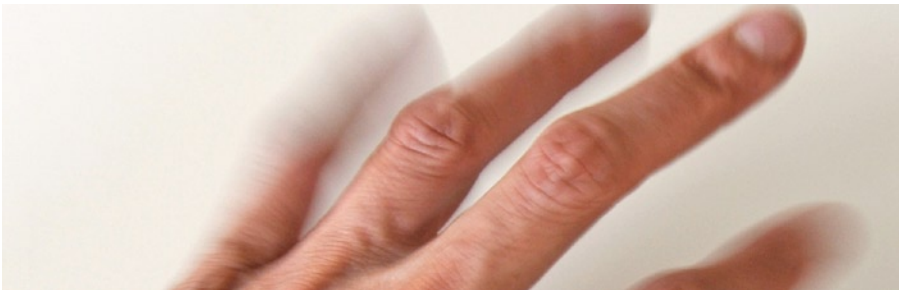
September 2008 · Issue 03

EHDN News

EUROPEAN HUNTINGTON'S DISEASE NETWORK



Hand tapping, a marker of motor dysfunction - read more on page 6.

FEATURE ARTICLE

By Michael Orth, EHDN Central Coordination, Ulm (Germany)
and Anne Rosser, University Hospital of Wales, Cardiff (United Kingdom)
on behalf of the EHDN Scientific and Bioethics Advisory Committee (SBAC)

Research applications and the Scientific and Bioethics Advisory Committee

The European Huntington's Disease Network (EHDN) is committed to facilitating research on Huntington's disease (HD). A major aim of the network is to provide an unparalleled collection of clinical data and biomaterials that will enable research projects to be conducted on a scale that has not previously been possible. In order to take full advantage of this unique resource, the EHDN is committed to an 'open access policy' and to fostering collaborative projects between its members. To this end EHDN encourages its members to establish working groups (https://www.euro-hd.net/html/network/groups) to focus on specific HD research projects essential to the overall goal of developing treatments for HD. In parallel, EHDN is building the infrastructure required to conduct systematic clinical trials of potential therapeutics.

There are three schemes through which EHDN members can apply to gain access to the resources of EHDN. Details of these schemes and the application procedure are detailed below:

1. Data mining projects

Any member of the EHDN may apply to the Scientific and Bioethics Advisory Committee (SBAC) (https://www.euro-hd.net/html/network/project/sbac) to gain access to the clinical data that is archived in the REGISTRY database and/or biomaterials that are stored at the BioRep biorepository. Investigators who are planning a project that would mine the clinical data in REGISTRY are advised to familiarise themselves with the content of the REGISTRY case report forms (https://www.euro-hd.net/html/registry/). The first biosamples that will become available on a large scale are DNA prepared from lymphoblastoid cell lines as well as the cell lines themselves. The endorsement of a project that requests access to biomaterials will require that any new sample-level data arising from that project be deposited with EHDN for use by the HD research community. An example would be the genotyping data resulting from genome wide association studies of EHDN samples that are searching for genetic modifiers of HD. >>

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By Michael Orth, EHDN Central Coordination, Ulm (Germany)
and Anne Rosser, University Hospital of Wales, Cardiff (United Kingdom)
on behalf of the EHDN Scientific and Bioethics Advisory Committee (SBAC)

2. Clinical Trials

Similarly, any member of EHDN may apply to the SBAC for endorsement of an EHDN clinical trial. In most cases, the aim will be to evaluate the effects of a certain drug on the progression of HD or on a particular clinical feature of the disease. HD trials may involve a single HD centre or several centres and all trials must follow the European Clinical Trials Directive for good clinical practice. Applications for clinical trials require the registration of trials whose primary purpose is to affect clinical practice (http://eudract.emea.europa.eu). All trials must of course comply with European and local requirements for ethical approval.

All endorsed EHDN clinical trials and steering committees can make use of services provided by Central Coordination and Language Area Coordination of EHDN. Trial policies governing confidentiality, human subjects, clinical practice, conflict-of-interest and publication need to be consistent with policies contained in the EHDN constitution (http://www.euro-hd.net/html/network/project/constitution2006).

3. Seed fund applications

EHDN working groups can apply for seed funds. These are intended to fast track the provision of limited funds to investigators for pilot studies to support the generation of preliminary data that will facilitate the submission of applications for larger grants from other organisations, or provide estimates of the power needed for e.g. clinical trials. Studies funded through this scheme should result in answers to clear hypotheses underlying the study. The maximum sum available per study is €50,000.

