For Lowell General Hospital Pediatric Rounds

# PANS/PANDAS

Yujuan (Julia) Zhang, MD
Pediatric Rheumatology Division
Tufts Medicine Pediatrics
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# Disclosure

- No Financial Conflicts
- Member of *Mass DPH PANDAS/PANS Advisory Council
- Seeing PANS/PANDAS patients since 2016

# Objectives

- Overview of concept of PANS/PANDAS
- Review evidence of PANS/PANDAS as neuroimmune condition
- Introduction of PANS/PANDAS management at our clinic
- Review challenges in PANS/PANDAS

# References (or PMID)


- PMID: 37808558;  PMID: 36446706;  PMID: 35964340;  PMID: 33559023;
- PMID: 40367585;  PMID 39165391;  PMID: 37908968;  PMID 39084540;
- PMID: 38239595;  PMID: 39556906;  PMID: 39421743;  PMID: 39079372;
- PMID: 39334578;  PMID 39556906;  PMID: 36383096;  PMID: 36101642;
- PMID: 39910009;  PMID: 36514161;  PMID: 38874750;  PMID: 34197525;
- PMID: 39461376;  PMID: 40599669;  PMID: 40407889;  PMID: 33601937;
- PMID: 40127994;  PMID: 29722936;  PMID: 28358599;  PMID: 29309797;
- PMID: 33601937;  PMID: 39334578;  PMID: 37742615;  PMID: 35543072;
- PMID: 25329522;  PMID: 25325534;  PMID: 31111754;  PMID: 28722464;
- PMID: 26906964; PMID: 27663941
- Pediatrics Volume 155, Issue 3, March 2025:e2024070334
- *JAMA Psychiatry.* 2025;82(10):1030–1046. doi:10.1001/jamapsychiatry.2025.1369
- Cold Spring Harb Perspect Med 2012;2:a009621

# PANS/PANDAS Resources

- PANDAS Physicians Network (https://www.pandasppn.org/)
- PANS Clinic at Stanford (https://med.stanford.edu/pans.html)
- Neuroimmune Foundation (https://neuroimmune.org/)
- Q & A at NIH (https://www.nimh.nih.gov/health/publications/pandas)
- AAP Clinical Report. Pediatrics Vol 155(3), March 2025:e2024070334
- DPH PANDAS/PANS Advisory Council (https://www.mass.gov/orgs/pandaspans-advisory-council)

# Scenario 1

- Tom is a previously healthy 5 year old boy
- Sudden onset of anxiety, rages, OCDs
- Sibling had strep infection last week, but Tom has no strep symptoms
- Tom’s strep test is positive
- His behaviors improve significantly with amoxicillin and ibuprofen
- After amoxicillin 10-day course was done, behaviors worsened again
- The diagnosis of PANDAS is considered

# Scenario 2

- James is 15 year old boy with known ADHD
- Worsening rages, oppositional behaviors for the past few weeks, considered from ADHD vs teen behaviors?
- Bedwetting incident, previously dry since age 4
- James had pneumonia a few weeks ago treated with azithromycin x 5 days
- Labs show elevated mycoplasma IgG, IgM (IFA negative)
- Possible PANS considered, attempted longer course azithromycin + naproxen, significant improvement

# PANS (Pediatric Acute-onset Neuropsychiatric Syndrome)

- PANS: sudden onset of **obsessive-compulsive symptoms (OCD) or eating restrictions**, concomitant with acute behavioral deterioration in at least two designated domains:
  - anxiety
  - sensory amplification or motor abnormalities
  - behavioral regression
  - deterioration in school performance
  - mood disorder
  - urinary symptoms
  - sleep disturbances
- PANS does not require a known trigger, although it is believed to be triggered by one or more pathogens.
- **Symptoms are not better explained by a known neurologic or medical disorder**

# PANDAS

- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections
- PANS/PANDAS on the same spectrum
- ICD-10 code available (D89.89)

# Incidence and Prevalence of PANS/PANDAS

- Cases reported since 1980
  - PITANDs in 1995, PANDAS 1998, PANS 2010, CANS 2012
- Incidence estimated 1/11,765 between age 3~12
  - Juvenile arthritis 1.6-23/100,000
  - Lupus (in adults and pediatrics) 5/100,000
- Prevalence estimated 1:200 (to be verified)
  - Juvenile arthritis 1:1000
  - Lupus (in adults and pediatrics) 1:200


PMID: 37808558; PMID: 36446706

# PANS is a clinical diagnosis requiring OCD and/or restrictive food intake...

restricted intake

...as well as two or more of the following symptoms:

OCD

emotional lability

aggression

depression

irritability

deterioration in school work

oppositional behaviors

urinary frequency

anxiety

sleep disturbances

regression

sensory abnormalities

enuresis

# OCDs and PANS/PANDAS

- OCDs in PANS/PANDAS vs OCDs in non-PANS group
- Consider PANS more if
  - Patients presenting with a wide range of symptoms at onset,
  - Patients have a rapid escalation in severity


PMID: 33559023; PMID: 40367585

# Eating Disorders and PANS/PANDAS

- Gut-brain link
  - Gut dysbiosis→anxiety/depression
  - Stress/anxiety→IBS/constipation

- PANS and Eating Disorder are not mutually exclusive
  - Eating restriction in half of PANS cases
  - Eating disorder can be triggered by infection, manifesting as PANS
    - Half of patients with eating disorder have PANS?

| | AN | PANDAS "anorexia" | ARFID | PANS disordered eating |
|---|---|---|---|---|
| **Onset** | Insidious and usually pubertal or postpubertal | Acute and prepubertal | Acute and prepubertal (most common) | Acute and prepubertal |
| **Prevalence** | Females > > Males | Females > Males | Females = Males | Females < Males |
| **Trigger** | Genetic predisposition, neurochemical imbalance, cultural pressure | Infection, genetic predisposition | Environmental, temperamental, genetic and physiological | Infection |
| **Fears** | Fears of being "fat," fear of weight gain; body image distortions | Contamination, sensory, irrational thinking (e.g., food seems inedible, mechanical swallowing, food smells) | Sensory, lack of interest in food; conditioned negative response to food | Contamination, sensory, irrational thinking (e.g., food seems inedible, mechanical swallowing, food smells) |
| **Resolution of symptoms and weight restoration** | Slow, relapse common, high mortality rate | Relatively rapid with PANDAS symptoms | Slow, need to address comorbidities | Relatively rapid with PANS symptoms |



PMID: 35543072; PMID: 25329522; PMID: 25329522; PMID: 39910009; PMID: 36514161

# Other Symptoms: at least two of the following

- Anxiety
- Sensory amplification or Motor abnormalities
  - Tics*, handwriting change, pain, texture issue
- Behavioral regression
- Deterioration in school performance
- Mood disorder
- Urinary symptoms
- Sleep disturbances



*Overlap with Tourette syndrome



https://northlandchildpsychiatry.com/blog/2023/08/11/recognizing-the-early-signs-of-tourette-syndrome-in-children/

# Other symptoms of PANS/PANDAS

- Dizziness
- Fatigue
- Narcolepsy
- Speech issue: Stuttering, selective mutism


[PMID: 39079372; PMID: 35964340]

# Triggers of PANS/PANDAS—Often Unrecognized!

- Infectious Triggers
  - Strep
  - Mycoplasma
  - Viral infection
  - Other infections: Lyme, other tick-borne

- Evidence of infection might be absent
  - Exposure to infection
  - None or minimal infectious symptoms
  - Often not seeking medical care


PMID: **37742615**

# Triggers of PANS/PANDAS—Often Unrecognized!

- Non-infectious Triggers
  - Loose tooth
  - Injury/trauma: concussion, fracture
  - Allergic reaction
  - Vaccinations


PMID: **37742615**

# Questioning the Diagnosis of PANS/PANDAS??

- Situational behavioral dysregulation
  - Often worst behaviors at home, when with primary care-giver
- Disagreement between parents and teens
  - PANS related oppositional behaviors vs “just teenagers”
- Suspected Munchausen by proxy (Factitious Disorder Imposed on Another, FDIA) in some cases

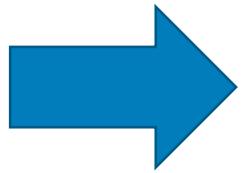
# Clinical Course of PANS/PANDAS

- Operative criteria for flare (>4 days)
- PANS Clinical Course:
  - 2/34 remitted
  - 20/34 relapsing-remitting
  - 12/34 chronic-static/progressive


PMID: **37742615,** PMID: 35964340

# Evidence of Neuroinflammation

- Connection with acute rheumatic fever and Sydenham Chorea
- Some research findings re cytokines especially the IL-17 and blood-brain barrier (BBB)
- Higher chance of family history of autoimmune diseases
- Findings of infections involved in psychiatric conditions



# AAP Clinic Report--NOT a Guideline for Providers

- The AAP recognizes that PANS is likely a valid diagnosis, although the diagnostic process is challenged by a lack of well-accepted evidence to guide the clinician

- Interventions focusing on psychiatric/behavioral interventions
  - Antibiotic treatment only if evidence of GAS infection; and
  - Immunomodulatory treatment not considered needed

