# LEARNING PROBLEMS AND NEUROBEHAVIORAL DISORDERS IN DUCHENNE

Action Duchenne

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# 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

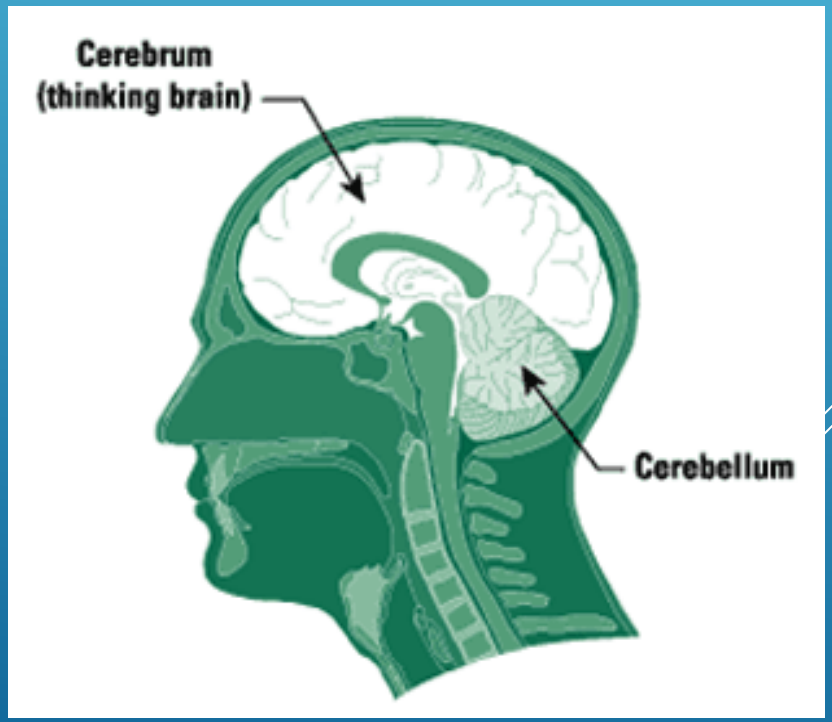
# POTENTIAL CAUSES

- 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)

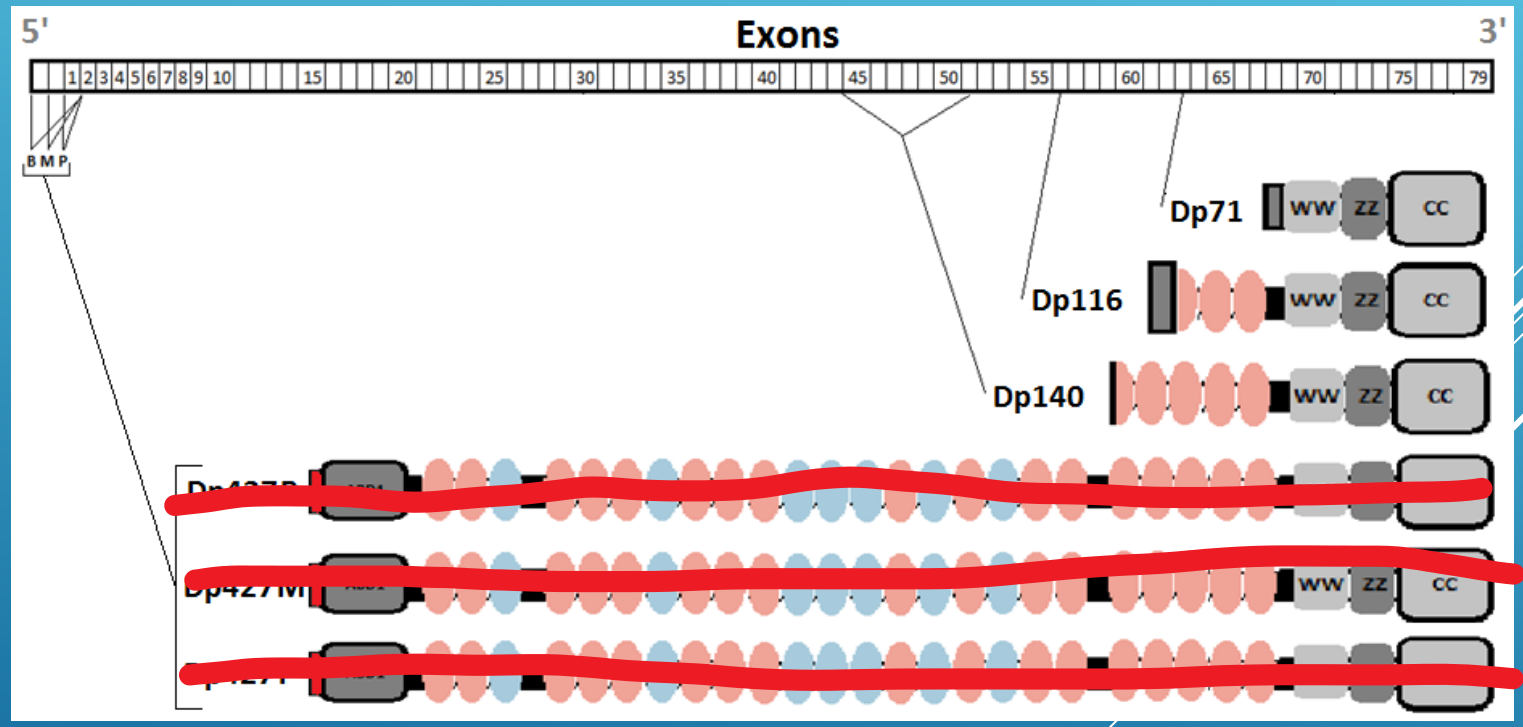
Usually found in different brain areas:

- 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

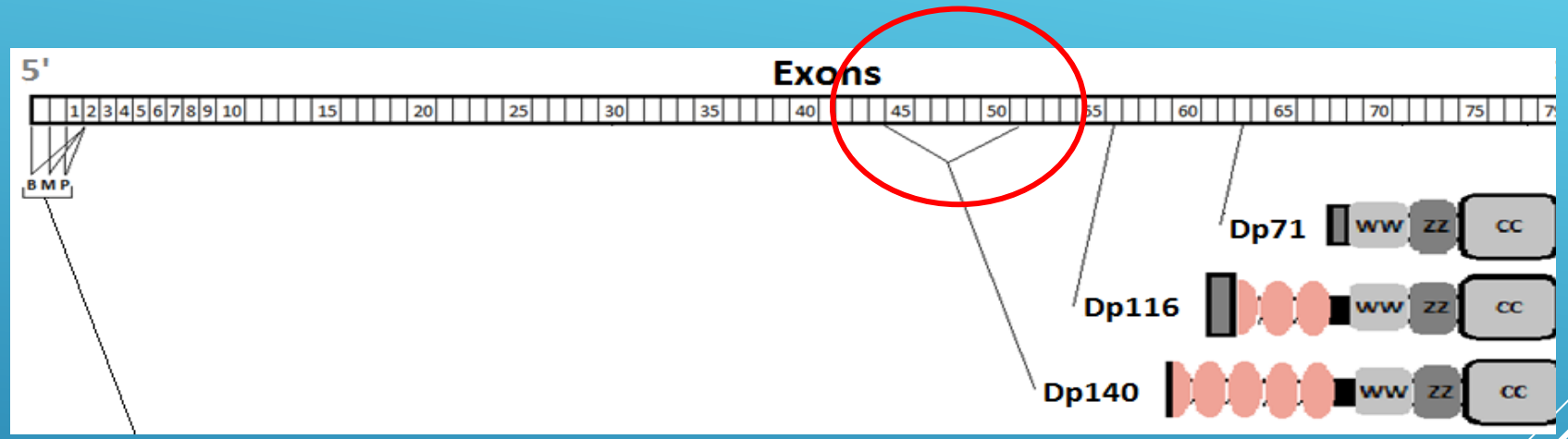
- Neurons
  - Ion channels not clustered correctly
    - less efficient in sending signals to each other
    - less ready for new signals
  - Changes in shape and size
  - Fewer neurons
  - Less new “connections”

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

- Functional
  - Differences in metabolism
  - Increase in choline-containing compounds
  - Higher incidence of abnormal EEG

Knuesel et al., 1999; Vaillend & Billard, 2002; Kueh, Head, Morley, 2008; Doorenweerd et al., 2014

# MISSING DYSTROPHIN IN THE BRAIN




- Some may also be missing smaller versions
- 55% of mutation breakpoints occur between introns 45 - 51

