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EHDN News

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

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EHDN organises its first virtual conference

Laura Spinney

On 11 September EHDN held its first ever virtual bridging meeting, an online conference designed as a partial replacement for the biannual plenary meeting, adapted to pandemic times. The postponed plenary, which was due to be held this month in Bologna, Italy, will be held next year in the same city, and will be organised jointly by EHDN and the European Huntington Association (EHA). Around 1,000 people registered for this year's bridging meeting, and 850 of those – hailing from an impressive 52 countries – tuned in for some or all of it.

The event was divided into two sessions reflecting two broad themes – scientific progress and clinical studies, chaired by Lesley Jones of Cardiff University and Jean-Marc Burgunder of the Swiss Huntington Centre in Gümligen respectively. After welcome messages from EHDN and EHA chairs Anne Rosser and Astri Arnesen, **Frédéric Saudou** of the Grenoble

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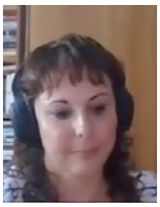
Alpes University kicked off the first session with an update of his lab's work on the basic functions of huntingtin protein (HTT). Using state-of-the-art technology, notably "HD on a chip" microfluidic chambers, his team has shown that HTT plays a critical role in axonal transport, defects in which are known to happen early on in the HD disease process and to have knock-on effects on cortical circuits. Among the other basic functions for which HTT is required, is ciliogenesis – the formation of cilia which constitutes a vital part of the cell cycle. Saudou's group has shown that the mutant form of HTT (mHTT) disrupts ciliogenesis, affecting both the circulation of cerebrospinal fluid (CSF) and brain homeostasis – a result that fits well with the recently published finding of his colleagues in Paris and Grenoble, that these are already disrupted in human fetuses carrying the HD mutation at 13 weeks' gestation. Saudou concluded that, while mHTT drives early pathological brain changes, restoring or preserving wild type HTT (wtHTT) is critical to brain health, whether or not that brain is affected by HD.

The correlation between the inherited number of CAG repeats in the *HTT* gene and age at onset of HD is well known, but it's also now known that this relationship is not simple. Variation in other genes can affect age at onset, and over a person's lifetime the number of CAG repeats can increase in some tissues – a phenomenon known as somatic instability. At the University of Glasgow, **Darren Monckton**'s team has been trying to quantify somatic instability using high-throughput sequencing of *HTT* alleles, or gene variants. They find that somatic expansion is not only age-dependent, it's also dependent on the inherited number of CAG repeats, and tissue-specific. There is an association between somatic expansion as measured in blood, disease severity and variation in genes involved in DNA repair. The latter observation opens up the possibility of modifying somatic expansion via therapies that target those DNA repair mechanisms, with potentially beneficial effects for carriers of the HD mutation.

TANK-binding kinase 1 (TBK1) is an enzyme that catalyses the phosphorylation – that is, the addition of a phospho "tag" – to HTT, regulating where the protein ends up inside a neuron, along with its aggregation, clearance and toxicity. Could TBK1 represent a viable drug target for HD? **Hilal Lashuel** of the Ecole Polytechnique Fédérale de Lausanne and colleagues, who first identified the enzyme, think it could. Lashuel described how, in cellular and *in vivo* models of HD, TBK1 acts on soluble forms of HTT to reduce its aggregation and toxicity, with measurable, beneficial effects on the disease phenotype – that is, how the disease manifests – in those models. Based on this preclinical work, therefore, selective and perhaps cell type-dependent upregulation of TBK1 represents a promising therapeutic strategy going forward – not only for HD, but potentially for other neurodegenerative diseases too.

