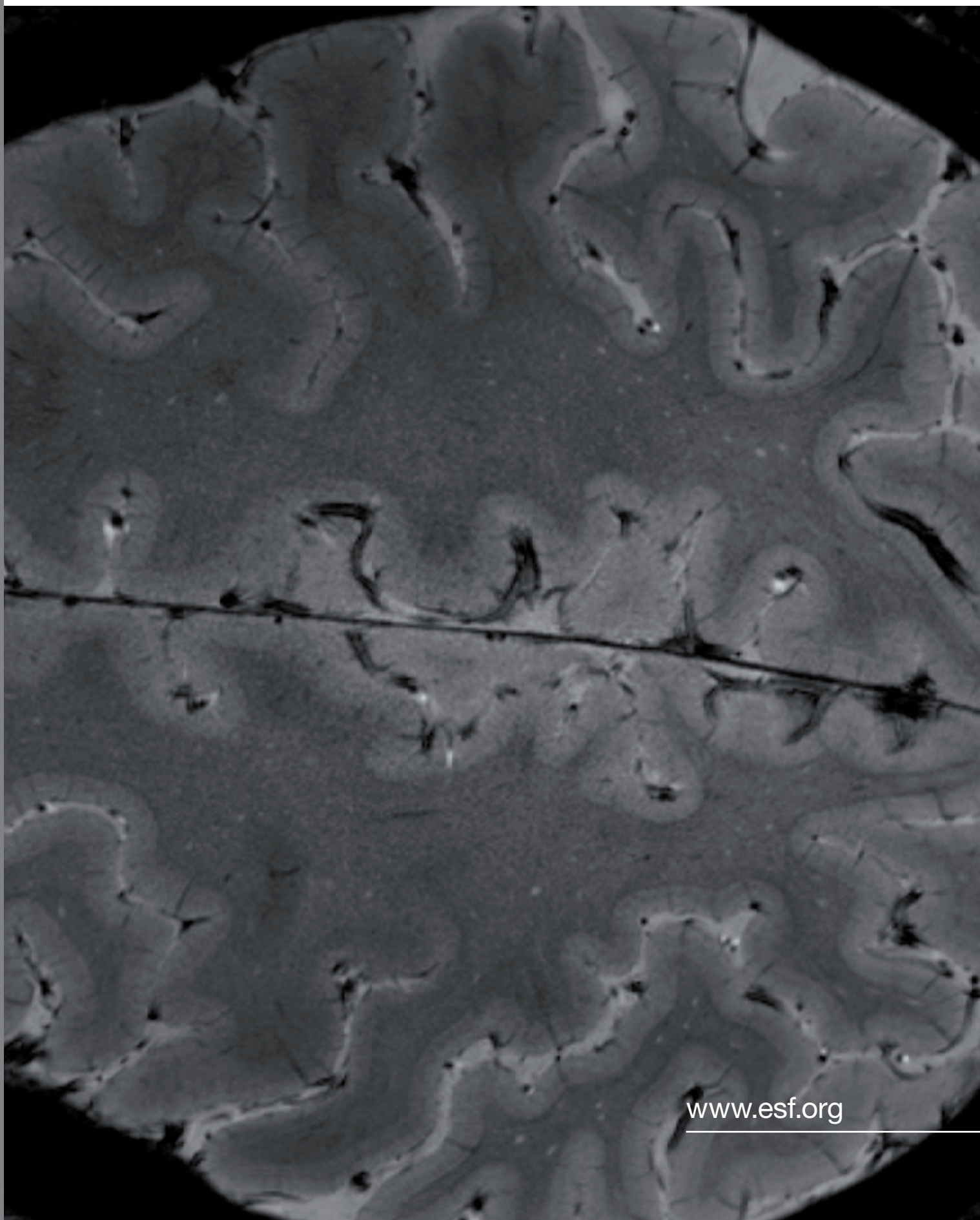
EUROPEAN SCIENCE FOUNDATION

SETTING SCIENCE AGENDAS FOR EUROPE

RESEARCH NETWORKING PROGRAMME

EUROPEAN RESEARCH NETWORK FOR INVESTIGATING HUMAN SENSORIMOTOR FUNCTION IN HEALTH AND DISEASE (ERNI-HSF)

