



*Is this Just the
Tip of an
Iceberg?*

*PANDAS/PANS and Other
Infection-Triggered
Autoimmune
Encephalopathies:
Interpretation of The
Cunningham Panel
Results*

*Craig Shimasaki, PhD, MBA
Co-founder & CEO, Moleculera Labs
December 3, 2019*

Disclosure Statement:

- I am President and CEO of Moleculera Labs, the company that performs the Cunningham Panel.
- No other disclosures

Topics We will Cover

1. Clinical Challenges with Neuropsychiatric and Behavioral Disorders

- Complexity of Complex Diseases
- Influences of genetics

2. Review of PANDAS/PANS

- Nomenclature and Acronyms
- Biological mechanism
- Medical model for other chronic neuropsychiatric and behavioral disorders

3. Common Infectious Triggers in Autoimmune Encephalopathies in Children and Adults

- Molecular Mimicry
- Multisystem Interaction and Genetic Predisposition

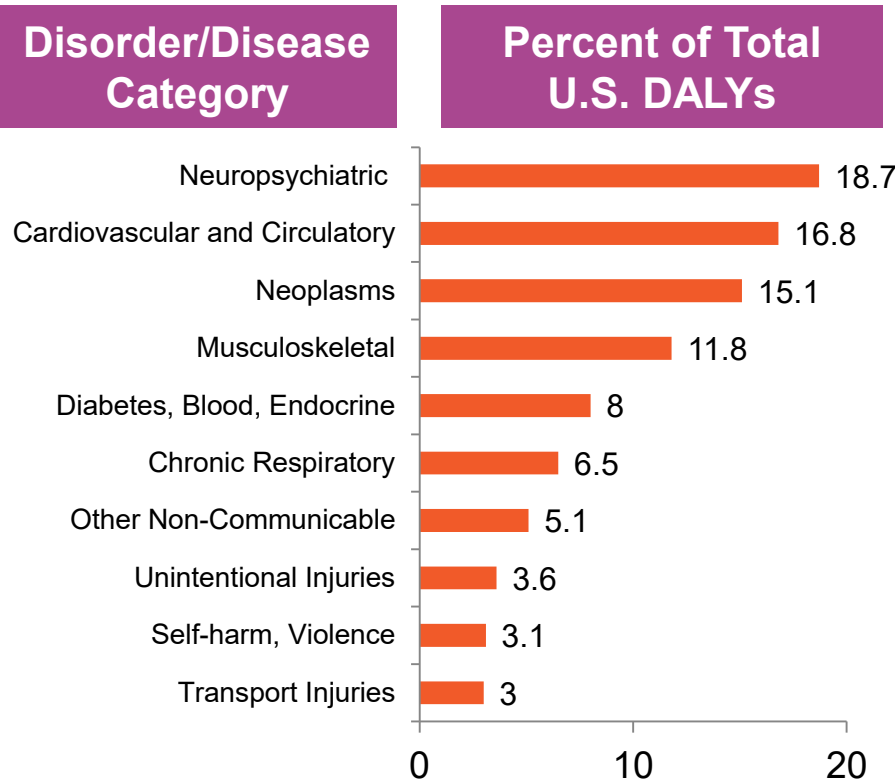
4. Biomarkers and Cell-Stimulation Assay in The Cunningham Panel

- Biological targets and associated symptoms
- Interpretation guidance



Neuropsychiatric Disorders Impact All Ages

NIH Top 10 Disease/Disorder Categories - U.S. Disability-Adjusted Life Years (DALYs)¹ = Total number of years lost to illness, disability, or premature death (Data 2010)



Children and Adults Suffer

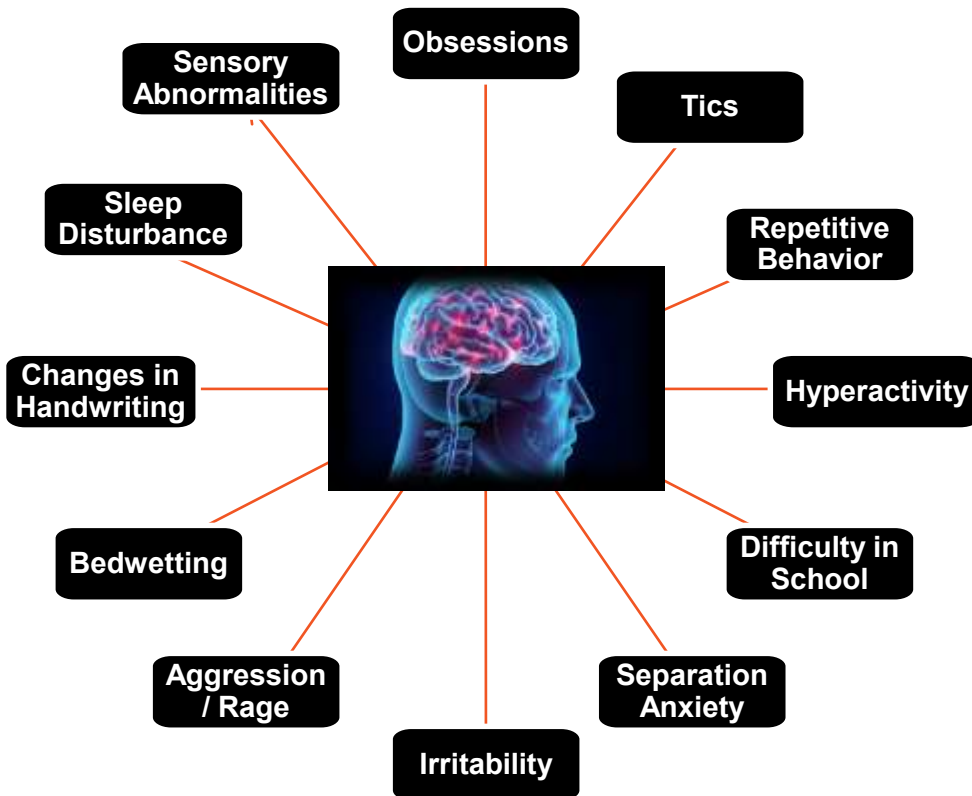


1. <http://www.nimh.nih.gov/health/statistics/disability/index.shtml> (DALYs) represent the total number of years lost to illness, disability, or premature death within a given population. Data from 2010.

Neuropsychiatric disorders outrank cardiac disease, diabetes, and cancer

Medical Challenge: Patients Assigned into Symptom-Based Categories – Considered “Incurable”