George McAllister of CHDI's HTT lowering pharmacology programme gave an overview of small molecule therapies for HD that are designed to be delivered orally. Like all HTT-lowering therapies, these fall into two broad categories – allele-selective, targeting only mHTT, and non-allele-selective, targeting both mHTT and wtHTT. Orally delivered therapies have both advantages and disadvantages. An obvious advantage is ease of administration, since one could envisage a once-a-day tablet titrated to an individual's needs. A potential disadvantage is that the whole organism is exposed to the drug, which could be detrimental in certain tissues or cell types. McAllister pointed out that these were exciting times for the field, with two molecules – those designed by Novartis and PTC Therapeutics – already in or close to clinical trials respectively. In fact, PTC disclosed the novel mechanism of its non-allele-selective, HTT-lowering small molecule in an update provided for his presentation. Treatment with this splicing modulator results in the insertion of a stop codon-containing "pseudo-exon" between exons 49 and 50 of HTT, which leads to the clearing of messenger RNA – and subsequent protein-lowering – by a process known as nonsense-mediated decay. PTC hopes to begin testing the drug clinically before the end of the year. Novartis has not yet disclosed the mechanism of its HTT-lowering small molecule, that is already in the clinic, but both companies have publications in preparation.



Introducing the second session, on clinical studies, University College London's **Sarah Tabrizi** gave an update on the GENERATION HD1 phase 3 clinical trial of the HTT-lowering therapy that is currently the most advanced in

development. This is Roche's intrathecally administered antisense oligonucleotide (ASO) tominersen, formerly known as RG6042. Despite the challenges presented by the Covid-19 pandemic, GENERATION HD1 – which got underway late last year – is now fully recruited, with 791 participants, and the study is ongoing with eight-weekly and 16-weekly dosing regimes.

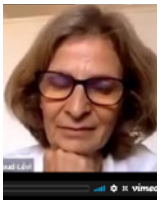
Anna Heinzmann, who works in Alexandra Durr's group at the Paris Brain Institute, reported on progress in the ongoing phase 1b/2a PRECISION-HD1 and -HD2 trials of the allele-specific stereopure oligonucleotides WVE-120101/2, which are sponsored by WAVE Life Sciences. An interim result is that the drug is safe up to and including a 16mg dosing regime, and that a statistically significant reduction of mHTT in CSF of more than 12% has been reported in all groups up to and including that dose (2, 4, 8 and 16mg). A 32mg arm is ongoing, and the trial is expected to report results in the first quarter of 2021.

On behalf of Triplet Therapeutics, **Anne Rosser** of Cardiff University presented SHIELD HD, a natural history study that is being conducted ahead of a therapeutic study due to get underway in late 2021. Building on findings (see Darren Monckton above) that somatic expansion is a key disease mechanism in HD – as it is in other repeat expansion disorders – SHIELD HD is investigating measures of clinical progression in premanifest and early HD, and how these correlate with somatic expansion. Triplet has a candidate ASO, TTX-3360, that targets a gene involved in DNA repair with a view to slowing somatic expansion. One reason this approach is considered promising is because there is evidence that some somatic expansion happens prior to full motor manifestation of the disease, meaning that it might be possible to prevent or at least delay disease onset. SHIELD HD started recruiting in May and is making progress despite the pandemic.

The drug pridopidine is well known to the HD scientific community, having been the subject of several previous clinical trials. These showed no clear clinical benefit, but did hint that the drug might slow decline in the long run. In the past, pridopidine was thought to work as a dopaminergic stabiliser, but recent evidence suggests that its action as a potent, selective sigma-1 receptor (S1R) agonist might be more relevant in the HD context. S1R regulates cellular processes that are known to contribute to the disease, such as calcium homeostasis and cytoskeleton dynamics, and is implicated in neuroprotection and cognitive function. In light of this,

Bernhard Landwehrmeyer of Ulm University explained, Prilenia Therapeutics is now sponsoring the PROOF-HD phase 3 trial to investigate whether longer term administration of the drug will generate clear clinical benefits. PROOF-HD, which has just been endorsed by EHDN, will get underway in early HD patients before the end of 2020.

Ralf Reilmann of the George Huntington Institute in Münster presented the first clinical trial of gene therapy in HD patients to have been given the green light by the US Food and Drug Administration, HD GeneTRX. In this phase 1/2a trial, which is being sponsored by UniQure Biopharma, an engineered microRNA called AMT-130 is delivered in combination with a safe viral vector – adeno-associated virus serotype 5 – into the brain's striatum via intracranial injection. Like ASOs, microRNAs have been shown to lower HTT levels preclinically, though they do so by a different mechanism – RNA interference. The trial got underway in September 2019 and is expected to last five years. It will recruit 26 patients, the first two of whom have already been safely treated.



