The Role of Medical Issues in Challenging Behaviors in Individuals with Autism

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What is behavior?

- Chronic /learned/conditioned response
- Adaptation to new environment or circumstance
- Symptoms of a psychiatric issue
- Medication side effects
- Symptoms of medical issues

- Ultimately Behavior IS communication

What is behavior?

- Chronic/learned/conditioned response
  - Chronic self-injurious behavior (SIB)as sensory seeking/soothing
- Adaptation to new environment or circumstance
  - New onset SIB as a coping mechanism
- Symptoms of a psychiatric issue
  - New onset SIB as anxiety disorder/OCD
- Medication side effects
  - New onset SIB related to confusion, cognitive issues, etc.
- Symptoms of medical issues
  - New onset SIB related to gastrointestinal/pain issues

- Ultimately Behavior is communication

Maladaptive behavior in autism

- As many as 40% of individuals with developmental disability may experience a period of disturbed behavior/function at some point in their lives
- Sudden change in behavior/functioning should prompt medical or clinical evaluation to identified any treatable medical causes
- Need to understand prior baseline behavior
- Need to coordinate with other providers such as neurologist, internist, pediatrician, behaviorist, therapist,etc.

Maladaptive behaviors-common
(or Reason for Psychiatric Referral)

- Aggression
- Mood lability/ irritability
- Low frustration tolerance/tantrums/property destruction
- Noncompliance/oppositional behavior
- Impulsive/Hyperactivity
- Sleep disturbance
- Regression in functioning
- Elopement

Maladaptive behaviors-less frequent

- Primarily present in individuals who are nonverbal or have more severe intellectual disability

- Stereotypies
  - Repetitive or ritualistic movements, posture or utterance
- Self injurious behavior (SIB)
  - Very intense/repetitive
- Fecal smearing
- Pica
  - Swallowing of nonfood items
- Rumination
  - Regurgitation of food following consumption.

Etiology of behavior in autism

- **Chronic behaviors**
  - **Stereotypies/SIB**
- **Adaptive dysfunction**
- **Psychiatric disorders**

- *Medication issues*
- *Medical issues*
  - *Pain*
  - *G.I.*
  - *Neurologic*
  - *Sleep*

✳ Often multiple causes/triggers

Stereotypical behavior

- Primarily present in individuals who are nonverbal or have more severe intellectual disability
- Stereotypies
  - Repetitive or ritualistic movements, posture or utterance
  - Typically chronic but can change over time
  - Frequency, intensity, circumstances, etc.
- Self injurious behavior (SIB)
  - Considered stereotypical behavior as well
  - Can vary from mild/low frequency (“habitual”) to very intense/ repetitive

Stereotypical behavior/SIB

- Need to determine what is baseline stereotypical behavior
- Chronic vs new/acute
- Distinguish from tics, dyskinesia (abnormal movements), dystonia (muscle stiffness), other abnormal movements
- Some of these could be medication side effects
  - Antipsychotics-risperidone, Abilify, etc.
  - Antinausea/G.I. drugs-Reglan
- Indicative of medical issues
  - Gastrointestinal-reflux, constipation, gastritis, etc.
  - Pain-dental, ear, etc.
  - PANDAS/PANS

Adaptive dysfunction

- Mismatch between needs, abilities, goals of individual and environment/ circumstances/expectations
  - Home
  - Residence
  - School
  - Day program

  - Change in parents/care providers
  - Change in health-illness/pregnancy/death
  - Change in environment
  - Change in people-staff, students, residents
  - Change in schedule-home, school, day program, residence

“Diagnostic overshadowing”

- =tendency to assess comorbid psychopathology in persons with intellectual disability less accurately than persons without *(Rice, Leviton + Szyszko (1982))*
- Assume that cognitive deficits negatively impact clinician judgments about psychopathology
- May impact
  - Severity-how severe the symptoms are?
  - Category/diagnosis-what diagnosis the person has
  - Treatment-how the disorder should be treated
    - *Jopp, Keys, diagnostic overshadowing reviewed and reconsidered, Am J MR, 2001*

Developmental Disability + Psychopathology

- Psychopathology in persons with ID is 3-4x higher vs gen pop
- 35-40% of children/adolescents with ID-diagnosable psychiatric disorder
- 30-42% vs 7%- Isle of Wight study

