

LEARNING PROBLEMS AND NEUROBEHAVIORAL DISORDERS IN DUCHENNE

Duchenne ACTT NOW Conference

Melbourne, March 8 – 9, 2020

JAMES POYSKY, PHD

Clinical Assistant Professor

Baylor College of Medicine



Baylor
College of
Medicine®

OUTLINE

1) Causes

2) Learning Problems

- ▶ General Learning Problems
- ▶ Specific Learning Disorders
 - ▶ Dyslexia
 - ▶ Dyscalculia
 - ▶ Dysgraphia

3) Neurobehavioral Disorders

- ▶ Externalizing
- ▶ Internalizing

4) What to do about it

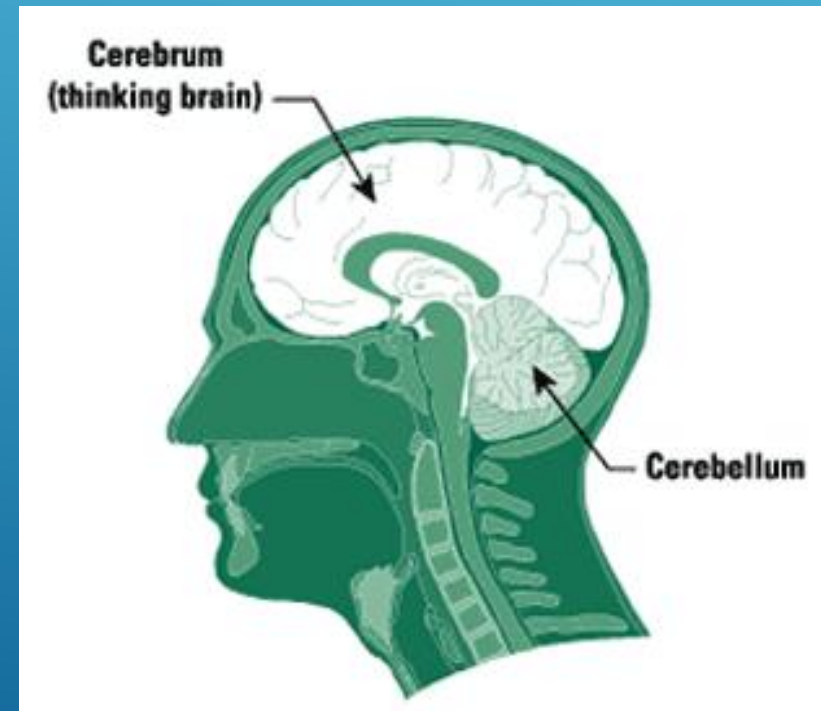
POTENTIAL CAUSES

- Psychological
 - Coping with DMD
 - Psychosocial Factors
 - Family stress/conflict
 - Parenting
 - Peer interactions
 - Teachers/adults
 - **DMD impact on brain functioning**
 - Medical factors
 - Steroids
 - Fatigue/sleep
 - Medical procedures
 - Blood sugar
- 

FULL- LENGTH DYSTROPHIN (DP 427)