Standing Committee for the Medical Sciences
(European Medical Research Councils, EMRC)



www.esf.org

The European Science Foundation (ESF) is an independent, non-governmental organisation, the members of which are 80 national funding agencies, research-performing agencies, academies and learned societies from 30 countries.
The strength of ESF lies in the influential membership and in its ability to bring together the different domains of European science in order to meet the challenges of the future.
Since its establishment in 1974, ESF, which has its headquarters in Strasbourg with offices in Brussels and Ostend, has assembled a host of organisations that span all disciplines of science, to create a common platform for cross-border cooperation in Europe.
ESF is dedicated to promote collaboration in scientific research, funding of research and science policy across Europe. Through its activities and instruments ESF has made major contributions to science in a global context. The ESF covers the following scientific domains:

- Humanities
- Life, Earth and Environmental Sciences
- Medical Sciences
- Physical and Engineering Sciences
- Social Sciences
- Marine Sciences
- Nuclear Physics
- Polar Sciences
- Radio Astronomy Frequencies
- Space Sciences

Cover picture:
An axial magnetic resonance image of human sensorimotor cortex obtained using ultra high-field (7 Tesla) magnetic resonance imaging (MRI) with a resolution of 0.25mm x 0.25mm x 1.0mm. Images were acquired at the University of Nottingham, UK using a Philips 7 Tesla MRI scanner and multi-channel SENSE head coil running a T2* weighted sequence. The increased signal-to-noise at 7 Tesla makes it possible to observe anatomical detail with far greater acuity than can be obtained at conventional field strengths. Clinical applications of 7 Tesla brain imaging include the observation of lesions in cortical grey matter in multiple sclerosis and the localisation of functional microlesions in stroke patients (e.g., Sumner et al. (2007) *Neuron* 54(5), 697-711).

Introduction

The parietal cortex plays an important role in how we represent our body and the space around the body. It also participates in planning and controlling our voluntary movements. In humans, damage to the parietal cortex can lead to disorders in the representation of spatial relationships and impairments in the planning and control of goal-directed movements. For this reason understanding the nature of the sensorimotor transformations carried out by the parietal cortex is a fundamental problem for neuroscience and is of considerable clinical importance in treating the consequences of stroke and other neurological and psychiatric disorders that affect this brain area.

Stroke is the third most common cause of death and by far the most common cause of human disability. Damage to the parietal cortex is a common outcome of stroke that frequently results in impairments of spatial representation or in the planning and control of goal-directed actions. *Visuospatial neglect* is a neurological disorder in which the individual ignores or fails to become aware of objects or events in the region of space contralateral (i.e., opposite to) their brain damage. Individuals with visuospatial neglect may fail to shave one side of their face, ignore the food on one side of their plate, and bump into objects on one side of their body. Visuospatial neglect affects 60-70% of right hemisphere stroke patients acutely. By contrast, *ideomotor apraxia*, which is a neurological disorder of skilled action in which the individual makes spatial and timing errors when carrying out goal-directed movements, affects approximately 50% of those admitted to hospital following a left hemisphere stroke. The presence of disorders such as visuospatial neglect seriously hampers rehabilitation after stroke, and reduces an individual's ability to regain functional independence.

The primary aim of the ERNI-HSF Research Networking Programme is to establish an interdisciplinary research forum that will drive forward our understanding of human sensorimotor function in health and disease through the foundation of a pan-European network that makes possible collaborative work practices that could not be achieved by individual scientists working alone.

The running period of the ESF ERNI-HSF Research Networking Programme is for five years from May 2007 to May 2012.