Common Symptoms



Diagnostic Categories

*Pediatric
Acute-Onset
Neuropsychiatric
Syndrome
(PANS)*

*Autism
Spectrum
Disorders*

*Asperger's
Syndrome*

*Tourette's
Syndrome*

*Pervasive
Developmental
Delay (PDD)*

*Chronic
Depression*

Schizophrenia

*Bipolar
Disorder*

*Developmental
Delay*

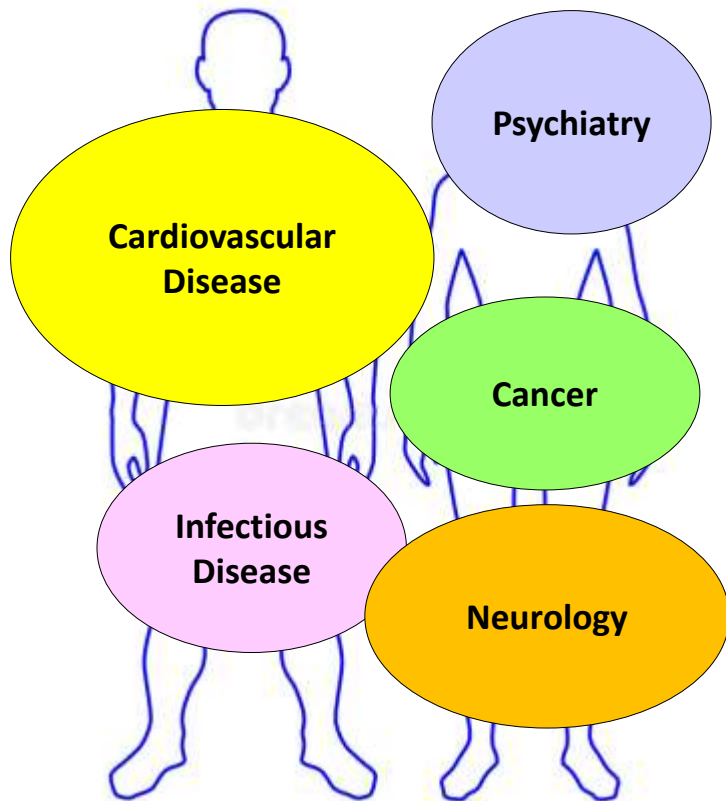
*Anxiety
Disorder*

*Seizure
Disorders*

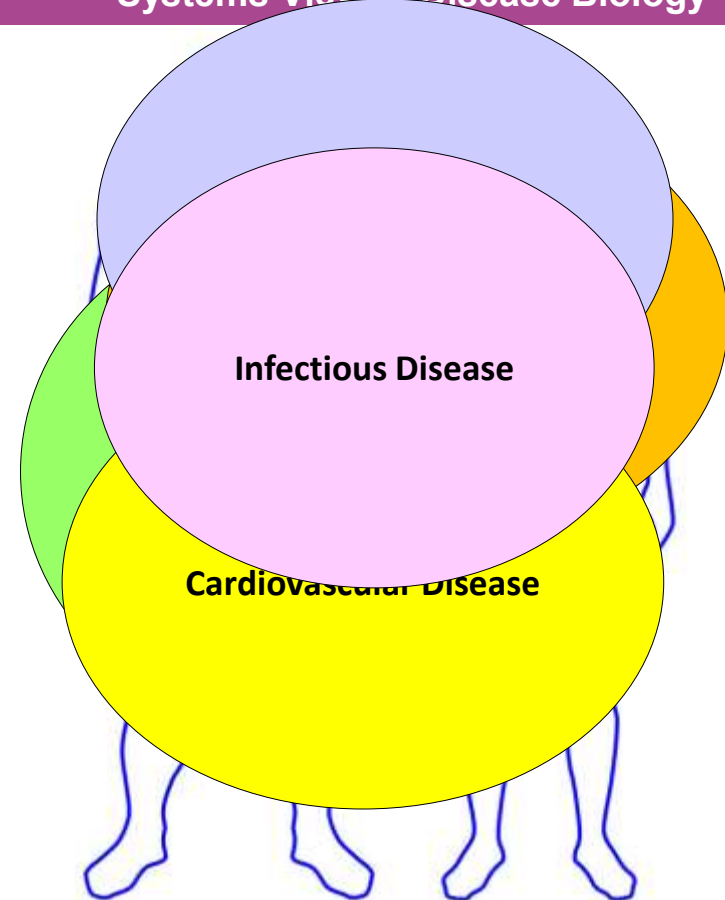
Epilepsy

Impact of Specialization in Medicine

Prevailing Understanding of Disease Biology

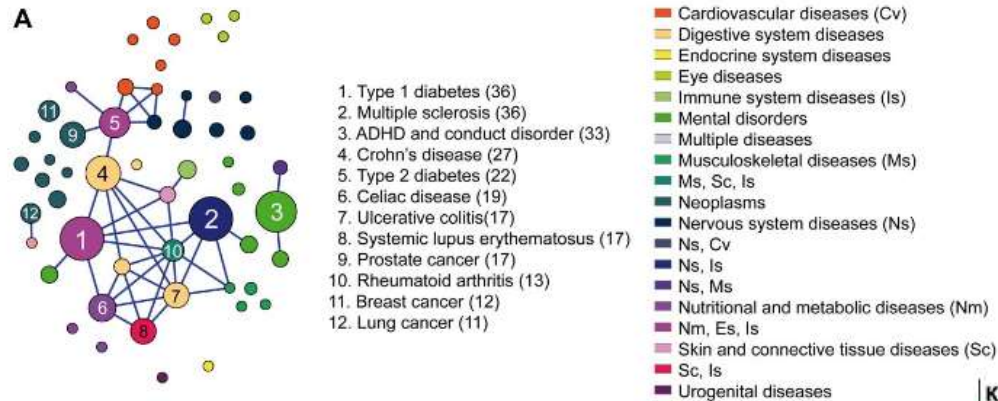


Systems View of Disease Biology

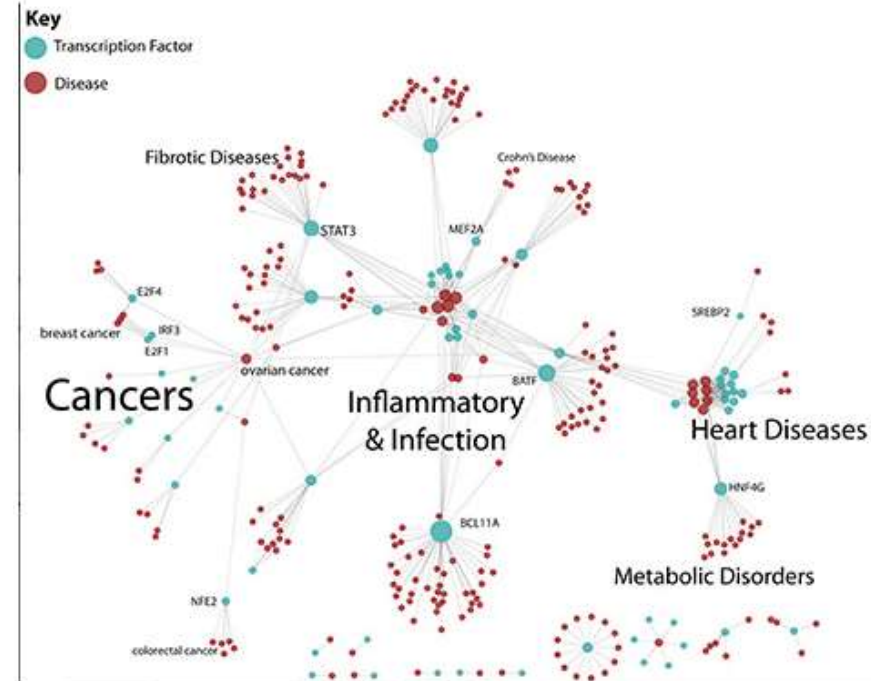
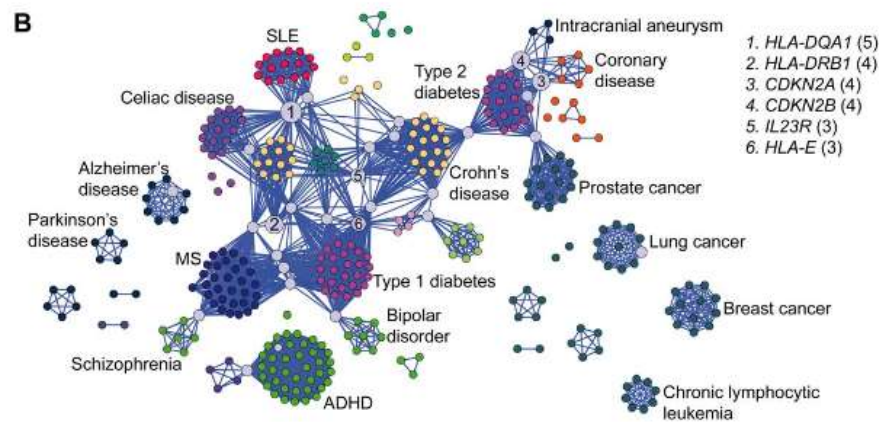


Identical symptoms/disorders can have different etiologies
but resolution is only possible with an understanding of the etiology

Complex Diseases are MultiFactorial and MultiSystem They are Complex...



Unlocking the Genetics of Complex Diseases:
GWAS and Beyond
Kristin Sainani
Biomedical Computation Review
Winter 2014/2015
Mobilize Center, an NIH Big Data Knowledge Center of
Excellence



OPEN ACCESS Freely available online

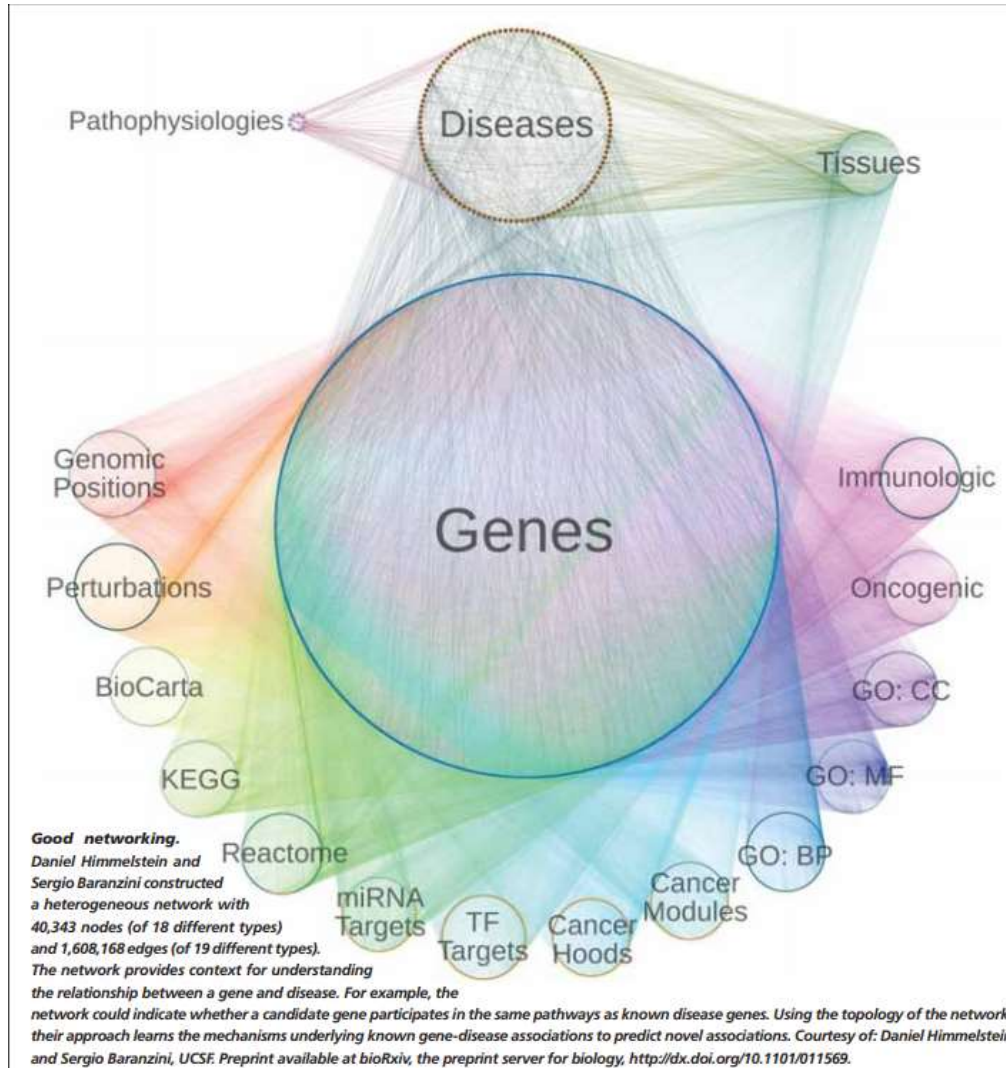
Network Properties of Complex Human Disease Genes Identified through Genome-Wide Association Studies

Fredrik Barrenas^{1,2,3}, Sreenivas Chavali^{1,3}, Petter Holme^{2,3}, Reza Mobini¹, Mikael Benson¹

¹The Unit for Clinical Systems Biology, University of Gothenburg, Gothenburg, Sweden, ²Department of Physics, Umeå University, Umeå, Sweden, ³Department of Energy Science, Sungkyunkwan University, Suwon, Korea

Complex Diseases are MultiFactorial and MultiSystem

They are Complex...



Unlocking the Genetics of Complex Diseases: GWAS
and Beyond

Kristin Sainani

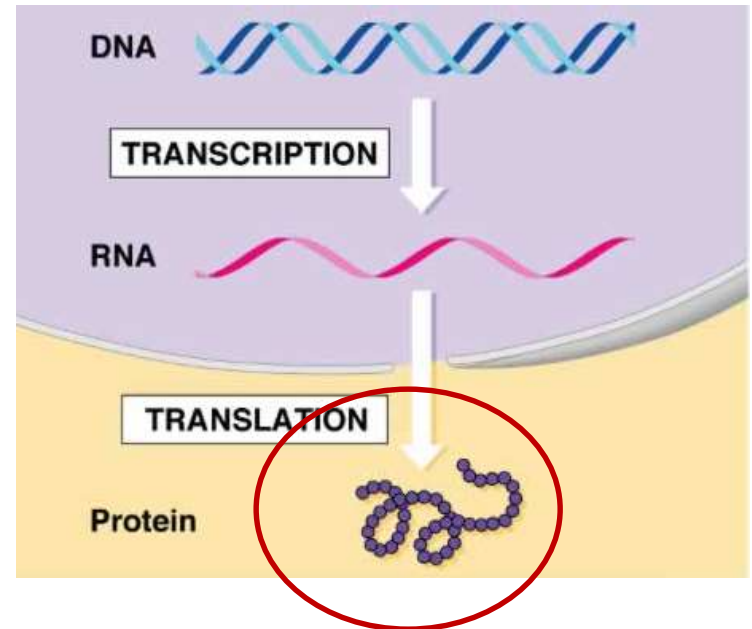
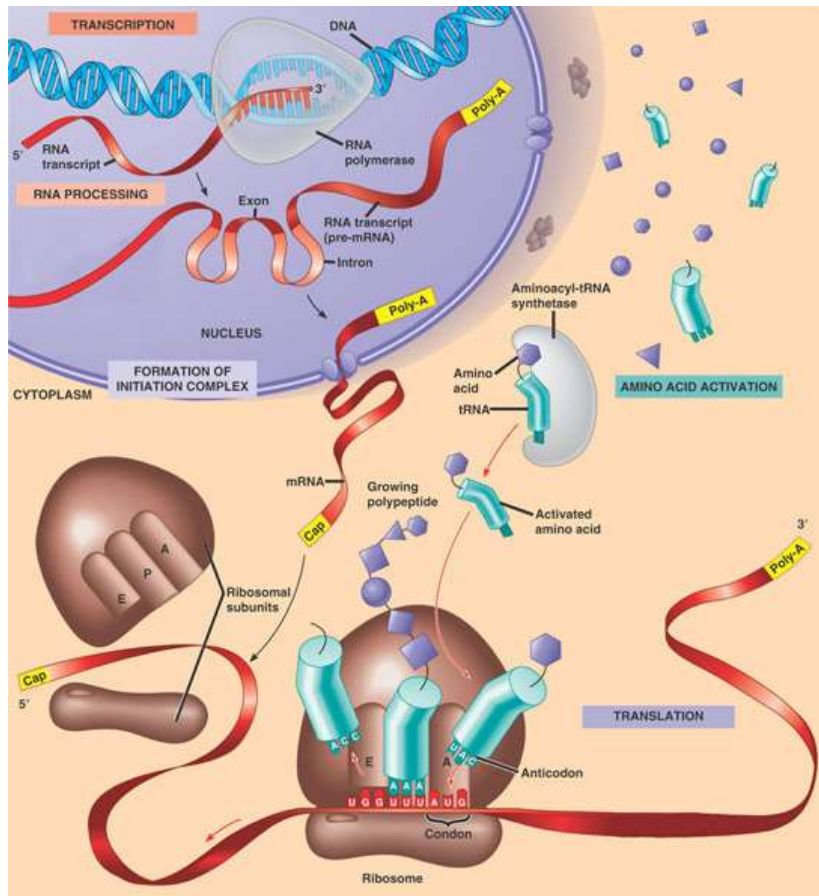
Biomedical Computation Review

Winter 2014/2015

Mobilize Center, an NIH Big Data Knowledge Center of Excellence

Genes Plays a Role

But Genes are not the Sole Determinant of Disease or Disorder



Example of Lung Cancer: Genetic Factor Impact

Lung Cancer >90% are smokers



Only ~15% of smokers succumb to Lung Cancer

Why do only “some” people get lung cancer?



Difference in Genes that Control

- Cell cycle
- DNA repair
- Carcinogen metabolism
- Other genetics

Topics We will Cover

1. Clinical Challenges with Neuropsychiatric and Behavioral Disorders

- Complexity of Complex Diseases
- Influences of genetics

2. Review of PANDAS/PANS

- Nomenclature and Acronyms
- Biological mechanism
- Medical model for other chronic neuropsychiatric and behavioral disorders

3. Common Infectious Triggers in Autoimmune Encephalopathies in Children and Adults

- Molecular Mimicry
- Multisystem Interaction and Genetic Predisposition

4. Biomarkers and Cell-Stimulation Assay in The Cunningham Panel

- Biological targets and associated symptoms
- Interpretation guidance

What is PANDAS?

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection



Pediatric Autoimmune Neuropsychiatric Disorders
Associated With Streptococcal Infections:
Clinical Description of the First 50 Cases

Susan E. Swedo, M.D., Henrietta L. Leonard, M.D., Marjorie Garvey, M.D.,
Barbara Mittleman, M.D., Albert J. Allen, M.D., Ph.D., Susan Perlmutter, M.D.,
Lorraine Lougee, L.C.S.W., Sara Dow, B.A., Jason Zamkoff, B.A., and Billinda K. Dubbert, M.S.N.

(1998) *Am J Psychiatry* **155**(2): 264-271.

