June 2008 · Issue 02

EHDN News

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

This year the EHDN Plenary Meeting takes place in Lisbon on September 5th and 6th. Registration deadline: July 31st, 2008. – Read more on page 3!

FEATURE ARTICLE

By Robi Blumenstein, CHDI Management, New York (USA)
on behalf of the EHDN Executive Committee

EHDN promotes collaboration and sharing – proposed changes to the Constitution

Having spent several years, first drafting, and then working with the Constitution and By-laws of the European Huntington's Disease Network (EHDN), the Executive Committee is now proposing changes for consideration by the membership at the upcoming EHDN Plenary Meeting in September 2008.

The purpose of these changes is threefold: 1) To better embody the EHDN philosophy of collaborative, open-access science; 2) To provide more flexibility for the Executive Committee to adopt policies and procedures to implement this philosophy; and 3) To ensure consistency of style and message.

Behind the proposed changes is the belief that collaborative, open-access science (or "Science 2.0" as it is being called) is a more productive way to conduct science and likely to lead to treatments for Huntington's disease more quickly. The premise of Science 2.0 is that sharing enables science – sharing of time spent in clinical research, of biological samples donated by people with Huntington's disease, of ideas, data, results and effort by scientists, and of financial and physical resources by our sponsors. EHDN is uniquely positioned to forge this collaborative network and enable Huntington's disease research.

As the physicist Richard Feynman said:
The principle of science, the definition, almost, is the following: ***The test of all knowledge is experiment…*** *But what is the source of knowledge? Where do the laws that are to be tested come from? Experiment, itself, helps to produce these laws, in the sense that it gives us hints. But also needed is* ***imagination*** *to create from these hints the great generalizations – to guess at the wonderful, simple, but very strange patterns beneath them all, and then to experiment again to check if we have made the right guess.*

EHDN cannot supply the imagination – that must spring from the minds of its Members – but by collecting samples and data and nurturing a culture of

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The EHDN Newsletter was originally conceived by **Prof. Justo García de Yébenes** and **Prof. G. Bernhard Landwehrmeyer**. We thank all people who have contributed to the first and second issues of the Newsletter, especially Prof. Justo García de Yébenes (Ramón y Cajal Hospital, Spain) and Gabriel Plaza (Ibáñez & Plaza Asociados, Spain).

By Robi Blumenstein, CHDI Management, New York (USA)
on behalf of the EHDN Executive Committee

sharing widely, it can enable the experiments that give us the hints that will hopefully lead to the imaginative insights we need.

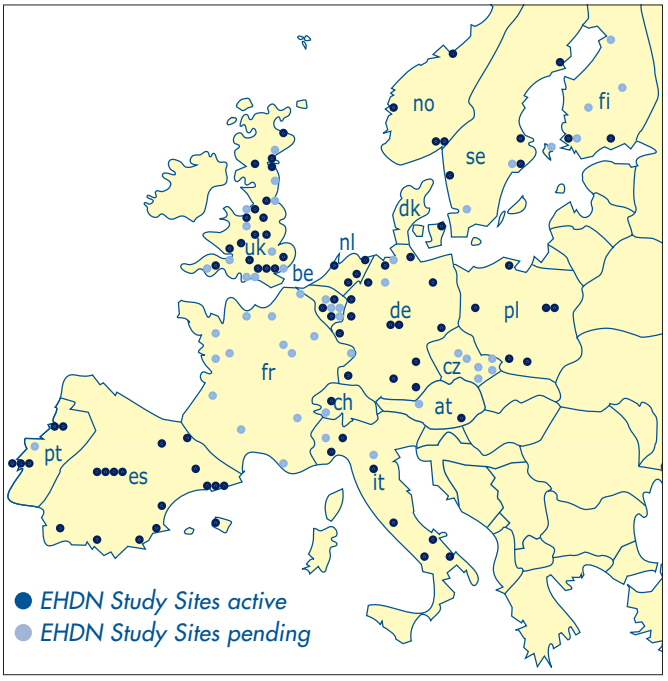
The Scientific Review Committee has been restyled to become the Scientific and Bioethics Advisory Committee (SBAC). Unlike the scientific board of a grant-funding organisation, this committee is charged with advising on scientific and bioethical issues to *facilitate* projects. Rather than find reasons to stop experiments taking place, this committee is intended to make science happen! Rather than duplicate a review that will be performed by other funding agencies, the SBAC can help those sponsors by bringing to bear the Network's Huntington's disease expertise to endorse appropriate projects.

The same philosophy extends to the data and biomaterials collected in the course of REGISTRY and other EHDN clinical research studies. Much of the biomaterials EHDN collects (e.g., DNA and cell lines) are inexhaustible in the sense they can be replicated. In general, these data and materials will be made available to investigators who propose experiments with relevance to Huntington's disease without regard to impact. Greater scrutiny will be given to requests for materials of finite quantity.