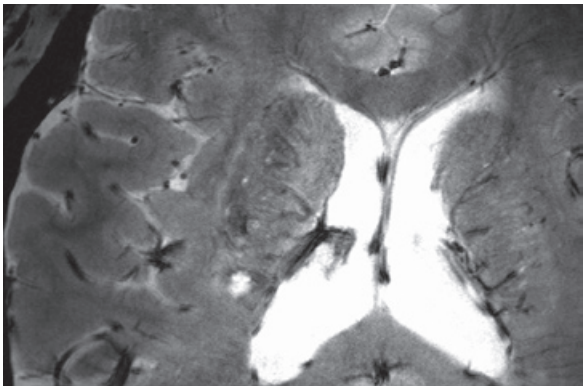


Figure 1: Illustrates a magnetic resonance image from a patient recovering from a small stroke using ultra high-field (7 Tesla) MRI. The scan revealed a small 'microlesion' located in the right putamen. The image is shown in radiological convention (i.e., the right brain is presented on the left of the image and left brain on the right). The images were obtained with an in-plane resolution 0.25mm × 0.25mm and a slice thickness of 1.25mm using a T1-weighted sequence using a Philips 7 Tesla MRI scanner.

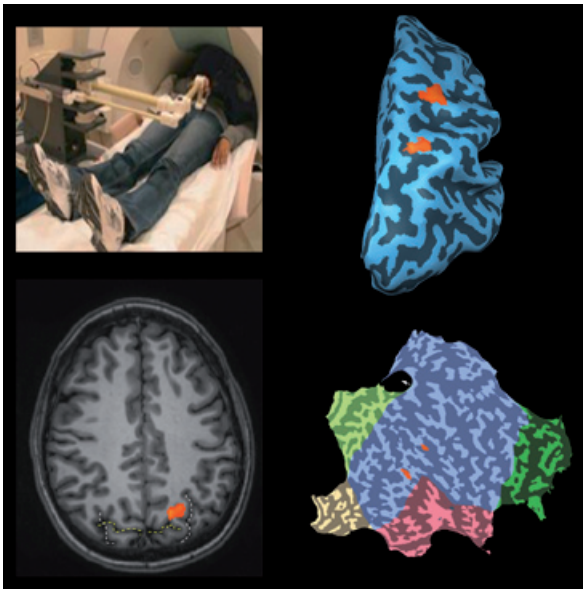


Figure 2: Illustrates studies investigating the brain processes involved in the planning and control of reaching movements. **Upper left panel** shows an MR-compatible two-link robot that is used to study upper-limb movements within the MRI scanner. An important aspect of this robot is that forces can be applied at the hand through the operation of pneumatic pistons, making it a useful tool for studying motor learning. **Lower left panel** shows the location of BOLD activation associated with reaching to a posturally defined location within the MRI scanner. This area, just anterior to the parietal-occipital sulcus, has been referred to as the human equivalent of the so-called 'parietal reach region' identified in the monkey brain. **Upper right panel** illustrates BOLD activations associated with reaching to novel, posturally defined, target locations superimposed on a semi-inflated brain. **Lower right panel** illustrates these same BOLD activations superimposed on a flattened map of the brain.

Comparative studies of primate sensorimotor function

Much of our current understanding of how sensorimotor transformations are implemented within the parietal cortex of the human brain comes from electrophysiological recording and lesion studies of non-human primates. These studies have been very successful in identifying multiple representations of space in the monkey parietal cortex, each of which is associated with different types or combinations of action (e.g., saccadic eye movements, and reaching or grasping movements of the upper limb). However, despite the success of this approach for understanding the functional organisation of the monkey parietal cortex, its relevance for understanding how the *human parietal cortex* represents space and contributes to the planning and control of goal-directed movements remains open to question. Specifically, whereas studies of the monkey parietal cortex may have proven useful in understanding human sensory and motor functions, it is unclear whether this approach can provide the accurate models of human parietal function in health and disease that are required for developing clinically useful models of mental function and dysfunction.

