Huntington's Disease Society of America

Workshop: June 26, 2010

Living Positively at Risk – Healthy Lifestyles

Jang-Ho Cha, MD PhD

Presenter Disclosures

Jang-Ho Cha

The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

- Merck Research Laboratories (employee)
- Lundbeck (Medical Advisory Board)

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The information provided by speakers in workshops, forums, sharing/networking sessions and any other educational presentation made as part of the 2009 HDSA convention program is for informational use only.

HDSA encourages all attendees to consult with their primary care provider, neurologist or other healthcare provider about any advice, exercise, medication, treatment, nutritional supplement or regimen that may have been mentioned as part of any presentation.

No medications have been approved to slow the progression or delay the onset of HD. I will discuss some of these.

Jang-Ho Cha, MD PhD: My Background

- 1991 – 2000: Venezuela HD Study
- Neurologist at Massachusetts General Hospital for 17 years
- 1997: Traveling Fellowship Award from HDSA
- 1998: HDSA Research Fellowship
- 2000 – 2010: HDSA *Coalition for the Cure* Investigator
- 2007 – present: Board of Trustees, Chair, CPEAC committee
- 2010: Merck Research Laboratories

What we don’t know

- Nothing proven to slow the progression or delay the onset of HD
- If treatments that work in symptomatic HD patients will have benefit for gene-positive individuals
- When to start a treatment
  - Early genetic diagnosis possible
  - All drugs have side effects, likely cumulative
  - Ability to predict onset is poor
    - When does it occur?
    - What is onset?

Commercial #1: Get Involved with Research

- We need persons with HD to participate in research trials in order to answer these important questions
- HDTrials.org
- PREDICT Trial
- COHORT = Cooperative Huntington's Observational Research Trial

What supplements should I take?
Many supplements have been talked about:

- Creatine
- Coenzyme Q10
- Ethyl-eicosapentanoic acid (ethyl-EPA)
- docosahexanoic acid (DHA)
- Blueberries
- Vitamin E
- Vitamin C
- Taurodeoxycholic acid (TUDCA)
- Trehalose (NeuroCoat)
- S-adenosyl-methionine (SAM)
- Lecithin
- Ginkgo biloba
- Selenium
- minocycline

Supplements: Questions for the audience

- How many people here are taking supplements?
- How many people think supplements work?
- Who would like to have more definite proof about whether supplements work?

Commercial #2: Supplements

- HD Drugworks
- Interested in collecting “n of 1” experiences of individual patients

Something has been shown to help HD mice. What would you like to know?

- Will this drug work in humans?
- What is the right dose?
- Is this drug safe?
- Is this drug harmful?
- What are the long-term side effects?
- How will I know if it's working for me?
- Has another lab reproduced this result?

Beware of **Publication Bias**

- Scientific literature: much easier to publish a positive result than a negative result
  - Most things do not work
  - Sometimes things “work” by *chance alone*
- Scientists: little incentive to repeat the work of others
  - Not as prestigious
  - Feelings get hurt
  - Disproving something does not lead to grant funding
- *Don’t believe everything you hear!*

My recommendation regarding supplements

- For the most part, I don’t know enough about the safety and efficacy of supplements to recommend supplements for symptomatic or pre-symptomatic HD patients.

Creatine

- Widely used nutritional supplement
- Popular with athletes; thought to add muscle
- Helps cells by boosting energy (mitochondria)
- Helps HD mice
  - Delays onset of symptoms
  - Extends lifespan
- Will it work in humans?
  - High likelihood to be safe
  - Unknown dose
  - Limited effect if any

Commercial #3: creatine

- CREST-E Study
- www.huntington-study-group.org
- For symptomatic patients

Coenzyme Q10 (CoQ10)

- Like creatine, thought help cells by boosting energy (mitochondria)
- Helps HD mice
  - Delays onset of symptoms
  - Extends lifespan
- Will it work in humans?
  - Expensive
  - Unknown dose
  - Limited effect if any

Commercial #4: Coenzyme Q10

- 2CARE Study: high-dose Coenzyme Q10 in symptomatic patients
- PREQUEL: Coenzyme Q10 in pre-symptomatic subjects
- www.huntington-study-group.org