  Rutter, et al., Isle of Wight studies 1964-1974, Psych Med, 1976

Medical causes of challenging behaviors

- Medication issues
  - Drug interactions
  - Side effects
  - Generics vs Brand
- Medical issues
  - Cardiac-bradycardia
  - GI reflux pica constipation
  - Pain- dental ear
  - Hormonal
  - Sleep-apnea
  - Neurologic-HA, seizures

- Often multiple causes

Medication Effects

- Drug interactions
- Side Effects
- Generics vs Branded

- Multiple medications
- Confounded by
  - Multiple providers
  - Current + historical information often limited
  - Medication noncompliance

Medication –Drug interactions

- Anticonvulsants
  - Some can induce metabolism via impact on liver enzyme function
    - Carbamazepine/Tegretol, valproic acid/Depakote, phenobarbital
  - As a consequence, the effective dose of other drug is **decreased**
    - Thus may require higher doses in the presence of these anticonvulsants
- Antidepressants
  - Inhibit metabolism via impact on liver enzymes(cytochromes)
    - Fluoxetine/Prozac, paroxetine/Paxil
  - As a consequence the effective dose of another drug can be **increased**
    - Risperidone in the presence of either drug could be effectively increased twofold

Medication Side Effects-anticonvulsants

- Phenobarbital
  - Not commonly used
  - Attention, other aspects of cognition, hyperactivity, depression
- Topiramate/Topomax
  - Memory issues,word finding difficulties
- Gabapentin/Neurontin
  - Typically very well tolerated especially in adults
  - Psychosis especially in younger individuals
- Leviteracetam/Keppra
  - Widely used because of lack of drug interactions
  - Well-established mood symptoms-20%
  - Irritability, agitation, aggression and depression
  - May benefit from treatment with vitamin B12 (50-100 mg)

Medication Side Effects-benzodiazepines

- Drowsiness
- Confusion/mental clouding
- Memory problems
  - especially if older+ long-term use
- Disinhibition?
  - Appear as if intoxicated
  - More likely in individuals with developmental issues?

Medication Side Effects-benzodiazepines

- Long acting/half-life-Clonazepam (Klonopin)
  - Accumulate>drowsiness & mental clouding+ confusion
- Short-acting/half life-Alprazolam(Xanax)
  - Interdose rebound symptoms
    - Worsening of anxiety prior to scheduled doses>higher doses>dependence/tolerance
  - Risk of seizures in the presence of abrupt discontinuation

Medication Side Effects-antipsychotics

- Risperidone/Risperdal, aripiprazole/Abilify
  - Parkinsonism/akathisia (restlessness)
    - Confused with worsening agitation
    - Can lead to counterproductive increase in dose
  - Alertness/mental performance
    - Some have more negative cognitive impact-haloperidol
  - Precipitous reduction in dosage
    - >agitation, behavioral deterioration
    - > worsening abnormal involuntary movements(transient withdrawal dyskinesias)

Atypical Antipsychotic -Side Effects

- Weight gain
  - Can be substantial 20-40 pounds
  - Creates new issues
- ↑ Glucose levels
  - New onset diabetes
- ↑ Lipid levels
- ↑ Prolactin levels
  - Gynecomastia(breast growth)

Generic vs Branded Medications

- Branded + generic medications do indeed contain the <u>exact same</u> active ingredient or DRUG
  - Generics are **BIOEQUILIVENT**
- Branded +generic medications may **<u>differ</u>** in 2 significant ways
  - As established by the FDA, generic products are considered bioequivalent if they contain 80-125% dose of the active compound
    - Generic medications usually contain less rather than more
  - Brands typically vary by only 3-5% of the dose
  - Packing, fillers, colors may differ significantly
- These differences may impact efficacy and side effects
  - Can impact drug breakdown, absorption, blood level rise, etc.
  - Therefore, not all generics are considered to have the same **BIOAVAILABILITY**

