



Juvenile Huntington's Disease

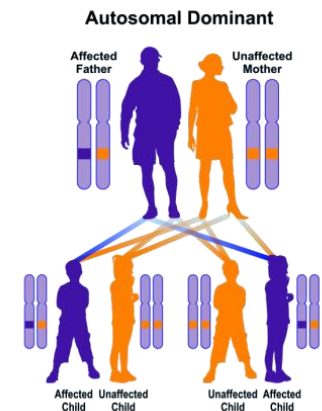
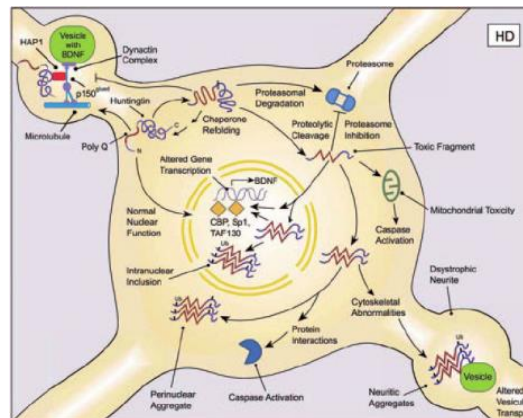
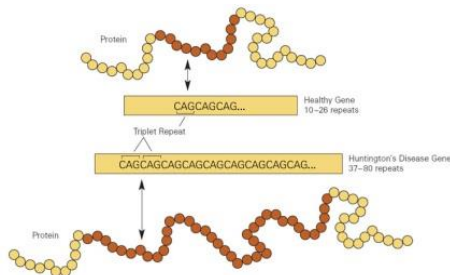
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HDSA Center of Excellence at UC Davis



Juvenile Huntington's Disease

- Genetically inherited neuropsychiatric degenerative disease
- Caused by abnormal CAG expansion of the HD gene leading to a mutated huntingtin protein which causes cellular disturbances and dysfunction
- 50/50 chance of inheriting the gene from an affected parent



Juvenile Huntington's Disease

- Symptom onset before the age of 20
- CAG repeats of > 50
- Fewer than 10% of people with HD have JHD
- Only 1-2% of people with HD have childhood onset before the age of

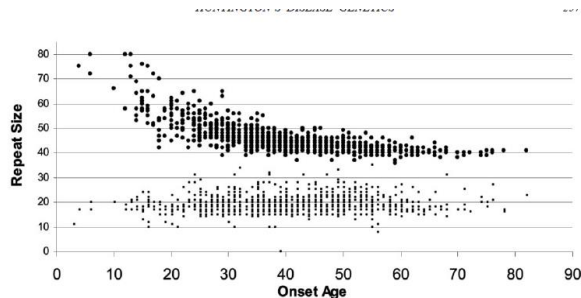


FIG. 3. HD repeat size and onset age. The relationship between the repeat size and the age at onset is presented. Persons with repeats of 60 or larger commonly have very young onset, before the age of 20, and among these large repeats there is a clear relationship between repeat size and onset age. For persons with 55 repeats or fewer, the relationship between repeat size and onset age is much weaker and the repeat size is not predictive of onset age.

