PANS & PANDAS Update

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Overview

1. Background
2. Understanding PANDAS and PANS
3. Treatment

PANDAS vs PANS

- **PANDAS**
  - **P**ediatric **A**utoimmune **N**europsychiatric **D**isorders **A**ssociated with **S**treptococcal Infections
  - Subset of children and adolescent who have acute- onset OCD and/or tic disorders in which symptoms worsen following strep infection
- **PANS**
  - **P**ediatric **A**cute-onset **N**europsychiatric **S**yndrome
  - Larger class of acute-onset OCD cases
  - Includes all cases of abrupt onset OCD (not just those associated with strep)

Background

- Initial description of PANDAS published in 1998
- Research at NIMH - Dr. Susan Swedo
  - Children with OCD
  - Subgroup of children with atypical course
    - Abrupt onset (max intensity within 24 – 48 hours)
    - Relapsing-remitting course
    - Significant neuropsychiatric comorbidities
      - ADHD, motor tics, separation anxiety
    - OCD frequently preceded by a bacterial or viral infection
      - “PITANDS” – Pediatric Infection-Triggered Autoimmune Neuropsychiatric Disorders

Why the interest in Group A Strep?

- Rheumatic Fever = inflammatory disease which is a complication of untreated or partially treated strep infection (strep throat, scarlet fever)
- Protein on Group A Strep similar to one on certain body tissues
- Immune system cells (antibodies) that would normally target the bacteria attack the body's own tissues as if they were infectious agents
- Primarily affects heart, joints, skin and CNS and cause inflammation
- Symptoms: carditis, arthritis, skin abnormalities and neurologic symptoms (Sydenham Chorea) = Rheumatic Fever
- Onset = 2-4 weeks after strep infection

Sydenham Chorea

- Clinical manifestation of rheumatic fever
- Cross-reactive antibodies attack tissues in the brain (basal ganglia)
- Quick, uncoordinated jerky movements mainly affecting the face, hands, and feet
- Movements are involuntary, brief, and irregular
- Associated with emotional lability

What's the connection to OCD?

- NIMH investigators found a high prevalance of obsessive-compulsive symptoms in children and adolescents with Sydenham's Chorea
- Obsessions and compulsions present in 60 – 75% of children affected by Sydenham's Chorea
- Led to an interest in studying the association between Group A strep infection and OCD
- A definitive association between infection and OCD is yet to be established!

PANDAS Criteria

1. Presence of clinically significant obsessions, compulsions, and/or tics

2. Prepubertal onset of symptoms

3. Acute/abrupt symptom onset and episodic (relapsing-remitting) course

4. Temporal relationship between Group A strep infection and symptom onset/exacerbations

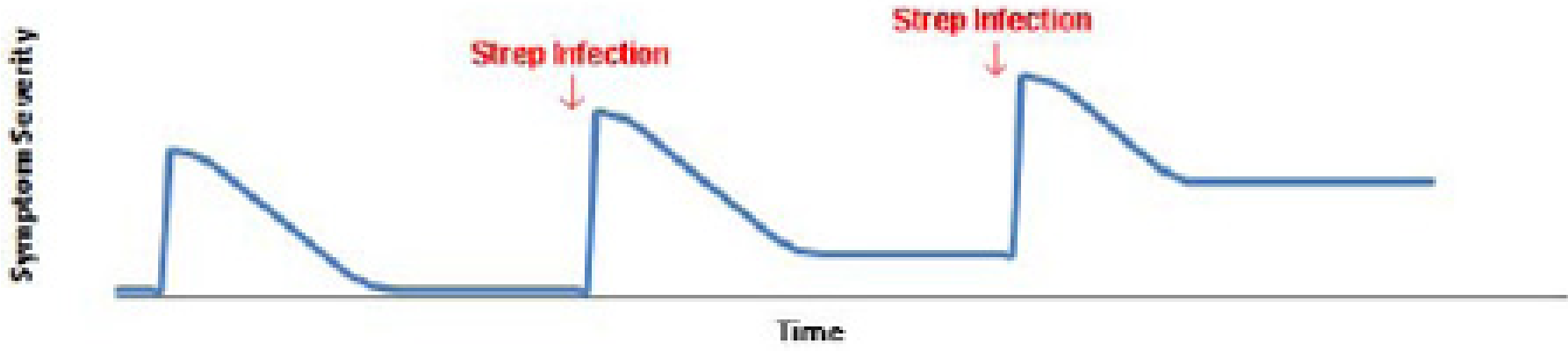
5. Association with other neuropsychiatric symptoms