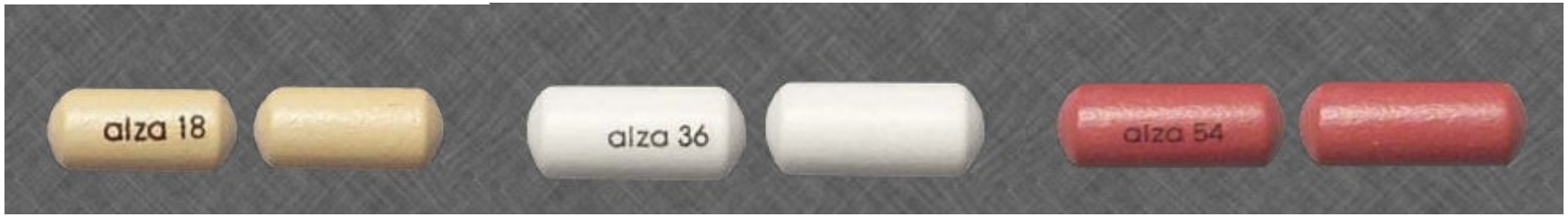
Generic vs Branded Medications
Concerta Problem

- BRAND
  - Originally manufactured by Ortho McNeil Janssen
  - Very specific release mechanism (OROS) responsible for the extended release
  - Specifically designed and patented barrel shaped capsule
- GENERICS
  - When Concerta went generic in 2014, several generic alternatives emerged including Watson (purchased by Actavis) and several others
  - These are very different in terms of size, shape, design and ultimately release.
  - Many of these are **NOT** OROS design

Generic vs Branded Medications

Concerta Problem

- Concerta problems
- Originally manufactured by Ortho McNeil Janssen + subsequently by Watson/Actavis



- Versions by Malinckrodt + Kudco

Generic vs Branded Medications

Concerta Problem

- Concerta/methylphenidate ER was designed to release the drug over a period of 10-12 hours
- Analysis by the FDA revealed that Mallinckrodt and Kudco products they delivered the drug at a slower rate of 7-12 hours
- As a result, the FDA change the **therapeutic equivalence** rating for these products from AB to BX
  - These products are still approved and can be prescribed that are no longer recommended as automatic substitution that the pharmacy for Concerta
  - FDA requested that these manufacturers confirm the bioequivalence of their products or voluntarily withdraw them from the market
  - http://www.fda.gov/Drugs/DrugSafety/ucm422568.htm

Medical causes of challenging behaviors

- *Medication*
  - *Drug interactions*
  - *Side effects*
  - *Generics vs Brand*
- Medical issues
  - General
  - Gastrointestinal
  - Pain
  - Hormonal
  - Sleep
  - Neurological
- Often multiple causes

Medical Evaluation of Persons with MR referred for Psychiatric Assessment (Ryan, Sunada, 1997)

- Interdisciplinary team evaluation clinic specifically for those with ID and behavioral challenges
- Consecutive sample of 1135 adults
  - ave age 32.9yrs
  - ID (moderate to severe)
  - 50% nonverbal
  - 46% nonpsychiatric meds
- Evaluated by 2-step process (physical exam + screening labs followed by selective testing)

Medical Evaluation of Persons with MR referred for Psychiatric Assessment (Ryan, Sunada, 1997)

Condition	% of cases
Epilepsy (untreated or undiagnosed)	45.8
Hypothyroidism	12.7
Tourette's syndrome	11.5
Gastroesophageal reflux	9.7
Severe closed head trauma	8.8
Chronic pain	8.7
Cerebral palsy (complicated)	6.5
Open brain injury	6.3
Abnormal (spike-wave) EEG	5.4
Arthritis (autoimmune)	5.0
Hypertension, symptomatic	4.7
Scoliosis (untreated)	4.1
Peptic ulcer disease	4.0

Medical Evaluation of Persons with MR referred for Psychiatric Assessment (Ryan, Sunada, 1997)

- Results
  - 75% had >1 undiagnosed/untreated medical problems
  - Almost all had NO diagnosis other than ID before the study
  - Most common psychiatric diagnosis-anxiety, depression
- Comments
  - Common conditions present atypically
  - Conditions considered “uncommon” may occur more frequently
  - Greater number of tests may be necessary because history often not available or helpful
  - Workup considered complete when person is improving or has a specific terminal diagnosis and is comfortable