The application process and endorsement

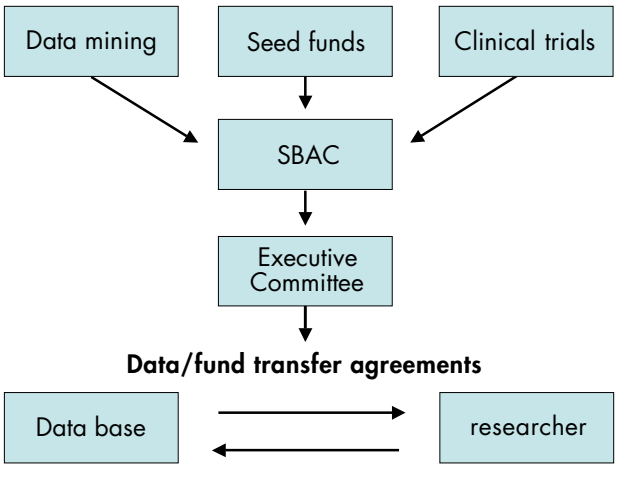
Project applications should be submitted electronically through the EHDN website. To submit a project application, please go to https://www.euro-hd.net/html/projects/proposals/file and click on 'new proposals'. Once you have completed all entries in the 'submission' form, press 'enter'. Your application will be given a project number once you open the 'submission' form. However, your application will only be processed if you press 'enter'. If you want your application to be removed, please contact the EHDN support team (support@euro-hd.net) at the EHDN central coordination.

EHDN central coordination now offers help with planning a project application. Applicants can contact Michael Orth (michael.orth@uni-ulm.de) to find out whether their project is feasible given the available data. The database currently stores data from close to 4,000 HD patients that have been collected on one or more visits to the clinic. However, not all data sets are complete. Therefore, applicants are encouraged to seek advice from Central Coordination in order to define exactly what data would be needed for a given project and then to determine how to search the database accordingly.

Upon submission, an application follows a defined path (see figure below) culminating in a final decision by the Executive Committee. Every application will be reviewed by the SBAC. The SBAC will consider a number of issues including

- aims and objectives,
- scientific and clinical adequacy of the applications,
- qualifications and capabilities of the investigators,
- the report of the bioethics advisor,
- any other factors it deems appropriate.

The SBAC's recommendations will then be considered by the EHDN Executive Committee. The final decision regarding endorsement of an application rests with the EHDN Executive Committee. Applicants will be informed about the progress of their application from submission to SBAC review and EC decision.



Once applications have been endorsed, access to data and/or biomaterials will be granted. In order to provide access, a contract detailing the project and the transfer of the data/material will be put in place between the applicants and EHDN. A short lay summary of the project will be posted on the 'studies in progress' area of the EHDN public website. This is intended to keep the HD community informed of ongoing research activities.

By Olivia Handley, REGISTRY Project Manager, EHDN, London (United Kingdom)
September 2008 · Issue 03

REGISTRY: Collection of biosamples

Since November 2005, REGISTRY has been collecting biosamples for use in HD research. The donation of biosamples is an optional component of REGISTRY. Participants are invited to donate blood and urine samples for use in studies searching for genetic modifiers and biological markers of HD, and for HD genetic testing (re-genotyping of the CAG repeat of the HD gene).