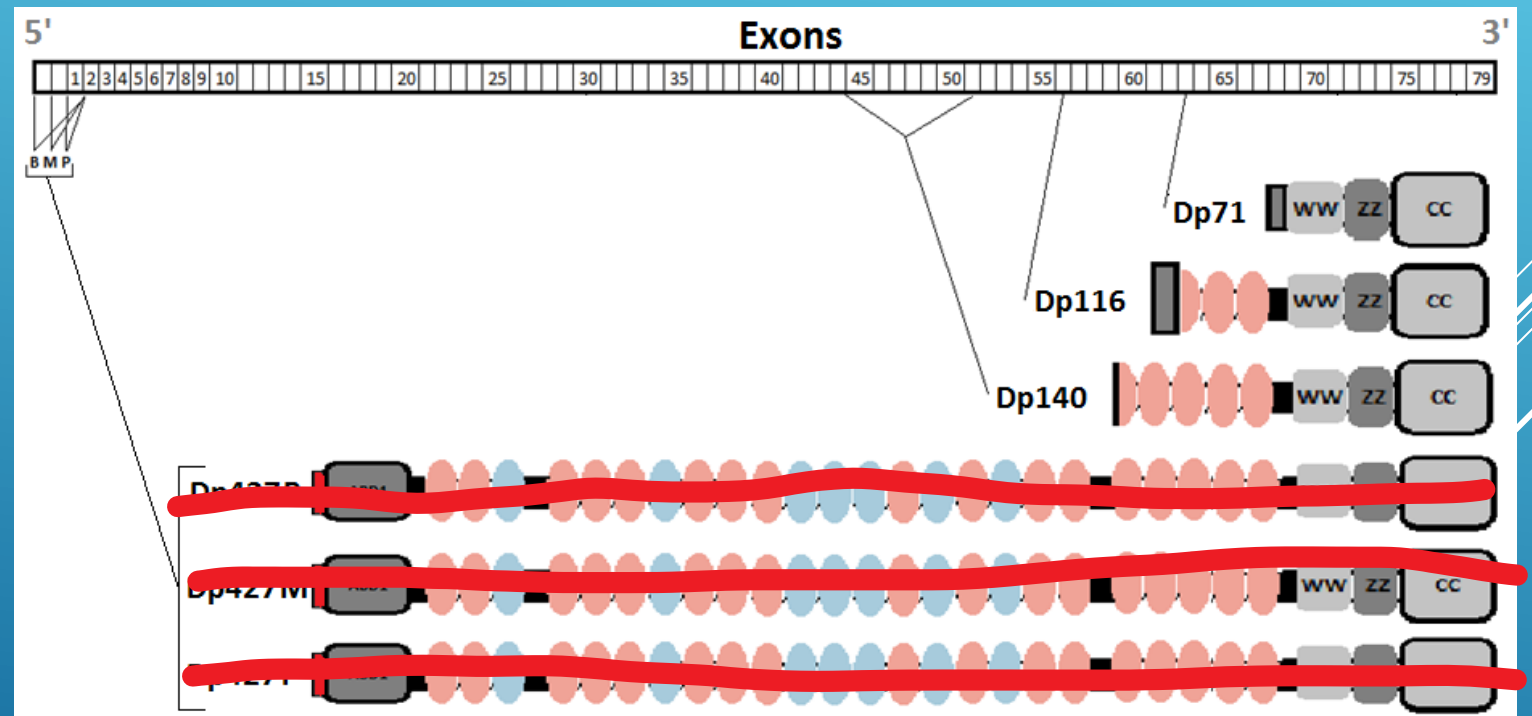
Usually found in different brain areas:

- ▶ Cerebral cortex
- ▶ Subcortical structures
- ▶ Hippocampus
- ▶ Cerebellum – Purkinje Cells
- ▶ GABA neurons – primary inhibitory mechanism of brain
- ▶ Also glutamate, acetylcholine, NMDA



DYSTROPHIN IN THE BRAIN

- ▶ Everyone with DMD is missing Dp427



MISSING DYSTROPHIN IN THE BRAIN

▶ Neurons

- ▶ Ion channels not clustered correctly
 - ▶ less efficient in sending signals to each other
 - ▶ less ready for new signals
- ▶ Changes in shape and size
- ▶ Fewer neurons
- ▶ Less new “connections”

▶ Structural

- ▶ Blood brain barrier less “tight”
- ▶ Smaller grey matter
- ▶ Less white matter density

▶ Functional

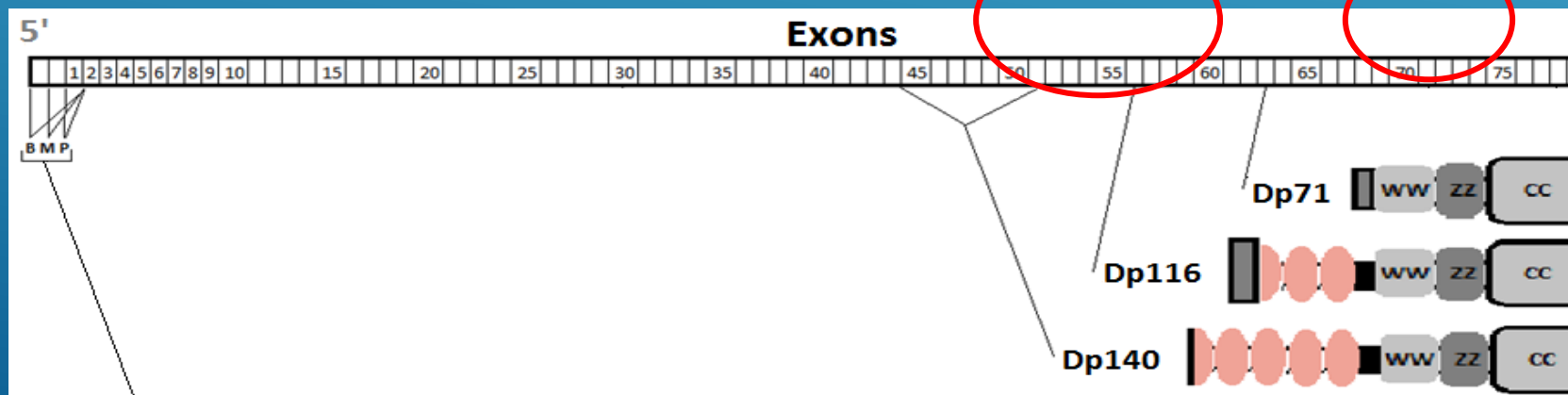
- ▶ Differences in metabolism (glucose hypometabolism) and blood flow (17% less)
- ▶ Increase in choline-containing compounds
- ▶ Higher incidence of abnormal EEG