THE AMERICAN JOURNAL OF
PSYCHIATRY

What's In a Name? Commonalities

PANDAS

Pediatric Autoimmune Neuropsychiatric
Disorder Associated with Streptococcal infection
(Dr. Susan Swedo)

ANDAL

Autoimmune Neuropsychiatric Disorder
Associated with Lyme
(Dr. Amiram Katz)

**Infectious Autoimmune
Encephalopathy or Encephalitis**

**Infectious Autoimmune Disorder
of the Brain (Basal Ganglia)**

1. Infection-Triggered

- Bacterial, Viral, Parasitic, Fungal or possibly environmental?

2. Autoimmune

- Immune-mediated through the adaptive Immune system

3. Neuropsychiatric Symptoms

- OCD, tics, urinary, emotional lability, sleep disorders, anxiety, depression etc.

4. Directed against portions of the brain

- Basal ganglia

5. Acute-Onset

- PANDAS/PANS but not observed in all conditions

6. Age-limitation

- Pediatric in PANDAS/PANS, but also observed in adults

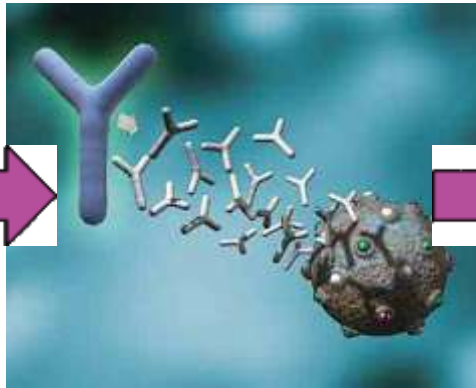
Autoimmune Mechanism for Multiple Neuropsychiatric Behavioral Disorders



Microbial, Viral, Fungal Infection Occurs



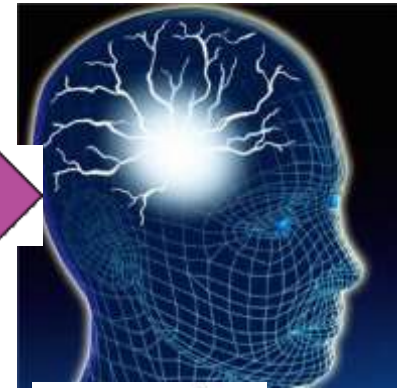
Body Produces Antibodies That Recognize Infectious Agent



Antibodies Cross-React With Neurologic Receptors (molecular mimicry)



Reaction Disrupts Brain Function (friendly fire)

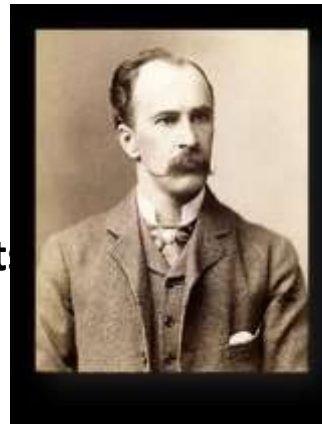


Neuropsychiatric Symptoms Including Anxiety, Aggression, Rage, OCD, Tics, Depression, Hyperactivity, Insomnia, Phobias

Sydenham Chorea is the Medical Model for PANDAS/PANS and Other Autoimmune Encephalopathies

Chorea: “Dance-like,” otherwise known as St. Vitus' dance”

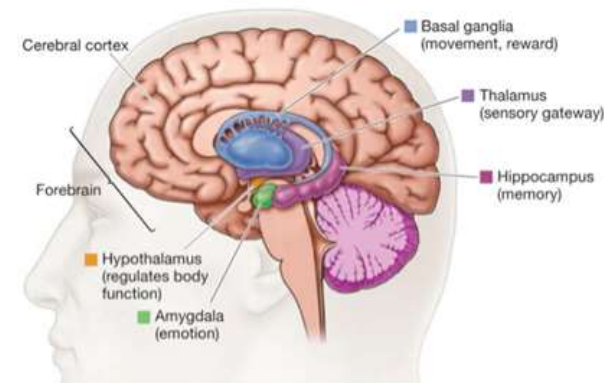
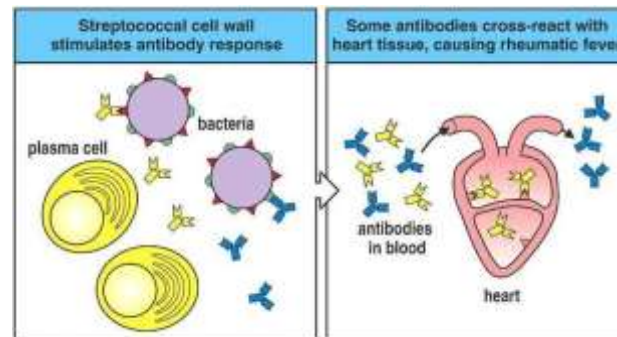
- abnormal movement
- Loss of fine-motor control
- Loss of emotional control



1894, Sir William Osler described “**bizarre**” and “**perseverative behaviors**” of children with “**chorea minor**,” and first made the relationship between obsessive-compulsive OCD symptoms and Sydenham’s chorea (SC)

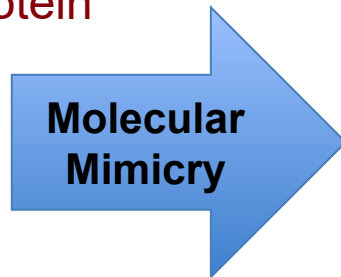
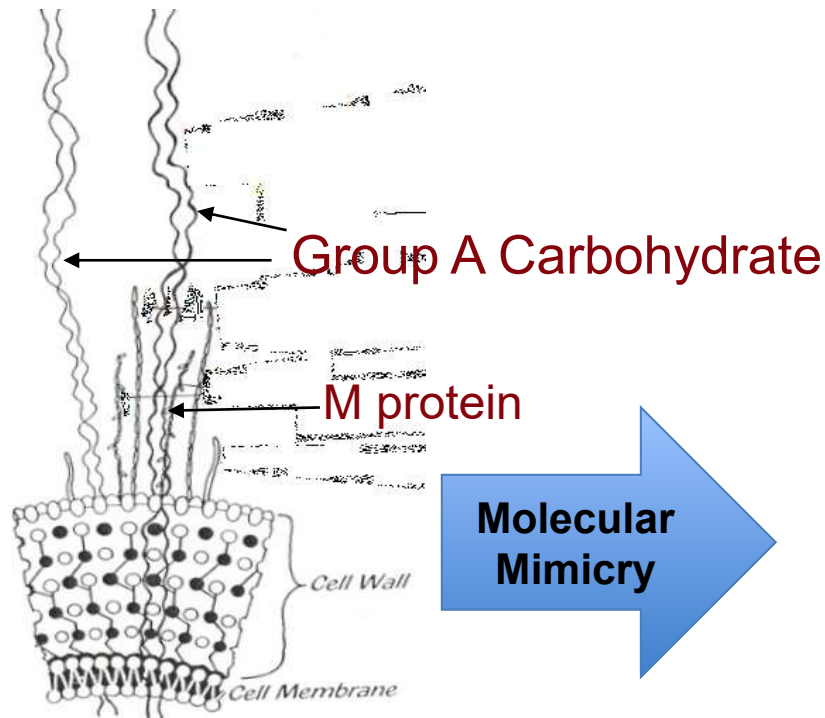
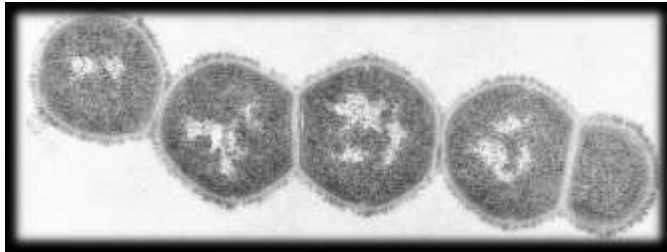
Triggered by Group A Streptococcus (GAS) autoimmune reaction involving the brain

Sydenham Chorea is the neurological manifestation of Acute Rheumatic Fever

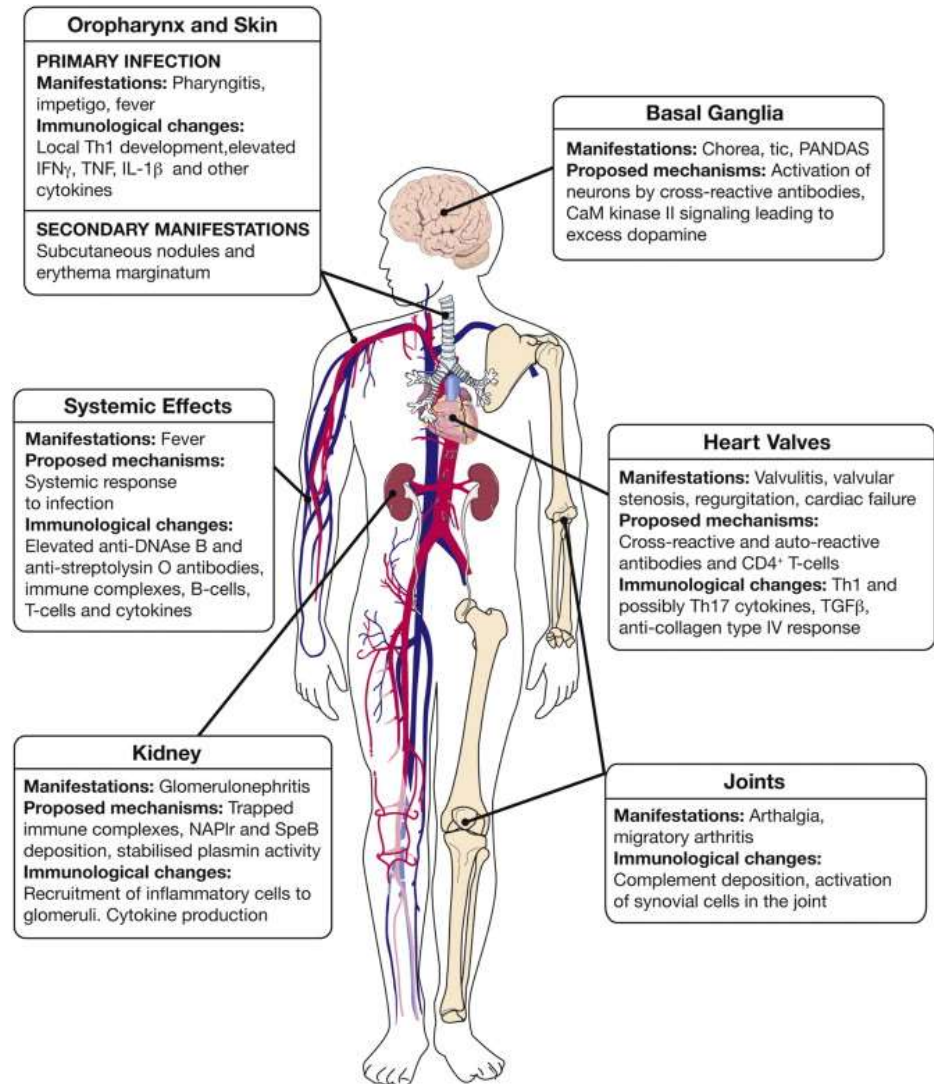


Molecular Mimicry Between Strep and Self-Antigens

Similar antigenic determinants between host and infecting microorganisms




Streptococcal Cell Wall



PANDAS/PANS results from an Infection-Triggered Autoimmune Response - Molecular Mimicry

Molecular Mimicry = “Friendly Fire”

A photograph showing soldiers in a desert environment. In the foreground, a soldier is seen from behind, wearing a helmet and carrying a large backpack. Other soldiers are visible in the mid-ground, some crouching and others standing. In the background, a military helicopter is flying in the sky. The terrain is rocky and arid, with mountains visible in the distance.

