

UCL Institute of Neurology Functional Neurosurgery Unit Annual Report 2008/09

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 Functional Neurosurgery Unit 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), a technique for correcting abnormal function in brain circuits. The mission of the Unit is to provide first-rate treatment for patients with Parkinson's disease and other movement and brain disorders, and to lead 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, which occupies a complete floor in the Centre, is now 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 (Edmond J. Safra Chair of Functional Neurosurgery)
Dr Patricia Limousin (Consultant Neurologist and Reader)
Professor Marjan Jahanshahi (Consultant Neuropsychologist)
Mr Ludvic Zrinzo (Consultant Neurosurgeon and Senior Clinical Researcher)
Dr Thomas Foltynie (Clinical Senior Lecturer and Honorary Consultant neurologist)
Ms Elina Tripoliti (Speech Therapist, Research Fellow)
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 (neurologist, research fellow and hon clin assistant)

Dr. Iciar Aviles-Olmos (neurologist, research fellow)
 Mr Ignacio Obeso (Psychology PhD student)
 Dr. Etienne Holl (neurosurgeon, research fellow)
 Dr. Erica Petersen (neurosurgeon, research fellow)
 Dr Takeshi Nakajima (Visiting Research Associate)

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 develops, there is increasing staff funding support from the NHS (Limousin, Foltynie, Tripoliti), from ION/UCL HEFCE funds (Jahanshahi, Taib), and from the Parkinson's Appeal (Foltynie). In addition, recent research grant awards have been secured from the Wellcome Trust, MRC, Parkinson's Disease Society, Brain Research Trust, Dystonia Medical Foundation, and the Michael J Fox Foundation.

Clinical Activity

To date, a total of 205 patients have been treated using DBS in the Unit, including patients with Parkinson's disease, dystonia, essential tremor, post-traumatic tremor, 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. A significant number of those patients who were operated on during the first years of the Unit have undergone successful replacement of their depleted, or almost depleted, batteries.

Research Strategy

The research strategy of the Unit is clinical and patient-centred, with the primary objective being to improve further the outcome of Functional Neurosurgery and the quality of life of the patients. The approach is multidisciplinary and involves neurology, neurosurgery, neuropsychology, neurophysiology, neuropsychiatry and neurogenetics.

The principal research aims are:

- To better understand how DBS works and what it affects;
- To improve the imaging and accuracy of existing brain targets;
- To expand DBS to the treatment of other disorders of the brain;
- To evaluate novel surgical and non-surgical therapies which do not involve electrical brain stimulation.

Current Projects

- **Accuracy of image guided functional stereotaxis and accuracy of 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 of midbrain following implantation of DBS electrodes**
- **Pathophysiology of brain plasticity in Parkinson's 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).
 - Pathophysiology of speech and brain plasticity in PD and dystonia.
- **Neuropsychology: Current research strategies focus on five main issues:**
 - Investigation of cognitive safety of surgical therapy.
 - 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.
 - Modulatory influence of dopamine on response selection under conflict and learning.
 - Application of experimental findings to improve motor function eg investigation of virtual reality glasses as a mobility aid in PD.
 - 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 about to start.
 - European Multicentre study (Queen Square only UK centre) of subgenual cingulum DBS for depression, (planned)
 - Posteromedial hypothalamic DBS for cluster headache (funding obtained)
 - PPN DBS in Parkinson's disease.
- **Existing therapy**
 - PD Surg multicentre UK study of surgery versus medical treatments.
 - Pallidal DBS in Dystonia
 - Pallidal DBS in pediatric populations (planned)
 - Intraduodenal delivery of levodopa in a European multicentre trial
- **Cell therapies for advanced Parkinson's disease**
 - Collaboration involving UK, Sweden, Germany, US, Canada. Phase I/II clinical trial to validate an optimised protocol for dopamine cell transplantation in patients with moderately severe Parkinson's disease (PD). Submitted MJF

Grant Awards 2008/09

Wellcome Trust Equipment Grant: "A multi-user facility for analysis of large-volume movements for investigation of motor control processes in health and disease" (Professor Hariz co-applicant with Prof Brian Day): £192,950

Fondacion Caja Madrid. Professor Jahanshahi. Fellowship for Ignacio Obeso, 42,672 Euros.

