2-27-2020

At Therapeutics Conference, landmark study of young gene carriers highlights how Huntington's disease researchers seek to solve critical puzzles

Kenneth P. Serbin
University of San Diego

At Risk for Huntington's Disease

HD is a genetically caused brain disorder that causes uncontrollable bodily movements and robs people's ability to walk, talk, eat, and think. The final result is a slow, ugly death. Children of parents with HD have a 50-50 chance of inheriting the disease. There is no cure or treatment.

Blog Archive

- ► 2021 (12)
- ▼ 2020 (16)
  - ► December (1)
  - ► November (3)
  - ► October (1)
  - ► August (1)
  - ► July (1)
  - ► May (1)
  - ► April (1)
  - ► March (3)
  - ▼ February (3)
    - At Therapeutics Conference, landmark study of youn...
    - Striving to overcome the doom of Huntington's disease
    - I'm a Huntington's disease gene carrier at age 60,...
  - ► January (1)
- ► 2019 (19)
- ► 2018 (16)
- ► 2017 (14)
- ► 2016 (13)
- ► 2015 (24)
- ► 2014 (24)
- ► 2013 (30)
- ► 2012 (26)
- ► 2011 (33)
- ► 2010 (26)
- ► 2009 (21)
- ► 2008 (7)
- ► 2007 (7)
- ► 2006 (4)
- ► 2005 (17)

About Me

GENE VERITAS

View my complete profile

HD Links

THURSDAY, FEBRUARY 27, 2020

At Therapeutics Conference, landmark study of young gene carriers highlights how Huntington's disease researchers seek to solve critical puzzles

Armed with ever more impressive data and a deeper understanding of Huntington's disease, scientists and drug hunters convened at the 15th Annual HD Therapeutics Conference this week, facing the complex puzzles that still hinder the quest for treatments for this deadly neurological disorder.

One of those puzzles: how to not only treat symptoms, but to *prevent* them, especially in young presymptomatic carriers of the HD gene, so that they don't have to spend their lives fearing the currently inevitable onset of this devastating disease.

On February 26, Sarah Tabrizi, FRCP, Ph.D., of University College London, answered key questions about what kinds of health consequences young presymptomatic gene carriers suffer decades before they're likely to develop the disease in midlife.

Previous studies have demonstrated that brain shrinkage can occur as early as 15 to 18 years before predicted age of onset. Ranging in age from 18-40, the 64 gene carriers in Dr. Tabrizi's HD Young Adult Study went through state-of-the art brain scans and cognitive testing, and also provided samples of blood and cerebrospinal fluid (CSF) for analysis. These at-risk volunteers are, on average, 24 years from estimated onset.

This study, in line with "The Path to Prevention" (one of five major themes of the 2020 conference), is aimed at helping identify the optimal time to treat gene carriers to slow or prevent their neurological decline.

"Comprehensive cognitive testing was normal," as compared to 67 non-HD-affected individuals, reported Dr. Tabrizi in her presentation to the conference. "There were no significant psychiatric differences, which I found very interesting, because I would have predicted they would've been big differences."

Dr. Tabrizi said that "there's always been a thought that carrying the HD gene hard-wired you for psychiatric burden," but the Young Adult Study suggests that such symptoms become more prominent closer to onset.

"I think that was – and I don't say this lightly – a landmark presentation," Robert Pacifici, Ph.D., the chief scientific officer for CHDI Foundation, Inc., the conference sponsor, told me today, adding that Dr. Tabrizi's team carried out the study with "a high degree of rigor and granularity."