The most relevant genetic factors for Autoimmune Diseases are genes located in the **Major Histocompatibility Complex (MHC)** and, in particular, loci from **Human Leukocyte Antigen (HLA) class I and class II**

Topics We will Cover

1. Clinical Challenges with Neuropsychiatric and Behavioral Disorders

- Complexity of Complex Diseases
- Influences of genetics

2. Review of PANDAS/PANS

- Nomenclature and Acronyms
- Biological mechanism
- Medical model for other chronic neuropsychiatric and behavioral disorders

3. Common Infectious Triggers in Autoimmune Encephalopathies in Children and Adults

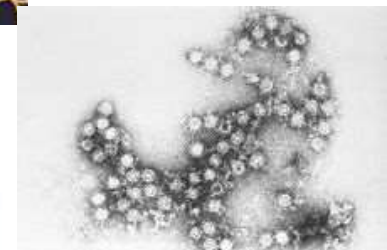
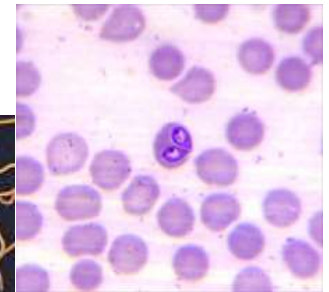
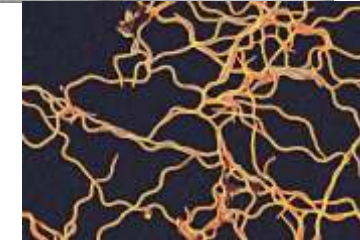
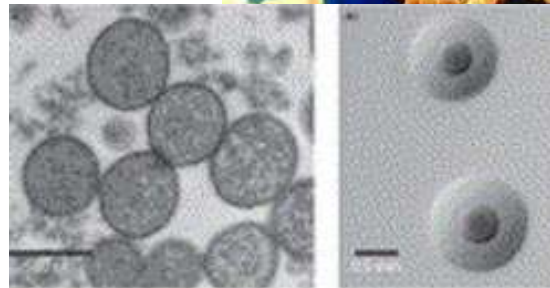
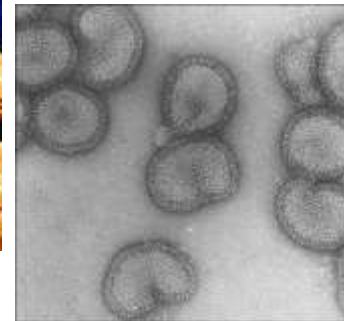
- Molecular Mimicry
- Multisystem Interaction and Genetic Predisposition

4. Biomarkers and Cell-Stimulation Assay in The Cunningham Panel

- Biological targets and associated symptoms
- Interpretation guidance

Multiple Infectious Triggers Associated with Autoimmune Encephalopathies

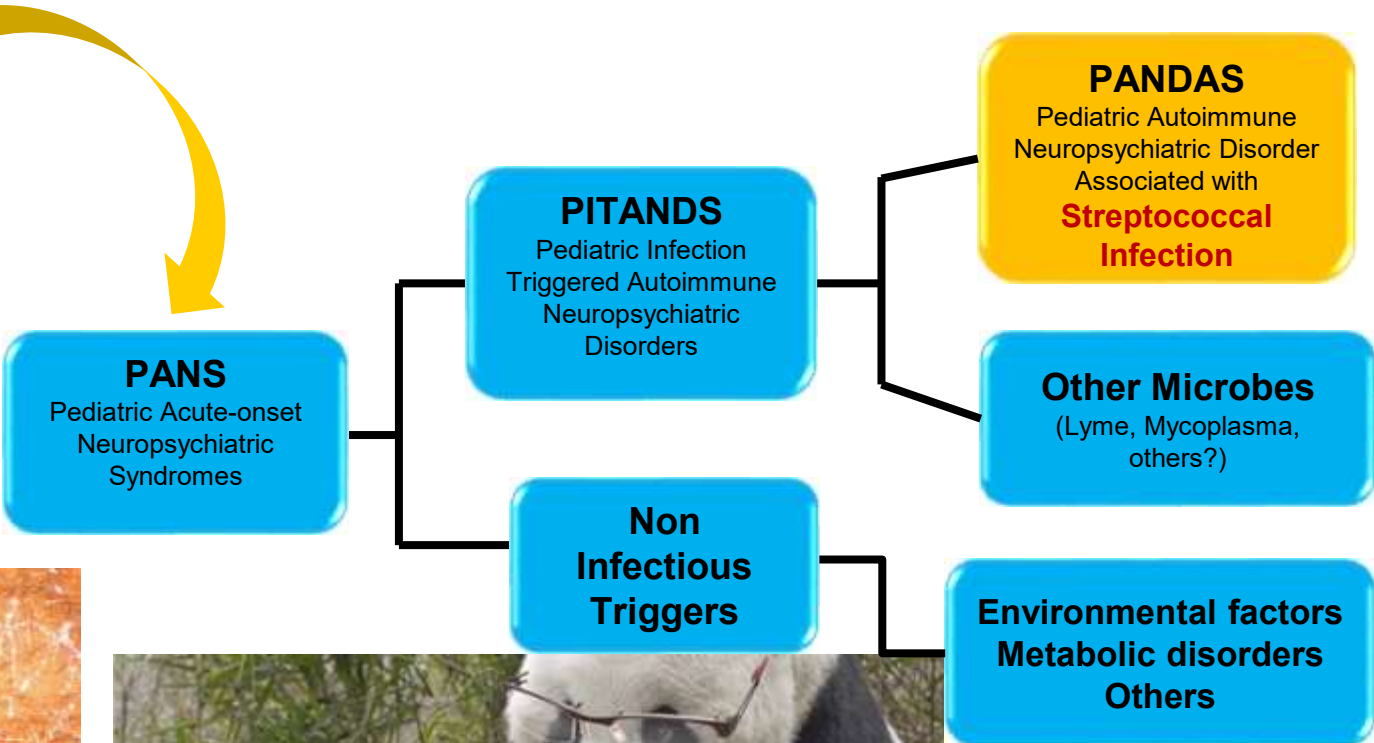
- **Group A streptococci**
- **Influenza A**
- **Varicella (chickenpox)**
- **Mycoplasma**
- **Lyme disease**
- **Babesia**
- **Bartonella**
- **Coxsackie virus**



Patients often have more than one infection, and can be subclinical

Lyme Disease is a Commonly Identified Infection-Triggered Autoimmune Neuropsychiatric Disorder Similar to PANDAS

**Babesia,
Bartonella,
Borrelia,
Ehrlichia,
Mycoplasma
are Included**



Infection-Triggers that affect the CNS and other Systems

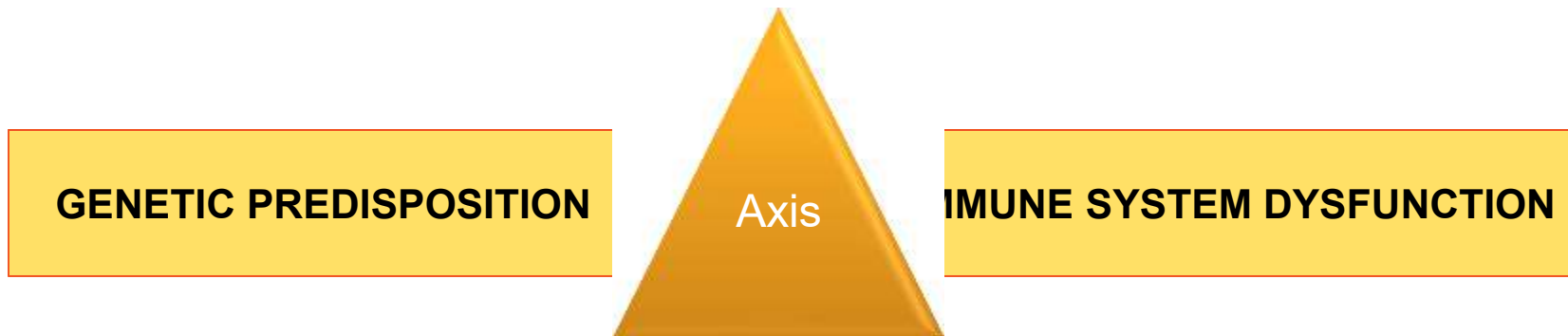
- **Guillain-Barré Syndrome**
 - Campylobacter jejuni
- **Sydenham Chorea**
 - Group A Streptococcus
- **Systemic Lupus Erythematosus (Lupus)**
 - Epstein-Barr virus (EBV nuclear antigen -1)
- **Multiple Sclerosis**
 - EBV, measles and HHV-6
- **Myasthenia Gravis**
 - Herpes Simplex Virus Type 1 (gpD)
- **Cardiomyopathy (myocarditis)**
 - Coxsackie virus, Group A Streptococcus
- **Crohn's Disease**
 - Gram-positive bacterial peptidoglycans
- **Diabetes Type 1**
 - Coxsackie B virus, rubella, herpesvirus, rotavirus
- **Psoriasis**
 - Streptococcus pyogenes (Streptococcal M Protein)

*M.F. Cusick, et. al., Clin Rev Allergy Immunol. 2012 February, 42(1): 102-111

Complex Interconnection Between Infection, the Immune System and the Brain

Brain Function

(Neurological and Neuropsychiatric symptoms)



GENETIC PREDISPOSITION

Axis

IMMUNE SYSTEM DYSFUNCTION

Infectious/Non-Infectious Triggers

(Environmental, bacteria, microbiome, viruses, parasites)

Immune System

(inflammation, microglia activation, cytokines, mast cell activation, autoimmune antibodies)

Topics We will Cover

1. Clinical Challenges with Neuropsychiatric and Behavioral Disorders

- Complexity of Complex Diseases
- Influences of genetics

2. Review of PANDAS/PANS

- Nomenclature and Acronyms
- Biological mechanism
- Medical model for other chronic neuropsychiatric and behavioral disorders

3. Common Infectious Triggers in Autoimmune Encephalopathies in Children and Adults

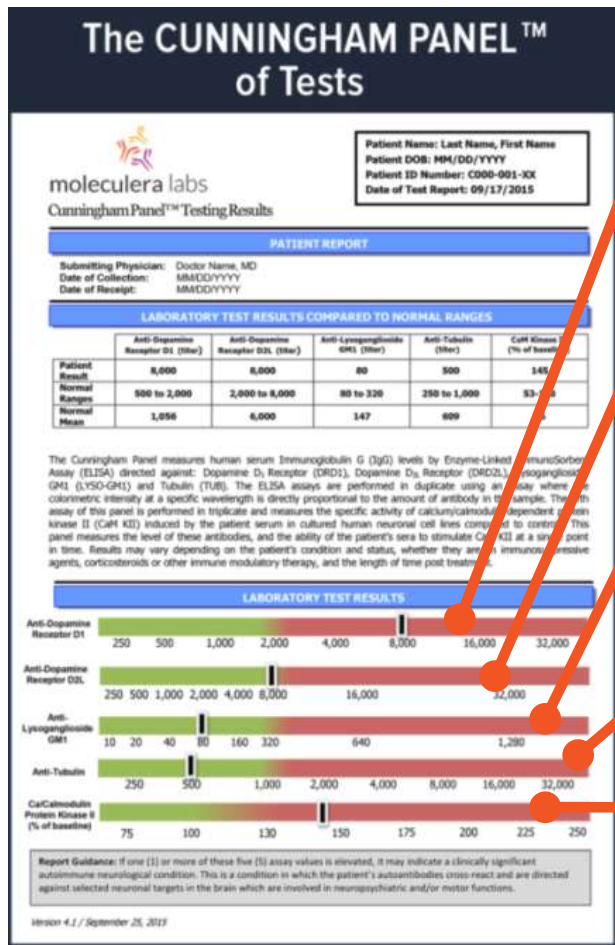
- Molecular Mimicry
- Multisystem Interaction and Genetic Predisposition

4. Biomarkers and Cell-Stimulation Assay in The Cunningham Panel

- Biological targets and associated symptoms
- Interpretation guidance

The Cunningham Panel™ Biomarker Components

The Cunningham Panel is an aid in a physician's diagnosis of Autoimmune Encephalopathies such as PANDAS/PANS and others



1) Anti-Dopamine D1

Often positive with psychiatric symptoms including psychosis⁽¹⁾

2) Anti-Dopamine D2L

Often positive with movement disorders and impulsivity⁽¹⁾

3) Anti-Lysoganglioside GM1

Often positive with neuropathic symptoms including tics⁽¹⁾

4) Anti-Tubulin

Often positive with cognitive complaints, OCD and brain fog⁽¹⁾

5) CaM KII Activity

Often positive with involuntary movements and any symptom of adrenergic activation⁽¹⁾

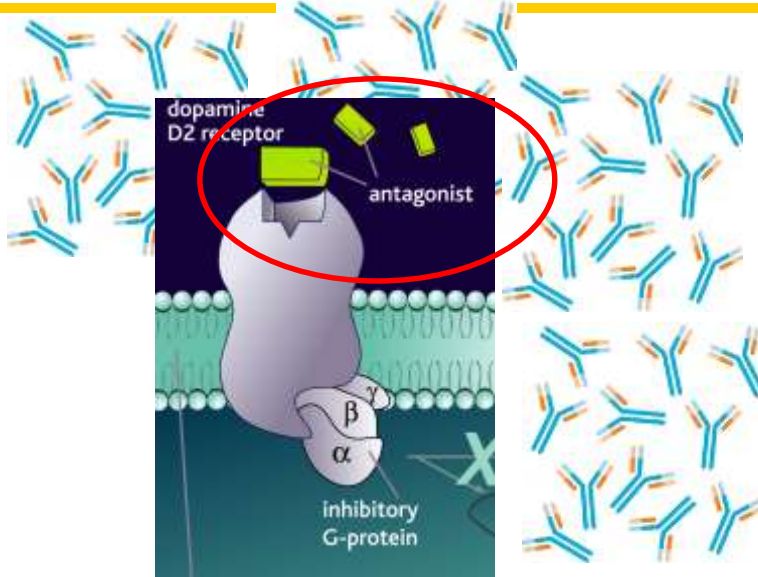
ELISAs

Enzyme-Linked Immunosorbent Assay (Testing Format)

Cell Stimulation Assay

Ref: (1) Reported by Dr. Amirm Katz base upon his 112 patients studied and our patient responses

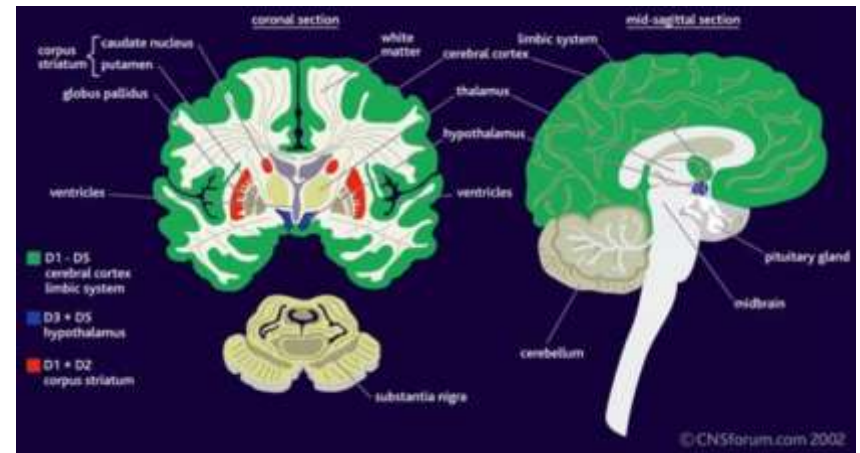
Anti-Human Dopamine D1 and D2L Receptors



Dopamine D1: informally referred to as the “psychiatric” band, tends to correlate with mood instability, anxiety, irritability, aggression and, in some cases, psychosis.