MISSING DYSTROPHIN IN THE BRAIN

- ▶ Dp140
- ▶ Only present in fetal brain
- ▶ 55% of mutation breakpoints occur between introns 45 - 51
 - ▶ Missing Dp140 related to smallest brain grey matter
 - ▶ Greater risk for learning/neurobehavioural problems
- ▶ Dp70
- ▶ Mutations in exons ≥ 68
 - ▶ Rare
 - ▶ Also missing other dystrophin isoforms
- ▶ Associated with most severe intellectual impairments

Naidoo & Anthony 2019

Pane et al 2012

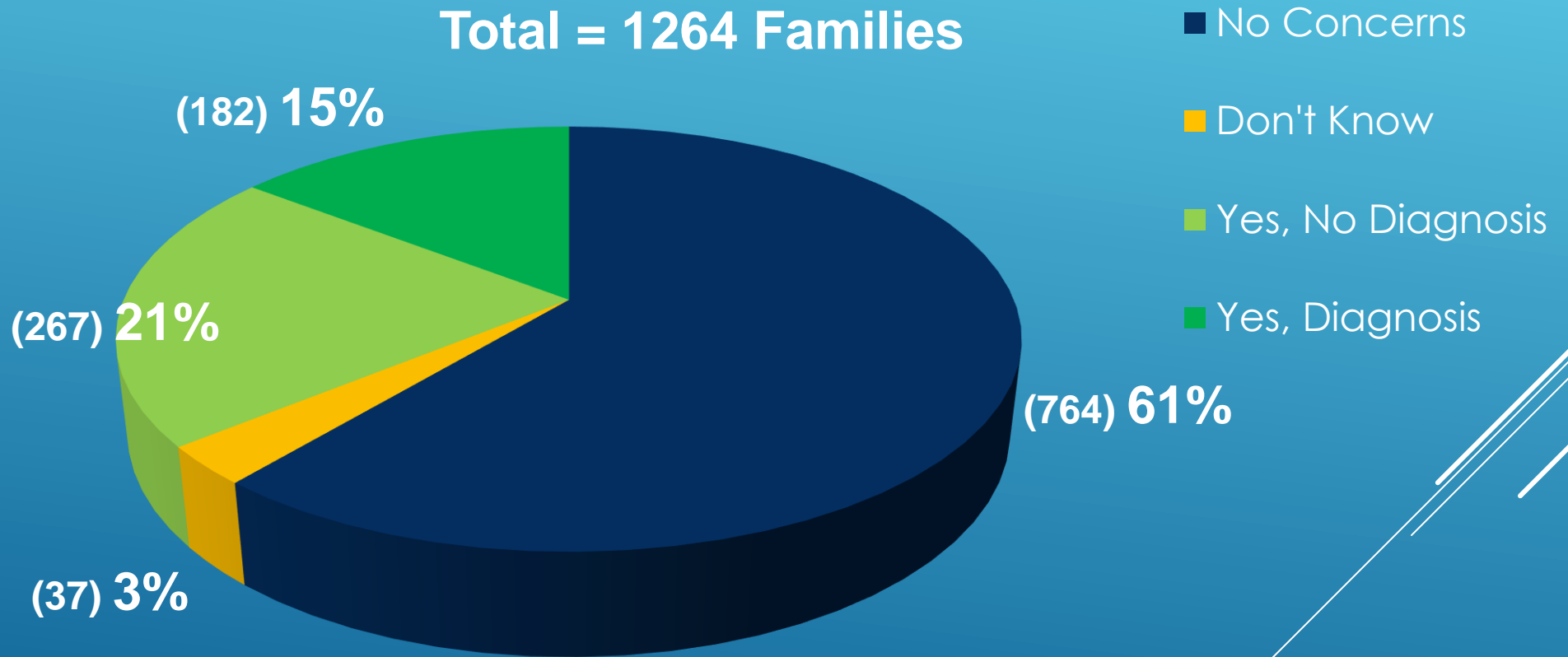


DYSTROPHIN IN THE BRAIN

- ▶ WHY DOES MY SON/DAUGHTER WITH DMD HAVE PROBLEMS WITH.....(fill in the blank)?

ANSWER: IT'S NEUROLOGICAL

LEARNING CONCERNS IN DMD



DuchenneConnect (preliminary data that may change before publication)

GENERAL LEARNING PROBLEMS: INTELLIGENCE

- ▶ Most have IQ in the normal range
- ▶ Average IQ score lower (80)
- ▶ Increased amount in the intellectual disability range (19-35% below 70)
- ▶ Verbal scores lower than visual-spatial scores

Cotton, S, N. Voudouris, and K. M. Greenwood. 2001

Cotton, S, N. Voudouris, and K. M. Greenwood. 2005.

Ricotti, Mandy, Scotto et al 2016

GENERAL LEARNING PROBLEMS: LANGUAGE

- ▶ Greater chance of delays in language development
- ▶ Greater problems in younger children
- ▶ Normal vocabulary
- ▶ Problems with:
 - ▶ complex comprehension and verbal fluency
 - ▶ About two years behind

Cyrluk, S.E., Fee, R., Batchelder, A., Kiefel, J., Goldstein, E., & V.J. Hinton. 2008;

Cyrluk, S., Fee, R., De Vivo, D.C. & V. J. Hinton.. 2007

