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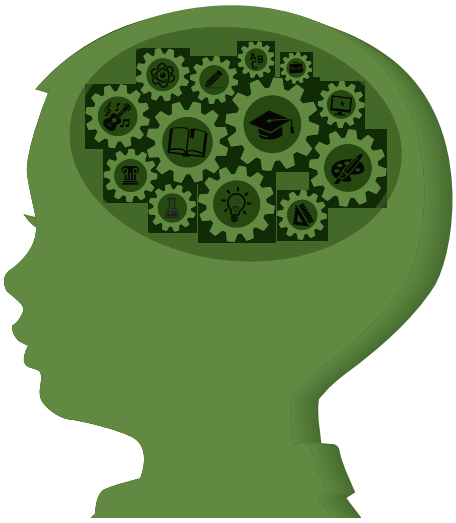

This month's issue features articles on the topic of **Pediatric Neuropsychiatry**. In an editorial, Aaron J. Hauptman, M.D., discusses the relevance of utilizing the neuropsychiatric approach in the complex care of children. Ross E. Goodwin, M.D., examines diagnostic differences between pediatric bipolar disorder and attention deficit hyperactivity disorder (ADHD), emphasizing the deleterious effects of misdiagnosis. Muhammad Puri, M.D., M.P.H., analyzes the challenge of diagnosing ADHD in traumatized children. Vanita Sahasranaman, M.D., examines pediatric anti-*N*-methyl-D-aspartate encephalitis, including discussion on clinical presentation, pathophysiology, and treatment. Taranjeet Singh Jolly, M.D., investigates a case of Guillain-Barré syndrome masquerading as conversion disorder in an 8-year-old female patient. Jennifer Severe, M.D., provides discussion on delineating pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections and pediatric acute-onset neuropsychiatric syndrome in the case of an 8-year-old patient. Lastly, Venkata B. Kolli, M.B.B.S, M.R.C.Psych., presents a review of *Clinical Topics in Child and Adolescent Psychiatry*.

EDITORIAL

Pediatric Neuropsychiatry: A Conceptual Framework

Aaron J. Hauptman, M.D.

What is the purpose of pediatric neuropsychiatry distinct from the separate notions of neurology and psychiatry? There are ways to approach conditions traditionally within the catchment of psychiatry but with an acute sense of the neurobiological, just as one can attend to historically neurological conditions with attention to behaviors, psychodynamics, and developmental courses affected. One might argue that a good psychiatrist or neurologist is doing this already, but special knowledge and skill sets are needed in the complex care of children whose conditions exist in watershed or overlapping realms; hence, neuropsychiatry.

A good example of such integration is in traumatic brain injury (TBI). Neuropsychiatric approaches to work-up and management of children with TBI are strongly recommended (1). Why? Pediatric TBI can result in neurocognitive, attentional, mood, psychotic, anxiety, and personality changes; it both interacts with family dynamics and requires management of medical injury-associated complications (1). The neurologist traditionally focuses on localizable symptoms, the child psychiatrist on behavioral and psychological phenomena. The child requires a highly integrated skill set outside the purview of either specialty alone as traditionally realized.

The historical divide between neurology and psychiatry is traced by some to the philosophical mind-body problem and the centuries-old debate within medicine between dualism and materialism (2). A conceptual separation of mental and physical, though still present (3), has decreased somewhat with a philosophical shift in both psychiatry and neurology (2). This was aided by the advent of neuroimaging, DSM theoretical shifts, increased appreciation of the primacy of brain as influencing behavior, etc. (2).

The neurologist traditionally focuses on localizable symptoms, the child psychiatrist on behavioral and psychological phenomena.

This neuropsychiatric approach to addressing illness becomes a study not only of injury but of context, not of disentangling behaviors from their neural roots but of reintegrating them (4). In medicine, we have grown accustomed to the disintegrated divvying between fields: the present volume argues that integration is feasible, an alternative to silos.

This issue of the Residents' Journal includes conditions historically considered primarily by the neurologist; similarly, it includes those traditionally viewed as behavioral. What is unique about considering these conditions through the lens of neuropsychiatry is that each is framed in the context of the other. Á propos of this philosophy, for example, anti-N-methyl-d-aspartate encephalopathy, might be considered with close attention to its frequent behavioral presentation that results in 75% of cases being seen first by psychiatrists (5). Similarly, antisocial personality disorder would be viewed closely attending to neurocircuitry, neurochemistry, and cross-correlation with acquired brain injury.

This is not to say that to be an effective clinician every doctor needs to know every fact about each surrounding discipline. But one hopes, as psychiatrists, we can integrate neurobiological understanding into our appreciation of development, attachment, and trauma and gain further understanding of the myriad forms of brain injury and its psychiatric impacts while interacting in creative ways with colleagues in neurology, behavioral pediatrics, and other pediatric subspecialties. It is less a call for a new fund of knowledge as it is a call for our curiosity to lead us to explore what underlies development, brain injury, and behavioral manifestations of mental illness.

Dr. Hauptman is a fourth-year resident in the Department of Child and Adolescent Psychiatry at New York University and the Guest Section Editor for this issue of the *Residents' Journal.*

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ARTICLE

Advances in Differentiating Pediatric Bipolar Disorder From Attention Deficit Hyperactivity Disorder

Ross E. Goodwin, M.D.

Pediatric bipolar disorder and attention deficit hyperactivity disorder (ADHD) share many symptoms in common, including impulsivity, inattention, hyperactivity, and irritability (1). Both disorders are prevalent in childhood, with prevalence rates of 1%–3% for pediatric bipolar disorder and 5% for ADHD (1–3). Further blurring their distinction is the high incidence of depression in ADHD, a common characteristic also of bipolar disorder (1). Mistakes in the differential diagnosis between ADHD and pediatric bipolar disorder lead to deleterious impacts on child development and higher rates of abuse, suicidality, and legal trouble (1). Prompt and accurate diagnosis of bipolar disorder is crucial, as early treatment improves prognosis, and stimulants or antidepressants can exacerbate mania if pediatric bipolar disorder is incorrectly labeled as ADHD (1). Further complicating the matter is that ADHD is the most prevalent comorbidity with pediatric bipolar disorder, at 60%–90% (1, 4). While there are 20 Food and Drug Administration-approved medications for ADHD, there are no medications approved to treat children younger than 10 years old with bipolar disorder (5). A multifaceted approach to differential diagnosis is necessary in order to accurately differentiate pediatric bipolar disorder from ADHD, including symptom profiles, family history, and future techniques in imaging and other biomarkers. The present article is a review of these various diagnostic domains to facilitate differentiation and decrease confusion between these two illnesses.

DIAGNOSTIC CRITERIA

Individuals with pediatric bipolar disorder may have increased activity, poor concentration, and increased impulsivity, but these features are episodic, occurring several days at a time. In pediatric bipolar disorder, increased impulsivity or inattention are accompanied by elevated mood, grandiosity, and other specific bipolar features such as flight of ideas, decreased need for sleep, hypersexuality, and hallucinations (DSM-5). While children with ADHD may show significant changes in mood within the same day, such lability differs from a manic episode, which must last 4 or more days. Pediatric bipolar disorder is also less common than ADHD (DSM-5).

As stated previously, both pediatric bipolar disorder and ADHD include hyperactivity, impulsivity, low frustration tolerance, distractibility, and increased talkativeness (1, 6). Bipolar disorder may be present if overlapping symptoms intensify during a mood episode (7). Children with ADHD may have initial insomnia, but this is due to hyperactivity, and the child feels tired the following day.