CAG

10-26 Normal

27-35 Intermediate

36-39 Reduced penetrance

40+ Full penetrance



HD

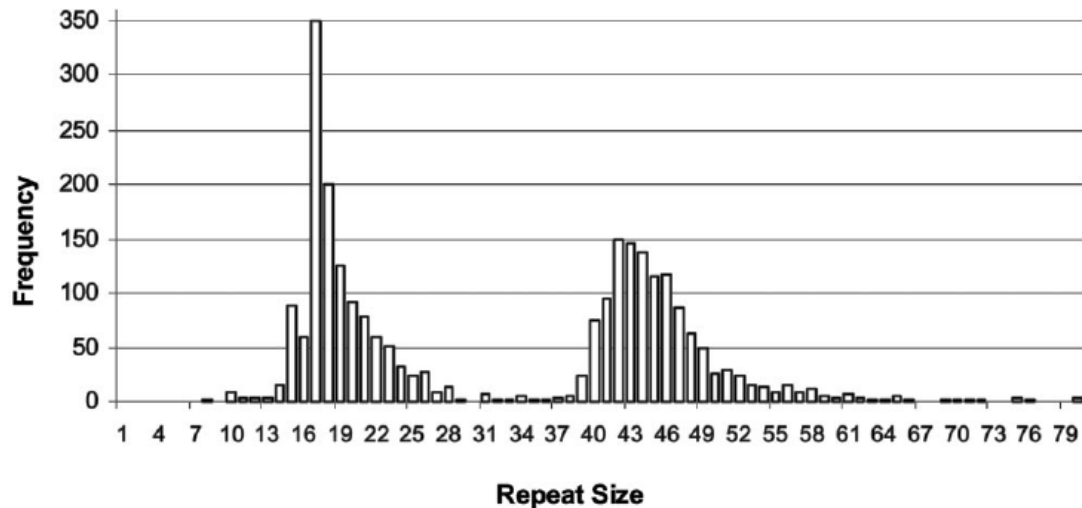


FIG. 2. Normal and expanded HD repeat sizes. The distribution of repeats for Huntington's disease may be divided into four categories. Repeats of 26 or fewer are normal. Repeats between 27 and 35 are rare and are not associated with the expression of the disease, but occasionally fathers with repeats in this range will transmit a repeat to descendants that is expanded to the range for expression of the illness. Repeats between 36 and 39 are associated with reduced penetrance whereby some individuals will develop HD and others will not. Repeats of 40 or larger are associated with the expression of HD. Persons carrying repeats in this range will develop HD, assuming they do not die of other causes before onset.

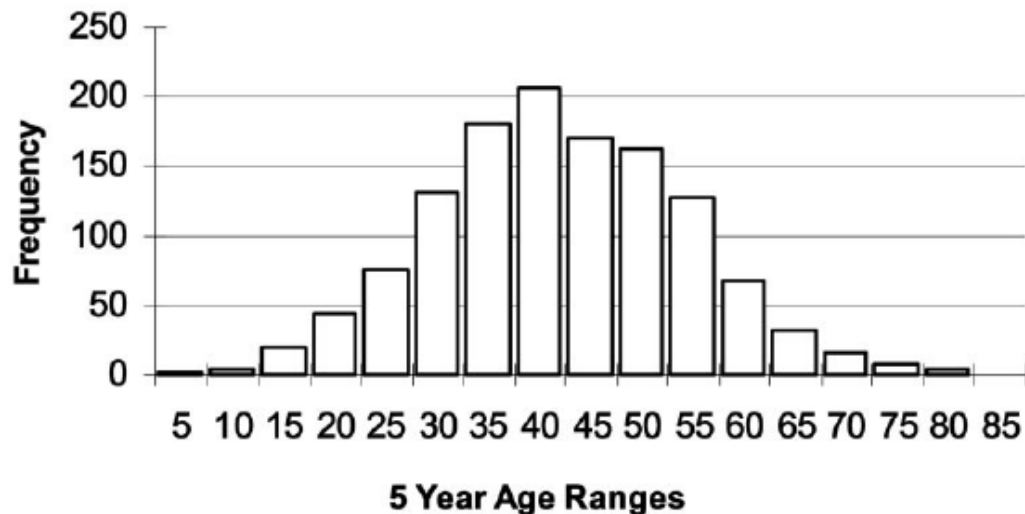


FIG. 1. Huntington's disease onset ages. The age at onset distribution in Huntington's disease is very broad and may vary from as young as 3 or 4 years of age to as old as 85. Onset presented here represents initial signs of motor impairment.