GENERAL LEARNING PROBLEMS: SHORT-TERM MEMORY

- ▶ Weaknesses in short-term memory
 - ▶ Worst for verbal information
 - ▶ Pattern seen at all IQ levels and ages

Hinton, V. J., N. E. Nereo, D. C. DeVivo, E. Goldstein, and Y. Stern. 2000.

Hinton, V. J., N. E. Nereo, D. C. DeVivo, E. Goldstein, and Y. Stern. 2001.

Hinton V. J. , Fee R., Goldstein, E.& D.C. De Vivo. 2007.

SPECIFIC LEARNING DISORDERS IN DMD

- ▶ About 40% have one or more learning disorders:

Dyslexia: Difficulty learning to read

Dyscalculia: Difficulty learning math

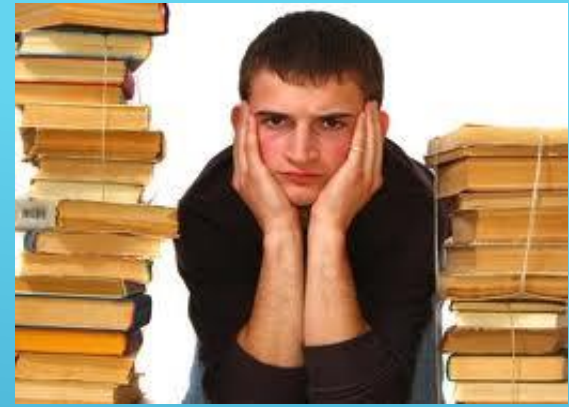
Dysgraphia: Difficulty with writing

SPECIFIC LEARNING DISORDERS: DYSLEXIA

- ▶ It is NOT a visual problem!
- ▶ It IS a sound problem!
 - ▶ Phonological processing
 - ▶ Understanding that small sounds make up the words we speak
 - ▶ Ability to manipulate those sounds
 - ▶ Word decoding
 - ▶ Matching sounds with letters and letter groups
 - ▶ Recognizing patterns that make syllables and words
 - ▶ Blending sounds together to make words
 - ▶ Making these skills fast and “automatic”

SIGNS OF DYSLEXIA

- ▶ Difficulty learning letter names/sounds
- ▶ Difficulty “sounding out” words
- ▶ Looking at the first few letters and guessing at the rest
- ▶ Dropping word endings while reading
- ▶ Adding words
- ▶ Tries to memorize how a word looks (sight-word strategy)
- ▶ Spelling problems
- ▶ Slow reading speed
- ▶ Poor comprehension
- ▶ Hates reading