Anne-Catherine Bachoud-Lévi of the Henri Mondor-Albert Chenevier Hospital in Créteil presented the Multicentric Intracerebral Grafting in HD (MIG-HD) trial, the first randomised, phase 2 cell transplant study in HD. Earlier open pilot studies of human fetal cell therapy in HD produced disappointing results, with only four unequivocal successes out of 71 patients who received transplants between 1998 and 2014. MIG-HD was not able to replicate those four successes, presumably because of slight changes in the protocol. It raised many questions, such as why some grafts restored atrophied tissue and others did not – and whether this was mediated by alloimmunisation, where the body produces antibodies against the graft. Despite having resolved many surgical issues, the researchers wondered whether MIG-HD justified pursuing the approach further. Their conclusion was that it still has potential – potentially as an adjunct to disease-modifying therapies – but that they need to go

back to the bench first, to refine the technique before testing it again in humans.

Hugh Rickards of Birmingham University closed the meeting with a discussion of the need to ensure fair access to any drugs that ongoing clinical trials determine to be effective in HD. He pointed out that even after a drug is licensed, there are barriers to its equitable distribution that the HD community has not properly considered. One of these is the question of who pays for the drug, which is determined on the basis of a health technology assessment. This involves a calculation of the impact the drug will have on a person's quality of life – which is often expressed in terms of quality-adjusted life years (QALYs). However, existing instruments for measuring QALYs are not well tailored to HD, Rickards said, meaning that the benefit any drug could bring to an HD patient risks being underestimated. Another potential hurdle is securing the capacity to deliver the therapy to everyone who needs it, which in turn relies on accurately estimating disease prevalence. Research conducted by Jean-Marc Burgunder and others indicates that only a fraction of specialised HD clinics in Europe currently have the capacity to deliver a drug such as tominersen – which is administered intrathecally – to all those who would benefit from it. These hurdles need to be addressed urgently by the HD community in all countries, and Rickards and others have created an EHDN task force – Huntington's Equal Access to Effective Drugs (HEATED) – to support them in doing so.

Bernhard Landwehrmeyer and Anne Rosser closed the meeting by thanking EHDN co-chair Patrick Weydt – who led the programme committee – and Katrin Barth, Sina Bartosch and Katharina Berndt for its smooth organisation. It is a rich time for HD therapeutics, they said, but the session on scientific progress had reminded us that there is still much about the complex biology of HD that we don't understand, and it is therefore important to remain inclusive and agnostic. The virtual format of the meeting seemed to have been appreciated, Rosser said, and future meetings adopting the same format may well be planned – pandemic or not.

The presentations from the virtual bridging event are available here.

Kathrin Reetz

Anne Rosser

EHDN endorsement: what does it mean and how does it work?

Kathrin Reetz, Chair, EHDN Scientific and Bioethics Advisory Committee; Anne Rosser, Chair, EHDN Executive Committee; and the EHDN leadership

What does endorsement mean?

Endorsement of research projects, clinical studies and trials has been part of EHDN's remit since its foundation, and is incorporated into its constitution. When the EHDN Executive Committee (EC) endorses a study, it gives that study its stamp of approval, judging that it has met EHDN's standards of scientific rigour and ethical conduct. This can be of considerable value to the study team, because it counts as evidence of independent peer review for ethical and regulatory submissions. It is also a signal to the EHDN membership, including patients and families, that the network considers the study to be both valuable and appropriately designed.

Most requests for endorsement to date have been for clinical trials – mainly commercially sponsored studies but also some investigator-led ones. Hence, the explanation of the endorsement process provided below largely reflects our approach to this kind of trial. Endorsed studies obtain visibility through the EHDN website and scientific meetings, and gain access to the scientific and clinical expertise of the EHDN membership. In return, lead investigators are expected to keep the network informed of the study's progress and of any amendments to its protocol, and EHDN

members conducting endorsed studies are expected to comply with the network's constitution. EHDN may provide additional practical assistance through its network of language area coordinators and the Enroll-HD study team, for studies that are also accepted by its Clinical Trials Committee. This assistance may include access to listings of Enroll-HD participants who potentially satisfy the study's inclusion criteria.

How does endorsement work?

