Pediatric Grand Rounds

Ashlee Loughan PhD

Christen Holder PhD, Amanda Rach MS

Alison Wilkinson-Smith PhD, Benjamin Greenberg MD

Renee Lajiness-O'Neill PhD, Christine Salinas PhD, Michael Westerveld PhD, Philip Fastenau PhD

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Megalencephaly-Capillary Malformation Polymicrogyria (M-CAP): A Case Study

Ashlee R. Loughan, Ph.D.
Clinical Neuropsychologist
Assistant Professor of Neurology
Virginia Commonwealth University
Massey Cancer Center

Other contributing authors include:
Murphy Harrell, M.S.
Robert Perna, RN, Ph.D.
Aslyn Allen, M.S.
Brian Suddarth, MD

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Objectives

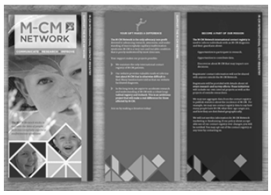
- **M-CAP**
  - Diagnostic Criteria
  - Identifiable Characteristics
  - Literature
  - Treatment
- **Case Study**
  - Demographics
  - History
  - Evaluation Results
  - Recommendations

Demographics

- Rare syndrome first described in 1997
  - Multiple name changes given defining characteristics (M-CMTC, M-CM, M-CAP)
  - In 2012, Genetic mutation identified in gene PIK3CA
  - Mutation is thought to always occur after cell division begins - de novo mutation
- Website Registry = 181 cases

Age	# Registered
0-2 yrs	32
3-10 yrs	100
11-18 yrs	37
18+ yrs	12

- Literature Reports = 150 cases
- Across genders
- Across ethnicities



http://works-progress.com/portfolio/m-cm-network/

Diagnostic Criteria

- Proposed Clinical Criteria for Diagnosis (Martínez-Glez et al., 2010)

Major Criteria (requires 3)	Minor Criteria (requires 2)
• Macrocephaly * • Capillary malformation(s) * • Overgrowth/asymmetry * • Neuroimaging alterations: o Ventriculomegaly * o Cavum septum pellucidum or cavum septum vergae o Cerebellar tonsillar herniation o Cerebral and/or cerebellar asymmetry *	• Midline facial capillary malformation • Neonatal hypotonia • Syndactyly/polydactyly * • Connective tissue abnormalities • Frontal bossing • Hydrocephalus * • Developmental delay *

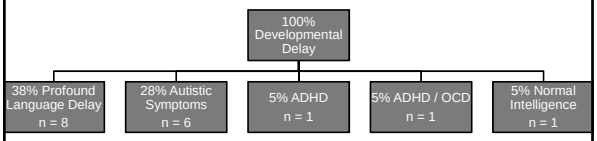
Martinez-Glez et al. were able to diagnose 94% of 136 previously reported cases using their criteria.

Identifiable Characteristics

- Macrocephaly
  http://undiagnosed.org.uk/archives/tag/macrocephaly
  http://www.m-cm.net/
- Capillary Malformation(s)
  http://www.saintluc.be/en/services/vascular-anomalies/
- Overgrowth / Asymmetry
  https://www.edmcasereports.com/
  http://www.m-cm.net
- Neonatal Hypotonia
  http://autism.wikia.com/wiki/Hypotonia
- Syndactyly / Polydactyly
  https://www.m-cm.net
  http://www.wikipedia.org

Literature

- Limited cognitive / neuropsychological data
- Most studies suggest developmental delays ranging from mild to moderate impairment
- For example: Mirzaa et al. (2012) examined 21 MCAP children



Literature Cont…

- **Important Note:**
  - To date, MCAP does not appear to be a condition associated with regression or decline in a person's cognitive functioning; unless an exacerbation of neuropathological processes occurs.
  - Children with MCAP are expected to make slow progress developmentally.
  - However, most children with this disorder continue to be consistently behind their peers in both academic and functional abilities.

CHALLENGE

This diverse presentation proves to be an obstacle when trying to identify cognitive or behavioral patterns in MCAP.

