'Buzzilia' from the Huntington's Disease World Congress: day 4

#Buzzilia, day 4: Jeff and Ed's roundup of happenings from the closing day of the HD World Congress in Rio de Janeiro

By Dr Jeff Carroll on September 18, 2013
Edited by Dr Ed Wild

Our final report from the last morning of the World Congress on Huntington's Disease in Rio de Janeiro, Brazil.

08:12 - **Bernhard Landwehrmeyer**, of Ulm and CHDI, starts off the therapeutic session of the WCHD with a discussion of drugs under development.

08:15 - **Landwehrmeyer:** There are at least 4 companies developing drugs for one specific target in HD - called "phosphodiesterases". The goal is in clear view, the path to the top is not! He suggests we have a "high class problem", which is too many possible treatments that we could try in HD. So how do we set priorities? Which of all the possible new drugs should we test first? How much evidence do we need? We have a path. We can run multiple therapeutic trials in parallel, with experienced study sites on 4 continents.

Bernhard Landwerhmeyer gives an overview of the many recent, current and planned HD drug trials

08:28 - **David Craufurd** (University of Manchester UK) addresses the treatment of 'psychiatric' or 'behavioral' symptoms in HD.

08:29 - **Craufurd:** behavioral problems (like anxiety and depression) are common and can be distressing, but are also treatable in most cases. Our ability to treat behavioral symptoms (and HD in general) through expert multidisciplinary care has dramatically improved. Patients looked after in HD clinics are leading better quality lives for longer. Apathy (loss of motivation) is a particularly big challenge. Common in HD and difficult to treat. Different from depression. Behavioral probs often need high doses and combinations of drugs, so specialist psychiatry input is essential (eg HD clinic). Drug treatments for depression etc often need to be continued for much longer in HD because it's a physical brain disease.

08:53 - **Binit Shah**, a neurologist working in HD, is describing " deep brain stimulation" (DBS) in HD. In DBS, surgeons insert a fine electrode directly into the brain, allowing them to simulate any particular part of the brain. The idea is that if a particular part of the brain isn't working

enough in HD, perhaps we can directly zap it into working normally. Based on the loss of tissue in HD brains, surgeons and neurologists have a particular brain region they'd like to target in HD.

09:03 - **Shah:** The first case of DBS in HD was reported in 2004 when surgeons performed it in a single HD patient, with positive effects on movements. Though the patient who received DBS in HD had better movements after the treatment, it didn't seem to help his daily function much. Since then, several more DBS attempts in HD have been reported with variably encouraging results.

09:14 - Addendum to **Prof Landwehrmeyer's** talk: Huntington Study Group is running a trial of a modified version of tetrabenazine for chorea. HSG's trial is called FIRST-HD.

09:25 - **Dr Francis Walker** is talking about speech and swallowing problems in HD which are also very common.

09:26 - **Walker:** Speech and language therapists already have expertise in this but HD requires specialist knowledge. Ultrasound can be a useful tool to get an idea of why swallowing may be problematic in HD. Swallowing problems are caused by combination of extra unwanted movements, loss of voluntary movts and psychological changes. A big problem is impulsivity - wolfing the food down and not coordinating swallowing and breathing. The good news is that expert assessment can lead to useful advice and exercises to help swallowing and keep it safe.

10:19 - We've started the session on gene silencing at the WCHD, beginning with a talk from **Neil Aronin**, who's working on this approach to HD. Aronin's group is working on a type of therapy called "RNAi". The goal is to shut down, or silence, a specific gene. For HD therapy, we'd like to be able to silence the HD gene, which is the root cause of the disease. Aronin's approach relies on using deactivated viruses, injected in the brain, which deliver the silencing drug. After Aronin's team injects the delivery viruses into a mouse brain, they observe reductions in the HD gene.

> "For things to happen as quickly as possible, we all need to work together."

