Comorbidity in Schizophrenia: A review in children and adolescents

Marcos Altable Pérez *

[1]*Department of Pediatric Neurology and Neurodevelopment, Virgen de África Polyclinic, Spain*

Corresponding Author*

Marcos Altable Pérez

Master in Pediatric Neurology and Neurodevelopment and EEG Consultation at Virgen de África Polyclinic; Spain.

Tel: 263777970592

Email: neuroceuta@gmail.com

Received 04 August 2020; **Accepted** 15 September 2020; **Published** 21 September 2020

Abstract

Studies using standardized diagnostic interviews report particularly high comorbidity rates in children and adolescents with schizophrenia. However, the volume of symptoms other than those required to make the diagnosis of schizophrenia remains the subject of controversy. The question is to consider these symptoms as an additional diagnosis, or as associated characteristics. Be that as it may, the frequency of these symptoms highlights the problems of differential diagnosis encountered in early-onset schizophrenia, particularly during the initial phase of the disorder.

Keywords: Schizophrenia • Substance abuse • Disorders

Pervasive developmental disorders

Many studies raise the problem of possible kinship and the diagnostic limits between schizophrenia and autistic disorder. In the study by Asarnow and Ben-Meir, four of the schizophrenic children studied (23.5%) also had an associated diagnosis of pervasive developmental disorder [1-5]. Other studies also highlight the frequency of children who met the diagnostic criteria for autism before the onset of schizophrenia: 23% of cases in the study by Cantor [6], and 39% in the analysis by Watkins [7]. In the study by Alaghband-Rad et al., 35% of schizophrenic children studied had shown signs of pervasive developmental disorder (PDD), including 13% with the complete criteria for autistic disorder [8]. Russell also found in 26% of children before the onset of schizophrenia, various symptoms, such as echolalia and motor stereotypies, usually observed in pervasive developmental disorders, without that these children nevertheless have all the criteria necessary for the diagnosis of autistic disorder [9]. It appears that a large number of schizophrenic children manifest early developmental delays and behavioral abnormalities that do not meet the strict diagnostic criteria for autistic disorder.

Thus, Kolvin notes that while echolalia is found in 6% of schizophrenic children, 49% show a delay in psychomotor development, and 46% a delay in language [10]. However, other studies show that the risk of schizophrenia is no higher in children with a pervasive developmental disorder than in the general population [11,12]. Since schizophrenia appears to be a neurodevelopmental disorder, it may share common signs and symptoms with autistic disorder, even if the current data support a clear distinction between the two disorders [13,14].

Multiple and complex developmental disorders

In the same way, several authors have identified a group of children with marked impairment in functioning in multiple areas (particularly on the cognitive and social levels) in whom the diagnosis of schizophrenia was often wrongly posed. All of these children had presented with delays or developmental problems in early childhood. All of them presented, to varying degrees, neuropsychological deficits affecting the visuospatial domain, attention, impulse control, regulation of emotions, and language, in particular in its receptive aspect. All had significant social adjustment difficulties, but without presenting the qualitative changes in social interactions characteristic of pervasive developmental disorders. Clinically, one or more symptoms corresponding to various diagnostic categories, such as borderline or schizotypal personality disorders or conduct disorder, were generally found; however, they had not met all the required criteria. Similarly, attention deficit hyperactivity disorder (ADHD) was frequently found. Finally, all these children reported intermittent or subclinical psychotic symptoms: hallucinatory experiences, excessive and age-inappropriate fantasies, and mood instability [15-17]. In the absence of a precise diagnostic category capable of accounting for these children's clinical picture, Towbin proposed the term “multiple and complex developmental disorders” [18]. However, the question remains whether this clinical picture can be considered an autonomous diagnostic entity or whether it is only the early expression of a later evolution towards schizophrenia or other psychotic troubles [19]. Therapeutically, these children would not respond to antipsychotic treatment.

Mood disorders

Mood disturbances are usually reported in early-onset schizophrenia, with a frequency of about 27 to 83% [20-22]. Studies that have used standardized diagnostic interviews find mood disorders characterized by depressive type (depression, dysthymia) in children and adolescents with schizophrenia in 30 to 37% of cases, and in manic type in 4% of cases. Schizophrenia and affective psychoses share many common symptoms in children and adolescents, of athymic and psychotic nature [23,24]. All these data raise the problem of the diagnostic boundaries between schizophrenia, bipolar disorder, and schizoaffective disorder. They can also account for the frequency of diagnostic errors observed at this age of life [25-28]. About 50% of adolescents with bipolar disorder are first diagnosed as schizophrenic [29].