Differential Diagnosis in nonverbal individuals

http://www.ddhealthinfo.org/

General pain/discomfort

(high activity, rocking, head-banging, or other behavior)

- Arthritis
- Bone fracture
- Cervical body subluxation

- Cardiac disease

- Constipation
- Intestinal obstruction
- Gastroesophageal reflux (w/ or w/o esophagitis)
- Hernia
- Rectal fissure

- Dental pathology

- Dehydration
- Electrolyte or glucose abnormality

- Pneumonia

- Headache or migraine
- Hydrocephalus
- Ocular and vision problems
- Seizures
- Change of consciousness

- Sepsis
- Occult infection (sinusitis, otitis media, dental, urinary tract infection, vaginitis, prostatitis)

- Medication toxicity

- Trauma including abuse or neglect
- Psychiatric disorders including depression

Hands/Fingers in Mouth

- Sinus problem
- Eustachian tube
- Middle ear problem
- Dental pathology
- Gastroesophageal reflux
- Asthma
- Nausea

Sudden Sitting

- Cardiac problems
- Seizures
- Syncope or orthostasis
- Vertigo
- Atlanto-axial dislocation

Medical causes of behavior-Allergies

- Environmental/hayfever, food allergies, atopic dermatitis, allergic asthma
- Can occur for the first time when setting or environment is changed
  - Change in weather/seasons
- Potentially undiagnosed in nonverbal individuals as many symptoms may not be apparent and could impact behavior
  - Symptoms (runny nose, itchiness, red eyes, shortness of breath, swelling, etc.) & associated discomfort can impact behavior
  - Uncomfortability >irritability, anxiety, agitation, SIB
- Associated medications also have side effects
  - Antihistamines-sedation +mood changes (especially Zyrtec)

Medical causes of behavior-Allergies

- Correlation of allergies/asthma with behavioral issues and ASD has not been examined in depth
- Medical comorbidities like allergies in the general population are often related to increased irritability and poor functional outcomes in children *(Jyonouchi, 2010)*
- ***Asthma & Allergies in Children with Autism Spectrum Disorders: Results from the CHARGE Study*** *(Lyall, et al., 2015)*
  - Overall allergy in children with ASD was associated with higher stereotypy scores as measured by the Aberrant Behavioral Checklist (ABC)

Medical causes of behavior-allergies

- ***Case example***
- 45-year-old nonverbal male with profound intellectual disability + autism who would repeatedly forcibly insert his hands in his mouth/throat and also had severe SIB (banging his head with his hands)
- Discovered that he had severe environmental allergies which caused a irritation/itching of his palette (roof of his mouth) which was the trigger for the insertion of his hands in his mouth
- Antihistamine hydroxyzine and other relevant interventions has produced some benefit including the elimination of this behavior but continues to have SIB

Medical causes of behavior-cardiac

- ***Case example***
- 60-year-old verbal male with mild ID, autism, possible mood disorder including bipolar with sudden onset of dropping to the floor including in public
- Viewed by staff as noncompliance possible associated with anxiety
- Ultimately diagnosed with bradycardia(slow heart rate) which required placement of a pacemaker.
- Following this, no further dropping behavior or noncompliance and anxiety was overall reduced

Medical causes of behavior-pain

- Many medical/dental issues can go undiagnosed in individuals with developmental disabilities and lead to the development of pain
- Pain maybe experienced very differently in individuals with developmental disabilities
  - Diminished or higher pain threshold many
  - Heightened sensitivity in some individuals perhaps related to sensory issues
- Awareness but lack of understanding and still impact behavior/ functioning
  - Discomfort, anxiety, irritability, agitation, aggression, SIB, insomnia

Medical causes of behavior-pain

- Dental issues
  - Dental visits/cleanings are often very limited/in frequent or not possible in some individuals
  - As a result various issues can develop (i.e. impacted teeth, infection, gum issues, etc.) which can cause discomfort/pain and associated behavioral manifestations
  - Lose teeth + braces can also be problematic
- Sinus/ear/nasal issues
  - Can be acute or chronic and significantly impact behavior
- Both could potentially contribute to discomfort and associated irritability, SIB (headbanging, slapping) and/or aggression towards others

