UCL Institute of Neurology
Functional Neurosurgery Unit
Annual Report 2010/11

Background

The Functional Neurosurgery Unit (FNU) is based in the Sobell Department of Motor Neuroscience and Movement Disorders at the UCL Institute of Neurology (IoN), Queen Square. The Unit was established in October 2002, when Professor Marwan Hariz was appointed to the first established University Chair of Functional Neurosurgery (The Edmond J. Safra Chair), and as Honorary Consultant Neurosurgeon at the National Hospital for Neurology and Neurosurgery (NHNN). The FNU was established through the generous support of The Parkinson's Appeal, led by Mrs Lyn Rothman.

The Unit is dedicated to the treatment of patients with Parkinson's disease and other movement and brain disorders using Deep Brain Stimulation (DBS); the technique for correcting abnormal function in brain circuits. The mission of the Unit is to provide the best possible treatment for patients with Parkinson's disease and other movement and brain disorders, to provide comprehensive training and education in this field and to engage in extensive research aimed at understanding, improving and extending the use of the DBS treatment.

Premises

In autumn 2008, the Unit moved to purpose-built facilities in the new Clinical Neuroscience Centre at 33, Queen Square: a £12m building which provides an integrated clinical and academic research facility on the east side of Queen Square, in close proximity to the inpatient and outpatient facilities of the NHNN: in particular the operating theatres, surgical ITU, and the Advanced Neuroimaging Suite with Interventional Surgical MRI.

The Unit occupies the entire 2nd floor, housed alongside the clinical research teams in the areas of epilepsy, Parkinson's disease and human movement and balance, together with the outpatient facilities for patients attending with those neurological conditions.

Current Staff

Professor Marwan Hariz, MD, PhD (Edmond J. Safra Chair of Functional Neurosurgery)
Dr Patricia Limousin, MD, PhD (Consultant Neurologist and Reader)
Professor Marjan Jahanshahi, PhD (Consultant Neuropsychologist)
Mr Ludvic Zrinzo, MD PhD (Consultant Neurosurgeon)
Dr Thomas Foltynie, PhD (Clinical Senior Lecturer and Honorary Consultant neurologist)
Dr Elina Tripoliti, PhD (Speech Therapist)
Mr Joseph Candelario (Movement Disorder Specialist Nurse)
Ms Linda Taib (PA to Professor Hariz and Secretary to the Unit)
Ms Karen Baylis (PA and secretary to Drs Foltynie, Limousin and Zrinzo)
Dr. Diana Ruge, MD, PhD (neurologist, research fellow and hon clin assistant)
Dr. Iciar Aviles-Olmos (neurologist, research fellow)
Dr. Zinovia Kefalopolou (Neurology clinical research fellow)

Dr. Concha del Rio (neurologist, clinical research fellow)
Dr Takeshi Nakajima (Neurosurgeon, Visiting Research Associate)
Dr Katerina Aggeli (Neurologist, Visiting Research Associate)
Mr Ignacio Obeso (Psychology PhD student)
Mr Mazda Beigi (Psychology PhD student)
Dr. Louise McDonald (Psychology, post-doc)
Dr Laura Madeley (Psychology, post-doc)
Ms Mariam Torkamani (Psychologist)
Ms Agata Ryterska (Psychology, PhD student)
Ms Catherine Cheung (Psychology graduate)

Funding

The core funding to support the Chair and Unit continues to come from the Monument Trust and from the Edmond J Safra Philanthropic Foundation, following renewal of their grants for a further five years to 2012. However, as the Unit has developed, there has been an increase in funding support from other sources: from the NHS (Limousin, Tripoliti, Zrinzo); from ION/UCL HEFCE funds (Jahanshahi, Taib, Zrinzo); and from the Parkinson's Appeal (Foltynie). In addition to previous research grant awards from the Wellcome Trust, MRC, Parkinson's Disease Society, Brain Research Trust, Dystonia Medical Foundation, Michael J Fox Foundation, Cure Parkinson's Trust and the European Union, further new grant funding has been awarded from the NIHR Comprehensive Local Research Network, European Commission and Brain Research Trust.

Clinical Activity

To date, a total of 296 patients have undergone surgery in the Unit, with over 500 surgical procedures performed. An increasing number of patients who were operated on during the first years of the Unit have required further surgery for replacement of their depleted, or almost depleted, batteries. Surgically treated patients include patients with Parkinson´s disease, dystonia, essential tremor, post-traumatic tremor, orthostatic tremor, multiple sclerosis, deafferentation pain, Tourette's syndrome, and cluster headache. The success rate of the Unit remains very good, and the safety of the procedures remains excellent with neither fatality, nor brain haemorrhage nor paralysis occurring in any patient.