Recent technological developments, particularly in magnetic resonance imaging (MRI), have made it possible to investigate the functional anatomy of sensorimotor function within the human brain. To date, these studies can be characterised largely as attempts to identify human homologues of functional brain areas in the parietal cortex, identified within the monkey using electrophysiological recording techniques. A more promising approach that will be a core focus of the ERNI-HSF Research Networking Programme may be to make use of the *same* brain imaging techniques (e.g., structural and functional MRI, transcranial magnetic stimulation, electrophysiological recording) in humans and monkeys. Figure 3 illustrates recent attempts by members of ERNI-HSF to make use of probabilistic diffusion tractography and functional MRI to compare directly the human and macaque sensorimotor systems using similar paradigms.

Correspondence between brain imaging and lesion techniques

The recent development of functional brain imaging techniques that are based upon measuring blood oxygenation, volume and flow has raised a number of important methodological questions concerning the relationship between these measures and the physiology of neuronal communication. A core focus of ERNI-HSF concerns the degree to which human functional brain imaging studies produce comparable findings to those obtained from lesion studies in neurological patients. This is because there has often been poor correspondence between functional brain areas identified in neuropsychological studies (e.g., using lesion overlay methods) and brain regions identified in functional brain imaging (e.g., functional MRI) studies. For this reason the interpretation of functional MRI data in the human parietal cortex requires validation using techniques that permit stronger inferences to be drawn about functional causality (e.g., TMS and/or lesion studies). The use of lesion overlap analyses based upon the co-registration of anatomical magnetic resonance images (Figure 4) is an important and rapidly developing technique that poses a number of technical challenges. To explore this issue further the first of several ERNI-HSF workshops, focusing on *Recent advances in magnetic resonance imaging and lesion reconstruction techniques for understanding*

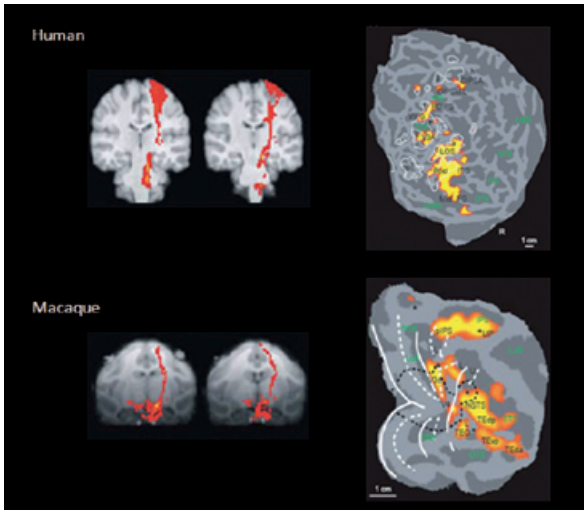


Figure 3: The upper and lower panels on the left of the figure illustrate the results of a recent study reported by Matthew Rushworth and colleagues that directly compared patterns of white-matter connectivity in the human and macaque brain using probabilistic diffusion-weighted tractography [images adapted from Croxson et al. (2005) *Journal of Neuroscience* 25: 8854–8866]. The upper and lower panels on the right of the figure illustrate the results of a recent study reported by Guy Orban and colleagues that conducted parallel functional MRI studies in humans and awake monkeys to compare directly the functional properties of the intraparietal sulcus (IPS), an area extensively investigated in the macaque using electrophysiological recording techniques [images adapted from Orban et al. (2006) *Neuropsychologia* 44: 2647–2667]. A crucial observation in both studies was that while there were a number of clear similarities between the macaque and human brain, there were also many important differences anatomically and in terms of function between the monkey and human brain.