SYMPTOM PROFILES

Certain symptom profiles in children are useful to predict future onset of bipolar disorder, thereby differentiating from ADHD at an early age. Retrospective rating scales completed by parents reveal that the total number of certain dysfunctional symptoms in children is much higher prior to childhood onset bipolar disorder than before ADHD (8). These symptoms also coincide with earlier age at onset and have more rapid accumulation prior to pediatric bipolar disorder. A subgroup of dysfunction symptoms relating to mania (brief or extended mood elevation, pressured speech, racing thoughts, bizarre behavior, grandiosity or delusions) is significantly more common prior to pediatric bipolar disorder as well. Similarly, more common antecedent symptoms are those relating to behavioral dysfunction (temper tantrums, aggression, irritability, poor frustration tolerance). Symptoms relating to anxiety also help predict pediatric bipolar disorder, but only after the age of 5, since in younger children the quantity of anxiety symptoms is similar in both conditions and thus not useful for differentiation (8).

Other symptoms are not as useful for predicting which child will develop bipolar disorder versus ADHD. These include depressive symptoms, as well as symptoms typical in ADHD (inattention, hyperactivity, impulsivity). The overlapping prevalence of these symptom clusters in both ADHD and pediatric bipolar disorder do not significantly differentiate the two disorders (8).

RATING SCALES

Rating scales such as the Child Behavior Checklist comprise another modality for distinguishing pediatric bipolar disorder from ADHD. In one study, the parent of each participant completed the Child Behavior Checklist, accounting for any symptoms observed during ages 4–18. The Severe Dysregulation Profile within the checklist sums the attention, aggression, and anxious/depressed subscales. A score of 2 standard deviations above the mean on this Severe Dysregulation Profile suggests bipolar type I disorder in children (9). The manifestation of bipolar disorder predicted by the Severe Dysregulation Profile is one that includes prominent delinquent behavior, aggression, with-

drawal, somatic complaints, anxiety, depression, and thought disorder. Children in this category have an earlier age at onset, higher tendency for psychiatric hospitalization, and greater comorbidity with other conditions such as major depression, oppositional defiant disorder, social anxiety, panic disorder, and generalized anxiety disorder. Overall, this pattern indicates a more severe form of bipolar disorder. Using the Severe Dysregulation Profile score, the sensitivity and specificity for distinguishing bipolar disorder from ADHD are 57% and 92%, respectively (9).

FAMILY HISTORY

In addition to characteristic symptom profiles, a child's family history can inform the risk of bipolar disorder compared with ADHD. Both disorders are highly heritable (1), and a history of bipolar disorder in the family portends at least a five-fold increase in risk for a child to develop bipolar disorder (10). Furthermore, children with comorbid bipolar disorder and ADHD tend to have a group of relatives with this same combined condition, suggesting that there may be a distinct genetic subtype of combined bipolar and ADHD (11).

One standardized tool for distilling family history into diagnostic risk stratification is the Family Index of Risk for Mood issues. This inexpensive and clinically practical method for gathering family history has been shown to improve detection of pediatric bipolar disorder (12). The assessment consists of 25 checkboxes in an array of questions about mental health history (regarding suicide, depression, mania, hospitalization, and substance use) for each of several relatives (including the primary caregiver's grandparents, parents, aunts and uncles, siblings, and other children). The Family Index of Risk for Mood score consists of the sum of items endorsed for established risk factors related to bipolar disorder.

In a study using the Family Index of Risk for Mood, a simple sum of familial mood issues discriminated children with bipolar disorder from all other cases. High scores were specific to children with a mood disorder, rather than ADHD or disruptive behavior disorders (12).

The utility of family history to predict bipolar disorder versus ADHD is further supported by research into familial association of the two disorders and the degree of bipolar and ADHD symptoms in parents of children with either bipolar disorder or ADHD. One study examined children with comorbid bipolar disorder and ADHD, as well as children with bipolar disorder alone, ADHD alone, and neither disorder. The rate of parental manic symptoms was similar in the comorbid and bipolar-alone groups, and this rate was significantly greater than the rates in the ADHD alone and neither disorder groups. ADHD symptoms in parents of children with bipolar disorder alone were significantly less frequent than symptoms in parents of children with ADHD (alone or comorbid) and also no greater than symptoms in parents of children with neither diagnosis. Overall, parental symptomatology specifically matched the child's constellation of both manic and ADHD symptoms, separately. These findings therefore demonstrate the heritability of each disorder separately with coincident overlap (13).

IMAGING AND OTHER BIOMARKERS

Beyond symptom reports and family history, future diagnostic clarification between pediatric bipolar disorder and ADHD may come by way of imaging techniques and other biomarkers. Functional MRI has shown differences in amygdala activity when children rate their perception of fear in neutral faces. Children with ADHD demonstrate left amygdala hyperactivity compared with children with bipolar disorder or no mental illness (14). These findings highlight the amygdala's role in mediating emotional processing and comprehending facial affect. Interestingly, children with bipolar disorder and severe mood dysregulation were more afraid of neutral faces than healthy or ADHD-positive comparison subjects.

Proton magnetic resonance spectroscopy is another research imaging modality showing promise for differentiating bipolar disorder from ADHD. By measuring the ratios of certain cerebral metabolites, proton magnetic resonance spectroscopy can suggest patterns characteristic of specific disorders (15). Certain cerebral metabolites are useful to characterize these ratios: creatine plus phosphocreatine (Cr), myo-inositol compounds (Ino), and glutamate plus glutamine (Glx). In one study, children with ADHD exhibited a higher Glx-to-Cr ratio in the prefrontal cortex and frontal lobe, compared with healthy controls (15). This finding aligns with the hypothesis that abnormal glutamate function in terminal areas of dopaminergic neurons contributes to ADHD. Pharmacotherapeutic strategies exploit this purported mechanism, as dopamine inhibits glutamate release from prefrontal cortical afferents in the nucleus accumbens, and stimulants increase extracellular dopamine by blocking dopamine reuptake.

In the above-mentioned study, a higher ratio of Ino-to-Cr was present in the cingulate cortex and frontal gray matter in children with bipolar disorder (15). This finding supports the implication of inositol-1-phosphate and the phosphatidylinositol cycle in affective disorders (15). In fact, mood stabilizers, such as lithium, valproate, and carbamazepine, reduce inositol levels (15). Additionally, children with ADHD alone have significantly higher ratios of Glx-to-Ino than do children with combined ADHD and bipolar disorder. In the future, Glx-to-Ino ratio could be used to differentiate between youths with ADHD who do or do not have comorbid bipolar disorder (15).

CONCLUSIONS

A multidimensional combination of several clinical risk factors like family history and early mood dysregulation symptoms, combined with imaging differences or other biomarkers, can suggest high index of suspicion for pediatric bipolar disorder. Through

KEY POINTS/CLINICAL PEARLS

- Symptoms of behavioral dysfunction, such as temper tantrums, aggression, irritability, and poor frustration tolerance, are more common antecedents of pediatric bipolar disorder than of attention deficit hyperactivity disorder (ADHD). Depressive symptoms and those symptoms typical of ADHD, including inattention, hyperactivity, and impulsivity, are not statistically useful to predict the onset of bipolar disorder versus ADHD.
- High scores on the Family Index of Risk for Mood issues are most specific to children with a mood disorder, rather than ADHD or disruptive behavior disorder.
- Children with ADHD demonstrate left amygdala hyperactivity compared with children who have bipolar disorder. By measuring ratios of certain cerebral metabolites, proton magnetic resonance spectroscopy is another imaging modality that holds promise in differentiating bipolar disorder from ADHD.

timely recognition of a child's risk for bipolar disorder—rather than a premature diagnosis of ADHD—intervention including early family-focused therapy may mitigate the effects of otherwise misdiagnosed and unmanaged pediatric bipolar disorder.

Dr. Goodwin is a third-year resident in the Department of Psychiatry and Behavioral Sciences, George Washington University, Washington, DC.

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ARTICLE

The Challenge of Diagnosing and Managing Attention Deficit Hyperactivity Disorder in the Traumatized Child

Muhammad Puri, M.D., M.P.H.