Medical causes of behavior-gastrointestinal

- Studies suggest that children with ASD are at increased risk for gastrointestinal problems *(Ibrahim et al , 2009)*
- Frequent G.I. complaints including constipation, reflux, food allergies/ sensitivities
- ***Gastrointestinal Symptoms in Autism Spectrum Disorder: A Meta Analysis***, *McElhanon, et al, 2015*
  - Analysis of 15 peer-reviewed studies (1980-2012)
  - Children with ASD experienced significantly more G.I. symptoms
  - Diarrhea (OR, 3.63/95% CI 1.82-7.23), constipation (OR 3.86/2.23-6.71), abdominal pain (OR 2.45/1.19-5.07).

Medical causes of behavior-gastrointestinal

- Studies suggest that children with ASD are at increased risk for gastrointestinal problems *(Ibrahim et al , 2009)* and may be more difficult to evaluate (Buie et. al., 2015)
- Further suggested that certain behavioral problems in children with ASD may be indicative of a child's response to or an attempt to communicate the pain or discomfort of this underlying G.I. issue *(Horvath, et al. 1999, Williams at all 2010, Bauman, 2010)*
- Specific suggested behaviors include sleep disturbance, stereotypical repetitive behaviors, self injurious behaviors (SIB), aggression, oppositionality, irritability, tantrums, and other mood disturbances

Medical causes of behavior-gastrointestinal

- ***Brief report: Association between behavioral features & gastrointestinal problems among children with autism spectrum disorder***, *Maener, et al, 2011*
- Cross-sectional study of children with ASD 35/487 (7.2percent) had documented history of G.I. issues
  - Constipation, abdominal pain, diarrhea, encopresis, gastroesophageal reflux disease (GERD), gastritis, abdominal bloating, disaccharide ace deficiencies, inflammation of GI tract, abnormalities of enteric nervous system, functional abdominal pain, irritable bowel syndrome (IBS), flatulence, celiac disease
- Constipation, encopresis, GERD-most common documented
- Significant association -Unusual sleeping ($p < 0.01$) or eating habits ($p < .02$), oppositional behavior ($P < 0.04$)
- Association but not significant-Mood disturbance ($P < .08$), tantrums ($p < 0.05$)
- No association-stereotypic/repetitive behaviors + SIB
  - Unusual sleeping or eating habits and oppositional behavior were significantly associated with GI problems

Medical causes of behavior-gastrointestinal

- Pica
  - Persistent eating of non-nutritive, nonfood substances over a period of 1 month (DSM V)
  - Paper, soap, cloth, hair, string, wool, soil, chalk, paint, gum, metal, pebbles, ice, coins
  - Occurs in the context of intellectual disability, autism, schizophrenia or other medical condition including pregnancy
- **Case example**
  - 39-year-old male with a history of severe intellectual disability and childhood TBI with a chronic history of pica
  - Would often swallow balloons or rubber gloves which could cause G.I. irritation including constipation
- Constipation/holding of stooling
  - Perhaps related to sensory/pain issues individuals may not be aware of the associated discomfort and impact on behavior

Medical causes of behavior-hormonal

- Most menstruating women experience some premenstrual symptoms
- Approximately 20-40% consider them severe enough to seek medical help
- **Premenstrual dysphoric disorder**
  - includes mood lability, irritability, dysphoria and anxiety symptoms that occurs repeatedly during the premenstrual phase of the cycle and remit around the onset of menses or shortly thereafter
  - Also includes physical and behavioral symptoms
  - 12 month prevalence = 1.8-5.8% of menstruating women

Medical causes of behavior-hormonal

- **Prevalence of premenstrual syndrome and autism: a prospective observator rated study,** *Obaydi + Puri 2008*
  - Compared women with autism + learning disability (26) with a group with learning disability only (36)
  - 24/26 (92%) met criteria for late luteal phase dysphoric disorder vs 11% of controls ($p<.000001$)
  - Increased symptoms-affective lability, anger or irritability, clumsiness, anxiety or tension, depressed mood, impairment of work performance, social activities relationship, social withdrawal, isolation and decreased interest in usual activities, decreased concentration, temper tantrums, physical aggression, self harm, stereotypies or repetitive movements, destructive behavior, hypersomnia, insomnia, change in appetite or specific food craving, headache

