



Struggling with a grant application?
Looking for new opportunities for collaboration?
The EHDN Grant Manager is here to help.
Find out more on page 6.

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HD Therapeutics 2015: Big Data in the spotlight

Michael Orth, Central Coordination

BIG DATA was a central theme at the 10th HD Therapeutics conference in Palm Springs in February, as researchers presented a raft of insights generated by the application of 21st century technology to large datasets.

Clearly much can be learned from a holistic as opposed to a “keyhole” approach to data analysis. For example, Ryan Michalek (Metabolon) presented an analysis of chemical indicators of cell metabolism, while Jong-Min Lee (Harvard Medical School) gave an update on the work of the GeM consortium, a major collaborative effort to identify genetic modifiers of HD, and Hongwei Dong (University of Southern California) described his group’s attempts to map neuronal connections systematically across the whole brain in healthy and HD mice.

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Editorial Board of EHDN News:

[Laura Spinney](#), Editor (Paris, France)

[Gabriele Stautner Artifax Communication Design](#) (Ulm, Germany).

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As Diane Stephenson (Critical Path Institute) told the meeting, large-scale collaboration and data-sharing are becoming increasingly critical to these kinds of efforts. Platforms that make large amounts of annotated data available to the community will ultimately reduce the cost of research and accelerate discovery. An example is the [HDinHD](#) platform unveiled by Jim Rosinski (CHDI), that houses maps of interacting proteins and gene expression data, and is accessible to researchers free of charge.

It is too early to say how this new knowledge will feed into the development of therapies for HD. The complexity of the datasets means that, for the moment, researchers are working in the realm of unknowns, generating information that is of potential therapeutic relevance without yet knowing what that relevance might be.

Meanwhile, the development of therapies continues apace. Isis Pharmaceuticals is now ready to launch a human safety trial of a drug called HTT-Rx, an antisense oligonucleotide that works by blocking the RNA transcript of the mutant *Htt* gene, and so blocking the synthesis of the abnormal protein. Other huntingtin-lowering approaches are also producing encouraging results, but questions remain over how best to deliver them to the brain. Tools that measure their ability to reach their targets are being developed in parallel, and Ed Wild (UCL) described his group's progress in measuring different forms of huntingtin protein in the cerebrospinal fluid—the fluid that bathes the brain. More work is needed to develop drugs that reach the striatum, a structure deep in the brain that is particularly damaged in HD, along with techniques for measuring the efficacy of such drugs. ■

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John Eden, Chief Executive of the Scottish Huntington's Association, and Louise McCabe of Stirling University, after collecting their Scottish Charity Award

CPD in Scotland

The Scottish Huntington's Association will run its second Continuous Professional Development course in HD this autumn. Aimed at practitioners in health, social care and advocacy, as well as members of community organisations who work with people with HD, it may also be of interest to HD family members and supporters. The patient-centred learning module, which has just picked up a Scottish Charity Award 2015, will draw on current research and practice to better equip students to treat, care and support those affected by HD. It will run over 14 weeks and begin with two study days at Stirling University on 7-8 September 2015. The cost is £675. For more information and an application form please contact Stirling University on telephone number +44 1786 467744 or email DempPG@stir.ac.uk.

Mindfulness-based therapy

An EHDN seed fund has been awarded to Jane Simpson (Lancaster University), David Craufurd (Manchester University), Alistair Smith (independent clinical psychologist) and Fiona Eccles (Lancaster University) to study the acceptability and utility of mindfulness-based cognitive therapy for those with HD who experience psychological symptoms including low mood and anxiety. Such symptoms are known to affect those with HD at different stages of the disease (both symptomatic and presymptomatic), but medication is not always effective and psychological therapies present a possible alternative. Though mindfulness-based cognitive therapy has an established evidence base, it is not known whether it is effective in the context of HD. This study will be the first to explore its impact on low mood in HD.



Jane Simpson



David Craufurd

Chorea, choreographer

Laura Spinney

It's not by chance that the words have the same Greek root, and for French dancer Philippe Chéhère, whose own family is affected by HD, the idea of asking HD patients to channel their involuntary movements into dance was the most natural thing in the world. Many of them agreed with him, and a research project is underway to determine if the benefits they report are more than anecdotal.

"Since I was a teenager I've watched people dance in spite of themselves," says Chéhère, whose father died of HD. He went on to become a dancer himself, and eventually came under the influence of choreographers working with dancers with a wide range of disorders. Inspired, he approached HD specialists Alexandra Dürr and Marcela Gargiulo at the Pitié-Salpêtrière Hospital in Paris, about dancing with HD patients. Initially they were sceptical, but they put him in touch with dancer Julie Salgues, and together the pair created Huntington + Dance.