The detrimental effects of childhood trauma result in a variety of behavioral and emotional symptoms, as well as abnormalities in cognitive and neurobiological processes. The literature supports that patients with posttraumatic stress disorder (PTSD) often have additional deficits in attention, executive functions, memory, and learning (1). Children often respond to trauma through dissociation, which can be misinterpreted as deficits in attention (2). The focus of the present review is to raise awareness of the importance of screening for trauma prior to diagnosing attention deficit hyperactivity disorder (ADHD) in the pediatric population and to acquaint providers with the appropriate guidelines for diagnosis and treatment in cases with co-occurrence of these disorders.

ADHD is a neurodevelopmental disorder presenting with symptoms of inattention, hyperactivity, and impulsivity present for at least 6 months in two or more settings that interfere with quality of life (3).

The prevalence of ADHD is 5%, with a male-to-female ratio of 3:1 (2). PTSD, like adjustment and acute stress disorder, is one of the few psychiatric diagnoses triggered by an external event, namely physical, sexual, or psychological abuse or neglect. The disorder was formally recognized in 1989 when it was incorporated in DSM-III-R (4). A child with PTSD often presents with distinct symptomatology from adults; symptoms in children include aggression, difficulties with concentration, and trouble modulating arousal (3). Consequently, PTSD may present similarly to ADHD. The diagnostic challenge ascends from the considerable symptomatic overlap between the two disorders, underscoring the importance of screening regularly for trauma prior to arriving at an ADHD diagnosis.

Failure to detect the early signs and symptoms of PTSD in children can result in misdiagnosis and delay of effective treatments (5). ADHD and PTSD can also coexist in children who are victims of childhood trauma, presenting a diagnostic challenge and complicating the treatment plan (4). This topic is also relevant because when ADHD and PTSD coexist, children often present with greater clinical severity and psychosocial dysfunction (6).

CHILDHOOD TRAUMA AND THE DEVELOPMENT OF PSYCHOPATHOLOGY

One early theory by Spitz (7) discussing the impact of childhood trauma hypothesized that traumatic events experienced before the generation of stable memory may lead to changes in later personality development and hinder the ability to form close interpersonal attachments. Spitz further hypothesized that despite lacking recollection of the trauma, children might subsequently display symptoms of anxiety, impulsivity, and poor concentration (7).

A community-based epidemiology study was conducted to screen pediatric trauma patients in the emergency department for ADHD (8). The Conners' Parent Rating Scale, widely used in ADHD evaluation, was utilized to assess the effect of trauma on patients ages 3–17 who presented to the emergency department. The control group consisted of patients in the same age group who were not exposed to trauma. One hundred and eight children participated in this study during their visit to the emergency department. The children were asked about the nature of their injuries, which were either accidental or due to physical abuse. The study concluded that the children presenting with trauma-related injuries had higher mean scores for impulsivity and hyperactivity in comparison to those treated for non-trauma-related injury (8). This study raises thought-provoking questions about the relationship between traumatic events and ADHD-like symptoms, and further research on the trauma-ADHD relationship will help guide diagnosis and treatment.

DSM-5 has shifted its focus to behavioral aspects of trauma, which can further complicate the clinical picture. While diagnostic criteria still include re-experiencing in the form of flashbacks and nightmares, as well as avoidance, hypervigilance is now more behaviorally defined with a focus on hyperarousal in the form of aggressive and at times agitated conduct. DSM-5 also includes another criterion labeled "negative cognitions and mood," which may manifest as diminished interest, feelings of estrangement, and lapses in memory (3). Interestingly, children are more likely to develop symptoms of PTSD than adults (9). However, a child's ability to verbalize past trauma may be limited as a result of certain biological processes resultant from the trauma (10), and thus clinicians may need to rely on other resources beyond simply self-report to screen for trauma.

DIAGNOSTIC INSTRUMENTS IN EVALUATING TRAUMA IN CHILDREN

The U.S. Department of Veterans Affairs has reported several PTSD inventory scales and diagnostic tools, which can

be utilized when a history of trauma is known or suspected. These scales vary in cost and time required to conduct the assessment, but none is considered superior to the other (11).

Childhood PTSD Interview.
The Childhood PTSD Interview is a 95-item semistructured interview available in child and parent versions assessing DSM-IV PTSD diagnosis (12).

Child PTSD Symptom Scale.
The Child PTSD Symptom Scale is a 24-item self-report questionnaire with a 7-item scale to assess functional impairment and a 17-item PTSD symptom scale. The score range is 1–4, with a score of 4 indicating increased severity of PTSD (12).

Children's PTSD Inventory.
The Children's PTSD Inventory is a clinician-administered measure for ages 6–18 based on DSM-IV diagnostic criteria for PTSD (12).

Clinician-Administered PTSD Scale for Children and Adolescents.
The Clinician-Administered PTSD Scale for Children and Adolescents is a 33-item clinician-administered PTSD scale for ages 8–18 measuring the intensity and frequency of symptoms, with a total of 5 points for each symptom (12).

Clinicians should provide compulsory screening for trauma in children who struggle with attention or present with hyperactivity/hyperarousal. These symptoms could be directly linked to childhood trauma, or they may be a reflection of underlying ADHD. There is also a possibility that these children may actually be suffering from both PTSD and ADHD (4).

ADHD OR ADHD-LIKE SYNDROME

Failure to report abuse to clinicians is common due to fear, shame, and difficulty with recall, presenting major barriers for providers in detecting PTSD and increasing the likelihood of misinterpreting symptoms as ADHD (4). In children, the clinical similarities between these two disorders can be greater than their differences, thus elevating the risk of misdiagnosis. Disrupted neurobiology and physiology may explain some of the symptomatic similarities between the two disorders. The sympathetic nervous system is physiologically set off in response to danger; however, this response becomes futile in cases of protracted childhood trauma, as the child is unable to escape from the potential danger. The child is in a chronic state of hyperarousal, conditioned to continuously survey the environment for danger. This results in excessive processing of stimuli that overburdens the child's cognitive reserve, creating a clinical picture of anxiety, impaired attention, and poor concentration due to inability to tune out extraneous information (4).

MANAGING THE SYMPTOMS OF ADHD AND PTSD WITH LIMITED TREATMENT OPTIONS

Managing PTSD

Management of PTSD is challenging because of noncompliance and a dropout rate of up to 81.1% during treatment (13). Children can benefit from psychotherapy, such as exposure therapy, mindfulness-based meditation, extensive education, eye-movement desensitization and reprocessing, and trauma-focused cognitive-behavioral therapy (14). Pharmacotherapy can be supportive, although no clear-cut medication guidelines exist and management remains the same for children and adults. However, most psychiatrists agree that selective serotonin reuptake inhibitors and prazosin, an alpha blocker, are the first choice (15). However, carbamazepine can be used to help control flashbacks (16). Clonidine and propranolol can be used to prevent PTSD by decreasing sympathetic outflow (16).

Managing ADHD

Psychological therapies, such as behavioral therapies, school-based interventions, interpersonal psychotherapy, social skills training, neuro-feedback, and family therapy, are recommended, along with the use of medications (17). Stimulant medications, such as methyphenidate and dextroamphetamines, are first-line medications; however, nonstimulant medications, such as amoxapine, a tricyclic antidepressant, as well as atomoxetine, a norepinephrine reuptake inhibitor, can also be used (18). Clonidine, a nonstimulant medication, can be used to treat both ADHD and PTSD (18).

