

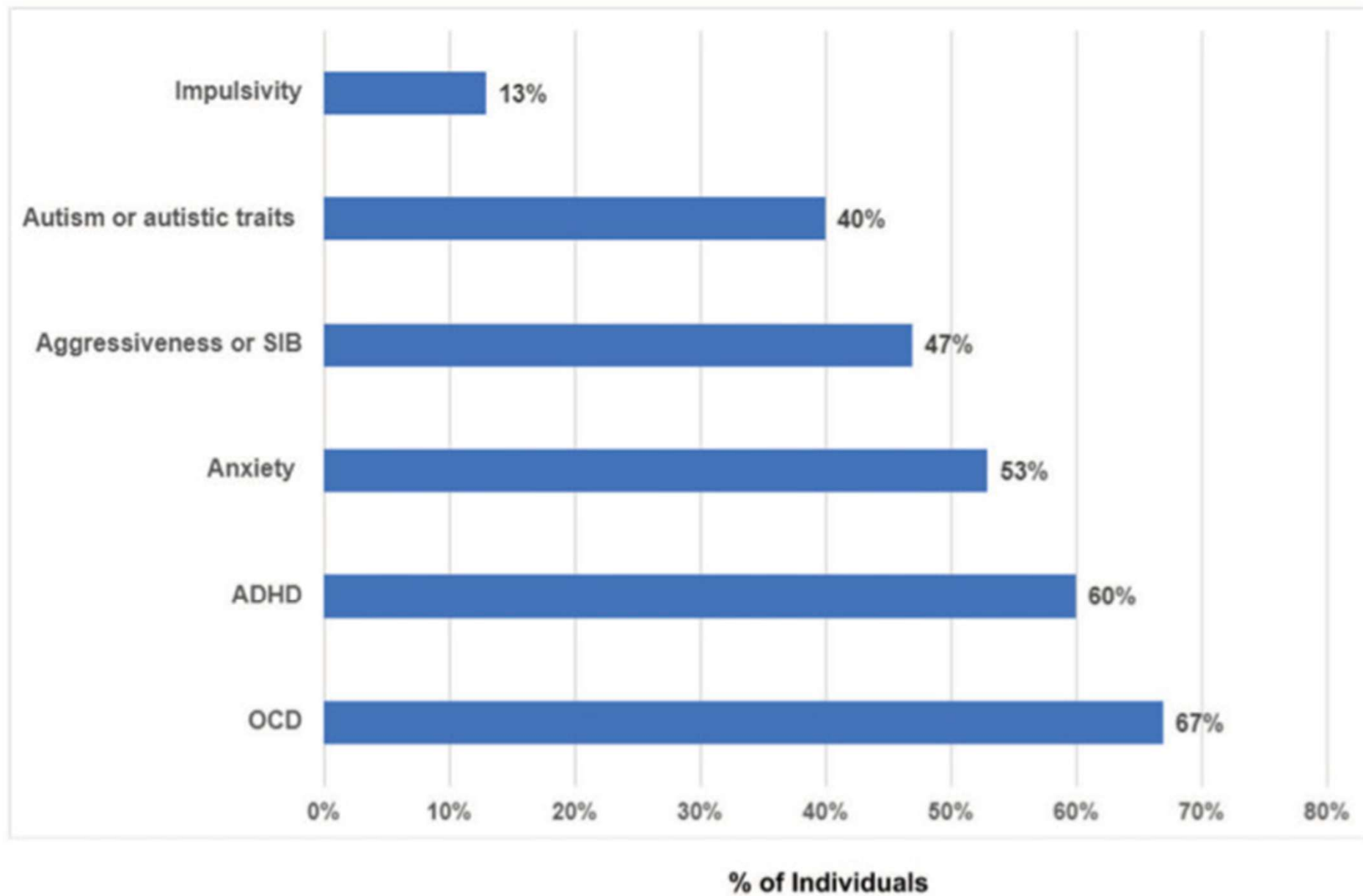
Managing Behavioral Challenges in DESSH and other Neurodevelopmental Disorders

