J Exp Clin Med 2014;6(6):179–186

Contents lists available at ScienceDirect

Journal of Experimental and Clinical Medicine

journal homepage: http://www.jecm-online.com

REVIEW ARTICLE

Prevalence of Comorbid Psychiatric Disorders in Children and Adolescents with Autism Spectrum Disorder

Luke Y. Tsai [1, 2 *]

[1] Department of Psychiatry, University of Michigan Medical School, Ann Arbor, MI, USA
[2] Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, USA

ARTICLE INFO

Article history:
Received: Sep 19, 2014
Revised: Sep 24, 2014
Accepted: Oct 2, 2014

KEY WORDS:
anxiety disorders;
attention-deficit/hyperactivity disorder;
autism spectrum disorder;
children and adolescents;
mood disorders;
pervasive developmental disorder

This review is based on an extensive literature search to determine the prevalence of comorbid psychiatric disorders in children and adolescents with autism spectrum disorder (ASD) and shows that case reports and clinic- and community-based studies are available with which to assess this prevalence. Attention-deficit/hyperactivity disorder, anxiety disorders, and mood disorders frequently present in children and adolescents with ASD. However, a valid and reliable prevalence of comorbid psychiatric disorders in children and adolescents with ASD has not been established as a result of the limited number and small sample sizes of the reported studies.

1. Introduction

1.1. Evolution of definition

In 1943, Kanner[1] described a group of 11 children with a previously unrecognized disorder. He noted that these children had a number of characteristic features, such as an inability to develop relationships with people, extreme aloofness, a delay in speech development, and noncommunicative use of speech. Other features included repeated simple patterns of play activities and islets of ability. He adopted the term early infantile autism to describe this disorder and drew attention to the fact that its symptoms were already evident in infancy.

1.2. Diagnostic changes of definition of autism in DSM and ICD systems

The 1980 edition of the *International Classification of Diseases, 9th edition* (*ICD-9-CM*)[2] of the World Health Organization and the 1980 edition of the *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition* (*DSM-III*)[3] of the American Psychiatric Association both set definition and diagnostic criteria for infantile autism. *ICD-9-CM* and *DSM-III* have similar definitions and diagnostic criteria for infantile autism. However, the concepts of autism are different in these two publications. In *ICD-9-CM*, infantile autism is classified as a subtype of "psychoses with origin specific to childhood," whereas in *DSM-III*, and later in *DSM-III*-R,[4] infantile autism is viewed as a type of pervasive developmental disorder (PDD), which is defined as a group of severe, early developmental disorders characterized by delays and distortions in the development of social skills, cognition, and communication.

In 1994, the American Psychiatric Association published *DSM-IV*,[5] which continued to adopt the diagnostic term PDD. In *DSM-IV*,[5] these disorders include: autistic disorder (AD); Rett's disorder; childhood disintegrative disorder; Asperger's syndrome (AS); and PDD not otherwise specified (PDDNOS; including atypical autism). *DSM-IV*[5] also offers operational diagnostic criteria for all of the subtypes of PDD, except PDDNOS. This approach supports the taxonomic validity of each subtype and aims to facilitate research in the subclassification of these disorders. Since 1992, such a diagnostic subclassification has also been adopted in *ICD-10*.[6]

Despite the publication of the definition and diagnostic subclassification of PDD in *DSM-IV*[5] and *ICD-10*,[6] many non-medical professionals in the field of autism research prefer to use the term of autism spectrum disorder (ASD) to describe the disorders that are classified by the *DSM-IV*[5] and *ICD-10*[6] as AD, AS, and PDDNOS. One difference between the two diagnostic concepts (i.e., PDD and ASD) is that the PDD concept considers that AD, AS, and PDDNOS are three distinct clinical disorders, whereas the ASD

Conflicts of interest: None.

* Luke Y. Tsai, Department of Psychiatry, University of Michigan Medical School, 2385 Placid Way, Ann Arbor, MI 48105, USA.
E-mail: <lyctsai@umich.edu>.

http://dx.doi.org/10.1016/j.jecm.2014.10.005

concept generally considers these three disorders as a disorder on a continuum (i.e., AD as a severe form on one end, AS as a mild form on the other end, and PDDNOS as a moderate form in the middle). The recently published *DSM-5*[7] has adopted the ASD concept and has set up diagnostic guidelines.

1.3. Comorbid psychiatric conditions in ASD

Despite the changes in diagnostic terms and criteria, the field of ASD has consistently agreed that the core features are impairment in social interaction, impairment in communication, and restricted, repetitive, and stereotyped patterns of behavior, interests, and activities. Nevertheless, many patients with ASD also develop other behavioral and/or psychiatric symptoms in addition to the core features of ASD. The additional behavioral and/or psychiatric symptoms were described by many investigators prior to the early 1990s. Simons[8] reported in 1974 that compulsive behavior is observed in every child with a clear-cut diagnosis of autism. Ando and Yoshimura[9] reported in 1979 that among 47 autistic children (age range 6–14 years), 36% had hyperactivity, 68% had stereotyped behavior, 43% had self-injury, and 17% had fear. In a follow-up study of autistic adult men, Rumsey et al[10] reported in 1985 that 86% of these men continued to demonstrate stereotyped, compulsive behaviors, including arranging objects, and phonic tics. Le Couteur et al[11] in 1989 described that in 16 patients with autism (mean ± SD age 13.26 ± 3.38 years), 73% had separation anxiety, 89% had stereotyped utterances, 88% had unusual preoccupations, 55% had verbal rituals, 81% had compulsions/rituals, 69% showed hand–-finger mannerisms, and 63% had unusual sensory interests. Fombonne[12] in 1992 observed that in 20 French patients with autism (age range 11–26 years), 74% showed separation anxiety, 50% had stereotyped utterances, 53% had unusual preoccupations, 16% had compulsions or rituals, 74% showed hand–finger mannerisms, and 42% had unusual sensory interests. In a follow-up study of 66 patients with autism in Hong Kong, Chung et al[13] in 1990 noted that 47% of these children were hyperactive, 64% had poor attention and concentration, 24% showed self-injurious behaviors, 23% showed fears or phobias, 9% had depressive moods, 44% showed irritability or agitation, 29% showed inappropriate affects, 11% had sleep problems, and 8% exhibited tics.

