Desktop Mount system (SR Research, Mississauga, ON, Canada). To control the eye tracker, EyeLink 1000 Plus Host software was used on a Host PC.

During stimulus presentation, the camera recorded gaze location and pupil diameter for both eyes based on the reflection of near-infrared light from the cornea and pupil. Gaze and pupil information was sampled binocular at a frequency of 1,000 Hz with a 2 mm lens and with a spatial resolution of 0.01°. System specifications included an average accuracy of 0.25–0.5 degrees of visual angle and a tolerance of head movements within a range of 22 × 22 cm. Participants were seated on a chair in front of a display screen (24 inch LCD screen monitor, resolution 1,920 × 1,080 pixels), with a distance of 90 cm from the display and 60 cm from the eye tracker, respectively. The recording was performed in remote mode, where the pupil could be tracked using a forehead "sticker" as reference point.

The associated Display PC presented the stimuli through EyeLink Experiment Builder (SR Research Ltd., version 2.1.140).

Procedure

Calibration and Validation

For processing the tasks and simultaneous recording of eye movements the participants were tested individually inside a lit cabin. The luminance directly in front of the participants' eyes was measured by a digital Peaktech 5,035 light meter with a range of 0–2,000 lx (Ahrensburg, Germany) and kept constant across participants by dimming the test room light down to 70–80 lx directly in front of the participants' eyes. They were seated in an adjustable chair in front of the display screen. The eye tracker was positioned below and slightly in front of the screen.

At the beginning of the eye tracking experiment, participants completed a 13-point calibration. If the gaze accuracy was within 1° for both eyes, the gaze positions were considered as calibrated. A validation of the calibration followed. If validation was successful, the task began. If validation was unsuccessful, the eye tracker and chair were adjusted and the calibration and validation procedure was rerun until it successfully measured gaze at all locations.

Before each trial a drift correction using a central fixation point was performed to continually ensure the eye tracker was adequately tracking gaze. If the gaze accuracy was within 0.5° for both eyes drift correction was accepted. Whenever necessary, adjustments to the calibration were made.

Stimuli Presentation

One examiner gave the instructions while sitting next to the participant inside the cabin. A second examiner was sitting in an adjoining room and monitored eye movements to ensure that participants remained attentive and completed the tasks according to the instructions. The present free viewing task was part of a larger test battery comprising of different saccade and fixation tasks, a visual search task as well as different free viewing tasks, during a two-and a half-hours session, interleaved by three 10-min breaks. The order of the tasks was counterbalanced across participants of each group. As a reward for their participation in the study, participants could choose between cinema or book vouchers worth 7.50€ per hour.

Before the start of the task, participants were asked by standardized verbal instructions to look at the faces as they appeared on the screen and to answer a question after the presentation. Each trial began with the presentation of a written instruction on screen, to look at the faces for 15 s. The following instruction on the screen asked the participants to focus on a cross in the center of the screen. The participants had to look within an area of interest (AOI: 1.6 × 1°) around a fixation cross for at least 1,000 ms to start the trial. After that, a set of faces was shown for 15 s following a 1,000 ms inter-stimulus interval during which the screen was blank. The screen background color was kept gray during both stimuli presentation and interstimulus interval. After the presentation of each trial the instructor asked which emotions they had just seen on the screen.

Data Analysis

The validity of the eye movement data was assessed with a proportion of missing values, which was acceptable for all groups (TD: 1.6%, SCZ: 5.2%, ADHD: 1.4%, ASD: 1.1%), albeit significantly higher in the SCZ compared to all other groups (GROUP: $F_{3,124} = 10.960$, $p < 0.001$, $\eta^2 = 0.210$). Data analysis

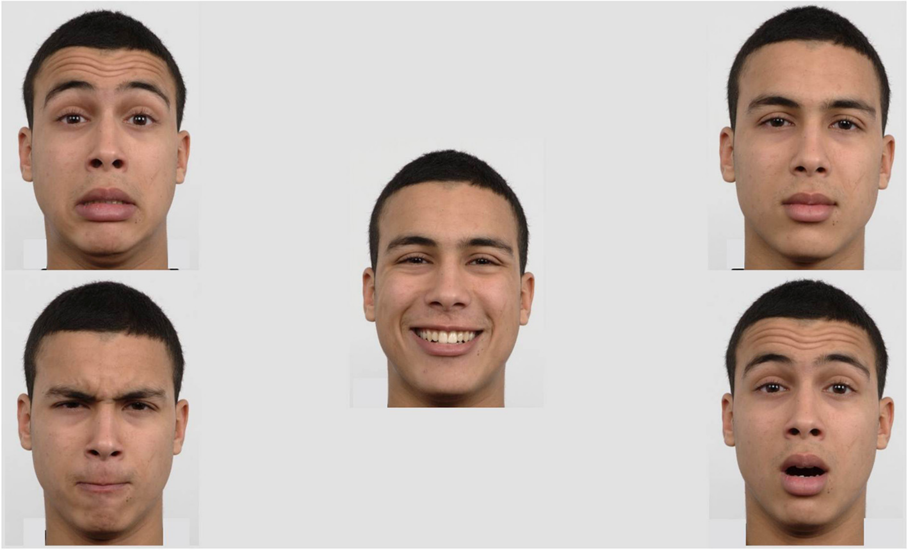


FIGURE 1 | Exemplary stimulus: The five emotional expressions (happy, neutral, surprised, angry, and scared) of one identity were presented simultaneously on five different positions (center, top right, bottom right, bottom left, and top left).

was performed using the data analysis program EyeLink Data Viewer (SR Research Ltd., version 3.1.97). Any period that was no blink or saccade, was defined as "fixation" according to the proprietary analysis algorithm.

Five different AOIs of equal size, one for each face, were defined for each of the stimuli. From these, dwell time and numbers of fixations ("fixation count") were derived for each AOI, both in absolute terms and as proportions of times participants were actually looking at the stimuli (rather than producing artifacts like blinks, or looking away from the screen). As absolute and relative measures yielded largely consistent results, we focus here on the relative measures unless conclusions to be drawn from these results conflict with each other. Such measures have been validated in previous studies to capture visual attention (62, 84–89).

A 5 × 5 × 4 mixed ANOVA with the within-subjects factors EMOTION (levels: Happy, fearful, angry, surprised, or neutral expression) and POSITION (levels: Center, top right, bottom right, bottom left, top left), and the between-subject factor GROUP (levels: ADHD, ASD, SCZ, TD) was used for each of the dependent variables. Furthermore, we ran subsequent mixed ANOVAs between each clinical group and the TD group with related contrast analyses as well as Bonferroni-adjusted *post-hoc* analyses for comparisons between groups and emotions. Additionally, we executed pairwise ANOVA's between the clinical groups. As a control analysis, the interaction between the two factors EMOTION and POSITION was examined. Further control analyses showed that neither age nor gender influenced the free viewing results significantly. Regarding gender, there was a significant chi-square test and therefore we included gender as a variable in different kinds of ANOVAs using the three groups TD, ADHD, and SCZ (in the ASD group, this was unfeasible as this group included only one female participant). We neither found any significant gender effects in these three groups analyzed separately, nor was there any significant gender * group interaction when either of the two clinical groups alone or both clinical groups together were compared with TD. Given the aforementioned gender imbalance between groups, we also explored potential gender effects of the stimulus materials by comparing dwell times and fixation counts for male vs. female faces. We found that within the contemplation period of 15 s and across all participants, female faces were looked at some 38 ms longer than male faces ($p = 0.06$, *Cohen's* $d = 0.625$). Neither did this effect interact with group status (TD, ASD, ADHD, SCZ) nor the subjects own gender. In order to check out the stability of our ANOVA findings for group differences in IQ, IQ was added as a covariate according to the suggestions by Schneider et al. (90), that is, after mean-centering the covariates when the design contains within-subject factors, using ANCOVA. This resulted in only negligible changes in the results presented here. Given that the correction for IQ differences is a controversial (91) and apparently not yet settled issue, we report the ANOVA results throughout.

Analyses were performed with SPSS software, Version 27 (SPSS Institute Inc., Cary, NC, USA). A significance level of $\alpha = 0.05$ was adopted for all statistical analyses and partial η^2 (η^2) quantified effect sizes.

Given the sample size, it can be assumed that the mixed ANOVA is sufficiently robust to violations of the normal distribution (92–94). Greenhouse-Geisser adjustments were made to correct for violations of sphericity. Homogeneity of the error variances was not met for all variables, as assessed by Levene's test. There was homogeneity of covariances, as assessed by Box's test ($p = 0.002$). Overall, the robustness of the analysis with respect to the preconditions is given.

According to G*Power (95), a group size of at least 20 subjects per group allows us to find an effect (f) of 0.25 at an alpha level of 0.05 with a test power of 0.90 ($N = 80$, $df = 3$). The final sample satisfied these requirements.

RESULTS

The subsequent results section is split into three major parts. In *part 1*, results on dwell time and results on fixation counts are presented. For each of these variables we found significant EMOTION * GROUP interactions suggesting group-specific processing of emotional faces. To disentangle these interactions, we first looked at the EMOTION effects for controls, followed by pairwise comparisons between controls on the one side, an each of the clinical groups on the other. In *part 2*, we compared the clinical groups (ASD, ADHD, SCZ) with each to directly address commonalities and differences. In *part 3*, we present additional, secondary findings.

Comparisons Between the Clinical Groups on the One Side and Controls on the Other

Dwell Time

Mixed ANOVA for proportion of dwell time and all groups with a Greenhouse-Geisser correction revealed a significant effect of the within-subject factor EMOTION on dwell time ($F_{2,999,371.833} = 8.211$, $p < 0.001$, $\eta^2 = 0.062$) which was further qualified by an overall EMOTION * GROUP interaction ($F_{8.996,371.833} = 2.113$, $p = 0.028$, $\eta^2 = 0.049$). This indicates that the dwell times for the different emotional expressions differed between the groups. To break down this interaction, subsequent mixed ANOVAs were conducted between each clinical group and the control group.

When looking at the TD group's viewing behavior only (see **Figure 2**), to begin with, it turned out that controls' gazes dwelled longest on fearful faces and shortest on angry faces (EMOTION: $F_{2.515,100.616} = 2.941$, $p = 0.045$, $\eta^2 = 0.068$). Contrast analyses between each emotional face and the neutral one revealed no significant differences though ($p > 0.05$). Otherwise, Bonferroni-adjusted *post-hoc* analysis revealed a significant difference in dwell time just between the fearful faces and the angry faces [0.028, 95% CI (0.004, 0.052), $p = 0.011$], but not between any other expressions ($p > 0.05$).