Treatment

Currently, there is no cure for M-CAP

Treatment varies depending on a multitude of factors including the presence and severity of specific impairments

CASE STUDY

- Frances "Franny" Brown
- Diagnosed with M-CAP at age 4 months
- Referral
  - Global delays
  - Reported inattention
  - Recent academic deficits / regression

Gender	Female
Age	7
Education	1st grade public education
Handedness	Right
Ethnicity	Caucasian
Socioeconomic Status	Upper Middle Class
Parental Education	Bachelors Degree

Developmental History

- Prenatal history uncomplicated
- Upon delivery, presented with
  - Cutis marmorata
  - Port wine stains
  - Large head (95th percentile – then "off the chart")
  - Feet malformations
- Genetic testing - none
- All developmental milestones delayed
- Continued motor deficits

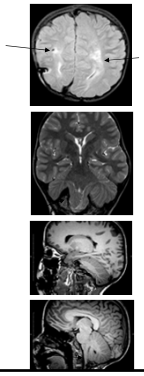
Medical History

- **Macrocephaly ****
- **Hemihyperplasia ****
- **Capillary malformations ****
- Headaches
- **Hydrocephalus ***
- Partial complex seizures (age 2 ½)
- **Syndactyly / polydactyly ***
- Muscle spasms
- Bladder incontinence
- Chronic ear infections
  - Comorbid hearing impairment
  - Currently wears hearing aids in both ears

- Surgery History (to date):
  - Ventriculoperitoneal shunt
    - (2 revisions)
  - Fourth ventricle shunt
    - (1 revision)
  - Tonsillectomy
  - Adenoidectomy
  - Spinal fenestration of an arachnoid cyst
  - Chiari decompressions (3)
  - Spinal shunt
    - (1 revision)
- Medications
  - Keppra, Trileptal, prevacid

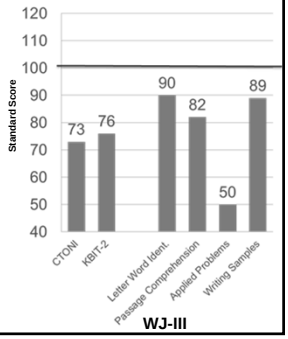
Medical History

- **Neuroimaging (MRI) Findings:**
  - Brain asymmetry / left hemimegalencephaly
  - Hydrocephalus (shunt placements)
  - Chiari malformations
  - Distortion of cerebellar hemisphere
  - White matter signal hyperintensities



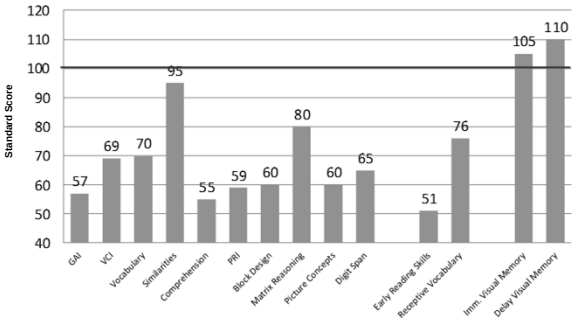
Previous Evaluation

2012



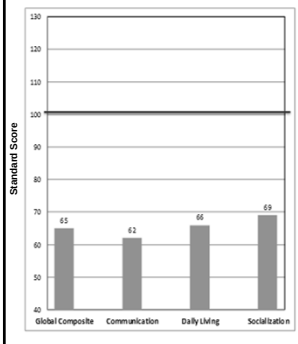
WJ-III

Test Results: Intelligence / Achievement / Memory



WISC-IV **WIAT-III** **LEITER-R**

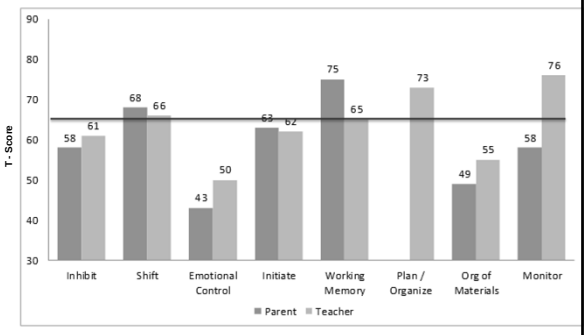
Test Results: Adaptive Functioning



Domain	Age Equivalent
Communication	
Receptive	1:10
Expressive	2:6
Written	3:1
Daily Living	
Personal	2:9
Domestic	2:8
Community	3:7
Socialization	
Interpersonal	2:3
Play and Leisure	2:11
Coping	2:11