CONCLUSIONS

The experiences of significant trauma in childhood can harvest ever-lasting effects. Clinical manifestations are variable, complicating the diagnostic workup and resulting in misdiagnosis. A historical view of the large percentage of children diagnosed with ADHD over the years has prompted the American Psychiatric Association to reassess the diagnostic criteria and treatments for ADHD. The Centers for Disease Control and Prevention reported 6.4 million children ages 4–17 with the diagnosis of ADHD as of 2001, and the percentage continues to grow each year. There has been approximately a 5% per-year increase in the diagnosis of ADHD from 2003 to 2011 (19). These findings may, in part, be explained in that childhood trauma is overlooked, resulting in misdiagnosis of PTSD as ADHD. The

KEY POINTS/CLINICAL PEARLS

- Attention deficit hyperactivity disorder (ADHD) and posttraumatic stress disorder (PTSD) can also coexist in children who are victims of childhood trauma, presenting a diagnostic challenge.
- Failure to detect the early signs and symptoms of PTSD in children can result in misdiagnosis and delay of effective treatments.
- The relationship between traumatic events and ADHD-like symptoms and further research on the trauma-ADHD relationship will help guide diagnosis and treatment.

consequences of incorrectly diagnosing and/or treating PTSD as though it were ADHD may perpetuate and exacerbate PTSD symptoms. There is ongoing research to further explore this predicament and to develop more effective methods of diagnosing and managing PTSD in children.

Dr. Puri is a first-year fellow at Institute of Living, Hartford, Conn.

The author thanks Dr. Edward Hall, Chief of Child Unit, Bergen Regional Medical Center, and Dr. Tahira Akbar, Research Fellow, Bergen Regional Medical Center.

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Submissions should include the following:

1. Two to three Board review-style questions with four to five answer choices.
2. Answers should be complete and include detailed explanations with references from pertinent peer-reviewed journals, textbooks, or reference manuals.

**Please direct all inquiries to Katherine Pier, Senior Deputy Editor (katherine.pier@mssm.edu).*

ARTICLE

Pediatric Anti-NMDA Receptor Encephalitis

Vanita Sahasranaman, M.D.

Autoimmune synaptic protein encephalopathy syndromes are a group of serious, yet treatable, disorders arising from antibodies targeting neuronal synaptic proteins. Among these conditions, antibodies to the N-methyl-D-aspartate (NMDA) receptor are the most common and best understood (1). First described in 2005 in four young women with ovarian teratomas (2), anti-NMDA receptor encephalitis is a multistage neuropsychiatric illness. The condition predominantly affects children and young adults, has a strong female preponderance, and is associated with ovarian teratomas. With prompt, aggressive treatment, 80% of diagnosed patients experience complete or near-complete recovery. Symptom relapse has been reported in 20% of children (1, 3–5).

CLINICAL PRESENTATION

Anti-NMDA receptor encephalitis typically starts with a prodromal phase of fever, headache, or viral-like symptoms (1). This can be followed in a few days to weeks by onset of psychiatric and behavioral problems, including anxiety, paranoid thoughts, grandiose or hyperreligious delusions, and insomnia. This evolves into a fulminant stage characterized by decreased level of consciousness, seizures, dyskinesias, choreoathetoid movements, autonomic instability, and central hypoventilation, which may require ventilator support (5–9).

Initial presentation includes psychosis, memory deficits, seizures, and language disintegration. Regardless of the initial presentation, more than 90% of patients develop at least three of the following groups of symptoms within one month of onset: psychiatric disorders, memory disturbance, speech disorder, seizures, dyskinesias, decreased consciousness, autonomic instability, or hypoventilation (1, 3). Movement disorders were observed significantly more often in cases of anti-NMDA receptor encephalitis (63%; $p<0.01$) compared with enteroviral and West Nile virus cases, which demonstrate no such findings (4).

The most common presentations in children under 12 years old are abnormal behaviors, seizures, movement disorders, and vague, nonspecific behavior changes such as new-onset temper tantrums and changes in mood or personality. Parents also report changes in speech, including reduced speech, mutism, echolalia, and perseveration (3, 9). Autonomic dysfunction, severe cardiac dysrhythmias, and clinically significant cardiac pauses are less frequent in children compared with adults (3). Anti-NMDA receptor encephalitis has occurred both with and without tumor association; up to 40% of cases occur without detection of a tumor. Most tumors are found in females between 12 and 45 years old (4). Ovarian teratomas occur most often, but other neoplasms, such as breast, lung, pancreatic, and thymic carcinomas, have also been reported (5, 6). In males, association with tumors, such as testicular teratomas, is rare. In one study of 107 male patients, only 6% of patients, all adults, presented with neoplasms of any kind. Detection of teratomas or other tumors is less common in preadolescent children (6, 10).

PATHOPHYSIOLOGY

Anti-NMDA receptor encephalitis results from immunoglobulin G antibodies against the glutamate N1 subunit of the NMDA receptor on the cell surface (11, 12). Injection of patients' antibodies into cultures of dissociated rat hippocampal neurons shows a titer-dependent decrease of synaptic NMDA receptor clusters without affecting cell viability, dendritic complexity, or other synaptic receptors; this is reversible upon removing the antibodies from the culture media. These findings, along with the apparent lack of complement-mediated mechanisms, may explain the potential reversibility of symptoms, even in patients who have been severely ill or with a low level of consciousness for several months (3, 13).

EPIDEMIOLOGY

Anti-NMDA receptor encephalitis is a leading cause of autoimmune encephalitis in children and adolescents. Forty percent of cases present in individuals younger than 18 years old. The condition has been identified as the second most common cause of encephalitis in this age range, exceeded only by acute disseminated encephalomyelitis (3, 14). In a cohort of 761 patients ≤30 years old with encephalitis of unknown origin, one study identified anti-NMDA receptor encephalitis four times more frequently than herpes simplex virus-1 encephalitis and six times more frequently than encephalitis caused by West Nile virus or varicella zoster virus. Absolute rates of anti-NMDA receptor encephalitis were higher than those of enteroviral encephalitis, at 41% versus 38%, with all values reaching statistical significance ($p<0.01$) (4). Median age of symptom onset is around 21 years, which is similar to that of encephalitis due to viral etiologies (herpes simplex virus-1, varicella zoster virus, West Nile virus, enterovirus). Eighty percent of cases occur in females (5). Male sex is associated with bimodal age distribution. Associated germ cell tumors are found more often in Asian and African American patients; this suggests a possible genetic risk for developing the condition (5, 6).

IMAGING

MRI

T2-fluid-attenuated MRI studies in children and adults have shown cortical, subcortical, and cerebellar abnormalities. Brain MRI is abnormal in about 55% of cases, including cortical and subcortical T2-fluid attenuated inversion recovery signal abnormalities that sometimes occur with transient cortical meningeal enhancement. T2-fluid attenuated inversion recovery signal abnormalities are also seen in the brainstem and cerebellum, despite the fact that related symptoms are rare. In children, MRI abnormalities occur less frequently than in adults. One study of a series of 32 children diagnosed with anti-NMDA receptor encephalitis found that 31% had abnormal MRI (3).

EEG

EEG is abnormal in almost all patients with anti-NMDA receptor encephalitis. EEG usually shows diffuse background slowing in the delta-theta range, though some patients may have focal slowing. Electrographic seizures during continuous EEG monitoring occur in approximately 60% of patients (3). Thirty percent of adult patients with anti-NMDA receptor encephalitis have a unique EEG pattern called "extreme delta brush," a nearly continuous combination of delta frequency waves with superimposed fast activity in the beta range occurring in a symmetric and synchronous pattern involving all head regions. This pattern occurred independently of sedation and episodes of dystonia or abnormal movements. Whether or not this pattern also occurs in children with anti-NMDA receptor encephalitis is an issue still under investigation (15).

DIFFERENTIAL DIAGNOSIS

Differential diagnoses include acute psychosis, temporal lobe seizures, toxic and metabolic disorders (including drug ingestion), focal brain lesions, or encephalitides (viral or autoimmune). Neuroleptic malignant syndrome should be considered given muscle rigidity, autonomic instability, and elevated creatinine kinase (16) (Table 1).