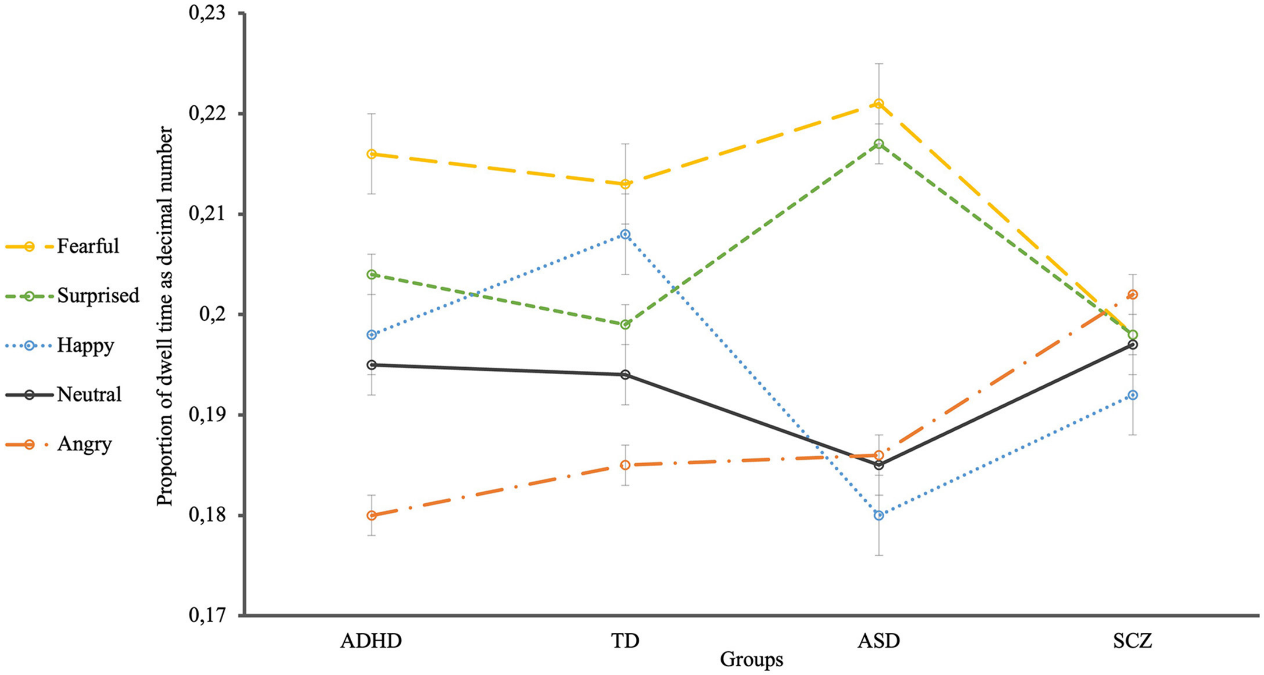
To disentangle the overall ANOVA results for all groups, "pairwise" ANOVAs comparing the TD group with one of the clinical groups were accomplished. With one exception, these ANOVAs revealed non-significant GROUP effects (TD vs. clinical group) both for the relative and the absolute dwell times. The exception was the absolute dwell time for the comparison including SCZ participants, as outlined below.

The comparison of the *ASD group* with controls showed a significant interaction between EMOTION and GROUP ($F_{2.807,188.100} = 3.481$, $p = 0.019$, $\eta^2 = 0.049$; EMOTION: $F_{2.807,\ 188.100} = 7.977$, $p < 0.001$, $\eta^2 = 0.106$). This interaction revealed significantly longer dwell times for surprised faces and shorter ones for happy faces in the ASD group, compared to controls. Contrast analyses with the neutral expression as reference category revealed a significant interaction between EMOTION and GROUP in comparison with the surprised expression ($F_{1,67} = 6.878$, $p = 0.011$, $\eta^2 = 0.093$). The EMOTION effect for the ASD group alone turned out highly significant (EMOTION: $F_{3.192,86.175} = 10.032$, $p < 0.001$, $\eta^2 = 0.271$), showing that compared to neutral faces fearful and surprised faces were significantly longer looked at ($p = 0.001$). *Post-hoc* analyses additionally showed significantly longer dwell times for fearful and surprised faces compared to happy and angry faces ($p < 0.05$).

The mixed ANOVA between the *ADHD group* and the TD group showed differences in dwell times for the different emotions but no significant interaction with group membership (EMOTION * GROUP: $F_{2.409,185.519} = 0.516$, $p = 0.632$, $\eta^2 = 0.007$). For the effect of EMOTION ($F_{2.409,185.519} = 7.888$, $p < 0.001$, $\eta^2 = 0.093$), contrast analysis with the neutral expression as reference showed that fearful faces were significantly longer viewed ($F_{1,77} = 7.691$, $p = 0.007$, $\eta^2 = 0.091$) and angry faces significantly shorter than the neutral ones ($F_{1,77} = 7.037$, $p = 0.010$, $\eta^2 = 0.084$). Similar to controls, participants with ADHD showed an effect of the considered emotion on dwell time (EMOTION: $F_{2.047,75.729} = 6.395$, $p = 0.003$, $\eta^2 = 0.147$). Contrast analyses for the ADHD group showed that fearful faces were viewed significantly longer ($F_{1,37} = 4.874$, $p = 0.034$, $\eta^2 = 0.116$) and angry faces were viewed significantly shorter ($F_{1,37} = 4.727$, $p = 0.036$, $\eta^2 = 0.113$) compared to neutral faces. Furthermore, pairwise comparisons according to Bonferroni adjusted *post-hoc* analyses revealed that fearful and surprised faces were significantly longer viewed than angry faces ($p < 0.001$).

The comparison between the *SCZ group* and the TD group revealed neither a significant main effect of EMOTION on dwell time ($F_{3.151,189.074} = 0.728$, $p = 0.543$, $\eta^2 = 0.012$), nor a significant EMOTION * GROUP interaction ($F_{3.151,189.074} = 1.466$, $p = 0.224$, $\eta^2 = 0.024$). Despite the non-significance of the EMOTION * GROUP interaction, **Figure 2** revealed a lack of differentiation of emotions by dwell times in the SCZ group for which not only the EMOTION simple effect was non-significant (EMOTION: $F_{4,80} = 0.138$, $p = 0.968$, $\eta^2 = 0.007$) but also all contrasts of the different emotions with the neutral facial expression ($p > 0.6$) as well as the *post-hoc* analyses between the different emotions ($p > 0.05$). The SCZ group was the only group that showed significantly shorter overall dwell times when compared to controls. This effect was very strong for the absolute (GROUP: $F_{1,60} = 44.869$, $p < 0.001$, $\eta^2 = 0.428$) and considerable weaker for the relative dwell times (GROUP: $F_{1,60} = 3.869$, $p = 0.054$, $\eta^2 = 0.061$) that took into account the somewhat greater proportion of missing data in this group.

To summarize the described results, three different viewing patterns have emerged for the different clinical groups: Both the ADHD and the ASD group differed descriptively from controls in the proportions of dwell times for the different emotions, but all contemplated fear longest. While the ADHD group did not differ significantly from the TD group regarding the patterns of dwell times for the different emotions, the ASD and TD



Simple effect of Emotion	$F_{2.047,75.729} = 6.395$, **$p = .003$**, $\eta^2 = .147$	$F_{2.515,100.616} = 2.941$, **$p = .045$**, $\eta^2 = .068$	$F_{3.192,86.175} = 10.032$, **$p < .001$**, $\eta^2 = .271$	$F_{4,80} = 0.138$, $p = .968$, $\eta^2 = .007$
Emotion * Group (Clinical Group vs. TD)	$F_{2.409,185.519} = 0.516$, $p = .632$, $\eta^2 = .007$		$F_{2.807,188.100} = 3.481$, **$p = .019$**, $\eta^2 = .049$	$F_{3.151,189.074} = 1.466$, $p = .224$, $\eta^2 = .024$

FIGURE 2 | Proportion of dwell time for the four groups. The groups are located on the horizontal axis with the different emotions as single lines. The table shows the statistics of the simple effects of EMOTION as well as the interaction effects EMOTION * GROUP.

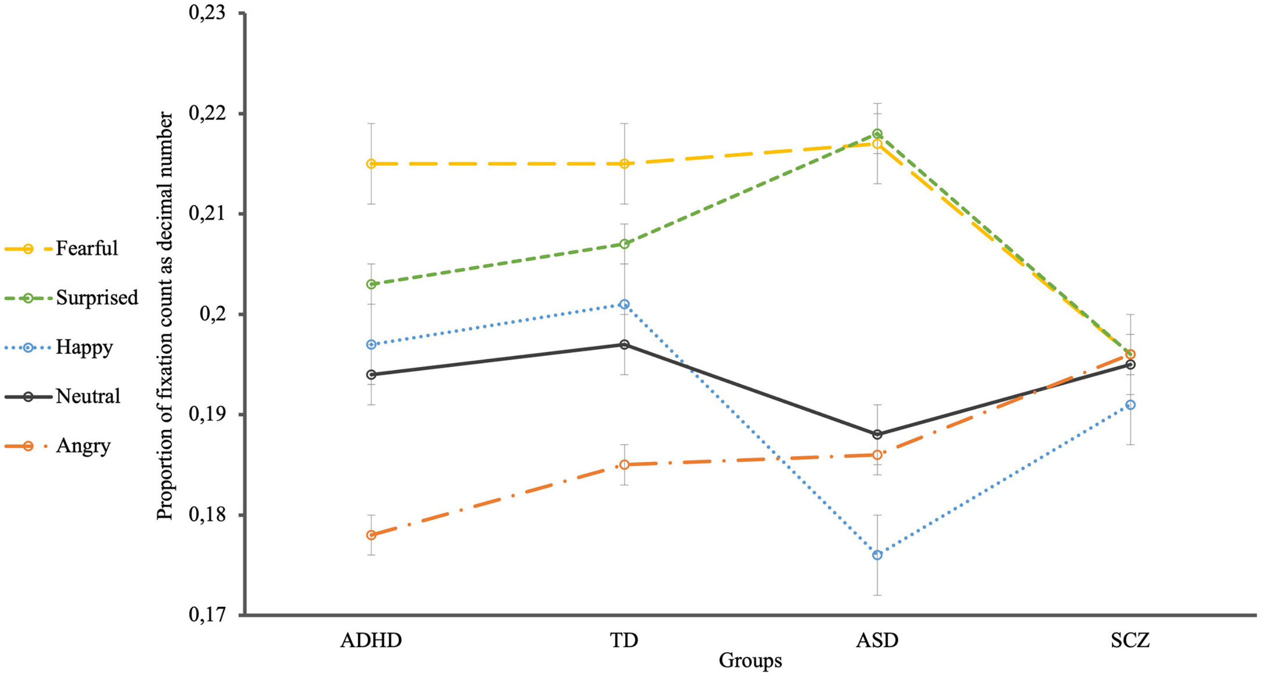
groups entered a significant interaction EMOTION * GROUP showing a partially different "ranking" of dwell durations for different emotions, especially regarding the emotion of surprise and overall greater dwell time differences across emotions in ASD compared to TD. For the SCZ group, dwell times showed significantly shorter viewing times in comparison with TD (more so for absolute than relative dwell times), but also no significant interaction EMOTION * GROUP.