There is an implicit bargain made when people with Huntington's disease graciously participate in studies and share their biomaterials with scientists: data and materials in exchange for ideas and effort. Another proposed amendment to the Constitution makes this bargain explicit:

Sharing Data and Materials: EHDN is committed to enabling well-powered, conclusive studies of Huntington's disease by making data and biomaterials provided by patients and collected through the efforts of many contributing sites available to competent scientific investigators who propose ethically sound projects. In exchange, Members conducting scientific projects or clinical studies using biomaterials obtained from EHDN are expected to promptly submit all sample-level data derived in the course of the scientific project or clinical study back to EHDN to further annotate the biomaterials used.

In the interest of accelerating research the quid pro quo for access to data and biomaterials collected by others is a willingness to promptly share sample-level data collected by oneself. In several places it is proposed to clarify the responsibility of the Executive Committee to publish policies and procedures to give effect to the principles in the Constitution. For example, the detailed mechanics for implementing the Publication and Authorship principles articulated in Article 10 would be deleted from the Constitution and replaced by a Statement of Policy and Procedure. Similarly, Statements of Policy and Procedure may be issued concerning the endorsement of research projects and clinical studies, access to data and biomaterials, ethics and conflicts-of-interest and other matters related to the administration and operation of the Network.



Study Sites of the EHDN REGISTRY Project. Map provided by Olivia Handley (REGISTRY Project Manager, EHDN, UK).

On the administrative level it is proposed that the Constitutional requirement to hold a Plenary Meeting every year be relaxed to every second year. This proposal stems in part from calendar considerations, in part from the fact that the biennial World Congress on Huntington's Disease will not be held in Europe for a number of years, and in part from the expectation that the support that would otherwise be used for Annual Plenary Meetings will be used to support working group and other similar activities during the off years.

The full text of the proposed amendments to the Constitution and By-laws of the European Huntington's Disease Network can be found at http://www.euro-hd.net/html/network/project/constitution. EHDN members are invited to comment on the proposed changes. All comments will be posted on the website.

Mosteiro dos Jerónimos, Lisbon

The EHDN Plenary Meeting 2008 in Lisbon

It is our great pleasure to invite you to attend the 5th Annual Plenary Meeting of the European Huntington's Disease Network (EHDN) to be held in Lisbon (Portugal) on September 5th and 6th, 2008, in conjunction with the 12th Bi-annual Meeting of the European Huntington Association (EHA).

All sessions of the EHDN Meeting are open to clinicians, scientists, representatives of the EHA and members of families affected by HD. Simultaneous translation of the sessions into Portuguese and Spanish will be provided.

The programme includes:

- "hot topics" discussion session
- recent advances in HD
- new EHDN endorsed projects
- keynote lectures in basic science and drug development.

Visit the EHDN Working Group booths for an update of their activities or listen to Working Group presentations. Meet old friends and colleagues, or make new ones at the social events.

To attend the EHDN Meeting, you must **register by July 31st, 2008**, using the online registration form at http://www.euro-hd.net/html/ehdn2008/registration.
A limited number of hotel rooms have been reserved for meeting participants. Please **book your accommodation** following the instructions at http://www.euro-hd.net/html/ehdn2008/location/accommodation by July 15th, 2008.
For **more information** on the EHDN Meeting, please visit http://www.euro-hd.net/html/ehdn2008.

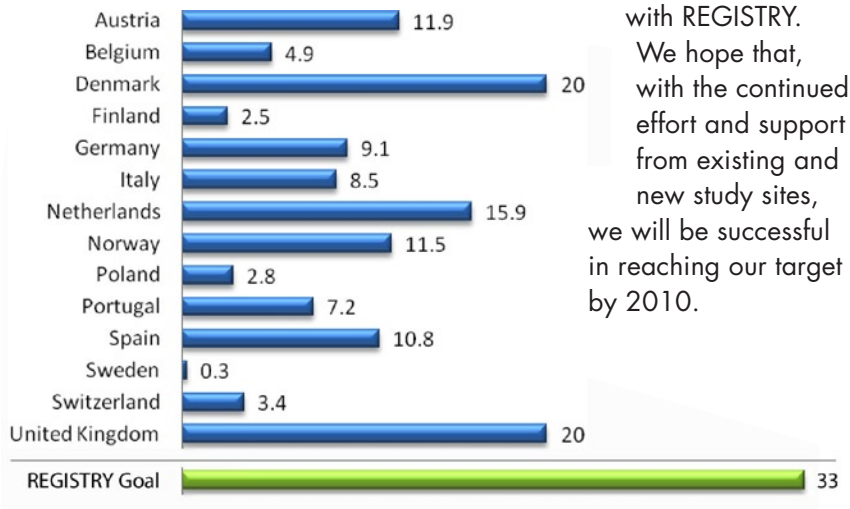
We look forward to meeting you in Lisbon!
Esperamos vê-lo em Lisboa!