PANDAS

- Course – episodic/relapsing-remitting
  - Sudden, dramatic onset of symptoms followed by a slow, gradual improvement in symptoms
  - Symptoms decrease significantly between episodes and sometimes resolve
  - Repeat strep infection leads to acute/sudden exacerbation of symptoms

- “Regular” OCD/tics - symptoms almost always present at a largely consistent level and not episodic in nature; not explosive/abrupt

Episodic Course of PANDAS



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PANDAS

- Symptoms tend to emerge 7- 14 days after group A strep infection
- Symptom flares occur months to years after initial onset
- Variable prognosis:
  - Full remission after initial episode
  - Dramatic flares followed by significant improvement, but not fully remitting
  - Progressively deteriorative course with each relapse

PANDAS

- Are laboratory tests useful in making a diagnosis?
  - Help document a current or recent strep infection
    - Throat culture – Group A beta-hemolytic strep
    - Blood test - Anti-streptococcal titers
      - Requires 2 separate blood tests, several weeks apart
      - **Demonstrate rising titer**
  - But…the presence of strep alone does not make a diagnosis. Must meet full diagnostic criteria!

PANDAS

- Neuropsychiatric symptoms
  - ADHD-like symptoms, motoric hyperactivity/restlessness
  - Separation anxiety
  - Enuresis
  - Generalized anxiety
  - Sensory abnormalities
  - Concentration difficulties/academic difficulties
  - Irritability/emotional lability
  - Developmental regression – tantrums, handwriting deterioration
- Associated neuropsychiatric symptoms begin at the same time or within 1-2 days of the OCD symptoms and are equally acute in onset

From PANDAS to PANS

- Controversy
  - Is there enough research to substantiate a link between strep/other infections and OCD/tics?
  - Concern about over use of antibiotics and other potentially dangerous treatments
  - Numerous patients meet criteria except for presence of preceding strep infection
  - Agreement on symptom set, but not etiology
- 2010 – Attempt at consensus:
  - Dr. Susan Swedo and colleagues at NIMH propose new, broader category to describe children with this same subset of symptoms but without the link to Group A strep
  - **PANS** = **P**ediatric **A**cute-onset **N**europsychiatric **S**yndrome