Anyone may apply to EHDN for endorsement of a project, by submitting the information requested by the EC. Proposals are considered by the Scientific and Bioethics Advisory Committee (SBAC) and the EC, ably supported by the EHDN Central Coordination (CC) team. It should be emphasised that, although many studies are submitted only once the final protocol is available, EHDN also welcomes submissions at an earlier stage. It can offer advice at that stage, pending a full review later on.

As well as reviewing data mining projects that require access to Registry data and biosamples, and seed fund proposals, the SBAC independently reviews endorsement requests. For clinical trials, a sub-group of SBAC members and advisors (including clinicians, researchers, statisticians, bioethics experts and patient representatives) pre-reviews the proposal data ahead of a discussion (usually via Zoom) with the entire SBAC team if that is deemed necessary. At that meeting, the following issues are discussed in depth:

- Is the proposal based on a sound rationale? Assessing this involves consideration of: the preclinical and clinical data supporting the proposal (eg drug evaluation, animal models, phase 1 and 2 data); the trial methodology (eg eligibility, randomisation, recruitment, sample size estimates, controlled-arm, efficacy, study duration and nature of follow-up, how the primary endpoint has been chosen, and primary analysis plan); and whether the proposal demonstrates appropriate quality assurance and pharmacovigilance processes.
- Based on previous clinical data (eg regarding adverse events), are there any safety or ethical concerns and how can safety and risk assessment be further improved? How are data protection and privacy issues addressed?
- Is the proposed trial protocol feasible and acceptable to clinicians, coordinators, patients and their families, in terms of the frequency of visits, the mode of application of a drug or other intervention, and the burden of assessments?
- Are there any conflicts of interest? These might concern sponsors, other companies or industry partners implicated in the project, potential sites, clinicians and researchers.

The information provided on these issues, along with the SBAC's overall recommendation, is considered by the EC, whose members have previously perused the submitted documentation. The EC's collective consideration of the proposal usually takes place at one of its scheduled meetings and is subject to a vote, the outcome of which is fed back to the study team along with any recommendations.

It may be possible to agree endorsement on a first pass through this system, with or without caveats or recommendations, but sometimes questions are raised that require addressing by the study's lead investigators and further deliberation on the part of the EC and/or SBAC. An uncomplicated request can usually be processed within one-to-two months, at present, although this depends on circumstances – including the SBAC's and EC's workload.

More information about endorsed projects and the SBAC, EC and CC teams can be found at www.ehdn.org.


Photo: G. Stautner, Artifox

Update: Clinical trials

Tim McLean, Clinical Operation Manager, EHDN

Much attention has been paid in recent editions of the newsletter to large, commercially sponsored clinical trials that have been endorsed by EHDN. There are, however, a number of well designed and well conducted non-commercial clinical trials that are underway, with EHDN's endorsement, that will be highlighted here.

These are usually investigator-led studies that are run out of an academic institution or a consortium of such institutions. In general, they are not designed to test the safety and efficacy of a pharmaceutical product, but rather to evaluate a procedure with potential therapeutic benefit or with a view to informing future research. They are often run on a smaller budget than commercial studies, being funded by grants from private foundations or governmental bodies. Nevertheless, they represent an important contribution to the quest for effective treatments and to improve the lives of those affected by HD.

EHDN reviews non-commercial studies in the same way it does commercial ones. First, the Scientific Bioethics Advisory Committee reviews the study, making its recommendations to the Executive Committee which then decides whether or not to endorse the study formally. An important feature of this process is that it may generate useful comments or recommendations regarding the design or conduct of the study.

The following are examples of non-commercial clinical trials that EHDN has endorsed:

HD-DBS

This study of deep brain stimulation (DBS) of the globus pallidus is coordinated by Jan Vesper and Alfons Schnitzler of the University of Düsseldorf, and funded by the German Research Foundation (DFG). It is a prospective, randomised, controlled multi-centre study that is designed to assess the safety and efficacy of DBS as measured by change in Unified Huntington's Disease Rating Scale (UHDRS) total motor score after 12 weeks. The study has recruited participants at eight sites (five in Germany and one each in Switzerland, France and Austria), but recruitment has been challenging due to the specific combination of entry criteria. Nevertheless, the study team has worked hard to maintain recruitment momentum, and after a hiatus due to the imposition of pandemic-related restrictions between March and June of this year, it is just four treated participants short of its target of 45.

