Therapeutic treatment of rapid-onset autoimmune encephalopathies
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Purpose
The purpose of this discussion is to introduce a particular type of Autoimmune Encephalopathy known as Pediatric Acute-Onset Neuropsychiatric Syndrome, or PANS, and to summarize recent management guidelines, with a focus on the use of therapies, supportive interventions, and other daily behavioral and lifestyle management strategies.

Summary
While little is known about PANS diagnosis and treatment, studies have found that treatment focusing on the whole patient seems to be the most beneficial in returning children to baseline. Apart from pharmaceutical treatments, remedies targeting behavioral changes and school accommodations are vital in helping reduce the negative symptoms of the disorder. Therefore, treatment emphasizes the participation of both behavioral therapists and school administration officials, where flexibility in dealing with symptoms and their effects is crucial in providing the highest possible care to the child.

Introduction
Autoimmune encephalopathies are a group of conditions in which the body’s natural immune system perceives molecules in the brain as foreign and the attack causes inflammation in areas of the brain. In the past two decades, a new group of rapid-onset autoimmune encephalopathies has been identified. Originally thought to be triggered by group A streptococcal infections, the definition has since expanded to include any illness or environmental triggers. The term proposed for these conditions is Pediatric Acute-Onset Neuropsychiatric Syndrome or PANS. This brief summarizes the recent management guidelines issued by a group of national experts who have been treating PANS over the last decade. Particular emphasis is paid to the use of therapies and other interventions as daily management strategies for the children affected with these conditions and their families.
Diagnostics Criteria for Pediatric Acute Onset Neuropsychiatric Syndrome

1. An abrupt, acute, dramatic onset of obsessive-compulsive disorder or severely restricted food intake.
2. Concurrent presence of additional neuropsychiatric symptoms with similarly severe and acute onset from at least two of the following:
   - Anxiety
   - Emotional Lability and/or Depression
   - Irritability, Aggression, and/or Severe Oppositional
   - Behavioral (Developmental) Regression
   - Sudden Deterioration in School Performance
   - Motor or Sensory Abnormalities
   - Somatic Signs & Symptoms, including Sleep Disturbances, Enuresis, or Urinary Frequency
3. Symptoms are not better explained by a known neurologic or medical disorder.

PANS is currently a clinical diagnosis of exclusion, meaning the diagnosis is made through comprehensive clinical examination confirming that other known neurological and medical disorders do not better explain the symptoms and clinical history of the child. The above list provides the diagnostic criteria for PANS.

Several psychotropic, anti-inflammatory, antimicrobial and immunomodulatory medications are recommended for management of psychiatric symptoms and the initial autoimmune response; however, the more critical management for day-to-day function occurs through non-pharmacological interventions and therapies. The remainder of this review will focus on therapeutic and supportive interventions recommended by the series of articles.

Best Available Evidence

As with many other neurodevelopmental conditions, every case is unique in symptom presentation and severity. The safety of the child is the priority and overrides any other symptom management when safety concerns are present. Threat of harm to self or others and clinically significant concerns of malnutrition due to reduced food or fluid intake need to be addressed before any other behavioral therapies can be introduced.

Behavioral Therapies

Standard established therapies for tics, anxiety, and obsessive-compulsive disorder can be used to extinguish or decreased the distress caused by these behaviors. Table 1 provides a summary on recommended therapeutic interventions for presenting symptoms. Meeting with or counseling the family may be warranted to facilitate consistency and limit unnecessary accommodations that could be exacerbating behaviors, particularly if the family has fears of recurrence. Furthermore, the sudden and dramatic change in their child can incite stress in the families. During the most acute stage of the presentation, family structures often need to change to ensure one parent can be home with the child to provide 24-7 care, support, and supervision. The recency of recognition of this condition and some of the controversy surrounding whether PANS should be treated as an encephalopathy or only as a psychiatric condition puts an added burden on the parent when seeking an initial diagnosis and symptom relief from unconvinced clinicians. Recommendations for determining whether or not the presenting symptoms are due to a relapse involves asking the child whether they attribute their symptoms to unwanted behaviors or if they believe they are relapsing.
School Accommodations

Many of the children affected with PANS are acutely aware of their behavioral and emotional changes and most will require some form of accommodations geared towards symptom management. Because of the relapse-remit cycle of PANS, schools should allow for accommodations that address the child’s needs when they are at their worst and in an active flare. It is paramount they provide flexibility and adjustments based on presentation during the course of illness.\(^4\) This allows the school and teachers to address the child’s needs based on their current symptom presentation and severity without drawing undo attention to the situation.\(^4\) Some of the more common areas where flexibility may be needed include: alternate methods of assignment completion when OCD is interfering or handwriting regression is evident; reduced academic load during times of reduced physical and mental stamina; and flexibility to leave the classroom as needed when urinary urgency or frequency is present. Other accommodations are more in line with standard educational accommodation needs such as regression in skills, slow processing speeds, and new onset difficulties in specific subjects.\(^4\) These recommendations are included in Table 1.