Several elements can help in the differential diagnosis between schizophrenia and affective psychoses. Clinically, several studies show that in children and adolescents, the onset of disorders most often appears insidious in schizophrenia, while in bipolar disorder it is most often acute, marked by disturbances of not only more frequent but also more severe moods. Similarly, the duration of the psychotic episode appears longer in schizophrenia, and the post-critical status is significantly more altered [30,31]. The study of premorbid history may also have some diagnostic value. In general, the premorbid history of schizophrenic children and adolescents shows significantly higher disturbances (developmental delays and disorders, social withdrawal, deterioration in peer relationships) than in children and adolescents with bipolar disorder or a schizoaffective disorder [32,33]. Finally, the study of family history shows that a history of schizophrenia is significantly more frequently found in the first degree parents of schizophrenic children and adolescents, while in the first degree parents of children and adolescents with a disorder bipolar or schizoaffective disorder are more frequently observed with a history of mood disorders [34,35].

Non-psychotic emotional and behavioral disorders

Several studies emphasize the frequency of emotional and behavioral disorders observed in schizophrenic children and adolescents, the most frequently found diagnoses including, in order of decreasing frequency, attention deficit hyperactivity disorder, the oppositional defiant disorder (ODD), separation anxiety disorder, generalized anxiety disorder and simple phobias [36]. At the same time, numerous studies emphasize the frequency of apparently psychotic symptoms (hallucinations, relational instability, affective instability, disorganized behavior) found in children and adolescents with non-psychotic emotional and behavioral disorders, the latter possibly being wrongly diagnosed as schizophrenic [37-39]. Compared to schizophrenic children and adolescents, they have little or no negative symptoms, behavioral irregularities, and disturbances in the thought process [40]. Follow-up studies show that they tend to progress more towards non-psychotic personality disorders, in particular of the borderline or antisocial type [41].

Furthermore, psychotic symptoms are frequently reported in mistreated children and adolescents, in particular in those with post-traumatic stress disorder [42]. Again, these children and adolescents can be misdiagnosed as schizophrenic, especially since a history of abuse is not uncommon in early-onset schizophrenia. The psychotic symptoms reported in children and adolescents with post-traumatic stress disorder correspond to anxious and dissociative phenomena, including fears and intrusive thoughts as well as feelings of unreality or depersonalization [43].

Obsessive-Compulsive Disorder

The difference between obsessive-compulsive disorder and schizophrenia is not always clear in children and adolescents. The seemingly almost delirious tenacity and irrationality of specific obsessive fears observed in children and adolescents, the quirkiness of their rituals, the irresistible nature of the agitation, aggression, and tantrums that they can manifest in connection with their obsessions and their compulsions, could lead to evoking the diagnosis of schizophrenia. The absence of hallucinations and disturbances and the preservation of contact with reality outside of obsessive-compulsive concerns generally allow this diagnosis to be ruled out. On the other hand, about 20% of schizophrenic children and adolescents also have an associated obsessive-compulsive disorder.

Substance abuse

Numerous studies have highlighted the frequency of substance abuse found among schizophrenic adolescents, with comorbidity rates of up to 50%. They also show that it is not uncommon for substance abuse to be observed when first psychotic symptoms appear [44-46]. In these cases, the question may arise of a psychotic disorder induced by the substance or substances consumed. The persistence of symptoms after a sufficiently long period of abstinence (generally more than a week) should suggest the diagnosis of schizophrenia. However, it now seems demonstrated that substance abuse can precipitate the onset of schizophrenia in adolescents at risk, presenting in particular schizotypal personality characteristics or a family history of schizophrenia [47-51].

Medical conditions

Many medical conditions are likely to induce psychotic disorders: epilepsies, lesions of the central nervous system (brain tumors, congenital malformations, traumatic brain injuries), neurodegenerative diseases, metabolic diseases and genetic abnormalities (endocrinopathies, Wilson disease), toxic encephalopathies, and infectious diseases (encephalitis, meningitis, infection with the human immunodeficiency virus). Some of these conditions may have an etiological role in the onset of schizophrenia, as is the case, for example, for bicycle-cardio-facial syndrome [52,53].

Conclusion

Studies using standardized diagnostic interviews report particularly high comorbidity rates in children and adolescents with schizophrenia. It appears that a large number of schizophrenic children manifest early developmental delays and behavioral abnormalities that do not meet the strict diagnostic criteria for autistic disorder. In the absence of a precise diagnostic category capable of accounting for these children's clinical picture, Towbin proposed the term “multiple and complex developmental disorders”. The premorbid history of schizophrenic children and adolescents shows significantly higher disturbances than in children and adolescents with bipolar disorder or a schizoaffective disorder. Compared to schizophrenic children and adolescents, they have little or no negative symptoms, behavioral irregularities, and disturbances in the thought process. The persistence of symptoms after a sufficiently long period of abstinence (generally more than a week) should suggest the diagnosis of schizophrenia.