Other Anti-Dopamine D1 Receptor Symptom Association:

- Mood dysregulation/lability, depression, anxiety, poor concentration and occasionally, delusions and psychosis
- 54% of these patients experience symptoms of OCD
- 50% experience sensory or motor abnormalities and/or sleep disturbance.
- (Total N=131)



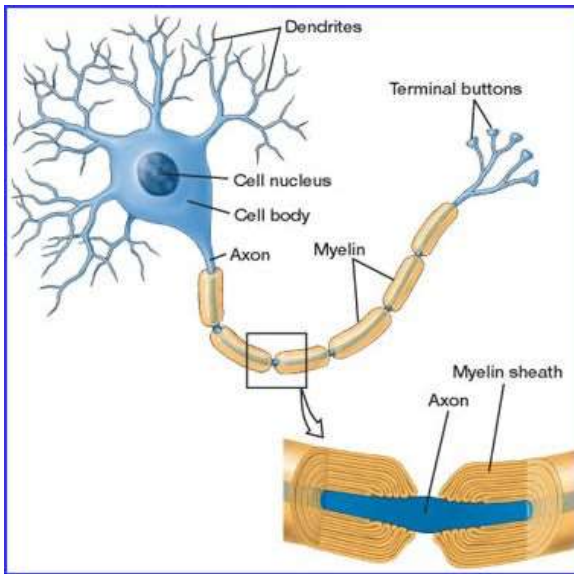
Dopamine D2L: informally referred to as the “movement” band, tends to correlate with choreiform movements, myoclonus, and exacerbations of hyperactivity

Other Anti-Dopamine D2 Receptor Symptom Association:

- Motor or movement disorders (including choreiform movements), hyperactivity, and impulsive behaviors including self-injurious behaviors
- Over 60% experience sleep disturbance, behavioral regression and OCD
- Over 50% of patients experience sensory or motor abnormalities
- (Total N=48)

Anti-Lysoganglioside GM1

Gangliosides are lipid components of neuronal cell membranes and found in Myelin Sheath

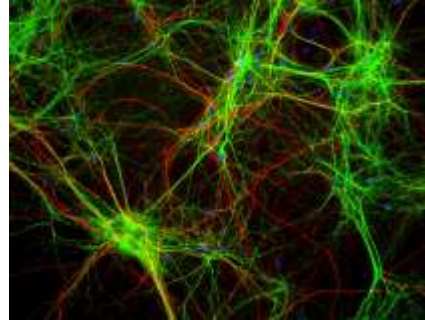
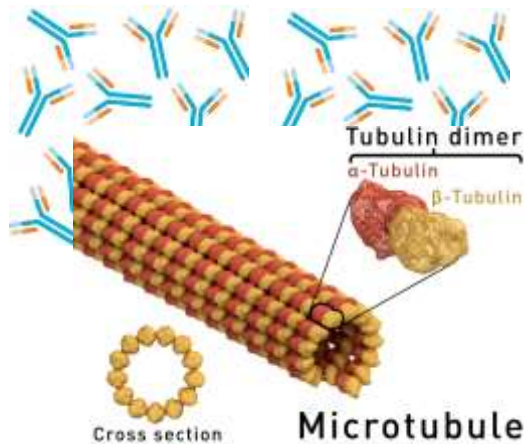


Anti-Lysoganglioside GM1: informally referred to as the “tic” band, tends to correlate with tics and complaints of joint or connective tissue pain

Other Anti-Lysoganglioside GM1 Symptom Association:

- Tics (72%) and joint or connective tissue pain
- Sleep disturbance (67%)
- OCD (67%)
- Sensory or motor abnormalities (67%)
- Behavioral regression (62%)
- (Total N=40)

Anti-Tubulin



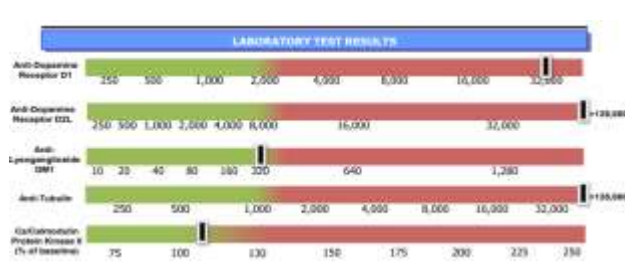
Anti-Tubulin: informally referred to as the “OCD” band, tends to correlate with cognitive interference, “brain fog”, difficulty with focus and concentration and symptoms of obsessions and compulsions

Other Anti-Tubulin Symptom Association:

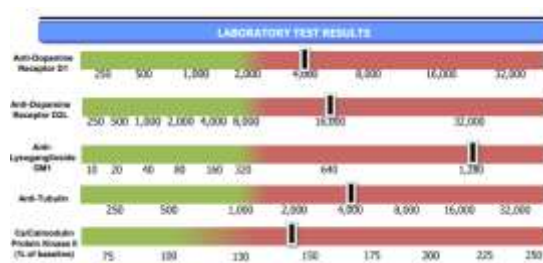
- OCD and “brain fog” or inattentive, disengaged, “tuned out”, struggle with concentration, memory and comprehension (82%)
- Aggressive and/or rage behaviors (50%)
- Sensory or motor abnormalities (74%)
- Emotional lability (73%)
- OCD (69%)
- Behavioral regression (69%)
- Sleep disturbances (69%)
- Tics (53%)
- (Total N= 552).

Other Interpretation Considerations

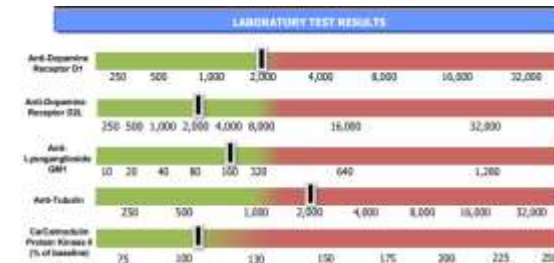
- Only 1 elevation required for positive interpretation
- Correlation with symptoms is strong
- Generally, correlation with severity is less strong
 - Low elevations can be seen with severe symptoms
 - Moderate elevations are seen with mild symptoms
 - Extremely high elevations have a stronger correlation with degree of symptom severity



Bed bound patient



Ambulatory, unable to work

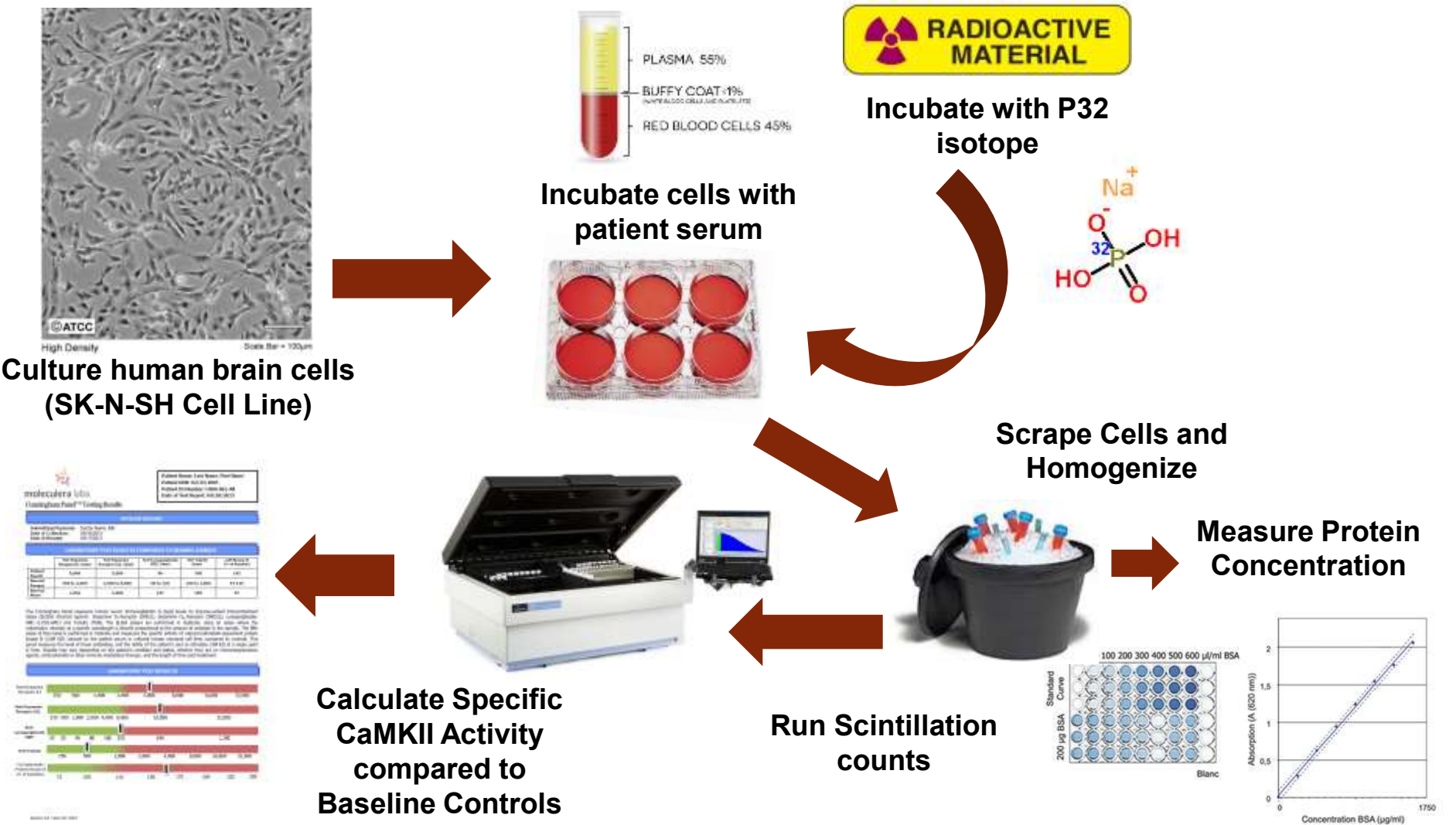


Institutionalized in state psychiatric hospital





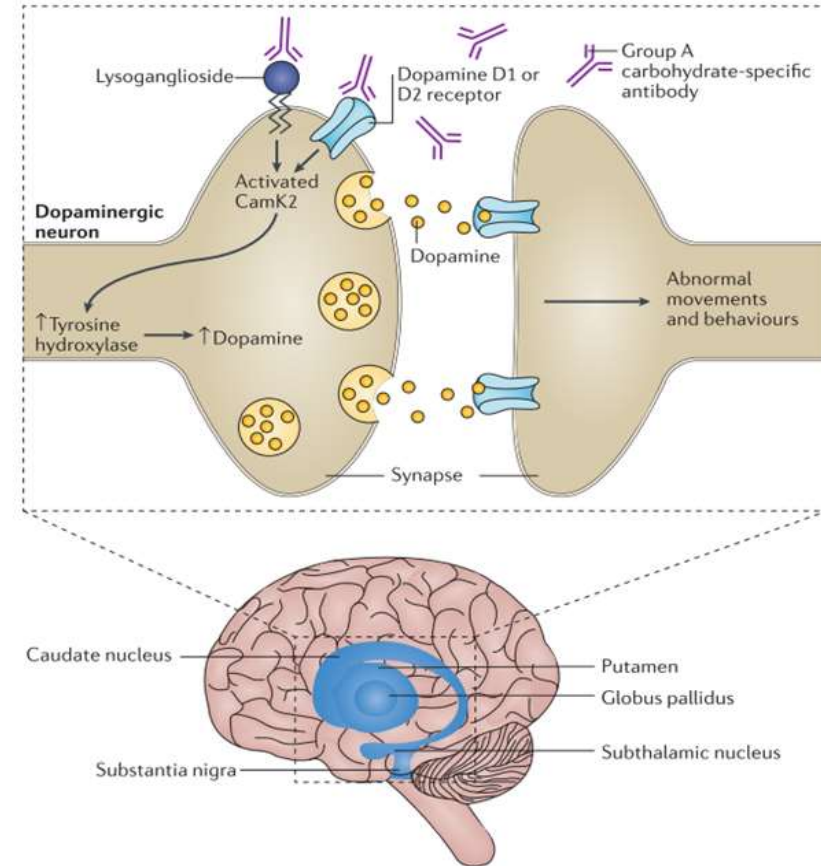
CaMKII – Cell Stimulation Assay Test



Autoantibodies that Stimulate CaMKII Increase Dopamine Production in the Brain

Elevation in the level of CaMKII tends to correlate with

- sympathetic nervous system activation symptoms
- fight or flight behavior
- separation anxiety
- urinary problems, bedwetting
- sensory sensitivities
- Elevated CaMKII suggests that there is still active infection(s) of some kind