<table>
<thead>
<tr>
<th>Area</th>
<th>Symptom</th>
<th>Accommodation/Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral Approaches</td>
<td>Obsessive Compulsive Disorder</td>
<td>Cognitive behavior therapy (CBT); Exposure/response prevention (ERP); Parent management techniques (PMT)</td>
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<tr>
<td>Anxiety</td>
<td></td>
<td>Cognitive behavior therapy (CBT); Exposure with response prevention (ERP); Occupational therapy interventions for fear management</td>
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<tr>
<td>Tics</td>
<td></td>
<td>Comprehensive behavioral intervention for tics (CBIT); Habit reversal training (HRT); ERP when severe; Relaxation techniques and family reinforcement of HRT</td>
</tr>
<tr>
<td>Irritability &amp; Aggression</td>
<td></td>
<td>Environmental interventions including reduced stimulation, sleep hygiene vigilance, and distraction during outbursts</td>
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<tr>
<td>Depression/Dysphoria (not severe)</td>
<td></td>
<td>Family or individual supportive therapy</td>
</tr>
<tr>
<td>School Accommodations</td>
<td>Prolonged Absences Due to Flares</td>
<td>Excusing absences or not requiring extensive makeup work</td>
</tr>
<tr>
<td>Separation Anxiety</td>
<td></td>
<td>Permitting parent in the classroom</td>
</tr>
<tr>
<td>OCD Symptoms</td>
<td></td>
<td>Excusing participation in certain activities or permitting alternate completion methods</td>
</tr>
<tr>
<td>Urinary Urgency/Frequency</td>
<td></td>
<td>Permitting child to leave class without requiring permission request</td>
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<tr>
<td>Dysgraphia, Dyscalculia, or general topical difficulties</td>
<td></td>
<td>Providing supports, resources, tutors or other tools to facilitate completion</td>
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<tr>
<td>Slowed Processing Speed</td>
<td></td>
<td>Decreasing assignments, allowing extra time or providing directions in a variety of formats</td>
</tr>
<tr>
<td>Decreased Stamina</td>
<td></td>
<td>Reduced school day or academic load, or permitting rest periods</td>
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Implications

Due to the wide array of symptoms and their severities, the treatment of PANS is by no means a simple task. It requires the delicate coordination of providers, families, and teachers to implement a treatment plan that best suites the needs of the child. Using a combination of pharmacological treatments with behavior and lifestyle modifications, patients have a greater chance of returning to baseline and living a normal life. However, as providers, it is important to consider that the child’s severity may vary from day-to-day or week-to-week, and thus this process is not a stagnant one, but rather one of constant adjustment.

During the acute phase, clinical management is important in getting the symptoms under control and attempting to return the patient to their baseline. Just as important, long-term treatment stems from management of PANS on the school and community-wide level, where both places play a vital role in improving the quality of life for both the patient and their families. While treatment regimens vary according to severity, patient, and situation, the one constant factor is a need for flexibility in treatment that can be constantly altered according to the child’s needs and symptoms.

Resources

The University of Arizona Steele Children’s Research Center’s Center for Postinfectious Autoimmune Encephalopathy is one of the few multidisciplinary clinics in the country focused on the diagnosis and treatment of PANS.
http://peds.arizona.edu/cpae

The PANDAS Physician Network provides clinical management guidelines and a library of resources, published research and other relevant information on PANS for practitioners. https://www.pandasppn.org/

References


About the Authors

Mathew Murray is a research technician with the Center for Postinfectious Autoimmune Encephalopathy at the University Arizona Health Sciences Center (CPAE). Mathew is responsible for recruitment, consenting and sample collection. Linnette is the Research Coordinator for CPAE and manages all related grants. Jennifer is Director of Research for the Division of Genetics and Developmental Pediatrics.