Fixation Count

Mixed ANOVA for all four groups for proportion of fixation count with a Greenhouse-Geisser correction revealed a significant effect of EMOTION ($F_{2.953,366.179} = 12.902$, $p < 0.001$, $\eta^2 = 0.094$) as well as for the between-subject factor GROUP ($F_{3,124} = 5.859$, $p < 0.001$, $\eta^2 = 0.124$), which was further qualified by an EMOTION * GROUP interaction ($F_{8.859,366.179} = 2.276$, $p = 0.018$, $\eta^2 = 0.052$). To describe what this interaction was due to, subsequent mixed ANOVAs were conducted between each clinical group and the control group.

Looking at the TD group's viewing behavior alone (see **Figure 3**), it was shown that controls spent the most fixations regarding fearful faces and the least on angry faces (EMOTION: $F_{2.712,108.492} = 3.802$, $p = 0.015$, $\eta^2 = 0.087$). Contrast analyses between each emotional face and the neutral one revealed no significant differences though ($p > 0.05$). Only the comparison between the neutral face and the fearful face was on the verge of significance ($F_{1,40} = 4.082$, $p = 0.050$, $\eta^2 = 0.093$). Furthermore, Bonferroni-adjusted *post-hoc* analysis revealed significant more fixations for the fearful faces compared to angry faces [0.030, 95%-CI (0.009, 0.050), $p = 0.001$], and likewise for surprised faces compared to angry faces [0.022, 95%-CI (0.002, 0.042), $p = 0.025$], but no differences between any other expressions (*p-values*>0.05).

The comparison of the *ASD group* with controls revealed, additionally to the effect of GROUP ($F_{1,67} = 5.418$, $p = 0.023$, $\eta^2 = 0.075$) and EMOTION ($F_{2.880,192.950} = 11.873$, $p < 0.001$, $\eta^2 = 0.151$), a significant interaction between EMOTION and GROUP ($F_{2.880,192.950} = 2.835$, $p = 0.042$, $\eta^2 = 0.041$). This interaction was due to significantly more fixations for surprised faces and fewer fixations for happy faces in the ASD group, compared to controls. Contrast analyses with the neutral expression as reference category revealed a significant interaction between EMOTION and GROUP in comparison with the surprised expression ($F_{1,67} = 4.776$, $p = 0.032$, $\eta^2 = 0.067$). For the ASD group alone the EMOTION effect was highly significant (EMOTION: $F_{3.022,81.602} = 13.001$, $p < 0.001$, $\eta^2 = 0.325$), with an effect size almost four times as large as in controls ($\eta^2 = 0.087$, see above), showing that compared to neutral faces



Simple effect of Emotion	$F_{1.980,73.262} = 10.153$, $\boldsymbol{p < .001}$, $\eta^2 = .215$	$F_{2.712,108.492} = 3.802$, $\boldsymbol{p = .015}$, $\eta^2 = .087$	$F_{3.022,81.602} = 13.001$, $\boldsymbol{p < .001}$, $\eta^2 = .325$	$F_{4,80} = 0.084$, $p = .987$, $\eta^2 = .004$
Emotion * Group (Clinical Group vs. TD)	$F_{2.485,191.335} = 0.149$, $p = .901$, $\eta^2 = .002$		$F_{2.880,192.950} = 2.835$, $\boldsymbol{p = .042}$, $\eta^2 = .041$	$F_{3.200,192.005} = 1.365$, $p = .253$, $\eta^2 = .022$

FIGURE 3 | Proportion of fixation count for the four groups. The groups are located on the horizontal axis with the different emotions as single lines. The table shows the statistics of the simple effects of EMOTION as well as the interaction effects EMOTION * GROUP.

fearful and surprised faces were significantly more often fixated ($p < 0.003$). Furthermore, *post-hoc* analyses revealed significantly more fixations for fearful and surprised faces compared to happy and angry faces ($p < 0.05$).

The mixed ANOVA between the *ADHD group* and the TD group showed an effect of the different emotions on the proportion of fixation count but no significant interaction with group membership (EMOTION * GROUP: $F_{2.485,\,191.335} = 0.149$, $p = 0.901$, $\eta^2 = 0.002$) but a generally lower proportion of fixations for the ADHD group (GROUP: $F_{1,77} = 6.081$, $p = 0.016$, $\eta^2 = 0.073$). For the effect of EMOTION ($F_{2.485,191.335} = 11.776$, $p < 0.001$, $\eta^2 = 0.133$), contrast analyses with the neutral expression as reference showed that fearful faces ($F_{1,77} = 11.767$, $p = 0.001$, $\eta^2 = 0.133$), and surprised faces ($F_{1,77} = 5.478$, $p = 0.022$, $\eta^2 = 0.066$) received significantly more, and angry faces significantly less fixations than the neutral ones ($F_{1,77} = 11.849$, $p = 0.001$, $\eta^2 = 0.133$). Equal to the TD group, participants with ADHD showed an effect of the considered emotion on fixation count (EMOTION: $F_{1.980,73.262} = 10.153$, $p < 0.001$, $\eta^2 = 0.215$). Contrast analyses for the ADHD group showed that fearful faces were fixated significantly more often ($F_{1,37} = 8.800$, $p = 0.005$, $\eta^2 = 0.192$) while angry faces were fixated significantly less often ($F_{1,37} = 11.446$, $p = 0.002$, $\eta^2 = 0.236$) compared to neutral faces. Pairwise comparisons according to Bonferroni adjusted *post-hoc* analyses revealed that fearful and surprised faces were significantly more often fixated than angry faces ($p < 0.001$).

The analysis including the *SCZ group* and the TD group revealed neither a significant main effect of EMOTION on proportion of fixation count ($F_{3.200,\,192.005} = 1.429$, $p = 0.234$, $\eta^2 = 0.023$), nor a significant EMOTION * GROUP interaction ($F_{3.200,\,192.005} = 1.365$, $p = 0.253$, $\eta^2 = 0.022$), but a main effect of GROUP ($F_{1,60} = 8.931$, $p = 0.004$, $\eta^2 = 0.130$), showing a significantly lower proportion of fixation count for the SCZ Group Regarding the Faces. For the SCZ Group Alone There Was a Lack of Differentiation of emotions by fixation count for which not only the EMOTION simple effect was non-significant (EMOTION: $F_{4,80} = 0.084$, $p = 0.987$, $\eta^2 = 0.004$) but also all contrasts of the different emotions with the neutral facial expression ($p > 0.7$).

In summary, similar results were found for fixation counts as for viewing times. The ADHD group did not differ significantly from the TD group regarding to patterns of fixation count, even showed the same "ranking" of emotions. A significant EMOTION * GROUP interaction was found only when comparing the ASD group with TD and pointed to more fixations falling on surprise in ASD compared to TD. The SCZ group again did not differentiate between emotions and again did not interact with the TD group with regard to fixation counts. Despite these differences between the clinical groups, they all showed overall a lower proportion of fixation counts compared to TD.

Comparisons Between the Clinical Groups

Dwell Time

Further, we ran pairwise mixed ANOVA's between the clinical groups for *proportion of dwell times* and fixation counts (see **Table 2** for all results).

The analysis for the *ASD and ADHD groups* for the proportion of dwell times revealed a significant effect of EMOTION ($F_{2.669,170.826} = 14.634$, $p < 0.001$, $\eta^2 = 0.186$) but no other significant effects or interactions ($p > 0.05$).

The analysis including the *ASD* and the *SCZ group*, by contrast showed a significant interaction between EMOTION and GROUP ($F_{4,188} = 3.186$, $p = 0.015$, $\eta^2 = 0.063$; EMOTION: $F_{4,188} = 3.904$, $p = 0.005$, $\eta^2 = 0.077$).Contrast analyses with the neutral expression as reference category revealed a significant interaction between EMOTION and GROUP in comparison with the surprised expression ($F_{1,47} = 4.553$, $p = 0.038$, $\eta^2 = 0.088$), showing significantly longer dwell times for surprised faces in the ASD group, compared to SCZ.

For the comparison of the *ADHD group* and the *SCZ group*, there was no significant effect of EMOTION ($F_{3.049,173.807} = 1.689$, $p = 0.166$, $\eta^2 = 0.029$) or GROUP ($F_{1,57} = 1.931$, $p = 0.170$, $\eta^2 = 0.033$) and no significant interaction ($p > 0.05$).

Fixation Count

The pairwise mixed ANOVAs between the clinical groups for proportion of *fixation counts* all revealed significant effects of EMOTION ($2.9 \leq F \leq 4.1$; $0.007 \leq p \leq 0.04$) and significant interactions between EMOTION and GROUP.

Regarding *SCZ vs. ADHD* contrast analyses between the emotional faces and the neutral expression as reference showed no significant effect ($p > 0.05$).

Comparing the comparison between *SCZ* and *ASD*, our analysis showed significant more fixations for surprised faces compared to the neutral faces ($F_{1,47} = 6.949$, $p = 0.011$, $\eta^2 = 0.129$). The significant interaction of GROUP and EMOTION ($F_{1,47} = 5.889$, $p = 0.019$, $\eta^2 = 0.111$) was primarily due to the faces showing surprise and eliciting more fixations in the ASD compared to the SCZ group.

Comparisons of the *ADHD* and the *ASD group* revealed a significant GROUP * EMOTION interaction ($F_{2.504,160.241} = 4.068$, $p = 0.012$, $\eta^2 = 0.060$) that was nourished by more fixations for surprised, fearful and angry faces in the ASD compared to the ADHD group.

For the comparison between the *SCZ* and the *ADHD group,* there was significant effect of GROUP ($F_{1,57} = 4.538$, $p = 0.037$, $\eta^2 = 0.074$) on proportions of fixation count, showing more fixations for the ADHD than for the SCZ group. However, the interaction of GROUP * EMOTION turned out significant ($F_{2.890,164.746} = 2.938$, $p = 0.037$, $\eta^2 = 0.049$), contrast analysis between the emotional faces and the neutral expression as reference showed no significant effect ($p > 0.05$). The interaction is therefore due to more fixations for the fearful faces and less fixations to the angry faces in the ADHD group, compared to the SCZ group, which looked at both emotions equally often.