TABLE 1. Differential Diagnosis for Anti-N-Methyl-D-Aspartate Receptor Encephalitis[a]

Infectious	
Bacterial	Pneumococcus Mycoplasma Syphilis
Viral	Enterovirus Varicella zoster virus Herpes simplex virus HIV Human herpes virus-6 Epstein-Barr virus Cytomegalovirus Arbovirus Rabies virus
Fungal	Cryptococcus Toxoplasma
Autoimmune	Systemic lupus erythematosus Anti-phospholipid antibody syndrome Sjogren's syndrome Angitis (primary or systemic) Hashimoto's encephalopathy CNS vasculitis
Malignancy	Other paraneoplastic syndromes due to primary malignancy
Toxic	Carbon monoxide Methanol Cyanide Drugs of abuse
Endocrine	Hashimoto's thyroiditis Grave's disease
Hematological	Porphyria
Neurological	Multiple sclerosis
Psychiatric	Schizophreniform disorder Schizophrenia Impulse control disorder Neuroleptic malignant syndrome Serotonin syndrome Catatonia

[a] For more details on the differential diagnosis, see Gable et al. (4), Florance et al. (10), Granerod et al. (14), and Kruse et al. (20).

DIAGNOSIS

The typical patient is a previously healthy young female presenting with acute, severe emotional distress and cognitive disturbance (16). Diagnosis is confirmed by the presence of NMDA-receptor antibodies in serum or CSF. Intrathecal synthesis of immunoglobulin G antibodies occurs in virtually all patients; antibody levels in CSF correlate better with symptom outcome than serum immunoglobulin G antibody levels (17). All patients should be examined for an underlying tumor, mainly an ovarian teratoma or a testicular germ-cell tumor. The most useful screening tests are MRI or CT of the abdomen and pelvis, ultrasound of the pelvis, or transvaginal ultrasound if appropriate (16). MRI of the abdomen and pelvis is the test of choice to identify ovarian teratomas (3). Serological tumor markers (CA-125, beta-hCG, alpha-fetoprotein, or testosterone) are negative in many patients (16). Patients with anti-NMDA receptor encephalitis may meet DSM criteria for delirium, psychotic disorder, or catatonic disorder due to a general medical condition.

TREATMENT

Medical

Initial treatment includes acyclovir until herpes simplex virus encephalitis can be excluded. Tumor removal, when appropriate, and prompt immunotherapies improve outcomes. First-line immunotherapies include corticosteroids,

KEY POINTS/CLINICAL PEARLS

- Suspect anti-NMDA receptor encephalitis in a previously healthy young female with viral-like symptoms rapidly progressing to altered behavior/consciousness and autonomic instability.
- First-line treatment: immunotherapy; use neuroleptics with caution given potential for dystonia, seizures, and cardiac arrhythmias.
- Eighty percent of patients experience complete or near-complete

intravenous immunoglobulin, or plasma exchange; however, in 30%–40% of cases, these treatments fail (1).

Increasing evidence shows that rituximab is an effective alternative, either with intravenous immunoglobulin and steroids or after first-line immunotherapies (18). Cyclophosphamide is considered in children with caution only after exhausting all other treatment modalities due to adverse effects (malignancy, infertility). Efficacy of azathioprine or mycophenolate mofeteil in preventing relapse remains unknown (1, 19).

Psychiatric

Evidence-based psychiatric management is equivocal. Case reports show that benzodiazepines may improve agitation and insomnia, anticholinergic agents may improve dystonias, and carbidopa-levodopa may effectively treat muscle rigidity; however, in other cases, patients had minimal to no response to these treatments. Neuroleptics used to treat psychosis must be used cautiously due to potential for dystonia, seizures, and cardiac arrhythmias.

ECT and benzodiazepines may be effective for associated catatonia. Case reports show that ECT may be effective in adults with anti-NMDA-receptor-associated catatonia. In younger patients, ECT may be a useful adjunct to benzodiazepines and immunotherapy; one case described a 14-year-old girl who showed dramatic improvement in malignant catatonia with this combination (20).

OUTCOMES

When rapidly identified and treated, the prognosis is good. A cohort study of 360 patients found that 80% of patients experienced near-complete or full recovery. Another study suggested that some patients improve up to 2 years after initial presentation. Autonomic instability, level of consciousness, seizures, and dyskinesias improve first. After patients regain consciousness, however, psychiatric symptoms can re-emerge, with manifestations such as behavioral disinhibition, impulsivity, problems with attention and planning, and memory deficits (1).

Fully recovered patients may have detectable antibody levels in serum or CSF, leading to immune response reactivation. Symptom relapse has been reported in 20% of children. This may require continued treatment, including neuroleptics, or short-term treatment during symptom exacerbation (1). After recovery, females should be screened periodically for 2 years for ovarian teratomas (6). Mortality is low, at 7% in 24 months after initial presentation (1).

Dr. Sahasranaman is a fourth-year resident in the Department of Psychiatry at Rosalind Franklin University of Medicine and Science, North Chicago, Ill.

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CASE REPORT

A Patient With Guillain-Barré Syndrome Masquerading as Conversion Disorder

Taranjeet Singh Jolly, M.D.

Guillain-Barré syndrome is an immune-mediated acute polyradiculoneuritis most frequently preceded by an unspecific infection (1). Guillain-Barré syndrome is the most common cause of acute flaccid paralysis in healthy infants and children (2). It occurs worldwide, with an overall incidence of 1 to 2 per 100,000 per year (3, 4). While all age groups are affected, the incidence is lower in children than in adults and increases by approximately 20% with every 10-year increase in age beyond the first decade of life. Guillain-Barré syndrome occurs rarely in children younger than 2 years old but can occur in infants (5, 6). Males are affected approximately 1.5 times more often than females in all age groups.

Guillain-Barré syndrome manifests as rapidly evolving areflexic motor paralysis with or without sensory disturbance, the usual pattern being ascending flaccid paralysis. Weakness typically evolves over hours to a few days and is frequently accompanied by tingling dysaesthesias in the extremities (7). Autonomic involvement is common, the usual manifestations being loss of vasomotor control with wide fluctuations in blood pressure, postural hypotension, and cardiac arrhythmias (7). According to pediatric literature, children usually recover in shorter time than adults, with a mortality rate of 3%–5%. Severe neurological disability leading to ventilatory insufficiency and autonomic failure are the main causes of death (1, 8). Although the etiology is not clearly known, about 70% of cases are preceded by acute infectious processes 1–3 weeks before the onset of neurologic symptoms. Electro-physiologically Guillain-Barré syndrome is characterized by acute motor axonal neuropathy. Immunoglobulins and plasmapharesis have made a significant change in the course of the illness (9).

The present case report describes Guillain-Barré syndrome, with symptoms similar to conversion disorder, in a young child.

CASE

"Sarah" is an 8-year-old Caucasian girl with no prior psychiatric history who was taken to our emergency department for mood outbursts, crying spells, and difficulty ambulating. For the past 3 weeks, she had intermittent back and hip pain. Early in the course of illness, she had 3 days of fevers up to 102°F, and her pediatrician diagnosed a viral syndrome and recommended conservative treatment. She presented to an outside hospital with progressive back and hip pain and difficulty walking, along with crying spells. An X-ray of her abdomen revealed constipation. A head CT, MRI of the right hip, and MRI of the lumbar spine were all read as normal. She was treated for her constipation and medically cleared despite being unable to ambulate throughout her hospitalization. Psychiatry was consulted, and she was diagnosed with major depressive disorder with possible "conversion disorder" manifesting as gait disturbance, with recommendation for inpatient psychiatric treatment.

The patient was brought to our emergency department 5 days after her discharge from the hospital with ongoing difficulty ambulating and worsening mood outbursts. A review of her records from the recent hospitalization was made, and acute medical or neurological causes were ruled out in the emergency department. No further tests were conducted in the emergency department. On admission to inpatient psychiatry, the patient was reported to have poor sleep, poor appetite, and increasing irritability for the past 3 weeks. Her parents reported self-harmful behavior, such as "hitting her head on the wall," when she became frustrated. Her behaviors were particularly worse since her recent hospitalization. Mental status examination results were significant for an obese, 8-year-old Caucasian girl who was irritable, belligerent, and crying on examination. We were unable to assess her mood, thought process, thought content, and perceptual disturbances because the patient was not cooperating. Her family history was significant for depression and anxiety on both the maternal and paternal sides. She had a normal birth and early developmental history with no delay in her developmental milestones. She had no pertinent psychiatric history. Her medical history was significant for a history of constipation, and she had been treated with polyethylene glycol for the past year.

