space neglect). Since unilateral visuospatial neglect is a complex syndrome that can affect different aspects of space cognition,6 different types of visuospatial neglect may have different effects on navigational abilities.7 Navigational abilities are crucial for neurological rehabilitation. Right brain damaged patients might be confronted with several spatial deficits while navigating in their wheelchair or walking with a left hemiparesis. Assessment and rehabilitation of navigation using a virtual environment is an interesting tool to train for navigational skills while not being embedded by the motor impairment or fatigability, yet respecting an ecological environment.

We are now proposing assessment and rehabilitation to all right brain damaged patients. Since the beginning of the study, six patients have benefited from VR rehabilitation sessions.

Anne Peskine,1 Charlotte Rosso,2,3 Natacha Box,4 Aurélie Galland,1 Elsa Caron,1 Gilles Rautureau,5,6 Roland Jouvent,5,6 Pascale Pradat-Diehl1,7
1 AP-HP, Pitié-Salpêtrière, Physical Medicine and Rehabilitation Unit, Paris, France; 2 UMR 7225, UMR S 975, Centre de Recherche de l’Institut du Cerveau et de la Moelle épinière (CICICM); COGIMAGE, Paris, France; 3 AP-HP, Pitié-Salpêtrière, Stroke Unit, Paris, France; 4 Cabinet de soins psychologiques et psychothérapeutiques CSPP, Paris, France; 5 Centre Emotion, CNRS-UPMC UMR 7593, Paris, France; 6 AP-HP, Pitié-Salpêtrière, Psychiatry Unit, Paris, France; 7 Université Pierre et Marie Curie-Paris 6, Paris, France

Correspondence to Dr A Peskine, AP-HP Service de Médecine Physique et de Réadaptation, Groupe Hospitalier Pitié-Salpêtrière, 47-83 bvd de l’Hôpital, 75651 Paris cedex 13, France; anne.peskine@psl.aphp.fr

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

Received 11 May 2010
Revised 2 August 2010
Accepted 5 August 2010
Published Online First 22 October 2010

J Neurol Neurosurg Psychiatry 2011;82:1407—1409. doi:10.1136/jnp.2010.217513

REFERENCES
1. Heilman KM, Watson RT, Valenstein E. Neglect and related disorders. In: Heilman KM, Valenstein E, eds. Clinical neuropsychology. New York:Oxford University Press, 1992:279—336.
2. Azouvi P, Bartolomeo P, Beis JM, et al. A battery of tests for the quantitative assessment of unilateral neglect. Restor Neurologi Neurosci 2006;24:273—85.
3. Rose FD, Brooks BM, Rizzo AA. Virtual reality in brain damage rehabilitation: review. Cybersysth Sel Behav 2005;8:263—71.
4. Tsalin I, Dupinix E, Chokron S, et al. Uses of virtual reality for diagnosis, rehabilitation and study of unilateral spatial neglect: review and analysis. Cybersysth Sel Behav 2009;12:175—81.
5. Urbanski M, Theibaut de Schotten M, Rodrigo S, et al. Brain networks of spatial awareness: evidence from diffusion tensor imaging tractography. J Neurol Neurosurg Psychiatry 2006;79:598—601.
6. Catani M, Theibaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections. Cortex 2008;44:1105—32.
7. Halligan PW, Pink GR, Marshall JC, et al. Spatial cognition: evidence from visual neglect. Trends Cogn Sci. 2003;7:125—33.
8. Guariglia C, Piccardi L, Iaria G, et al. Representational neglect and navigation in real space. Neuropsychologia 2005;43:1138—43.

Observing Huntington’s disease: the European Huntington’s Disease Network’s REGISTRY

Huntington’s disease (HD) is an autosomal dominant neurodegenerative disorder caused by a CAG repeat expansion in the HTT gene. HD usually manifests in adult life, causing motor impairments, cognitive decline and behavioural/psychiatric alterations. HD is devastating and inevitably fatal; currently, no disease modifying treatment is established.1

Historically, the study of HD has benefited strikingly from multicentre research initiatives, typified by the international collaborative effort that identified the causative CAG repeat expansion in the HTT gene in 1993.2 Much effort at present is focused on identifying therapeutic targets and developing treatments that may delay onset of the disease, or slow down or stop the progression of HD once it manifests. With a prevalence of 5—8/100,000, manifest HD is relatively rare. Thus we need advanced, multicenter, multinational research frameworks that allow us to study simultaneously multiple complementary aspects of HD. This includes the natural history of HD, its management and the collection of clinical information and biosamples for research. The European Huntington’s Disease Network (EHDN; http://www.euro-hd.net), established in 2004, is a collaborative network of HD researchers, HD clinicians, people affected by HD and their relatives. It strives to lay the foundations on which to advance knowledge about HD, how to optimally assess disease progression and factors that modify the phenotype. This initiative aims to develop new symptomatic therapies and provide the infrastructure to test rapidly putative disease modifying treatments in a multicentre, multinational setting with the ultimate goal of improving the quality of life of people affected by the disease.

