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EHDN News

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

TRACK-HD: 360 people have signed up for the three annual tests including Charles Sabine.

FEATURE ARTICLE

By Charles Sabine

A day in the life of a human guinea pig

The best view of London's Mecklenburgh Square comes from the Wolfson Centre, in its middle. Because it is the only view without the Wolfson Centre in it.

The *TRACK-HD* office's concrete walls may match the drabness of the corridors inside, but both are lit up by the occupants' sense of purpose. It is difficult to overstate the importance of the work that is conducted here and in sister clinics in Paris, Vancouver and Leiden. Because Huntington's disease (HD) holds the answers to so many questions for the future of *all* diseases, HD research is vastly magnified in significance, despite it being a relatively rare disorder. And whatever treatments or cure might be developed in the future for HD, they will never reach the homes of victims like me without biomarkers to measure their effect in clinical trials. All of which is a very good thing, because it is a long day for us 360 Guinea Pigs who have signed up for the three annual tests.

Immediately following registration and a cup of tea comes the worst bit – a blood test. For a late-rising trypanophobic[1] like me, the injury of having metal stuck in your arm is compounded by the insult of it happening at 9:30 in the morning, necessitating a 6:00 am departure from home. Even the dogs wouldn't get up to say goodbye. (TRACK-HD, in fact, offers a night in a hotel as well as the transport costs – in my case 50 pence a mile for the 200 mile round trip.)

I always hated blood tests, even before I took the one that told me I would get HD. But *this* is the mother of all blood tests: NINE vials! NINE! 50 millilitres! "That's a glass of wine", I whine. The pain is not even relieved by the feeling that it is for a good cause, since its purpose – unlike most of the other tests – isn't obvious to the layman. I feel that I shouldn't ask. There's an unspoken code in the room, as if asking questions might break some sort of spell. Like asking if Santa is real. >>

[1]Trypanophobia means needle phobia.

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(AM) = Article of the Month

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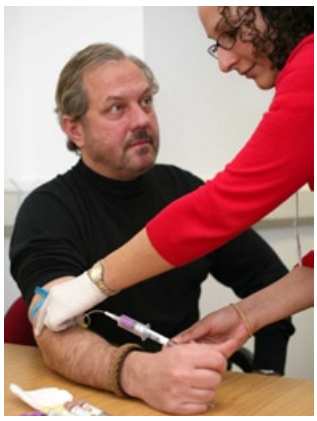
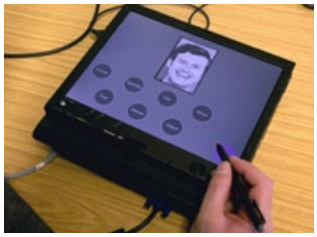
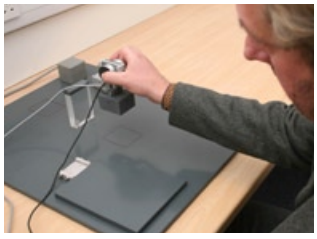
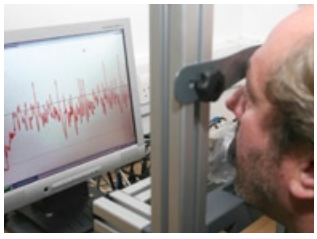


In fact, while access to the rationale of the tests may be ambiguous, the results of the tests are definitely out of bounds. I, for one, would like to know mine. But Nayana Lahiri, a 30 year old Clinical Registrar from London who is completing a PhD in HD, and currently inspecting a syringe full of my blood, says that it is not a common request. "I think over time, people will want to know", she says. "But right now, even *we* won't know the meaning of the tests until the three years are over and the data are analysed."







It's a long day – eight and a half hours – but softened by the pleasant nature of the site staff. They say they are inspired by the spirit in the HD community. "Seeing the motivation of the gene carriers and their families, and hearing their stories, I feel honoured to have a common purpose with them", says Miranda Say, a 28-year-old clinical neuro-psychologist from Sydney. Miranda gets to preside over the fun part of the day - two hours of puzzles and parlour games that include lifting blocks, making a meter move with your tongue (always a source of innuendo), drawing circles blindfold, and so on. Some are surprising in their nature – like a smelling test - others amusing in their technology. When set the task of identifying the emotion of faces shown on a screen, the biggest difficulty comes from the pictures appearing to be from a 1950s American college yearbook, making the hairstyles mightily distracting. At one point, Miranda brings up the suggestion of 'homework' to take away. A request too far, I think.