Her examination was positive for absent reflexes in the upper and lower limbs and narrow-based gait. Her evaluation was negative for eye, ear nose and throat, respiratory, cardiology, gastrointestinal, genitourinary, dermatologic, and endocrine abnormalities. Vitals signs were within normal limits.

Pediatric neurology was consulted because of concerns for absent reflexes and gait disturbances. Neurological examination revealed decreased hip flexion 3/5 bilaterally, as well as absent reflexes. The patient's gait was narrow based; with use of a walker, she was able to lift both feet off the ground, flex her knees, and flex her hips, with frequent imbalance backwards and near falls.

Neurology recommended CT head, MRI–L spine and T-spine, and MRI of hip. The initial preliminary diagnosis was diffuse/multifocal polyneuropathy. MRI hip was unremarkable.

MRI of lumbar spine was notable for mild thickening and smooth enhancement of the pial surface of the conus and cauda equina nerve roots in the lumbosacral region, which was most likely consistent with an inflammatory condition such as Guillain-Barré syndrome. At this time, the patient was transferred to the neurology service for further workup for inflammatory processes. She was monitored for ascending paralysis, with specific examination for symptoms such as urinary retention or respiratory depression. Her workup was consistent with the diagnosis including MRI with nerve root enhancement. A lumbar puncture was performed, which revealed cytoalbuminologic dissociation with elevated protein (261 mg/dL) but relatively normal white blood cell count (8/cu mm). Electromyogram revealed increased distal latencies and mildly decreased amplitudes.

Investigations (conducted in neurology service) for CSF glucose levels, mononuclear CSF, immunoglobulin G, immunoglobulin A, and complete metabolic panel revealed no abnormalities. Elevated CSF protein (261 mg/dL [range: 15 mg/dL–45 mg/dL]) was observed.

Intravenous immunoglobulin treatment was initiated and continued for 5 days (400 mg/kg/day). Immunoglobulin A was within normal limits. The patient was tested for cytomegalovirus, herpes simplex virus, Epstein-Barr virus, enterovirus, varicella zoster virus, and West Nile virus, with all negative results. Psychiatry was consulted for follow-up, and we recommended continuation of fluoxetine (10 mg/day) to help with depression. The patient was also started on gabapentin (100 mg b.i.d.) for neuropathic pain. Physical medicine and rehabilitation was involved, and the patient was receiving regular physical therapy. Behavioral psychology was also consulted for behavioral management during the treatment. The patient was discharged from the inpatient unit to the physical rehabilitation unit, and she was seen by behavioral psychology who worked with her on pain and relaxation techniques, as well as on development of coping skills. By the time of discharge from the rehabilitation unit, the patient had hip flexion 4/5 and ankle dorsi-flexion 4/5. She was discharged back to her home with recommended physical therapy at home. No further follow-up information was made available.

DISCUSSION

Conversion disorder is defined as a symptom or deficit in voluntary motor function in patients without an anatomic or physiologic basis. Conversion disorder is also called functional neurological symptom disorder in DSM-5. It can consist of the following subtypes: with weakness or paralysis, with abnormal movement (e.g., tremor, dystonic movement, myoclonus, gait disorder), with swallowing symptoms, with speech symptoms (e.g., dysphonia, slurred speech), with attacks or seizures, with anesthesia or sensory loss, with special sensory symptom (e.g., visual, olfactory, or hearing disturbance), or with mixed symptoms. A high rate of misdiagnosis of conversion symptoms was reported in early studies, but this rate has been only 4% on average in studies of this diagnosis since 1970 (Table 1) (13). In children, conversion disorder occurs more commonly in girls than in boys and is most prevalent in children between the ages of 10 and 15 (11, 12). Risk factors include prior sexual abuse and preexisting psychiatric disease (e.g., anxiety, depression). In children, symptoms are most commonly related to motor function and often start following emotional stress or minor injury. In most cases, a detailed history identifies domestic stress, feelings of parental rejection, unresolved grief, and/or problems at school (11). Physical examination often provides early diagnosis without extensive laboratory evaluation or ancillary studies. Key findings include reciprocal contraction during attempts to move apparently paralyzed muscle groups, presence of normal tendon reflexes in flaccid extremities, or physically implausible presentations. Successful treatment involves early referral for psychiatric care and avoidance of extensive investigation for an organic cause. Although the occurrence of Guillain-Barré syndrome in children is relatively rare, it is the most common cause of acute flaccid paralysis in infants and children during the post-polio eradication era. It is impor-

TABLE 1. Common Conditions Misdiagnosed as Conversion Disorder[a]

Condition
Frontal lobe epilepsy
Amyotropic lateral sclerosis
Myasthenia gravis
Multiple sclerosis
CNS tumor
Peripheral nerve palsy
Cerebrovascular accident
Systemic lupus erythematosus

[a] For more details on these conditions, see Crimlisk et al. (14) and Moene et al. (15).

KEY POINTS/CLINICAL PEARLS

- Guillain-Barré syndrome is the most common cause of acute flaccid paralysis in healthy infants and children, with an overall incidence of 1 to 2 per 100,000 per year.
- The incidence of Guillain-Barré syndrome is lower in children than in adults and increases by approximately 20% with every 10-year increase in age beyond the first decade of life.
- In children, conversion disorder occurs more commonly in girls than boys and is most prevalent in children between the ages of 10 and 15. Risk factors include prior sexual abuse and preexisting psychiatric disease (e.g., anxiety, depression).
- It is important to consider and rule out neurological and general medical causes of acute change in mental status or gait disturbance before considering a diagnosis of conversion disorder or psychogenic gait disorder.

tant to consider and rule out neurological and general medical causes of acute change in mental status or gait disturbance before considering a diagnosis of conversion disorder or psychogenic gait disorder.

Dr. Jolly is a child and adolescent psychiatry fellow at the Johns Hopkins Hospital, Baltimore.

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CASE REPORT

Delineating PANDAS/PANS Diagnosis

Jennifer Severe, M.D.

Researchers have continued to investigate symptoms of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS). The present case report is of an 8-year-old girl diagnosed with PANDAS.

CASE

"Mary" is an 8-year-old Caucasian girl with a medical history of asthma. She is an only child, high-achieving, and a perfectionist. She has no prior psychiatric history, and her family history is positive only for anxiety in both parents and an aunt. She presented to a pediatric emergency department with 2 weeks of sudden emergence of random and intense intrusive thoughts, which she referred to as "pops" (indicating the thoughts "popping" into her head). She categorized the pops by topic, ranging from sexualized obsessions (including sex, pregnancy, giving birth, and seeing genitals of others, which prompted online searches on sex and episodes of masturbation) to violent thoughts involving killing herself or others (shooting or stabbing) and obsessional ideas about swearing and making racist comments. She used to enjoy going to church with her parents but could no longer tolerate it due to experiencing intense hatred against God and emerging doubts about the veracity of the Bible.

At the same time, the patient also developed a sore throat, which was accompanied with fear of choking on small objects such as candy and popcorn, contrasted with irresistible thoughts of putting bottle caps into her mouth. She became anxious and distraught, wishing her life was less complicated and wishing she was dead. This presentation, along with 24 hours of poor oral intake, prompted her parents to seek medical care. Around the time of her presentation, Mary had been undergoing significant stressors, including that she and her parents had been in the process of relocating to another state and they were moving in and out with relatives.