PACE-HD

The Physical ACtivity and Exercise outcomes in HD study is led by Monica Busse of Cardiff University and Lori Quinn of Columbia University, New York, and funded by the Gossweiler Foundation. It has two components: a one-year prospective evaluation of physical activity and physical fitness in individuals with HD, conducted alongside annual Enroll-HD assessments; and a within-cohort, randomised, controlled trial of a one-year exercise intervention in HD, that compares a supported and structured aerobic exercise training programme with usual activity. 116 participants were recruited between February 2018 and May 2019, at six sites (two in Germany, two in Spain and two in the US). Of those participants, 59 were assigned to the prospective cohort and 57 to the randomised trial. The last participant completed the 24-month exercise period in June 2020, and results are expected before the end of 2020.

DOMINO-HD

Monica Busse is also leading the Multi-Domain Lifestyle Targets for Improving PrognOsis in HD observational study, which is funded by the EU Joint Programme – Neurodegenerative Disease Research. DOMINO-HD is designed to provide new insights into whether behaviour and lifestyle factors are linked to HD genetic risk and progression. 300 participants in the Enroll-HD study will be recruited to this study at five sites in Germany, Poland, Spain, Switzerland and the UK. Participants' physical activity, sleep and diet will be monitored at their homes over a 12-month period, in part by means of a wearable activity tracker. Monitoring will also include an intensive seven-day/night assessment and two in-clinic assessments at baseline and 12 months. A number of site-specific sub-studies will be conducted in parallel with the main study, involving different sub-sets of participants. Recruitment was due to get underway in October 2020.


Photo: G. Stautner, Artifox

Update: Enroll-HD

Olivia Handley, Enroll-HD Global Platform Manager

Enroll-HD is now well established as a clinical research platform that supports clinical studies and therapeutic trials for HD with a wide range of resources. How is it being used?

An important first step for any study team seeking to use the platform is to engage with the platform resource support management (PRSM) team (prsm@enroll-hd.org). This is a small team drawn from CHDI and Enroll-HD whose members have 50 years of experience of setting up HD studies between them. Having described the study design, timeline and operational requirements, the study team works with PRSM to identify which aspects of the platform could provide useful support for the study.

Enroll-HD adopts a risk-based data monitoring approach that uses standardised edit checks, centralised statistical monitoring and quality control checks, as well as on-site source data review, meaning its data is verified to a high level and represents an attractive resource for other studies to draw on. A growing number of studies have used or will use Enroll-HD data to date, of which the CHDI-funded longitudinal CSF collection study HDClarity is an example. Since participants in HDClarity must also be participating in Enroll-HD, Enroll-HD data can be shared with HDClarity, thereby reducing the burden on participants in terms of avoiding the unnecessary repetition of assessments, relieving site resources associated with those assessments, and avoiding the entry of duplicate data. In other words, the advantages of joint participation in the two studies are felt at the levels of participant, site and study.

Enroll-HD platform monitoring activities are not restricted to Enroll-HD data. To date, seven studies have used or will use Enroll-HD monitors to review their data on-site – for checking data sources and verifying informed consent forms, for example. This monitoring resource is in high demand and managing that demand requires careful planning on the part of the Enroll-HD platform monitoring oversight team (PMOT). The PMOT works with study teams to identify their requirements and ensure clear communication regarding expectations and timelines. The optimal approach, which is to schedule study and Enroll-HD monitoring visits to coincide, has been successfully adopted for HDClarity, PACE-HD, FuRST 2.0 and HD-Charge, and will also be used in studies planned for 2021 and beyond. It has many advantages: visits can be planned in advance, monitoring resource (number of monitors, days required on site) can be accurately estimated, and sites can prepare to cover multiple studies in a single monitoring visit. There is one limitation, however: the Enroll-HD schedule determines monitoring visit frequency, and study teams are asked to comply with this schedule as far as possible. Otherwise it becomes impossible to manage competing demands for a resource that may be required across several studies at a time.