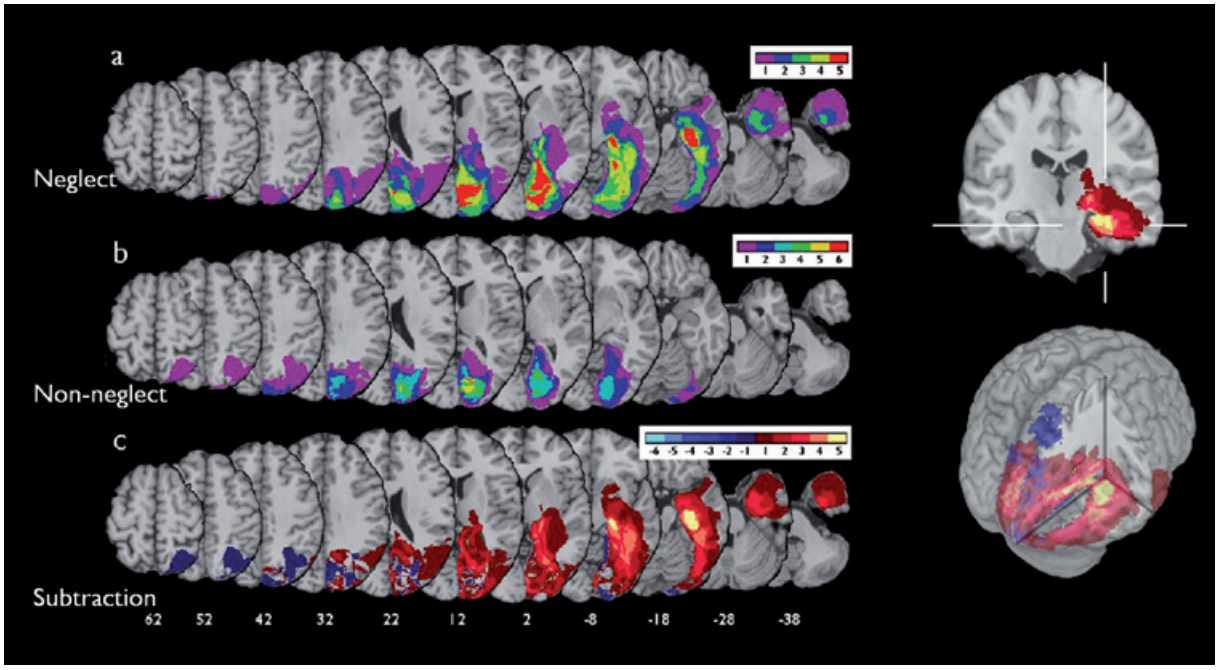


Figure 4: Illustrates how lesion overlap studies based upon the use of spatially normalised magnetic resonance images can be used to identify spatially localised brain regions in which damage is highly predictive of particular forms of functional impairment. The figure shows the results of a recent lesion overlap analysis of visual hemineglect reported by Masud Husain and colleagues [images are adapted from Mort et al. (2003) *Brain* 126: 1986-1997].

human brain function, was held in Budapest, Hungary in April 2008. Future ERNI-HSF workshops will focus on the best technical practice of using *diffusion tensor imaging* and on the difficulties and benefits of using *ultra high-field (7 Tesla) magnetic resonance imaging* for studying human brain function.

Human brain atlases based upon magnetic resonance imaging

Lesion overlap studies of neurological syndromes are clearly important and can be extremely influential. A serious limitation of such studies is, however, that it often takes many years to accumulate a sufficiently large cohort of appropriate individuals. This has sometimes resulted in the publication of studies that are based upon relatively small numbers of participants (~20) which may be considered sub-optimal. As such studies will clearly benefit from the use of very large cohorts (i.e., several hundred participants), a core focus of ERNI-HSF is to develop a human brain atlas based upon archived structural MRI data. Such an atlas would have tremendous scientific and clinical importance. We plan to explore how data might be collected from scientific groups across a wide range of countries within the EU. Key to the success of this project will be the development of agreed imaging protocols that are adhered to by all collaborating groups. Preliminary discussion of this issue was carried out at the April 2008 ERNI-HSF workshop held in Budapest.