Another task: tapping in time to a rhythmic beat. My first thought is that surely some people just have bad rhythm. But the second guessing that lurks all day in my 'guinea-pig subconscious' reminds me that, of course, it is not about comparisons with other people, but rather with myself, year on year. A small sigh accompanies this depressing reminder of why I am here.

A one-hour lunch break flies by (food courtesy of *TRACK-HD*), and it's back into the fray. Joy Read, an oncology nurse from Oxfordshire, has drawn the short straw of supervising the more tedious section of my day – two hours of questioning about mood and depression (which feels a bit intrusive), and then conducting the eye movement tests – a really boring process of following dots illuminated on a wall. But despite the boring bits, there has been no difficulty finding recruits. "People with the HD gene seem really motivated", says Nayana.

By 3 o'clock I am nearing the 'had enough' stage. It is a bad time to start on my second worst bit - the MRI scan. There are two reasons why this is bad for me. First, I really hate the feeling of having your head hammered by a pneumatic drill, and second, I have mild claustrophobia. By 4 pm, it's back to Nayana for a half an hour of the standard scale of rating HD symptoms. Now I really feel we are in overtime and sure that my eyes are crossed. Luckily there are good pubs nearby!

So in the end, if like me you get bored easily, or hate syringes, or are claustrophobic, this may not seem like your perfect day. But if you want to contribute to a more hopeful future for your children, then who cares about a bit of discomfort?

TRACK-HD

TRACK-HD is a three year initiative led by Dr. Sarah Tabrizi and funded by the CHDI Foundation. It commenced in 2007 and aims to identify and compare head-to-head clinical, imaging and molecular biomarker assessment tools to track the emergence of HD in premanifest gene carriers and its progression in early stage disease. A total of 120 people with premanifest HD, 120 with early stage HD and 120 controls have been recruited from clinics in London, Paris, Leiden and Vancouver.

REGISTRY Data Collection and Retention

By Olivia Handley, REGISTRY Project Manager, London (United Kingdom)

The rate of enrolment into REGISTRY over the past year has increased by one third, with a total of 4,282 participants registered on the web portal. As the REGISTRY cohort continues to expand, study sites are encouraged to balance their efforts between recruitment and retention to ensure that the collection of high-quality data is sustained at its current volume.

REGISTRY is an open-ended study inviting participants to attend prospective annual visits. The assessment protocol is designed to promote the collection of clinical data and biological specimens that will allow us to study the natural history and clinical care of individuals affected by and at risk of developing Huntington's disease (HD). A minimum core assessment is administered to all REGISTRY participants. Depending on the participants' wishes and the level of resources available at the study site, additional assessments and procedures may also be completed (see table). Here, we present figures for the total number of participants with complete datasets for core, extended and full assessments. Core data are available for 2,403 (56%) participants for a total of 4,819 visits. The extended REGISTRY assessment has been carried out on 871 (20%) participants across 1,161 visits. The full REGISTRY assessment (excluding optional components) has been obtained for 415 (10%) participants over 571 visits. Of the 4,282 REGISTRY participants currently enrolled, 3,047 are already eligible for follow-up visits (i.e. enrolled before 01 January 2008). To date, 2,130 (70%) participants have attended at least one follow-up visit.

Whilst the data collected represent an impressive and invaluable resource, a significant volume of core information remains to be entered onto the web portal. This presents a challenge for the EHDN Monitors whose task is to control the evaluation of plausibility and completeness of the REGISTRY database. EHDN Monitors maintain frequent contact with study site staff and complete on-site and online monitoring on a regular basis. This has, without doubt, improved the quality and volume of data entered into REGISTRY, and with additional monitoring visits already in place for 2009, the proportion of complete data will continue to increase.