REGISTRY: Enrolment update and progress

By Olivia Handley, REGISTRY Project Manager, EHDN (UK)

Progress toward finding a treatment or cure for Huntington's disease (HD) will depend on worldwide cooperation and collaboration. This is precisely the goal of the EHDN. Its core study REGISTRY is the first significant step towards establishing a well-characterised HD cohort that is eligible for participation in observational studies and interventional trials in Europe.

A major goal of REGISTRY is to recruit one third of the European HD population (~10,000 individuals) by 2010. At the close of 2007, 14 European countries were actively contributing to REGISTRY, and collectively had enrolled 2,948 (10.6%) individuals affected by, pre-manifest for, or at risk of HD. The percentage of each country's estimated HD population enrolled into REGISTRY is shown in the figure. So far, the Network has made excellent progress with REGISTRY. We hope that, with the continued effort and support from existing and new study sites, we will be successful in reaching our target by 2010.



REGISTRY participants before 2007-12-31 given as percentage of country's HD population (based on a prevalence of 8/100,000 individuals).

The BioRep facility for HD sample processing and storage

By Pasquale de Blasio and Michele Piovella, BioRep (Italy)

Biorepositories assure the long-term storage, viability, quality and distribution of biological materials. They serve as a key resource centre for large-scale genomic- and proteomic-based research. In addition, a centralised biorepository is of paramount importance in translational medicine, since it provides a high-quality source of biosamples that can be used to detect markers of disease state and progression and targets for therapeutic intervention.

Tank with liquid nitrogen for storage of biomaterials at BioRep (Italy).

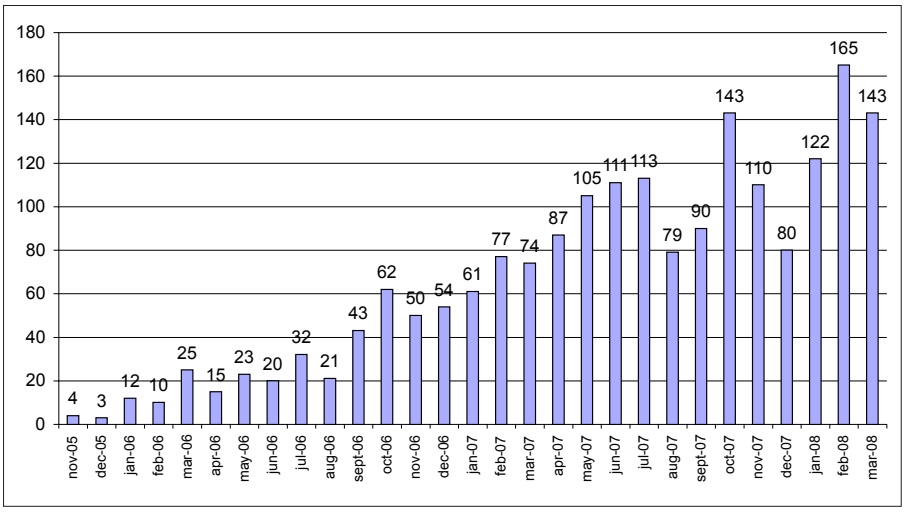
BioRep's ISO 9001/2000 certified facility is designed to provide a secure collection of biosamples. It is one of the few biorepositories in Europe which is able to guarantee safe storage (for three generations) of biological materials in liquid nitrogen, supported by monitoring and controlling systems based on PLC (programmable logic controller) technology. This technology is able to register and certificate all of the operative parameters of critical machines (incubators, tanks, cold rooms, etc), and to activate a very sophisticated alarm system (24 hours/day for 365 days/year) in case of emergency. BioRep has a partnership agreement with the Coriell Institute of Medical Research, one of the most prestigious cell line repository in the USA, allowing BioRep to use Coriell's Standard Operating Procedures (SOPs) that have been developed over more than 50 years.

BioRep has been the reference Biorepository of the **EHDN "REGISTRY"** Project since November 2005. It aims to guarantee the long-term control of samples that will be used to search for genetic modifiers of Huntington's disease and for biomarkers as indicators of disease progression. To date, BioRep has collected, transported, processed and stored more than 1,700 blood samples from people with Huntington's disease that have been collected from more than 120 centres spread over 16 European countries.

From each blood sample, BioRep establishes immortalised cell lines using isolated white blood cells (lymphocytes), extracts DNA from whole blood and from the derived cell lines, and stores the buffy coats (fraction of blood samples containing white blood cells and platelets). Biorep also stores urine for potential future metabolomic studies. Any stored sample will be destroyed on the request of the donor. They will soon start to store blood plasma that has been prepared at selected collection centres.

BioRep measures the CAG repeat in DNA from consenting patients **for research purposes only.** Because the accurate determination of CAG repeat size is important for many research projects, CAG repeat testing is performed in parallel at the Diagnostic Molecular Genetic Laboratory of the University Hospital of Tübingen, Germany. So far, only 0.6% of the CAG repeat sizes determined by the two labs differs by more than 2 CAG repeats, underscoring the uniformity of the procedures applied, whereas there can be a large difference in the results from tests performed by other diagnostic labs.