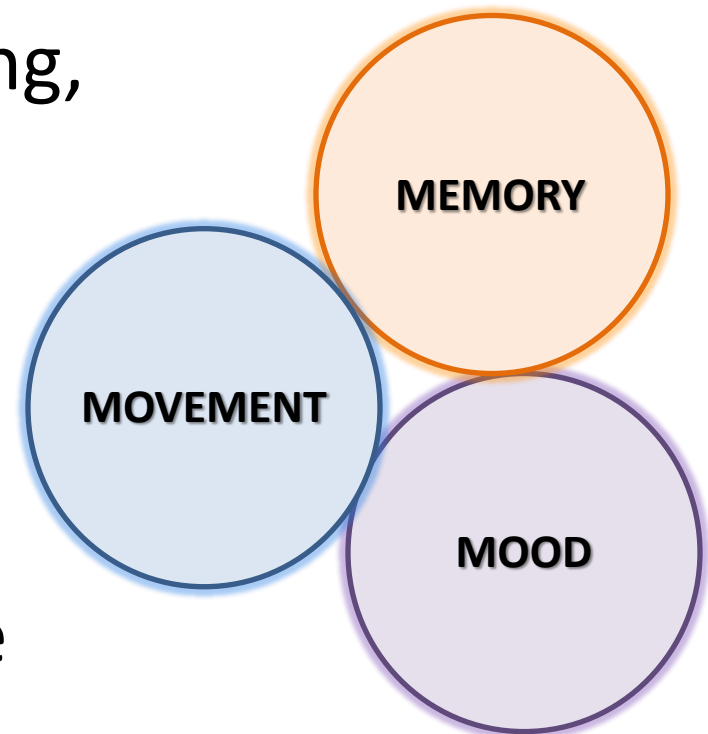
How do we get from 40 to 60?

- Mutable normal allele (27-35) and reduced penetrance
- “Mutable” gene is unstable and may undergo anticipation in that it may increase from one generation from the next
- Maternal transmission: +/- 2
- Paternal transmission: -2 to + 20 or more
- Paternal cases for most JHD cases (case reports from maternal inheritance)

HD Status	Predictive Test Result	CAG Repeat Length
Unaffected	Normal	10-26
	Intermediate	27-35
Affected	Reduced Penetrance	36-39
	Full Penetrance	40-Above

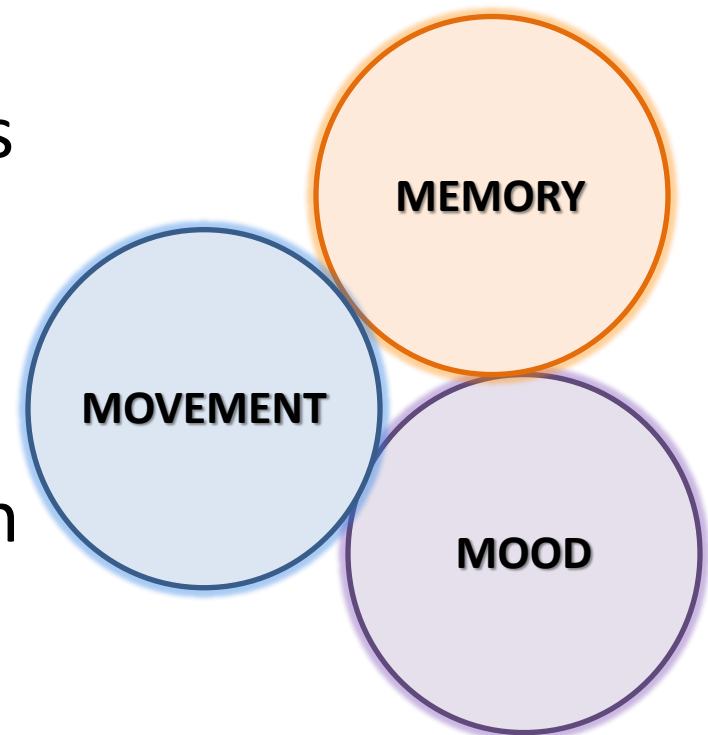
Juvenile Huntington's Disease

- Affects memory, movement and mood
- Leading to changes in thinking, difficulties with movements and psychiatric and behavioral disturbances
- Different from typical adult-onset HD, particularly a child under 10 years of age
- Unique challenges