Conflict of interest

The authors declare no conflict of interest.

References

1. Petty, L. K., et al. Autistic Children Who Become Schizophrenic. *Arch Gen Psychiatry*, 41 (1984): 129–135.
2. Ross, R. G., et al. High rates of comorbidity are found in childhood-onset schizophrenia. *Schizophr Res*, 88 (2006): 90–95
3. Hollis, C. Schizophrenia and Allied Disorders. In Rutter's Child and Adolescent Psychiatry: Fifth Edition. *Wiley Online Library*, (2009): 737–758.
4. McClellan, J., et al. Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. *J Am Acad Child Adolesc Psychiatry*, 40 (2001): 4S-23S.
5. Rosenbaum A.J., et al. Children With Schizophrenia Spectrum and Depressive Disorders: A Comparative Study of Premorbid Adjustment, Onset Pattern and Severity of Impairment. *J Child Psychol Psychiatry*, 29 (1998): 477–488.
6. Cantor, S., et al. Childhood schizphrenia: Present but not accounted for. *Am J Psychiatry*, 139 (1982): 758–762.
7. Watkins, J. M., et al. Symptom Development in Childhood Onset Schizophrenia. *J Child Psychol Psychiatry*, 29 (1988): 865–878.
8. Alaghband-Rad, J., et al. Childhood-Onset Schizophrenia: The Severity of Premorbid Course. *J Am Acad Child Adolesc Psychiatry*, 34 (1995): 1273–1283.
9. Russell, A. T., et al. The Phenomenology of Schizophrenia Occurring in Childhood. *J Am Acad Child Adolesc Psychiatry*, 28 (1989): 399–407.
10. Kolvin, I. Studies in the childhood psychoses. I. Diagnostic criteria and classification. *Br J Psychiatry*, 118 (1971), 381–384.
11. BURD, L., et al. A North Dakota Prevalence Study of Schizophrenia Presenting in Childhood. *J Am Acad Child Adolesc Psychiatry*, 26 (1987), 347–350.
12. Volkmar, F. R., et al. Comorbid association of autism and schizophrenia. *Am J Psychiatry*, 148 (1991): 1705–1707.
13. Harris, J. C. Schizophrenia : a neurodevelopmental disorder. *Dev Neuropsychol*, 2 (1998): 404-426.
14. Sporn, A. L., et al. Pervasive developmental disorder and childhood-onset schizophrenia: Comorbid disorder or a phenotypic variant of a very early onset illness? *Biol Psychiatry*, 55 (2004): 989–994.
15. Kumra, S., et al. 'Multidimensionally impaired disorder': Is it a variant of very early-onset schizophrenia? *J Am Acad Child Adolesc Psychiatry*, 37 (1998): 91–99.
16. Mckenna, K., et al. (1994). Looking for Childhood-Onset Schizophrenia: The First 71 Cases Screened. *J Am Acad Child Adolesc Psychiatry*, 33 (1994), 636–644.
17. Towbin, K. E., et al. Conceptualizing “Borderline Syndrome of Childhood” and “Childhood Schizophrenia” as a Developmental Disorder. *J Am Acad Child Adolesc Psychiatry*, 32 (1993), 775–782.
18. Towbin, K. E. (1997). Pervasive developmental disorder not otherwise specified. In Handbook of autism and pervasive developmental disorders. *Wiley Online Library* ,(1997): 123-147.
19. Sprong, M., et al. Pathways to psychosis: A comparison of the pervasive developmental disorder subtype Multiple Complex Developmental Disorder and the 'At Risk Mental State'. Schizophr Res, 99 (2008): 38–47.
20. Green, W. H., et al. A Comparison of Schizophrenic and Autistic Children. *J Am Acad Child Adolesc Psychiatry*, 23 (1984), 399–409.
21. Kydd, R. R., et al. Schizophrenia in children under 16 years. *J Autism Dev Disord*, 12 (1982), 343–357.
22. Volkmar, et al. Phenomenology and classification of the childhood psychoses. *Psychol Med*, 18 (1988), 191–201.
23. McClellan, et al. A follow-up study of early onset psychosis: Comparison between outcome diagnoses of schizophrenia, mood disorders, and personality disorders. *J Autism Dev Disord*, 23 (1993), 243–262.
24. Werry, et al. Childhood and Adolescent Schizophrenic, Bipolar, and Schizoaffective Disorders: A Clinical and Outcome Study. *J Am Acad Child Adolesc Psychiatry*, 30 (1991), 457–465.
25. Bailly, D., et al. Un diagnostic méconnu: la schizophrénie chez l'enfant. *Ann Med Psychol*, 161 (2003), 652–659.
26. Calderoni, D., et al. Differentiating childhood-onset schizophrenia from psychotic mood disorders. *J Am Acad Child Adolesc Psychiatry*, 40 (2001), 1190–1196.
27. Lofgren, D. P., et al. A prospective follow-up study of so-called borderline children. *Am J Psychiatry*, 148 (1991), 1541–1547.
28. McClellan, J., et al. Early onset psychotic disorders: Diagnostic stability and clinical characteristics. *Eur Child Adolesc Psychiatry*, 8 (1999).
29. Joyce, P. R. Age of onset in bipolar affective disorder and misdiagnosis as schizophrenia. Psychol Med, 14 (1998): 145–149.
30. Eisenberg, L.The Natural History of Psychiatric Disorder in Children. *Psychol Med*, 17 (1987): 784–786.
31. Gochman, P., et al. Childhood-onset schizophrenia: The challenge of diagnosis. *Curr Psychiatry Rep*, 13 (2011), 321–322.
32. Hollis, C. Child and adolescent (juvenile onset) schizophrenia. A case control study of premorbid developmental impairments. *Brit J Psychiat*, 166 (1995): 489–495.
33. McClellan, J M. Neurocognitive pathways in the development of schizophrenia. *Semin Clin Neurpsychiatry*, 3 (1998): 320–332.
34. Erlenmeyer-Kimling, L., et al. The New York High-Risk Project: Prevalence and comorbidity of Axis I disorders in offspring of schizophrenic parents at 25-year follow-up. *Arch Gen Psychiatry*, 54 (1997): 1096–1102.
35. Werry, John S. (1992). Child and adolescent (early onset) schizophrenia: A review in light of DSM-III-R. *J Autism Dev Disord*, 22 (1992), 601–624.