# Evaluating PANS/PANDAS at Our Rheum Clinic

- Clinical Diagnosis
  - Diagnosis of exclusion
- Explore potential infectious triggers
  - **Strep, mycoplasma, Lyme, other bacteria**
  - Other tick borne disease, bartonella
  - Fungal/yeast infection/mold exposure?
- Explore non-infectious associations
  - Allergens, Mast Cell Activation Syndrome?
  - **Celiac disease, Hashimoto thyroiditis**
- Rule out conditions that might mimic PANS/PANDAS
  - PANS/PANDAS can coexist with other inflammatory conditions

# Evaluating PANS/PANDAS at Our Rheum Clinic

- Workup (case by case)
  - Labs
    - CBC-D, CMP, +/-ESR, CRP, urinalysis with protein creatinine ratio
    - ASO, Dnase B, Mycoplasma IgG/IgM, Lyme screen
    - IgG subclass, IgA, +/-IgE
    - ANA, +/-APLs, +/-C3, C4, +/- HLA B27, +/-HLA B51
    - TSH, FT4, anti-TPO, anti-thyroglobulin, Celiac panel
    - Iron study, +/-vitamin D
  - Imaging
    - Brain MRI
    - EKG, EEG
    - Joint imaging

# Consider PANS/PANDAS a Differential Diagnosis

- Screen recent/current infections/exposure to infections
  - Negative strep does NOT rule out PANS/PANDAS
- Connect the patient to a specialist who is familiar with PANS/PANDAS
  - psychiatrist, neurologist, rheumatologist, therapist, infectious disease, etc.
- Validate the family/caregivers' concerns
  - Munchausen by proxy 0.5-2.8/100,000 < 1/11,765 for PANS/PANDAS
  - If true suspicion for Munchausen by proxy (FDIA), do what you believe is right!

# Subspecialties often involved

- Psychiatry/Behavioral Therapy/Psychology
- Neurology
- ENT
- Endocrinology
- GI/Nutrition
- Allergy/Immunology
- Cardiology

# PANS vs Autoimmune Encephalitis

- Consider **autoimmune encephalitis workup** if one of the following prominent
  - 1) Delirium, psychosis, and/or diffuse encephalopathy;
  - 2) pervasive cognitive decline;
  - 3) persistent memory impairment;
  - 4) pervasive behavior deterioration;
  - 5) seizures; and
  - 6) movement abnormality not consistent with tics.
- **Workup for autoimmune encephalitis**
  - Neuroimaging such as brain MRI/MRA
  - electroencephalogram (EEG)
  - neuronal antibody testing (e.g., N-Methyl-d-aspartate [NMDA] receptor antibodies, voltage gated potassium channel antibodies) in serum and cerebrospinal fluid (CSF), thyroid antibodies (thyroglobulin antibodies, thyroperoxidase antibodies), and paraneoplastic evaluations.


PMID: **25325534**

# Diagnostic Criteria for Autoimmune Encephalitis
-------All three of the following criteria met

- Subacute onset (rapid progression of less than 3 months) of working memory deficits (short term memory loss), altered mental status (change in consciousness, lethargy, or personality change), or psychiatric symptoms
- At least one of the following: new focal CNS findings; seizure not explained by a previously known seizure disorder; CSF pleocytosis (WBC>5/mm3); MRI features suggestive of encephalitis *
- Reasonable exclusion of alternative causes

* Hyperintense signal on T2 weighted fluid-attenuated inversion recovery sequences highly restricted to one or both medial temporal lobes or in multifocal areas involving grey matter, white matter or both compatible with demyelination or inflammation

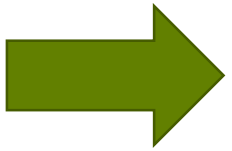

PMID: 26906964

# Treatment--Multidisciplinary approach

- Treat possible infectious or non-infectious trigger
  - Antibiotics, anti-histamine, etc
- Anti-inflammatory interventions
  - Anti-inflammatory, Immunomodulatory
- Symptom relief/supportive care
  - Behavioral, Neuropsychiatric, Family/School support

# PANS/PANDAS Medical Treatment Efficacy

- There IS evidence of medical treatment efficacy in PANS/PANDAS
  - Antibiotics
  - NSAIDs
  - IVIG
  - Others
- Strength of evidence is mostly weak
  - Mostly case reports, observational data
  - Some trials, often open label
- Skeptics might be more critical of PANS/PANDAS in terms of evidence



# Considering PANS/PANDAS……

When suspecting PANS/waiting for workup/specialist

- A Trial of NSAIDs/Celebrex
  - Ibuprofen
  - Naproxen
  - Celebrex

# Treating Possible Infectious Trigger

- Consider Antibiotics if possible infectious trigger per history/workup
  - Covering strep
  - Covering mycoplasma
  - Evidence of active infection often absent
  - Longer course antibiotics often necessary