Paul E.A. Glaser MD, PhD
Department of Psychiatry
Division of Child Psychiatry
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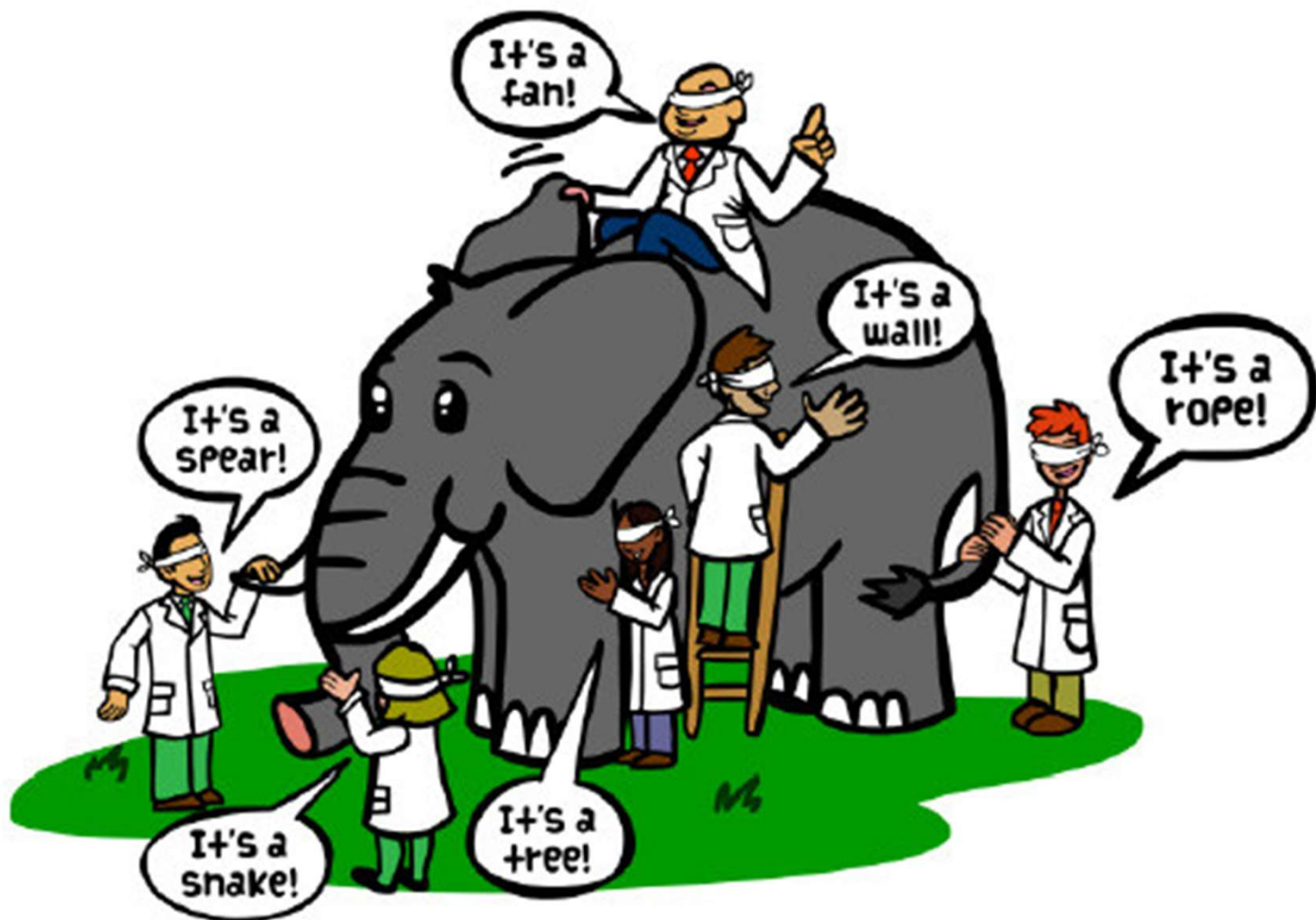
Characteristic Behavioral Troubles in DESSH

- Anxiety Disorders
- ADHD (includes impulsivity-inattention-hyper)
- Aggression
- Autism Spectrum Disorder (or features of Autism)
- Mood Swings (now called DMDD - Disruptive Mood Dysregulation Disorder)



Reynolds M, Weisenberg J, Shinawi M, Jensen R.
Mo Med. 2024 Jul-Aug;121(4):304-309.

Core Behavioral Problem?