Secondary Results—Effect of Position

As a secondary result, a significant effect of the within-subject factor POSITION was found for both the proportion of dwell time ($F_{1.754,21.444} = 153.779$, $p < 0.001$, $\eta^2 = 0.554$) and of number of fixations ($F_{2.382,295.396} = 209.528$, $p < 0.001$, $\eta^2 = 0.628$), which can be further differentiated by a POSITION * GROUP interaction.

Accordingly, dwell times and fixation counts for the different positions differed between groups and emotions. To break down these interactions, we looked at the subsequent mixed ANOVAs between each clinical group and the control group.

For all groups, there was a significant effect of POSITION, in the sense that the central position was viewed significantly longer and fixated more often than all other positions ($p < 0.001$). This "central bias" was more pronounced in the SCZ group and in the ASD group compared to TD, shown by significant POSITION * GROUP interactions (POSITION effects for: (a) dwell times—SCZ: $F_{2.039,122.347} = 4.947$, $p = 0.008$, $\eta^2 = 0.076$; ASD: $F_{1.806,120.994} = 6.218$, $p = 0.004$, $\eta^2 = 0.085$; (b) fixation counts—SCZ: $F_{2.619,157.125} = 6.493$, $p = 0.001$, $\eta^2 = 0.098$; ASD: $F_{2.538,170.022} = 4.489$, $p = 0.007$, $\eta^2 = 0.063$). Comparing the POSITION effects directly between the ASD and SCZ groups we found no significant interaction between GROUP and POSITION [(a) dwell times—$F_{1.657,77.901} = 0.025$, $p = 0.958$, $\eta^2 = 0.001$; (b) fixation counts—$F_{1.979,93.035} = 0.575$, $p = 0.563$, $\eta^2 = 0.012$; simple effects of POSITION: (a) dwell times—$F_{1.657,77.901} = 71.282$, $p < 0.001$, $\eta^2 = 0.603$; (b) fixation counts—$F_{1.979.93.035} = 110.477$, $p < 0.001$, $\eta^2 = 0.702$].

DISCUSSION

The present study examined young adults with ASD, ADHD, or schizophrenia under the assumption of overlapping pathophysiological mechanisms, with the aim of investigating similarities and differences between these groups regarding visual exploration of emotional faces. To that end, the three clinical groups were each compared with a control group regarding the visual exploration of five different facial emotions presented simultaneously while eye fixations were recorded to analyse dwell times and fixation counts.

We found the following main results: (a) The *ASD group* differed significantly from TD in differentiating more strongly between emotions and "ranking" emotions partially differently regarding dwell times and fixation counts. (b) The TD and *ADHD groups* showed rather similar corresponding fixation patterns for the different emotions, both regarding dwell times and fixation counts. (c) The *SCZ group*, by contrast, differentiated not at all between emotions and exhibited reduced dwell times compared to controls. (d) While the ASD group and the SCZ group differed from ADHD in fixation counts and not in dwell times, regarding the attentional preferences for different emotions, dwell times differentiated the ASD and the SCZ group in that aspect, additionally to fixation counts. Furthermore, the total amount of fixations differentiated the ADHD and SCZ group.

The healthy control subjects looked at the different emotions for different lengths of time and fixated them with different

TABLE 2 | Pairwise mixed ANOVA's between the clinical groups.

Dependent variable	**ADHD–ASD**			**ADHD–SCZ**			**ASD–SCZ**		
	F	***p***	η^2	***F***	***p***	η^2	***F***	***p***	η^2
Proportion of dwell time									
EMOTION	14.634	**<0.001**	0.186	1.689	0.170	0.029	3.904	**0.005**	0.077
EMOTION * GROUP	2.484	0.070	0.037	2.273	0.081	0.038	3.186	**0.015**	0.063
GROUP	0.528	0.470	0.008	1.931	0.170	0.033	0.123	0.728	0.003
POSITION	87.432	**<0.001**	0.577	74.417	**<0.001**	0.566	71.282	**<0.001**	0.603
POSITION * GROUP	0.905	0.385	0.014	0.578	0.535	0.010	0.025	0.958	0.001
Proportion of fixation count									
EMOTION	20.152	**<0.001**	0.239	3.097	**0.030**	0.052	5.458	**0.001**	0.104
EMOTION * GROUP	4.068	**0.012**	0.060	2.938	**0.037**	0.049	4.003	**0.007**	0.078
GROUP	0.162	0.689	0.003	4.538	**0.037**	0.074	2.399	0.128	0.049
POSITION	131.285	**<0.001**	0.672	105.479	**<0.001**	0.649	110.477	**<0.001**	0.702
POSITION * GROUP	1.336	0.267	0.020	2.993	0.051	0.050	0.575	0.563	0.012

Bold values indicate significant results.

frequencies. This speaks to our prediction of an influence of emotional facial expression on visual exploration behavior. In particular, this was shown to be significant for the difference between the emotions fear and anger for both viewing duration and fixation number. These facial emotional expressions had been highlighted in previous studies already. For example, Green et al. (47) found increased numbers and duration of fixations for fear and anger compared to other emotions (happy, sad, neutral). While many studies suggested that negative information and, consequently, negative emotions attract more attention than positive information (47, 96, 97), other studies showed that there are in addition different responses to different negative emotions (49, 98–100). Accordingly, the mere valence of emotions cannot fully explain the observed viewing patterns. Also, we found that that fearful faces were viewed the longest and fixated the most, while angry faces were viewed the shortest and fixated the least frequently. Within the domain of emotions with negative valence, we thus found opposing viewing patterns. Such opposing patterns of attentional preferences may reflect an threat-based attentional bias (99) as well as more avoidance tendencies on angry faces (101). Importantly, in many studies not showing such results, only one of the two negative emotions were presented, that is either fear or anger, which may have led to increased exploration of either of these facial expressions in comparison to other ones [e.g., (102, 103)].

By contrast, Mühlenbeck et al. (49) looked at both of these emotions in their study and did so within pairwise comparisons with neutral and happy faces. Similar to our results, they found the longest viewing times for fearful facial expressions and the lowest for angry ones, and accordingly argued against a general negative attention bias. While both emotions have threat connotations, they are shown in real life for different reasons and consequently require different responses (49). Fearful faces are shown as a response to a threat in the environment, this source has to be recognized and therefore attention is directed to the fearful face (104). An angry face, on the other hand, represents a direct threat from a counterpart and consequently results in avoidance behavior (105). To avoid harmful consequences, both fearful and angry faces require very specific responses compared to positive emotions, whose response behavior is more flexible (49).

Mogg et al. (106) suggested that these behavioral patterns arise from the fact that initially angry as well as fearful faces automatically attract attention, and in a later phase gaze is averted from angry faces while being maintained for fearful faces in order to determine an appropriate response. For the first phase of attentional alignment, this is consistent with Green et al. (47) idea of increased vigilance, relative to socially threatening stimuli.

For the *ASD group*, consistent with our prediction, we found emotion-specific deviations from the TD group in viewing time and fixation number. In this group, the emotion effect showed the strongest effect size and the greatest differentiation between emotions. This attentional weighting of emotions interacts with the TD's exploration behavior. This suggests that ASD subjects process emotions in different ways as suggested by the different "rankings" of emotions regarding viewing time and fixation number. This finding, hence, cannot be explained by threat-related assumptions alone. Fan et al. (59) found in their meta-analysis a small but significant effect for a bias toward threatening faces compared to happy faces in ASD participants. Likewise, ASD subjects in our study viewed fearful faces the longest, even when compared to happy faces. The finding that fear is viewed the longest, both in ASD and TD is found in a variety of studies that showed marked scanning behavior with respect to threatening facial expressions [e.g., (47, 107–109)]. However, this enhanced attention does not apply to the further threat-related emotion anger. Similar response mechanisms to TD could be hypothesized here, making angry faces more likely to be avoided, especially in more anxious subjects (101).

Atypical fixation patterns in the ASD participants of our study referred particularly to the significantly longer viewed and more frequently fixated facial expressions of surprise (and shorter viewed and less frequently fixated happy emotion expression). In line with this result, there are studies suggesting increased attentional orienting in ASD regarding the emotion of surprise (23, 110, 111), possibly in consequence of a less frequent experience and engagement with this emotion. In agreement with this reasoning is the common observation that experienced special educators avoid surprised reactions and surprising situations when working with individuals with autism, knowing that rigidity and thus little tolerance for surprises is core to their symptomatology (23). This may be due to surprise being a particularly "cognitive" emotion according to Baron-Cohen et al. (112). The notion here is that surprise differs from the other basic emotions in that it is not evoked by a situation alone, but can only be understood if the emotion-expressing subject's belief is understood. With appropriate reasoning regarding the "Theory of Mind," individuals with autism seem to exhibit partial difficulties (113–115), which could result in an increased attentional focus regarding such surprised expressions. Another peculiarity in the eye movements in the ASD group is shown by a more pronounced central bias, i.e., the consideration of the central position, which has not been shown so far for ASD, but has been shown for SCZ (see below).

Consistent with our prediction and previous studies, relative fixation preferences as revealed by the "ranking" of facial emotions were similar between *patients with ADHD* and control subjects. Both groups paid the most attention to the fearful facial expression and the least to the angry one. While we found minor differences for dwell times on surprised and happy expressions between TD and ADHD, the two groups showed the same ranking of emotions in terms of the proportion of fixation number. The only difference between the groups was in the proportion of fixation count, with patients with ADHD showing generally fewer fixations. Nevertheless, the similarities support the assumption that in ADHD the basic emotion processing skills are intact and not core to the symptomatology (27). Overall, it can be concluded on the basis of our results that participants with ADHD have similar attentional preferences for facial emotions as TD and thus presumably intact emotion processing. It should be noted, that from a statistical point of view not rejecting the null hypothesis does not amount to accepting it. Based on the psychopathology of ADHD, which does not include affective disturbances as core symptoms, as well as the pertinent literature (see introduction), finding no differences between participants with ADHD and neurotypical controls is the expected outcome of the comparison.

For the *SCZ group*, we found no emotion-related differences in viewing times as well as in fixation numbers. Consequently, there was no differentiation based on these eye movement parameters between emotions, which is consistent with our prediction. This group, in addition, showed significantly shorter dwell times and smaller proportions of fixation numbers for the faces, when compared to the TD group. Overall, our results indicate a generally impaired and constrained visual exploration behavior.