She had to change schools as a result of these frequent relocations. On two recent occasions, she had witnessed her mother faint, which generated a great deal of anxiety. She cultured positive for group A streptococcus the day of her presentation to the emergency department. She was put on amoxicillin but was switched to clindamycin after the first dose due to developing an allergic reaction. She was assessed by a child psychiatrist and began treatment with fluoxetine and in-home cognitive-behavioral therapy (CBT) with her mother, with the working diagnosis of PANDAS. Titration of her fluoxetine dose was very slow due to emergence of increased restlessness with an increase from 5 mg to 10 mg daily. Four months after her initial presentation, her symptoms subsided except for episodic anxiety. Her mother stated, "We are seeing smiles."

DISCUSSION

Disease Overview

Symptoms of PANDAS and PANS are progressively coming to light, yet the diagnoses remain controversial. Since Sydenham and Osler in the mid-19th century, researchers have dedicated efforts toward investigating the potential associations between bacterial infection and new-onset of obsessive compulsive disorder (OCD), tics, and Sydenham chorea in children (1). In 1998, Swedo et al. (2) observed a novel group of 50 patients with OCD and tic disorder associated with group A streptococcal infection and formulated the diagnostic criteria for PANDAS (Table 1). The concurrent group A streptococcal infection in association with the acuity of symptom onset constitutes the cornerstone for PANDAS diagnosis as shown in the above case report. In one study, children with elevated antistreptolysin O titer showed a pattern toward greater OCD severity and, consequently, more impaired neurocognitive processing (3, 4). Strangely enough, a higher susceptibility to group A streptococcal infections is reported in youths with tics and/or OCD compared to healthy controls, estimated at 0.42 versus 0.28 infections per subject per year, respectively (1). An additional risk factor may be a maternal autoimmune history, particularly Hashimoto's thyroiditis (5).

Researchers continue to explore etiologic factors other than group A streptococcal infection linked to the condition, and concurrent infection with mycoplasma pneumonia, Borrelia burgdorferi, influenza, and Epstein-Barr virus have been reported (1, 3, 6, 7). Noninfectious etiologies, such as autoimmune and inflammatory diseases and perhaps certain psychosocial stressors, also warrant consideration (1, 3, 6, 7). The countless cases of sudden-onset OCD with or without tic disorder failing to reasonably meet the rigid and limited criteria for PANDAS prompted a group of experts at the National Institutes of Health to widen the scope of the syndrome in 2010 (6), and thus PANS was designated as a single diagnostic category (Table 1). Presently, PANDAS is regarded as a subtype of PANS.

For some researchers, PANDAS/PANS is seen as "a yet-unproven hypothesis" (8); for others, it is a real but not well-defined clinical entity (9). The incidence of PANS OCD is yet to be determined, though estimated at 0.2%–

TABLE 1. PANDAS/PANS Diagnostic Criteria

PANDAS	PANS
Presence of obsessive-compulsive disorder (OCD) or a tic disorder; Acute symptom onset and episodic course	An abrupt and dramatic onset of OCD or food restriction
Prepubertal symptom onset	Area of dissimilarity
Temporally associated with group A streptococcal infection and symptom onset/exacerbations	
Associated with neurological abnormalities, particularly motoric hyperactivity and choreiform movements	
Area of dissimilarity	Symptoms are not better explained by a known neurologic or medical disorder
	At least two similarly severe and acute neuropsychiatric symptoms, including anxiety, emotional lability and/or depression irritability, aggression and/or oppositionality, behavioral regression, deterioration in school performance, sensory or motor abnormalities, and somatic signs and symptoms (e.g., enuresis or sleep disturbances)

0.4% (1). Children with PANDAS/PANS are anecdotally described as being "changed overnight," a perplexing and distressing phenomenon not only to the affected children but also to families. The prevailing theory of pathogenesis is the induction of abnormal immune response by group A streptococcal infection, which generates cross-reactive antineuronal antibodies for both group A streptococcal cellular components and basal ganglia tissue (7, 10). This engenders a volumetric increase of the caudate, putamen, and globus pallidus, which is believed to create a dopamine dysregulation leading to the neuropsychiatric manifestations (1, 7, 10). As with most forms of psychopathology, quality of life is significantly affected (3). The prognosis of youths diagnosed with PANDAS/PANS is not entirely known.

Differential Diagnosis

PANS is a "diagnosis of exclusion" (7). While the diagnosis of PANDAS/PANS seemed more evident as the above clinical case unfolded, the diagnostic decision-making deserves up-close and in-depth attention considering the associated psychosocial entanglement and contextual conditions. The patient was portrayed as a perfectionist by her family; nonetheless, there was no clinical evidence of OCD prior to her group A streptococcal infection. Her anxiety

TABLE 2. Obsessive-Compulsive Disorder (OCD) Versus PANS OCD[a]

Variable	OCD	PANS OCD
Age at onset (years)	10	<7
Gender relatedness	Age <15 years; males slightly higher than females; female/male ratio increases post puberty	Nearly 5:1 male:female ratio under age 8
Course	Insidious onset; not episodic	Dramatic and severe onset; episodic or saw-tooth course; long-term prognosis unknown
Incidence	2% of youths	Unknown, estimate is 10%–20% of pediatric OCD
Infectious trigger	Unknown	Proposed association with infection but not required
Motor signs	Increased findings of neurological soft signs, including choreiform movements	Choreiform movements
Neurocognitive findings	Oculomotor response inhibition deficits; deficits in set shifting and inhibition; deficits in cognitive flexibility and planning	Poor attention and visual-spatial abilities; acute math and reading deficits; impulsivity; deficits in fine motor speed
Involvement of basal ganglia	Strong support	Good support
Immune therapy response	No	Some support for Intravenous immunoglobulin, antibiotics
Response to CBT	Yes	Yes
Response to serotonergic reuptake inhibitors	Yes	Yes, but may be prone to activation
Comorbidity (%)	Any tic disorder: 15–30	Any tic disorder: 55.3
	ADHD: 11–12	ADHD:44.6
	Separation anxiety: 30–52	Separation anxiety: 21
	Affective disorder: 25–62	Affective disorder: 43
	Anxiety disorder: 26–75	Anxiety disorder: 31

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KEY POINTS/CLINICAL PEARLS

- Pediatric acute-onset neuropsychiatric syndrome (PANS) is a diagnosis of exclusion.
- Careful delineation of symptoms, including the acuity and severity of onset, is essential to PANS diagnostic framework.
- Infectious and noninfectious etiologies have come into light in the development of PANS and define the therapeutic interventions.
- Be aware of the potential behavioral activation following selective serotonin reuptake inhibitor initiation for treatment of the obsessive-compulsive disorder symptoms.

regarding her mother's health, her tendency of internalizing, her family history of anxiety disorder, along with the stressful disruption in schooling, peer relationships, and living situation, made tangible other anxiety-spectrum phenotypes. PANS symptoms overlap with a variety of psychiatric disorders, especially OCD (Table 2), as well as attention deficit hyperactive disorder, separation anxiety disorder, generalized anxiety disorder, anorexia nervosa, oppositional defiant disorder, bipolar disorder, and sometimes depression (3, 7, 11). Clinicians should be mindful of children's reluctance and shameful or guilty feeling to disclose the entire scope of their symptoms, as this can complicate the history. The main differential diagnosis of PANDAS/PANS also includes Tourette's syndrome, transient tic disorder, Sydenham chorea, Wilson's disease, avoidant/restrictive food intake disorder, secondary enuresis, autoimmune encephalitis, and systemic autoimmune disease (3, 7). A drastic course and type of the symptoms are the most important factors for an accurate diagnosis.

Treatment

Promising therapeutic interventions for children with PANDAS/PANS include 1) an appropriate course of antibiotics, such as penicillin, cephalosporin, and macrolides for treatment of underlying bacterial infections; 2) selective serotonin reuptake inhibitors (SSRIs); 3) antidopaminergic or prednisone for tics; 4) CBT; and 5) intravenous immunoglobulin and therapeutic plasma exchange for treatment-refractory cases (1, 6, 12) .It is important to be aware that group A streptococcal infections are suspected to, at times, lead to tryptophan degradation, which may influence serotonin function and induce behavioral activation following SSRI initiation (13). Contrary to expectations, the available research does not support tonsillectomy or adenotonsillectomy as likely affecting symptom progression or the presumed autoimmunologic response (14).