Other CaMKII Symptom Association:

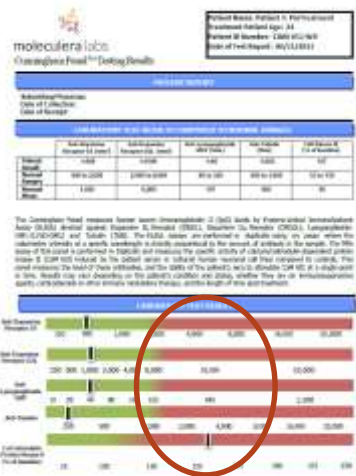
- Involuntary movements which can be brief and of low amplitude
- Early stage illness (estimated to be <18 months)
- Apparent re-activation of a previous infection or the onset of a new infection
- Mydriasis, fight or flight behavior, increased pulse rate, anxiety, and insomnia
- (Total N=200)



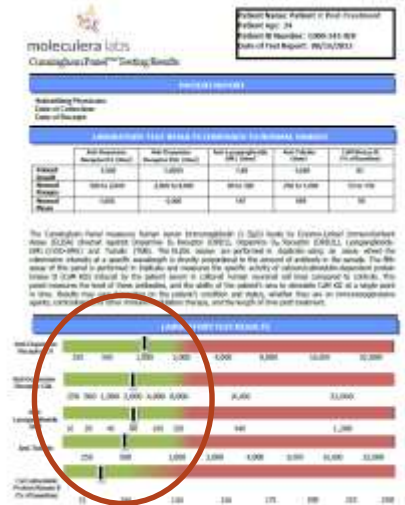
Case Studies (>200 Similar Case Studies)

Case Study #1

24 y/o Male: Presenting symptoms: OCD, tics, decreased appetite with 30 pound weight loss, inability to concentrate, sensory abnormalities, emotional lability, behavioral regression, separation anxiety, et al.



Treatment: Patient treated with IVIG and plasmapheresis resulted in symptom reduction

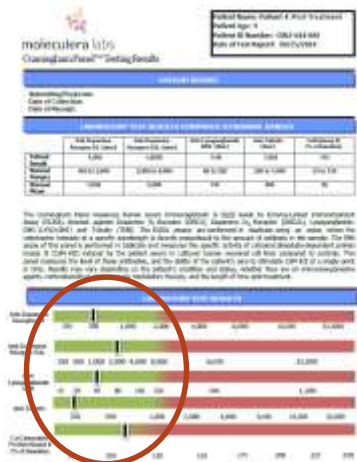


Case Study #2

9 y/o Female: obsessive-compulsive behaviors, verbal tics and “stimming”, inability to concentrate, sensory and motor abnormalities, emotional lability, behavioral regression, urinary and sleep problems, dysgraphia, and aggressiveness, Relapsing and remitting in nature



Treatment: Patient was treated with azithromycin with rapid improvement in symptoms

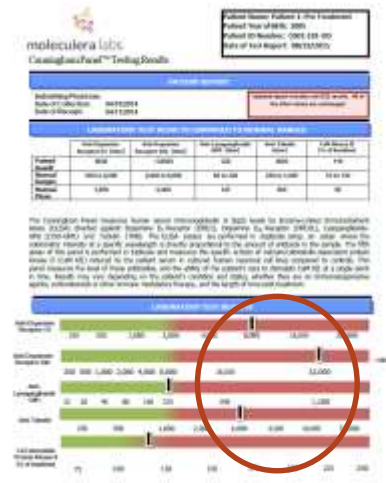
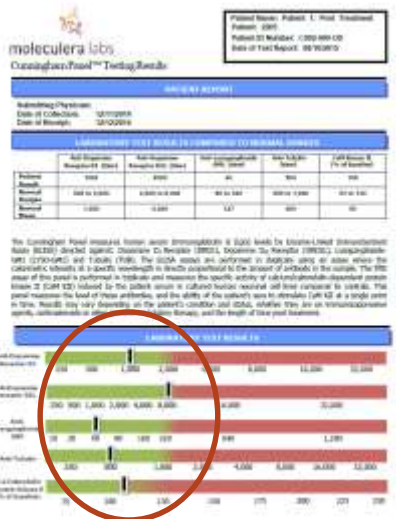




Case Studies (>200 Similar Case Studies)

Case Study #3

9 y/o Female: Presenting with unknown origin of neuropsychiatric symptoms. Lyme disease positive by Western Blot, Child said during a bout of strep, ***"Mom, something happened to my brain"***



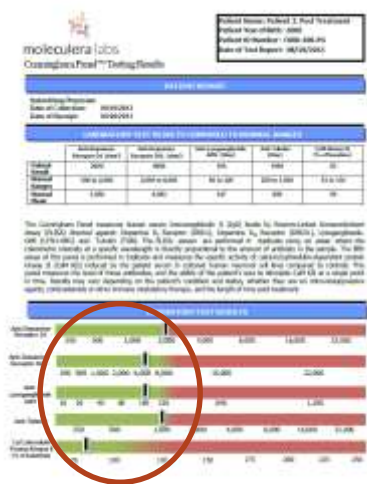
Treatment: azithromax, naproxen, omnicef, and Bactrim, Tindamax (anti parasitic) 3 IVIG treatments; complete symptom regression

Case Study #4

9 y/o Male: Presenting 30 days post confirmed strep infection with OCD, Tics, inability to concentrate, sensory abnormalities, emotional lability, separation anxiety, developmental regression, urinary frequency and urgency, sleep disturbance, dysgraphia, aggressiveness, choreiform movements, relapsing and remitting symptoms.



Treatment: Patient had IVIG within one month of diagnosis with complete symptom elimination.



Autism Spectrum Disorder

Cunningham Panel Predicted IVIG Treatment Responders

Connery et al. Translational Psychiatry (2018) 8:148
DOI: 10.1038/s41398-018-0214-7

Translational Psychiatry

ARTICLE

Open Access

Intravenous immunoglobulin for the treatment of autoimmune encephalopathy in children with autism

Kathleen Connery¹, Marie Tippet¹, Leanna M. Delhey¹, Shannon Rose¹, John C. Slattery², Stephen G. Kahler¹, Juergen Hahn^{1,4}, Uwe Kruger³, Madeleine W. Cunningham², Craig Shimasaki⁶ and Richard E. Frye^{1,2,6}

Abstract

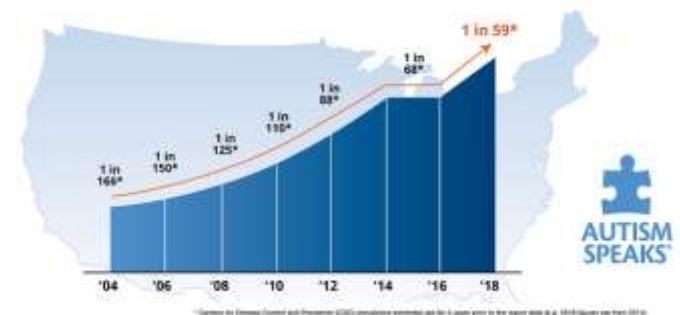
The identification of brain-targeted autoantibodies in children with autism spectrum disorder (ASD) raises the possibility of autoimmune encephalopathy (AIE). Intravenous immunoglobulin (IVIg) is effective for AIE and for some children with ASD. Here, we present the largest case series of children with ASD treated with IVIG. Through an ASD clinic, we screened 82 children for AIE, 80 of them with ASD. IVIG was recommended for 49 (60%) with 31 (38%) receiving the treatment under our care team. The majority of parents (90%) reported some improvement with 71% reporting improvements in two or more symptoms. In a subset of patients, Aberrant Behavior Checklist (ABC) and/or Social Responsiveness Scale (SRS) were completed before and after IVIG treatment. Patients with a 10% or greater improvement in SRS scores were included in the analysis. The majority of patients (90%) reported some improvement with 71% reporting improvements in two or more symptoms. In a subset of patients, Aberrant Behavior Checklist (ABC) and/or Social Responsiveness Scale (SRS) were completed before and after IVIG treatment. Patients with a 10% or greater improvement in SRS scores were included in the analysis.

“The majority of the ASD patients who had autoantibodies demonstrated elevations in autoantibodies measured by the Cunningham panel along with an elevation in the activation of CaMKII.”

“The Cunningham panel predicted response to IVIG treatment with an accuracy of 81% with a sensitivity of 90% and a specificity of 67% based on the ABC scores; with an accuracy of 88% with a sensitivity of 100% and a specificity of 75% based on the SRS scores; and with an accuracy of 88% with a sensitivity of 100% and a specificity of 67% based on parental scores.”

- In 82 patients with Autism Spectrum Disorder (ASD), 49 patients had autoantibodies (60%)
- IVIG was completed for 36 of these patients (73%)
- Cunningham Panel predicted with accuracy (81% to 88%) those patients who improved and responded to IVIG therapy

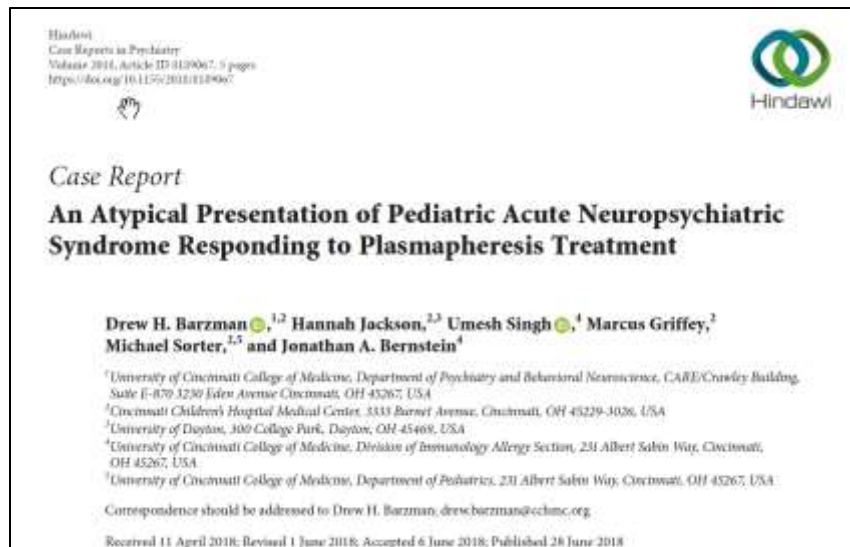
Estimated Autism Prevalence 2018



The cost of caring for Americans with autism reached \$268 billion in 2015 and would rise to \$461 billion by 2025 in the absence of more-effective interventions and support across the life span.