Constrained fixation during visual exploration in participants with schizophrenia has been well-replicated (116), and "minimal scanning behavior" or "staring" has been found to be positively correlated with blunted affect [e.g., (117–119)], a negative symptom of the disorder and one of the "four As" in Bleuler's conceptualization of schizophrenia. While it seems clinically intuitive to associate reduced exploration of emotional faces with affective flattening, it has been shown in various studies that this viewing pattern seems to be independent of the (emotional) content of the displayed pictures (116), calling for a broader explanatory construct. Visual exploration requires voluntary initiation and continuation of a specific form of behavior, the re-construction of complex visual stimuli by self-controlled and selective spatial sequencing of fixations. As such, decreased visual exploration resembles at the construct level "avolition," another negative symptom of schizophrenia, typically defined as decrease in the ability to initiate and persist in self-directed purposeful activities. While blunted affect and avolition are different facets of negative symptomatology, finding stable two-factorial solutions to self-reported symptoms that distinguish "positive" and "negative" symptoms in schizophrenia and schizotypy (120), may point to common underlying pathophysiological "mechanisms" [e.g., in fronto-temporal or cortico-basal networks, (121)]. The restricted exploration behavior is further supported by the observation of a stronger central bias in the SCZ group compared to TD, as also reported in previous studies (67, 117). It should be noted that the SCZ participants tested here were all early-onset SCZ cases, having developed psychoses before the age of 18 years. Only about 0.1–1.0% of all SCZ cases show such an early onset, putatively due to high genetic load and with an overall poor prognosis (122).

Both in the SCZ and the ASD sample we found an increased central bias, possibly pointing to a commonality between these two disorders in a general feature of visual exploration. However, as has been shown for smooth pursuit eye movements, ASD and SCZ may exhibit dissimilar neurophysiological "mechanisms" (123) underlying similar functional deficits (124). Such topics obviously should be resolved ideally in combined functional and neurophysiological studies.

LIMITATIONS, CONCLUSIONS, AND FUTURE DIRECTIONS

Several limitations of the study should be noted. First, the sample size was small, especially for the SCZ group, necessitating replication using larger groups. This is a potential limitation of the generalizability of our findings and limits the possibility of explaining within-group heterogeneity (by analyses of inter-dependencies). Second, another limitation is that all schizophrenia patients were receiving anti-psychotic medication. There is, hence, a confounder between diagnosis and medication status. For obvious ethical reasons, excluding this confounder is practically very difficult. Nevertheless, future studies measuring emotional preferences in drug naive patients could address this crucial issue. That said, other studies did either not report any relation between visual exploration and medication (65, 125, 126) or that, if anything, medication seems to "normalize" distorted processes, sliding study outcomes toward the null hypothesis rather than producing seeming "deficits" (127). Third, given the high number of different analyses between groups and emotions, the possibility of Type I error should be noted. Given the fairly "lenient" significance threshold of $p < 0.05$, it is important to consider the statistical problems of multiple tests, that is, the inflation of the alpha error. In addition of the requirements of an independent replication of our results, this problem enhances the need for discussions of effect sizes. Fourth, a further limitation of our study is the rather long testing duration, which may lead to different time-on-task effects for a given task between individuals, depending on the position of the task in test battery. While the counter-balanced task order reduces differences between tasks regarding general time-on-task effects—as well as group differences herein—, it increases within-group heterogeneity and thus the ANOVA error term. Importantly, such effects would push statistical results toward the null hypotheses and thus reduce rather than produce significant findings. Fifth, unfortunately, not all matching criteria were adequately considered. Gender in particular was not well-balanced between groups. Gender effects in various domains, for instance in face recognition (128), have been reported in the literature. We are, however, not aware of any studies reporting gender effects in emotional preferences. Therefore, we undertook several *post-hoc* analyses of gender effects within the TD, SCZ and ADHD groups as well as interaction effects of gender and group in comparisons between SCZ and ADHD on the one side and TD on the other. All these *post-hoc* analyses showed that the present paradigm did *not* unveil any significant gender effects (see methods Section). This potential threat to the internal validity of our study design had in fact no impact on our results. As a general comment, it should be noted that if gender imbalance characterizes a clinical population as is the case with all neurodevelopmental disorders, balancing gender between such clinical groups and controls impacts the external validity of a study. Moreover, previous studies showed no effect of gender on eye-movement parameters among others also in the study of emotional face processing (129–131).

Co-morbidity with other psychiatric disorders is a key feature of all neurodevelopmental disorders as the vast majority of such patients has at least one co-morbid diagnosis. Recruiting, for instance, ASD or ADHD patients without co-morbid disorder(s) is therefore not only a highly cumbersome undertaking, is also limits the generalizability of any finding seriously. We therefore decided to constrain our exclusion criteria to serious other psychiatric, neurological and medical conditions like psychosis or substance use (for the ASD and ADHD groups) epilepsy or preterm birth. Furthermore, the participants in the SCZ group had a main diagnosis of schizophrenia, schizophreniform or schizoaffective disorder. Given that all of them were early-onset SCZ cases, this sample is very rare and in addition co-morbidities are typically present [for a review see (132, 133)]. The co-morbidities could be statistically controlled for by studies of very large samples, which is very difficult to achieve. Conversely, excluding comorbid cases would render the sample non-representative of the population. Accordingly we decided not to limit generalizability by employing further exclusion criteria.

The present study also has a number of important implications. A methodological innovation of the present study that is based on Owen and O'Donovan (6) is the direct comparison of three disorders with neurodevelopmental etiology that have been grouped on the basis of qualitatively similar cognitive impairment. In our study we could show that attention for emotional expressions differed between the ASD and SCZ clinical groups compared to TD, whereas the ADHD group showed similar gaze behavior. Likewise, the ASD and SCZ differed whereas ADHD and SCZ did not. Accordingly, the ASD group showed primarily qualitative differences in attentional preferences for facial emotions, the SCZ differed mainly quantitatively from TD, and the ADHD group showed the same "ranking" of emotions as controls. Pending replication in larger samples, such different fixation patterns would suggest that attention for emotion does not tap into pathophysiological mechanism that are common to ASD, ADHD, and SCZ. Here, other processes unrelated to emotion processing may show opposite results, as recently shown by Canu et al. (134).

The approach of the present study implies support of the *National Institute of Mental Health's Research Domain Criteria* (RDoC) project to provide a framework for future research classification systems for mental disorders [see Cuthbert (135)]. This project focuses on functional dimensions of behavior as well as cognitive and affective processes as studied across the entire range of functioning and breaks up current heterogeneous disorder categories (136). The present study considered three clinical disorders in the light of Owen and O'Donovan's (6) model of a continuum of neurodevelopmental disorders.

The coexistence of commonalities and differences between ASD, ADHD, and SCZ in no way argues against the concept of the continuum, but rather for its multi-dimensionality, by means of which the disorder patterns can be adequately described with their individual as well as common impairments, but also intact functions. Thapar et al. (2) also describe the overlap of the three disorders in many areas of cognitive functioning, but still heterogeneous in terms of clinical characteristics. Accordingly, emotion processing is not equally impaired in all these disorders, but is an aspect that differentiates between them, along with similar deviations of other cognitive functions [see Canu et al. (134)]. In general, the concept of continuum should encourage to not use clinical categories too rigidly and to not assign them exclusively based on cut-off values of diagnostic instruments (2). This goal also underlies the RDoC approach. Therefore, the results presented here provide further information for the implementation of such an alternative approach to future diagnostic practice that integrates advances in genetics, neuroscience and cognitive science with the goal of more effective diagnostic and treatment (137).

As this is the first study to use eye tracking to compare emotion perception across the three clinical disorders ADHD, ASD, and SCZ, the results represent an important reference point for future research. As recommended by previous studies, we captured visual attention during emotion viewing [see Berggren et al. (45)]. However, in future research further aspects should be considered such as the use of more natural stimulus materials such as social scenes, as well as the control of facial configuration skills and implicit emotion recognition (45). Our paradigm proved to be an effective measure of attentional alignment and might allow differentiation of clinical groups based on three different eye movement patterns.

Finding impairments in eye movement patterns underscores the unique contribution of this methodology to the study of cognition as well as to differential diagnosis. The results of this study highlight the usefulness and importance of a joint investigation of disorders with neurodevelopmental etiology to examine commonalities and differences in multi-dimensional variable spaces to possibly reveal common pathophysiological mechanisms.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the University of Freiburg. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