REGISTRY is EHDN’s core observational study. REGISTRY is a multicentre, prospective, observational study with annual follow-up visits that enrolls manifest and pre-manifest HD expansion mutation carriers, individuals at risk of HD, non-mutation gene carriers and controls (no family history of HD) (figure 1). Participants give informed written consent according to the International Conference on Harmonisation—Good Clinical Practice (ICH-GCP) guidelines (http://www.ich.org/LOB/media/MEDIA482.pdf). For participants who lack the capacity to consent, study sites adhere to country specific guidelines for obtaining consent. Minors assent with both parents consenting for them. Ethics approval was obtained from the local ethics committee for each study site contributing to REGISTRY. Data collection uses electronic case report forms available in Czech, Danish, Dutch, English, Finnish, French, German, Italian, Norwegian, Polish, Portuguese, Spanish, Swedish and Russian. At each study site, clinicians with longstanding experience in HD take a careful history and examine patients clinically; motor,

Figure 1 Flowchart illustrating REGISTRY study design. SF-36, Short Form-36; TFC, total functional capacity; UHDRS, Unified Huntington’s Disease Rating Scale.
psychiatric and cognitive signs are scored using the Unified Huntington’s Disease Rating Scale (UHDRS).\textsuperscript{3} Assessments are complemented by self-rating scales that probe mood, quality of life and health economics (for an overview see figure 1). Disease stage is derived from the total functional capacity scores.\textsuperscript{4} All participants are assigned a nine digit pseudonym created using a secure one way hash algorithm. No identifying data are stored on the EHDN server. Data are entered online using an electronic web based data capture system (http://www.euro-hd.net) where a username determines access rights within the web portal. Entries for medication are coded according to the Anatomical Therapeutic Chemical classification (http://www.whocc.no/atcddd), and co-morbidities are coded according to ICD-10. Data entry onto the web portal is subject to automatic plausibility checks. In addition, study site monitors are annually trained, assessed and certified to reduce inter- and intra-rater variability. Following data entry, data are monitored online and on site by monitors fluent in the language of the contributing study site. Data monitoring adheres to the principles laid out in ICH-GCP.

Blood is collected and shipped to BioRep at room temperature for genetic analysis and lymphoblastoid cell line creation (BioRep, Milan, Italy). DNA is extracted, and HTT gene CAG repeat length analysis\textsuperscript{5} (PCR amplification followed by capillary electrophoresis using the MegaBace Fragment Filser Software from General Electric, Buckinghamshire, UK). A second independent accredited laboratory in Tübingen, Germany, duplicated CAG repeat analyses (Applied Biosystems, California, USA) in 342 DNA samples for quality comparison. Comparisons between BioRep and Tübingen resulted in agreement of 99% with respect to CAG expansion size for the larger and smaller allele: only 3/342 size determinations for the larger allele differed by two or more repeats (k = 0.98). Mid stream urine samples are collected. DNA and urine are stored at –20°C. To date (August 2010), REGISTRY includes 6476 participants from 136 study sites in 16 countries. Of these, 663 are larger allele differed by two or more repeats (k = 0.98). Mid stream urine samples are collected. DNA and urine are stored at –20°C. To date (August 2010), REGISTRY includes 6476 participants from 136 study sites in 16 countries. Of these, 663 are participating in 5183 patients. BioRep has so far isolated DNA from whole blood in 4510 participants with CAG repeat measurements available from 3506. A total of 4053 lymphoblastoid cell lines have been established.

The strength of our study is the large number of participants with data collected across Europe following the same study protocol. We demonstrate that such studies can be conducted effectively across different countries and multiple languages. In addition, investigators are regularly trained and certified to improve data quality. REGISTRY, unlike many observational clinical research initiatives, engages data monitoring based on the principles of ICH-GCP. Participating sites are visited regularly by a team of trained monitors in order to ensure the plausibility and accuracy of the data, and to promote adherence to the study protocol and its procedures. Data monitoring is not a prerequisite for cohort studies but it is an investment to enhance the collection of more robust and reliable data. The unparalleled large collection of clinical data and biomaterials in REGISTRY will enable research projects to be conducted on a scale that has not previously been possible. The initiative will expedite the search for disease modifiers (genetic and environmental) of age at onset and phase of progression that could be harnessed for the development of novel treatments, thus offering a promising new direction towards slowing down or preventing this debilitating disease.