Professor Paul Krack, neurologist from Grenoble, France, has characterised the achievements of the Unit as a *"new Benchmark"* in the surgical management of Parkinson's disease in a recent Editorial. (Krack P: Subthalamic stimulation for Parkinson's disease: a new benchmark. J Neurol Neurosurg Psychiatry. 2011 Apr;82(4):356-7).

In June 2011, Sir John Tooke, Vice-Provost (Health), commented on the impact case study of our Unit as follows: *"This is specific and well referenced with documented improvements in clinical outcome."*

Recently, surgery for DBS has moved from the usual surgical theatres to the Interventional Surgical MRI (iMRI) suite. This move allows for more rapid surgery, avoiding patient transfer between MRI and theatres, and has the potential of permitting an increase in the number of patients operated.

Research Strategy

The research strategy of the Unit continues to be clinical and patient-centred, with the primary objective being to further improve the outcome of Functional Neurosurgery and the quality of life of the patients and to extend the therapy to other functional brain disorders. Additionally, translational research projects with external collaborators have been initiated with the aim of testing new strategies to treat Parkinson's disease and other functional brain disorders. The approach is multidisciplinary, multicentre,and multinational. Disciplines involved include neurology, neurosurgery, neuroradiology, neuropsychology, neurophysiology, neuropsychiatry, neurogenetics, neurorehabilitaion, neuroengineering, and nano-technology.

The principal research aims are to:

- Better understand how DBS works and what it affects by use of tractography, functional MRI, recording of local field potentials, Magnetoencephalography (MEG) and Transcranial Magnetic Stimulation (TMS);
- Improve the imaging and accuracy of existing brain targets by use of high Tesla MRI
- Expand DBS to the treatment of other disorders of the brain
- Evaluate novel surgical and non-surgical therapies which do not involve electrical brain stimulation
- Expand DBS to the treatment of other disorders of the brain, in particular through national and international multicentre studies
- Document the impact of DBS and understand the mechanisms of its effects on cognition, mood and behaviour
- Develop and validate alternative methods for management of mobility and cognitive problems in PD
- Perform in depth evaluation of the effects of DBS on quality of life
- Explore novel strategies for surgical delivery of therapies using nano-technology.

Ongoing and planned Projects

- Accuracy and precision of image guided stereotactic targeting using higher Tesla MRIs as well as interventional MRI
- Electric field simulation in deep brain stimulation; impact on effects and side effects of DBS
- High Tesla (9.4T) MRI imaging following implantation of DBS electrodes
- Functional imaging studies on patients with Parkinson's disease and dystonia on chronic deep brain stimulation
- Local Field Potentials and Magnetoencephalography studies on patients with DBS for Parkinson's disease
- Diffusion tensor imaging studies on basal ganglia connections
- Pathophysiology of speech and brain plasticity in Parkinson's disease and dystonia
- The relationship between candidate genetic polymorphisms, the development of dyskinesias in PD and the response to DBS (measured clinically and using fMRI and rTMS)
- Brain plasticity following long term DBS in dystonia patients
- Image-guided DBS in general anaesthesia: safety, accuracy and efficacy
- Gender-related aspects of DBS in patients with Parkinson´s disease
- Qualitative evaluation of DBS in dystonia

- Nano-technology for experimental surgical treatment of Rodent-PD
- Can Deep Brain Stimulation improve the cognitive deficits associated with Parkinson's Disease?
- Can Deep Brain Stimulation improve the cognitive deficits associated with Lewy Body Dementia?
- Development of Wireless DBS techniques
- Exenatide as a treatment for Parkinson's disease
- Transeuro "Neural transplantation in the treatment of Parkinson's disease"
- Generation of predictive models utilising multimodal imaging techniques for the assessment of response to deep brain stimulator surgery in corresponding surgical cohorts
- Genetic Influence on Response to treatment in Parkinson's disease
- DBS for Tourette Syndrome - pilot trial
- PROBAND study "Parkinson's Repository of Biosamples and Networked Datasets".
- Intraduodenal delivery of levodopa in a European multicentre trial.
- Investigation of modulatory influence of attention and motivation on movement speed in PD and healthy controls.
- -Surgical therapy as a method of gaining access to or modulating the function of deep brain structures, such as the STN or GPi, and investigating their role in movement, cognition and emotion.
- Can access to a computerized platform improve the care of patients with Parkinson's disease and dementia at home and reduce the burden on carers?
- Impact of movement disorders on psychosocial functioning and quality of life of patients, carers and children and how surgical interventions influence these.