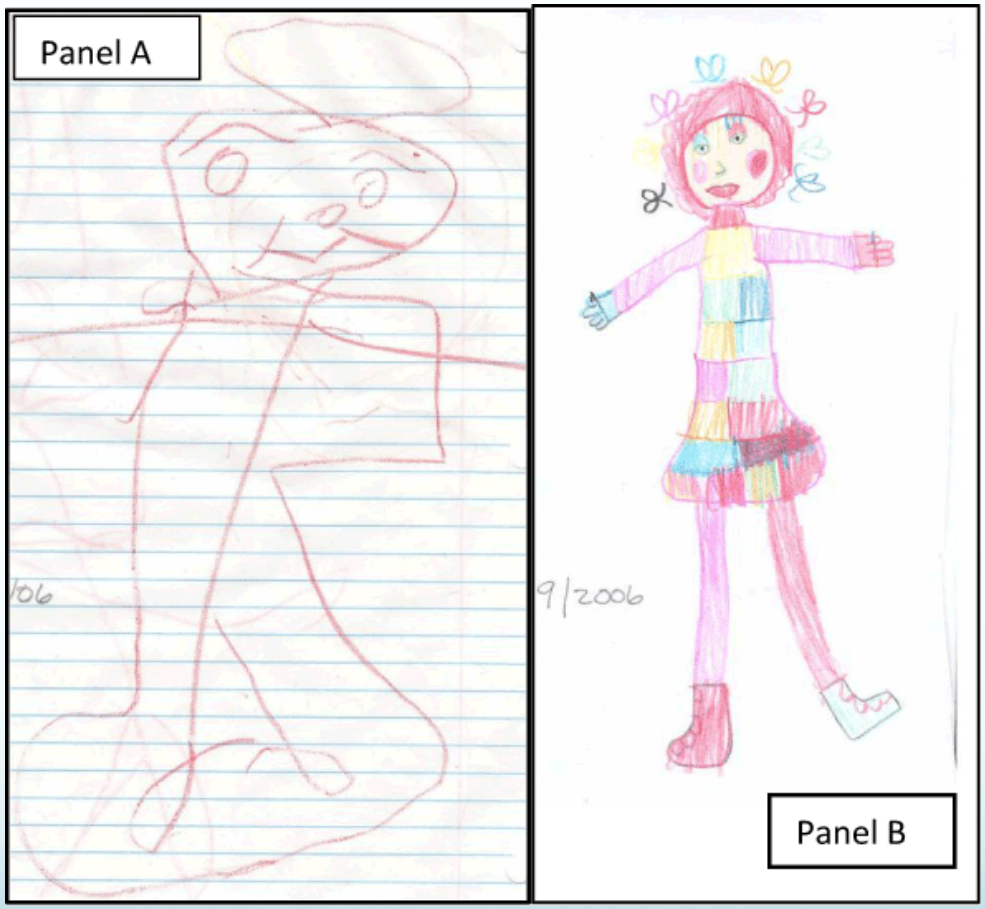
PANS Criteria

1. Abrupt, dramatic onset of OCD or severely restricted food intake
2. Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least 2 of the following 7 categories:
   - Anxiety
   - Emotional lability and/or depression
   - Irritability, aggression, and/or severe oppositional behaviors
   - Behavioral/developmental regression
   - Deterioration in school performance
   - Sensory or motor abnormalities – (dysgraphia, tics)
   - Somatic signs and symptoms – enuresis, sleep disturbance, urinary frequency
3. Symptoms not better explained by a known neurologic or medical disorder

PANS

- 5:1 male to female ratio (under age 8)
- Accounts for approximately 10-20% of pediatric OCD cases