Formal Behavioral Management

Parent training in behavior management

ADHD

Disruptive behavior disorders (DMDD, ODD)

Child behavior therapy

ADHD

Disruptive behavior disorders

Cognitive-behavior therapy

Disruptive behavior disorder

Depression, Anxiety, and PTSD

Applied Behavior Analysis (ABA Therapy)

- Rooted in behavioral techniques originally described by B.F. Skinner
- Should be overseen by Board-Certified Behavioral Analysts (BCBAs) and implemented by Registered Behavioral Therapists (RBTs)
 - Systematically observes, describes, and assesses behaviors
 - Works with the patient and family on finding reliable rewards
 - Devises plan to shape behaviors that lead to safer outcomes
- Wide range of evidence supporting its utility
- **Usually requires diagnosis of Autism in USA**

Parent-Child Interaction Therapy

- Indicated for ADHD and oppositional behaviors/emotion dysregulation
- Parent training, typically “coached” by therapists who are observing through “bug in the ear”, video feedback sessions
- Works to establish warmth between parent and child, in addition to approaching problem behaviors and interactions
- Does require higher communication capacity than ABA

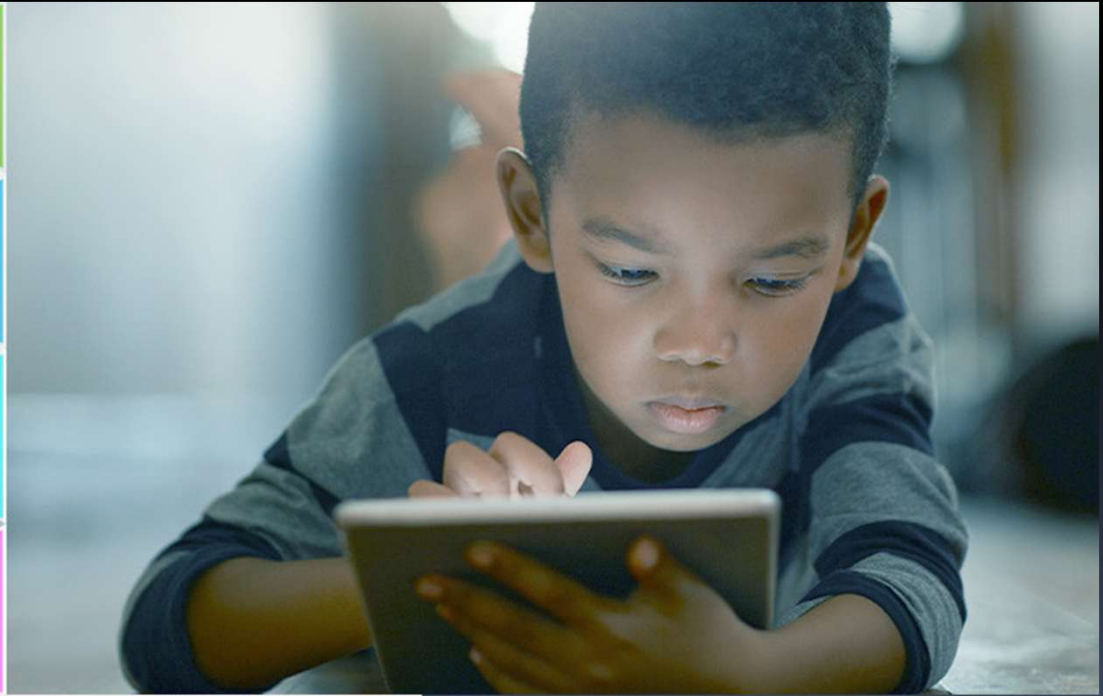


Add-Ons to Behavioral Management

- When Sensory Issues are a Trigger for Extreme Behaviors:
 - Occupational Therapy
- When Communication Issues are a Trigger for Extreme Behaviors:
 - Speech Therapy
 - Assistive-Communication Devices
- Dispelling Energy
 - Physical Therapy
 - Sports, Outdoor exercise

What about “stimming” behaviors?

Ipad Therapy?



Practical Behavioral Management

- Most families want to know if there are best ways to respond to certain behaviors

ECLECTIC THERAPY - aka, try interventions that have worked for other families and see if they work for your child

- Support Groups - How have other families dealt with the behaviors unique to DESSH syndrome
- Book Therapy - Find a Parenting advice book with a method that resonates with your philosophy of parenting (or that works for your child)

Practical Behavioral Management

- One Method “Raising Your Spirited Child”
 - 1) You’re Not Alone
 - 2) You Did Not Make Your Child Spirited
 - 3) You are Not Powerless
 - 4) You Have Permission To Take Care of Yourself
 - 5) You May Celebrate and Enjoy the Delights of Your Spirited Child

Introduces useful idea - “Choose your battles”

What about behavioral troubles as a teen or as an adult?

