Training Module

Autism & Schizophrenia

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Emerging study results suggest that there are both clinical and biological links between autism and schizophrenia. The question regarding whether there is phenotypic overlap or comorbidity between autism and schizophrenia dates back to 1943, when Kanner[1] first used the term "autism" to describe egocentricity. The distinction between the two disorders remained unclear for nearly 30 years, until DSM-II included children with autism under the diagnostic umbrella of schizophrenia, childhood type. In 1971, Kolvin[2] conducted seminal research that highlighted the distinction between autism and schizophrenia, which influenced the decision to include the disorders as 2 separate categories in DSM-III.

The patient's age at the onset of symptoms and the clinical presentation distinguish autism from early- onset schizophrenia. Also, the disorders are treated differently.[2,3] Schizophrenia is thought to develop at a chance rate in individuals with autism. It is noteworthy, however, that children who have childhood- onset schizophrenia (COS) show fairly high premorbid rates of early developmental abnormalities.[2,4-7]

This article highlights the biological and clinical links between autism and schizophrenia. Childhood- onset schizophrenia COS-the onset of psychosis before age 13 years-is considered a rare and severe form of schizophrenia. Systematic studies of COS show high rates of the disorder being either preceded by or comorbid with autistic spectrum disorders (ASD).[7]

The first to describe the severity and frequency of prepsychotic developmental disorders in COS was Kolvin,[2] who noted deficits in communication, motor development, and social relatedness. These deficits were found in 28% to 55% of children with ASD, and these observations have been replicated in multiple studies.[6-8]

Retrospective studies of children with schizophrenia reveal delays in language acquisition and visual- motor coordination during early childhood before the onset of psychotic symptoms.[9] Alaghband-Rad and colleagues[10] reviewed the premorbid histories of children with COS and noted language delays and transient motor stereotypies (patterned repetitive movements, postures, and utterances). Their findings suggest early developmental abnormalities of the temporal and frontal lobes as evidenced by prepsychotic language difficulties; the early transient motor stereotypies indicate developmental abnormalities of the basal ganglia.

Shared Clinical Features

Although the disorders are distinct, they have shared clinical features. Social withdrawal, communication impairment, and poor eye contact seen in ASD are similar to the negative symptoms seen in youths with schizophrenia.[11] When higher-functioning individuals with autism are stressed, they become highly anxious and at times may appear thought-disordered and paranoid, particularly when they are asked to shift set (such as being asked to change a topic of conversation or to stop an activitythat they are engaged in and begin a new activity).[12] A subset of children (28%) in the ongoing NIMH study of COS have been reported to have comorbid COS and ASD.[7]

A number of researchers use different terms to describe this complex mix of psychiatric comorbidity and developmental psychopathology. At the Yale Child Study Center, a subgroup of children with ASD was labeled as having multiplex developmental disorder.[13,14] Researchers in the Netherlands used the term "multiple complex developmental disorders" (MCDD) to describe children who met criteria for ASD and also exhibited affect dysregulation and disordered thinking.[15-18] Of significant interest are follow-up studies, which showed that psychosis developed by adulthood in 64% of children with MCDD.[16]

Similarly, a study by Sprong and colleagues[19] that compared youths with MCDD with youths at risk for psychosis found that although the groups clearly had differing early developmental and treatment histories, there were no differences in schizotypal traits, disorganization, and general prodromal symptoms. In that study, 78% of the MCDD group met criteria for at-risk mental state. The authors concluded that children with MCDD are at high risk for psychosis later in life.

What is already known about autism and schizophrenia?

Although autism has long been recognized as a separate diagnostic entity from schizophrenia, both disorders share clinical features. Childhood-onset schizophrenia (COS), considered a rare and severe form of schizophrenia, frequently presents with premorbid developmental abnormalities. This prepsychotic developmental disorder includes deficits in communication, social relatedness, and motor development, similar to those seen in autism spectrum disorders (ASD).

What new information does this article add?

This article highlights the biological and clinical links between the two disorders, reviewing shared genetics, brain changes, and similarities and differences in clinical presentations.

What are the Implications for psychiatric practice?

Autism and schizophrenia may present as 2 separate disorders that need to be differentiated, or as comorbid conditions. It is important to remember that some individuals may have both COS and ASD, which has implications when designing appropriate biopsychosocial interventions. Adult psychiatrists may benefit from additional training in the diagnosis of ASD in

adults, whereas child psychiatrists may benefit from increased comfort with identifying primary psychotic symptoms in autistic youth.

Case Vignette

George is a 14-year-old boy who first presented to Dr. Frazier at age 8 with a diagnosis of ASD. The diagnosis had initially been made when George was 27 months old and had been reconfirmed by numerous well-regarded autism experts over the years. George had received the usual autism-specific services, and although he made gains, he continued to present with atypical behaviors. George was referred to Dr. Frazier because of an increase in the intensity and frequency of unusual and disturbing preoccupations that often had a morbid theme. Those who worked with him had difficulty in getting him off of these disturbing topics.

George also had unusual behaviors and mood-regulation difficulties. When he first presented to the clinic, he was disinhibited, emotionally unstable, and talked at length about his "other world." His thoughts were loosely connected and he spoke about the friends in his other world who were talking to him. Initially, these friends were humming to him or saying hello. Because of a history of at least one depressive episode and what appeared to be more of a chronic euphoric state with affective ability, George was given a provisional comorbid diagnosis of bipolar disorder with psychotic features. Over the ensuing years, despite a number of medication trials including atypical antipsychotics and mood stabilizers, he became tortured by more persistent auditory hallucinations. "She" was particularly disturbing to him and he wanted her to go away.