Clinical Trials

- **New DBS applications and new brain targets for DBS**
  - Multicentre (UK) study using DBS for Tourette's syndrome, is continuing.
  - European Multicentre study of subgenual cingulum DBS for depression, has commenced.
  - Posteromedial hypothalamic DBS for cluster headache. The development of DBS for cluster headache has commenced successfully in the Unit, in collaboration with Dr Manjit Matharu. An application for funding of a clinical trial has been submitted.
  - PPN DBS in Parkinson's disease and PSP
  - DBS for severe obsessive compulsive disorder; planned trial

- **Cell therapies for advanced Parkinson's disease**
  -Collaboration involving UK, Sweden, Germany, US, Canada is continuing through the Phase I/II clinical trial to validate an optimised protocol for dopamine cell transplantation in patients with moderately severe Parkinson's disease (PD).

- **Efficacy of DBS in cases of severe OCD**
  -The aim of establishing the potential and efficacy of DBS for people with severe obsessive compulsive disorder (OCD), is the subject of a recent grant application (September 2011) to the MRC under the Experimental Medicine Call. The PI is Professor Eileen Joyce (UCL Chair in Neuropsychiatry), with Co-Investigators from the FNU team, together with the Universities of Cambridge, Dundee and London, and the Hertfordshire NHS Foundation Trust.

Grant Awards 2010/11

MRC Sweden 2011-2013: Trials of DBS for Depression, OCD, and Tourette syndrome. **Professor Hariz**, (Co-Applicant with Associate Professors Patric Blomstedt and Ove Bodlund). SEK 1.200.000.

Weizmann Institute-UK Joint Programme 2010-2011. "The Impact of Emotion on Time Perception". **Professor Jahanshahi** (Co-Applicant with Dr Rony Paz and Dr G Dirnberger). $100,000

European Commission AAL Joint Programme ALADDIN 2009-2012. "A technology pLatform for the Assisted living of Dementia elDerly INdividuals and their carers". **Professor Jahanshahi** (Co-Applicant with Institute of Communication & Computer Systems, Greece; Fraunhofer FOKUS, Germany; University of Bologna, Italy; Mario Negri Institute, Italy; DAFNI Attica Psychiatric Hospital, Greece; Badalona Serveis Assistencials, Spain.). Euros 228,800.

NIHR Comprehensive Local Research Network 2011-12. "Exendin-4 as a treatment for Parkinson's disease - pilot trial", Portfolio ID 8302; **Dr T.Foltynie**. £19,806.

NIHR Comprehensive Local Research Network 2011-12. "Genetic Influences on Treatment response in Parkinson's disease & Dystonia", Portfolio ID 7449; **Dr T. Foltynie**. £27,617.

Brain Research Trust: Parkinson's Appeal Fund 2011-2014: "Can Deep Brain Stimulation improve the cognitive deficits associated with Parkinson's disease?". **Dr T. Foltynie.** £229,023.

Professor Hariz & Dr Foltynie were named Key Researchers in the Novel Therapies Section of the successful application submitted by the UCLH Trust and UCL to the NHS National Institute for Health Research to establish a **NIHR Biomedical Research Unit (Dementia)**. The successful delivery of DBS
to novel groups of patients e.g. individuals with severe Tourette Syndrome, was highlighted as a specific example of translating research findings for the benefit of patients. Funding of £5 million has been awarded (September 2011).

Collaborations

The Unit collaborates with other research groups on research projects across the ION, including neuroradiology, headache and pain, neuropathology, neuropsychiatry, dementia, and with the Functional Imaging Laboratory. External collaborations include: Hammersmith Hospital (PET studies); Universities of Birmingham (Tourette DBS) and Oxford (DBS in depression); University of Edinburgh (wireless DBS); as well as with the group of Professor Kostas Kostarelos, Chair of Nanomedicine, Centre for Drug Delivery Research, School of Pharmacy, University of London. International collaboration includes Swedish Universities of Umea (neurosurgery for neuropsychiatric illnesses); Lund (cell therapy for PD); and Linkoeping (studies of electrical fields of DBS); University of Malta (accuracy and cadaver studies); CIREN in Havana, Cuba; and Department of Neurology, Pamplona, Spain

(neuropsychology studies in suthalamotomy patients); University of Montpellier (plasticity in dystonia).