In March 2008, BioRep began to distribute DNA samples in 96-well microtiter plates to authorised research labs which have signed appropriate material transfer agreements with the EHDN Central Coordination. BioRep aims to establish 5,000 cell lines from the participants of the EHDN REGISTRY Project by 2010.



Number of samples monthly collected for REGISTRY by all participating Study Sites since November 2005.

Standard of Care Working Group

By Sheila Simpson, University of Aberdeen (UK)

Establishing Standards of Care in Huntington's disease

There is little peer reviewed literature on the care of the Huntington's patient. Internationally approved guidelines for care have not been developed, since the evidence for best practice is lacking. This partly reflects the fact that in many countries there are no designated clinics for this patient group, and within some countries the care provided varies widely. Clinicians with varying experience (some extensive) have adopted their own methods of working, but audit of this is rare, with publication of evidence even more so.

Services available

We sought to document the services available to those affected by Huntington's disease (HD) within Europe. A poster was presented at the third World Congress on Huntington's disease, which described the specialities of those involved in providing care and their tools. A publication is in preparation with greater detail of these data. Clinicians have sent details of their work, as well as ongoing projects with which they are involved, which will add to the literature.

Help for asymptomatic individuals

It is clear that those who are as yet asymptomatic, but who carry the mutation for HD, are rarely offered comprehensive follow up and assessment. This is an important group and their needs are significant. Information about research programmes and testing of pregnancies are two of the issues raised by them.

Objectives

The Standard of Care Working Group has therefore several objectives, which include the gathering of information about different approaches around Europe to the management of HD, so that evidence based guidelines for best practice can be created. A framework for care has been designed (see figure) and accepted by the group, and our energies are now directed towards gathering and creating evidence for this managed care network.

Cooperation

Liaison with other EHDN working groups, such as the Quality of Life Working Group, and with international family organisations allows us the opportunity to document the wishes of the Huntington's patient and to assess the impact of various treatment regimens. Of particular importance is our investigation of groups that are disadvantaged in their access to clinical review because of language or cultural barriers. Our group is investigating the use of interpreters and leaflets as aids.

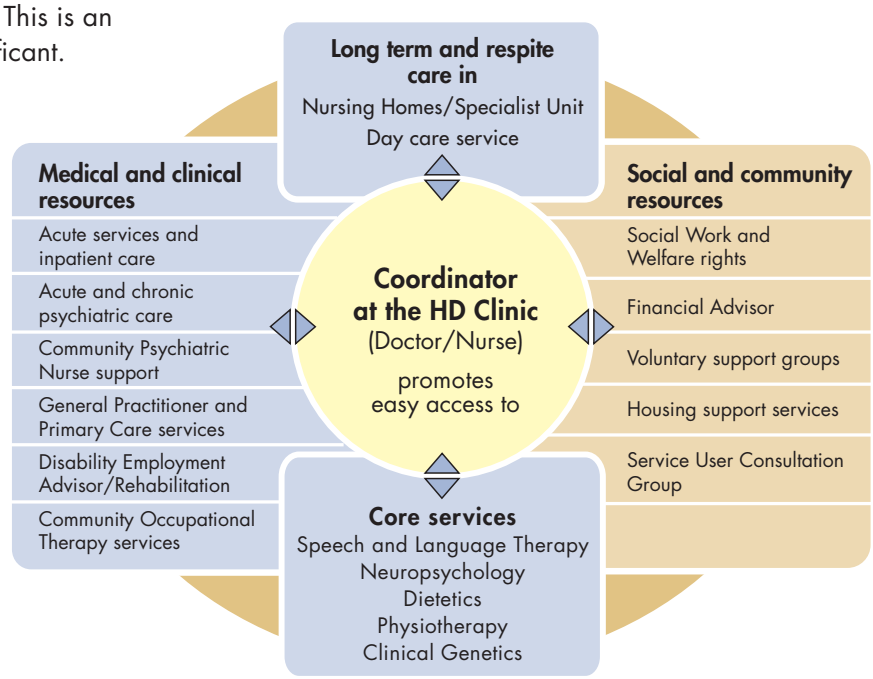
Database

The group is creating a database of relevant literature on care issues, drugs, aids and other resources, and is to install these databases on the EHDN website for all to access. Country specific sources of expert advice are planned.

Information

Knowledge of the pathophysiology of HD is an essential component of research into its cause and prevention. Without detailed and accurate clinical information, such research cannot proceed. Regular assessment and documentation of stages of disease are essential for this process. Trials of therapy will depend on the ability to properly compare progress before and after intervention. Management review clinics allow for the collection of such data from consenting patients.

The "Managed Care Network": A model developed by the Standard of Care Working Group for integrating different specialised services for HD patients.



Biomarkers Working Group

By Edward Wild and Sarah Tabrizi, University College London (UK)

Searching for biomarkers of Huntington's disease

What is a biomarker?