Typical Initial Symptoms of JHD

- + family history, usually in the father
- Stiffness in the legs
- Clumsiness in the arm and legs
- Decline in cognitive function
- Changes in behavior
- Seizures
- Changes in oral motor function
- Chorea in adolescent
- Behavioral disturbances





MEMORY

- Decline in cognitive function (thinking and reasoning)
- Initially subtle following by progression
- May appear distracted, easily be overwhelmed and/or having difficulty completing tasks
- Loss of skills previously gain (milestones) and difficulty learning new skills
- Decline in school performance
- Attention and concentration difficulties
- Problems with multitasking and decision making



MOVEMENT

- Worsening of motor skills
- Changes in speech, riding a bicycle, or throwing a ball
- Rigidity or stiffness
- Dystonia (abnormal tightness and posturing)
- Difficulty walking
- Clumsiness
- Poor oral control with drooling and difficulty swallowing
- Chorea is rare but can be seen in adolescent onset



MOOD

- Psychiatric and behavioral changes
- Depression: sadness, tearful, feeling hopeless, changes in sleep, appetite, energy, and overall performance
- Attention difficulties or hyperactivity
- Hypersexuality
- Aggressiveness, impulsivity, explosive behavior
- Obsessive thinking

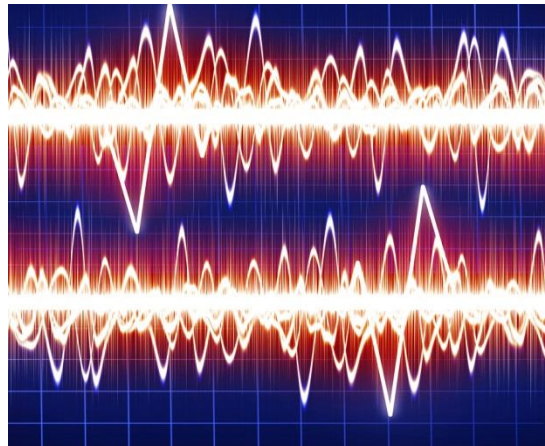


MOOD

- Affect of disease on the brain verses psychological stress of the disease
- Behaviors can be unpredictable and difficult to manage (disease verses normal changes and urges of being a teenager)
- Can lead to substance abuse (drugs or alcohol)
- Causes disruptions in family or social life

Seizures

- Can be the presenting symptom
- About 25% of children with JHD
- May be any type and differ in severity
- Babies and children can have seizures due to many other causes not related to JHD



Young Adult HD

- The young adult with features of JHD and HD
- Not everyone fits perfectly into JHD and adult onset HD
- Special attention to an individuals' presentation and particular needs
- You can be a part of both JHD and HD



Challenges in diagnosing JHD

- Many symptoms found in other conditions
 - What else could it be?
- + HD genetic testing does not necessarily mean that the symptoms are due to JHD
- Complicated family history
 - Parent not affected yet
 - Early death of a parent (before they were affected)
 - Misdiagnosis or lack of diagnosis in affected parent
 - Non-paternity
 - adoption



Evaluation for possible JHD

- Talk to your health care provider
- Seek referral or reach out to a HD Center
- What to expect:
 - Medical and neurological history
 - Family history
 - Developmental history
 - Neurological exam
 - Discussion about impression and plan
 - Do not be afraid to ask questions
 - A diagnosis of JHD takes time
 - Routine follow-up



Genetic testing?