Aims and Objectives

The primary aim of the ERNI-HSF Research Networking Programme is to establish an interdisciplinary scientific forum that can drive forward our understanding of human sensorimotor function in health and disease. A key aspect of this forum is the foundation of a pan-European research network that makes possible collaborative work practices that could not be achieved by individual scientists working alone. The activities of ERNI-HSF are facilitated by a Steering Committee, the members of which are drawn from a wide range of scientific disciplines relevant to the investigation of human sensorimotor function in health and disease. An important function of the Steering Committee is to identify thematic topics or issues that are considered to be critical for initiating major scientific advances, and to oversee the organisation of appropriate technical workshops and scientific meetings.

A further, and very important, objective of ERNI-HSF is to establish mechanisms for sharing scientific knowledge and technical expertise, including current "best practice" in the use of rapidly emerging brain imaging techniques. This type of activity is best achieved by a series of technical workshops in which a small number of acknowledged experts in a particular approach or technique are brought together. The key technical issues raised within each workshop are then rapidly disseminated to the wider scientific community via electronic media. Technical workshops completed or currently being planned include:

- Techniques involved in studying brain structure/function relationships based upon lesion reconstruction and lesion overlay analyses;
- Benefits and challenges of human neuroimaging studies at ultra high-field strengths (7 Tesla);
- Challenges involved in combining brain imaging techniques (e.g., transcranial magnetic stimulation and fMRI, EEG recording and fMRI);
- Difficulties involved in the use and analyses of functional neuroimaging with neurological groups (e.g., those presenting with vascular impairments).

Another important objective of ERNI-HSF will be to promote and facilitate the training of young basic and clinical scientists across the EU. General scientific training will be provided by awarding support for postgraduate and postdoctoral students to attend ERNI-HSF-organised scientific meetings and workshops. Specialist training in particular scientific techniques, including hands-on experience with new techniques or methods (e.g., ultra high-field neuroimaging), will be provided as part of a programme of technical workshops and training courses.

Finally, and most importantly, a key aim of ERNI-HSF will be to coordinate the establishment of a European-wide database of brain imaging data. This database might include the following:

- An archive of structural MRI data obtained from neurologically healthy individuals that would form the basis of a European MRI atlas of human brain structure;
- An archive of structural MRI data obtained from a large number of individuals presenting with neurological disease (e.g., recovering from stroke) that could be correlated with data from agreed, standardised behavioural measurements to yield an atlas of structure/function relationships based upon lesion reconstruction and lesion overlay analyses.