Medical causes of behavior-hormonal

- ***Case example***
- 23-year-old largely nonverbal female with autism, prior diagnosis of ADHD and bipolar disorder beginning in late teens
- Developed cyclical mood changes in addition to hormonal changes in mood
- Responded well to mood stabilizers/antipsychotics as well as the addition of transdermal birth control
- With this combination cyclical and hormonal mood changes are largely under control

Medical causes of behavior-sleep disorders

- Sleep wake cycle in individuals with autism appears to be abnormal
- Sleep problems
  - Common in children with ASD-45-86% *Liu, Hubbard, Fabes & Adam, 2006, Maskey et al., 2008*
  - More chronic –remission 8.3% vs 52.4% *Silversen et al., 2012*
  - Considered as a coexisting symptom of ASD not significantly influenced by race, gender, age or IQ *Mayes & Calhoun 2009*
- Impact on the individual and the family/care providers is profound
  - Significant stress to families
  - Short sleep duration associated with higher rates of stereotypical behavior 33 as well as social deficits 32
  - May worsen daytime behaviors including inattention/hyperactivity 28

Medical causes of behavior-insomnia

- Insomnia =Difficulty initiating or maintaining sleep
- Types-Prolonged sleep latency (time to fall asleep), bedtime resistance, decreased sleep efficiency, decreased sleep duration + continuity and increased awakenings
- Sleep onset insomnia is more prevalent than sleep maintenance insomnia 17, 34
- Many possible contributing factors
  - Aberrations of neurotransmitter systems that are related to sleep + regular sleep wake cycle(e.g. melatonin)
  - Psychiatric disorders-anxiety/depression, ADHD, obsessive/repetitive behavior
  - Medical issues that disrupt sleep continuity-epilepsy, G.I. disorders, pain, constipation, breathing issues/asthma
  - Neurologic issues-sleep apnea, periodic limb movement, restless leg syndrome
  - Difficulty establishing a proper bedtime behavior and routine
  - Sensory issues

Medical causes of behavior-sleep apnea

- Sleep disordered breathing includes disorders related to airway obstruction / obstructive sleep apnea
- Common in the general pediatric population including those with autism
- Contributing factors-allergies, tonsillitis, hypotonia, medication related sedation
- Contributes to daytime sleepiness which can impact behavior, mood, attention, etc.

Medical causes of behavior-headaches

- Prevalence
  - 37-51% during elementary school years, 57-82%-high school
  - Frequent/severe headaches including migraine-17% of children + adolescence
- Migraine headaches= moderate/severe recurrent headaches
  - others symptoms including nausea, vomiting, sensitivities (light, sound, smell), visual/vision disturbances, frequent triggers
  - Family history
  - Hormonal + other triggers
- In those with language/communication difficulties headaches may be hard to diagnose but can cause significant impact on pain
- Empirical treatment?

Medical causes of behavior-neurological

- Prevalence of epilepsy in ASD ranges 11-39%
- More severe cognitive dysfunction associated with higher risk of seizures
- EEG abnormalities can be found in 8-31% of those without epilepsy
- More commonly associated with *regression* – seen in about 30% of ASD, usually 18-24 mos
  - In this subset, up to 80% in one study had epileptiform activity on EEG *during sleep (ESES or CSWS)*
  - Onset of ESES commonly associated with onset of seizures, most frequently absence

Medical causes of behavior-neurological

- Epilepsy= Recurrent seizures

- Complex partial seizures/temporal lobe epilepsy
- Absence seizures/petite mal
- Frontal lobe seizures

- Mixed seizure types/syndromes
  - Lennox Gastaut Syndrome

- Continuous spike waves in slow wave sleep (CSWS)
- Landau Kleffner Syndrome

Medical causes of behavior-neurological

- Epilepsy= Recurrent seizures
- Frequent seizures especially at night can impact cognition/development
- When very frequent can contribute to the development of a chronic confused state (encephalopathy).
- The addition of required medication can further contribute to this confused state
- The location of being abnormal electrical activity can be relevant to functioning of the brain in that area including behavior.