Non-medication approaches

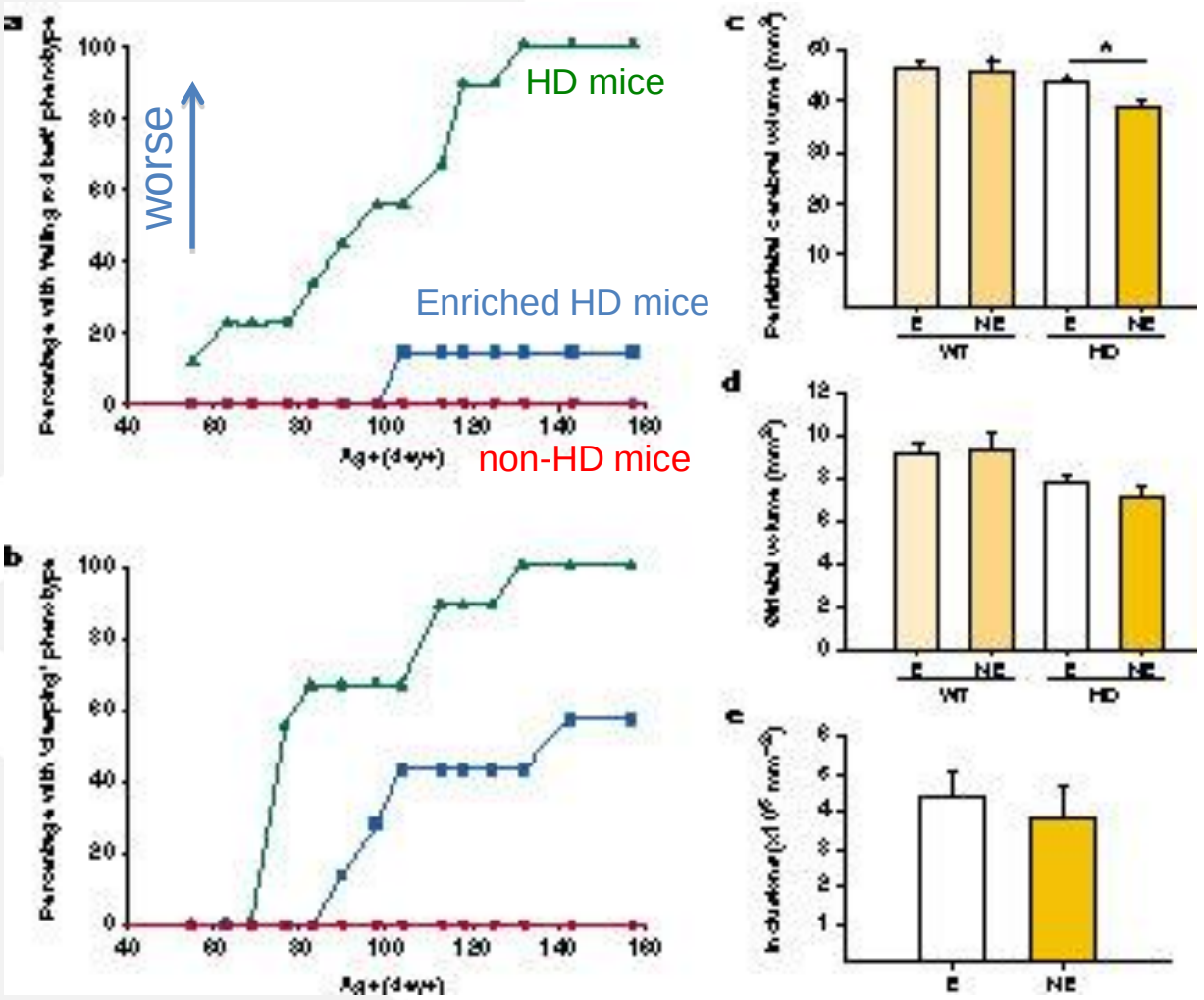
Environmental enrichment works in mice!

brief communications

Delaying the onset of Huntington's in mice

This unremitting disease develops later in animals stimulated by their environment.

van Dellen A, Blakemore C, Deacon R, York D, Hannan AJ (2000) Environmental enrichment delays disease onset in a mouse model of Huntington's disease. *Nature* ***404:721-722.***



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Article to be published in August…

J Neuropathol Exp Neurol
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August 2010
pp. 00–00

ORIGINAL ARTICLE

Environmental Enrichment Reduces Neuronal Intranuclear Inclusion Load But Has No Effect on Messenger RNA Expression in a Mouse Model of Huntington Disease