That was in 2003. Participation in the group is free, and for 10 years they kept the project going without any financial support, because they could see that there was a demand for it. Magali, for example, was busy working and looking after her father, who had advanced HD.



Photos: Laura Spinney

Philippe Chéhère

After he died in 2009 she started coming regularly, and she is now one of the longest dancing members of the group, which meets in the Marais area of Paris. "It's a priority in my week," she says, "A moment of joy and relaxation that I don't find anywhere else."

Magali believes dance helps improve her ability to walk without falling and to retain information, including those all-important PIN numbers. With others in the group, she has taken part in a five-month-long study being run by cognitive neuroscientist Iris Trinkler, also based at the Pitié-Salpêtrière, to see if those improvements can be detected in clinical assessments and MRI scans. The study will end in August, and the data will be analysed after that.

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One thing already seems clear though. The sessions provide the dancers with a much needed opportunity to break out of the isolation that the disease imposes on them, and to abandon themselves to the movements that otherwise cause them so much difficulty, in an environment where there is time and space to do so. "The raw material is the movement that disturbs, the movement that frightens," says Chéhère. But the outcome, in his view, is that each dancer learns to relate to their own body, and to others', in new ways.

Happiness, laughter and human kindness characterise the sessions. The dancers form a tightly knit group, and not just because they share a diagnosis. Dancing together forces them to place their trust in one another. They have even put on performances in which clinicians and carers participate, including one in which dancers and their doctors were literally taped together, back-to-back. Through such "multidisciplinary" art, the different parties are bound together via a medium other than the disease.

Chéhère has also taken the group on home visits when members have become too ill to make the journey to him. That was what happened with Dominique, who died last year after having danced in a documentary about the project, *Eloge du Mouvement (Elegy for movement)*, made by [David Gil](#). At Dominique's home, Chéhère explains, the group danced as usual, simply adapting themselves to the new space. The improvisation never stops, and inevitably it informs his own experiments in dance—notably a performance he gave in 2009, called *Perseveration Above the Clouds*, that was inspired by memories of his father.

More information about Philippe Chéhère, Julie Salgues and Huntington + Dance can be found [here](#). In February, the pair launched a second dance group at the Henri Mondor Hospital in Créteil, on the outskirts of Paris. ■





Update: Enroll-HD

Olivia Handley, Global Project Manager, Enroll-HD

Transition from Registry to Enroll-HD continues apace in Europe. In two countries, Poland and Denmark, all sites have completed transition. A further four countries—Germany, UK, Italy and the Netherlands—are nearing completion, with many of their sites now activated and enrolling in the new study.

Over the next three months, France, Spain and Ireland will be activated, with the first of their sites anticipated to begin enrolling by September. In Austria, Switzerland, the Czech Republic and Belgium, ethics review board (ERB) submissions are underway and the first round of ERB feedback has been received. For the remaining countries, which include Russia, Norway and Sweden, initial ERB submission is expected to take place during the next quarter. Over one third (56) of the 132 European sites have now undergone transition from Registry to Enroll-HD, while 12 new sites have joined the study. Transition is expected to continue into the first half of 2016.

Europe continues to make an exponential impact on global recruitment in Enroll-HD. Based on its current rate of recruitment, it is expected to become the largest recruiting region within a couple of months. Indeed, the George Huntington Institute in Münster, Germany (principal investigator Ralf Reilmann) has recently become the highest recruiting site globally.

The European transition from Registry to Enroll-HD remains one of EHDN's central activities, and upcoming regional investigator meetings will focus on Enroll-HD. The regions have been grouped into four investigator meetings that will take place between May and October (see box for details). Each meeting lasts two days and covers topics including a global update, platform activities, and tips and tricks for database collection,



along with training sessions and scientific updates. Also included are interactive sessions at which representatives of two local sites share their site arrangements, and in particular how they manage their clinics to accommodate Enroll-HD.