A biomarker is anything that we can measure reliably to give us an idea of how a disease is progressing, or how it is expected to progress in future. It may also tell us whether a possible treatment is working. Many of the features which we already measure in HD can be seen as biomarkers, for example the neurological examinations and cognitive tests that patients undergo in the clinic. But other tests could be more accurate at monitoring disease progression.

Possible biomarkers include:

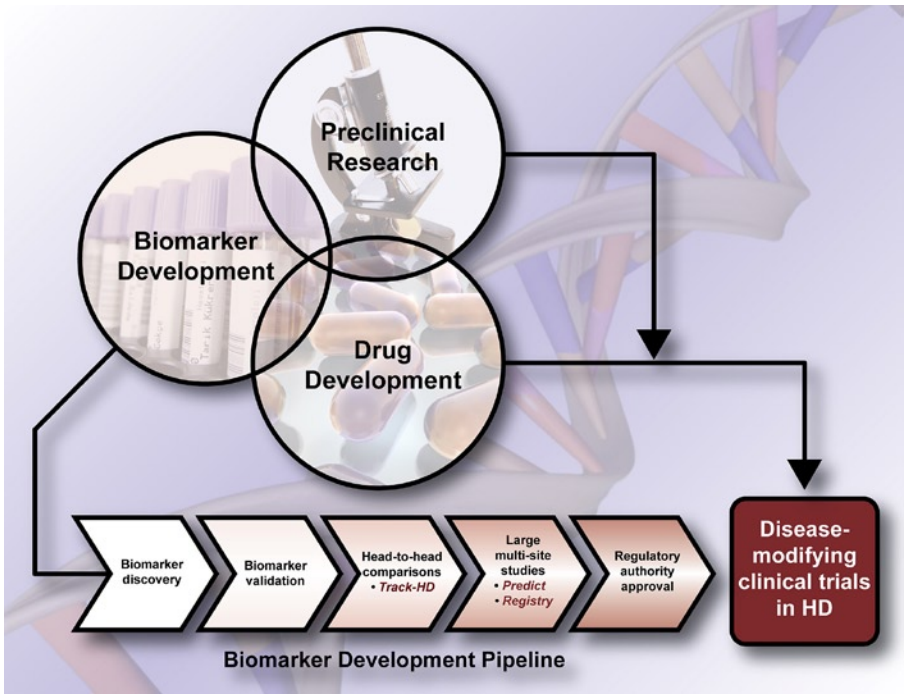
- Chemical tests on blood or urine that reflect what is happening in the brain
- Measures calculated from brain scans
- New cognitive tests with increased accuracy and consistency
- Computerised tests of limb and eye movements.

Why do we need biomarkers for HD?

The genetic test can tell us reliably which people at risk of HD will develop the disease. However, it cannot tell us when the disease itself will start to develop, or which symptoms the person will get. HD usually progresses slowly, and symptoms vary from person to person. The clinical assessments used currently to measure disease progression are not accurate enough. This is an important problem for the evaluation of possible treatments for HD. For instance, therapies that slow down disease progression would need clinical trials involving hundreds of patients over many years. This scenario becomes more complex when we consider HD gene carriers who have no symptoms at all. Dozens of treatments may need to be tested in the next few years, and we therefore need ways to reduce the number of participants and duration of clinical trials. We hope that biomarkers will help us identify the most promising drugs.

How is the Biomarkers Working Group helping biomarker research?

The EHDN Biomarkers Working Group (BMWG) encourages researchers from throughout Europe - and beyond - to share their results, ideas and patient samples to facilitate biomarker research. Our scientific meetings are characterised by lively debate, cooperation and sharing of data. For instance, the new TRACK-HD study, which aims to compare the best biomarker candidates head-to-head, arose from ideas and discussions of the BMWG. Biomarker research, pre-clinical (laboratory) research and drug development go hand-in-hand (see figure). The BMWG members are key contributors to the EHDN REGISTRY study, which promises to generate a major collection of samples for biomarker research.



Biomarker research is connected with pre-clinical and drug development research. The "biomarker development pipeline" sets out the steps required for each possible biomarker. When researchers identify a putative biomarker, it needs validating to see how it changes in patients over time and across populations. Next, biomarkers need to be compared head-to-head under tightly controlled conditions. This is exactly the aim of TRACK-HD. The most promising combination of biomarkers can then be tested in larger studies.

Effects of an intensive rehabilitation programme on patients with Huntington's disease: a pilot study

Paola Zinzi et al., Clinical Rehabilitation 2007; 21: 603–613

Rehabilitation in HD

This interesting publication reports the results of a pilot study aimed to investigate the effects of an intensive, multidisciplinary, inpatient rehabilitation programme on people affected by HD. Rehabilitation therapy has been shown to improve quality of life for patients with certain neurodegenerative disorders. In HD, however, most studies on the use of physiotherapy have not been scientifically robust enough to be able to make strong recommendations.