"The participants seem to be remarkably well," Dr. Pacifici observed. The absence of many of the neurological and other problems typical of HD is an encouraging prospect for developing safe and well-tolerated treatments that could "not just

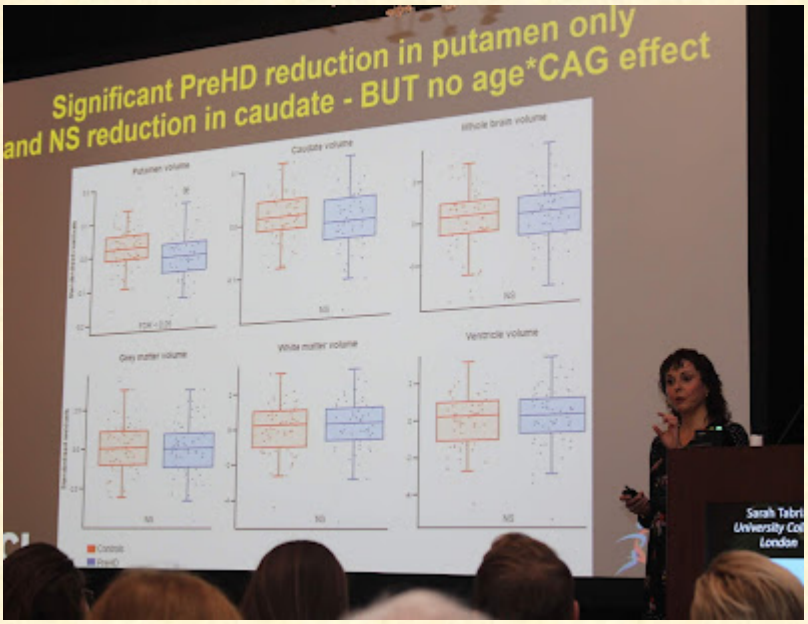
Huntington's Disease Society of America
International Huntington Association
Huntington's Disease Drug Works
Huntington's Disease Lighthouse
Hereditary Disease Foundation
Huntington's Disease Advocacy Center
Thomas Cellini Huntington's Foundation
HDSA Orange County (CA) Affiliate
HD Free with PGD!
Stanford HOPES
Earth Source CoQ10, Inc.

HD Blogs and Individuals

Chris Furbee: Huntingtons Dance
Angela F.: Surviving Huntington's?
Heather's Huntington's Disease Page

reverse, but actually prevent" HD, he said.

Dr. Pacifici lauded the study volunteers for their "unbelievably selfless participation," including submitting to the study's "incredibly rigorous battery."



Above, Dr. Sarah Tabrizi presenting her talk on the HD Young Adult Study at the 2020 HD Therapeutics Conference, February 26, 2020, and, below, a closeup of Dr. Tabrizi (photos by Gene Veritas, aka Kenneth P. Serbin)

Overall, 'good news' for young gene carriers

The young gene carriers in the study did appear to go through a small change in the area of the forebrain known as the striatum, consisting primarily of the

putamen and the caudate, the deep brain regions that are most affected by HD. The striatum helps to control our movements and rewards system.

The study found a significant reduction in the size of the putamen, but an insignificant reduction in the caudate. Nevertheless, Dr. Tabrizi explained that, based on this study, these differences (in comparison with the normal subjects) were "not associated with predicted years to onset."

"So what we now know, based on the data, is that the striatum never appears to be the same size as the control group," she explained.

The "very slightly smaller" striatum may suggest a "neurodevelopmental effect" (the way the brain develops) that is "well compensated for," Dr. Tabrizi said, meaning that the brain adjusts without clear damage. She added that it "might be why the striatum is vulnerable later in life, because it has a double hit." As mentioned by Dr. Tabrizi, this interpretation resonates with the research of Peg Nopoulos, M.D., who has studied the compromised development of the brains of people affected by juvenile HD.

Alternatively, neurodegeneration early on could be "too subtle and variable" to associate with predicated age of onset, Dr. Tabrizi noted.

Other imaging results showed no decrease in the white matter (the tissue in the brain made of nerve fibers and possibly involved in cognitive problems in HD) or any other aspect of the brain measured in the study, indicating that the subjects were still "very far from onset," Dr. Tabrizi continued.

"This is really good news," Dr. Tabrizi stated.

Douglas Langbehn, M.D., Ph.D., a psychiatrist and biostatistician at the University of Iowa who did the statistical analysis for the HD Young Adult Study, listens to Dr. Tabrizi at the Therapeutics Conference (photo by Gene Veritas).