Medical causes of behavior-neurological

- **CSWS – Continuous spike waves in slow wave sleep**

- Present with regression – loss of language and temporospatial skills, hyperactivity, aggression
- May have motor deficits – ataxia, apraxia, dyspraxia
- Mostly expressive aphasia(receptive usually spared)
- Seizures are presenting symptom in up to 80%
- Age of onset variable, mean 4- 8 years
  - Younger onset, worse prognosis

Medical causes of behavior-neurological-Landau Kleffner Syndrome

- Onset-3-8 years with peak 4-5 years
- Acquired aphasia
  - Normal development until 4-6yrs
  - Language arrest>jargonized speech
- Other symptoms
  - Hyperactive/impulsive, autistic like
- Seizures
  - Present and 70-80%
  - EEG-Bilateral independent temp/parietal spike/wave or focal temporal
- Differential-Autism

Medical causes of behavior-neurological-PANDAS

- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections
  - Specifically, group A beta-hemolytic Streptococcus (GABHS)
- First described in 1998 with a case series of 50 cases by Susan Swedo at the NIH.
  - *Swedo SE, Leonard HL, Garvey M, et al. PANDAS: Clinical Description of the First 50 Cases. American Journal of Psychiatry 1998; 155: 264-271.*
- Antibodies generated against GABHS cross-react with self-antigens expressed in the basal ganglia and/or other brain structures (molecular mimicry).

PANDAS Criteria

1. **Tic disorder** or **Obsessive Compulsive Disorder** meeting DSM criteria
2. Onset prior to puberty (usually 3-12)
3. **Abrupt** onset of symptoms or episodic course (severe)
4. **Temporal association** of symptom exacerbation and **streptococcal infections** (onset + one exacerbation, or at least two exacerbations confirmed by culture or repeated rising anti-streptolysin O/anti DNAse B titers)
5. Presence of neurological abnormalities during periods of symptoms exacerbation (e.g. - choreiform movements (but not chorea), tremor, cognitive deficits, motoric hyperactivity)

Medical causes of behavior-neurological-PANDAS

- Additional research revealed association between PANDAS in the presence of comorbid ADHD, separation anxiety, vocal and motor tics, frequent urination, handwriting deterioration, and decline in school performance.
- Children with PANDAS were more like to present with dramatic onset of symptoms, complete remission, temporal association of symptoms with GAS infection and clumsiness.

Medical causes of behavior-neurological-PANS

- Pediatric Acute onset Neuropsychiatric Syndrome
  - Consensus conference May 2013
  - Journal of Academy of Child & Adolescent Psychopharmacology
- PANDAS "morphed" as research identified potential infectious triggers beyond Group A streptococcus as well as noninfectious or metabolic factors
- Clinicians confronted with the difficulty diagnosing youth who meet all but one criteria of the PANDAS subtype, evidence of GAS infection before symptom onset.
  - Increasing evidence suggesting absence of significant role for GAS infection
- Proposed a broader term that encompasses acute onset neuropsychiatric symptoms without a specific environmental or immune related trigger *(Swedo et al., 2012)*

Medical causes of behavior-neurological-PANS

- Clinicians confronted with the difficulty diagnosing youth who meet all but one criteria of the PANDAS subtype, evidence of GAS infection before symptom onset.
- Increasing evidence suggesting absence of significant role for GAS infection
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Medical causes of behavior-neurological-PANS

- **PANS Criteria**
- Abrupt, dramatic onset of OCD OR **severely restricted food intake** +
- 2 or more concurrent neuropsychiatric symptoms also with acute onset
  - Sensory symptoms
  - Handwriting deterioration
  - Separation anxiety
  - Emotional lability

Medical causes of behavior-neurological-PANS

- **Other features**
  - Anxiety
  - Emotionally lability, depression, or both
  - Irritability, aggression or severe oppositional behavior or combination
  - Behavioral regression
  - Deterioration in school performance
  - Sensory motor abnormalities
  - Somatic signs or symptoms including sleep disturbance, enuresis or urinary frequency

Medical causes of behavior-neurological-PANS

- **Laboratory tests –PANS**
- ASO titer elevations began one week after infection and peak after 2-3 weeks
- Anti-DNAse B titer elevations after 4-8 weeks
- Use of both reduces the possibility of obtaining false negatives

Thank you