Probably the most sought-after resource provided by the Enroll-HD platform – which more than 30 studies and trials have drawn on to date – is intelligence regarding site selection and participant feasibility or eligibility. Study teams use these to guide them in site start-up activities and recruitment respectively. The platform has the unique advantage of having collected information on approximately 200 sites across the globe, of which more than 150 take part in Enroll-HD. Valuable insights have been gained at site, region and country levels, and these are shared to assist study teams in their site selection strategies. *In silico* screening via the Enroll-HD platform means they have easy and up-to-date access to listings of potentially eligible participants, too. It is unquestionably one of the platform's greatest strengths, that it has at its core a high-quality dataset on an HD population, which can be used to expedite recruitment to HD research.

Photo kindly provided by Rosanna Tortelli

Rosanna Tortelli

Photo: G. Stautner, Artifox

Ed Wild

New seed fund awarded

EHDN has approved seed funding for the NEVADA-HD study, a project proposed by Rosanna Tortelli and Ed Wild of University College London.

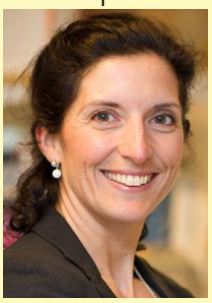
Though impressive progress has been made in the field of biomarkers, HD researchers still need better biomarkers of the HD disease process as it unfolds inside the brain. One promising candidate is exosomes, tiny vesicles containing proteins, RNA and lipids that are released by most cell types – both in health and in disease – and whose contents reflect the functional state of the cell that released them. Exosomes can be isolated from biological fluids and their contents can be analysed, providing a "fingerprint" of the tissue of origin. NEVADA-HD aims to optimise the isolation of exosomes generated by neurons, both from the cerebrospinal fluid and the blood of individuals with premanifest and manifest HD. The project will test different techniques for doing so, and evaluate them comparatively.

Seed funds are intended to support pilot studies that will eventually kickstart larger projects. More information about the programme and how to apply can be found here.

Get in touch with the think tank!

The EHDN's HD Science Think Tank brings together EHDN members and staff who are closely involved in supporting scientific research – including members of the Executive Committee, Central Coordination and the working groups – and it engages with the HD research community in three ways:

- Researchers may contact the think tank for help in identifying potential collaborators or funding opportunities, or to discuss scientific ideas
- The think tank welcomes suggestions of research topics, and has provided a contact form on its website via which these can be submitted
- The think tank may occasionally propose specific research topics that could be addressed by a dedicated task force working for a defined period of time



For more information about the think tank, please contact Kristina Bečanović: kristina.becanovic@euro-hd.net

Send us your photos!

In this photo, a patient's daughter hugs her while neurologist Nacho Aracil of the Movement Disorders Unit at the Santa Creu i Sant Pau Hospital in Barcelona administers the experimental drug tominersen to her, in the context of the Generation HD1 clinical trial that is sponsored by Roche. The photo was kindly provided by Saül Martínez-Horta, a neuropsychologist at the unit and a former EHDN language area coordinator, who took it in March 2019.

"It was a really emotional moment for us," Saül explains, "because it was the first time we were administering this drug and the patient was one of the first in Europe to receive it."

Another reason the moment was significant for the team, he adds, was because of the extraordinary efforts they had made over a decade, to have the Movement Disorders Unit recognised as an HD reference site. The photo was taken and is published with the permission of the patient and her daughter.

Our photo experiment continues!

Whether you're affected by HD personally, or you're a carer, clinician or scientist working in the field, we'd like to publish your images in the newsletter. If you have a photo that provides an insight into your daily life, that you think might interest or inspire other EHDN members – or make them think differently about the disease – please send it to us along with a few words explaining who you are and what the image shows: newsletter@euro-hd.net

Photos kindly provided by Katrin Barth

Behind the scenes at EHDN:

Interview with Katin Barth

Katrin Barth's official job description, within EHDN'S Central Coordination, is "IT support", but that doesn't do justice to the person who helps ensure the smooth day-to-day running of the network, and without whose team the biannual celebrations of science and community we call the EHDN plenary meeting would never come together so apparently effortlessly. She's hard to extract from her office in Ulm, Germany, these days, so we booted up Zoom and followed her in there…

What initially drew you to EHDN?