- If the history and examination are strongly suggestive of HD then may proceed with confirmatory genetic testing
- If symptoms are not typical or exam is not clear then genetic testing should not necessarily be pursued at that time
- **GOAL:** make an appropriate and timely diagnosis while avoiding the potential risks of testing a child inappropriately or prematurely



Your Medical Team

- HD COE: Neurologist, Psychiatrist, Social Worker, Genetic Counselor, Therapist, Research Coordinator
- Therapy: Physical, occupational and speech
- Dietician
- Primary care physician
- Dental care



HDSA Center of Excellence at UC Davis

JP Roberson Foundation
Charles and Margaret Pue Foundation

HUNTINGTON'S DISEASE Center Of Excellence

OUR MISSION:

- *To provide excellent, comprehensive and compassionate care and outreach to families*
- *To provide expert education to families, researchers and health care providers*
- *To advance Huntington's Disease research*

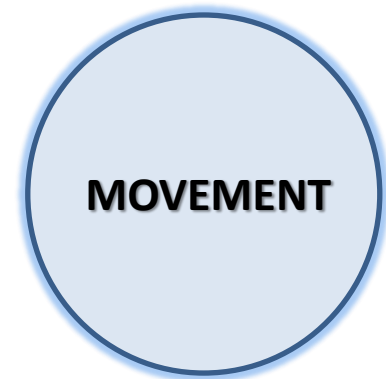


Your Medical Care

- Each person has their own individual course with medical care tailored to their needs
- Treatment focuses on
 - Education
 - Movement disorders
 - Cognitive disorders
 - Behavioral and Psychiatric issues
 - Seizures
 - Psychosocial dynamics

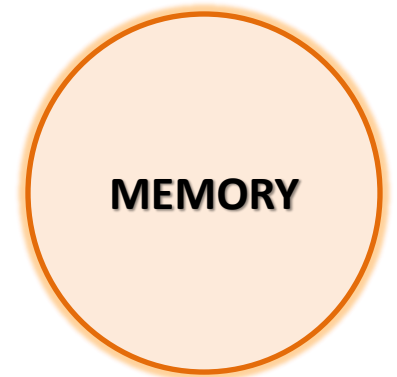
Movement Disorder Treatment

- Early intervention
- Safety devices and equipment assessment
- Physical therapy and range of motion exercises
- Safety measures and fall prevention
- Rigidity
 - Sinemet, Amantadine, Botulinum toxin therapy
- Spasticity and dystonia
 - Baclofen, Tizanidine, Clonazepam
- Chorea
 - Tetrabenazine (Xenazine)
 - Neuroleptics: Zyprexa, Risperdal, Abilify, Haldol, etc



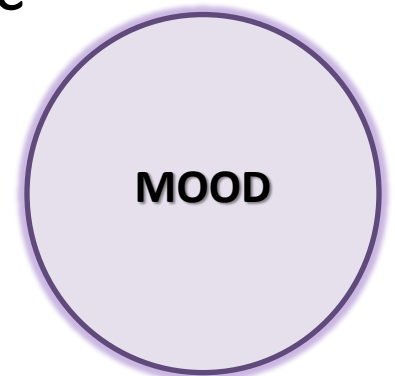
Cognitive Impairment Management

- Provide a stable and predictable environment
- Create daily schedule
- Minimize distractions and noise
- Simplify tasks and decisions
- Re-orientation
- Creative reminders
- Modifications at school (Individual Education Plan)



Behavioral and Psychiatric Management

- Affect of disease on the brain verses psychological stress of the disease
- Depression: sadness, tearful, feeling hopeless, changes in sleep, appetite, energy, and overall performance
 - Anti-depressants (SSRI, SNRI, TCA, other): Zoloft, Celexa, Effexor, Wellbutrin, Remeron, etc



Behavioral and Psychiatric Management

- Behaviors can be unpredictable and difficult to manage (disease verses normal changes and urges of being a teenager)
- Aggressiveness, impulsivity, explosive behavior
 - Behavioral and environmental modification, safety plan
 - Antipsychotics, mood stabilizers or anti-anxiety Rx
- Obsessive thinking
 - Reassurance and redirection
 - Anti-depressants/ SSRI's