- ▶ Problems in 3 main areas

- ▶ Math concepts

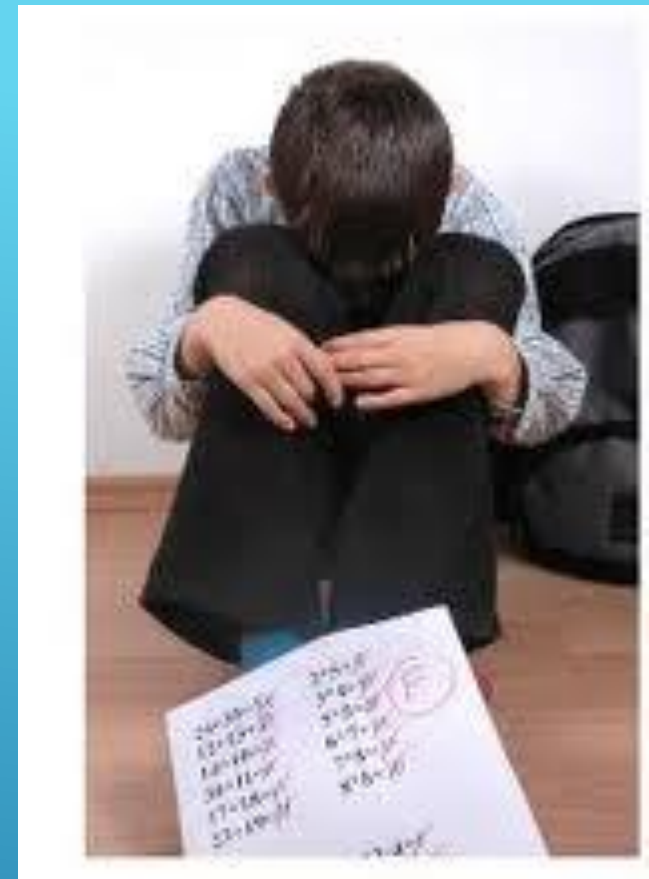
- ▶ symbolic relationships, seeing patterns, estimating value, “visualizing” the problem, identifying key information

- ▶ Math operations

- ▶ remembering the correct steps, internal number line


- ▶ Speed for math facts

- ▶ memorizing facts, becoming quick and “automatic” instead of counting on fingers



SPECIFIC LEARNING DISORDERS: DYSCALCULIA

DYSGRAPHIA IN DMD

- ▶ Can have problems in 3 main areas:
 - ▶ Fine motor (letter formation/spacing, speed)
 - ▶ Writing mechanics (grammar, punctuation, spelling, capitalization)
 - ▶ Topic/content (generating, organizing, and sequencing ideas)
- 
- A decorative graphic consisting of several parallel white lines of varying lengths, slanted upwards from left to right, located in the bottom right corner of the slide.

- ▶ Anxiety related to specific subject
- ▶ Shutting down, overwhelmed
- ▶ Frustration, exploding
- ▶ Poor performance relative to other subjects
- ▶ Says “I hate _____!” (reading, math, writing)

OTHER SIGNS OF A LEARNING DISORDER

NEUROBEHAVIORAL DISORDERS

- ▶ Behavior and emotional problems that are believed to be related to brain (dys)function.
- ▶ Most people with DMD have at least one of these problems (73%), and 2/3 have more than one*.

Darmahkasih, Rybalsky, Tian, Shellenberger, Horn, Lambert, & Wong 2020

Ricotti, Mandy, & Scoto 2016

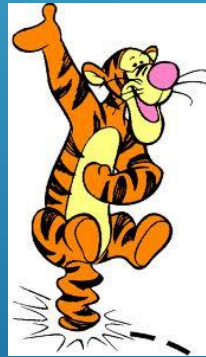
* Including learning and language delays.

NEUROBEHAVIORAL DISORDERS IN DMD

Attention-deficit disorder: 12% – 44% in DMD
(with or without hyperactivity-impulsivity)

Signs to look for:

Impulsive
Blurts things out
Interrupts
Impatient
Fidgets
Easily frustrated
Too loud



Avoids work
Overly focused on fun
Easily distracted
Messy and disorganized
Forgetful
Daydreams
Difficulty following directions



NEUROBEHAVIORAL DISORDERS IN DMD

Oppositional, argumentative, & explosive behavior:
15% - 52% of boys with DMD?