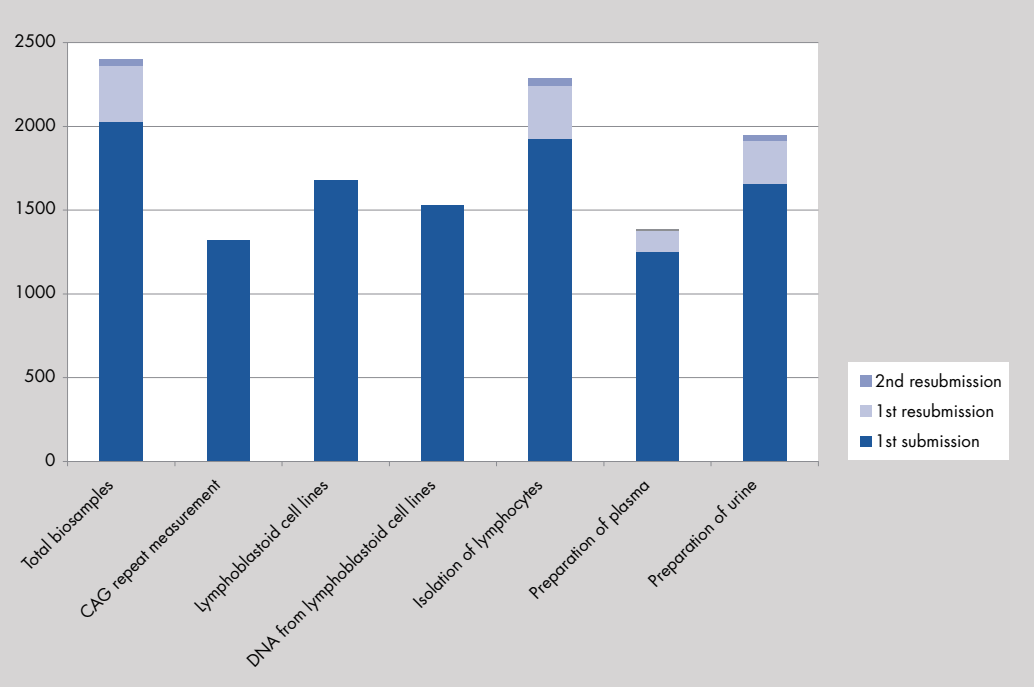
Thanks to the support of the EHDN study sites, there are currently more than 2,400 biosamples held at BioRep, the centralised biorepository for EHDN based in Milan, Italy. The contribution of these biosamples is fundamental to the Network's aim to host a unique clinical and biological data repository that can be used to deliver high quality research. The overall numbers of biosamples submitted and processed are detailed in the figure below.

BioRep processes blood samples in order to isolate lymphocytes (white blood cells) and derive lymphoblastoid cell lines (cultures in which white blood cells continuously divide). Cells are grown in culture and then stored indefinitely in liquid nitrogen. DNA is extracted from the cell lines, thus providing an unlimited supply of DNA to researchers. This DNA, as well as urine samples received from each centre, are divided into small amounts and stored in freezers. BioRep has also prepared plasma from blood although, unfortunately, these samples did not meet quality control standards. The REGISTRY Steering Committee and BioRep are in the process of conducting a pilot study to determine whether it is possible to collect high-quality plasma on a large scale across the Network. A revised initiative for plasma collection will be launched based on the outcome of these results.

Biosamples may be accessed by the scientific community pending review by the Scientific and Bioethics Advisory Committee (SBAC) and Executive Committee of the EHDN. Successful applicants must sign a material transfer agreement. The EHDN Central Coordination identifies suitable biosamples for shipment and forwards a request to BioRep. The list of biosamples includes for instance 96-well microtiter plates coated with DNA (2.5 µg of DNA per well) for genetic studies. All exported data is re-coded using a project-specific pseudonym.

Applications to access the REGISTRY clinical and biosample repository are very welcome and should be submitted online to the SBAC for review (http://www.euro-hd.net/html/projects/proposals).

REGISTRY biorepository summary (June 30th, 2008).



LANCOs: Overcoming language barriers within Europe

By Jenny Naji, Cardiff University, Cardiff (United Kingdom)

The language coordination team is pivotal to the success of the European Huntington's Disease Network (EHDN) across Europe. The wide range of languages spoken throughout Europe has previously been a major barrier to internationally collaborative research. This language barrier has been overcome in the EHDN by recruiting language area coordinators (LANCOs) who are also fluent English speakers.

Members of EHDN Language Coordination and Central Coordination, Ulm (Germany), June 9th, 2008.

EHDN LANCO Team:

Language area	LANCOs	Based in
Czech	Pavla Šašinková	Náchod, Czech Republic
Dutch: The Netherlands and Belgium	Reineke Bos and Marie-Noëlle Witjes-Ané	Leiden, The Netherlands
English: United Kingdom and Ireland	Jenny Naji	Cardiff, United Kingdom
French: France, Belgium, Switzerland	Hélène Padieu and Marie-Noëlle Witjes-Ané (Belgium)	Créteil, France
German: Germany, Austria, Switzerland	Michael Orth and Katrin Barth	Ulm, Germany
Italian	Daniela Monza	Milan, Italy
Polish	Daniel Zielonka	Poznan, Poland
Portuguese	Tiago Mestre	Lisbon, Portugal
Nordic countries: Denmark, Finland, Norway, Sweden	Marleen van Walsem, Niini Heinonen and Marie-Noëlle Witjes-Ané (Denmark)	Oslo, Norway
Spanish	Asunción Martínez Descals and Patricia Trigo Cubillo	Madrid, Spain

For more details on EHDN Language Coordination, please visit http://www.euro-hd.net/html/network/project/langcoord.