George's affective instability continued, but his thought disorder and psychosis have been the most enduring symptoms, even in the absence of mood dysregulation. His comorbid diagnosis was changed to schizoaffective disorder and, more recently, to schizophrenia. He is currently taking a typical antipsychotic. His thoughts are more linear, he rarely talks about "she," and he is much more able to engage in his schoolwork.

Although George's psychotic symptoms are well controlled by the medication, symptoms of ASD persist, including poor eye contact, ongoing failure to develop appropriate peer relationships, inability to sustain a conversation with others, encompassing preoccupation with restricted patterns of interest, stereotypies, and repetitive motor mannerisms. These symptoms, present since early childhood, predated his symptoms of psychosis and continue to require the support of autism-specific services.

Genetics

Although epidemiological studies of the genetic relationship between autism and schizophrenia are deficient, evidence does exist for shared genetic factors.[20] As with the majority of psychiatric disorders and other common conditions, genetic complexity is compounded by phenotypic complexity. Copy number variant and rare allele studies have found a relationship between autism and point and structural mutations in neurologins, neurexins, and related genes.[7] There have also been reports that implicate the neurexin family in schizophrenia.

Neurologins are a family of postsynaptic proteins that bind transsynaptically to neurexins, which are presynaptic proteins that seem necessary for both excitatory and inhibitory synaptogenesis and synapse maturation. This fits with the neurodevelopmental insult and imbalance in excitatory and inhibitory transmission hypothesis for both autism and schizophrenia.[20]

Specific deletions associated with schizophrenia include 22q11.2, 1q21.1, and 15q13.3, which have been found to be associated with autism, attention-deficit disorder, and mental retardation.20 In individuals with velocardiofacial syndrome (chromosome 22q11), rates of ASD and psychosis are higher.[21] Similarly, 16p11.2 microdeletions or microduplications have been reported in 1% of cases of autism and in 2% of the NIMH COS cohort.[22-24] These copy number variants confer a risk for a range of neurodevelopmental phenotypes that include autism and schizophrenia.[20] Although there have not been systemic comparisons of genome-wide association studies for autism and schizophrenia, some functional links have been reported at voltage-gated calcium channel genes, which are integral to presynaptic function and plasticity, across phenotypes.[20]

Brain Changes

Both autism and schizophrenia have accelerated trajectories of brain development around the age of symptom onset: those with autism have an acceleration or brain overgrowth during the first 3 years of life, and those with COS have an acceleration of brain development (pruning) during adolescence.[7]

Cheung and colleagues[25] attempted to quantify brain structural similarities and differences in ASD and schizophrenia using a quantified anatomical likelihood estimation approach to synthesize existing brain imaging datasets. Using this model, they extracted 313 foci from 25 voxel-based studies comprising 660 patients (308 ASD, 352 first-episode schizophrenia) and 801 controls. Those with ASD and schizophrenia had lower gray matter volumes within limbic-striato-thalamic neurocircuitry than did controls. Unique features included lower gray matter volume in the amygdala, caudate, and frontal and medial gyrus for schizophrenia, and lower gray matter volume in the putamen for autism. The researchers concluded that in terms of brain volumetrics, ASD and schizophrenia have a clear degree of overlap that may reflect shared etiological mechanisms.[25]

Treatments

A variety of psychosocial and educational interventions that support children with COS and children with ASD exist to address core deficits in socialization, communication, and behavior and the associated developmental and medical conditions. A thorough description is beyond the scope of this article, however. Atypical antipsychotics are the mainstay of pharmacotherapy for schizophrenia at any age, and they have also been used to manage certain symptoms, particularly irritability, associated with ASD.[26-28]

Conclusion

Developmental delays are described premorbidly in samples of children and adults with schizophrenia. More recently, the notion that ASD and schizophrenia can present comorbidly in a subset of patients has received further attention in the literature.[7,29] Yet our current diagnostic hierarchy implies that the two conditions are distinct.

The differential diagnosis between these disorders and the comorbid diagnoses of the two conditions is often a bit of a quagmire for clinicians. Our program is frequently asked to rule out ASD, schizotypal personality disorder and/or schizophreniform disorder, and first-episode schizophrenia in youths and young adults. We see children with ASD who have emerging psychotic symptoms. In these children, the hallucinations or delusional preoccupations may initially be attributed to the developmental disorder. Conversely, we also see adolescents or young adults with schizophrenia who have a developmental history consistent with ASD (typically higher functioning) and who continue to have comorbid ASD. Yet some have not previously received a diagnosis of ASD. Appropriate identification of comorbid conditions can enhance intervention efforts (eg, autism-related services for those with comorbid ASD and/or use of antipsychotics in patients who have comorbid ASD and a psychotic disorder).

The key take-away point is that there are some individuals who may have both COS and ASD. Adult psychiatrists and mental health professionals would benefit from further training in the diagnosis of ASD in adults, and child mental health professionals would benefit from training in the diagnosis of schizophrenia spectrum disorders in youths. Given the complex symptom profile in youths with schizophrenia spectrum disorders, there tends to be a delay in diagnosis, even when symptoms are present for years.[30] In addition, child mental health professionals would benefit from training in more specific identification of primary psychotic disorders in youths with ASD. Finally, care must be provided in an integrative manner-using a biopsychosocial model-for these multi-complex patients and their families.

Systematic long-term follow-up studies that include individuals with ASD and with COS are indicated to further inform the field regarding similarities and differences between autism and schizophrenia. These studies would benefit from the inclusion of genetics and characterization of family members to get a clearer sense of the genotype-phenotype associations and predictors of outcome.

See more at: http://www.psychiatrictimes.com/autism/autism-and-schizophrenia#sthash.QK2p6bav.dpu

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