Will they ever be independent? Who will take care of my child when I am older?

What is the possible reason?

- Hannah C Rudolph et al. Biology (Basel). 2023 Apr 12;12(4):589. Structure-Function of the Human WAC Protein in GABAergic Neurons: Towards an Understanding of Autosomal Dominant DeSanto-Shinawi Syndrome
- This would suggest that dysfunction in GABA neurons may lead to a hyperglutaminergic state in DESSH

What is the possible reason?

- Nishikawa, Med Mol Morphol. 2023 Dec;56(4):266-273. Expression analyses of WAC, a responsible gene for neurodevelopmental disorders, during mouse brain development
- Expression was found in the brain in cortical, hippocampal, and cerebellar areas during critical periods of early brain development
- This would suggest that dysfunction in DESSH is likely due to an alteration in brain development that would affect development of brain structures involved in behavioral control, emotional control, reward and memory circuits, focus, and balance

What is the possible reason?

- Lee, Vogt et al. bioRxiv, [Preprint]. 2024 May.
- Complimentary vertebrate Wac models exhibit phenotypes relevant to DeSanto-Shinawi Syndrome
- This would suggest that dysfunction in GABA neurons may lead to a hyperglutaminergic state in DESSH (Dr. Glaser's unproven hypothesis)
- Memory deficits (Dr. Glaser would suggest that behavioral interventions might have limited success)

When should we consider medications?

If Anxiety/Mood Is a Problem?

- Try SSRI (selective serotonin reuptake inhibitor)
 - Zoloft (sertraline)
 - Prozac (fluoxetine)
 - Lexapro (escitalopram)
 - Celexa (citalopram)
 - Luvox (fluvoxamine)

May also help a little with OCD/rigidity symptoms

- Others
 - Cymbalta (duloxetine)
 - Effexor (venlafaxine)
 - Pristiq (desvenlafaxine)
 - Buspar (buspirone)

If Aggression Is Severe

- Atypical Antipsychotics
 - Risperdal (risperidone) FDA approved for Autism
 - Zyprexa (olanzapine)
 - Seroquel (sertraline)
 - Geodon (ziprasidone)
 - Abilify (aripiprazole) FDA approved for Autism
 - lurasidone (Latuda)
 - cariprazine (Vraylar)
- Others
 - Naltrexone (Revia) - mostly for repetitive self-harm
 - Lithium
 - Amantadine

If Impulsivity/Attention Is a Problem

- Stimulants (sometimes do not work)
 - Concerta, Metadate, Ritalin., Focalin (methylphenidate)
 - Adderall, Vyvanse (amphetamines)
- Clonidine (clonidine)
- Tenex (guanfacine), Intuniv
- Strattera (atomoxetine)
- Wellbutrin (bupropion)

- Memantine (Namenda)

Anti-Seizure Medications That Modulate Glutamate/GABA balance

- Lamictal (lamotrigine)
 - Topamax (topiramate)
 - Trileptal (oxcarbazepine)
 - Depakote (valproic acid)
 - Tegretol (carbamazepine)
 - Neurontin (gabapentin)
 - Klonopin (clonazepam)
- These or many other anti-seizure medications such as levetiracetam (Keppra) may be used for your child's seizure disorder - may worsen or improve behavior

Sleep Troubles

- Do they need a sleep study?
- Good Sleep Hygiene
- Bedtime Routine
- Melatonin (regular or time-release)
- Clonidine
- diphenhydramine (Benadryl)
- Older children (or difficult to treat sleep troubles)
- Trazodone
- Mirtazapine (Remeron)
- Quetiapine (Seroquel)
- Benzodiazepines (Clonazepam)

Repurposed Medication Trials

USA

- DESSH Foundation remains in regular communication with the team at Mayo Clinic
- Receives funding from Cures Within Reach

UK

- Rare People - (www.rarepeople.org) is funding
- Guy's and St Thomas' Hospital in London.

The Best “Medications”

- Structure
- Sameness
- Predictability
- Keeping Promises
- Simplicity
- Family Focus
- Consistent Discipline

Questions?

