

# Neurodevelopmental Manifestations of Sotos Syndrome

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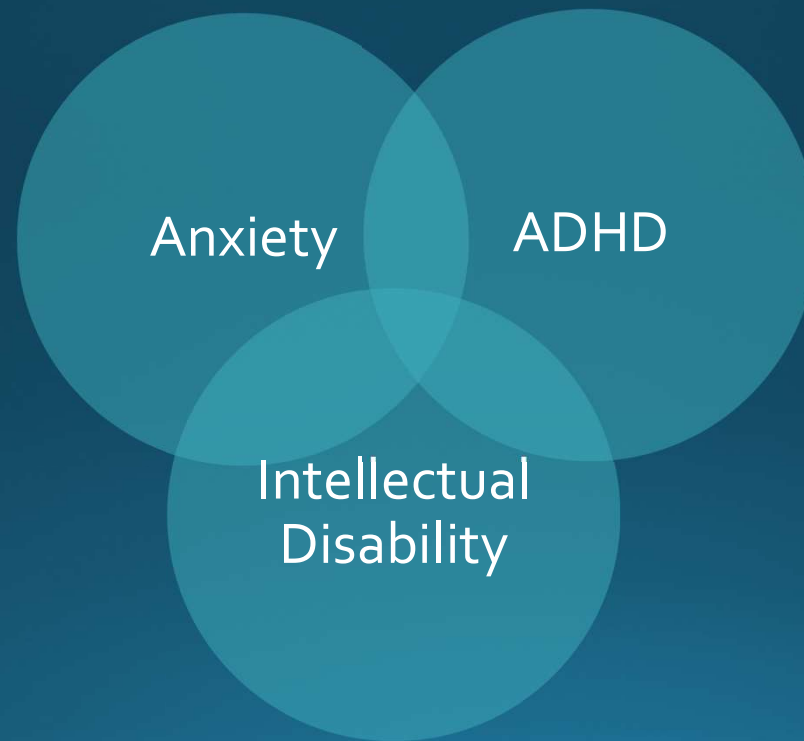
# Overview

- Intro to Neurodevelopmental Disabilities
- Specific Neurodevelopmental Disabilities in Sotos syndrome
- Potential Clinical, Behavioral, and Educational Strategies for Right Now

# Overview of Neurodevelopmental Disabilities

- Intellectual disability
- ADHD
- Autism spectrum disorder
- Specific learning disabilities
- Cerebral palsy
- Language disorder
- Anxiety
- Epilepsy
- And More.....

# Overlap and Multiple Disabilities are the Rule Not the Exception



# Certain Patterns of Cognitive Strengths and Weaknesses Have Been Associated with Specific Genetic Syndromes

|                   | Intellectual Disability | Language Disability | Visual-Spatial Problems | ADHD | Anxiety | Autistic Features | Seizures |
|-------------------|-------------------------|---------------------|-------------------------|------|---------|-------------------|----------|
| Williams Syndrome | +                       | -                   | +                       | +/-  | +       | -                 | -        |
| Angelman Syndrome | +                       | +                   | -                       | -    | -       | +/-               | +        |
| Rett Syndrome     | +                       | +                   | -                       | -    | +       | +                 | +        |
| Down Syndrome     | +                       | +                   | -                       | -    | -       | +/-               | -        |
| Kabuki Syndrome   | +                       | -                   | +                       | +/-  | +       | -                 | +/-      |

# Does Sotos Syndrome have a Particular Neurologic, Cognitive, or Behavioral Profile?

- Yes, but more work needs to be done to characterize it. Most of this has been published just in the last 5 years.
- Mild to moderate intellectual disability
  - Verbal and visuospatial memory strengths
  - Quantitative reasoning (math) very weak
- Anxiety, ADHD, autism spectrum disorder
- Early hypotonia that improves with age, fine motor problems persist
- Sleep problems common
- Seizures in less than half, mostly easily controlled
- Ventriculomegaly and large extra-axial spaces on MRI