Caroline L. Benn, PhD, Ruth Luthi-Carter, PhD, Alexandre Kuhn, PhD, Ghazaleh Sadri-Vakili, PhD, Kwabena L. Blankson, BSc, MD, Sudeb C. Dalai, BSc, Darlene R. Goldstein, PhD, Tara L. Spires, PhD, Joel Pritchard, MSc, James M. Olson, MD, PhD, Anton van Dellen, PhD, Anthony J. Hannan, PhD, and Jang-Ho J. Cha, MD, PhD

Environmental enrichment decreases abnormal protein inclusions in HD mouse brain

What do you think environmental enrichment will do in your brain?

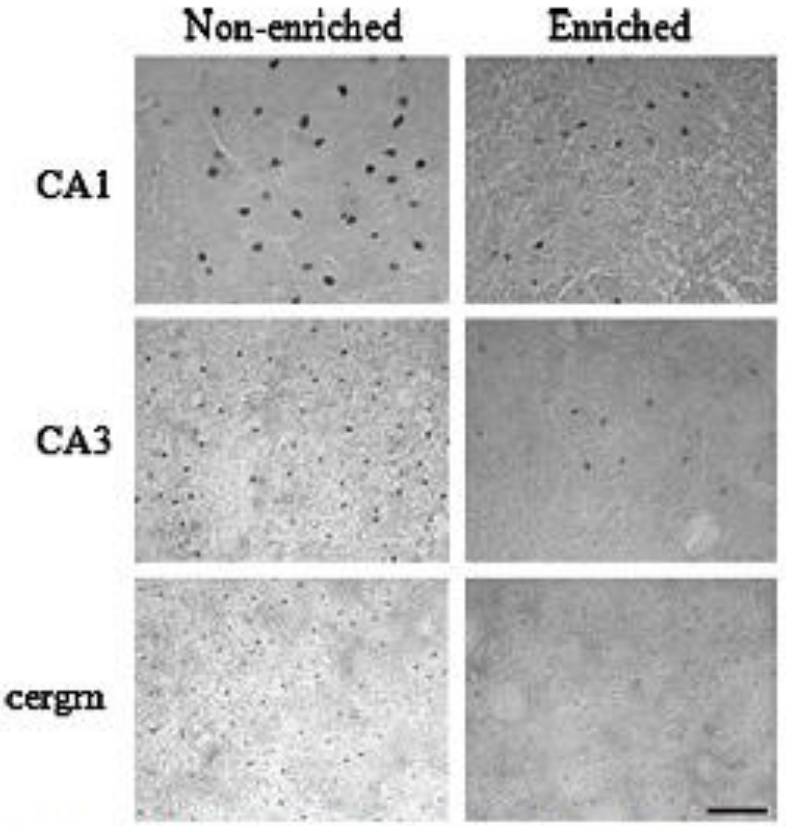
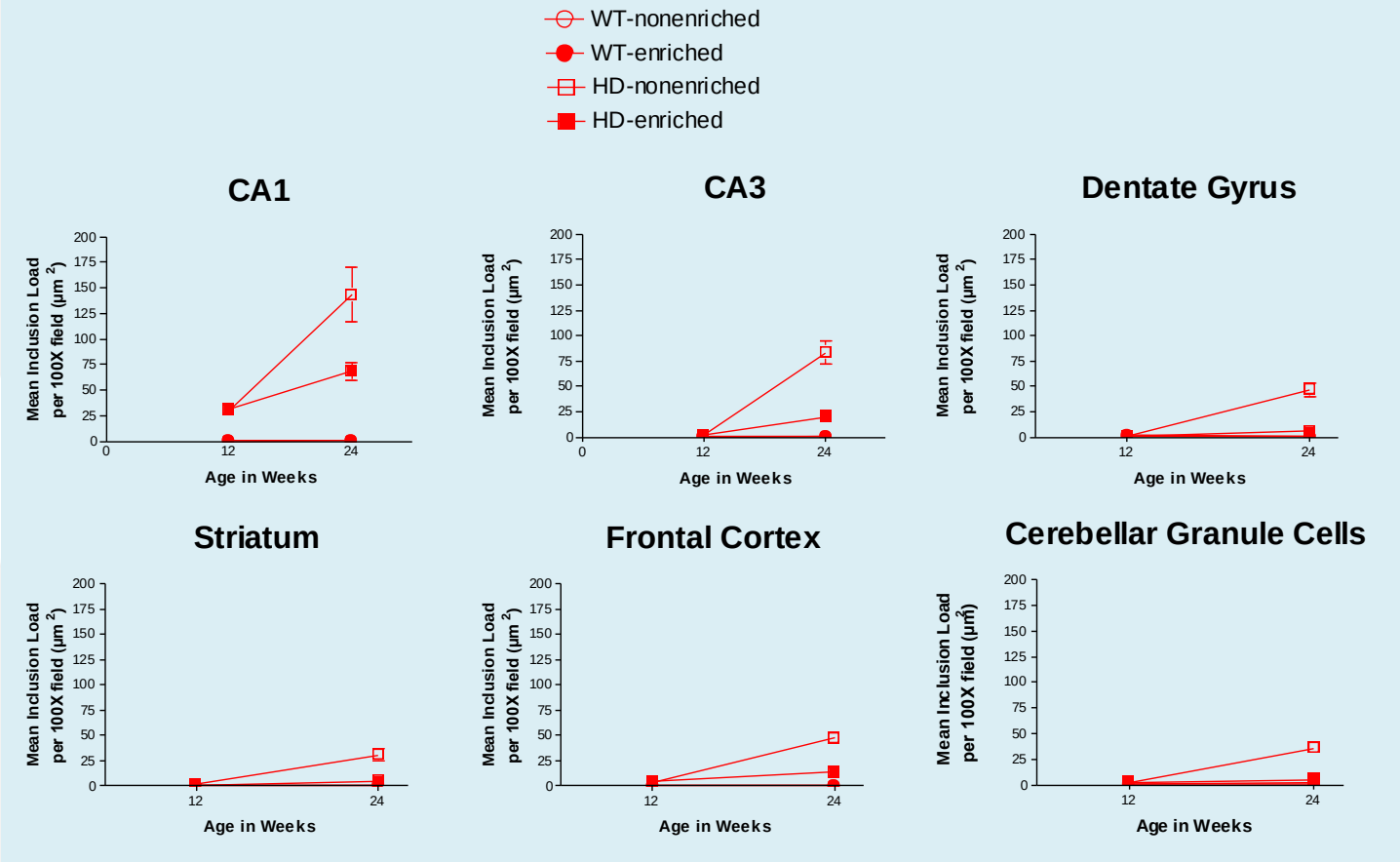