These investigators, however, did not consider that these additional symptoms might be those of comorbid disorders and they did not specifically investigate the incidence of diagnosable psychiatric disorders based on any commonly used diagnostic criteria in their samples. This approach might be influenced by the *DSM-III*, *DSM-IIIR*, and *DSM-IV* diagnostic classification systems, which consider these additional symptoms as "associated features" of ASD. However, since the late 1980s there have been a number of case reports describing specific types of psychiatric disorders occurring in patients with ASD (reviewed by Tsai[14] in 1996). It is conceivable that some of the "associated features" may be the diagnostic features of other coexisting psychiatric disorders. The question addressed in this review is: How frequently do these comorbid psychiatric disorders exist?

2. Methods used to identify the relevant literature

Two approaches have been used in the published literature to address the question of whether patients with ASD have comorbid psychiatric disorders and the prevalence of these disorders. The focus of this review is to provide information on studies that have reported patients with ASD who have comorbid psychiatric disorders and the prevalence of comorbid psychiatric disorders in children and adolescents with ASD.

A systematic search of the literature was conducted to locate studies published between 1980 and 2014 that examined the comorbid psychiatric disorders of patients with ASD. The search was limited to English-language journal articles. Publications were identified by conducting searches in the major databases *PubMed*, *MEDLINE*, *PsycINFO*, and *ERIC*. Searches were conducted by entering the following terms: autism, pervasive developmental disorder, autism spectrum disorder, and comorbid psychiatric disorders. Reference lists from relevant articles (e.g., literature reviews) and recent editions of key journals (e.g., *Journal of Child Psychology and Psychiatry*, *Autism, Journal of Autism and Developmental Disorders*, and *Research of Autism Spectrum Disorder*) were also used to identify relevant articles. The search of the databases and reference lists was extended to the end of September 2014. Studies were included if they used the *DSM-III*, *DSM-III-R*, *DSM-IV*,[5] *DSM-IV-TR*, *ICD-10*,[6] *Autism Diagnostic Interview* (*ADI*),[11] *ADI-Revised*, *Autism Diagnostic Observation Scale* (ADOS)[15] criteria to diagnose patients and to include them in the studies.

3. Published work on comorbid psychiatric disorders in patients with ASD

3.1. Case reports of comorbid psychiatric disorders

Although case reports do not give information on the prevalence of comorbid psychiatric disorders in patients with ASD, they do provide some evidence to support the proposal that there are other important psychiatric disorders that often coexist with ASD.

3.1.1. Attention-deficit/hyperactivity disorder

In 2004, Goldstein and Schwebach[16] carried out a study to determine whether a sample of children meeting the diagnostic criteria for PDD displayed symptoms of impairment-related attention-deficit/hyperactivity disorder (ADHD) sufficient to warrant a comorbid diagnosis of ADHD. They found that of 57 children diagnosed with *DSM-IV* AD or PDDNOS, 26% also met the *DSM-IV* criteria for the combined type of ADHD and 33% met the diagnostic criteria for the inattentive type of ADHD. Yoshida and Uchiyama[17] found that 36 of 53 child and adolescent patients with a *DSM-IV* diagnosis of PDD also met the *DSM-IV* criteria for ADHD and that the co-occurrence rate of AS/PDDNOS (85%) was higher than for AD (57.6%).

In a retrospective study of stimulant response in children with ADHD and comorbid ASD, Santosh et al[18] identified 61 children who met the *DSM-IV* criteria for coexisting ADHD and ASD (7 with AD, 13 with AS and 41 with PDDNOS). In a prospective study, they found that 27 children met the *DSM-IV* criteria for coexisting ADHD and ASD.

Sinzig et al[19] compared the neuropsychological profiles of the attention functions of children with ASD and comorbid ADHD and identified 30 children aged from 6 years to 18 years. In a study of group differences to better understand the clinical phenotypes, Gadow et al[20] identified 88 children diagnosed with *DSM-IV* ASD and combined ADHD. In an assessment of the influence of psychiatric comorbidity on social skill treatment outcomes for children with ASD, Antshel et al[21] identified 25 children with ASD and comorbid anxiety disorder.

Clarke et al[22] studied electroencephalography differences to support the evidence for comorbid disorders and identified that 60 children with ADHD also had ASD diagnostic criteria of the developmental behavior checklist.[23] To study the efficacy and tolerability of atomoxetine in children with high-functioning ASD and combined ADHD, Zeiner et al[24] recruited 14 boys who qualified for the inclusion criteria. Jang et al[25] studied the rates of comorbid