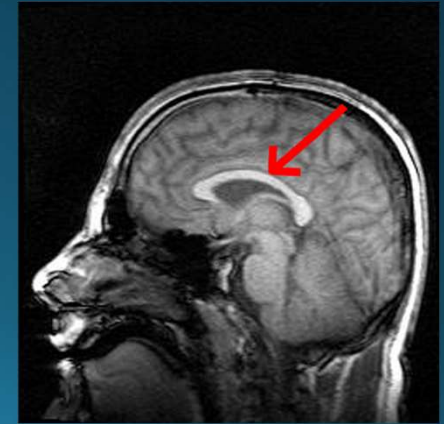
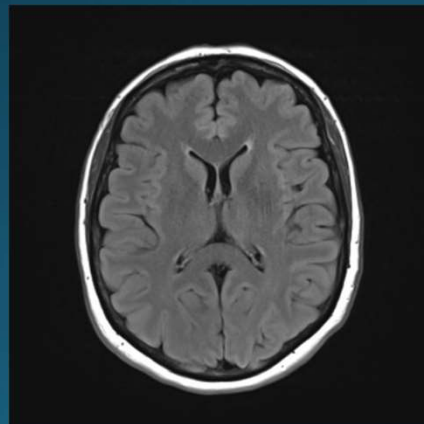
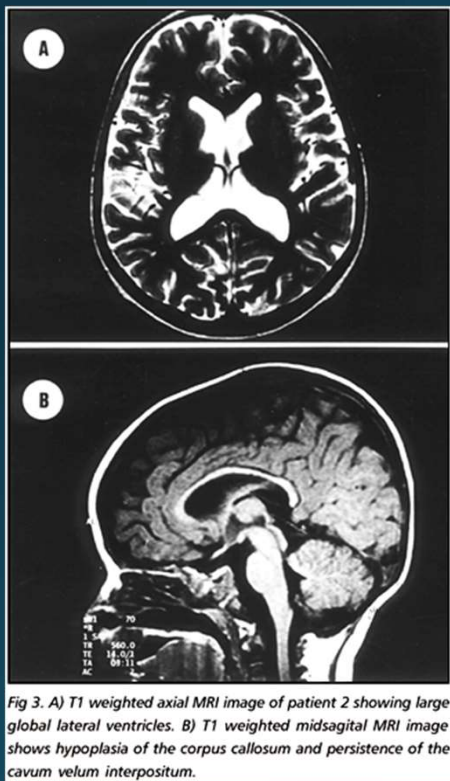
# Neurologic - Hypotonia

- Present in almost all infants with Sotos syndrome, in most it is significant
- Low muscle tone: can result in delayed acquisition of motor milestones, balance and coordination issues
- Treatment is physical and occupational therapy
- Worst in infancy and toddler ages and gets better with age
- One study showed that development in Sotos syndrome appears worse early and improves as time goes on, likely due to the early hypotonia
- Fine motor issues persist throughout life



# Neurologic - Brain MRI Findings

- Present in about 3/4 of people with Sotos syndrome
- Generally benign findings with no clinical significance
- According to Schaefer et al. most common findings are ventriculomegaly, enlarged extra-axial spaces, and midline anomalies including cavum septum pellucidum and underdevelopment of corpus callosum
  - Enlarged ventricles seldom related to increased pressure





# Neurologic - Seizures

- Present in 15-40% of people with Sotos syndrome depending on the study
- A study published by Fortin et al (2021) suggests that all seizure types are present in Sotos syndrome
  - Staring spells, febrile convulsions most common then generalized tonic clonic
  - Multiple seizure types present in most
- Seizures typically easily controlled on 0-1 medication but some cases can be refractory