- Adjust Treatment based on response to above treatment

# Medical Treatment

When PANS/PANDAS confirmed AND longer term treatment needed

- Consider safer longer term options
  - Low dose naltrexone (LDN) especially if intolerance of NSAIDs/Celebrex

- Long term antibiotics sometimes needed

# Medical Treatment

- For Moderate to Severe cases
  - IVIG/SCIG
  - DMARDs: colchicine, hydroxychloroquine, azathioprine
  - Biologics: anti-IL-17, JAK inhibitor, anti-TNF, anti-CD20 (Rituximab)

- Other Treatment: methotrexate, mycophenolate, plasmapheresis, functional/homeopathic treatments

# Medical Treatment--Immunoglobulin

- IVIG/SCIG
  - 1~2 grams/kg per month
    - Some patients could only tolerate very low dose and show good response to low dose
  - PANS patients tend to be MORE sensitive to IG side effects
    - Adequate hydration, pre-medications, post-medications
  - Response 3~6 months after initial treatment
  - Treatment course individualized

# Vaccinations for Children with PANS/PANDAS

- Benefit outweighs risks
  - Flares more after COVID infection compared to COVID vaccine

- We SUPPORT usual vaccinations for PANS/PANDAS patients


PMID: 40127994

# Vaccinations for Children with PANS/PANDAS

- Special considerations
  - Ideally, avoid vaccination when having an active flare in PANS/PANDAS
    - If flare difficult to control, will vaccinate if benefit outweighs the risks
  - If possible, do one vaccine at a time for PANS/PANDAS patients (at least 1 week apart between vaccines)
  - If history of a major flare in PANS triggered by a particular vaccine, we often agree to avoid the same vaccine in the future


PMID: 40127994

# Challenges—Families/Patients

- **Neuropsychiatric symptoms might be the only symptoms**
- **Impact on family and Caregiver Burnout**
  - The psychological toll on the family living in a constant state of "high alert.“
  - Family Medical Leave
- **Inadequate Access to PANS/PANDAS providers/treatments**
- **Care-coordination:** PANS sits at the intersection of Neurology, Rheumatology, Immunology, Infectious disease and Psychiatry. The patient/family often act as the “case manager”.

# Challenges--For Providers

- **PANS/PANDAS is a condition involving the medical and psychiatric field.**
  - Neuropsychiatric symptoms might be the only symptoms
  - Symptom Overlap: ADHD, Tourette's, Anorexia, etc

- **PANS/PANDAS might have an unremarkable workup**
  - Lab tests often non-specific.
  - It remains a clinical diagnosis, which creates uncertainty for providers.

- **Flare Management:** The "Two Steps Forward, One Step Back" nature of recovery. A simple cold can trigger a total relapse, which is exhausting for the patient.

# Challenges—For Providers

- **Frequent flares often require frequent or even long term medications**
  - Debate over long-term antibiotics, anti-inflammatory treatment.

- **Access and Cost:** The challenge of getting insurance coverage for expensive treatments like Intravenous Immunoglobulin or biologics (such as Rituximab).

- **Outcome measurement not standardized**

# Challenges—For Providers

- **Inadequate Research Funding/Support**
- **Workforce Shortage**
  - **Provider Burnout**

# Challenges—School and Community

- **Educational Barriers**
  - Schools often struggle to understand/accommodate
  - Missing school/decline in school performance

- **Social Isolation**
  - The "invisible" nature of the illness. Because the child might look physically healthy, their behavioral outbursts are often mislabeled as "bad parenting" or "poor discipline."

# Challenges—For the System

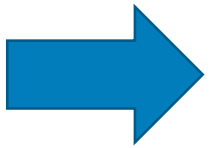
- **Standardizing Care:** The need for consensus diagnostic and therapeutic protocols
  - AAP clinic report recognizes PANS as a valid condition
  - AAP clinic report is NOT a guideline for clinicians

- **The Path Forward: Advocacy and Education**

- **Legislative Hurdles**

# Cases

- PANS and lupus
  - Lupus is a typical autoimmune disease mediated by autoantibodies
- PANS and Behcet's like disease
  - Behcet's is a rare rheumatic disease mainly involving innate immune system
- PANS and Functional Neurologic Disorder (FND)
  - FND usually managed by psychiatric/behavioral support