Features of HD

Huntington's disease (HD) is characterised by motor (movement), behavioural (mood) and cognitive (thinking) disturbances. The major motor signs of HD include an excess of involuntary movements (chorea = dance-like movements), a slowing of voluntary movements (bradykinesia), a tendency to abnormal, sustained posturing (dystonia) and an abnormal increase in muscle tone (rigidity). Posture, balance and gait become increasingly impaired with disease progression. Speech gradually becomes more slurred. Difficulties with swallowing usually develop, increasing the risk of choking and aspiration pneumonia, and contributing to weight loss. Behavioural and cognitive symptoms include depression, apathy, intellectual deterioration and memory problems. As there is currently no cure for HD, drug therapies can only provide symptomatic benefits, and these are often associated with side effects. Hence, efforts are in progress to identify and develop non-pharmacological therapies to improve both the physical and psychological symptoms of HD.

HD patients doing physiotherapy at the Home Care "Nova Salus" (Italy).

Study Design

The aim of the study was to provide evidence to support physiotherapy for the management of symptoms in HD. The programme comprised physical, occupational and speech therapies, as well as respiratory and cognitive exercises. The treatment was divided into three-week admission periods with an intensive regimen of 44 hours per week and could be repeated three times a year. The exercises were performed both individually and in groups. Forty HD patients in early to mid-stage disease were enrolled in the study.

The tools used to measure therapy outcomes comprised:

- Barthel Index (activities of daily living)
- Tinetti Scale (balance and gait)
- Physical Performance Test (PPT; functional tasks)
- Depression scale (Zung).

Results

The readouts after treatment were better than those before treatment. Each admission resulted in improvements in motor performance and activities of daily living. The average increase was 4.7 for Tinetti and 5.2 for PPT scores. Improvements in depression scores were also noted. No motor decline was detected over two years, indicating that patients maintained their levels of functional, cognitive and motor performance. Maintenance of a baseline level over such a period can be seen as a positive outcome, since HD is a progressive disease with constant decline in performance and clinical instability. This pilot study shows that intensive rehabilitation can be beneficial for HD patients.

Riluzole in Huntington's disease: a 3-year, randomized controlled study

G. Bernhard Landwehrmeyer et al., Annals of Neurology 2007; 62: 262–272

Prof. G. Bernhard Landwehrmeyer, Chair of the Executive Committee of the EHDN (Germany).

Since its foundation in November 2003, the European Huntington's Disease Network (EHDN) has been committed to supporting scientific and clinical efforts to develop and test therapeutic interventions able to improve the quality of life of people affected by Huntington's disease (HD). The EHDN has evolved from an interventional clinical trial named European Huntington's Disease Initiative (EHDI), which was set up to test the efficacy and safety of riluzole for treating HD.

Riluzole

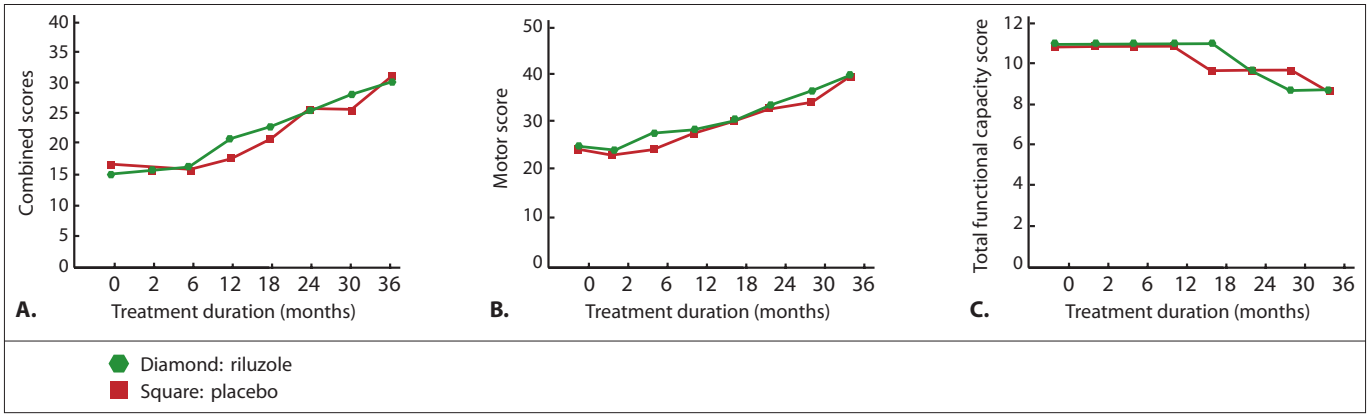
Currently, treatment of HD is restricted to symptom relief, despite the intensive search for disease-modifying therapies. One candidate drug is riluzole, an anti-excitotoxic agent approved for the treatment of amyotrophic lateral sclerosis (ALS), another neurodegenerative disease.The EHDI rationale was based on some neuroprotective effects of riluzole in animal models of HD, as well as on the results of three pilot studies performed in HD patients which showed short-term improvements of choreic movements.