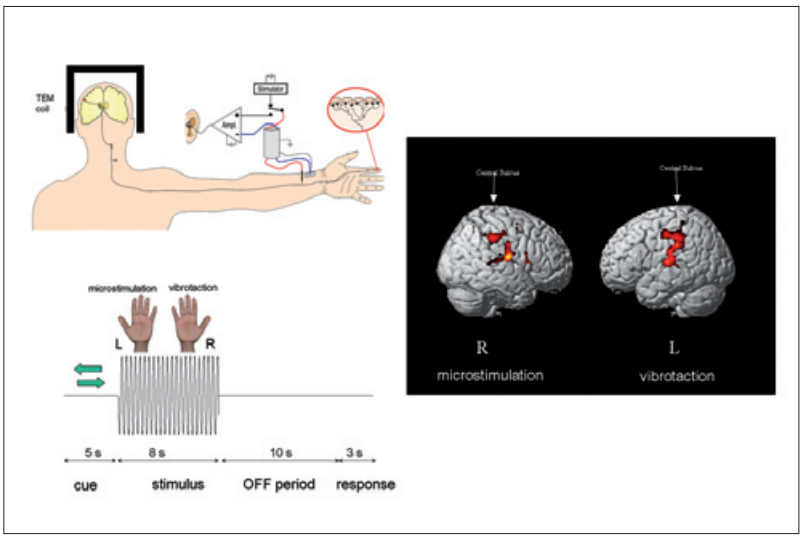


Figure 5: Microstimulation and vibration studies of human somatosensation using magnetic resonance imaging techniques. **Upper left panel** illustrates the experimental setup used for combined functional magnetic resonance imaging (fMRI) and microneurography studies. In these studies a microelectrode is inserted into the arm just above the wrist and individual mechanoreceptors within the median nerve bundle are stimulated. Brain activity (BOLD activation) associated with median nerve stimulation is then recorded using a surface coil. **Lower left panel** illustrates the time course of stimulation used in the microstimulation and vibration studies. **Right panel** shows how BOLD activations produced by microstimulation of the median nerve and vibrotactile stimulation of the finger tips produce similar patterns of brain activation. See McGlone et al. *Behavioural Brain Research* 135 (2002) for further details.

Programme Activities

Scientific collaboration and training will be facilitated through thematic or technical **workshops** or scientific **meetings**. Following a series of very successful international themed workshops on the topic of *body representation*, latterly funded by the UK Economic and Social Research Council (ESRC), ERNI-HSF continues to support annual scientific workshops on this topic. Two such ERNI-HSF *Body representation* workshops have taken place. The first took place in October 2007, in Rovereto, Italy (organisers: Dr. Massimiliano Zampini and Dr. Francesco Pavani), and the second took place in April 2008 in Nottingham, UK (organiser: Professor Stephen Jackson). A third *Body representation* workshop is planned for 2009, to be held in Switzerland and organised by Professor Olaf Blanke and colleagues.

Other workshops recently convened within the ERNI-HSF Research Networking Programme have included a two-day workshop entitled *Recent advances in magnetic resonance imaging and lesion reconstruction techniques for understanding human brain function*. This workshop was held in April 2008 at the Hungarian Academy of Sciences, Budapest, Hungary (organisers: Professor Masud Husain, UK, and Hans-Otto Karnath, Germany). A two-day workshop on **Computational principles of sensorimotor learning** will be held from 13-15 September 2009 in Kloster Irsee, Germany, with the aim to develop an atlas of human brain structure/function relationships (organisers: Joern Diedrichsen, Chris Miall and Daniel Wolpert, UK).

A larger **scientific meeting**, focusing on the *role played by the parietal cortex in sensorimotor function*, will be held in Amsterdam in 2010 (organisers: Professor Edward de Haan and Dr. Chris Dijkerman, The Netherlands). This meeting will coincide with the bi-annual meeting of the Federation of European Neuropsychology Societies in Amsterdam.

Training courses will be organised to train a new generation of young scientists and technicians in new or emerging approaches or techniques (particularly those associated with brain imaging techniques). **Bursaries** are available through science meeting organisers to facilitate the attendance of young scientists. **Exchange grants** promote mobility of researchers between laboratories in different European countries and contribute to training and to advancing basic research projects. Programme information is disseminated through the ESF and ERNI-HSF **websites**.

Funding

ESF Research Networking Programmes are principally funded by the Foundation's Member Organisations on an *à la carte* basis. ERNI-HSF is supported by:

- **Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (FWF)**
  Austrian Science Research Fund, Austria
- **Fonds voor Wetenschappelijk Onderzoek-Vlaanderen (FWO)**
  Research Foundation Flanders, Belgium
- **Suomen Akatemia/Finlands Akademi**
  Academy of Finland, Finland
- **Deutsche Forschungsgemeinschaft (DFG)**
  German Research Foundation, Germany
- **Magyar Tudományos Akadémia (MTA)**
  Hungarian Academy of Sciences, Hungary
- **Országos Tudományos Kutatási Alapprogramok (OTKA)**
  Hungarian Scientific Research Fund, Hungary
- **Health Research Board (HRB)**
  Ireland
- **Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO)**
  Netherlands Organisation for Scientific Research, The Netherlands
- **Norges Forskningsråd**
  Research Council of Norway, Norway
- **Schweizerischer Nationalfonds (SNF)**
  Swiss National Science Foundation, Switzerland
- **Medical Research Council (MRC)**
  United Kingdom