Regional investigator meetings 2015

Germany, Poland, Czech Republic, Switzerland, Austria	Berlin, 21-22 May
UK, Ireland, Netherlands, Denmark, Norway, Sweden, Belgium (Flemish-speaking)	London, 4-5 June
Spain, Italy, Portugal, France, Belgium (French-speaking)	Madrid, 1-2 October
Russia	To be confirmed

As at previous meetings, there are sessions dedicated to local scientific updates and breakout sessions for discussion of country-specific issues. The training component focuses on core assessments used in Enroll-HD such as the short version of the problem behaviours assessment (PBA-s), cognitive and motor tests and the HD clinical characteristics (HDCC) assessment, along with "drop-in clinics" that provide guidance on the electronic data capture and Greenphire (payment) systems. The format of these meetings has been carefully prepared to ensure that they are informative and useful for participants, while also building on the success of Enroll-HD in Europe to date.

For further information, please contact EnrollHD@quintiles.com or visit www.enroll-hd.org



Roundup: funding news

Fionnuala Margreiter, Grant Manager

News

- Following the successful submission of an HD-related gene therapy project to stage 1 of Horizon 2020's rare diseases funding call, a stage 2 proposal was recently submitted by the project consortium's leader, Dutch industry partner uniQure. EHDN is participating as a communication and dissemination partner.
- EHDN is participating in another stage 2 proposal in the context of Horizon 2020, for the HD component of a gene therapy project for rare diseases, led by the University of Tübingen in Germany.
- A new draft programme for Horizon 2020 (personalised medicine) in 2016-2017 is available—please contact Fionnuala Margreiter for details. Besides the rare diseases funding call, there are other calls of potential interest to HD researchers.
- The EHDN's Fellowship Exchange Programme received 16 high quality applications, of which eight were selected for funding.



Funding opportunities

- Up to CHF30,000 is available to Swiss researchers who want to organise a 2-5 day [international exploratory workshop](#) in Switzerland, with colleagues working in their field abroad. The next deadline for applications is **7 October 2015**.
- The [Thyssen Foundation](#) supports German researchers pursuing projects on molecular causes in the development of illnesses. The next deadline is **30 September 2015**.
- The UK's Wellcome Trust provides [Pathfinder Awards](#) to kick-start pilot projects whose goal is to develop innovative products that address unmet needs in healthcare. There are four deadlines a year.
- The Marie Curie [research and innovation staff exchange](#) programme funds short-term exchanges for staff to develop careers combining scientific excellence with exposure to other countries and sectors (academic, private). The next deadline is **14 April 2016**.
- The European Molecular Biology Organisation (EMBO) offers [awards and financial support](#) for scientists at all stages of their careers.
- The international [Human Frontier Science Programme](#) provides postdoctoral fellowships to encourage early-career scientists to broaden their research skills by moving into new areas of study while working in a new country. The next deadline for applications is **13 August 2015**. The programme also provides research grants, for which the next deadline is expected to be in **March 2016**.

IMPORTANT: support available to EHDN researchers!

To discuss your project idea, find out about funding calls, request assistance with your application or scope out opportunities for collaboration, please contact Fionnuala Margreiter:
fionnuala.margreiter@euro-hd.net

Interlude: poem

Cattaneolab, University of Milan

Huntington, the story of a gene in search of a better future

*This is the story
of an ancient gene,
its name is Huntington.*

*It lives inside all humans,
on the tip
of our chromosome 4.*

*It originated in an amoeba
millions and millions of years ago.
We think there was a good reason for its birth—
shaping the first society of organised cells!
It was born without sin.*

*As millennia went by
and newer species appeared
something unexpected came up in the sequence:
...CAG...CAG...*

*at first it did not exist, but then
2 of them appeared in the good sea urchin
4 in fish, reptiles and amphibians
7 in mice
8 in rats
10 in sheep
12 in elephants
15 in monkeys*

*That chain of intruding letters
which repeat themselves
reaches out to us humans
who have quite a few of them.*



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*The errors of evolution are opportunities too.
There are more of those letters
in the more recent species,
and there must be a good reason, we think,
why they behave that way.*

*Do they take part, perhaps, in developing
more and more functional nervous systems?*

*Those who suffer from Huntington's disease
have too many of those intruding letters,
...CAG...CAG...CAG...CAG...CAG...
But those people too are part of this evolution.*

*Telling the story of this ancient gene will not change,
for the moment, the course of their tragic disease.
But the need to understand more brings us together—
we all have that ancient gene.*

*Huntington's is not "only" a disease
we are trying to defeat
but also a story about ourselves
as human beings.*

HD doesn't recognise borders, neither should we

At the 10th Annual HD Therapeutics Conference in Palm Springs in February, Charles Sabine sat down with CHDI President Robi Blumenstein and asked him about CHDI, EHDN and his own journey to the heart of the HD community.

How did you come to be involved in HD—do you have a personal connection?