# Case: PANS and Lupus

- 10 yo F
- Age7-8: anxiety, school refusal, depression, treated with CBT, SSRI, developed rages, hair pulling, tics, food restrictions
- Age 9: flu infection, all above worse, multiple psychiatric meds, clear response to antibiotics, difficulty weaning off antibiotics, worse bruises when on NSAIDs
- Age 10: sent to us rheumatology
- Family Hx: extensive autoimmunity
- Workup positive SSB non-specific
- Hydroxychloroquine: very helpful
- IVIG as needed: very helpful
- Age 12: developed chronic arthritis, later a cutaneous lupus rash, low C3, C4, dx of lupus. No CSF yet.
- Age 16: worsening EKG, cardiac MRI suggesting myocardial inflammation. Started Rinvoq

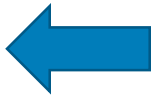
# Case: PANS and Behcet's Like Disease

- 15 yo M
- Frequent ear infections as a child
- Age 8: mild tics
- Age 13: COVID, weeks after, anxiety, OCDs, severe tics, hallucinations, rages, food restrictions, poor response to psych meds
- Age 14:  PANS suspected, positive HSV PCR (no report, unclear details), HSV IgG, strep titers, positive candida IgG. Treated with abx, NSAIDs, anti-viral, for a week, no help; dx of Tourette's, treated with Risperidone, worse
- Age 15: PANS suspected again, changed abx, restarted NSAIDs, no help. Antiviral started again with possible help. Sent to us rheumatology.

- Hx of large oral ulcers since young age, back stiffness, worse recently
- Family history: oral ulcers, psoriasis, thyroid disease, lupus and PANS/PANDAS
- HLA B51 positive; normal brain MRI, CSF, HSV encephalitis ruled out, neuro-Behcet unlikely per neurology
- Prednisone x 5 days mild help, IV Solumedrol pulse once, brief help.
- Colchicine side effects
- IVIG not available yet. Azathioprine: clear help for oral ulcers AND behaviors within a month
- IVIG added 3 months later: additional help
- Signs of worsening oral ulcers/worse behavior if missing Azathioprine; worsening behavior if overdue for IVIG
- Recently changed Azathioprine to anti-TNF (adalimumab) but not as effective

# Case: PANS and Functional Neurologic Disorder

- 13 yo F
- Age 7: Anxiety shortly after a concussion, worse after a cold, PANDAS considered, but strep negative→PANDAS "ruled out"
- Age 8~Age 13: tics, OCDs, seizure like activities later dx of FND, refractory to neuropsychiatric medications/partial program/psychiatric inpatient care
- Age 13: symptoms worse, PANS reconsidered, sent to us rheumatology, no response to Naproxen→ PANS "less likely"
- Age 13: Back to Psychiatric care only
- Age 14: family found ibuprofen works well for her anxiety; PANS reconsidered
- Significant improvement after LDN, antibiotics, IVIG
  - Gradually weaning off psych medications, still difficulty weaning off antibiotics, IVIG



# My Bias

- Very high index of suspicion in PANS/PANDAS

- All About Inflammation! Inadequate consideration in
  - infectious workup/metabolic workup
  - Psychosocial impact/family dynamic

# Thank You!

- Open conversation about PANS/PANDAS
- All providers support each other and learn together
- If any questions
  - Yzhang5@tuftsmedicalcenter.org
  - T:617-636-7285; F: 617-636-8388

# Evidence of Neuroinflammation

- A couple of good reviews
  - Vreeland A, et al. Dev Neurosci. 2023;45(6):361-374. doi: 10.1159/000534261. Epub 2023 Sep 22. Postinfectious Inflammation, Autoimmunity, and Obsessive-Compulsive Disorder: Sydenham Chorea, Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection, and Pediatric Acute-Onset Neuropsychiatric Disorder
  - Leonardi L et al. Children (Basel). 2024 Aug 27;11(9):1043. doi: 10.3390/children11091043. Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS): Immunological Features Underpinning Controversial Entities

# Neuroinflammation

## --Association with Acute Rheumatic Fever and Sydenham Chorea

- Approximately 25% of ARF cases manifest Sydenham chorea.

- Among patients diagnosed with SC, up to 80% exhibit obsessive-compulsive symptoms, along with other neuropsychiatric symptoms including restlessness, irritability, emotional lability, distractibility, anxiety, night terrors, and outbursts of inappropriate and/or violent behavior.


PMID: **39334578** [Cold Spring Harb Perspect Med 2012;2:a009621] PMID: **37742615**

# Neuroinflammation

## --Association with Acute Rheumatic Fever and Sydenham Chorea

- Basal ganglia dopamine dysfunction associated with dystonia, chorea, tics, obsessive compulsive disorders, and alterations of mood
- In humans, multiple MRI analyses have revealed both abnormal T1 and T2 signals in the basal ganglia of SC subjects, and persistent alterations in MRI
- Brain imaging studies point towards the basal ganglia as the most prominently affected part of the brain
  - Swelling of the basal ganglia in the acute stage;
  - microglia activation most prominently affects the basal ganglia structures in the caudate and putamen
  - microstructural changes in the basal ganglia

# Neuroinflammation
## --Association with Cytokine and BBB

- Preliminary studies of BBB models indicate that plasma from patients with PANS disrupts the BBB compared to plasma from matched controls.