Acknowledgements We wish to acknowledge the time and effort of all participants in this study.

Michael Orth, The European Huntington’s Disease Network

Correspondence to M Orth, Department of Neurology, Universitätsklinikum Ulm, Oberer Eselsberg 45/1, 89081 Ulm, Germany; michael.orth@uni-ulm.de

Funding The European Huntington’s Disease Network is funded by the CHDI Foundation, Inc.

Competing interests None.

Ethics approval This study was conducted with the approval of each of the contributing study sites.

Contributors Writing committee: M Orth, OJ Handley, C Schwenke, SJ Tabrizi, EF Wild, SJ Traubi, GB Landwehrmeyer.

Registry Steering committee: A-C Bachoud-Levi, AR Dunnett, EJ Wild, SJ Tabrizi, GB Landwehrmeyer, J Lewy, JE Nielsen, DM Vinter, AJ Walshe, M Mirzaei, JF Knott, M Pa¨ivi¨aru¨ta, C Verellen-Dumoulin, JU Jacobsen, Jørgen Nielsen.

Biostatistics: JF Wild, SJ Traubi, GB Landwehrmeyer, J Lewy, JE Nielsen, DM Vinter, AJ Walshe, M Mirzaei, JF Knott, M Pa¨ivi¨aru¨ta, C Verellen-Dumoulin, JU Jacobsen, Jørgen Nielsen.

Biospecimen handling: Annamaria Painold, Sabina Debruxelles; Daniel Zielonka, Anna-Christine Flamme-Painold.

Central coordination and Language coordinators: Katrin Barth, Leonor Correa Guedes, Ana Maria Finisterra, Monica Bascaralien Garde, R Bos, Sabrina Burg, Daniel Ecker, Olivia J Handley, Christine Held, Kerstin Koppers; Mathilde Lauré, Asuncion Martinez Descals, Tim McLean, Tiago Mestre, Sara Minster, Daniela Monza, Jenny Townhill (formerly Naji), Michael Orth, Helene Pedieu, Laurent Paterski, Nadia Peppa, Susana Pro Kirovstva, Amandine Rialland, Nino Ranen (formerly Heinenon) Pavia Šaškinová, Patricia Trigo Cubillo, Christine Tricht, Marlene R van Walters, Maria-Noelle Witjes-Ané, Elizaveta Yudina (formerly Tarasova), Daniel Zienkon, Eugenius Zienkon, Paolo Zini.

AUSTRIA

Graz (UKH Graz, Abteilung für Psychiatrie): Raphael M. Bonelli; Brigitte Herrenhoft; Anna Holl (formerly Hötli); Hans-Peter Kapfhammer; Michael Koppitz; Markus Magnet; Daniela Otti; Annamaria Painold; Karin Reisinger; Monika Scheit; Karen Hecht; Sabine Lick; Nicole Müller; Helmut Schöngärtner; Jassmin Ulrich

Belgien

Charleroi (Institut de Pathologie et de Génétique (IPG)): Pascal iBai; Christine Verellen-Dumoulin.

Brussels (VUB Neurology): Anja Flamez; V Moree; Sylvie de Haedt.

Leuven (Universitair Ziekenhuis Gasthuisberg): Andrea Verellen-Dumoulin; Wim Vandenberghe; Dimpna van Reijen.

CZECH REPUBLIC

Prague (Extrapramidové centrum, Neurologická klinika, 1. LF UK a VFN): Jiří Klempíř; Martin Kuchařik; Jan Roth.

Olomouc (Neurologická klinika, Fakultní nemocnice Olomouc): Zuana Senkarová.

DENMARK

Copenhagen (Hukommelsesklinikken, Rigshospitalet): Lis Hasholt; Lena E. Hjermdal; Oda Jakobsen; Anne Nørreman; Sven Asger Sørensen; Jette Stokholm; Jørn Nielsen.

FINLAND

Turku-Suviuitti (Rehabilitation Centre Suviuitti): Heila Hivola; Kirsti Martikanen; Katrin Tuha.

Helsinki (Department of Medical Genetics The Family Federation of Finland): Maarit Peippo; Marjaatta Sipponen.

Oulu (Dep. of Neurology): Jaakko Ignatius; Mikko Karpinski; Jaana Armin.

Tampere (Tervestyalo Healthcare Service Centre): Maita Santala.

FRANCE

Angers (CHU d’Angers): Philippe Allain; Marie-Anne Guerin; Bénédicte Gohier; Audrey Olivier; Adriana Prunduvan; Clarisse Scherer-Gegg; Christophe Verney.