FIGURE 4. Ubiquitin immunohistochemistry of NIIs in enriched and NE R6/1 mice. Representative images of NII in the CA1 and CA3 regions of the hippocampus and cerebellar granule cell layer (cergrn) in 24-week-old R6/1 mice. Bar, 10 μm.

Benn et al. *J Neuropathol Exp Neurol* 2010***, in press***

Environmental enrichment decreases abnormal protein blobs in the brains of HD mice



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Take home message:

The way you interact with the environment modifies how the mutant huntingtin protein affects your brain.

Does environmental enrichment work in humans?

- What do you think?
- Experience with human subjects
- Example: Remotivation Therapy
  - Sullivan FR, Bird ED, Alpay M, Cha JH (2001) Remotivation therapy and Huntington's disease. *J Neurosci Nurs* ***33:136-142.***
- Remotivation Therapy: A discipline in which clients are approached as individuals, seeking those factors that can help motivate
- Patients receiving RT required less staffing, achieved higher functional levels

Beneficial effects of exercise on neurological disease

- Alzheimer's disease
- Parkinson's disease
- Multiple sclerosis
- Huntington's disease?

My best educated guesses

- Daily exercise
  - At least 30 min for 6 days a week
- Mental activity
  - Engagement is key factor
  - Humans are evolved to interact with other humans
- Sleep
  - Emerging data: lack of sleep as harmful as smoking on overall mortality
- Consider taking creatine and/or coenzyme Q10

In other words, persons at-risk for HD should do what we **all** should be doing!

Resources

- www.HDTrials.org
- PREDICT & COHORT Studies: www.huntington-study-group.org
- hddrugworks.org
- van Dellen A, Blakemore C, Deacon R, York D, Hannan AJ (2000) Environmental enrichment delays disease onset in a mouse model of Huntington's disease. *Nature* **404:**721-722*.*
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Questions & Discussion

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