- ▶ Rigid expectations
- ▶ Difficulty adjusting to unexpected outcomes
- ▶ Argues often
- ▶ Easily irritated, angry outbursts
- ▶ Blames others
- ▶ Hard time predicting consequences
- ▶ Keeps making same mistakes
- ▶ Punishment increases anger and escalates outbursts

NEUROBEHAVIORAL DISORDERS IN DMD

Oppositional, argumentative, & explosive behavior:
15% - 52% of boys with DMD?

- ▶ Rigid expectations
- ▶ Difficulty adjusting to unexpected outcomes
- ▶ Argues often
- ▶ Easily irritated, angry outbursts
- ▶ Blames others
- ▶ Hard time predicting consequences
- ▶ Keeps making same mistakes
- ▶ Punishment increases anger and escalates outbursts



NEUROBEHAVIORAL DISORDERS IN DMD

Oppositional, argumentative, & explosive behavior:
15% - 52% of boys with DMD?

- ▶ Rigid expectations
- ▶ Difficulty adjusting to unexpected outcomes
- ▶ Argues often
- ▶ Easily irritated, angry outbursts
- ▶ Blames others
- ▶ Hard time predicting consequences
- ▶ Keeps making same mistakes
- ▶ Punishment increases anger and escalates outbursts

NEUROBEHAVIORAL DISORDERS IN DMD



Autism: 3-21%
Signs to look for:

- ▶ Delayed language development
- ▶ Excessive and unusual interests/obsessions and routines
- ▶ **Impaired understanding of social interactions**

Wu et al. 2005; Hendriksen & Vles, 2008; Darke, Bushby, Le Couteur, McConachie, 2006; Hinton et al 2009; Ricotti et al 2015

- ▶ INCREASED RISK OF ANXIETY
- ▶ Generalized Anxiety
 - ▶ Worrying, stressing, feeling tense, about what might happen or has already happened
 - ▶ May seek reassurance from others repetitively
 - ▶ Too hard on themselves for mistakes
 - ▶ Keep replaying things in their mind
 - ▶ Has to know what is going to happen
 - ▶ Changes from day to day
 - ▶ Associated with being rigid/stubborn in thought process

NEUROBEHAVIORAL DISORDERS IN DMD

- ▶ INCREASED RISK OF ANXIETY

- ▶ Social Anxiety

- ▶ Very shy, uncomfortable around people they don't know well
- ▶ Avoids eye contact, won't say much, may ignore other's when they say "What's up?"
- ▶ Worried about others watching/judging them
- ▶ Afraid they will do/say something embarrassing
- ▶ Avoid/leave situations where they might have to interact
- ▶ Use electronics so they don't have to have conversations

NEUROBEHAVIORAL DISORDERS IN DMD

- ▶ INCREASED RISK FOR ANXIETY
- ▶ Obsessive-Compulsive Disorder
 - ▶ Rituals and excessive routines
 - ▶ Very particular about things being even, lined up, etc.
 - ▶ Repetitive behaviors
 - ▶ Intrusive thoughts/images
 - ▶ Too sensitive to how things feel

NEUROBEHAVIORAL DISORDERS IN DMD

“HANGRY” = Hungry + Angry

- ▶ Blood sugar starts to drop
 - ▶ Angry
 - ▶ Irrational
 - ▶ Mean/aggressive
 - ▶ Emotionally sensitive/labile
- ▶ Don't feel hungry
- ▶ Blood sugar may still technically be in the normal range




LEARNING AND BEHAVIOR TREATMENT RECOMMENDATIONS

Bushby K, Finkel R, Birnkrant DJ, Case L, Clemens P, Cripe L, Kaul A, Kinnett K, McDonald C, Pandya S, Poysky J, Shapiro F, Tomezsko J, Constantin C, DMD Care Considerations Working Group. [The diagnosis and management of Duchenne muscular dystrophy – part 1. Diagnosis, pharmacological and psychosocial management.](#) The Lancet Neurology 2010;9(1):77-93.