Schizophrenia

Cunningham Panel Changed Treatment and Recovery

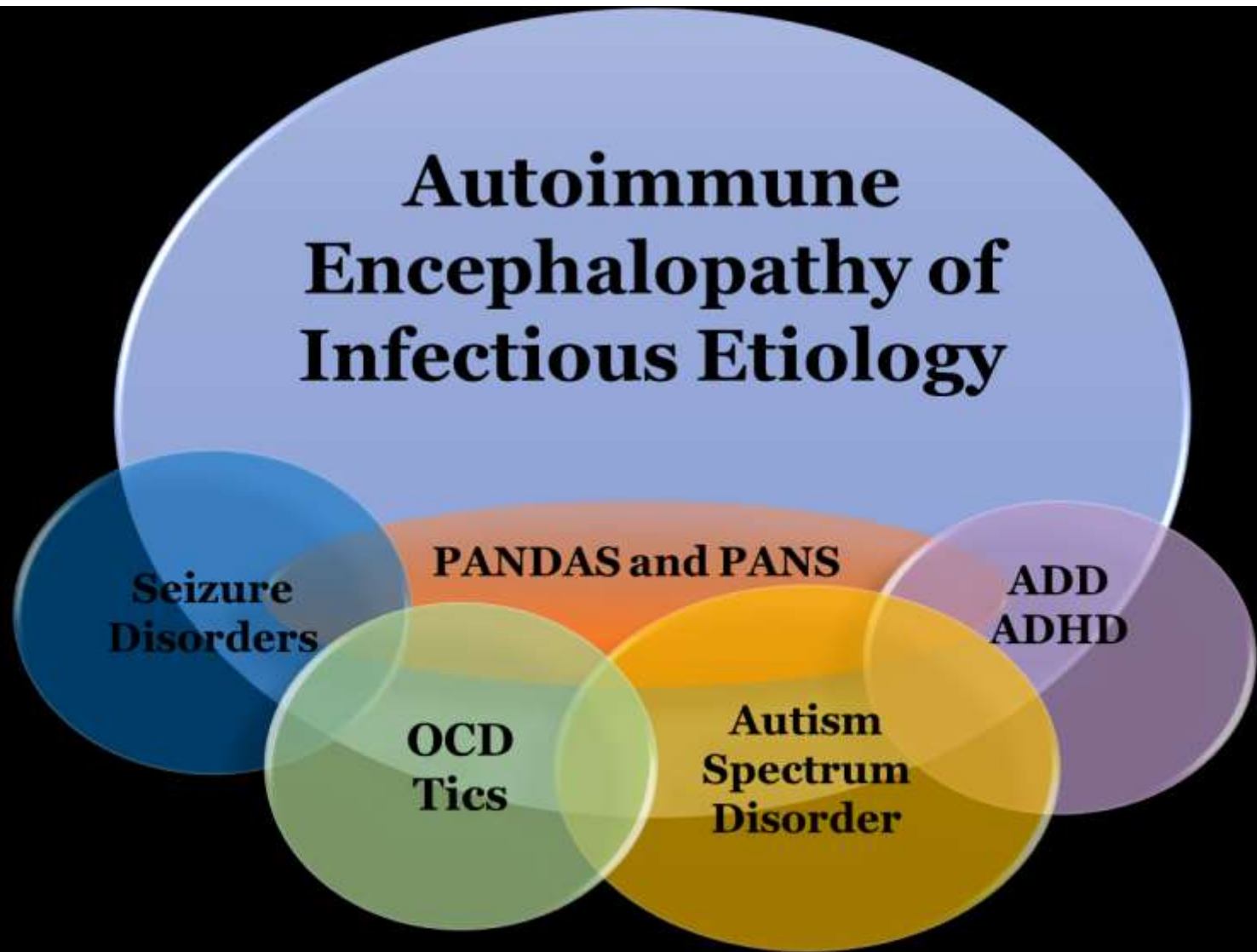


- Cincinnati Children's Hospital
- 15-year-old female who had been diagnosed and treated unsuccessfully for schizophrenia with psychosis, severe anxiety, and depression
- In and out of treatment facilities

A Cunningham panel was ordered, which measures anti-neuronal IgG antibodies (Cunningham panel) directed against dopamine 1 and 2 receptors, lysoganglioside-GM1, tubulin, and calcium/calmodulin-dependent protein kinase II (CaMKII). The results of this test revealed significant elevation of the first four antibodies and a borderline increase for CaMKII."

"After one course of plasmapheresis was administered..., the patient had complete resolution of her psychotic, OCD, and anxiety symptoms. She was able to be weaned off olanzapine and resume many of her normal activities including tennis, within 2 weeks after plasmapheresis. This response has now been sustained for over six months consistent with previous studies"

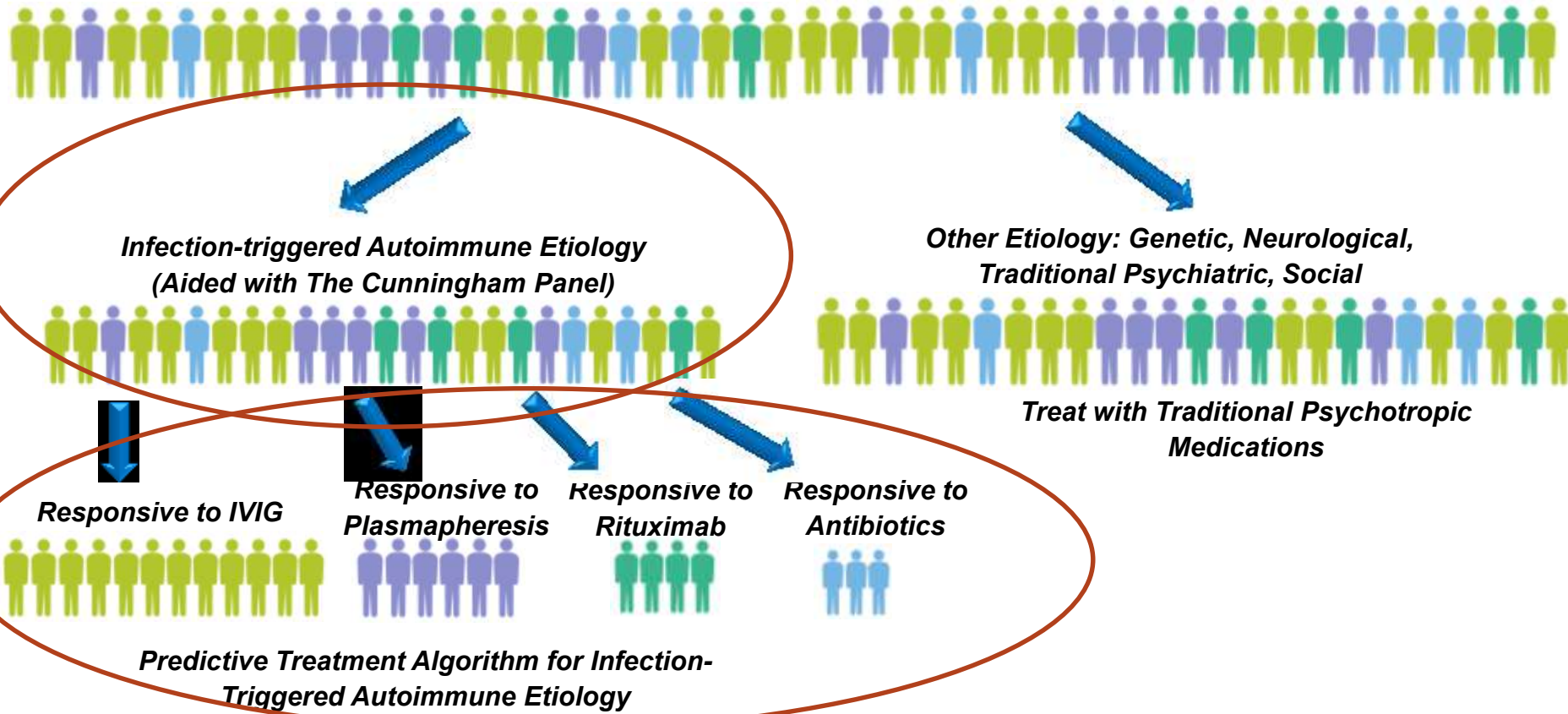
PANDAS and PANS may be a Medical Model for *Portions* of Many other Neuropsychiatric Disorders





Goal of Personalized and Precision Medicine

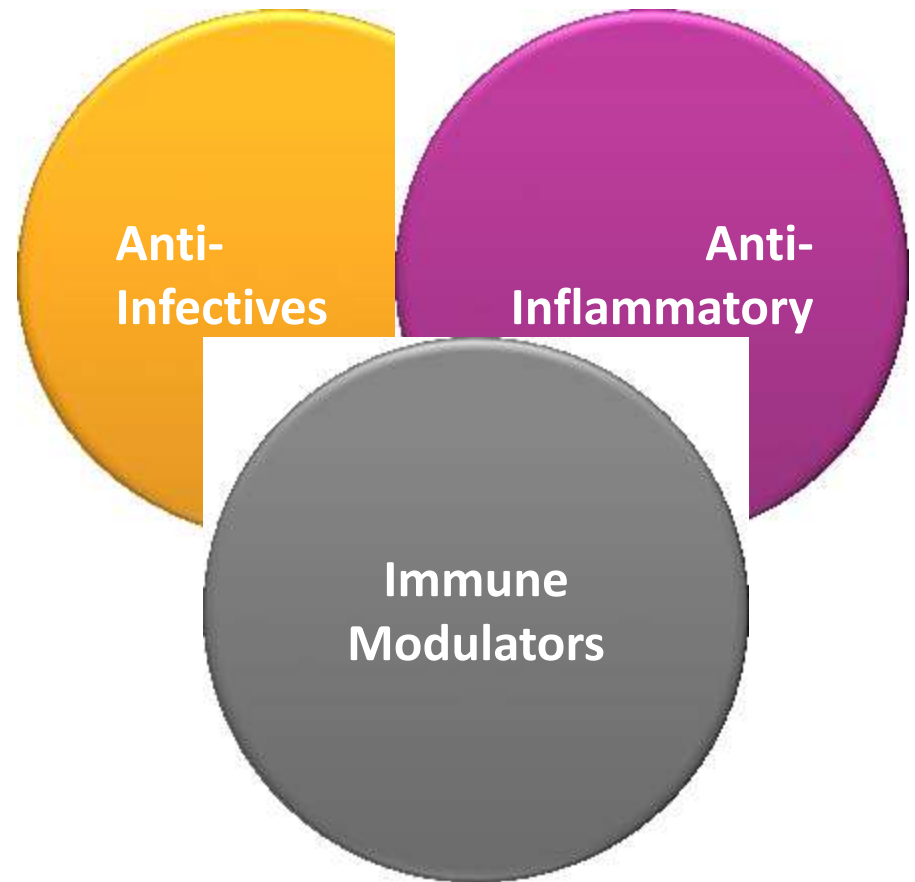
Patients with Neuropsychiatric and Behavioral Disorders





Existing Treatments have Remarkable Responses

- **Anti-microbials**
- **Steroids and NSAIDs**
- **Plasmapheresis (Plasma exchange)**
- **Intravenous Immunoglobulins (IVIG)**
- **Immune modulating medications**
- **Symptomatic Treatment**
 - **Cognitive Behavioral Therapy**
 - **Low dose SSRIs**



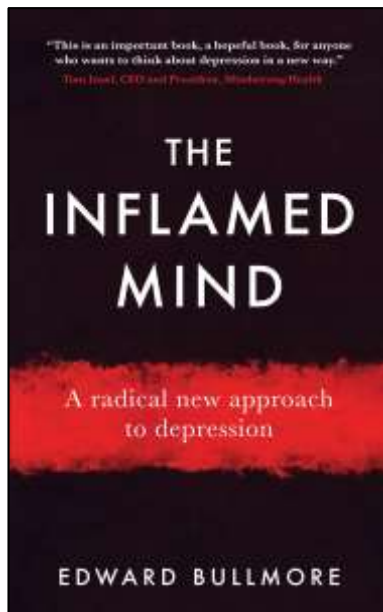
JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 27, Number 7, 2017
© Mary Ann Liebert, Inc.
Pp. 1–4
DOI: 10.1089/jcap.2017.0042

Introduction

Overview of Treatment of Pediatric Acute-Onset
Neuropsychiatric Syndrome

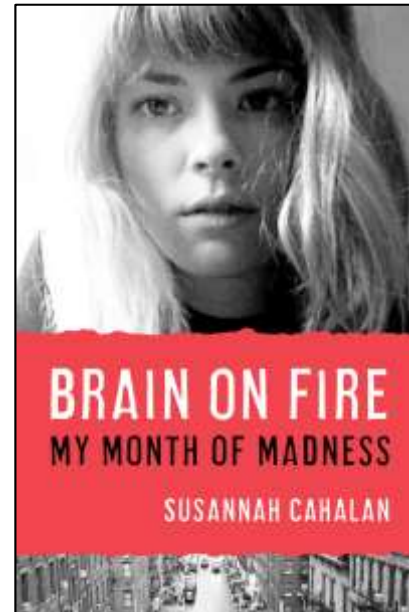
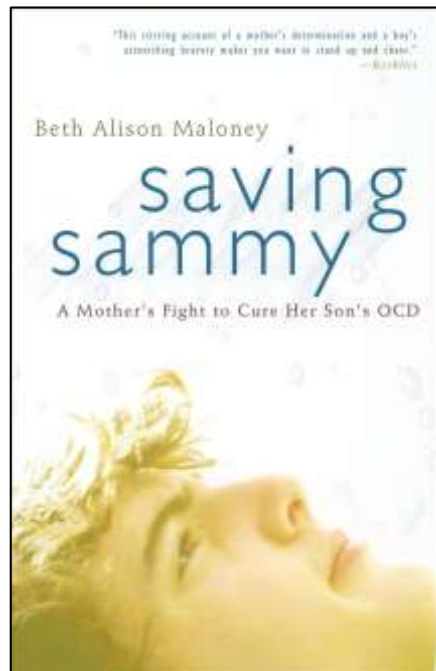
Susan E. Swedo, MD,¹ Jennifer Frankovich, MD, MS^{2,3} and Tanya K. Murphy, MD, MS⁴