PANS



Adapted from Swedo et al 2012

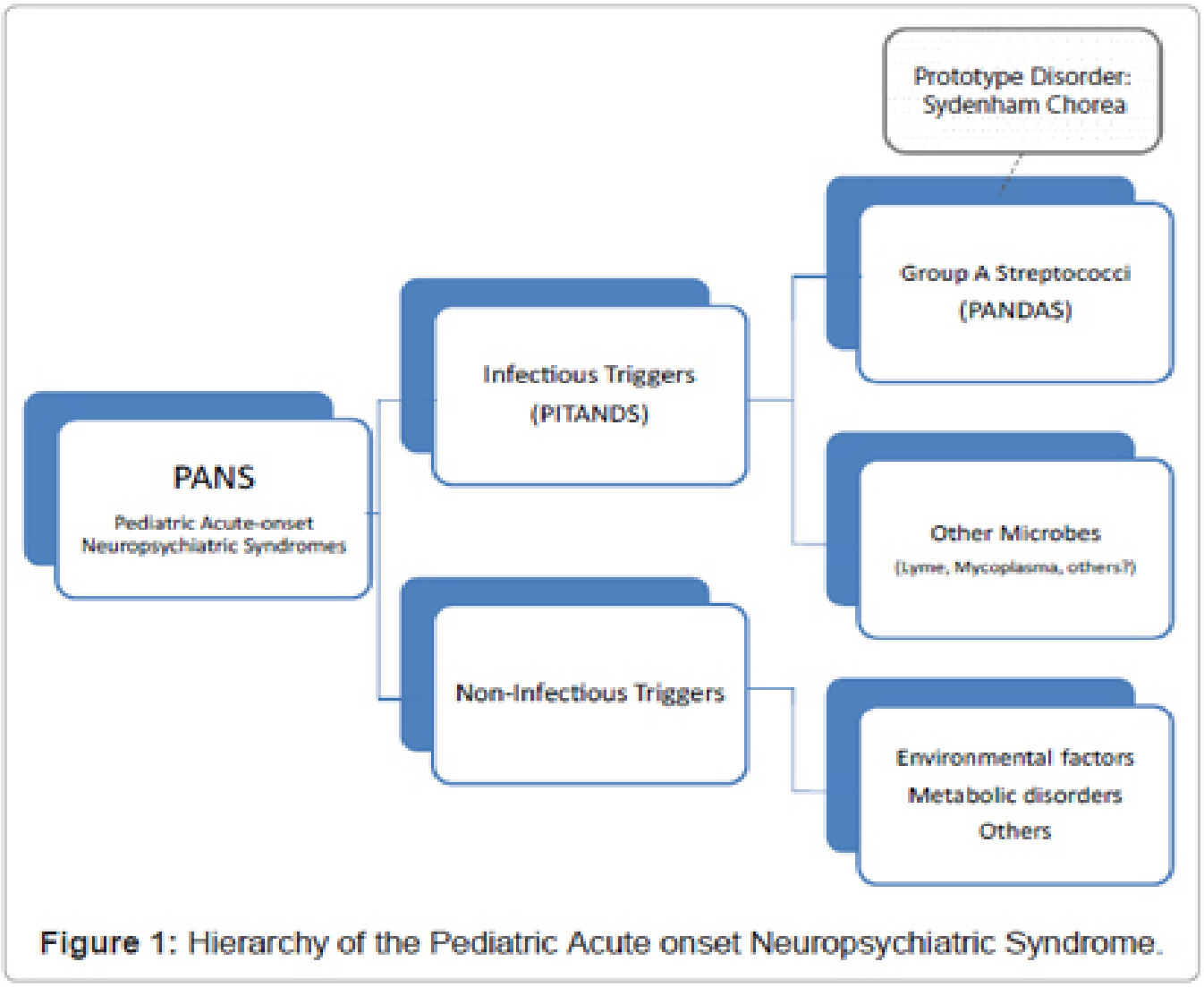


Figure 1: Hierarchy of the Pediatric Acute onset Neuropsychiatric Syndrome.

Image borrowed from "From Research Subgroup to Clinical Syndrome: Modifying the PANDAS Criteria to Describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome)"

Swedo et al. 2012

PANS Treatment

- No etiologic trigger
  - CBT, OT
  - Medication (SSRI's for OCD)
  - Supportive therapy to patient and family
- Infectious trigger
  - Treatment of infection may reduce symptom severity
- Children with PANS particularly sensitive to medication side effects
- No good treatment trials