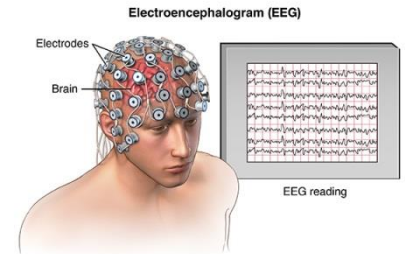


Behavior Management: Sexuality

- JHD verses adolescent/teenager(s) changing body and hormonal urges
- Managing menstrual hygiene
- Contraceptive medication
- Education about sex
- Discussing and redirecting inappropriate sexual behavior (touching self in public)
- Possible treatment with medication

Treatment of Seizures

- Appropriate work-up: brain imaging, electroencephalogram, possible blood tests
- Many different types of seizures
- Seizure precautions discussed
- Importance of medication compliance
- Medication treatment (depending on seizure type): Keppra, Depakote, Lamictal, Tegretol, Topamax, Zonegran, etc



Other Medical Issues

- Choking (dysphagia)
 - Avoidance of aspiration
 - Use of a straw and modification of food consistency
 - Small and slow
- Nutrition
 - Nutritious high calorie food
 - Frequent snacks (milkshakes, ensure, muscle milk)
- Communication
 - Electronic communication devices
 - Hand gestures

Late Stage JHD

- Early discussions regarding possibilities and goals of care
- Severe stiffness in limbs leaving some children wheelchair or bed bound
- Treatment of any discomfort
- Attention to possible malnutrition, infections of the urine and lung and skin sores
- In home services and placement outside of the home
- Sensitive issues to discuss: feeding tube, goals of care, palliative care, hospice care
- Advance directive

Caregivers

- Handling the emotions of such a diagnosis
- Managing your own feelings
- Practical and emotional support
- Outlets
- Caring for the caregiver
- Support groups
- Knowing your resources
- Respite
- Create your *HD family*

BE KIND TO
YOURSELF.

You Can Do
ANYTHING

But Not
EVERYTHING.

In the moment...

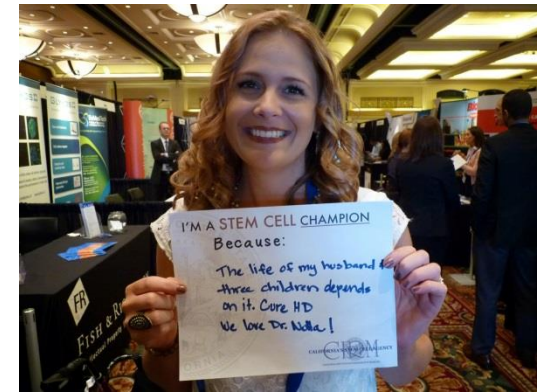
- Attempt to take pause and live in the moment
- Enjoy the simple things in life
- Have the moment be NOT about JHD

I love
RIGHT
NOW

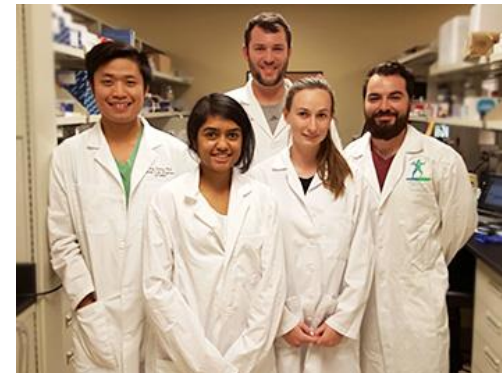


Key Points

- Education
- Know where to turn for help and support
- Advocate (HD warriors)
- And maintain hope through research!



Human Mesenchymal Stem Cells Genetically Engineered to Overexpress Brain-derived Neurotrophic Factor Improve Outcomes in Huntington's Disease Mouse Models



JROLOGY TODAY | NOVEMBER 19, 2015

NEWS FROM THE SOCIETY FOR NEUROSCIENCE ANNUAL MEETING

Gene Editing Techniques Show Promise in Silencing or Inhibiting the Mutant Huntington's Disease Gene

BY JAMIE TALAN





Help
4HD

Thank you to our JHD & HD families for your strength, courage, and inspiration!



Huntington's Disease Society of America