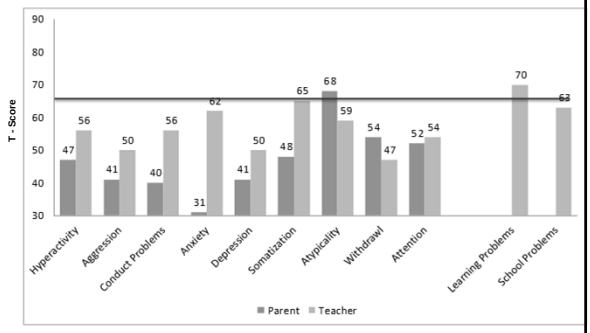
Vineland Adaptive Skills – 2nd Edition

Test Results: Executive Functioning



Behavior Rating Inventory of Executive Function

Test Results: Behavior and Emotional Screening



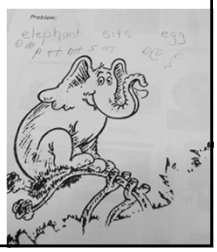
Behavior Assessment System for Children – 2nd Edition

Interpretation / Take Home

- Consistent with MCAP literature, Franny presented with multiple neurologic complications which should raise concerns and can impact cognitive development
- Testing demonstrated global developmental delays and many cognitive deficits
- Significant strength was evident in Frannys visual memory
- Most concerning was that cognitive performance had declined
  NOT TYPICAL
- Comorbid hearing impairment made for additional challenges

Recommendations

- Educational Placement
  - Individualized Education Plan (IEP)
  - Hearing impaired specialist for teacher
  - Instruction should take place in a 1-on-1
  - Integration into general education
  - Speech and Language Therapy, Occupational Therapy, and Physical Therapy
- Neurology Consultation
  - Urgent given regression
- Cognitive and Academic Recommendations:
  - Implement visual instruction / learning
  - Make learning meaningful
  - Focus on functionality
  - Repetition is key
  - Provide a structured and explicit learning environment
  - Attention
  - Reading
  - Rewards plan
- Neuropsychological Re-Evaluation.
  - Annually



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Questions and Discussion

Contact Information:

Ashlee R. Loughan, Ph.D., M.Ed.
Virginia Commonwealth University
Massey Cancer Center
Richmond, VA
804-828-9815
ashlee.loughan@vcuhealth.org

Neuropsychological Profile of Pediatric Pseudotumor Cerebri Syndrome: A Case Study

Christen M. Holder, Ph.D.[1]; Amanda M. Rach, M.S.[2]

[1]University of Tennessee Health Science Center,
[2]The University of Kansas Medical School- Wichita

Introduction

- Pseudotumor cerebri syndrome (PCS) is a progressive disorder marked by increased intracranial pressure without a known cause.
- A rare disorder in children, particularly prior to the age of 11
- Research on PCS related cognitive deficits have almost exclusively investigated adults.
- This presentation will provide a case study of childhood PCS

Pseudotumor Cerebri Syndrome (PCS)

Symptoms
- Mimics sx of brain tumor
- Headache
- Papilledema
- Blurred vision
- Increased CSF pressure

Course
- Develops over weeks or months
- Absence of enlarged ventricles or a mass
- Most common in obese adult women of childbearing age

Treatment
- Lumbar-peritoneal shunting
- Lumbar puncture
- Corticosteroids
- Weight reduction

Previous Literature

- Limited research into cognitive implications of PCS
  - Adult studies ranging from 20y – 56y, with one 15yo included
  - Almost exclusively female
- Most common findings
  - General verbal deficits in language, memory, and fluency
  - General memory deficits
  - Executive dysfunction and poor cognitive flexibility
  - Slowed processing speed and reaction time
  - Visual-spatial deficits
- Most patients do not show cognitive improvement, despite treatment
- No patients show evidence of brain damage/malformation on CT/MRI to indicate cause of impairment

Case study: 12-year-old female "K"

Reason for Referral
- Memory difficulties
- Academic difficulties
- Impaired sense of time
- Impaired hygiene
- Fatigue and poor sleep

Demographics
- 6th grade with 504 plan
- Right-handed
- PCS diagnosed in 2011 (9yo)
  - Papilledema
  - Daily headaches
- BMI – 97th percentile

Developmental history
- Unremarkable pregnancy/birth
- Milestones achieved within normal limits
- Medical history unremarkable