Continued enrolment of new participants and sustained annual follow-up visits is central to the success of REGISTRY's aim to prospectively track the onset, nature and progression of HD. The contribution of sites and participants involved in REGISTRY continues to be remarkable, and provides EHDN with a robust clinical and biological repository that will serve to expedite our understanding of this disease. We would like to take this opportunity to encourage EHDN members to apply for access to the REGISTRY database for research proposals. Please visit http://www.euro-hd.net/html/projects/proposals for further information.

REGISTRY assessment protocol		Core	Extended	Full
General	Medical History (medical, HD, psychiatric)	✔	✔	✔
	Demographics (Fixed & Variable)	✔	✔	✔
	Co-morbid conditions	✔	✔	✔
	Medication log	✔	✔	✔
	CAG result from local laboratory End of Study	✔ (✔)*	✔	✔
Clinical History	UHDRS '99 Motor UHDRS '99 Function	✔ ✔	✔ ✔	✔ ✔
Neuropsychiatric	UHDRS '99 Behaviour		✔	✔
	Becks Depression Inventory (self-report)			✔
	Hamilton Depression Rating Scale		✔	✔
Cognitive	UHDRS '99 Cognitive		✔	✔
Quality of Life	SF-36 (self-report) Caregiver Burden Inventory (self-report)			✔
Health economics	Client Service Receipt Inventory		✔	✔
Optional components	Biosample collection Family History questionnaire			

End of Study is included in the core assessment of the battery, but has not been included in the figures presented because it applies only to participants withdrawn from the study.

Photos from the Rehabilitation Home Care "Nova Salus" (Italy) kindly provided by Paola Zinzi

Physiotherapy Working Group

By Monica Busse and Lori Quinn, Cardiff University, Cardiff (United Kingdom)

Rationale and Aims

The progressive motor impairment in Huntington's disease (HD) leads to a loss of mobility with individuals eventually requiring assistance with all activities of daily living. There is some evidence to suggest that physiotherapy can play a role in helping people with HD to maintain their independence. However, well-controlled trials have yet to be conducted to establish whether or not physiotherapy makes a measurable difference to the lives of HD patients. Designing a systematic and well controlled trial of physiotherapy is difficult. The interpretation of studies that have been completed to date has been confounded by the small numbers of patients used, inconsistency of intervention content and a lack of sensitive outcome measures. Clinical judgement, personal experience, and 'trial and error' remain the major mechanisms through which interventions are currently justified. Therefore, to investigate whether or not physiotherapy is beneficial in HD, there is a need for evidence-based development and evaluation of complex physiotherapy interventions.

The Physiotherapy Working Group is developing guidelines for physiotherapy evaluations and interventions by describing current and best practice, and evaluating appropriate, standardised outcome measures relevant to physiotherapy and to the needs of patients. These are the important first steps in developing clinical intervention trials.

Activities

1. Guidance for Physiotherapy interventions

The first major project undertaken by the Physiotherapy Working Group was the development of a physiotherapy guidance document devised through a combination of the available scientific evidence and expert consensus. The first draft was disseminated for review at the 2008 EHDN Plenary Meeting. Planning for the development and publication of the final version of the guidance and also of associated patient education materials is now underway.

2. Seed funded Outcome Measures Project

One of the first steps in developing clinical intervention trials is to choose appropriate outcome measures that are both reliable and valid when applied to individuals with HD. It is essential that they are sensitive, so that changes attributed to an intervention can be measured above the background of natural variability and/or measurement error. The purpose of this planned multicentre study is to determine the reliability and minimal detectable difference of various outcome measures that are potentially suitable for use in HD. These outcome measures will be tested as part of REGISTRY Version 3.