Study Design

The EHDI study was designed as a randomised, placebo-controlled, double-blind clinical trial involving more than 500 patients with a clinical and genetic diagnosis of HD in early stages, who were treated either with riluzole (50 mg twice daily) or placebo in eight European countries for three years. The primary outcome measure was the change in a combined score derived from the motor and the total functional capacity scores of the Unified Huntington's Disease Rating Scale (UHDRS). Secondary efficacy outcome variables comprised the cognitive, behavioural, independence, functional assessment and clinical summaries of the UHDRS, including chorea and depression. Drug safety, i.e. the occurrence of adverse events, and the need for additional anti-choreic medication were also evaluated.

Results

Not all of the patients who were initially enrolled completed the three-year trial. 158 patients stopped taking the study medication earlier, in most cases because they required other medicines to reduce choreic movements. The effect of riluzole on HD was therefore evaluated in a total of 379 patients. Unfortunately, no difference in the primary outcome measure could be detected between the two treatment groups: The median change from baseline in the combined score was 13.7 in the placebo group and 14.3 in the riluzole group. Evaluation of the secondary efficacy outcome variables also showed no differences, except that patients taking placebo needed anti-choreic medication more frequently than the riluzole group. In general, riluzole was well-tolerated over the three years and no unexpected or serious adverse events were reported. Taken together, the results of the EHDI study showed that the tested dose of riluzole had no neuroprotective or beneficial symptomatic effects on the course of HD, but did demonstrate the feasibility of conducting large, long-term clinical trials for HD in Europe.



Evolution of UHDRS combined score (A), motor score (B), and total functional capacity (C) score over the course of the study. Squares denote placebo; diamonds denote riluzole.

Huntingtin interacting proteins are genetic modifiers of neurodegeneration

Linda S. Kaltenbach et al., PLoS Genetics, Volume 3, Issue 5, May 2007

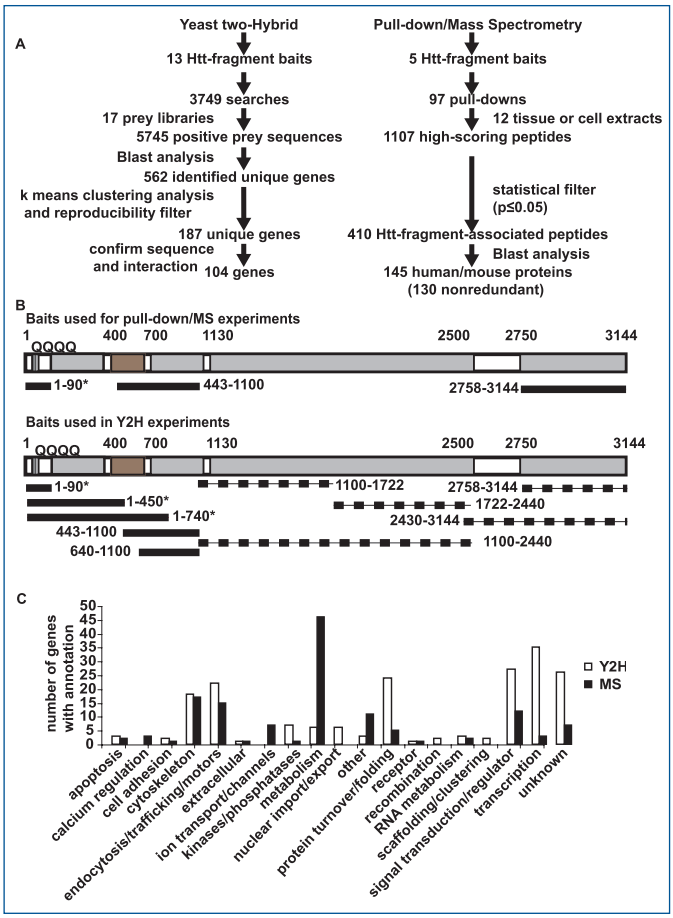
Huntington's disease (HD) is caused by an increase in the length (expansion) of the trinucleotide repeat CAG in the gene coding for a protein called huntingtin (Htt). The triplet CAG encodes the amino acid glutamine, a protein building block. Therefore, this mutation produces an abnormally long tract of glutamines (polyQ), which leads to malfunction and death of nerve cells in specific areas of the brain.

Huntingtin and its interactors

Htt is a large protein, present in every cell, which contains multiple regions that are important for interaction with other proteins. Almost 50 proteins capable of interacting directly with Htt or Htt fragments had been described previously. In HD, the expanded Htt protein is cleaved to short fragments encompassing the polyQ tract which form protein aggregates (small oligomers and inclusion bodies). A number of proteins have been found to bind to these aggregates. This provides evidence that mutant Htt may interfere with the normal function of different cellular proteins directly through protein interactions. The present study was based on the hypothesis that genetic modifiers, i.e. other genes that affect HD pathogenesis, should be enriched among Htt interacting partners. The identification of these Htt protein interactors may elucidate the mechanisms underlying HD neurodegeneration and may reveal new drug targets for treating the disease.