DC and CK: study planning. DC, MB, and CK: data collection. JB, DC, and CK: data analysis. All authors: manuscript preparation. All authors contributed to the article and approved the submitted version.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th edition. Washington, DC: APA (2013). doi: 10.1176/appi.books.9780890425596
2. Thapar A, Cooper M, Rutter M. Neurodevelopmental disorders. *Lancet Psychiatry.* (2017) 4:339–46. doi: 10.1016/S2215-0366(16)30376-5
3. Weinberger DR. Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry.* (1987) 44:660–9. doi: 10.1001/archpsyc.1987.01800190080012
4. Bora E, Pantelis C. Meta-analysis of social cognition in attention-deficit/hyperactivity disorder (ADHD): comparison with healthy controls and autistic spectrum disorder. *Psychol Med.* (2016) 46:699–716. doi: 10.1017/S0033291715002573
5. Savla GN, Vella L, Armstrong CC, Penn DL, Twamley EW. Deficits in domains of social cognition in schizophrenia: a meta-analysis of the empirical evidence. *Schizophr Bull.* (2013) 39:979–92. doi: 10.1093/schbul/sbs080
6. Owen MJ, O'Donovan MC. Schizophrenia and the neurodevelopmental continuum:evidence from genomics. *World Psychiatry.* (2017) 16:227–35. doi: 10.1002/wps.20440
7. Hoogman M, Van Rooij D, Klein M, Boedhoe P, Ilioska I, Li T, et al. Consortium neuroscience of attention deficit/hyperactivity disorder and autism spectrum disorder: the ENIGMA adventure. *Hum Brain Mapp.* (2022) 43:37–55. doi: 10.1002/hbm.25029
8. Spronk M, Keane BP, Ito T, Kulkarni K, Ji JL, Anticevic A, et al. A whole-brain and cross-diagnostic perspective on functional brain network dysfunction. *Cerebral Cortex.* (2021) 31:547–61. doi: 10.1093/cercor/bhaa242
9. Taurines R, Schwenck C, Westerwald E, Sachse M, Siniatchkin M, Freitag C. ADHD and autism: differential diagnosis or overlapping traits? A selective review. *Attent Deficit Hyperact Disord.* (2012) 4:115–39. doi: 10.1007/s12402-012-0086-2
10. Waddington F, Hartman C, de Bruijn Y, Lappenschaar M, Oerlemans A, Buitelaar J, et al. Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD. *Euro Neuropsychopharmacol.* (2018) 28:994–1005. doi: 10.1016/j.euroneuro.2018.06.009
11. Blair RJR. Facial expressions, their communicatory functions and neuro–cognitive substrates. *Philos Trans R Soc Lond Ser B Biol Sci.* (2003) 358:561–72. doi: 10.1098/rstb.2002.1220
12. Herbold AK. *Neuronale und Psychophysiologische Korrelate der Emotionsverarbeitung von Gesunden und Patienten mit Gehirnläsionen.* (Doctoral Dissertation). University of Erfurt, Erfurt, Germany (2010).
13. Darwin C. *The Expression of the Emotions in Man and Animals by Charles Darwin.* New York, NY: John Murray (1872). doi: 10.1037/10001-000
14. Mondloch CJ, Geldart S, Maurer D, Grand RL. Developmental changes in face processing skills. *J Exp Child Psychol.* (2003) 86:67–84. doi: 10.1016/S0022-0965(03)00102-4
15. Walker-Andrews AS. Emotions and social development: infants' recognition of emotions in others. *Pediatrics.* (1998) 102 (Supplement E1):1268–71. doi: 10.1542/peds.102.SE1.1268
16. Ekman P, Sorenson ER, Friesen WV. Pan-cultural elements in facial displays of emotion. *Science.* (1969) 164:86–8. doi: 10.1126/science.164.3875.86
17. Palermo R, Coltheart M. Photographs of facial expression: accuracy, response times, and ratings of intensity. *Behav Res Methods Instru Comp.* (2004) 36:634–8. doi: 10.3758/BF03206544
18. Young AW, Rowland D, Calder AJ, Etcoff NL, Seth A, Perrett DI. Facial expression megamix: tests of dimensional and category accounts of emotion recognition. *Cognition.* (1997) 63:271–313. doi: 10.1016/S0010-0277(97)00003-6
19. Ekman P, Friesen WV. Constants across cultures in the face and emotion. *J Pers Soc Psychol.* (1971) 17:124–9. doi: 10.1037/h0030377
20. Kim H, Somerville LH, Johnstone T, Polis S, Alexander AL, Shin LM, et al. Contextual modulation of amygdala responsivity to surprised faces. *J Cogn Neurosci.* (2004) 16:1730–45. doi: 10.1162/0898929042947865
21. Zhao K, Yan WJ, Chen YH, Zuo XN, Fu X. Amygdala volume predicts inter-individual differences in fearful face recognition. *PLoS ONE.* (2013) 8:e74096. doi: 10.1371/journal.pone.0074096
22. Castelli F. Understanding emotions from standardized facial expressions in autism and normal development. *Autism.* (2005) 9:428–49. doi: 10.1177/1362361305056082
23. Jones CRG, Pickles A, Falcaro M, Marsden AJS, Happé F, Scott SK, et al. A multimodal approach to emotion recognition ability in autism spectrum disorders: emotion recognition in autism spectrum disorders. *J Child Psychol Psychiatry.* (2011) 52:275–85. doi: 10.1111/j.1469-7610.2010.02328.x
24. Loveland KA, Tunali–Kotoski B, Chen YR, Ortegon J, Pearson DA, Brelsford KA, et al. Emotion recognition in autism: verbal and nonverbal information. *Dev Psychopathol.* (1997) 9:579–93. doi: 10.1017/S0954579497001351
25. Ozonoff S, Pennington BF, Rogers SJ. Are there emotion perception deficits in young autistic children? *J Child Psychol Psychiatry.* (1990) 31:343–61. doi: 10.1111/j.1469-7610.1990.tb01574.x
26. Tracy JL, Robins RW, Schriber RA, Solomon M. Is emotion recognition impaired in individuals with autism spectrum disorders? *J Autism Dev Disord.* (2011) 41:102–9. doi: 10.1007/s10803-010-1030-y
27. Schwenck C, Schneider T, Schreckenbach J, Zenglein Y, Gensthaler A, Taurines R, et al. Emotion recognition in children and adolescents with attention-deficit/hyperactivity disorder (ADHD). *Attent Defic Hyperact Disord.* (2013) 5:295–302. doi: 10.1007/s12402-013-0104-z
28. Wells EL, Day TN, Harmon SL, Groves NB, Kofler MJ. Are emotion recognition abilities intact in pediatric ADHD? *Emotion.* (2019) 19:1192–205. doi: 10.1037/emo0000520
29. Altschuler MR, Trevisan DA, Wolf JM, Naples AJ, Foss-Feig JH, Srihari VH, et al. Face perception predicts affective theory of mind in autism spectrum disorder but not schizophrenia or typical development. *J Abnorm Psychol.* (2021) 130:413–22. doi: 10.1037/abn0000621
30. Sasson NJ, Pinkham AE, Weittenhiller LP, Faso DJ, Simpson C. Context effects on facial affect recognition in schizophrenia and

autism: behavioral and eye-tracking evidence. *Schizophr Bull.* (2016) 42:675–83. doi: 10.1093/schbul/sbv176

31. Vaskinn A, Sundet K, Friis S, Simonsen C, Birkenæs AB, Engh JA, et al. The effect of gender on emotion perception in schizophrenia and bipolar disorder. *Acta Psychiatr Scand.* (2007) 116:263–70. doi: 10.1111/j.1600-0447.2007.00991.x
32. Bal E, Harden E, Lamb D, Van Hecke AV, Denver JW, Porges SW. Emotion recognition in children with autism spectrum disorders: relations to eye gaze and autonomic state. *J Autism Dev Disord.* (2010) 40:358–70. doi: 10.1007/s10803-009-0884-3
33. Wright B, Clarke N, Jordan J, Young AW, Clarke P, Miles J, et al. Emotion recognition in faces and the use of visual context Vo in young people with high-functioning autism spectrum disorders. *Autism.* (2008) 12:607–26. doi: 10.1177/1362361308097118
34. Cadesky EB, Mota VL, Schachar RJ. Beyond words: how do children with ADHD and/or conduct problems process nonverbal information about affect? *J Am Acad Child Adolesc Psychiatry.* (2000) 39:1160–7. doi: 10.1097/00004583-200009000-00016
35. Shapiro EG, Hughes SJ, August GJ, Bloomquist ML. Processing of emotional information in children with attention-deficit hyperactivity disorder. *Dev Neuropsychol.* (1993) 9:207–24. doi: 10.1080/87565649309540553
36. Singh SD, Ellis CR, Winton ASW, Singh NN, Leung JP, Oswald DP. Recognition of facial expressions of emotion by children with attention-deficit hyperactivity disorder. *Behav Modif.* (1998) 22:128–42. doi: 10.1177/01454455980222002
37. Edwards J, Jackson HJ, Pattison PE. Emotion recognition via facial expression and affective prosody in schizophrenia: a methodological review. *Clin Psychol Rev.* (2002) 22:789–832. doi: 10.1016/S0272-7358(02)00130-7
38. Mandal MK, Pandey R, Prasad AB. Facial expressions of emotions and schizophrenia: a review. *Schizophr Bull.* (1998) 24:399–412. doi: 10.1093/oxfordjournals.schbul.a033335
39. Walker E, Marwit S, Emory E. A cross-sectional study of emotion recognition in schizophrenics. *J Abnorm Psychol.* (1980) 89:428–36. doi: 10.1037/0021-843X.89.3.428
40. Harms MB, Martin A, Wallace GL. Facial emotion recognition in autism spectrum disorders: a review of behavioral and neuroimaging studies. *Neuropsychol Rev.* (2010) 20:290–322. doi: 10.1007/s11065-010-9138-6
41. Borhani K, Nejati V. Emotional face recognition in individuals withattention-deficit/hyperactivity disorder: a review article. *Dev Neuropsychol.* (2018) 43:256–77. doi: 10.1080/87565641.2018.1440295
42. Sachse M, Schlitt S, Hainz D, Ciaramidaro A, Walter H, Poustka F, et al. Facial emotion recognition in paranoid schizophrenia and autism spectrum disorder. *Schizophr Res.* (2014) 159:509–14. doi: 10.1016/j.schres.2014.08.030
43. Golan O, Gordon I, Fichman K, Keinan G. Specific patterns of emotion recognition from faces in children with ASD: results of a cross-modal matching paradigm. *J Autism Dev Disord.* (2018) 48:844–52. doi: 10.1007/s10803-017-3389-5
44. Rutherford MD, Towns AM. Scan path differences and similarities during emotion perception in those with and without autism spectrum disorders. *J Autism Dev Disord.* (2008) 38:1371–81. doi: 10.1007/s10803-007-0525-7
45. Berggren S, Engström AC, Bölte S. Facial affect recognition in autism, ADHD and typical development. *Cogn Neuropsychiatry.* (2016) 21:213–27. doi: 10.1080/13546805.2016.1171205
46. Noton D, Stark L. Eye movements and visual perception. *Sci Am.* (1971) 224:34–43. http://www.jstor.org/stable/24922750
47. Green M, Williams L, Davidson D. Brief report. *Cogn Emot.* (2003) 17:779–86. doi: 10.1080/02699930302282
48. Henderson JM, Williams CC, Castelhano MS, Falk RJ. Eye movements and picture processing during recognition. *Percept Psychophys.* (2003) 65:725–34. doi: 10.3758/BF03194809
49. Mühlenbeck C, Pritsch C, Wartenburger I, Telkemeyer S, Liebal K. Attentional bias to facial expressions of different emotions – a cross-cultural comparison of ≠ Akhoe Hai||om and German children and adolescents. *Front Psychol.* (2020) 11:795. doi: 10.3389/fpsyg.2020.00795
50. Sullivan LA, Kirkpatrick SW. Facial interpretation and component consistency. *Genet Soc Gen Psychol Monogr.* (1996) 122:389–404.
51. García-Blanco A, López-Soler C, Vento M, García-Blanco MC, Gago B, Perea M. Communication deficits and avoidance of angry faces in children with autism spectrum disorder. *Res Dev Disabil.* (2017) 62:218–26. doi: 10.1016/j.ridd.2017.02.002
52. Król ME, Król M. A novel machine learning analysis of eye-tracking data reveals suboptimal visual information extraction from facial stimuli in individuals with autism. *Neuropsychologia.* (2019) 129:397–406. doi: 10.1016/j.neuropsychologia.2019.04.022
53. Tang JSY, Chen NTM, Falkmer M, Bölte S, Girdler S. Atypical visual processing but comparable levels of emotion recognition in adults with autism during the processing of social scenes. *J Autism Dev Disord.* (2019) 49:4009–18. doi: 10.1007/s10803-019-04104-y
54. Tsang V. Eye-tracking study on facial emotion recognition tasks in individuals with high-functioning autism spectrum disorders. *Autism.* (2018) 22:161–70. doi: 10.1177/1362361316667830
55. Uono S, Sato W, Toichi M. Dynamic fearful gaze does not enhance attention orienting in individuals with Asperger's disorder. *Brain Cogn.* (2009) 71:229–33. doi: 10.1016/j.bandc.2009.08.015
56. Matsuda S, Minagawa Y, Yamamoto J. Gaze behavior of children with ASD toward pictures of facial expressions. *Autism Res Treat.* (2015) 2015:1–8. doi: 10.1155/2015/617190
57. Krysko KM, Rutherford MD. A threat-detection advantage in those with autism spectrum disorders. *Brain Cogn.* (2009) 69:472–80. doi: 10.1016/j.bandc.2008.10.002
58. Bochet A, Franchini M, Kojovic N, Glaser B, Schaer M. Emotional vs. neutral face exploration and habituation: an eye-tracking study of preschoolers with autism spectrum disorders. *Front Psychiatry.* (2021) 11:568997. doi: 10.3389/fpsyt.2020.568997
59. Fan XZ, Duan YW, Yi LX, He HZ. Attentional bias toward threatening emotional faces in individuals with autism spectrum disorder: a meta-analysis on reaction time tasks. *Res Autism Spectr Disord.* (2020) 78:101646. doi: 10.1016/j.rasd.2020.101646
60. Serrano VJ, Owens JS, Hallowell B. Where children with ADHD direct visual attention during emotion knowledge tasks: relationships to accuracy, response time, ADHD symptoms. *J Atten Disord.* (2018) 22:752–63. doi: 10.1177/1087054715593632
61. Ahmadi M, Judi M. Initial orientation of attention towards emotional faces in children with attention deficit hyperactivity disorder. *Iran J Psychiatry.* (2011) 6:87–91.
62. Pishyareh E, Tehrani-Doost M, Mahmoodi-Gharaie J, Khorrami A, Joudi M, Ahmadi M. Attentional bias towards emotional scenes in boys with attention deficit hyperactivity disorder. *Iran J Psychiatry.* (2012) 7:93–6.
63. Delerue C, Laprévote V, Verfaillie K, Boucart M. Gaze control during face exploration in schizophrenia. *Neurosci Lett.* (2010) 482:245–9. doi: 10.1016/j.neulet.2010.07.048
64. Li H, Chan RCK, McAlonan GM, Gong QY. Facial emotion processing in schizophrenia: a meta-analysis of functional neuroimaging data. *Schizophr Bull.* (2010) 36:1029–39. doi: 10.1093/schbul/sbn190
65. Loughland CM, Williams LM, Gordon E. Visual scanpaths to positive and negative facial emotions in an outpatient schizophrenia sample. *Schizophr Res.* (2002) 55:159–70. doi: 10.1016/S0920-9964(01)00186-4
66. Quirk SW, Strauss ME. Visual exploration of emotion eliciting images by patients with schizophrenia. *J Nerv Ment Dis.* (2001) 189:757–65. doi: 10.1097/00005053-200111000-00005
67. Bestelmeyer PEG, Tatler BW, Phillips LH, Fraser G, Benson PJ, St.Clair D. Global visual scanning abnormalities in schizophrenia and bipolar disorder. *Schizophr Res.* (2006) 87:212–22. doi: 10.1016/j.schres.2006.06.015
68. Silberg JE, Agtzidis I, Startsev M, Fasshauer T, Silling K, Sprenger A, et al. Free visual exploration of natural movies in schizophrenia. *Eur Arch Psychiatry Clin Neurosci.* (2019) 269:407–18. doi: 10.1007/s00406-017-0863-1
69. Asgharpour M, Tehrani-Doost M, Ahmadi M, Moshki H. Visual attention to emotional face in schizophrenia: an eye tracking study. *Iran J Psychiatry.* (2015) 10:13–8.
70. Green MJ, Williams LM, Davidson D. Visual scanpaths to threat-related faces in deluded schizophrenia. *Psychiatry Res.* (2003) 119:271–85. doi: 10.1016/S0165-1781(03)00129-X