Clinical Implications

Understanding the brain maturational and developmental processes, in conjunction with the plastic reorganization in response to a temporary or long-term PANDAS/PANS diagnosis, warrants further inquiry. Clear identification of PANDAS/PANS cases is of particular importance in gathering more insight to address the uncertainty of the condition.

Dr. Severe is a third-year resident in the Department of Psychiatry, Baystate Medical Center/Tufts University School of Medicine, Springfield, Mass.

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BOOK FORUM

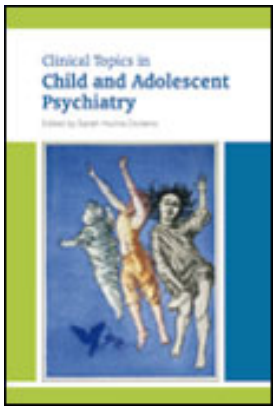
Clinical Topics in Child and Adolescent Psychiatry

Reviewed by Venkata B. Kolli, M.B.B.S., M.R.C.Psych.

Clinical Topics in Child and Adolescent Psychiatry, edited by Sarah Huline-Dickens, is a befitting addition to the long line of high-quality publications from the Royal College of Psychiatrists. This book is of value to psychiatrists and pediatricians interested in the behavioral health of children and adolescents. It discusses key mental health disorders with childhood onset and their continuation into adult life, integrating their biological and social etiology with a focus on recent advances in neurosciences.

Several chapters in this book have been adapted from the popular UK journal, *Advances in Psychiatric Treatment*, which publishes review articles. As mentioned in the preface, the book attempts to conceptualize core topics of child and adolescent psychiatry for the purpose of medical education. All of the chapters maintain this ethos, distilling key child psychiatry concepts into a meaningful and coherent manner.

The book starts off with an introductory chapter on Child Psychiatry and People Who Have Shaped It, which provides a background on child psychiatry evolution. The selection of clinical topics and their order is well-thought-out. The initial chapters of the book range from pragmatic topics like Fabrication and Induction of Illness in Children, which discusses risk factors, diagnosis, and management, to heavily theoretical but easy-to-read chapters such as Personality Disorders as Disorganization of Attachment and Affect Regulation. The latter lays the foundation for other topics like Post-traumatic Stress Disorder and Attachment: Possible Links with Borderline Personality Disorder, as well as Management of Antisocial Personality Disorders in Childhood. The mid-section of the book, chapters 6–10, discusses pharmacological and psychotherapeutic management of childhood psychiatric disorders. The book then moves on to discussing common childhood psychiatric conditions and their management (chapters 11–22). The final chapter is on Psychiatry of Children Aged 0–4 Years Old, an age group whose psychiatric care is universally challenging.



Edited by Sarah Huline-Dickens . London, RCPsych Publications, 2014, 416 pp., $46.90 (U.S.).

Even though the book seems to be written with a perspective of the National Health Service (United Kingdom), it might be of interest to American readers, with the recent and proposed changes to health care delivery in the United States. Throughout the book, landmark child psychiatry studies (e.g., Multimodal Treatment of ADHD) are well described, and there are discussions on American child psychiatry practice. There is a balanced approach with a discussion of both National Institute of Clinical Excellence and American Academy of Child and Adolescent Psychiatry guidelines. There is a review of both the ICD-10 and DSM-5 nosologies, improving its utility for a global audience.

The book is well written, and its educationally rich figures, tables, and textboxes further enhance its usefulness. This book is suitable for those looking for a quick update on child psychiatry and at the same time can serve as a practical reference guide for child psychiatrists. With its easy-to-read presentation, I believe this book to be beneficial for psychiatry trainees who are interested in or currently training in child psychiatry. I foresee its value in preparing for child psychiatry in-service examinations and American Board of Psychiatry and Neurology board examinations.

At the time this book review was accepted for publication, Dr. Kolli was a child psychiatry fellow at Creighton University, Omaha Neb.

Residents' Resources

Here we highlight upcoming national opportunities for medical students and trainees to be recognized for their hard work, dedication, and scholarship.

**To contribute to the Residents' Resources feature, contact Hun Millard, M.D., M.A., Deputy Editor (hun.millard@yale.edu).*

OCTOBER DEADLINES

Fellowship/Award and Deadline	Organization	Brief Description	Eligibility	Contact	Website
The Group for the Advancement of Psychiatry (GAP) Fellowship **Deadline:** October 1, 2015	GAP	Each Fellow: Attends four GAP meetings over 2-years; becomes a member of one of the working GAP committees; collaborates with other fellows on a plenary presentation to the general GAP membership; learns about group process in their GAP committee and with their fellowship group; and benefits from close interaction with peers and mentors.	PGY 2 or later at an accredited psychiatry residency program in the United States or Canada; have at least 2 years of training ahead (e.g., PGY-1 or 3, or first year of a 2-year fellowship).	e-mail: Frda1@airmail.net or telephone: 972-613-0985	http://ourgap.org/
Geriatric Mental Health Foundation's Honors Scholarships **Deadline:** October 1, 2015	American Association for Geriatric Psychiatry (AAGP)	Provides residents 1-year membership to AAGP; registration and travel costs to attend the AAGP Annual Meeting; Participation in an academic project related to geriatric psychiatry under the supervision of an assigned mentor.	PGY 1, 2, or 3 at an accredited psychiatry residency program	e-mail: main@AAGPonline.org or telephone: 703-556-9222	http://www.aagponline.org/
Geriatric Mental Health Foundation's General Scholarships **Deadline:** October 1, 2015	AAGP	Provides medical students 1-year membership to AAGP; registration and travel stipend to attend the AAGP Annual Meeting; voluntary participation in an academic project related to geriatric psychiatry under the supervision of an assigned mentor.	Medical students in a LCME or COCA accredited medical school.	e-mail: main@AAGPonline.org or telephone: 703-556-9222	http://www.aagponline.org/

NOVEMBER DEADLINES

Fellowship/Award and Deadline	Organization	Brief Description	Eligibility	Contact	Website
APA/Lily Psychiatric Research Fellowship **Deadline:** November 17, 2015	APA	This fellowship provides funding for 2 postgraduate psychiatry trainees, under the supervision and guidance of his/her mentor to design and conduct a research study on a major research topic.	APA RFM; Received M.D. or D.O. degree; Completed residency training in general psychiatry or child psychiatry prior to time fellowship commences; Not already an established investigator.	psychresearch@psych.org	http://www.psychiatry.org/researchers/research-training-and-career-distinction-awards/psychiatric-research-fellowship
American Psychiatric Foundation (APF) Schizophrenia Research Fellowship **Deadline:** November 17, 2015	APF	A 1-year psychiatric research fellowship for three postgraduate psychiatry trainees specifically to focus on research and personal scholarship. Minimal time (less than 15%) will be devoted to teaching, patient care, consultation, or other duties. The protection of time for research should be assured by the department chairman.	Received M.D. or D.O. degree; Completed residency training in general psychiatry or child psychiatry prior to time fellowship commences; Not already an established investigator.	Marilyn King e-mail: schizophrenia@psych.org or telephone: 703-907-8653	http://www.psychiatry.org/researchers/research-training-and-career-distinction-awards/schizophrenia-research-fellowship

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3. **Treatment in Psychiatry:** This article type begins with a brief, common clinical vignette and involves a description of the evaluation and management of a clinical scenario that house officers frequently encounter. This article type should also include 2-4 multiple choice questions based on the article's content. Limited to 1,500 words, 15 references, and one figure. This article type should also include a table of Key Points/Clinical Pearls with 3–4 teaching points.
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