New proteins found

In this study, a large number (234) of new proteins that bind to normal and mutant fragments of the Htt protein were identified using two complementary approaches: yeast two-hybrid screening and affinity pull down followed by mass spectrometry. The Htt interacting proteins that were identified are involved in signal transduction, synaptic transmission, regulation of gene expression, protein turnover, folding and trafficking, as well as in cytoskeletal organisation and biogenesis, and other metabolic processes.



Results of the interaction screens: Yeast two-hybrid and pull-down/mass spectrometry workflows (A), diagram of Htt baits used in both experiments (B), and functional analysis of the Htt protein interactors identified.

Validation

The specificity of these interactions was validated in a *Drosophila* (fruit fly) model of polyQ toxicity and in co-immunoprecipitation experiments with brain extracts from wild-type and transgenic HD mice. An arbitrary set of genes encoding Htt interacting proteins was tested for their ability to behave as genetic modifiers of neurodegeneration in the *Drosophila* model. This validation assay showed that 27 of the 60 genes tested were high-confidence genetic modifiers. Changing the expression of many of these proteins can modulate the pathological effects of Htt on fly neurones that deteriorate when they express the mutant protein. Among the modifiers, 17 conferred beneficial effects when their levels were decreased, and can be considered as potential targets for future drug design. This study demonstrates that high-throughput screening for protein interactions combined with genetic validation in a model organism is a powerful approach for identifying novel candidate modifiers of polyglutamine toxicity and targets for therapeutic intervention.

Upcoming Meetings 2008

Jun 3	40th European Human Genetics Conference (ESHG), Barcelona, Spain http://www.eshg.org/eshg2008
Jun 7–11	European Neurological Society (ENS), Nice, France http://www.akm.ch/ens2008/
Jun 12–15	TOXINS 2008, Baveno, Lake Maggiore, Italy http://www.toxins2008.org/index.asp
Jun 22–26	Movement Disorder Society (MDS), Chicago, USA International Congress of PD and Movement Disorders http://www.movementdisorders.org/congress/congress08/
Jun 27–Jul 1	International Special Neurochemistry (ISN) Conference, Beijing, China International Meeting for Brain Energy Metabolism "Neurodegeneration and Regeneration" http://www.isnbeijing2008.org/
Jun 28	Austrian Huntington Association Congress, Graz, Austria http://www.huntington.at
Jul 12–16	6th Forum of European Neuroscience (FENS), Geneva, Switzerland http://fens2008.neurosciences.asso.fr/
Jul 26–31	International Conference on Alzheimer's Disease (CIAD), Chicago, USA http://www.alz.org/icad/
Aug 4–7	IBC's 13th Annual World Congress Drug Discovery & development of Innovative Therapeutics (DDT), Boston, MA, USA http://www.drugdisc.com
Aug 8–10	Herediatry Disease Foundation Conference on Huntington's Disease The Milton Wexler Celebration of Life, Royal Sonesta Hotel, Cambridge, MA, USA
Aug 17–24	National Institute of Neurological Disorders and Stroke (NINDS), Vail, Colorado, USA http://www.neurologytrials.org.
Aug 23–26	European Federation of Neurological Societies (EFNS), Madrid, Spain http://www.kenes.com/efns/
Aug 30–Sep 3	European College of Neuropsychopharmacology (ECNP), Barcelona, Spain http://www.ecnp.eu/
Sep 5–6	**5th Annual Plenary Meeting of the European Huntington's Disease Network (EHDN), Lisbon, Portugal** http://www.euro-hd.net/html/ehdn2008
Sep 6–8	**12th bi-annual meeting of the European Huntington Association (EHA), Lisbon, Portugal** http://www.euro-hd.net/html/ehdn2008
Sep 15–17	British Society for Human Genetics Conference, University of York, UK www.bshg.org.uk
Sep 21–24	American Neurological Association (ANA), Salt Lake City, USA http://www.aneuroa.org/index.php?src=gendocs&ref=2008SLC_Home
Oct 3–5	Deutsche Huntington Hilfe e.V. (DHH), Annual Conference, Duderstadt, Germany http://www.huntington-hilfe.de/index.php/deutsch/Start/Termine
Oct 23–26	Controversies in Neurology (CONy), Hilton Hotel, Athens, Greece http://comtecmed.com/cony/2008
Nov 11–15	American Society of Human Genetics (ASHG), Philadelphia, PA, USA http://www.ashg.org/2008meeting/
Nov 12–15	Huntington Study Group meeting, St. Pete Beach, FL, USA http://www.huntington-study-group.org
Nov 15–19	Society for Neuroscience, Washington, DC, USA http://www.sfn.org/am2008