To begin with I came as an intern, to support work on the web portal. I was studying medical documentation and during a previous internship I had got to know Torsten Illmann of 2mt Software, the IT company that was collaborating with EHDN. But I also had training as a physician's assistant, and when a colleague left on maternity leave I took over from her, working with patients and as a language area coordinator (LanCo). It was 2005. The network was two years old, and the Registry study was just getting going.

What made you stay?

Coincidentally, I had been present at 2mt when Professor [Bernhard] Landwehrmeyer came to meet the team in 2003. He presented his vision for the network and how data collection would be at the heart of it. It was inspiring but also overwhelming. And then, when I got to know the patients and my colleagues at EHDN, I was hooked. I became involved emotionally. Gradually the community came to seem like a family to me. EHDN *is* a family, in fact, and the network and I have evolved together!

Is there a typical day for you?

On a typical day I'm sitting in front of the computer, reading and trying to respond to emails on a very wide range of subjects. I see myself as the IT support for the Enroll-HD observational study, so if someone is entering data for that study and encounters a problem, I act as the link between them and the IT team and I may be able to suggest a solution myself. I'm still involved with the LanCos and, more recently, in setting up new platform studies and other projects in collaboration with CHDI.

Do you travel a lot – or rather did you travel a lot, pre-Covid-19?

Yes – to CHDI platform study set-up meetings, and to LanCo and on-site monitoring meetings at the German-speaking study sites, with which I have a close relationship.

Organising the plenary meeting must require a huge effort. Tell us about it?

Planning for a plenary starts as soon as the previous one is over. This year's meeting was postponed, of course, but we already have the venue for the 2021 edition in Bologna, and an outline of the programme. For the last couple of years I've been a member of the organising committee. EHDN's project manager Katharina Berndt, event manager Sina Bartosch and I are the ones who oversee the logistics. My role is technical – organising wheelchair access for patients, for example, or microphones on stage, or someone to host the speaker ready room. This involves visiting the venue at least once prior to the meeting. During the meeting itself the entire Ulm team helps at the conference centre, providing technical support and on-site registration. We are about 20 in all, working in a container building – we call it the

Huntington Container – at the university hospital in Ulm.

Who arranges the flowers when these are presented on stage?

That might also be me!

How did the decision to organise a virtual bridging event come about?

Naturally, since the physical plenary could not go ahead. It seemed obvious to the programme committee and to us that something should take its place, to keep everyone with a connection to EHDN motivated and informed. After that it was mainly a question of slimming down the programme that had already been drawn up, and deciding on a format and duration.

It was the first time EHDN had organised such a meeting virtually. Were there any technical challenges?

We had to decide which communication platform to use – we chose Zoom – and then learn how to use it. It wasn't straightforward, and Zoom's technical support could have been better. It wasn't obvious, for example,

how to find out who had registered for the meeting. In the end, though, everything went according to plan. 850 people logged in, from 52 countries. I am very happy with that – and there was no need to organise flowers!

Were you able to listen to the presentations?

No, unfortunately, I was too busy making sure everybody else could hear them… But I heard enough to realise that these are exciting times, scientifically. My understanding is that the reason so many pharmaceutical companies are now active in HD research is because of our observational studies and the data they generate. I think that's wonderful, and I hope there will be treatments very soon, for those affected by HD.

In the meantime, will you return to organising next year's plenary?

Yes, and to working on the platform studies and other projects, some of which will get underway very soon. It's a pleasure for me to work for EHDN. Hopefully one day we can use the structures we have built to make HD treatments accessible.

• • •

Dates for your diary

Save the dates for:

- EHDN physiotherapy working group virtual meeting (open to all physiotherapists working with people with HD), 6 November 2020, 13h30-15h GMT, Meeting ID: 817 6608 0255, Password: 287940
- Webinar: "Functional movement disorders: a diagnostic guide", 1 December 2020, 15-16h CET
- Virtual meeting: "Neurodegenerative diseases: biology and therapeutics", Cold Spring Harbor, USA, 2-4 December 2020
- HDYO's International Young Adult Congress 2021, Glasgow, Scotland, 9-11 March 2021
- FENS Brain Conference: "RNA mechanisms and brain disease", Rungstedgaard, Denmark, 18-21 April 2021
- EHDN2021 plenary meeting, Bologna, Italy, 10-12 September 2021

Photo: Rungsteedgaard