Pane et al 2012

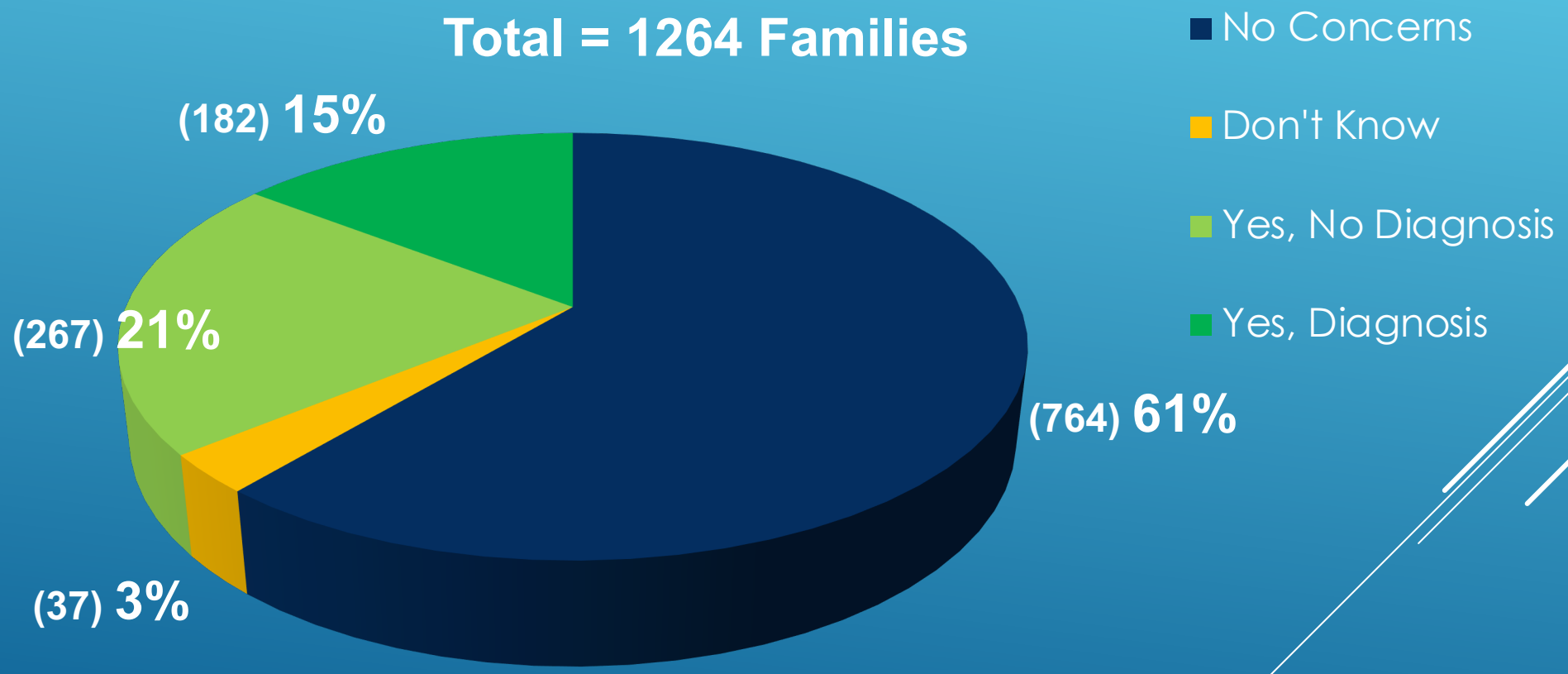
- Region for Dp140
  - Missing Dp140 related to smallest brain grey matter
  - Greater risk for cognitive/behaviour problems

# 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 (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.

# 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

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

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

# SPECIFIC LEARNING DISORDERS IN DMD

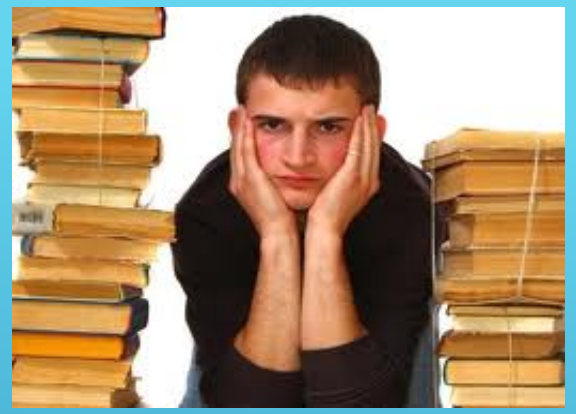
- About 40% have one or more learning disorders:
  - Dyslexia: Difficulty learning to read
  - Dyscalculia: Difficulty learning math
  - Dysgraphia: Difficulty with writing

Hendriksen & Vles 2006

# 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

# SPECIFIC LEARNING DISORDERS: DYSCALCULIA

- 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

# 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)

# OTHER SIGNS OF A LEARNING DISORDER

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

# 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

Hendriksen & Vles 2008; Poysky & Lotze, 2008; Hinton et al. 2006; Pane et al. 2012; Ricotti et al 2015

# 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/bad behavior

Poysky, Hodges, Lotze – unpublished data; Ricotti et al 2015; Conway et al 2015

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# NEUROBEHAVIORAL DISORDERS IN DMD


Autism: 3-21%
Signs to look for:

- Delayed language development
- Excessive and unusual interests/obsessions and routines, extreme sensory intolerances
- Impaired understanding of social interactions
  - Nonverbal communication (gestures, facial expressions)
  - Perspective taking/social judgement
  - Making inferences
  - Reciprocal ("back and forth") interactions
  - Social motivation

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

# NEUROBEHAVIORAL DISORDERS IN DMD

- INCREASED RISK OF ANXIETY
- Generalized Anxiety
  - Worrying 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
  - Easily stressed, overwhelmed, and agitated by unexpected events or changes in routine
    - Anxiety may come out as anger/irritability
  - Changes from day to day
  - Associated with being rigid/stubborn in thought process
  - Limited awareness of when they're feeling this way

# 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

# “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”

# 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

# NEUROBEHAVIORAL TREATMENT RECOMMENDATIONS

## 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

# 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

# COPING WITH DMD

- Talking to child about DMD
- Promoting independence
- Have high expectations
- Acknowledge challenges but focus on positives
- Clinical trials vs. family stability

- Caregiver mental health is important!
- Take time for yourself
- Ask for help
- GET INVOLVED!
- Others will not understand, but that is OK

# ADDITIONAL RESOURCES:

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