71. Wade J, Nichols HS, Ichinose M, Bian D, Bekele E, Snodgress M, et al. Extraction of emotional information via visual scanning patterns: a feasibility study of participants with schizophrenia and neurotypical individuals. *ACM Trans Access Comput.* (2018) 11:1–20. doi: 10.1145/3282434
72. Kerr SL, Neale JM. Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance?. *J Abnorm Psychol.* (1993) 102:312. doi: 10.1037/0021-843X.102.2.312
73. Silver H, Bilker W, Goodman C. Impaired recognition of happy, sad and neutral expressions in schizophrenia is emotion, but not valence, specific and context dependent. *Psychiatry Res.* (2009) 169:101–6. doi: 10.1016/j.psychres.2008.11.017
74. García-Blanco A, Salmerón L, Perea M, Livianos L. Attentional biases toward emotional images in the different episodes of bipolar disorder: an eye-tracking study. *Psychiatry Res.* (2014) 215:628–33. doi: 10.1016/j.psychres.2013.12.039
75. Christiansen H, Kis B, Hirsch O, Matthies S, Hebebrand J, Uekermann J, et al. German validation of the conners adult ADHD rating scales (CAARS) II: reliability, validity, diagnostic sensitivity and specificity. *Euro Psychiatry.* (2012) 27:321–8. doi: 10.1016/j.eurpsy.2010.12.010
76. Rühl D, Bölte S, Feineis-Matthews S, Poustka F. *Diagnostische Beobachtungsskala für Autistische Störungen (ADOS).* Huber: Deutsche Fassung der Autism Diagnostic Observation Schedule (2004).
77. Bölte S, Rühl D, Schmötzer G, Poustka F. *Diagnostisches Interview für Autistische Störungen Revidiert (ADI-R).* Huber: Deutsche Fassung des Autism Diagnostic Interview revised (2006).
78. Bölte S, Poustka F. *SRS: Skala zur Erfassung sozialer Reaktivität.* Huber: Dimensionale Autismus-Diagnostik. Deutsche Fassung der Social Responsiveness Scale (SRS) von John N. Constantino und Christian P. Gruber (2008).
79. Weiß RH, Weiß B. *CFT 20-R mit WS/ZF-R: Grundintelligenztest Skala 2-Revision (CFT 20-R) mit Wortschatztest und Zahlenfolgentest-Revision (WS/ZF-R).* Hogrefe (2008).
80. Petermann F, Petermann U. *Hamburg-Wechsler-Intelligenztest für Kinder IV (HAWIK-IV).* Hogrefe (2007).
81. Raven J, Raven JC, Court HH. *Raven manual: Section 3. Standard Progressive Matrices*. Oxford: Oxford Psychologists Press Ltd (2000).
82. Bilker WB, Hansen JA, Brensinger CM, Richard J, Gur RE, Gur RC. Development of abbreviated nine-item forms of the raven's standard progressive matrices test. *Assessment.* (2012) 19:354–69. doi: 10.1177/1073191112446655
83. Langner O, Dotsch R, Bijlstra G, Wigboldus DHJ, Hawk ST, van Knippenberg A. Presentation and validation of the radboud faces database. *Cogn Emot.* (2010) 24:1377–88. doi: 10.1080/02699930903485076
84. Eizenman M, Lawrence HY, Grupp L, Eizenman E, Ellenbogen M, Gemar M, et al. A naturalistic visual scanning approach to assess selective attention in major depressive disorder. *Psychiatry Res.* (2003) 118:117–28. doi: 10.1016/S0165-1781(03)00068-4
85. Kellough JL, Beevers CG, Ellis AJ, Wells TT. Time course of selective attention in clinically depressed young adults: An eye tracking study. *Behav Res Ther*. (2008) 46:1238–43. doi: 10.1016/j.brat.2008.07.004
86. Heuer S, Hallowell B. Visual attention in a multiple-choice task: Influences of image characteristics with and without presentation of a verbal stimulus. *Aphasiology* (2009) 23:351–63. doi: 10.1080/02687030701770474
87. Ellis AJ, Beevers CG, Wells TT. Attention allocation and incidental recognition of emotional information in dysphoria. *Cogn Ther Res.* (2011) 35:425–33. doi: 10.1007/s10608-010-9305-3
88. Sears CR, Thomas CL, LeHuquet JM, Johnson JC. Attentional biases in dysphoria: An eye-tracking study of the allocation and disengagement of attention. *Cogn Emot*. (2010) 24:1349–68. doi: 10.1080/02699930903399319
89. Leyman L, De Raedt R, Vaeyens R, Philippaerts RM. Attention for emotional facial expressions in dysphoria: an eye-movement registration study. *Cogn Emot.* (2011) 25:111–20. doi: 10.1080/02699931003593827
90. Schneider BA, Avivi-Reich M, Mozuraitis M. A cautionary note on the use of the analysis of covariance (ANCOVA) in classification designs with and without within-subject factors. *Front Psychol.* (2015) 6:474. doi: 10.3389/fpsyg.2015.00474
91. Dennis M, Francis DJ, Cirino PT, Schachar R, Barnes MA, Fletcher JM. Why IQ is not a covariate in cognitive studies of neurodevelopmental disorders. *J Int Neuropsychol Soc.* (2009) 15:331–43. doi: 10.1017/S1355617709090481
92. Glass GV, Peckham PD, Sanders JR. Consequences of failure to meet assumptions underlying the fixed effects analyses of variance and covariance. *Rev Educ Res.* (1972) 42:237–88. doi: 10.3102/00346543042003237
93. Harwell MR, Rubinstein EN, Hayes WS, Olds CC. Summarizing Monte Carlo results in methodological research: the one-and two-factor fixed effects ANOVA cases. *J Educ Stat.* (1992) 17:315–39. doi: 10.3102/10769986017004315
94. Salkind NJ, editor. *Encyclopedia of Research Design.* Vol. 1. Thousand Oaks, CA: Sage (2010). doi: 10.4135/9781412961288
95. Faul F, Erdfelder E, Lang AG, Buchner A. *G*Power (Version 3.1.9.6) [Software]*. (2014). Available online at: http://www.gpower.hhu.de/
96. Baumeister RF, Bratslavsky E, Finkenauer C, Vohs KD. Bad is stronger than good. *Rev Gen Psychol.* (2001) 5:323–70. doi: 10.1037/1089-2680.5.4.323
97. Rozin P, Royzman EB. Negativity bias, negativity dominance, and contagion. *Pers Soc Psychol Rev.* (2001) 5:296–320. doi: 10.1207/S15327957PSPR0504_2
98. Frischen A, Eastwood JD, Smilek D. Visual search for faces with emotional expressions. *Psychol Bull.* (2008) 134:662–76. doi: 10.1037/0033-2909.134.5.662
99. Vaish A, Grossmann T, Woodward A. Not all emotions are created equal: the negativity bias in social-emotional development. *Psychol Bull.* (2008) 134:383–403. doi: 10.1037/0033-2909.134.3.383
100. Yiend J. The effects of emotion on attention: a review of attentional processing of emotional information. *Cogn Emot.* (2010) 24:3–47. doi: 10.1080/02699930903205698
101. Lisk S, Vaswani A, Linetzky M, Bar-Haim Y, Lau JYF. Systematic review and meta-analysis: eye-tracking of attention to threat in child and adolescent anxiety. *J Am Acad Child Adolesc Psychiatry.* (2020) 59:88–99.e1. doi: 10.1016/j.jaac.2019.06.006
102. Hansen CH, Hansen RD. Finding the face in the crowd: an anger superiority effect. *J Pers Soc Psychol.* (1988) 54:917–24. doi: 10.1037/0022-3514.54.6.917
103. Rossignol M, Campanella S, Bissot C, Philippot P. Fear of negative evaluation and attentional bias for facial expressions: an event-related study. *Brain Cogn.* (2013) 82:344–52. doi: 10.1016/j.bandc.2013.05.008
104. Öhman A. Fear and anxiety. In: Lewis M, Haviland-Jones JM, Feldman L, editors. *Barrett Handbook of Emotions.* New York, NY: Guilford Press (2008). p. 709–29.
105. Marsh AA, Ambady N, Kleck RE. The effects of fear and anger facial expressions on approach- and avoidance-related behaviors. *Emotion.* (2005) 5:119–24. doi: 10.1037/1528-3542.5.1.119
106. Mogg K, Garner M, Bradley BP. Anxiety and orienting of gaze to angry and fearful faces. *Biol Psychol.* (2007) 76:163–9. doi: 10.1016/j.biopsycho.2007.07.005
107. de Wit TC, Falck-Ytter T, von Hofsten C. Young children with autism spectrum disorder look differently at positive versus negative emotional faces. *Res Autism Spectr Disord.* (2008) 2:651–9. doi: 10.1016/j.rasd.2008.01.004
108. Haviland JM, Walker-Andrews AS, Huffman LR, Toci L, Alton K. Intermodal perception of emotional expressions by children with autism. *J Dev Phys Disabil.* (1996) 8:77–88. doi: 10.1007/BF02578441
109. van der Geest JN, Kemner C, Verbaten MN, van Engeland H. Gaze behavior of children with pervasive developmental disorder toward human faces: a fixation time study. *J Child Psychol Psychiatry.* (2002) 43:669–78. doi: 10.1111/1469-7610.00055
110. Pino MC, Vagnetti R, Valenti M, Mazza M. Comparing virtual vs real faces expressing emotions in children with autism: an eye-tracking study. *Educ Inform Technol.* (2021) 26:5717–32. doi: 10.1007/s10639-021-10552-w
111. Wieckowski AT, White SW. Eye-Gaze analysis of facial emotion recognition and expression in adolescents with ASD. *J Clin Child Adolesc Psychol.* (2017) 46:110–24. doi: 10.1080/15374416.2016.1204924
112. Baron-Cohen S, Spitz A, Cross P. Do children with autism recognise surprise? A research note. *Cogn Emot.* (1993) 7:507–16. doi: 10.1080/02699939308409202
113. Baron-Cohen S, Jolliffe T, Mortimore C, Robertson M. Another advanced test of theory of mind: evidence from very high functioning adults with autism or asperger syndrome. *J Child Psychol Psychiatry.* (1997) 38:813–22.