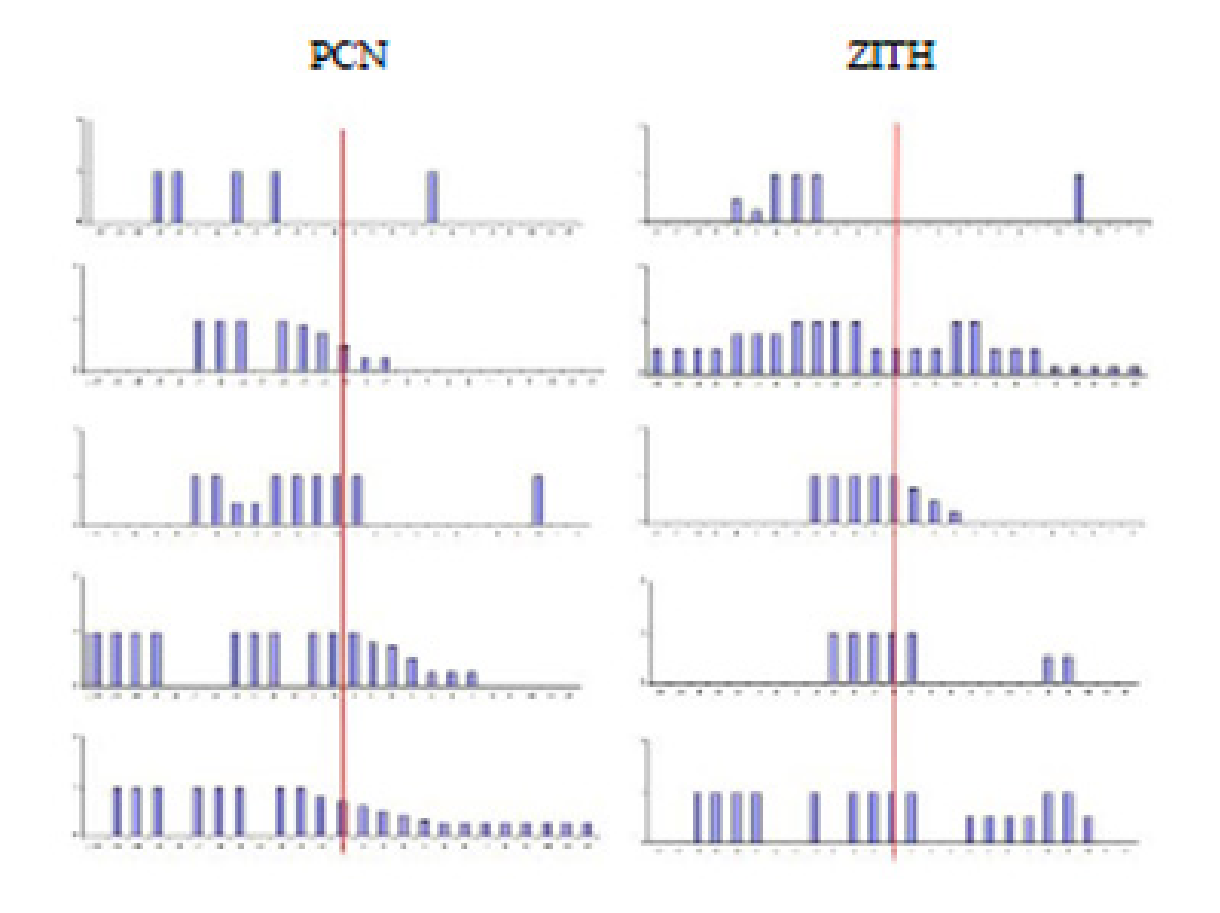
PANDAS Treatment

- Acute episode
  - Treat strep infection if still present
  - Single course of antibiotics (4 – 6 weeks)
    - Penicillin, amoxicillin, cephalosporin, azithromycin
    - Response to antibiotics can occur as quickly as within 24 – 48 hours, but may be delayed for up to 14 days
    - May require longer treatment if symptoms recur
  - 2nd line agents: NSAIDS, steroids
  - 3rd line agents: IVIG, plasmapheresis
- Also use conventional treatments – CBT, SSRI's, OT
  - Lessen severity of future flares

PANDAS – Prophylaxis???

- Two small clinical trials looking at prophylactic use of antibiotics in PANDAS to prevent strep infections
  - Prevention of group A strep infection is associated with:
    - Decreased number of neuropsychiatric symptom exacerbations
    - Overall improvement
  - Small sample size
  - Results cannot be generalized
  - Antibiotic prophylaxis not generally recommended

    (only treat acute strep infection!)



Adapted from nimh.nih.gov

Take home points

- PANS/PANDAS are associated with an acute/sudden onset of OCD symptoms
- PANDAS is a sub-category of PANS in which specific etiologic agent is group A strep
- Diagnosis is based on history and physical exam, exclusion of other medical causes, and cannot be made on laboratory values alone
- Treat with antibiotics only if known infectious agent is present
- Use of prophylaxis antibiotics not recommended at this time
- Need more research!

References

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