- Circulating IL-17 provokes BBB disruption by altering tight junctions (TJs) and cell adhesion molecule expression on endothelial cells.


PMID: **39334578** PMID: **37742615** PMID: 38239595

# Neuroinflammation
## --Association with Cytokine and BBB

- Disruption in the BBB allows for the entry of peripheral immune cells, including Th17 cells, monocytes, and neutrophils, into the CNS.

- Moreover, IL-17 prevents brain endothelial cells from producing NO (eNOS), which may lead to endothelial dysfunction and lower cerebral blood flow (CBF).


PMID: **39334578** PMID: **37742615** PMID: 38239595

# Neuroinflammation
## --Association with Cytokines

- Th17 response plays a crucial role in those pathological conditions characterized by a state of neuroinflammation as shown by studies on autoimmune encephalitis (AE) and multiple sclerosis (MS)

- Higher TNF-alpha, IL-17, lower C3 levels detected in PANDAS compared to control group.

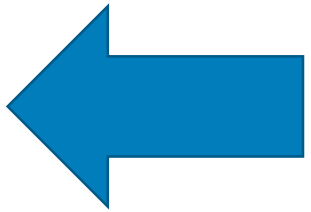
- IL-17 elevated in PANS serum compared to controls; CSF samples did not confirm the difference but controls were not age matched; PANS CSF IL-17 much higher than serum IL-17.


PMID: **38239595** PMID: 39556906

# Neuroinflammation
## --Other Supportive Evidence

- Family histories of PANS patients reveal remarkably high incidences of psychiatric disorders (51–78%) and autoimmune disorders (67–80%). Siblings of patients with PANS have a higher rate of immune disorders compared to controls (14% vs. 3%).

- Infections HSV, Borna disease, Strep, Borrelia spp, toxoplasma gondii, contributing to schizophrenia, mood disorders, autism, ADHD, anorexia nervosa, and PTSD




PMID: 36383096 PMID: **37742615** PMID: 36101642

# PANS/PANDAS Medical Treatment Efficacy

- Clinical Trials:
  - Penicillin prophylaxis 4 month no statistical benefit in OCDs
    - slightly better in penicillin group compared to placebo but no statistical significance
  - Azithromycin x 4 weeks, placebo controlled, severity in OCDs reduced on clinical global impression severity scale
    - QTc longer at the end of week 4 (P=0.06)
  - Non-PANS with OCDs or Tics treated with Cefdinir or placebo
    - no difference in OCD
    - Tics better with Cefdinir


PMID: **29722936**

# PANS/PANDAS Medical Treatment Efficacy

- Clinical Trials (no placebo control)
  - Penicillin or Azithromycin
    - Less strep infection
    - Less neuropsychiatric exacerbations compared to previous year


PMID: **29722936**

# PANS/PANDAS Medical Treatment Efficacy

- Observational studies:
  - Antibiotics associated with remission of neuropsychiatric symptoms: important clinical significance given the magnitude
  - Antibiotics help treat OCDs associated with PANS/PANDAS.
  - 698 patients with PANS
    - 90% of patients with infection-associated onset (65% of the total) reported receiving antibiotics for the infection
    - with 59% having a resolution of infection and
    - 31% having a resolution of PANS symptoms
- Case reports since 1996: many supportive cases