Teaching and Training

- All members of the Unit contribute frequently to teaching and training activity on site, including clinical and surgical training, supervising MSc students, as well as acting as invited faculty to national and international meetings, conferences and workshops. In the past year, some forty invitations were extended to the PIs in the Unit to meetings in the UK and abroad. Additionally, the Unit has had a record number of visitors from abroad – neurologists, neurosurgeons, neuropsychologists, occupational therapists, specialist nurses and medical students – for observing and learning.
- Prof Hariz and Dr Limousin are co-organisers of the regular meetings of the Queen Square Basal Ganglia Club.
- Members of the Unit have participated in examining PhD theses in Norway, Denmark, France, and Italy.
- Two members of the Unit have successfully defended their PhD theses: Elina Tripoliti and Ludvic Zrinzo.
- Ignacio Obeso is currently writing-up his PhD thesis and is due to be examined shortly.
- Dr Iciar Aviles-Olmos has recently registered for a PhD.
- Joshua Kahan was awarded a First in the UCL Intercalated BSc; with a research project: "The effect of therapeutic bilateral subthalamic deep brain stimulation on movement induced brain activity in patients with Parkinson's disease; a fMRI pilot study". He is due to commence PhD studies in the Unit in January 2012.
- The Intercalated BSc project completed by Ms Anam Anzak entitled "Involvement of the Subthalamic Nucleus in Cognitive Processing in Parkinson's Disease: A Local Field Potential Study", under the supervision of Professor Jahanshahi and Professor Brown, won the award for the best project across UCL.

Awards, Knowledge Transfer, Public Engagement & Media

- Carol Walton, President of the US Parkinson Alliance, visited the Unit.
- Members of the Unit have assisted with the first procedure in Portugal of DBS for Gilles de la Tourette Syndrome.
- The Unit has been instrumental in facilitating the introduction of DBS services to Malta.
- The Unit is planning to host an International Meeting on the occasion of its 10th anniversary in October 2012.

Professor Marwan Hariz:

- Appointed Board member of the World Society for Stereotactic and Functional Neurosurgery
- Appointed Chair of the Scientific Committee of the Interim Meeting of the World Society for Stereotactic and Functional Neurosurgery, to be held in November 2011 in Cape Town
- Appointed life-long member of the Swedish Movement Disorders Society, and proposed Vice Chairman of the Neurosurgical Interest Group of the International Movement Disorders Society
- One of his publications features among the 100 most cited works in Parkinson's disease (Ponce & Lozano: "The Most Cited Work in Parkinson´s Disease". Movement Disorders,

2011; 26: 380-390).

Mr Ludvic Zrinzo:

- Received an award for best presentation at the meeting of the European Society for Stereotactic & Functional Neurosurgery, held in Athens in September 2010.
- Awarded a PhD, by University College London in July 2011, for his thesis entitled "MRI guided and MRI verified deep brain stimulation: accuracy, safety and efficacy".
- A press release on DBS for cluster headache was issued by UCLH in December 2010. This was reported in the national and international media, and by the Brain Research Trust:

http://www.uclh.org/News/Pages/Newhopeforclusterheadachesufferers.aspx
http://www.dailymail.co.uk/health/article-1342067/Me-operation-The-cure-cluster-headaches--drilling-hole-head.html
http://www.bbc.co.uk/news/health-12013583
http://www.bbc.co.uk/blogs/thereporters/ferguswalsh/2010/12/brain_surgery_to_relieve_headaches.html
http://www.brt.org.uk/n/items/Cluster-headaches
http://articles.latimes.com/2010/dec/31/news/la-heb-cluster-headaches-20101231

As a result of Mr Zrinzo introducing the technique of Deep Brain Stimulation to the Maltese Islands, as a Visiting Consultant Neurosurgeon, the National Hospital and UCL were featured on Maltese national news.

http://www.doi.gov.mt/en/press_releases/2011/07/pr1452.pdf
http://www.timesofmalta.com/articles/view/20110730/local/deep-brain-stimulation-performed-at-mater-dei-hospital.378026

Professor Marjan Jahanshahi:

- Joined the Editorial Board of Parkinson's Disease.
- One of her publications features among the 100 most cited works in Parkinson's disease (Ponce &Lozano: "The Most Cited Work in Parkinson´s Disease". Movement Disorders, 2011; 26: 380-390).

Dr Patricia Limousin:

- Appointed to the Scientific Advisory Board of France Parkinson
- Member of the Care Advisory Board.
- Three of her publications feature among the 100 most cited works in Parkinson's disease (Ponce & Lozano, 2011, Movement Disorders, 26; 380-390).

Dr Tom Foltynie:

- Member of the Clinical Advisory Board of Parkinson's UK
- Member of the Queen Square Clinical Trials Committee
- Member of the Research Advisory Committee of Cure Parkinson's Trust
- Member of the Prosavin Data Monitoring Committee
- Podcast for BMJ in April 2011 re. interview on the success of DBS at Queen Square for patients with Parkinson's disease

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