Meetings and Membership

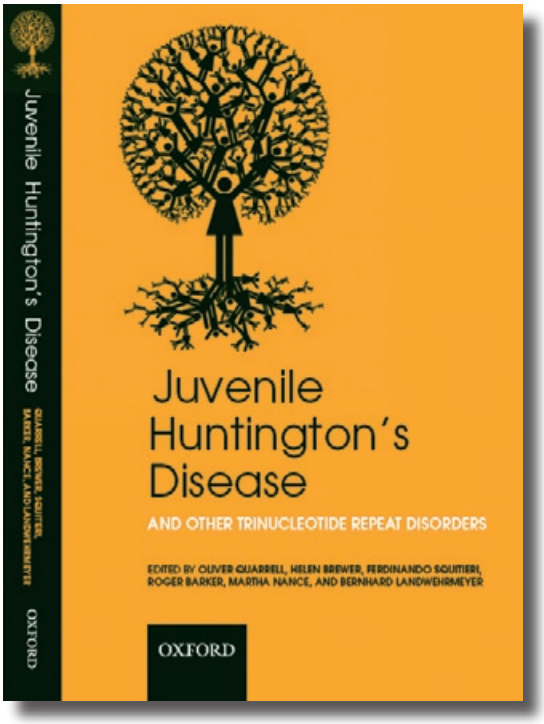
The Physiotherapy Working Group has active members based in the UK, Sweden, Norway, Germany, Italy and USA. Our long-term goal is to develop high-quality multi-site randomised controlled trials of physiotherapy. Any clinician with an interest or expertise in HD, as well as in rehabilitation or physiotherapy, is welcome to join the group and should contact Monica Busse at busseme@cardiff.ac.uk or Lori Quinn at quinnl1@Cardiff.ac.uk.

Juvenile Huntington's Disease Working Group

By Oliver Quarrell, Sheffield Children's Hospital, Sheffield (United Kingdom)

Why study juvenile Huntington's Disease?

The percentage of patients with juvenile Huntington's disease (JHD), in whom disease onset occurs before the age of 20, varies between studies, but 5% is a reasonable working figure. Patients with JHD often have a larger CAG repeat and more widespread pathology than those with adult onset HD. The median CAG repeat size that can cause JHD is approximately 60. Therefore, most individuals with more than 60 CAG repeats have JHD, and those with more than 80 repeats typically have disease onset before the age of 10. It also follows that half of the JHD cases have a repeat size of less than 60 repeats. Indeed, in some cases the length of the CAG repeat is in the range between 40 and 50. All mouse models carry CAG repeats that would cause an early childhood form of HD in humans, and therefore, may be models of JHD rather than of adult onset disease.



The new book on juvenile HD was published in January 2009 (ISBN-13: 978-0199236121).

Objectives

The JHD Working Group has a number of aims. The first has been to summarize what is currently known about this group of patients. This will be the starting point for developing further studies. We were originally supported in this aim by EHDN and the Novartis Foundation, which together helped arrange an international conference in London (UK) in November 2006. Subsequent support has come from Oxford University Press, which has just published a book based on the proceedings of that meeting (see figure). The book begins with a number of accounts from carers and from a patient, some of which is understandably difficult to read without feeling upset. In addition, there are chapters on the genetic, pathological, and molecular mechanisms of JHD, the current therapies available for treating the condition, as well as the challenges posed in diagnosing and assessing patients. Some sections of the book will be available on the EHDN website.

The current rating scales used both for monitoring HD and as outcome measures in treatment trials cannot be applied easily to juvenile patients. The typical symptoms of JHD are slow movements (bradykinesia), tremor, seizures and complex behavioural problems. Therefore, new rating scales need to be designed and tested. A JHD-specific rating scale is important, since treatments aimed at altering the natural history of HD, particularly if useful in the early stages of the condition, may show an effect more quickly in patients with greater pathological changes.

The current evidence base for treating patients with JHD is limited to case reports at best. Developing new rating scales will involve a dialogue with families, and will hopefully lead to a greater understanding of the condition. This will result in an improved evidence base for producing a new standard of care document for juvenile patients.

Next steps

The REGISTRY project is essential for identifying large numbers of JHD patients willing to participate in research projects. Qualitative studies need to be undertaken to inform those designing the new rating scales, which will need to be tested on a group of JHD patients. Their usefulness will need to be assessed formally, using both "traditional" and the "new" methods of psychometric analysis. Given the relative rarity of JHD, a worldwide collaboration is required so that this group of patients can be included in future clinical trials. We are now in a position to capitalise on collaborations within Europe, North America and Australia.