PMID: **29722936**

# PANS/PANDAS Medical Treatment Efficacy

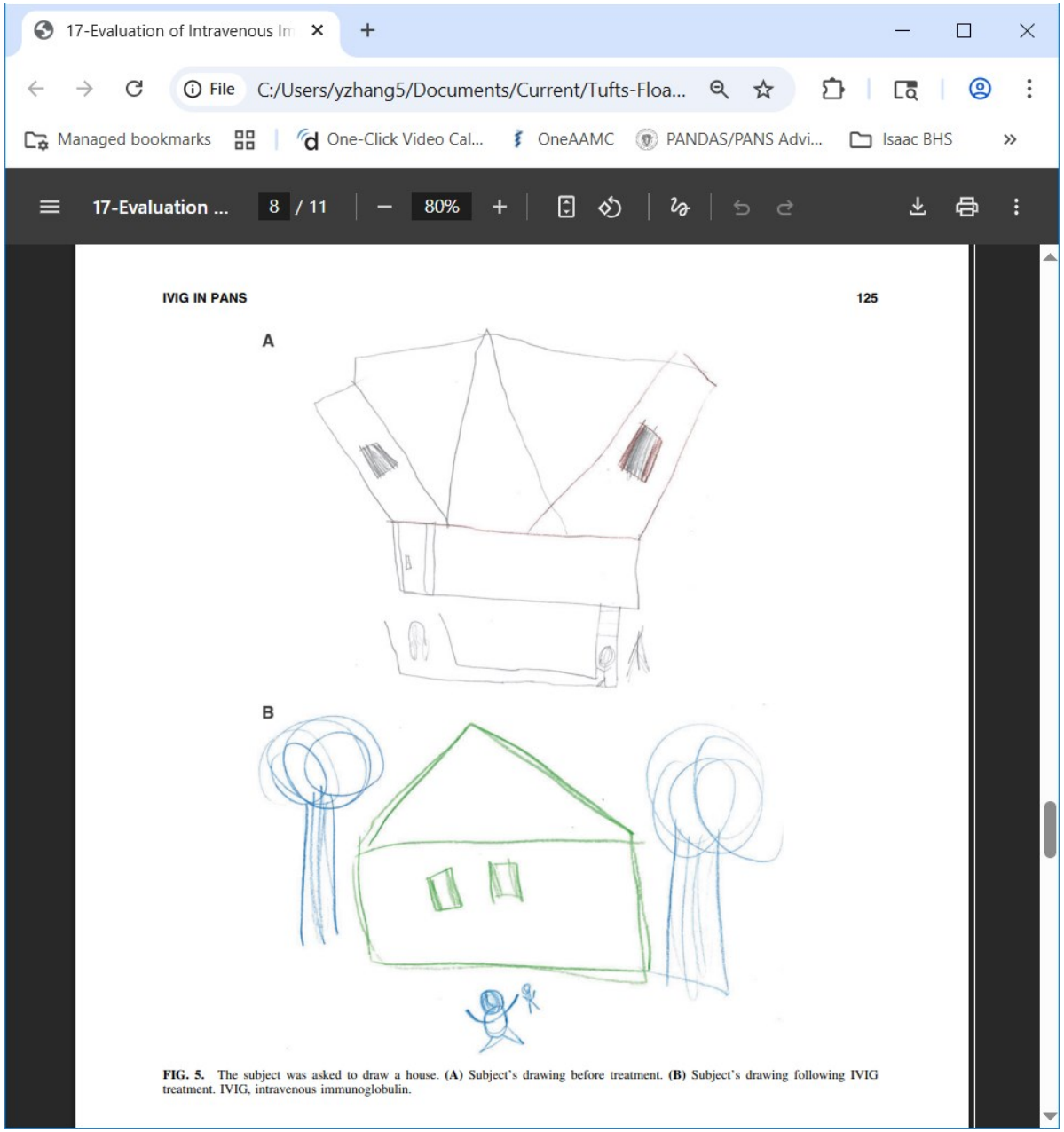
- Antibiotics role in modulation of neurotransmitter signaling, immune-modulating, neurogenesis
  - β-Lactams, macrolides
- SSRI role in immune modulating, neurogenesis
- CBT helps PANS related OCD group as well


PMID: **29722936**

# PANS/PANDAS Medical Treatment Efficacy

- One RCT did not see difference between IVIG and Placebo groups
- Open label study: IVIG (1 gram/kg every 3 weeks for 6 infusions) successfully ameliorated psychological symptoms/dysfunction with sustained benefits for over 8 weeks, up to 46 weeks in a subset of subjects
- PANS pro-inflammatory profile and psychometric scores improve following IVIG
- Neuropsychiatric testing improvement after one dose of IVIG in some areas (memory, sensory motor skills, visual motor integration)
- Improvement noticed in 11/12 patients after IVIG treatment (memory, sensory-motor, visual-motor)
- **Clinic trial with placebo group ongoing**: results suggesting IVIG more effective than placebo but primary endpoint not met yet (not published yet)