LANCOs are a link between the EHDN, the scientific community, physicians, other healthcare professionals and Huntington's disease (HD) families. They work in close cooperation with a clinical / scientific supervisor in their home countries. This person is an HD expert and an EHDN member, usually belonging to the Executive Committee, Scientific and Bioethics Advisory Committee or REGISTRY Steering Committee.

Within each language area, **LANCOs are a point of contact and source of information** for HD study sites. They are responsible for obtaining regulatory (e.g. ethical) approval, initiation and training of site personnel and setting up access to the online database. Once sites are entering data for REGISTRY, the core study of EHDN, **LANCOs have the task of monitoring case report forms** (CRFs) for accuracy and completeness, and, to fulfil this function, aim to visit each study site once per calendar quarter. LANCOs communicate with clinicians and scientists in their native language and translate all CRFs and other documents (e.g. texts about HD and recent publications), so that they can be used by patients and professionals who may not speak English.

LANCOs organise local site investigator meetings. They maintain strong links with the lay community and present the work of the Network in various forums, such as academic meetings, lay meetings and healthcare settings. At least one LANCO attends every EHDN Working Group meeting and provides support to the lead facilitator of that group.

To exchange information on the current status and progress of each language area, and discuss strategies to improve the Network, **LANCOs attend quarterly face-to-face meetings and communicate monthly via phone conferences.** They maintain regular contact with EHDN Working Groups and Central Coordination in Ulm (Germany) via phone conferences and e-mail.

The LANCOs themselves come from diverse backgrounds, mainly psychologists, physicians and nurses. Many of them also see patients on a regular basis at their local clinic.

Genetic testing/Genetic counselling Working Group

By Gerry Evers-Kiebooms, University Hospitals Leuven, Leuven (Belgium)

Communication of genetic test results: the burden of living with uncertainty

Uncertainty about the future and risk is inherent to all, but in families with Huntington's disease (HD), there are periods of pronounced uncertainty at various stages throughout life. Some of this is influenced by the length of the CAG repeat, abbreviated here as n(CAG). People undergoing predictive testing employ a wide range of strategies to cope with the uncertainty, which are partly influenced by a person's personality profile.

Communication about the consequences of the detection of a particular n(CAG) can be difficult because these are known to be complex and there are still gaps in our knowledge. Communication of the n(CAG) itself to individuals who have undergone predictive testing is not in accordance with the "Guidelines for the molecular genetics predictive test in Huntington's disease", that were drawn by an ad hoc committee consisting of representatives of the International Huntington Association (IHA) and the World Federation of Neurology (WFN) – Research Group on Huntington's disease, and published in 1994.

Uncertainty is not only concerned with the development of symptoms, but also affects reproductive confidence. This can be restored through prenatal diagnosis (PD) and preimplantation genetic diagnosis (PGD), but both are associated with a considerable psychological cost and with ethical problems. Guidelines for PD in HD have been available since 1994, but there are discrepancies in practice. There are no specific guidelines for PGD in HD.

Objectives

The aim of the Genetic testing/Genetic counselling Working Group is to address relevant issues related to the delivery of genetic test results and to prepare guidelines for predictive testing and counselling. It is important to consider the consequences of the predictive test on the applicant's future health, as well as on the transmission of the n(CAG) to the next generation(s), taking into account the instability of the repeat. Reduced penetrance alleles and intermediate alleles will receive major attention and were already the topic of presentations and discussions during the first working group meeting, as outlined below.

Activities

The initiative for this working group was taken in Dresden in September 2007. The first meeting took place in Leuven, Belgium, in May 2008, with the very active participation of more than 40 professionals from different disciplines, mostly from European countries, and three key members of the European Huntington Association (EHA). The meeting started by stressing the psychological complexity of genetic testing and by presenting the EHA's as well as a neurologist's perspective on the communication of the n(CAG).