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)

Weight loss in Huntington disease increases with higher CAG repeat number

N. Ahmad Aziz et al., Neurology (2008), 71:1506–1513

This study shows that the rate of weight loss in Huntington's disease is directly proportional to the length of the CAG repeat in the *HD* gene, and is likely to result from a hypermetabolic state.

Background

Huntington's disease (HD) is a genetic neurodegenerative disorder caused by the expansion of the CAG repeat in the *HD* gene. It is characterised by a clinical triad of motor, behavioural and cognitive disturbances. Weight loss is also a hallmark of HD, and has been observed both in humans and HD transgenic mice. Interestingly, in HD, a lower body mass index (BMI) has been associated with a higher rate of disease progression.

The cause of weight loss has been attributed to the following:

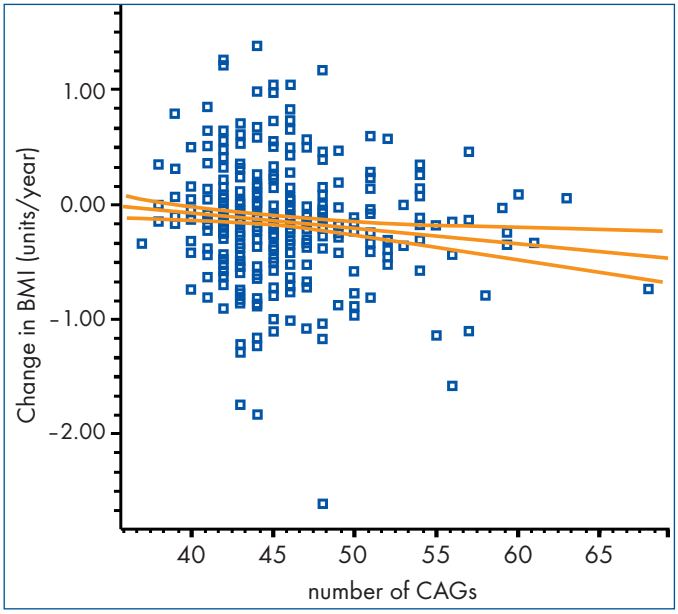
- Difficulties with swallowing that might lead to a decreased intake of calories. Note however that weight loss is already seen in pre-manifest HD individuals, and previous studies have shown that, at early stages, caloric intake is increased both in HD patients and HD transgenic mice.
- Increased motor activity caused by chorea (involuntary movements) that might lead to higher energy expenditure. However, the severity of choreic symptoms does not correlate with weight loss.
- An increased metabolic rate. Mutant huntingtin (Htt) has been shown to perturb a number of molecular and cellular systems that could impact on energy homeostasis. This effect could vary with the length of the polyglutamine tract in mutant Htt.

Methods

The aims of this study were:

- To investigate weight loss in early stage HD over three years
- To assess whether there is a correlation between weight loss and clinical symptoms
- To determine whether CAG repeat length is directly related to the rate of weight loss and caloric intake.

Participants (517 early stage HD patients) were recruited from the European Huntington's Disease Initiative, a phase III interventional clinical trial. Riluzole, the drug tested in this trial, does not affect body weight. Patients taking neuroleptic drugs were excluded. Clinical symptoms were assessed with the Unified Huntington's Disease Rating Scale (UHDRS) subscales for motor, behavioural, cognition and functional capacity. Data analysis was performed using linear mixed-effects models. The relationship between CAG repeat length, body weight and caloric intake was also studied in the R6/2 mouse model of HD.



HD patients with larger CAG repeats had a faster rate of weight loss.

Results

In HD patients, BMI significantly decreased by 0.15 units per year on average (normal BMI lies between 18–25). The rate of weight loss was greater in patients with a longer CAG repeat (see figure), although none of the symptoms assessed by the UHDRS correlated with weight loss. A correlation between weight loss and CAG repeat length was also observed in HD mice, despite the fact that mice with longer CAG repeats had increased caloric intake.

