



Fifth Annual Family Conference

DESSH Syndrome: One Neurologist's Perspective

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BEFORE WE BEGIN

Disclosure Statement



Dr. Weisenberg is a Professor of Neurology, employed by Washington University.



Financial

No financial interest, arrangement, or affiliation that would constitute a conflict of interest.



Non-financial

No non-financial arrangement or affiliation that would constitute a conflict of interest.

Neurologic Manifestations of DeSanto-Shinawi Syndrome



Low Muscle Tone

Hypotonia affecting posture & feeding



Developmental Delay

Intellectual disability spectrum



Apraxia

Difficulty planning speech & movement



Behavior Regulation

ADHD-type challenges



Epilepsy

Seen in a subset of individuals



Brain MRI Differences

Often subtle, around the ventricles

Symptoms vary in type and severity from person to person.

NEUROLOGIC MANIFESTATION

Hypotonia (Low Muscle Tone)



Tone is the tension in a relaxed muscle. **Hypotonia** means low tone — muscles feel less firm than expected at rest.

Hypotonia can be a problem in the:

Brain

Spinal cord

Peripheral nerve

Muscle itself

A thorough neurologic exam helps narrow down the source.

Functional impact can range from severe (affects walking, managing oral secretions and swallowing) to mild clumsiness.



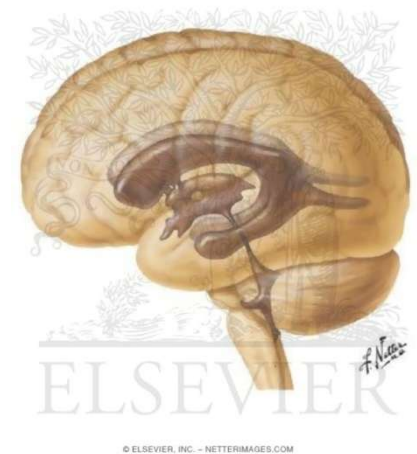
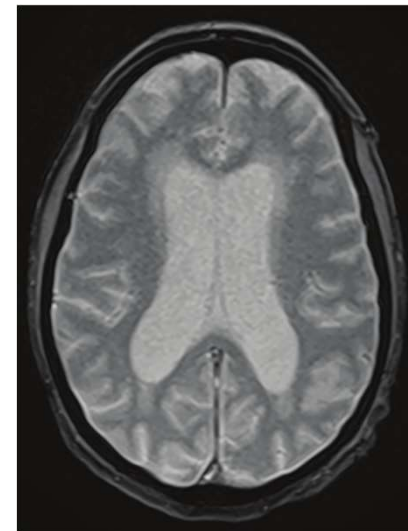
Clinical demonstration of low tone ("floppy" posture) in an infant.

NEUROLOGIC MANIFESTATION

Brain MRI Findings in DESSH



- Ventriculomegaly and/or thinned white matter are the most common findings
- Some nonspecific differences in the corpus callosum
- There is some correlation between MRI findings and severity

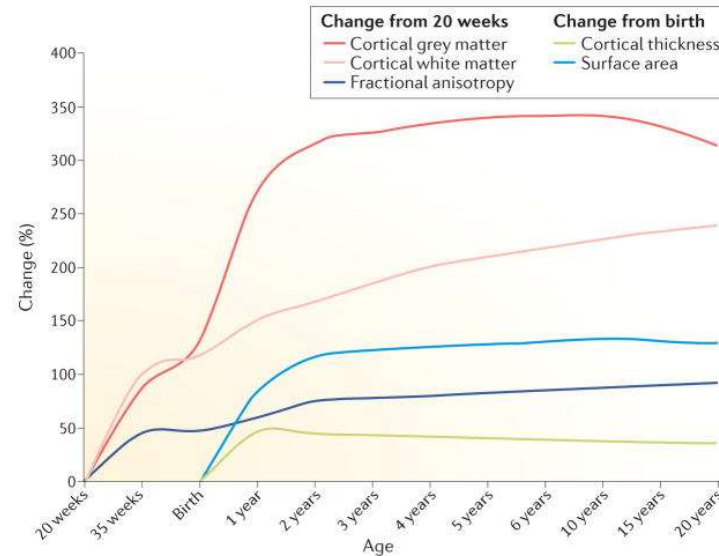


Axial MRI (left) and brain anatomy reference (right) illustrating regions commonly affected.