Current practice for delivery of test results

All meeting participants answered two questions for their centre or country:

- *Is the exact number of CAG repeats reported?*
  In most but not all centres, n(CAG) is given in the laboratory report to the clinicians. Most of the latter only communicate n(CAG) when it is explicitly requested by the person who has been tested. There are huge differences in practice.
- *To what extend are models for disease onset prediction used for counselling?*
  The inverse relationship between n(CAG) and age at disease onset is usually explained to people undergoing predictive tests, but the use of models is exceptional.

Some countries do not have qualified professionals involved in genetic counselling, and the EHA's point of view is that criteria for quality control in genetic counselling are necessary.

Discussion of laboratory, clinical and CAG communication issues in subgroups

This interactive part of the meeting was very fruitful with interesting reports to the whole group. The discussion will be continued during the meeting of the working group in September 2008 in Lisbon. All subgroups gave a positive answer to the question whether a revision of the 1994 guidelines on predictive testing is needed.

Future plans

Short-term aims:

Revision of the 1994 guidelines and elaboration of adequate information leaflets in several European languages, which will be available on the EHDN website.

Long-term aims:

Development of programs for participation in research.

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)
September 2008 · Issue 03

Hand tapping: A simple, reproducible, objective marker of motor dysfunction in Huntington's disease

Andrew W. Michell et al., Journal of Neurology 2008, May 13

The hand tapping test for assessing motor symptoms in HD provides many advantages: It is quick, extremely inexpensive and entirely objective, requires no training and can be performed at virtually all stages of the disease. This study demonstrates that two parameters of the test (total number of taps and variability of inter-tap interval) may be helpful clinical markers of disease progression in HD.

Assessment of motor symptoms in HD

Huntington's disease (HD) affects both voluntary and involuntary movements. Among others, the main motor signs comprise **chorea** (involuntary, dance-like movements), **bradykinesia** (slowing of voluntary movements), **dystonia** (sustained posturing) and impairments in balance and gait. Assessment of these motor deficits has been limited to the use of clinical rating scales, such as the Unified Huntington's Disease Rating Scale (UHDRS). However, these tools are subject to errors: For instance, they are susceptible to variation due to subjective rating of the tests, especially when performed by different physicians (inter-rater variability). **Hence, objective and quantitative tools to supplement standard clinical assessment of HD motor symptoms are urgently required.** This is particularly important in view of the pressing need for specific and sensitive clinical and biological markers able to track disease progression and evaluate drug efficacy. **The identification of disease markers that could be used as outcome measures in future clinical trials is essential for the development of new treatments for HD.**

The hand tapping device

As a means of objectively measuring impairment in motor function, the authors of this publication developed a device to assess hand movements based on a tapping test. The device consists of two buttons spaced 30 cm apart that have to be pushed alternately as quickly as possible for 30 seconds. The original device was improved by incorporating a timing system to record time between taps. **This enables an objective assessment of variability in tapping rhythm (inter-tap interval) and tiredness during the test.**

Study design

The aim of this study was to answer four key questions:

1. Was the hand tapping device able to detect a difference between HD patients and control subjects?
2. Did the severity of deficit correlate with the severity of clinical phenotype assessed with other rating scales?
3. How did this relationship change over time?
4. Were the tapping scores reproducible?

The original device was used to collect data from 178 HD patients at varying stages in disease progression from 2003 to 2005, and a further 15 patients were assessed using the improved tapping device. In addition, longitudinal data collected over 10 years were available from a subgroup of 17 patients in whom hand tapping measures were combined with UHDRS motor assessment, as well as measures of functional capacity and an independence score.

Results

The total number of taps in 30 seconds measured with the original device significantly correlated with the UHDRS motor score and independence score in the large study of the 178 HD patients. In the long-term study (17 patients) the total number of taps decreased continually over several years, during which the UHDRS motor scores reflected disease progression. Again, a correlation was found between UHDRS motor scores and number of taps over time. **Data from the updated device (see table below) demonstrated that HD patients made significantly fewer taps than control subjects** (with corresponding increased time between taps). They were more prone to become tired towards the end of the assessment period (shown by the increase in inter-tap interval). Furthermore, there was greater variability in the duration of inter-tap intervals among HD patients. **In other words, control subjects were able to tap the buttons more quickly and regularly.** Both the total number of taps in 30 seconds and the variability of inter-tap interval parameters were reproducible.