No, I'm not from an HD family. I was a wannabe filmmaker, lawyer and investment professional when, about 14 years ago, a friend and business acquaintance of mine approached me. This was the donor behind CHDI and EHDN. He was already involved in funding HD research, and he felt that the enterprise would benefit from some management expertise. I looked at the project and found it interesting, and that's how I became the manager of a scientific organisation.

It can't be easy to take on responsibility for the hopes of so many people around the world, who suffer from an untreatable disease. Do you ever regret it?

No, though I realise now that I was unbelievably naive when I took the project on. I thought that within five years I'd have put a management structure in place and my job would be done. Over to you, scientists! It turned out, of course, to be a much more complicated problem—one that required the creation of a new type of organisation. That process is ongoing.

This was the organisation that became CHDI. What was its initial purpose?

It was and is to find effective treatments for HD—and then go out of business. We never conceived of CHDI as a permanent fixture. Originally, like many other HD charities, our focus was on funding basic research, but it quickly became obvious to me that this wasn't enough. We needed to address translational and clinical aspects too, and so our remit became broader. We were fortunate in that we had the resources to take such a holistic approach.



CHDI operates out of three US sites—New York City, Princeton and Los Angeles—but it's not just an American organisation, is it?

CHDI is a global organisation because it's virtual by design. We manage and support research and help to build collaborations between researchers, whether they're at pharmaceutical companies, academic institutions or contract research organisations. Those partners are all over the world, so in a sense CHDI is too. A few years ago, at a meeting of the Huntington Society of Canada, somebody asked me how much of the research I was describing was going on in Canada. I said I didn't think about it in national terms. The disease is essentially the same everywhere, and so the research effort has to be global and collaborative. In the end it's about people, not geography.

How did EHDN come about?

I had been at the job for about a year when I attended a Gordon Research Conference in Italy. There I sat in on a discussion about how European HD scientists could organise themselves as their American counterparts had. I offered to support an effort to explore that possibility, and EHDN was the fruit of that effort. Its goal, again, was to facilitate clinical trials. But to pull off high-quality trials, a high-quality network was needed—one that would provide the patients and families needed to conduct those trials, and that would also, in a more bottom-up way, generate ideas for new research avenues to pursue.

The first step was to get European clinical investigators working together, so working groups were created that focused on different aspects of the disease—biomarkers, neuroprotection, symptomatic therapy and so on. Some of those groups met their goals and ceased to exist, some continue to exist in one form or other, others

fell by the wayside—which is natural. There were no trials in the pipeline then; there are now, and the focus has shifted to them. But the working groups were an essential preliminary step, in my view, to creating a culture of collaboration.

“European investigators came together in a fantastic way, and not just European investigators. One day, perhaps, EHDN will drop the E...”

How is EHDN funded?

The majority of its funding comes from CHDI. A small amount comes from trial sponsors who benefit from EHDN’s expertise in designing and running trials and contribute funds in exchange. Another potential source for the future is research grants—if and when EHDN is involved as a partner in grant-funded projects.

The biannual EHDN plenary seems increasingly to be THE go-to meeting in the world for patients and families. Would you agree?



The issue of meetings is complicated. Here geography does matter, because families can’t always travel long distances to attend. But we also need a cycle of meetings that

fulfils the needs of the different constituencies within the community. No one organisation can control the cycle, of course, but resources are scarce these days, so people are coming together to see how best they can satisfy those constituencies. There’s a lack of clinical meetings at the moment, for example, so we are planning meetings for investigators involved in the Enroll-HD global observational study.

How do you see EHDN evolving in future?

I see it having its hands full with clinical trials! There are three phase 2 trials underway (Pride-HD, Legato-HD and Amaryllyis), and others are planned. If the phase 2 trials are successful they will be followed by phase 3 trials. So there are trials as far as the eye can see. It’s a high-class problem!



Wikipedia – The Little Mermaid Statue by Edvard Eriksen; Photo by Avda 2013

Dates for your diary

Save the dates for

- [Orphan Drugs Summit](#), Copenhagen, Denmark, 17-18 September 2015
- European Huntington Association—[How to cope living with HD](#), Warsaw, Poland, 18-20 September 2015
- [2nd Conference on European Reference Networks](#), Lisbon, Portugal, 8-9 October 2015
- 3rd International Congress on Research of Rare and Orphan Diseases—[RE\(ACT\)](#), Barcelona, Spain, 9-12 March 2016
- [10th Federation of European Neuroscience Societies \(FENS\) Forum of Neuroscience](#), Copenhagen, Denmark, 2-6 July 2016