114. Happe F, Ehlers S, Fletcher P, Frith U, Johansson M, Gillberg C, et al. 'Theory of mind' in the brain. Evidence from a PET scan study of Asperger syndrome. *Neuroreport*. (1996) 8:197–201. doi: 10.1097/00001756-199612200-00040
115. Rutherford MD, Baron-Cohen S, Wheelwright S. Reading the mind in the voice: a study with normal adults and adults with asperger syndrome and high functioning autism. *J Autism Dev Disord.* (2002) 32:189–94. doi: 10.1023/A:1015497629971
116. Bestelmeyer PEG. Visual scanning abnormalities as biomarker for schizophrenia. In: *The Handbook of Neuropsychiatric Biomarkers, Endophenotypes and Genes*. Springer (2009). p. 221–6. doi: 10.1007/978-1-4020-9464-4_15
117. Gaebel W, Ulrich G, Frick K. Visuomotor performance of schizophrenic patients and normal controls in a picture viewing task. *Biol Psychiatry.* (1987) 22:1227–37. doi: 10.1016/0006-3223(87)90030-8
118. Kee KS, Horan WP, Wynn JK, Mintz J, Green MF. An analysis of categorical perception of facial emotion in schizophrenia. *Schizophr Res.* (2006) 87:228–37. doi: 10.1016/j.schres.2006.06.001
119. Kojima T, Potkin SG, Kharazmi M, Matsushima E, Herrera J, Shimazono Y. Limited eye movement patterns in chronic schizophrenic patients. *Psychiatry Res.* (1989) 28:307–14. doi: 10.1016/0165-1781(89)90211-4
120. Klein C, Berg P, Rockstroh B, Andresen B. Topography of the auditory P300 in schizotypal personality. *Biol Psychiatry*. (1999) 45:1612–21. doi: 10.1016/S0006-3223(98)00254-6
121. Correll CU, Schooler NR. Negative symptoms in schizophrenia: a review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatr Dis Treat.* (2020) 16:519. doi: 10.2147/NDT.S225643
122. Remschmidt H. Early-onset schizophrenia as a progressive-deteriorating developmental disorder: evidence from child psychiatry. *J Neural Transm.* (2002) 109:101–17. doi: 10.1007/s702-002-8240-3
123. Shishido E, Ogawa S, Miyata S, Yamamoto M, Inada T, Ozaki N. Application of eye trackers for understanding mental disorders: cases for schizophrenia and autism spectrum disorder. *Neuropsychopharmacol Rep.* (2019) 39:72–7. doi: 10.1002/npr2.12046
124. Takarae Y, Minshew NJ, Luna B, Krisky CM, Sweeney JA. Pursuit eye movement deficits in autism. *Brain.* (2004) 127:2584–94. doi: 10.1093/brain/awh307
125. Streit M, Wölwer W, Gaebel W. Facial-affect recognition and visual scanning behaviour in the course of schizophrenia. *Schizophr Res.* (1997) 24:311–7. doi: 10.1016/S0920-9964(96)00126-0
126. Zhu XL, Tan SP, De Yang F, Sun W, Song CS, Cui JF, et al. Visual scanning of emotional faces in schizophrenia. *Neurosci Lett.* (2013) 552:46–51. doi: 10.1016/j.neulet.2013.07.046
127. Williams LM, Loughland CM, Green MJ, Harris AW, Gordon E. Emotion perception in schizophrenia: an eye movement study comparing the effectiveness of risperidone vs. haloperidol. *Psychiatry Res.* (2003) 120:13–27. doi: 10.1016/S0165-1781(03)00166-5
128. Herlitz A, Lovén J. Sex differences and the own-gender bias in face recognition: a meta-analytic review. *Vis Cogn.* (2013) 21:1306–36. doi: 10.1080/13506285.2013.823140
129. Calvo MG, Lundqvist D. Facial expressions of emotion (KDEF): identification under different display-duration conditions. *Behav Res Methods.* (2008) 40:109–15. doi: 10.3758/BRM.40.1.109
130. Cangöz B, Altun A, Aşkar P, Baran Z, Mazman SG. Examining the visual screening patterns of emotional facial expressions with gender, age and lateralization. *J Eye Mov Res.* (2013) 118:1–15. doi: 10.16910/jemr.6.4.3
131. Grimshaw GM, Bulman-Fleming MB, Ngo C. A signal-detection analysis of sex differences in the perception of emotional faces. *Brain Cogn.* (2004) 54:248–50. doi: 10.1016/j.bandc.2004.02.029
132. De Berardis D, De Filippis S, Masi G, Vicari S, Zuddas A. A neurodevelopment approach for a transitional model of early onset schizophrenia. *Brain Sci.* (2021) 11:275. doi: 10.3390/brainsci11020275
133. Stentebjerg-Olesen M, Pagsberg AK, Fink-Jensen A, Correll CU, Jeppesen P. Clinical characteristics and predictors of outcome of schizophrenia-spectrum psychosis in children and adolescents: a systematic review. *J Child Adolesc Psychopharmacol.* (2016) 26:410–27. doi: 10.1089/cap.2015.0097
134. Canu D, Ioannou C, Müller K, Martin B, Fleischhaker C, Biscaldi M, et al. Visual search in neurodevelopmental disorders: evidence towards a continuum of impairment. *Eur Child Adolesc Psychiatry*. (2021) 1–18. doi: 10.1007/s00787-021-01756-z
135. Cuthbert BN. Research domain criteria: toward future psychiatric nosologies. *Dialogues Clin Neurosci.* (2015) 17:89–97. doi: 10.31887/DCNS.2015.17.1/bcuthbert
136. Cuthbert BN. The role of RDoC in future classification of mental disorders. *Dialogues Clin Neurosci.* (2020) 22:81–5. doi: 10.31887/DCNS.2020.22.1/bcuthbert
137. Cuthbert BN. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *World Psychiatry*. (2014) 13:28–35. doi: 10.1002/wps.20087

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Advantages of publishing in Frontiers

OPEN ACCESS
Articles are free to read
for greatest visibility
and readership

FAST PUBLICATION
Around 90 days
from submission
to decision

HIGH QUALITY PEER-REVIEW
Rigorous, collaborative,
and constructive
peer-review

TRANSPARENT PEER-REVIEW
Editors and reviewers
acknowledged by name
on published articles

Frontiers
Avenue du Tribunal-Fédéral 34
1005 Lausanne | Switzerland

Visit us: www.frontiersin.org
Contact us: frontiersin.org/about/contact

REPRODUCIBILITY OF RESEARCH
Support open data
and methods to enhance
research reproducibility

DIGITAL PUBLISHING
Articles designed
for optimal readership
across devices

FOLLOW US
@frontiersin

IMPACT METRICS
Advanced article metrics
track visibility across
digital media

EXTENSIVE PROMOTION
Marketing
and promotion
of impactful research

LOOP RESEARCH NETWORK
Our network
increases your
article's readership