Neuroinflammation, Autoimmunity and the Brain



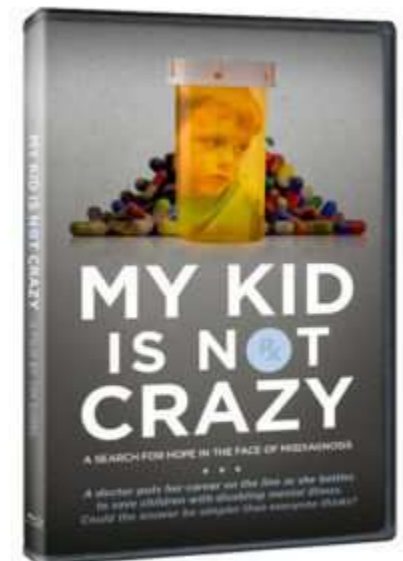
Dr. Bullmore is Co-Chair of Cambridge Neuroscience, Scientific Director of the Wolfson Brain Imaging Centre, and Head of the Department of Psychiatry at Cambridge University

Linking infection to "mental" illness, as strep antibodies are linked to the neurological Tourette's syndrome, has been rejected by many doctors since the rise of psychoanalysis, but Maloney insisted Sammy be tested for strep titers when he became unable to attend school and to walk. He was diagnosed with PANDAS. Antibiotics ended two torturous years for the family, and Sammy's regains came as rapidly as the symptoms had overtaken him



Susannah Cahalan is a news reporter at the *New York Post* who succumbed to an infection then began a painful journey to be diagnosed with an autoimmune disorder attacking her brain, and then the path to recovery after receiving the right treatment.

DVD: Documentary chronicling several families and their children suffering from PANDAS and what they went through to reach a diagnosis and begin recovery



Additional Information Sources



moleculara labs
molecularalabs.com



aonm.org



PANS PANDAS UK
awareness support education

panspandasuk.org

PANDAS PHYSICIANS NETWORK



A DIVISION OF THE FOUNDATION
FOR BRAIN SCIENCE AND IMMUNOLOGY

pandasppn.org



National Institute
of Mental Health

nimh.nih.gov



Pediatric Autoimmune Neuropsychiatric Disorders

pandasnetwork.org



*Our Mission is to Help Change How Medicine is
Practiced for Neuropsychiatric Disorders*

***Thank you for helping those suffering with this
disorder, to gain hope and get well!***

For More Information Contact:

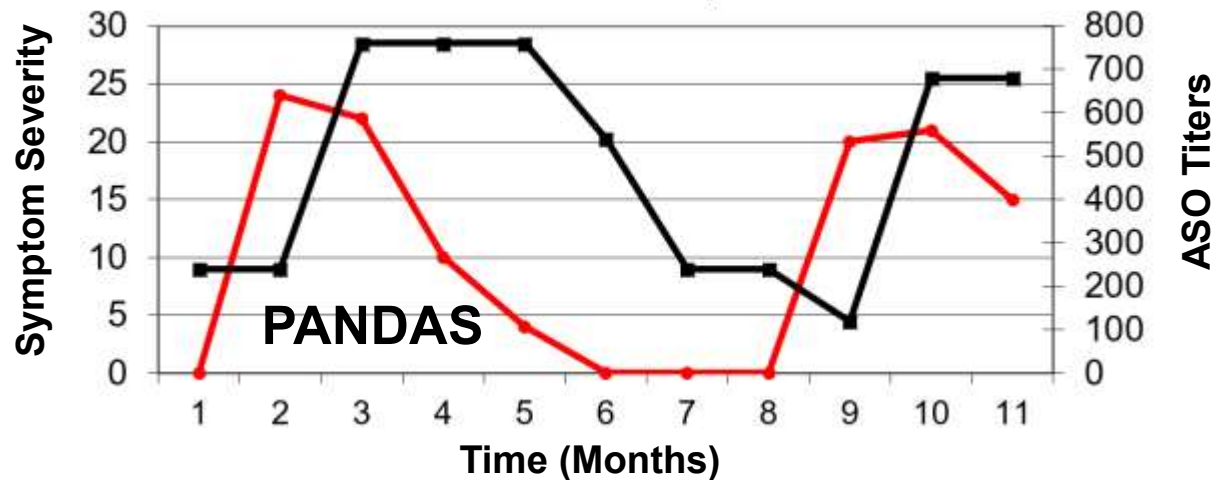
Craig Shimasaki, PhD, MBA

shimasakic@molecularera.com

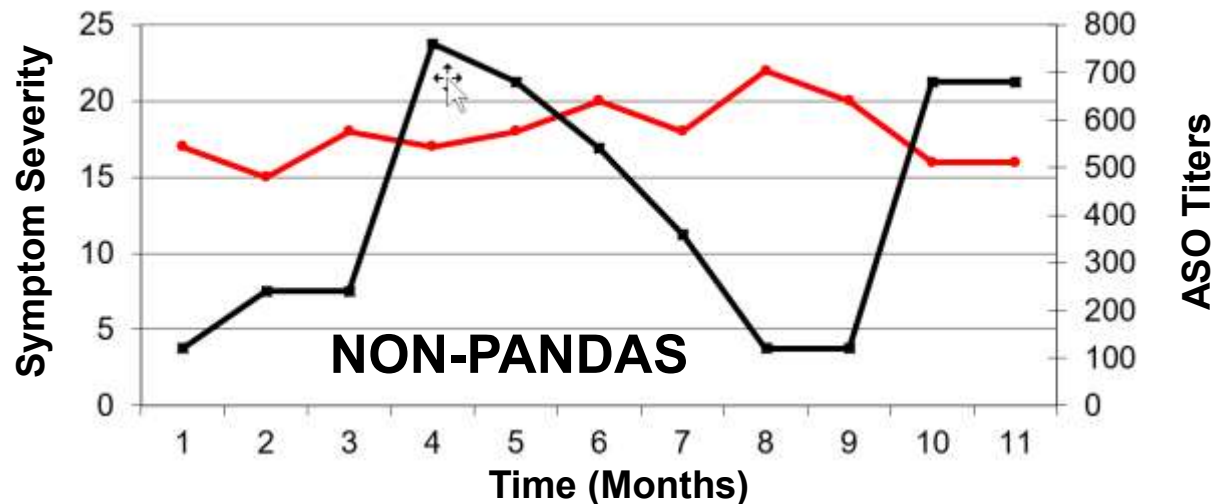
www.MoleculareraLabs.com

U.S. +1(405) 239-5250

Correlation vs. Causation: Anti-Streptolysin O Titers and OCD Symptom Severity



ASO TITER ---
Y-BOCS ---



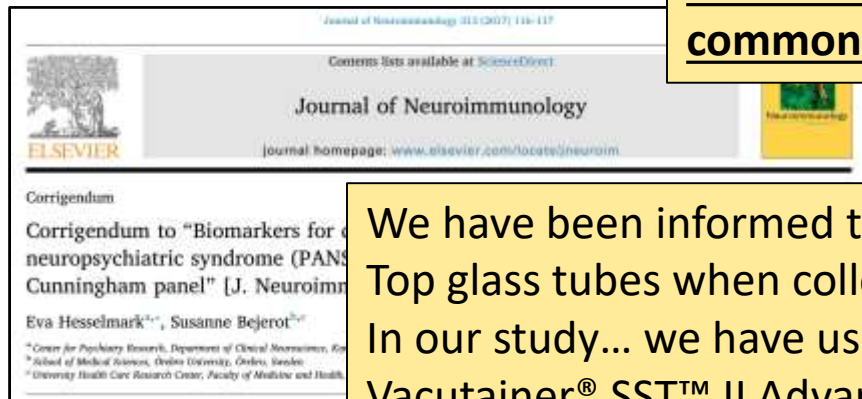
ASO TITER ---
Y-BOCS ---

Courtesy of Dr. Susan Swedo

Swedish Study of Cunningham Panel



Although our findings identified a moderate correlation between change in CaMKII and change in symptom severity in individuals with PANS or PANDAS, there was no indication that the Cunningham Panel can be used to diagnose PANS or PANDAS. Our results also suggest that **test-retest reliability of CaMKII may be insufficient, and that Cunningham Panel results are commonly elevated in healthy controls.**



We have been informed that Moleculera Labs recommend Red Top glass tubes when collecting blood for the Cunningham panel. In our study... we have used serum sampling tubes (BD Vacutainer® SST™ II Advance tubes, Gold Top) but erroneously reported sampling in “serum sampling tube (BD Vacutainer, yellow top)”... **The use of another blood collection tube than the one recommended by Moleculera could be viewed as a limitation in our study.**

Swedish Study of Cunningham Panel



Swedish Study Conclusions of Cunningham Panel

1. “...test-retest reliability of CaMKII may be insufficient”
2. “...results are commonly elevated in healthy controls”



SST Gold Top Blood Collection Tube

Invalid Blood Collection Tube

- Polymer Gel for serum separation
- **Interferes with assay results**

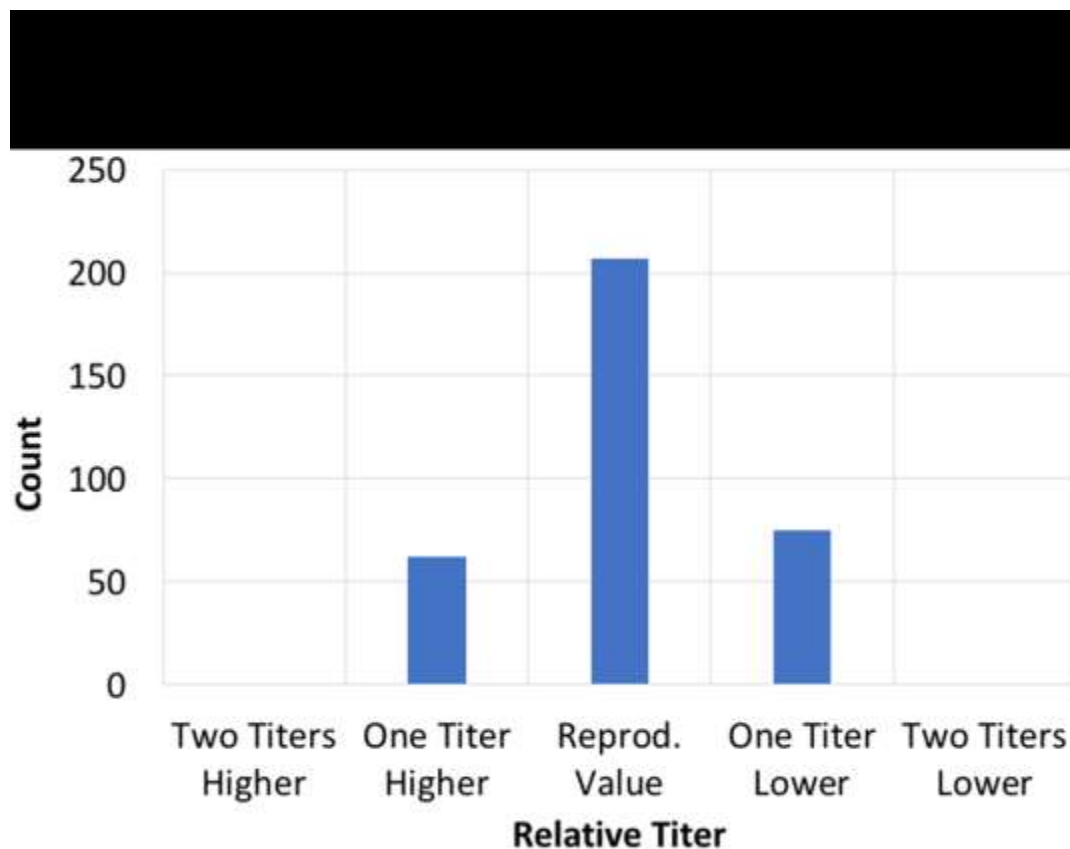


Red Top Glass Blood Collection Tube

Only validated Blood Collection Tube

- No Polymer Gel

Test-Retest Reproducibility in Tubes w/o Additives



Results of 344 individual repeated tests on 7 individual patients over several months

Seven patient samples collected in validated glass tubes with no additives (Red Top glass tubes) tested at random intervals over a period of several months for 344 individual tests. We observed 62 readings at one dilution higher, 207 readings at the most commonly observed dilution, and 75 readings at one dilution lower