10:29 - But mouse brains are small. To see if the silencing technique could work in bigger brains, Aronin's team is injecting sheep brains! Aronin's team is using sheep to try and determine the best type of virus, and amount of injection, to cover as much brain as possible. Encouragingly, Aronin's team hasn't seen any loss of brain cells or other kinds of toxicity resulting from these silencing injections. To do a larger scale safety trial, Aronin's team is heading to Australia to inject 60 sheep with HD silencing drugs. Aronin would like to develop methods to deliver silencing drugs without having to do brain injections, and is studying new options.

10:40 - Next up is another gene silencing talk from **Doug Macdonald** of CHDI, who are working with Isis Pharmaceuticals on a different approach. Like Aronin, the Isis team are silencing the HD gene, but using a different type of drug called "antisense oligonucleotides" or ASOs.

Macdonald reviews the wide range of technologies available to silence the HD gene - listing 13 different active efforts

10:54 - **Macdonald:** An ASO gene silencing approach with Isis and Roche is going well and is planned to enter human trials at the end of 2014. Unlike the viral studies described, ASOs are infused into the spinal fluid, rather than being injected into the brain. ASOs spread widely around the brain, but don't get into the deep parts of the brain as well as injected drugs.

10:57 - Macdonald and Aronin suggest that the injected viral approach and the infused ASO approach might be complementary to silence the HD gene.

10:59 - **Macdonald:** CHDI and Sangamo are developing an exciting new technology that cuts part of HD gene out of DNA. Macdonald shows early evidence that DNA editing technique not only works, but can discriminate between the 'good' and 'bad' HD genes. Before we go to the clinic with HD silencing drugs, we need to be able to accurately measure HD gene levels in people. Otherwise, it's hard to know whether your silencing drug worked!

11:06 - **Macdonald:** The team CHDI is working with thinks they might now be able to measure the HD gene product in the spinal fluid of patients. This would be a huge benefit, because it would let us prove that gene silencing drugs are actually working in humans. There's really amazing progress being made towards gene silencing for HD! If one approach doesn't work, there's others in the pipeline.

11:14 - **Joaquim Ferreira** reminds the audience that while there is currently no cure for HD, there are a number of treatments that help patients. Each stage of HD is a different disease, in terms of symptoms. So doctors working with HD patients need to react to change. Many of the treatments physicians use for HD don't have a large body of evidence, but are based on experience.

Today was the final day of the 2013 World Congress, but the science continues … 24/7/365.

11:45 - **Raymund Roos** (Leiden, Netherlands) talks about optimum care in later stage HD, often overlooked or beyond the reach of HD clinics.

11:51 - **Roos:** The Netherlands is one country where medical euthanasia is an option. It is very strictly regulated to ensure it is not abused. Most patients have thought about how they want their end-of-life care to be handled. Often overlooked in discussions with doctors.

12:00 - The Congress closes with gratitude to the local organizing committee and in particular Dr Francisco Cardoso and Dr Monica Haddad.

Sunset conclusions

During today's sessions, we almost lost count of the number of clinical trials of new treatments, designed with Huntington's disease in mind. Some are underway, others planned. Some are aimed at improving symptoms of HD, others at slowing or preventing its progression. For things

to happen as quickly as possible, we all need to work together. Researchers need to keep pressing ahead with the science, and HD family members need to stay aware, stay informed and be prepared to volunteer - not later, but now - for any and all patient-focused research to ensure that not a second is lost in bringing these treatments to the people who need them.

Farewell from Rio, look forward to videos of our 'Buzzilia' sessions and stay tuned to HDBuzz for updates on all the HD research news that matters.

The authors have no conflicts of interest to declare. For more information about our disclosure policy see our FAQ...

Glossary

ASOs A type of gene silencing treatment in which specially designed DNA molecules are used to switch off a gene

deep brain stimulation direct stimulation of the brain using electrical impulses through tiny wires.

gene silencing An approach to treating HD that uses targeted molecules to tell cells not to produce the harmful huntingtin protein

chorea Involuntary, irregular 'fidgety' movements that are common in HD

RNA interference A type of gene silencing treatment in which specially designed RNA molecules are used to switch off a gene

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