36. Hafner, H., et al. Epidemiology of schizophrenia. *Can J Psychiatry*, 42 (1997): 139–151.

37. Del Beccaro, M. A., et al. Hallucinations in Children: A Follow-up Study. *J Am Acad Child Adolesc Psychiatry*, 27 (1988): 462–465.

38. Garralda, M. E. Hallucinations in children with conduct and emotional disorders: I. The clinical phenomena. *Psychol Med*, 14 (1984): 589–596.

39. Hornstein, N. L., et al. Clinical Phenomenology of Child and Adolescent Dissociative Disorders. *J Am Acad Child Adolesc Psychiatry*, 31 (1992): 1077–1085.

40. Garralda, M. E. Characteristics of the psychoses of late onset in children and adolescents (A comparative study of hallucinating children). *J Adolesc*, 8 (1985): 195–207.

41. Thomsen, P. H. Schizophrenia with childhood and adolescent onset - A nationwide register-based study. *Acta Psychiatr Scand*, 94 (1996): 187–193.

42. Famularo, R., et al. Psychiatric Diagnoses of Maltreated Children: Preliminary Findings. *J Am Acad Child Adolesc Psychiatry*, 31 (1992): 863–867.

43. Altman, H., et al. Subclinical hallucinations and delusions in nonpsychotic adolescents. *J Child Psychol Psychiatry*, 38 (1997): 413–420.

44. Kutcher, S., et al. Substance abuse among adolescents with chronic mental illnesses: A pilot study of descriptive and differentiating features. *Can J Psychiatry*, 37 (1992): 428–431.

45. Pencer, A., et al. Outcome of a first episode of psychosis in adolescence: A 2-year follow-up. *Psychiatry Res*, 133 (2005), 35–43.

46. Shoval, G., et al. The use of illicit substances in adolescent schizophrenia inpatients. *Int J Adolesc Med Health*, 18 (2006): 643–648.

47. McGuire, P. K., et al. Morbid risk of schizophrenia for relatives of patients with cannabis-associated psychosis. *Schizophr Res*, 15 (1995), 277–281.

48. A, E., et al. Practitioner's guide to psychoactive drugs for children and adolescents. *Springer* ,(1998): 297–328.

49. Bailly, D. Adolescence and schizophrenia. *Encephale*, (2009): 35.

50. Stirling, J., et al. Cannabis-induced psychotic-like experiences are predicted by high schizotypy: Confirmation of preliminary results in a large cohort. *Psychopathology*, 41 (2008): 371–378.

51. Verdoux, H., et al. Impact of substance use on the onset and course of early psychosis. *Schizophr Res*, 79 (2005): 69–75.

52. Murphy, K. C., et al. Velo-cardio-facial syndrome: A model for understanding the genetics and pathogenesis of schizophrenia. *Brit J Psychiat*, 179 (2001): 397–402.

53. Usiskin, S. I., et al. Velocardiofacial syndrome in childhood-onset schizophrenia. *J Am Acad Child Adolesc Psychiatry*, 38 (1999): 1536–1543.