# Neurologic - Sleep

- Two recent studies by Stafford et al. (2021) and Frattale et al. (2024)
- Increase of sleep problems compared to typically developing
  - 71% in 2024 study of pediatric patients although underreported
- Longer sleep duration, more daytime sleepiness, more parasomnias
- Some suggestion of abnormal sleep stage breakdown
- Sleep disordered breathing more common than in other developmental disabilities



# Cognitive

- All patients with Sotos syndrome have some degree of neurodevelopmental disability although some can be quite mild
- Most people with Sotos syndrome fall in the mild intellectual disability range with some scattered in both directions
  - According to Siracusano et al. (2024) most individuals with mutation are borderline cognitive dysfunction
- Individuals with a deletion have significantly lower IQ scores and adaptive functioning than those with a NSD1 mutation

# Cognitive

- Lane et al. (2019) suggested that SS has a specific cognitive profile - verbal higher than nonverbal, quantitative reasoning a specific weakness, visuospatial memory a specific strength
- Foster et al. (2019) published that more than half of adults with SS are independent for most of their ADLs and employed although most need supports for community living and working

# Prognosis/Expectations for ID

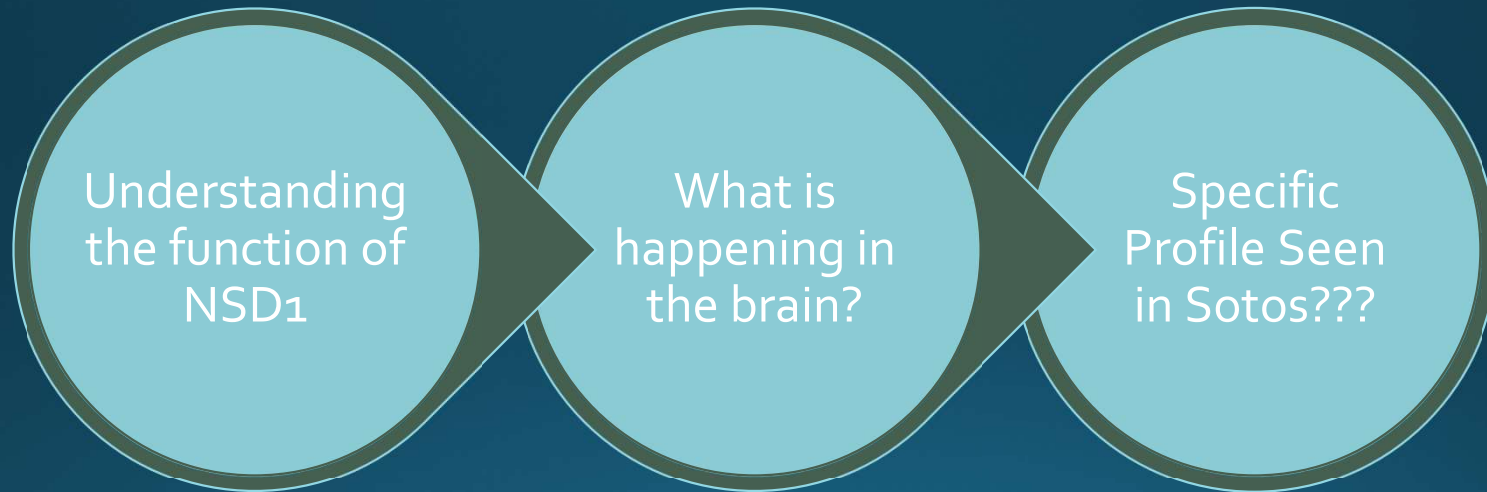
| Severity   | IQ range | Academic Potential  | Daily Living                                      | Work                              | Expected mental age as an Adult (yr) | Intensity of Support |
|------------|----------|---|---|-----------------------------------|--------------------------------------|----------------------|
| Borderline | 70-80    | 6 <sup>th</sup> grade   | Fully independent                                 | Employable ; may require training |                                      | Intermittent         |
| Mild       | 50-69    | Reading and writing to 4 <sup>th</sup> -5 <sup>th</sup> grade | Relatively independent with training              | Employable, often needs training  | 9-11                                 | Intermittent         |
| Moderate   | 35-49    | Reading to 1 <sup>st</sup> or 2 <sup>nd</sup> grade           | Dress w/o help, toileting, prepares food          | Sheltered employment              | 5-8                                  | Limited              |
| Severe     | 20-34    | Very unlikely to read or write                                | Toilet trained, help w/ dressing, signs name      | Sheltered employment              | 3-5                                  | Extensive            |
| Profound   | < 20     | None  | Rare toileting, help w/ dressing, often nonverbal | Very limited                      | <3                                   | Pervasive            |