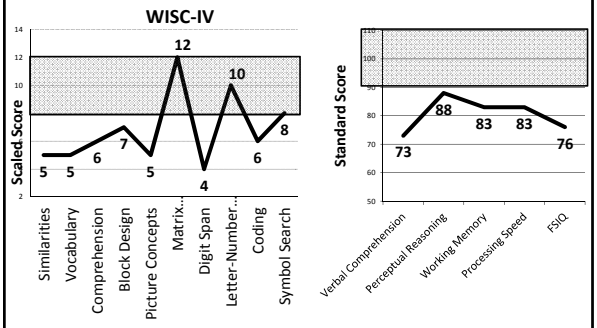
Current medical issues
- Optic Nerve Drusen w/papilledema
- 1-2 headaches per month
- Snoring and daytime sleepiness
- No prescribed medications
- Unremarkable MRI/MRV (repeat studies)

Surgical history
- Strabismus 2013, 2014
- Lumbar peritoneal shunt 2013

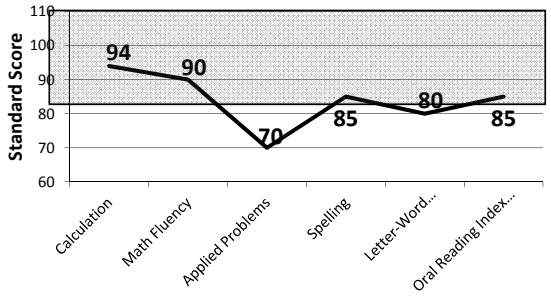
Tests Administered

Domain	Tests
Intelligence	Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV)
Academic Achievement	Woodcock-Johnson Tests of Achievement, Third Edition (WJ-III) Gray Oral Reading Tests, Fifth Edition (GORT-5)
Language	Boston Naming Test Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4) Expressive Vocabulary Test, Second Edition (EVT-2)
Motor	Grooved Pegboard Test
Visuoperceptual	Benton Judgment of Line Orientation (JLO) Beery Developmental Test of Visual Perception Beery Developmental Test of Visual-Motor Integration (VMI)
Memory	Test of Memory and Learning, Second Edition (TOMAL-2) Rey-Osterrieth Complex Figure Test (RCFT)
Executive Functioning	Delis-Kaplan Executive Function System (D-KEFS) Wisconsin Card Sorting Test (WCST)
Behavior and adaptive functioning	Adaptive Behavior Assessment System, Second Edition (ABAS-II) Behavior Rating Inventory of Executive Function (BRIEF) Behavior Assessment System for Children, Second Edition (BASC-2)