Conclusion

Weight loss in HD is directly correlated to CAG repeat length and likely to result from a hypermetabolic state. This correlation suggests that mutant Htt interferes directly with cellular energy homeostasis. Hypothalamic pathology, changes in the innate immune response and mitochondrial disturbances have all been described in HD, and could contribute to this process.

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)

Detection of Huntington's disease decades before diagnosis: the Predict-HD study

Jane S. Paulsen et al., J. Neurol. Neurosurg. Psychiatry (2008), 79:874–880

This study shows that small changes in clinical and neuroimaging parameters are detectable long before the predicted onset of Huntington's disease, and proposes a model establishing the relationship between different clinical outcomes and estimated age at diagnosis.

Background

Predict-HD is an international, multi-site, observational study aimed at identifying predictors of Huntington's disease (HD) onset in asymptomatic gene carriers. Given that the CAG repeat length determines only 50–70% of the variation in age of onset, there must be other modifying factors that influence the onset and progression of HD. Predict-HD investigates the nature and pattern of neurobiological and neurobehavioural changes (including cognition, emotion regulation, brain structure and function) that might occur prior to clinical diagnosis of HD. The study objectives are to identify 'state' markers of disease onset and early disease progression, and to develop sensitive tools both to track these changes and to detect putative modifiers of age of onset.

Methods

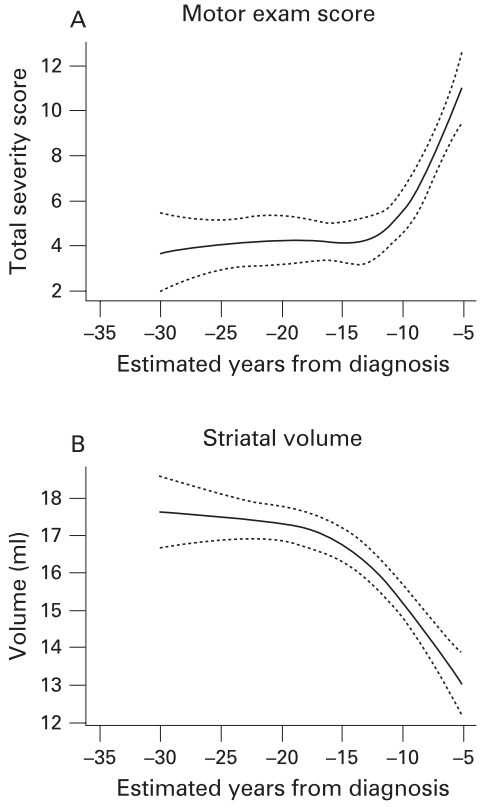
438 asymptomatic HD gene carriers were examined. Estimated time to clinical diagnosis was calculated based on the individual's CAG repeat length and current age. The features of HD that were assessed included striatal volume changes (using MRI[1]), motor ability (using UHDRS[2] and finger tapping tests), cognitive performance and odour recognition. The outcomes were used to develop a model aiming to examine the relationship between estimated time until clinical diagnosis and motor, cognitive, psychiatric and brain volumetric measures. The patients in the study had a mean estimated time to diagnosis of 13.9 years.

Results

Small changes in clinical outcomes were detectable 15–20 years prior to diagnosis. Estimated time to diagnosis was related to most of the clinical and neuroimaging markers. For all variables, the relationship was consistently non-linear, with the rate of decline increasing exponentially as the predicted time of symptom onset approaches (see figure for examples).

Conclusion

The relationships between estimated years to diagnosis and motor scores, striatal volume, odour retention and cognitive measures were strikingly consistent. Understanding the initial steps in HD pathogenesis could facilitate early clinical diagnosis, and improve trials of candidate drugs aimed at delaying disease onset or slowing the rate of disease progression. The authors propose a time scale model of disease onset and suggest candidate markers for use in therapeutic trials. The functional significance of these findings requires validation. This will be attempted with a Predict-HD longitudinal follow-up study.