PMID: 27663941; PMID: 39421743; PMID 39165391, doi:10.1001/jamapsychiatry.2025.1369; PMID: 37908968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80%
IVIG IN PANS
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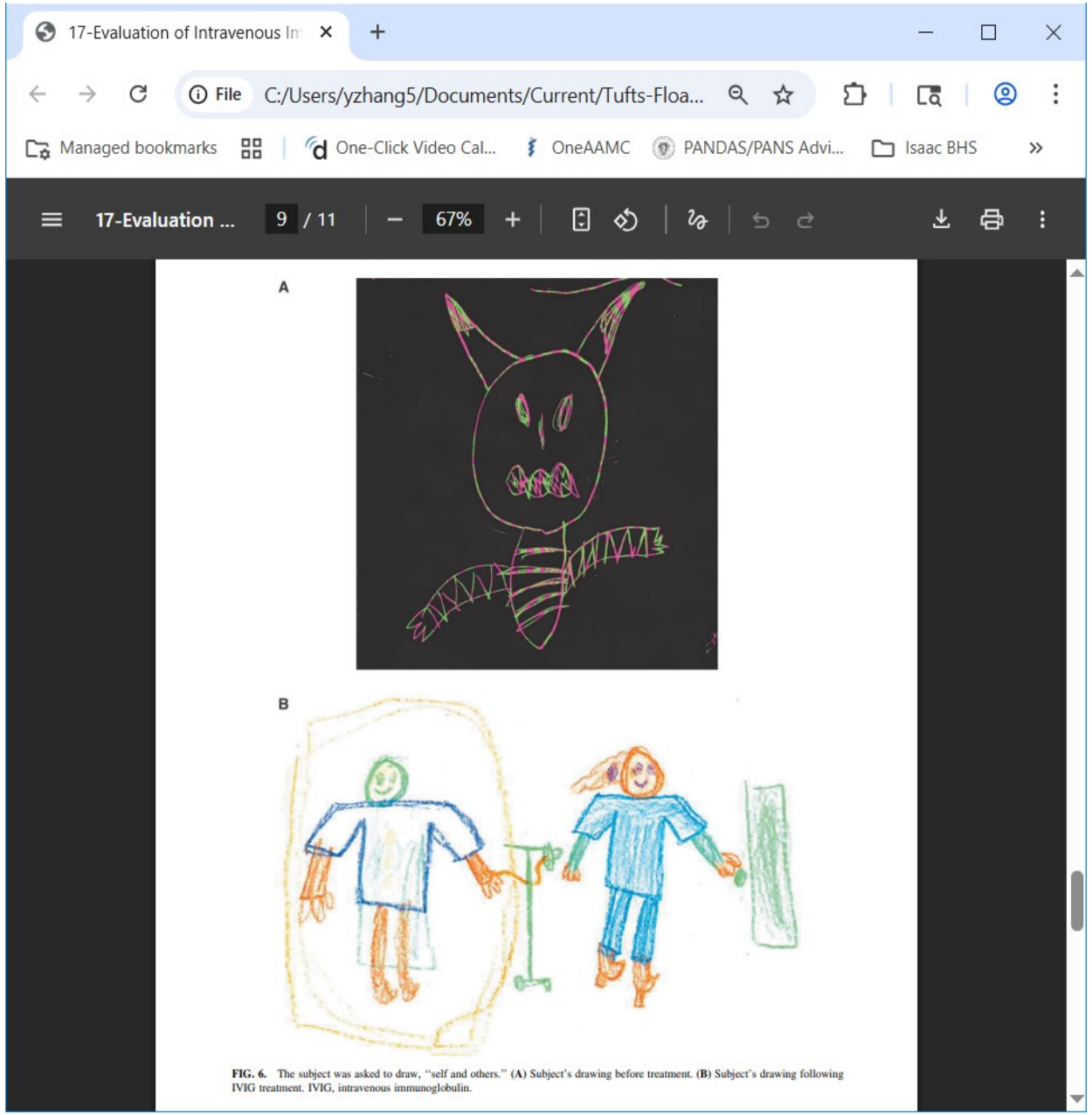
FIG. 5. The subject was asked to draw a house. (A) Subject's drawing before treatment. (B) Subject's drawing following IVIG treatment. IVIG, intravenous immunoglobulin.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67%
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FIG. 6. The subject was asked to draw, "self and others." (A) Subject's drawing before treatment. (B) Subject's drawing following IVIG treatment. IVIG, intravenous immunoglobulin.

# PANS/PANDAS Medical Treatment Efficacy

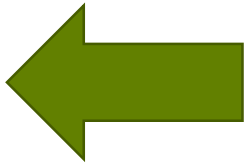
- Review INCONCLUSIVE re:
  - Antibiotics
  - Plasma Exchange
  - IVIG
  - CBT
  - NSAIDs
  - Steroids
  - SSRI
  - Weak in tonsillectomy+/-adenoidectomy.

- The lack of evidence for treatment efficacy is based not on the inefficacy of the treatments, but **on lack of systematic research**.


PMID: **29309797**

# PANS/PANDAS Medical Treatment Efficacy

- It may be noted that this evidence situation has similarities with the one regarding treatment of juvenile idiopathic arthritis (JIA), where reviews have shown that the level of evidence is mostly very low or low for COX-2 inhibitors, corticosteroids and other currently available medications.





PMID: 34197525