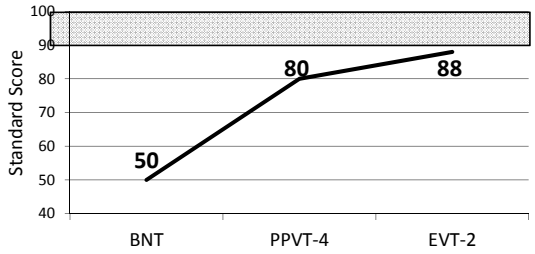
Results: Intelligence



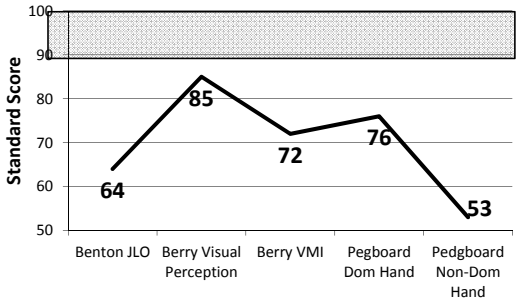
Results: Academic Achievement



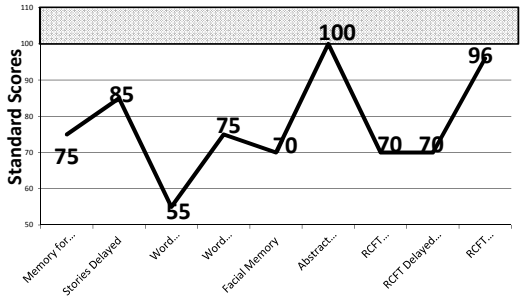
Results: Language



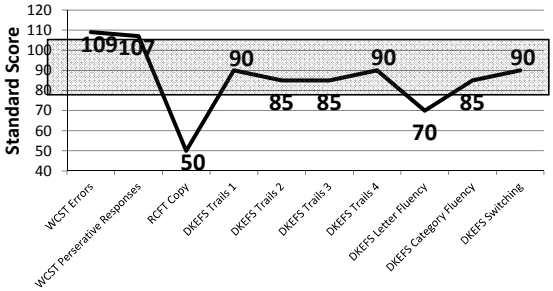
Results: Visuospatial and Motor



Results: Memory



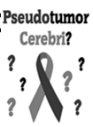
Results: Executive Functioning



Impressions

- Overall borderline impaired intellectual functioning and mildly impaired adaptive functioning
- Diffuse impairment in multiple areas of functioning
  - Comprehension
  - Memory across domains
  - Visual-perception and visual-construction
  - Motor speed/coordination
  - Confrontational visual naming/word retrieval
- Pockets of preserved cognition

Treatment Recommendati



- Changes to modifications/accommodations on implementation of IEP
- Strategies for slow learners emphasizing dividing tasks in to smaller units, repetition with frequent practice
- Use of visual memory aids and routines to maintain consistency
- Mathematics tutoring and reading comprehension intervention
- Chart system for hygiene
- Referral to the Sleep Disorders Clinic

Case in Context

- In comparison to previous literature
  - Pattern of deficits were largely consistent with previous literature.
  - Particularly notable is her Borderline IQ with greater deficits in Verbal Comprehension – many adults did not have general impairments in IQ
- Relevance to field
  - Although some view PCS as a "benign" condition, our findings suggest that diffuse cognitive deficits and impaired functioning are likely and will require intervention
  - Will the condition become more prevalent in children as childhood obesity rises?

Questions

References

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children's health Children's Medical Center | UT Southwestern Medical Center

The Princess and the P-Value:
Functional Neurological Symptoms and Rare Neuroimmunological Disease

Alison Wilkinson-Smith, Ph.D., ABPP
Benjamin Greenberg, M.D.

The Need for Collaboration

- Pediatric neuroimmunology is a rapidly changing field with many unknowns.
- Functional neurological symptoms are also poorly understood in children, and often considered only when medical causes are ruled out.
- This case highlights the need for collaboration between neuropsychologists and neurologists.

Demographics and Reason for Referral

- Kate: 12 year old Caucasian girl with suspected autoimmune encephalitis
- Normal early history until onset of symptoms two years ago
- Withdrew from rigorous private school in order to homeschool
- Participation in competitive gymnastics league
- Only child, living with both parents
- Family history noncontributory

Symptoms

- "Disney Princess" voice and mannerisms appeared following strep throat infection
- Approximately six months later developed additional neurological symptoms following urinary tract infection and flu mist vaccine
  - Dilated pupils
  - Agitation
  - Repetitive and tic-like behaviors
  - Dizziness
  - Headaches
  - Cognitive changes (memory, math, "brain fog")
  - Slurred/pressured speech
  - "Emotional fatigue"
- Symptoms worsened and she was "almost comatose"

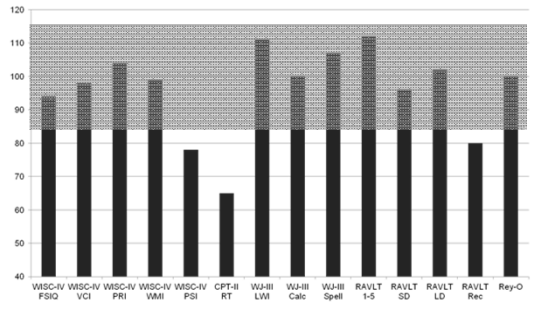
Medical Evaluations and Testing

- Multiple previous specialists
  - Neurology
  - Gastroenterology
  - Psychiatry
  - Infectious Disease
  - Chiropractic
  - Applied Behavior Analysis
  - Complementary and Alternative Medicine
- Negative strep titres
- Normal MRI of the brain
- Normal EEG
- **Abnormal CSF results**
  - **Elevated interleukin 6 and 8**
  - **S100B of unclear significance**