ERNI-HSF Steering Committee

Professor Stephen Jackson (Chair)
School of Psychology
University of Nottingham
Nottingham NG7 2RD
United Kingdom
Tel: +44 115 846 6020
Fax: +44 115 951 5324
Email: stephen.jackson@nottingham.ac.uk

Professor Eric Achten
MR-Department (-1K12)
Ghent University Hospital
De Pintelaan 185
9000 Ghent
Belgium
Tel: +32 9 240 4072
Email: rik.achten@ugent.be

Professor Olaf Blanke
Laboratory of Cognitive Neuroscience (LNCO)
Brain-Mind Institute
École Polytechnique Fédérale de Lausanne (EPFL)
1015 Lausanne
Switzerland
Tel: +41 21 693 96 21
Email: olaf.blanke@epfl.ch

Professor Synnöve Carlson
Institute of Biomedicine
Physiology
University of Helsinki
B123B
PL 63 (Haartmaninkatu 8)
00014 Helsingin Yliopisto
Finland
Tel: +358 191 25316/+358 191 25314
Email: Synnove.Carlson@helsinki.fi

Professor Edward de Haan
Faculty of Social and Behavioural Sciences
University of Amsterdam
Nieuwe Prinsengracht 130
1018 VZ Amsterdam
The Netherlands
Tel: +31 20 525 4868
Email: E.H.F.deHaan@uva.nl

Dr. Orla Hardiman
National Neuroscience Centre
Beaumont Hospital
Dublin 9
Ireland
Tel: +353 1 8376528
Email: ohard@iol.ie

Professor Hans-Otto Karnath
Centre of Neurology
University of Tübingen
Hoppe-Seyler-Strasse 3
72076 Tübingen
Germany
Tel: +49 7071 29 80465
Email: Karnath@uni-tuebingen.de

Professor Reinhold Schmidt
Department of Neurology
Medical University Graz
Auenbruggerplatz 22
8010 Graz
Austria
Tel: +43 316 385 3397
Fax: +43 316 325 520
Email: reinhold.schmidt@meduni-graz.at

Professor Håkan Sundberg
Department of Biological and Medical Psychology
Faculty of Psychology
University of Bergen
Jonas Lies vei 91
5009 Bergen
Norway
Tel: +47 55 58 62 24
Fax: +47 55 58 98 72
Email: hakan.sundberg@psybp.uib.no

Professor Zoltan Vidnyanszky
MR Research Centre
Szentagothai Knowledge Centre
Semmelweis University
Prater u. 50/a
1083 Budapest
Hungary
Tel: +36 1217 6937
Email: vidnyanszky@digitus.itk.ppke.hu

External Coordinator

Ms. Amy Parkinson
School of Psychology
University of Nottingham
Nottingham NG7 2RD
United Kingdom
Tel: +44 115 846 7241
Fax: +44 115 951 5324
Email: Amy.Parkinson@nottingham.ac.uk

EMRC Standing Committee Representative

Professor Albert Gjedde
Department of Neuroscience and Pharmacology
School of Medicine and Health Studies
University of Copenhagen
Panum Institutes, 3
Blegdamsvej
2200 Copenhagen
Denmark
Tel: +45 21 78 85 31
Fax: +45 89 49 16 62
Email: albert@pet.auh.dk

ESF Liaison

Dr. Stephane Berghmans
Science
Ms. Blanche Facchini-Schaller
Administration

Medical Sciences Unit
European Science Foundation
1 quai Lezay-Marnésia
BP 90015
67080 Strasbourg cedex
France
Tel: +33 (0)3 88 76 71 18
Fax: +33 (0)3 88 37 05 32
Email: bfacchini@esf.org

For the latest information on this Research Networking Programme consult the ERNI-HSF website: **www.esf.org/erni-hsf**

EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

1 quai Lezay-Marnésia | BP 90015
67080 Strasbourg cedex | France
Tel: +33 (0)3 88 76 71 00 | Fax: +33 (0)3 88 37 05 32
www.esf.org

Print run: 1500 – June 2009