Considerations with Brain MRI Findings



Typical brain development changes substantially through childhood — a single MRI is a snapshot, not the whole story.



Change in cortical grey matter, white matter, surface area, and fractional anisotropy from 20 weeks gestation through adulthood.

Developmental Diagnoses — Brief Descriptions



GDD

Global Developmental Delay —
young child (<5) with delays
across multiple skill areas



ID

Intellectual Developmental
Disorder — the diagnosis GDD
often evolves into after age 5



ASD

Autism Spectrum Disorder —
differences in social
communication & behavior



Apraxia

Difficulty planning purposeful,
multi-step actions — especially
speech & fine motor

Key message: Patients with DESSH syndrome consistently improve developmentally over time. As genetic testing becomes more accessible, more individuals with milder symptoms are being identified.

Management of Developmental Disorders



MEDICATIONS



Targeted treatment

Can treat ADHD or certain harmful behaviors with medication

OPTIMIZE DEVELOPMENT



Vision & hearing

Ensure both are good



Sleep!

A cornerstone of development



Nutrition

Healthy, balanced diet; consider a multivitamin if a child is extremely picky

THERAPIES



Physical therapy



Occupational therapy



Speech therapy



Behavioral therapy



Educational supports (IEP, 504 Plan)

UNDERSTANDING THE BASICS

Seizures / Epilepsy



Seizure

A single event caused by unhealthy electrical activity in the brain.



Epilepsy

A predisposition to have seizures: 2+ unprovoked seizures, or 1 seizure with high risk of more.



The description of the episode is the most important piece of information.



EEG is helpful — but is NOT the most important factor.



Seizures are treatable (though not all require treatment).

Role of EEG (Electroencephalogram)



EEG is a test that measures electrical activity in the brain at the time of the study.

EEG CAN...

- ✓ Identify a risk of seizure
- ✓ Tell where seizures come from
- ✓ Identify specific patterns
- ✓ Help classify events IF they happen during the test

EEG DOESN'T...

- ✗ Predict the next seizure
- ✗ Tell if a seizure happened in the past

A routine EEG can only address the surface of the brain, and only the moment in time it's recorded.

When Should an EEG Be Performed?



New, abnormal spells

To help determine whether new events could be seizures



Before medication changes or weans

To establish a baseline



To capture a spell

A prolonged EEG-video (1–7 days) can be used if events occur often



When considering brain surgery

To help evaluate options for treating epilepsy

Epilepsy in DESSH Syndrome



~1/3

of patients have been reported to have epilepsy

An abnormal EEG does not, by itself, mean someone has epilepsy.

Common: Treatable with medication

Uncommon: "Refractory" epilepsy

In general, epilepsy should present in childhood — by adolescence at the latest.

Terminology



Developmental Encephalopathy

A general term for a brain condition affecting development.

VS

Developmental Epileptic Encephalopathy

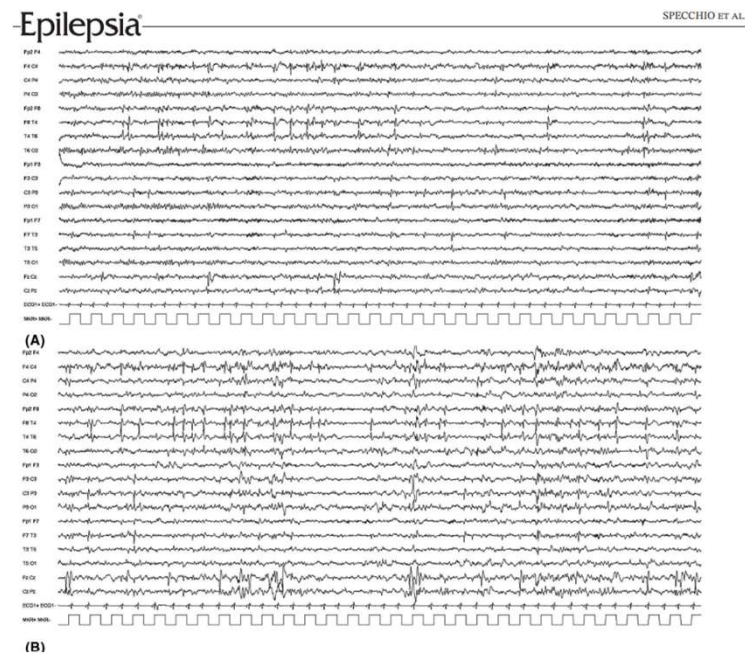
Development is affected both by the underlying condition and by ongoing epileptic activity.