The ongoing search for reliable biomarkers

The study also involved the ongoing search for reliable biomarkers (signs of disease and drug efficacy).

The study detected mutant huntingtin protein in the subjects' cerebrospinal fluid. "CSF mutant huntingtin was higher in those closer to [predicted] onset, suggesting that some injury is releasing mutant huntingtin [from the brain], but very subtle," Dr. Tabrizi said.

Several other biomarkers were elevated in the subjects' CSF, again indicating an early, subtle injury, but most of those subjects had readings showing levels very close to those of the unaffected control subjects, Dr. Tabrizi continued. Furthermore, six other biomarkers were normal, she added.

The Young Adult Study points to the one CSF biomarker in particular, neurofilament light, a marker of brain damage, as potentially helpful in measuring disease progression and treatment response in people decades from onset, Dr. Tabrizi concluded.

A drug that kept neurofilament light at very low levels could prevent degeneration of the brain, she added.

You can watch Dr. Tabrizi's presentation in the video below.

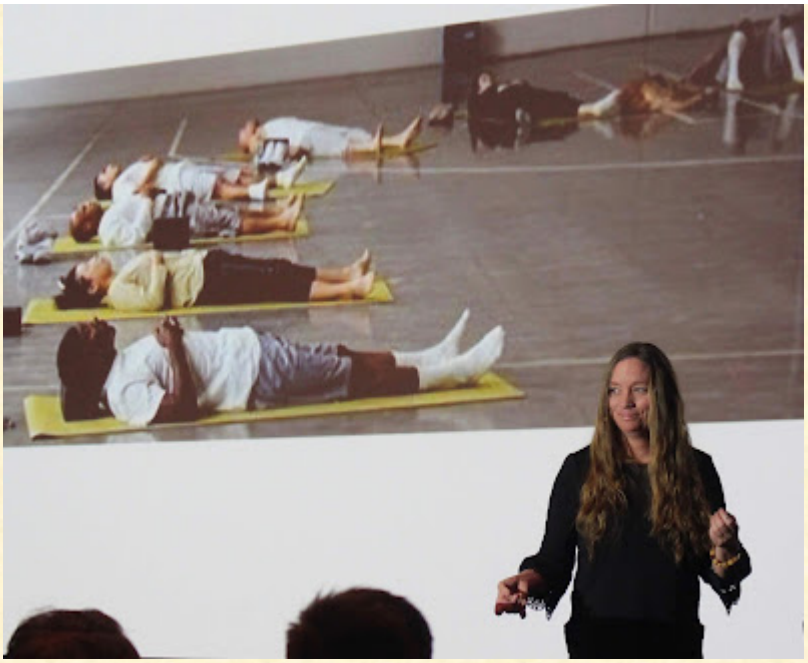
A moving keynote address

With a record attendance of 380, the conference opened on February 24 with a moving keynote speech by Amy Merkel, a 45-year-old nurse from Wisconsin and the founder of Starfish Yoga.

A small company, Starfish focuses on encouraging constructive coping skills, primarily for people affected by past imprisonment, sexual abuse, and neurological disorders, including HD.

Amy, who titled her talk "Life is Good," belongs to a family deeply affected by HD. She recounted her extended family's decades-long struggles with HD. Amy received a standing ovation.

Stay tuned to this blog for additional reporting on the conference, including an overview provided in my interview with Dr. Pacifici.



Above, HD advocate Amy Merkel addresses the 15th Annual Therapeutics Conference, and, below, poses with researchers Dr. Sarah Tabrizi (far left), Leslie Thompson, Ph.D. (second from right), and Gillian Bates, Ph.D. (photos by Gene Veritas).

Posted by Gene Veritas at 4:39 PM

Labels: at-risk , brain , HD Therapeutics Conference , HD Young Adult Study , Huntington's disease , onset , presymptomatic gene carrier , prevention , researchers , Sarah Tabrizi , symptoms , treatments , volunteers

No comments:

Post a Comment

Newer Post Home Older Post

Subscribe to: Post Comments (Atom)