Mean values	control subjects (n = 9)	HD patients (n = 15)	p-value
Number of taps in 30 s	104	79	< 0.01
Tiredness (%)	– 2.7	1.4	0.1
Inter-tap variability	56	148	< 0.02

Data adapted from Table 1 of original publication.

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)
September 2008 · Issue 03

Rapid eye movement sleep disturbances in Huntington Disease

Isabelle Arnulf et al., Archives of Neurology, Vol. 65, No. 4, April 2008

This study shows that HD patients frequently suffer from sleeplessness (mainly caused by problems in maintaining sleep), reduced REM sleep and increased motor activity during sleep. These sleep disturbances, which apparently do not correlate with the CAG repeat length, can be detected even in the asymptomatic phase. Importantly, the REM sleep dysfunction seems to be an early marker of HD which progresses with disease duration.

REM sleep

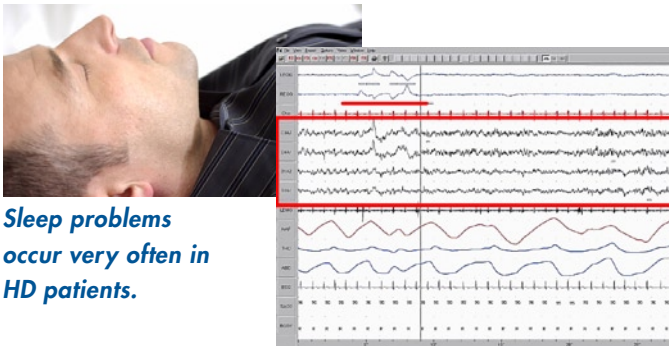
Rapid eye movement (REM) sleep is a normal stage of sleep characterised by rapid movements of the eyes, low muscle tone and a rapid, low voltage electroencephalogram (EEG), which is a test that measures the electrical activity of the brain. **In adults, REM sleep typically occupies 20-25% of total sleep.** During a normal night, people usually experience 4 or 5 periods of REM sleep. The function of REM sleep is not well understood, but it is thought to play a role in memory consolidation and brain development. Vividly recalled dreams mostly occur during REM sleep.

Sleep disturbances in HD

Sleep problems occur very often (up to 90%) in Huntington's disease (HD) patients. They include, for instance, difficulty falling asleep, sleeplessness, waking and movements during sleep, and daytime sleepiness. Sleeplessness may be caused by anxiety, depression, disturbed sleep/wake rhythms or chorea (involuntary, dance-like movements typically seen in HD).

Study design

The aim of this study was to evaluate the sleep/wake behaviour at various stages of HD and to determine if this correlates with the CAG repeat length of the HD gene. Sleep disturbances were investigated in HD patients in comparison to narcolepsy patients and controls (25 subjects each). Narcolepsy is a condition characterised by excessive daytime sleepiness and disturbed nighttime sleep. The HD group comprised patients with different disease severity scores: a) pre-manifest (i.e. asymptomatic) and very mild; b) mild; and c) moderate.



Sleep problems occur very often in HD patients.

Results

Almost two thirds of the HD patients complained of sleeplessness (16 HD patients compared to 4 control subjects). Although nighttime sleeplessness and daytime sleepiness increased with HD severity, differences in sleep patterns between the disease severity scores were not significant. No correlation between sleeplessness and length of CAG repeats could be detected. Sleeplessness was not associated with restless legs syndrome, a condition characterised by a compelling need to move the legs. According to self-reports, HD patients did not have more frequent daytime sleepiness or narcolepsy-like symptoms.

Compared to controls, **HD patients had lower sleep efficiencies and a longer duration of wakefulness after sleep onset**, but similar sleep-onset delays. This indicates that HD patients had problems primarily in maintaining sleep. They also spent more time in light sleep stages. Interestingly, HD patients had more frequent periodic leg movements, causing more arousals than in controls. For instance, one quarter of the HD patients had more than 15 movements per hour. **HD patients had normal non-REM sleep percentages**, including slow wave sleep. A comparison between HD patients with and without a complaint of sleeplessness revealed that both groups differed only in sleep efficiency, but not in total sleep time, sleep-onset delay, percentages and duration of sleep stages or arousal index.