EEG Data for DESSH Syndrome



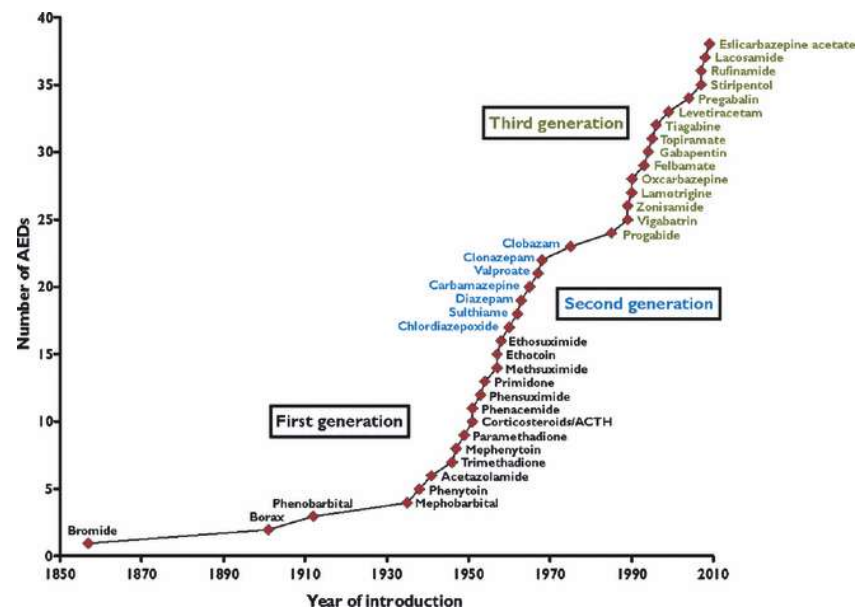
- Most common finding: focal sharp waves, particularly in the centrotemporal region
- This is a common finding across many childhood epilepsy & developmental syndromes — including SELECTS, Rett syndrome, and GRIN-related disorders
- Separate reports of ESES (now known as DEE-SWAS) have occurred in DESSH syndrome

SELECTS v. DEE-SWAS



(A) SELECTS-type pattern — focal sharp waves. **(B)** DEE-SWAS pattern — near-continuous spike-and-wave activity, especially in sleep.

A Word About Anti-Seizure Medications (ASM)



Growth in the number of available anti-seizure medications by generation, over time.

Considerations When Selecting an ASM



Type of Seizures



Epilepsy Syndrome



Side Effects



Cost



Efficacy



General principle: Thoughtfully make one change at a time, with a clear next-steps strategy.

DESSH-Specific Considerations



Typically focal seizures/epilepsy — but with some important nuances:



Sodium channel inhibitors can activate epileptiform activity.

Examples: oxcarbazepine, lamotrigine, and possibly lacosamide.



Avoid medications that may worsen negative behavioral symptoms.

Example: levetiracetam. Note — some ASMs are also mood stabilizers.



Individual responses vary significantly — your child is not one gene.

Clonazepam (Klonopin)



- Long-acting benzodiazepine
- Enhances GABA activity in the brain
- FDA approved in 1975; initial indication was epilepsy
- Prescribed for anxiety, sedation, calming aggressive behavior in psychiatric illness, and epilepsy
- Occasionally used at nighttime only, for DEE-SWAS

Clonazepam for DESSH



- If a research trial is pending, use could impact ability to participate or get clean data
- There is a range of dosing
- May affect EEG findings — an EEG including sleep should be obtained beforehand
- Understanding the full potential benefit and necessary duration of treatment will require many years of observation
- Could there be a biomarker?

THOUGHTS TO TAKE WITH YOU



Your child is not one gene.



Knowing a genetic diagnosis is a resource — not an identity.



Scientific questioning and critical thinking are key to progress and should not be a source of discouragement.

Neurologic Management in DESSH Syndrome



YOUR NEUROLOGIST



Monitors & optimizes development



Manages medications (seizures, behavior)



Connects you to therapies

ASSEMBLE YOUR TEAM



Therapists



Communicative, responsive medical team



School & community resources



Support groups

The DESSH Foundation — connect via social media and community groups.



Questions?



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