European Commission AAL Joint Programme. Professor Jahanshahi. “A technology platform for the assisted living of dementia elderly individuals and their carers”. 228,800 Euros (part of 1,998,961 Euros award with co-applicants: 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).

ESRC New Investigator Award. Professor Jahanshahi. “Everyday functional ability in the elderly: Assessment and inference using brief cognitive tasks” £ 99, 000 (Prof Jahanshahi named collaborator. Principal applicant Dr A Ho, University of Reading).

Parkinson’s Disease Society. Dr Limousin. Pump priming for movement disorder speech therapist Clinical Specialist position for two years £ 132,752.

NIH-Medtronic Joint Study “Neural control of movement and posture” £95,000 (Dr Limousin co-applicant, principal applicant Dr Corcos)

Medtronic. “STN Stimulation – Neural control of movement and posture”. Dr Limousin co-applicant: Prof J Rothwell \$175,000

MRC Project Grant. “A therapeutic approach to freezing in Parkinson’s disease”. Dr Limousin co-applicant: Professor B Day £309,588

Michael J Fox Foundation. “Encapsulated GDNF-producing cells for neuroprotection in Parkinson’s disease”, \$ 130,214 for this site (Dr Limousin co-applicant, coordinating principal applicant Dr Lindvall)

Fundacion Caja Madrid. Dr Limousin. Fellowship for Graduated Courses in Universities and Colleges, to support research fellow Dr Matinez Torres. 16,800 euros

Dystonia Medical Research Foundation “Long term plasticity in the dystonia patients treated with Deep Brain Stimulation”. \$64,544. Prof. J Rohwell for funding of Dr Diane Ruge.

Parkinson’s Disease Society Innovation Grant. Dr. Foltynie. “Genetic polymorphisms, dyskinesia risk and response to DBS in Parkinson’s disease”. £14,815.

Brain Research Trust. Dr. Foltynie. “Functional imaging and response to Deep Brain Stimulation in Parkinson’s disease”. £ 21,666.

Collaborations

The Unit collaborates with other research groups on research projects across the ION, including neuroradiology, headache and pain, neuropathology, neuropsychiatry, as well as external collaborations with Hammersmith Hospital (PET studies), Universities of Birmingham (Tourette DBS) and Oxford (DBS in depression), Swedish Universities of Umea (neurosurgery for neuropsychiatric illnesses, PPN DBS,) Lund (cell therapy for PD) and Linköping (studies of electrical fields of DBS), University of Malta (accuracy and cadaver

studies), Netherlands University in Groningen and UCLA (studies of targeting and trajectory accuracies), CIREN in Havana, Cuba, and Department of Neurology, Pamplona, Spain (neuropsychology studies in subthalamicotomy patients). Additional collaboration is planned with Prof Duncan and the Epilepsy Group at ION, in view of trials of DBS for Epilepsy, as well as with the group of Professor Kostas Kostarellos, Chair of Nanomedicine, Centre for Drug Delivery Research, School of Pharmacy, University of London.

Teaching and Conferences

All members of the Unit contribute frequently to teaching activity on site, including supervising MSc students, as well as acting as invited faculty to national and international meetings, conferences and workshops. Additionally, the Unit has regular visitors from abroad - neurologists, neurosurgeons and medical students - for observing and learning. The DBS support group had a very successful second meeting on 7th September 2009, organised by Professor Jahanshahi and Mr Joseph Candelario, and funded and supported by the Parkinson's Disease Society.

Distinctions and Awards

Professor Hariz was elected guest member of the Japan Society of Neurosurgery and a member of the Board of Directors of the World Society for Stereotactic and Functional Neurosurgery. He was elected member of the Movement Disorders Society's Task force for Neurosurgery, and the Task Force for Surgery of Dystonia. Recently he received the Swedish award in memory of Algot and Amanda Mangberg "For outstanding achievements in surgery for Parkinson's disease".

Mr Ludvic Zrinzo received an award for best presentation at the quadrennial meeting of the World Society for Stereotactic and Functional Neurosurgery, held in Toronto in May 2009.

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