Bordeaux (Hôpital Pellegrin): Blandine Babinol; Sabrina Debruxelles; Cyril Goizet; Danielle Lafourrière.

Lille-Amiens:

Lille (CHRU Roger Salengro): Christelle De Bruycker; Anne-Sophie Carette; Eric Decorte; Arnaud Deléglé; Kathy Dujardin; Mareriele Peter; Lucie Plomhouse; Clémence Simonny; Stéphanie Thibault-Tanchou.

Amiens (CHU Nord): Marcellin Bellon; Cécile Duru; Pierre Krystkowiak; Martine Rousset; Sandrine Wannepaan.

Marseille (Hôpital La Timone): Jean-Philippe Azoulay; Christelle Dabert; Dominique Delphin; Alexandre Eusebio; Hélène Grosjean; Laura Mullender; Marielle Nowak.

Strasbourg (Hôpital Civil): Gabrielle Rudolf; Gièle Steinmetz; Christine Tranchant; Caroline Wagner; Marie-Agathe Zimmermann.

Toulouse (Hôpital Purpan): Fabienne Calvez; Samia Cheriet; Jean-François Demontet; Monique Galtzky.

GARCHEN

Aachen (Universitätsklinikum Aachen, Neurologische Klinik): Christoph Michael Kosinski; Eva Milkeret; Daniela Probst; Christian Sass; Johannes Scheer; Christiane Schlangen; Cornelius J. Werner. Brain Research Center – Charité - Universitätsmedizin Berlin: Harald Gelderbloom; Josef Priller; Harald Prüß; Elke Jakob Spruth.

Bochum (Huntington-Zentrum (NRW) Bochum im St. Josef-Hospital): Jürgen Andrich; Rainer Hoffmann; Peter H. Kraus; Sabine Muth; Christian Pfehr; Carsten
What’s in a name? Neuronal intermediate filament inclusion disease (NIFID), frontotemporal lobar degeneration-intermediate filament (FTLD-IF) or frontotemporal lobar degeneration-fused in sarcoma (FTLD-FUS)?

Neuronal intermediate filament inclusion disease (NIFID) is a neurodegenerative disorder of a heterogeneous clinical phenotype, encompassing behavioural changes, language impairment, perseveration, executive dysfunction with or without early onset dementia, extrapyramidal features, and subclinical or clinical involvement of upper and lower motor neurons, with age at onset of reported cases ranging from 23 to 56 years (table 1). 1–5 NIFID was initially characterised neuropathologically on the basis of intraneuronal cytoplasmic inclusions of variable morphology which immunostained for all class IV intermediate filament (IF) proteins, namely NF-H, NF-M, NF-L and alpha-internexin. 1–3 More recently it has been shown that a much larger proportion of the inclusions in NIFID are immunoreactive with the fused in sarcoma (FUS) protein than with IF, leading to changes in the suggested nomenclature. 1–3 We present a further case demonstrating the broad phenotypic features, overlapping with both corticobasal degeneration and motor neuron disease.

A 62-year-old right-hand woman presented with a 2-year history of progressive difficulty with coordination and balance. She noticed weak grip and poor coordination in her right hand when playing tennis and had difficulty assembling familiar scuba diving equipment. She developed involuntary twitching of the fingers in the right hand and heaviness in the right arm. Over the next few months asymmetric leg weakness (right > left) developed, with difficulty initiating gait and climbing stairs with occasional falls. Dysarthria also became apparent, conversation became more laboured and her writing became smaller.

Examination showed bradykinesia and cogwheel rigidity in the right arm but no rest tremor. Myoclonic jerks were seen in the right little and index fingers, and there was exaggerated response to startle and sound. Neither muscle wasting nor fasciculations were seen; power was preserved. Reflexes were globally brisk with bilateral downgoing plantars. All modalities of sensation were normal. Gait showed slow initiation and wide base. The clinical picture of an asymmetric akinetic–rigid syndrome with some pyramidal features and myoclonus was thought most in keeping with a corticobasal syndrome.9

Salient findings on investigation were elevated creatine kinase (620 U/l, normal <175), normal MR brain imaging, EEG and CSF analysis. Formal neuropsychological assessment showed no evidence of cognitive decline. EMG showed active denervation and fasciculations in all limbs and paraspinal muscles. Hence the investigations indicated a subcortical anterior horn cell disorder typical of motor neuron disease.

Symptoms progressively deteriorated over the next 2 years. Although clonazepam improved the myoclonus, the extrapyramidal syndrome was levodopa unresponsive and the patient became wheelchair bound.