Relationship between estimated years to diagnosis of Huntington's disease (HD) and various other measures. Solid line plots the predicted response; broken lines are 95% confidence limits for the estimated mean response. All relationships are adjusted to a female with mean levels of the other variables for which we adjusted our models (age = 41.2 years, education = 14 years, premorbid IQ).

[1] Magnetic Resonance Imaging
[2] Unified Huntington's Disease Rating Scale

Summary by Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)

A comparison of Huntington disease and Huntington disease-like 2 neuropathology

Dobrila D. Rudnicki et al., J. Neuropathol. Exp. Neurol. (2008), 67:366–374

This study compared *post mortem* brains from Huntington's disease and Huntington's disease-like 2 patients. Neuropathological features of both diseases were very similar, suggesting that the pathogenic mechanisms underlying the two diseases might overlap.

Background

In recent years, a number of neurological disorders have been identified where patients present with a clinical picture similar to that seen in Huntington's disease (HD). To date, four "Huntington's disease-like" (HDL) syndromes have been recognised. One of these, HDL2, was identified in 2001 and accounts for approximately 1% of all cases referred for HD genetic testing in the USA. The prevalence is highest among black South Africans and African Americans. With the exception of a few cases in Brazil, HDL2 has not been reported in Caucasian or Asian individuals.

HD and HDL2 have several genetic and clinical features in common. In both

- inheritance is autosomal dominant
- the mutation is a trinucleotide repeat expansion (CAG located in exon 1 of the *HD* gene in HD, and CTG located in a variably spliced exon of the *junctophilin-3* gene in HDL2)
- age of onset correlates inversely with repeat length
- disease typically appears in adults
- the course is relentless, with death about 20 years after onset
- pathology shown by MRI brain scans is similar
- symptoms include movement disorders (chorea, slowing of voluntary movements, rigidity, tremor, dystonia and parkinsonism), behavioural symptoms (depression), cognitive impairment (dementia) and weight loss.

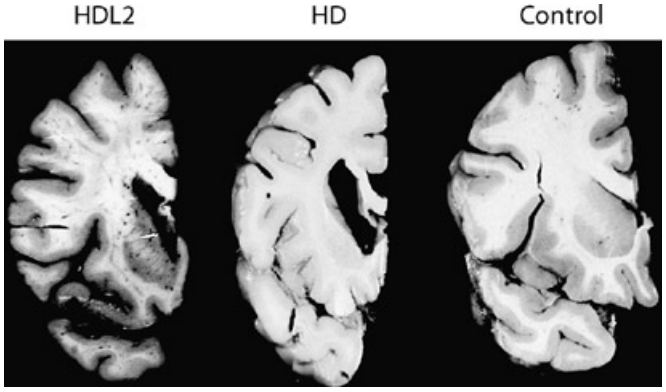
Results

Five HD and five HDL2 *post mortem* brains were examined using gross morphological parameters, immunohistochemistry, immunofluorescence and electron microscopy. The HD and HDL2 brains were indistinguishable upon gross examination. A remarkable similarity between the neuropathology of HD and HDL2 was also observed. In both diseases there was

- reduced brain weight
- marked volume loss (atrophy) of the striatum and cortex
- loss of neurones and proliferation of astrocytes in the striatum
- protein aggregates that were indistinguishable by immunostaining with anti-polyglutamine and anti-ubiquitin antibodies, and by electron microscopy. However, these were present in both the cell nucleus and cytoplasm in HD, but only in the nucleus in HDL2.
- a similar distribution and number of nuclear aggregates in the motor cortex and amygdala. However, nuclear aggregates were present in the pons and medulla of HD patients, but absent in all HDL2 cases.
- staining of nuclear aggregates with antibodies to the TATA-binding protein.

Conclusion

The neuropathological features of HD and HDL2 are extremely similar, with the only consistent differences being in the content and distribution of protein aggregates. The pathogenic mechanisms underlying HD and HDL2 may thus converge. Identifying the points of convergence should uncover useful therapeutic targets for both diseases.



Gross comparison of HDL2 and HD brains showing marked atrophy of the striatum and thinning of the cortex compared with a control brain.