HD patients had longer REM sleep delays and shorter REM sleep percentages (of total sleep time) than did controls, and these percentages decreased further with increasing disease severity. The mean percentage of REM sleep was 16.3% in the pre-manifest/very mild HD group, 16.4% in the mild HD group, and 9.7% in the moderate HD group, compared to 19% in the control group and 21% in the narcolepsy group. In addition, 12% of the HD patients showed REM sleep behaviour disorders, such as movements of lips, head, trunk, arms and hands.

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)
September 2008 · Issue 03

Identification and allele-specific silencing of the mutant huntingtin allele in Huntington's disease patient-derived fibroblasts

Paul H. J. van Bilsen et al., Human Gene Therapy, Vol. 19, No. 7, July 2008

HD: the features of a hereditary disease

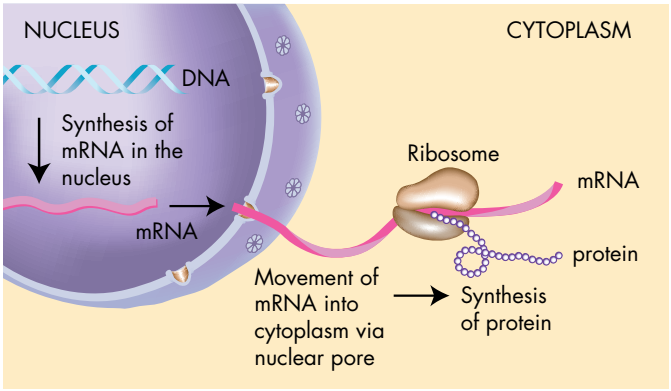
- Huntington's disease (HD) is an **inherited genetic** disease caused by a mutation (extra long CAG repeat) in the gene coding for a protein called **huntingtin** (Htt).
- Humans have two copies (or **alleles**) of each gene.
- Most HD patients are **heterozygous**, i.e., they have two different copies of the HD gene: one normal allele from the unaffected parent and one mutant allele from the affected parent.
- The DNA code for the two alleles may not be identical. Single nucleotides – adenine (A), guanine (G), cytosine (C) or thymine (T) – of the code may differ, allowing the alleles to be distinguished. This is called **single nucleotide polymorphism** (SNP).
- The normal and mutant HD alleles are first converted into **messenger RNA** (mRNA), from which the Htt protein is then made.
- The HD inheritance pattern is **autosomal dominant**, such that a single mutant allele is sufficient to cause the disease.

Basis for gene therapy

RNA interference (RNAi) is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. **This biological process has inspired the development of a new class of medicines, known as RNAi therapeutics.** Key components in the RNAi process are small interfering RNA (siRNA) molecules that complement and bind to the mRNA of the gene in question. RNAi therapeutics shuts down expression of target genes by cutting the respective mRNA, thereby preventing disease-causing proteins from being made.

New strategy for allele-specific treatment of HD

The presence of the mutant Htt protein causes dysfunction and death of nerve cells (neurones) in many areas of the brain, leading to the different symptoms of HD. **Therefore, supression of the production of the mutant protein, particularly in the brain, may be an effective treatment.** One means of reducing protein production in neurones is to deliver small interfering RNA (siRNA) molecules or a piece of DNA encoding short hairpin RNA



(shRNA) molecules (from which siRNA is made) into the brain. **Such strategies have been shown to be effective in HD mouse models.** The positive effects detected in several studies include, for instance, delay of disease onset, improvement of movement, behavioural and neuropathological abnormalities, and extension of life span.

However, it is vital that the normal Htt protein is still made from the normal Htt allele. **Hence, RNAi therapeutics needs to be able to distinguish between mutant and normal Htt alleles.** The activity of siRNA is highly specific, such that the siRNA and the target mRNA must match perfectly for the cutting to be efficient. Therefore, if an siRNA is targeted to a portion of mRNA containing the site of a single nucleotide polymorphism (SNP), the treatment may discriminate between the two Htt alleles.

This study presents a strategy for treating HD using RNAi technology that selectively blocks the production of the mutant Htt protein. The approach was based on specific siRNA targeting of an SNP in the HD gene in cells derived from an HD patient. The levels of mutant Htt mRNA were decreased by approximately 80%, while production of normal Htt mRNA remained essentially unchanged. Only the normal – and not the mutant – Htt protein could be detected.