Treatments

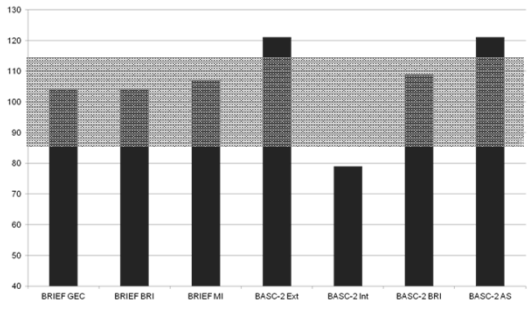
- Injection of rocephin (symptom improvement for 24 hours)
- Intravenous immunoglobulin (brief improvement)
- Plasmapheresis (brief improvement)
- Scheduled to undergo additional intravenous immunoglobulin treatments

Initial Testing: Selected Scores



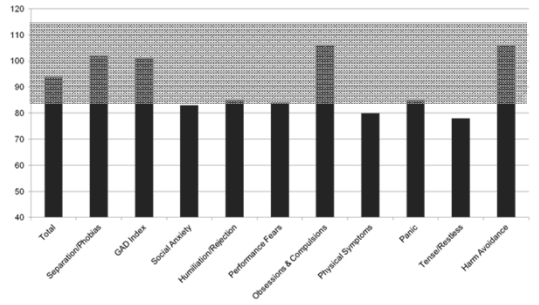
Performance on all tests represented as standard scores with higher scores reflecting optimal performance

Initial Testing: Parent Rating Selected Scores



Performance on all tests represented as standard scores with higher scores reflecting optimal performance

Initial Testing: Self-Report MASC-2



Performance on all tests represented as standard scores with higher scores reflecting optimal performance

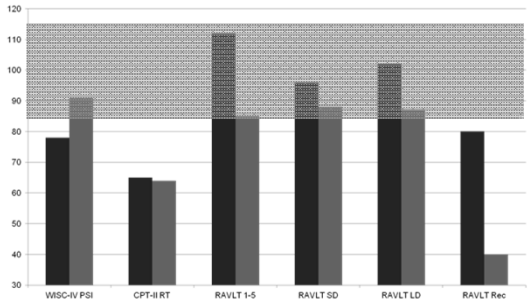
Impressions and Recommendations

- Autoimmune encephalitis
  - Continue with plan for intravenous immunoglobulin
  - Neuropsychological re-evaluation post-treatment
- Functional neurological symptoms
  - Consider psychotherapy for stress management and coping skills

Two Months Later

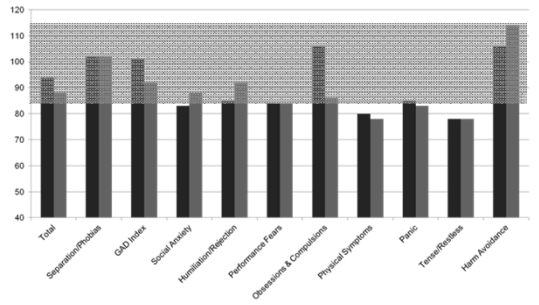
- Additional course of intravenous immunoglobulin completed
- No other treatments or changes
- Family reports improvements in symptoms
  - Memory problems and "brain fog"
  - Voice and mannerisms
  - Anxiety
- Improvements most noticeable immediately following treatment

Follow-Up Testing: Selected Scores



Performance on all tests represented as standard scores with higher scores reflecting optimal performance

Follow-Up Testing: Self-Report MASC-2



Performance on all tests represented as standard scores with higher scores reflecting optimal performance

Impressions and Recommendations

- Autoimmune encephalitis
  - Further treatment planning deferred to neurology
- Functional neurological symptoms
  - Consider psychotherapy for stress management and coping skills
  - Mindful return to school

Eight Months Later

- Enrolled in public school
- Non-competitive gymnastics club
- Noticeable improvements in voice and mannerisms
- Family complaints of residual mild memory deficits
- All other symptoms resolved

Lessons Learned

- Assessment of rare neuroimmunological disease is inexact and ever-evolving, particularly in pediatrics
- Functional neurological symptom exacerbation can be considered alongside medical etiology
- Multidisciplinary collaboration can promote the best outcomes for patients and families

Pediatric Grand Rounds

Ashlee Loughan PhD

Christen Holder PhD, Amanda Rach MS

Alison Wilkinson-Smith PhD, Benjamin Greenberg MD

Renee Lajiness-O'Neill PhD, Christine Salinas PhD, Michael Westerveld PhD, Philip Fastenau PhD