A submodule of EHDN provides information on and assessment tools for non-HD, hereditary choreatic syndromes under the heading "Neuroacanthocytosis", including HDL-2:
www.euro-hd.net/html/na/submodule
www.euro-hd.net/html/na/diseases/hdl2
A login can be requested for clinicians interested in contributing to this prospective cohort study (see website).

Upcoming Meetings 2009

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 Restoration 2009, Havana, Cuba http://www.ciren.cu/paginas/GRUPO_MENU_DERECHA/EVENTOS/Evento1.htm
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 25	Annual Neuroscience Day 2009, University of Edinburgh, UK
Mar 26-28	24th Conference of Alzheimer's Disease International, Singapore http://www.adi2009.org/
Apr 2-4	2nd International Conference on Psychogenic Movement Disorders and Other Conversion Disorders, Washington, DC, USA http://www.movementdisorders.org/education/pmd/
Apr 25-May 2	2009 Annual Meeting of the American Academy of Neurology, Seattle, WA, USA http://www.aan.com/go/am
Apr 27-30	4th Annual CHDI Huntington's Disease Therapeutics Conference, Cannes, France http://www.chdifoundation.org/news/event.php?neid=49
May 31-Jun 5	Gordon Research Conference on CAG Triplet Repeat Disorders, Waterville Valley, NH, USA http://www.grc.org/programs.aspx?year=2009&program=cag
Jun 5-7	Huntington's Disease Society of America (HDSA) 24th Annual Convention, Phoenix, AZ, USA http://www.hdsa.org/index/convention.html
Jun 7-11	13th Movement Disorder Society (MDS), Paris, France International Congress of PD and Movement Disorders http://www.movementdisorders.org/congress/congress09/
Jun 20-24	19th European Neurological Society (ENS), Milan, Italy http://www.akm.ch/ens2009/
Jun 22-26	Spanish Society of Neurology (SEN) and Association of British Neurologists (ABN), Liverpool, UK http://www.theabn.org/meetings/annual-meeting.php
Jul 11-16	Alzheimer's Association International Conference on Alzheimer's Disease, Vienna, Austria http://www.alz.org/icad/overview.asp
Aug 27-30	1st International Congress on Clinical Neuroepidemiology, Munich, Germany http://www.neuro2009.com/
Aug 31-Sep 2	British Society for Human Genetics Conference, University of Warwick, UK www.bshg.org.uk/2009BSHG.htm
Sep 12-15	World Congress on Huntington's Disease, Vancouver, BC, Canada http://www.worldcongress-hd.net
Sep 12-15	13th European Federation of Neurological Societies (EFNS) Congress, Florence, Italy http://efns2009.efns.org/
Sep 12-16	22nd European College of Neuropsychopharmacology (ECNP), Istanbul, Turkey http://www.ecnp.eu/emc.asp?pageId=1196
Sep 23-26	82nd Congress of the German Society for Neurology (DGN), Nuremberg, Germany http://www.akmcongress.com/dgn2009/
Oct 11	23rd Annual Symposium on Etiology, Pathogenesis, and Treatment of Parkinson's Disease and Other Movement Disorders (HSG/PSG/MDS) Baltimore, MD, USA http://www.parkinson-study-group.org/PSG23rdAnnlSymposia.asp
Oct 17-21	Neuroscience 2009 - 39th Annual Meeting of the Society for Neuroscience, Chicago, IL, USA http://www.sfn.org/index.cfm?pagename=annualMeeting
Oct 20-24	American Society of Human Genetics (ASHG), Honolulu, HI, USA http://www.ashg.org/2009meeting/
Oct 24-30	19th World Congress on Neurology, Bangkok, Thailand http://www.wcn2009bangkok.com/
Nov 21	3rd Huntington Disease Clinical Research Symposium (venue to be confirmed) http://www.huntington-study-group.org/NewsEvents/EventsUpcomingMeetings/HuntingtonDiseaseClinicalResearchSymposium/tabid/62/Default.aspx
Dec 13-16	XVII World Federation of Neurology Congress on Parkinson's Disease and Related Disorders, Miami Beach, FL, USA http://www2.kenes.com/parkinson/Pages/Home.aspx