The authors of this work developed a simple method for determining which copy of an SNP is located on the mutant allele and which on the normal allele of the HD gene. This information is essential for designing siRNA molecules that will block the production of the mutant and not the normal Htt protein. This method is effective even if the SNP site is not located close to the CAG repeat. Most importantly, this study suggests that allele-specific treatments for HD may be feasible. However, there are many other factors (e.g. delivery of the treatment to the brain) that need to be resolved before this approach could be considered clinically practical.

Upcoming Meetings 2008/2009

Sep 03-05	6th International Conference on Frontotemporal Dementia, Rotterdam, The Netherlands http://www.ftd2008.org/site/
Sep 05-06	5th Annual Plenary Meeting of the European Huntington's Disease Network (EHDN), Lisbon, Portugal https://www.euro-hd.net/html/ehdn2008
Sep 06-08	12th Bi-annual Meeting of the European Huntington Association (EHA), Lisbon, Portugal https://www.euro-hd.net/html/ehdn2008
Sep 10-13	81st Congress of the German Society for Neurologie (DGN), Hamburg, Germany http://www.dgn2008.de/
Sep 15-17	British Society for Human Genetics Conference, University of York, Heslington, York, UK http://www.bshg.org.uk/york2008.htm
Sep 20-25	XIV World Congress of Psychiatry, Prague, Czech Republic http://www.wpa-prague2008.cz/Text/home-page
Sep 21	22nd Annual Symposium on Etiology, Pathogenesis, and Treatment of Parkinson's Disease and Other Movement Disorders http://www.huntington-study-group.org/NewsEvents/EventsUpcomingMeetings/HSGMDSSymposium/.../Default.aspx
Sep 21–24	133rd Annual Meeting of the American Neurological Association (ANA), Salt Lake City, UT, USA http://www.aneuroa.org/
Oct 03-05	Deutsche Huntington Hilfe e.V. (DHH), Annual Conference, Duderstadt, Germany http://www.huntington-hilfe.de/index.php/.../Termine
Oct 06-07	9th International Conference on Alzheimer's Disease Drug Discovery, New York, NY, USA http://www.worldeventsforum.com/.../index.html
Oct 16-19	6th International Congress on Mental Dysfunctions & Other Non-Motor Features in Parkinson's Disease, Dresden, Germany http://www.kenes.com/pdment2008/
Oct 23-26	2nd World Congress on Controversies in Neurology (CONy), Athens, Greece http://comtecmed.com/cony/2008/
Nov 03-05	19th International Symposium on ALS/MND, Birmingham, UK http://www.mndassociation.org/.../index.html
Nov 11-15	58th Annual Meeting of the American Society of Human Genetics (ASHG), Philadelphia, PA, USA http://www.ashg.org/2008meeting/index.shtml
Nov 15	2nd Annual Huntington Disease Clinical Research Symposium, St. Pete Beach, FL, USA Information: http://www.huntington-study-group.org/NewsEvents/EventsUpcomingMeetings/...Default.aspx Registration: http://www.register123.com/event/profile/...Page=home
Nov 15-19	Neuroscience 2008 - 37th Annual Meeting of the Society for Neuroscience, Washington, DC, USA http://www.sfn.org/am2008/
Nov 16-18	International Symposium on Rare Diseases. Inherited Neuromuscular Diseases: Translation from Pathomechanisms to Therapies, Valencia, Spain http://www.fundacioncac.es/eng/...Actividad=77
Jan 17-22	International Conference on Unstable Microsatellites & Human Disease, Guanacaste, Costa Rica http://www.microsatellites.ca/about.html
Feb 17-22	Neurodegenerative Diseases: New Molecular Mechanisms, Keystone, CO, USA http://www.keystonesymposia.org/Meetings/...1003
Mar 07-11	40th Annual Meeting of the American Society for Neurochemistry, Charleston, SC, USA http://asneurochem.org/2009meeting/ASN2009.htm
Mar 09-13	Neurological Restauration 2009, Havana, Cuba http://www.ciren.cu/rn2009.pdf
Mar 11-15	9th International Conference on Alzheimer's and Parkinson's Diseases: Advances, Concepts and New Challenges, Prague, Czech Republic http://www.kenes.com/adpd/
Mar 26-28	24th Conference of Alzheimer's Disease International, Singapore http://www.adi2009.org/