David J Birnkrant, Katharine Bushby, Carla M Bann, Susan D Apkon, Angela Blackwell, Mary K Colvin, Linda Cripe, Adrienne R Herron, Annie Kennedy, Kathi Kinnett, James Naprawa, Garey Noritz, James Poysky, Natalie Street, Christina J Trout, David R Weber, Leanne M Ward. [Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan](#) The Lancet Neurology Published online: January 23, 2018

Colvin MK, Poysky J, Kinnett K, Damiani M, Gibbons M, Hoskin J, Moreland S, Trout CJ, Weidner N. [Psychosocial Management of the Patient with Duchenne Muscular Dystrophy](#) Pediatrics 2018 12(s2) – In Press

TREATMENT RECOMMENDATIONS

- ▶ Effective treatments! Same as for people without DMD
 - ▶ Don't wait if you have concerns
 - ▶ Mental health professional
 - ▶ Does not need to be “expert” in DMD
 - ▶ Willing to learn from, and listen to, patient, parents and other professionals
 - ▶ It is helpful if they have worked with other medical conditions
- 

LEARNING PROBLEMS: WHAT CAN I DO ABOUT IT?


PREVENTION (so it doesn't become a problem)

INTERVENTION (trying to fix the problem)

ACCOMMODATION (minimizing the impact)

MODIFICATION (changing teaching and/or evaluation methods)



- ▶ Evaluations
 - ▶ Neuropsychologist
 - ▶ School Psychologist
 - ▶ Special Education Case Manager
 - ▶ Psychiatrist
 - ▶ There may be more than one problem going on
 - ▶ Don't wait to see if he/she will "grow out of it"
- 
- A decorative graphic consisting of several parallel white lines of varying lengths, slanted upwards from left to right, located in the bottom right corner of the slide.

PROBLEMS AT SCHOOL

Special Education

- Individual education plan

- Interventions for learning problems

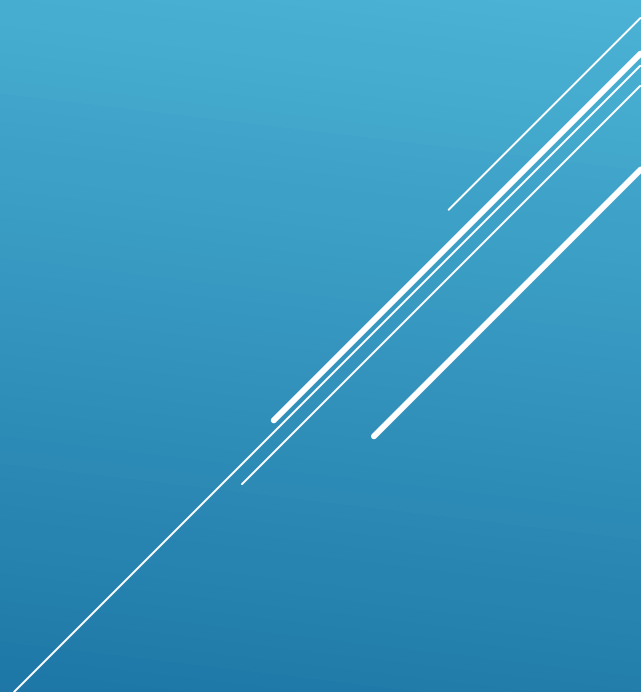
 - Tutoring, small-group instruction

 - Different teaching methods

- Behavioral support plans

 - Special reward systems

- Accommodate physical limitations



Psychotherapy

- ▶ **Parental behavior management training**
 - ▶ Noncompliance, disruptive behavior, temper meltdowns
- ▶ **Individual therapy**
 - ▶ Low self-esteem and depression, anxiety, obsessive-compulsive disorder, coping
- ▶ **Group therapy**
 - ▶ Social skills deficits
- ▶ **Applied Behavior Analysis**
 - ▶ Autism

NEUROBEHAVIORAL TREATMENT
RECOMMENDATIONS

TREATMENT RECOMMENDATIONS

Psychiatric Medication

- ▶ Remember, it is neurological!
 - ▶ Stimulants or alpha-agonists for ADHD
 - ▶ SSRI's for anxiety, depression, emotional reactivity

Ritalin + Prozac combination becoming more common



ADDITIONAL RESOURCES:

[Save Our Sons Teacher Resource Guide \(2017\)](#)

treat-nmd.eu

TREAT NMD: Family Care Guidelines

parentprojectmd.org

“DMD Learning and Behavior Guide” (Poysky)

“Psychology of Duchenne” (Hendriksen)

A Guide to Duchenne Muscular Dystrophy: Information and Advice for Teachers and Parents -Janet Hoskin – Editor. (Amazon)

The Explosive Child – Ross Greene