# Behavioral Issues

- Up to  $\frac{2}{3}$  of patients with Sotos syndrome meet criteria for autism - patients with lowest cognitive functioning at highest risk
- Executive dysfunction, aggression, self-injurious behaviors, impulsivity, hyperactivity all occur at high levels in Sotos syndrome (>40%)
- Behavioral issues are often a major concern in teenage and adult years
- Foster et al study of adults demonstrated that behavioral profiles stay mostly similar from childhood and it is rare but not unheard of for new diagnoses of mental illnesses to arise
- Recent studies just this year from the Italian group suggest rate of behaviors is overall not as high as some syndromes but anxiety and ADHD are the biggest

# So What Might the Neurodevelopmental Profile Look Like in Sotos syndrome?

|                | Intellectual Disability | Language Disability | Visual-Spatial Problems | Math Problems | ADHD/ Executive Dysfunction | Anxiety | Autistic Features | Seizures | Hypotonia   |
|----------------|-------------------------|---------------------|-------------------------|---------------|-----------------------------|---------|-------------------|----------|---|
| Sotos Syndrome | + (mild to moderate)    | -                   | -                       | +             | +                           | +       | +                 | +/-      | + (usually profound in early life and mild later) |





# What Can I Do Now For My Child's Neurodevelopmental Issues?

# Educational

- Develop a good IEP targeting areas of weakness – for many Sotos syndrome kids, math and behavioral plans should be areas of focus
- Obtain good neuropsych testing specific to your child to tailor an education program. Neuropsych should be done by someone used to testing children with significant disabilities
- Handwriting circumvention
- BIP (Behavior Intervention Plan) is necessary for many children with Sotos

# Therapies

- Early involvement with Infants and Toddlers
- Physical therapy if necessary, particularly with early hypotonia
- OT to help with ADLs and fine motor tasks
- SLP to help with articulation/speech production and later with higher order language
- ABA therapy when many autistic features, CBT when higher functioning and lots of anxiety
- Always have good balance – therapy is good but also need to maintain family sanity and allow children to be children and development to take its course

# Neurologic/Medical

- High suspicion for seizures and treat if present
- We are not currently aware that one seizure medicine is better than the others for Sotos
- Although MRI frequently shows enlarged ventricles, in a child with known Sotos, hydrocephalus is exceedingly uncommon and shunting should never be done based on enlarged ventricles alone
- Low threshold to order sleep study

# ADHD

- Should be treated similarly to ADHD in other scenarios with stimulants first line for school age children
- Alpha adrenergics commonly used also
- Appropriate 504-type accommodations in school

# Anxiety

- Anxiety is incredibly common in this syndrome
- Significant anxiety can look like autism but is treated differently. Although autism is very common in Sotos as well, make sure anxiety is looked for/addressed if an autism diagnosis is considered.
- Obsessive-compulsive behaviors and perseveration very common
- SSRIs should be first line pharmacological therapy for treatment of anxiety in Sotos syndrome

# Other Behavioral Issues

- ABA therapy for autistic features
- Behavioral therapy and/or medications as needed and appropriate for aggressive or self-injurious behaviors
- Important to have a good sleep routine and hygiene

Thank you and questions??